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Medication Errors in Paediatric Patients- The Role of the Clinical Pharmacist

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First and above all, I praise Allah, the almighty for helping and guiding me in my whole life and during my academic study and for all the blessings

Abstract

Six electronic databases were searched and 153 studies which identified the number or the rate of paediatric medication errors were identified; mainly from the US. These studies were compared to identify factors responsible for the great variations seen in reported error rates **(Chapter 2)**. The most important factors were the use of different denominators, different definitions of medication errors, and the use of different methods of data collection.

To explore further the reasons for the wide ranges of error rate identified in Chapter 2, the studies that used the same denominators, methods, and error types were compared, yet showed a difference between the highest and lowest error rate of more than 50% **(Chapter 3)**. Factors identified for the variation in error rates included differences in setting, drugs studied, participants, study design details and countries involved.

To try to clarify the relationship between the method of data collection and results obtained **(Chapter 3)**, the rates of specific types of medication errors reported by studies using different methods but the same denominator were compared. Conclusions were difficult to draw due to the heterogeneity of the current literature. Prescription errors are probably best studied using chart review and administration errors by direct observation.

The relationship between the clarity of definitions and results was investigated in **Chapter 3,** in terms of how clearly the studies had defined errors and the degree to which the definition(s) used matched each study's aim. Studies were too heterogeneous and unfortunately could not adequately be compared.

Chapter 3 also explores the interventional tools reported. Of all studies, 59 used interventional tools and assessed their benefit. These included dosing supporting tools, electronic prescribing, education, health and safety strategies, clinical pharmacist services and pre-printed forms among others. Most studies reported that their interventions effectively reduced or prevented medication errors, despite in some cases not measuring errors before and after interventions and even in some studies where error rates increased.

Chapter 3 also explores the UK studies. Very few studies occurred in the same setting and used both the same methodology and denominators to identify the rate of the same types of medication errors. It was difficult to draw firm conclusions but prescribing and administration errors seem to happen more often in paediatric units in general hospitals than in specialist children's hospitals. Most studies were of prescribing errors with other types of error rarely studied in the UK.

Four studies identified the time of day most associated with errors; three the time of day and days of the week most associated with errors; and one the days of the week most associated with errors **(Chapter 3)**. However, given the diversity of definitions of times of day, shifts, and weekdays, it was impossible to draw conclusions regarding the temporal aspect of medication errors from these studies.

A second systematic review was conducted to explore the current literature that examines the role of paediatric clinical pharmacists in reducing the rate of medication errors **(Chapter 4)**. Twenty-five studies published until the end of July 2013 were identified that reported pharmacists' activities in reducing or preventing medication

errors. The most commonly intercepted types of errors were wrong dose, wrong drug and wrong route of administration. The most common types of pharmacists' contributions were reactive information giving in response to other healthcare professionals' queries, education of healthcare professionals and cost saving.

Based on knowledge gained from the second systematic review, an observational study of the role of paediatric clinical pharmacists was conducted in two NHS Trusts in the UK **(Chapter 5)**. By shadowing pharmacists, they were observed during their day-to-day work and their contributions to health care were documented, as well as the errors that they identified and addressed. Having ultimately shadowed 14 pharmacists over the course of 197 ward visits, clinical pharmacists were found to play an important role in improving the health care services provided to paediatric patients and are effective in averting different types of medication errors. Pharmacists intercepted errors in 8.4% of all prescriptions and the overall contribution rate of all prescriptions was 54.8%. The most common types of errors intercepted by pharmacists were omission errors (27.9%), wrong dose (24%) and illegible prescribing (19.2%). The most common types of contributions were annotating prescriptions with information (e.g. administration instructions) (19.2% of all prescriptions), drug history check (97% of all new patients) and allergy status checked (100% of all new patients). The acceptance rate of pharmacists' recommendations by doctors was very high (99.5%).

Publications and Presentations Related to This Thesis

Paper:

- Alsenani A, Sammons H, Conroy S. Systematic review of factors influencing reported rates of medication errors. (Paper submitted to Archives of Disease in Childhood)

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1. What factors influence reported rates of paediatric medication errors?, 14th ESDPPP Congress, June 4th to 7th, 2013, Salzburg, Austria.
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3. The role of the paediatric clinical pharmacist in reducing medication errors: a systematic literature review, 20th NPPG Conference, November 7th to 9th, 2014, Nottingham, UK.
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Abbreviations

ACCP	The American College of Clinical Pharmacy
ADEs	Adverse Drug Events
ADRs	Adverse Drug Reactions
BID	Twice a day
BNF	British National Formulary
BSA	Body Surface Area
CDSS	Clinical Decision Support System
CPOE	Computerised Prescriber/Physician Order Entry
DCH	Derbyshire Children's Hospital
D.O.B.	Date Of Birth
ED	Emergency Department
EMRs	Electronic Medical Records
GIT	Gastrointestinal
GP	General Practitioner
ICU	Intensive Care Unit
IM	Intramuscular
IOM	The Institute of Medicine
IV	Intravenous
LASA	Look-Alike-Sound-Alike
MAEs	Medication Administration Errors
MARs	Medication Administration Records
MDEs	Medication Dispensing Errors
MEs	Medication Errors
mg	Milligram
ml	Millilitre
MMEs	Medication Monitoring Errors
MPEs	Medication Prescribing Errors
MTEs	Medication Transcribing Errors
NA	Not Available
NaCL	Sodium Chloride

NCC-MERP	The National Coordinating Council for Medication Error Reporting and Prevention
NCH	Nottingham Children's Hospital
NG	Nasogastric
NHS	National Health Service
NICU	Neonatal Intensive Care Unit
NOE	Nurse Order Entry
NPSA	National Patient Safety Agency
NRLS	The National Reporting and Learning Service
OD	Once Daily
OTC	Over-The-Counter
PCC	Poison Control Centre
PHDU	Paediatric High Dependency Unit
PICU	Paediatric Intensive Care Unit
POE	Physician Order Entry
TID	Three Times a day
TDM	Therapeutic Drug Monitoring
TPN	Total Parenteral Nutrition
U	Unit
UK	The United Kingdom
US	The United States
USP	United States Pharmacopeia

Chapter 1: Introduction

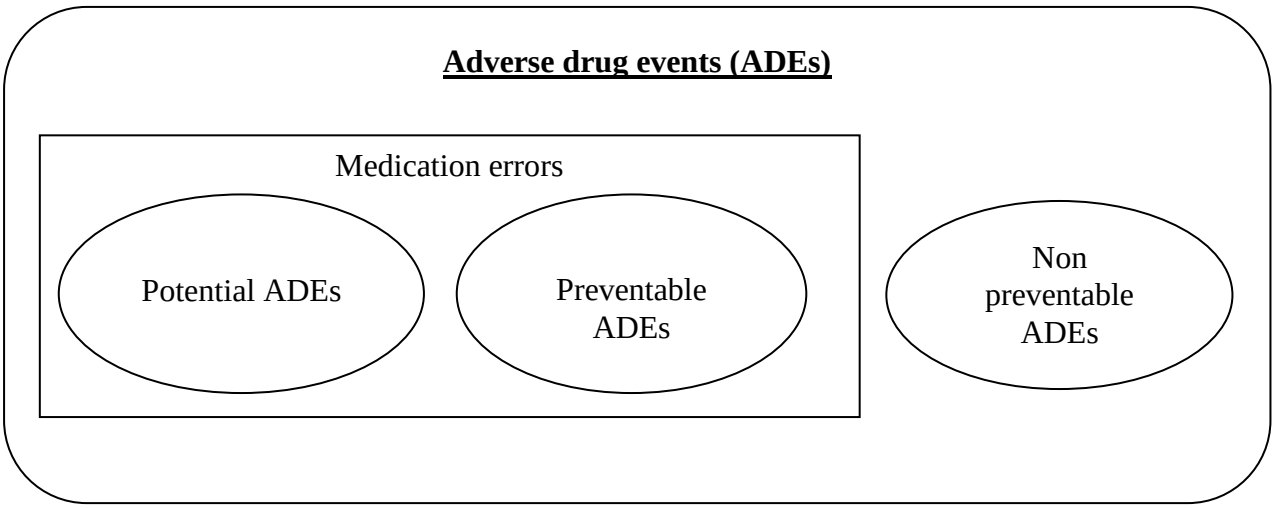
Medications are used generally to help improve health and decrease morbidity and mortality (1). There is an undoubtedly positive effect of using medications for treating and preventing diseases, but only if they are used safely and effectively. Improving patient health is an important goal to be achieved by healthcare facilities which can be improved by preventing medication errors (2). Medication errors comprise the largest portion of all types of medical errors (3). Medication errors might occur at any stage of therapeutic management (4). This involves the prescribing, transcribing, dispensing, preparing and administering, monitoring and documentation of medications and patients (4, 5). According to these stages, all healthcare providers taking part in therapeutic management may be involved in medication errors. It is important to find solutions to decrease harmful and potentially deadly errors (6).

Medication errors in general are an important topic to address, particularly with regard to the paediatric patient (7). Information regarding preventative strategies and detection tools is more commonly available for adult patients than paediatric patients (8). Medication errors are internationally recognised, and the challenge is more common in paediatric patients because they are at a greater risk of harm from medication errors than adult patients (9). Therefore, my thesis will look at the different aspects of medication errors with regard to children.

1.1. Background

Despite using medications effectively and safely, adverse drug events (ADEs) cannot always be prevented. Adverse drug reactions (ADRs) may occur (1). These are called non-preventable ADEs (1). These events are not caused by human mistakes but rather by the drugs themselves (1). Preventable ADEs, including "medication errors," follow human mistakes (1). Medication errors, if they are intercepted before reaching the patients, are called "near misses" or "potential ADEs" (10, 11). These also include medication errors which reached the patient but did not cause harm. Medication errors can be prevented, and most of them do not cause harm (11-13). Figure 1.1 illustrates the relationship between ADEs and medication errors.

Figure 1.1.: Relationship between preventable and non-preventable ADEs.



Adapted from Kaushal et al. (2002) (11).

The Institute of Medicine (IOM) in the US focused on issues related to patient safety and published a report "To err is Human: Building a Safer Health System," which discussed the high mortality and morbidity rates resulting from medical errors (3). The concern for patients' safety in general and medication errors in particular has clearly increased since the publication of this report in 1999 (14). The IOM recommends focusing on providing the correct treatment, instead of blaming people (3). They reported that: "It may be part of human nature to err, but it is also part of human nature to create solutions, find better alternatives and meet the challenges ahead" (3).

1.2. Definitions of medication errors

Terminology around the subject of medication errors can be confusing with numerous definitions having been used. Some examples are given below:

- Iatrogenic event: "Any event that occurred during hospitalization that compromised the safety of the patient, even if the patient was not harmed" (15).
- ADEs: "An injury resulting from medical intervention related to a drug" (16).
- Medical errors: "All errors that occur within the healthcare system including mishandled surgery, diagnostic errors, equipment failures, and medication errors" (17).
- Medication error: "Any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. Such events may be related to professional practice, health care products, procedures, and systems, including prescribing; order communication; product labelling,

packaging, and nomenclature; compounding; dispensing; distribution; administration; education; monitoring; and use" (18).

- Medication error: "A mistake made at any stage in the provision of a pharmaceutical product to a patient" (19).
- Medication error: "Any error in the medication use process including drug ordering, transcribing, dispensing, administering, or monitoring" (5).

1.2.1. Problems associated with definitions

In the previous studies on this topic no authoritative definition for medication error has emerged (17, 20). Consequently; results unsurprisingly will differ from one study to another, according to the definitions used. In a systematic literature review by Ghaleb et al. (2006) to identify the rate of medication errors in paediatric patients; it was found that some studies identified a rate of medication error without stating whether any definition was used and some studies used more than one definition to clarify different types of medication errors, e.g. a prescribing error (17).

Different types of medication errors are considered in some studies and not in others; making studies difficult to compare in terms of the rate of errors identified (17). Ghaleb et al. pointed out that most definitions for medication errors considered adult patients, without considering some important issues related to children, such as documenting patients' weights and using unlicensed and off-label drugs (17).

In a systematic literature review by Lisby et al. (2010) to identify definitions used for medication errors, it was found that 45 definitions appeared in 203 studies (of which, 17 used the National Coordinating Council for Medication Error Reporting and Prevention's (NCC-MERP) definition from the US) (20). The studies used different methods and different study designs, involved different populations and different ages, provided results using different denominators and were conducted in different settings in nine different countries (20). The authors stated that results cannot be summarised due to differences in methods and outcome measures (20). They also stated that the prevalence of medication error cannot be determined from studies which obtained their results from reporting systems, interview and questionnaires as there are no baseline data available to put the results into contexts (20).

Lisby et al found no relationship between definitions used and prevalence of medication errors in the studies identified. They stated that there is a need for standardised methods and a clear definition, using clear terminology to avoid wrong explanations and to provide an accurate rate of medication error. They concluded that as more types of errors are considered in definitions, this will lead to an increase in the rate of medication errors identified (20).

1.3. Classification of medication errors

Medication errors have been classified according to the stages of therapeutic management, degree of harm caused and a psychological approach. According to the stages of therapeutic management; errors can be classified into five types: prescribing, transcribing, dispensing, preparing and administering, and monitoring of medications and patients (5). According to the degree of harm caused; errors can be classified into five types: no harm, low harm, moderate harm, severe harm and death (21). Table 1.1 shows the definitions according to the degree of harm used by the UK National Patient Safety Agency (NPSA).

Table 1.1: Classifications of medication errors according to the degree of harm caused

Degree of harm	Definition by National Patient Safety Agency
No harm	Impact prevented: any patient safety incident that had the potential to cause harm but was prevented, resulting in no harm to the person(s) receiving NHS-funded care.
No harm	Impact not prevented: any patient safety incident that ran to completion but no harm occurred to the person(s) receiving NHS-funded care.
Low harm	Any patient safety incident that required extra observation or minor treatment, and caused minimal harm to the person(s) receiving NHS-funded care.
Moderate harm	Any patient safety incident that resulted in a moderate increase in treatment, and which caused significant but not permanent harm to the person(s) receiving NHS-funded care.
Severe harm	Any patient safety incident that resulted in permanent harm to the person(s) receiving NHS-funded care.
Death	Any patient safety incident that directly resulted in the death of the person(s) receiving NHS-funded care.

Adapted from the UK National Patient Safety Agency (21).

Using a psychological approach; medication errors have been classified into two types of error: mistakes and skill based errors (Table 1.2) (22).

Table 1.2: Classifications of medication errors according to the psychological approach

Type of error	Explanation	Classifications
Mistakes	Errors resulting from applying wrong plans.	▪ Knowledge based. ▪ Rule based (applying the rule incorrectly or applying the wrong rule).
Skill based	Errors resulting from applying right plans wrongly.	▪ Memory based (forgetfulness or inattention). ▪ Incorrect performance or poor technical skill.

Adapted from Ferner et al. (2006) (22).

1.3.1. Prescribing Errors

One definition is: "A clinically meaningful prescribing error occurs when, as a result of a prescribing decision or prescription writing process, there is an unintentional significant reduction in the probability of treatment being timely and effective or increase in the risk of harm when compared with generally accepted practice" (23).

These errors can involve incomplete prescriptions, wrong drug, dose, frequency, rate of infusion, route of administration, quantity, patient, transcribing, not considering important issues such as patients' weight, wrong indication or prescribing contraindicated drugs (24-26). The cause of medication error may sometimes be related to the clinical situation, e.g. a medication error could result from giving a regular dose of chemotherapy to a patient with a low neutrophil count instead of adjusting the dose according to the neutrophil count (27).

It has been suggested, that doctors should increase their knowledge of drugs used for paediatric patients and to consider drug interactions, contraindications, patients' allergy and weight; and to make sure all this information is documented clearly and accurately on patients' charts (28).

Tenfold errors are commonly seen in paediatric patients (e.g. 5 mg prescribed instead of 0.5) (29, 30). Tenfold errors can lead to death, especially with low therapeutic index drugs (29). It has been recommended for doctors to write down each step of a calculation and thereafter get this double checked by other healthcare providers (28).

Prescribing errors happen as a result of several different factors. Of these some are related to healthcare providers, some to the surrounding environment and some to the medication treatment process. The following factors may contribute to prescribing errors (25):

- Insufficient knowledge of medications prescribed, accurate doses and essential information about patients, such as allergies.
- Illegible handwriting.
- History including wrong medications being taken.
- Confusion in names of medications.
- Calculation mistakes, leading to tenfold errors in some situations.
- Use of inappropriate or unclear abbreviations (Table 1.3 illustrates examples of some dangerous abbreviations).
- Ordering medication verbally.
- Insufficient training.
- Lack of awareness of errors.

- Work environment and workload.
- Poor communication with other healthcare providers.
- Look-Alike-Sound-Alike (LASA) errors (Table 1.4 illustrates examples of drugs associated with LASA errors)

Table 1.3: Abbreviations associated with medication errors

Abbreviation	Common Error
U (Unit)	Read as 0 or 4.
µg (Micrograms)	Read as mg.
SC or SQ (Subcutaneous)	Read as SL (Sublingual).
TIW (Three Times a Week)	Read as TID (Three Times a Day).
IU (International Unit)	Read as IV (Intravenous) OR result in administration of large quantities e.g. 81 U instead of 8 IU.
.5 (0.5)	Read as 5 e.g. 5 ml or 5 mg

Adapted from the National Coordinating Council for Medication Error Reporting and Prevention (18).

Table 1.4: Examples of drugs associated with LASA errors.

Drug name	Confused drug name
Aminophylline	Amitriptyline
Amoxicillin	Ampicillin
Erythromycin	Azithromycin
Cefotaxime	Cefuroxime
Penicillamine	Penicillin
Cyclosporin	Cycloserine
Azithromycin	Erythromycin
Bisacodyl	Bisoprolol
Humulin®	Novolin®
Zantac®	Zyrtec®

Adapted from Derby Hospitals NHS Foundation Trust Formulary (31).

Many procedures have been recommended to minimise errors during the prescribing process. These include:

1. Clear and effective communications with other healthcare providers (31).
2. Completing prescriptions with all required information, and identifying drug allergy (31, 32).
3. Using generic names (31).
4. Avoiding abbreviations (of drug names, dosage units and instructions), verbal orders, unclear instructions and use of trailing zeroes (31, 32).
5. Making sure all drug related information is provided clearly, e.g. strengths, frequency, dose, volume and route of administration (32).
6. Use of reliable equipment (such as electronic prescribing) to help in increasing the safety of medication delivery, reduce time spent and avoiding risks such as calculation errors (28).
7. Ensuring correct calculations and patients' weight during prescribing drugs to children (32).
8. Hospital environment should be quiet and safe to avoid errors (32).
9. Healthcare professionals should be qualified and have an adequate level of training and education (28).
10. Prescribers should update their information regarding paediatric diseases and medications and to ensure that prescriptions are written correctly and safely (32).
11. Prescribers should use all available sources of information, including pharmacists, about medications if required (32).
12. Prescribers should know the hospital systems for prescribing drugs and current drugs used by patients (32).

13. Prescribers should provide patients with information related to their medications (32).
14. Non-punitive reporting systems should be provided in the hospital, and healthcare providers should be encouraged to report all incidents (28, 32).
15. Barriers to reporting incidents should be considered and healthcare providers should understand the importance of reporting incidents to learn from these events and to avoid such events in future (28).
16. LASA drugs showed be reviewed regularly, limit verbal orders and healthcare providers should be educated about their risks (33).

1.3.1.1. Junior doctors and trainees

In a study at a UK teaching hospital, Dean et al. 2002 found that junior doctors are responsible for the majority of prescribing and also the majority of prescribing errors (12). Doctors just graduating from medical school often feel that they are not ready to start prescribing and have emphasised the need for further education on accurate and safe prescribing for patients of all ages (34). The rate of prescribing error amongst foundation trainees has been shown to be 7% of medicine orders (52 errors per 100 admissions) (35).

1.3.1.2. Unlicensed and off-label drugs

Using unlicensed and off-label drugs for children has been suggested to increase the incidence of errors because of the need for calculating the dose and the need for manipulating the medicine (36). Conroy's (2011) study in a UK paediatric hospital found that unlicensed drugs are associated with more medication errors and greater harm to children than other medications (37). It has been estimated that 46-65% of all

paediatric prescriptions are either unlicensed or off-label (38, 39). Payne et al. (2007) suggested that when doctors prescribe off-label drugs, they need to apply their understanding of pharmacokinetics and pharmacodynamics in addition to their experience as a prescriber to these drugs (40). It has been estimated that around 75% of children's medications had not been studied sufficiently, despite the encouragement of federal legislation to do more studies into children's medications (41).

1.3.2. Dispensing errors

A dispensing error has been defined as: "Any deviation from the medical prescription in dispensing medication" (42). Errors can occur in all stages of dispensing starting from receiving prescriptions through to supplying drugs (3, 25). Errors may include the wrong dose, drug, concentration, dosage form and patient; missing doses; omission of drugs, dispensing expired medications and medications being stored inappropriately (25, 42). Typing errors may occur during computerised labelling and cause error (e.g. typing wrong drug name, patient name, dose, dosage form, quantity, instruction; wrong selection of drugs and selecting a wrong drug saved on the patient medical record) (25, 42-44).

Dispensing errors have many contributing factors such as (44):

- Similarity in drug names and containers (LASA drugs).
- Poor handwriting.
- Unclear prescriptions and direction.
- Interruptions, not concentrating, noise and poor light.
- Workload.

- Poor communication.
- Poor dispensing procedures.
- Lack of experience, training or knowledge.
- Systems used such as labelling computer programs.
- Continuous work without taking break, working alone, hunger, fatigue and stress.
- Not following guidelines.
- Drugs on shelves not arranged correctly.

The following steps have been advised when pharmacy staff deal with medications, patients and other healthcare professional:

1. Following the right steps during dispensing (25).
2. Dealing more carefully with LASA drugs and drugs associated with errors (such as potassium chloride, heparin and insulin) (25, 32).
3. Ensuring separating LASA drugs when storing medications (25).
4. Working in a quiet place to avoid disruptions (32).
5. Working in an organised and suitable place (32).
6. Ensuring correct transcribing of prescriptions (45).
7. Checking medications against correct times, drug interactions and duplication (46).
8. Checking that prescriptions and labels are correct and fully completed (45).
9. Taking care with calculations and abbreviations (45).
10. Reducing workload and stress (45).
11. Arranging and storing medications safely (45).
12. Double check before issuing to the patient (45).

13. Discussing medication prescribed with the patient (32).
14. Discussing with prescribers for confusing medications (32).
15. Checking patients' allergy before dispensing (46).
16. More reliable equipment (such as barcode technology) should be provided to help in increasing safety, reduce time spent and avoiding some risks such as calculation errors (28).
17. Non-punitive reporting systems should be in operation, and healthcare providers should be encouraged to report all incidents (28, 32).
18. Barriers to reporting incidents should be considered and healthcare providers should understand the importance of reporting incidents to learn from these events and to avoid such events in future (28).

1.3.3. Preparation and administration errors

A medication administration error has been defined as: "The administration of a dose of medication that deviates from the prescription, as written on the patient medication chart, or from standard hospital policy and procedures. This includes errors in the preparation, and administration of intravenous medicines on the ward" (24). Medication administration errors can cause more harm to patients than any other stages of therapeutic management, as being the final step are difficult to prevent (47).

Nurses and other healthcare professionals are required to consider the "Five Rights" (right dose, drug, patient, time and route) (25). The administration of drugs by the wrong route may lead to death (e.g. administering certain cytotoxic drugs such as vincristine intrathecally) (25). Administration errors can also include the omission of doses (more common), the administration of wrong or expired drugs, wrong rate of

administration, wrong time, wrong dose, wrong patient, wrong preparation or administration technique (24, 25).

Many things may contribute to administration errors including (25):

- Lack of knowledge of the risks associated with the administration process.
- Lack of knowledge of the right technique for administering and preparing medications.
- The complexity of equipment used for preparing or administering medications.
- Environmental issues, such as poor light or noise, and interruptions.
- Ignoring or forgetting to check patients' identity.
- Storing medication with similar appearance in one place.

Procedures suggested to improve patients' safety and decrease harm related to wrong administration technique include:

1. Checking patients' identities to ensure that the right drugs and doses are delivered to the right patients (25).
2. Ensuring medications are checked against the medication administration record (46).
3. Checking all prescribed medications, allergy status and past medication history (32).
4. Double check calculations with another healthcare professional before administering (32).
5. Working in a quiet and suitable place (25).
6. Decreasing interruptions during doing any task (25).
7. Familiarity with all equipment used for delivering medications (32).

8. Nurses being required to discuss with prescribers any confusing issues before administering medications (32).
9. More reliable equipment may help in increasing safety, reduce time spent and avoiding some risks (28).
10. Non-punitive reporting systems should be in operation, and healthcare providers should be encouraged to report all incidents (28, 32).
11. Barriers to reporting incidents should be considered and healthcare providers should understand the importance of reporting incidents to learn from these events and to avoid such events in future (28).

Parents and other caregivers may also contribute to administration errors. Poor health literacy and using a cup for measuring doses have been suggested to be the most common reasons for administration errors by parents (48). It is also known that using a kitchen spoon for liquid medications is associated with administration errors by parents (49, 50). The volume that can be measured by different spoonfuls ranges from 1.5 to 9 ml, which can lead to error if the wrong spoon is used (51, 52). Misreading and misunderstanding medication labels by caregivers has also led to overdose (53).

Despite all these recommendations for reducing errors at different stages of the medication management process, errors continue to occur.

1.4. Methods used to identify medication errors

Various methods have been used to identify medication errors including:

- Review of patients' charts (54).
- Direct observation of care provided to patients (54).
- Incident reporting systems (54).
- Analysing urine samples to detect omitted and unauthorised medications (54).
- Analysing doses returned to pharmacy (54).
- Review of medical malpractice claim files (55).
- Analysis and comparing administration data with prescriptions (54).
- Mortality certificate reviews (54).

The first three methods are most used and are discussed a little more below:

1.4.1. Chart review

This method is most commonly used for detecting medication errors, mainly prescribing errors (20). Underestimation of other types of errors is a problem with chart review (20). Chart review is also time consuming (56). Electronic Medical Records (EMRs) (if available) can be searched and reviewed to obtain the required data instead of reviewing charts (57).

1.4.2. Direct observation

This method is the most common method used for detecting dispensing and administration errors (20). Direct observation is a valuable method but is more expensive than other methods due to resources and time needed (54). Direct observation is usually not blind and participants know that their performances will be evaluated and this therefore may affect the accuracy of results (55). Poor reception by healthcare providers, such as nurses, has been noted (58).

1.4.3. Reviewing of incident reports

Many hospitals have an incident reporting system whereby all medication error incidents are reported. Reviewing incident reports does not measure the rate of medication error but gives an overview of the different types and nature of errors that occurred (17). The method provides less information about medication errors than chart review and direct observation methods (20).

In an incident report system, potentially relatively few errors will be reported (58). Typically, a poor reporting rate is seen because healthcare providers may be afraid of punishment or claims (54, 59-61). Low levels of reports may mean either that health care providers believe that the errors are not serious enough to be documented or that they did not recognise that medication errors had occurred (62).

The IOM stated that the reporting system is a valuable key to decrease the incidence of medication error, as it helps health care providers to learn from previous committed errors (3). A compulsory reporting system usually provides information about serious errors and death, whereas a voluntary reporting system may also provide information about potential errors such as near misses (63).

Using an anonymous reporting system in conjunction with safety strategies was found by Taylor et al. (2007) to increase the rate of reporting incidents by 54% in a paediatric hospital in the US (58). A non-punitive, continuous, anonymous and prospective reporting system was found, by Ligi et al. (2010), to be very effective in decreasing the rate of medication error and improving patients' safety in a neonatal centre in France (15). One example is MEDMARX, which is a US database accessed

on the Internet to report medication errors (64). This system was established by the United States Pharmacopeia (USP) in 1998 (6). The National Reporting and Learning Service (NRLS), part of the work of the National Patient Safety Agency in the UK; also collects and reviews incident reports from different healthcare sectors (65). The NRLS was established in 2001 and any healthcare professional can report any incident by filling an online report (65). Many studies have retrieved incident reports from MEDMARX and the NRLS and then performed analysis.

Incident reporting has its limitations including inability to identify the rate of errors (because the total number of prescriptions is unknown), the reporters may be unknown, reports are often are not completed either at all or completely, and nobody checks the accuracy of these reports (66).

1.5. Paediatric patients and medication errors

Ghaleb et al. (2006) stated that many studies have aimed to identify the rate of medication errors for adults but the information obtained regarding paediatric patients is not enough (17). The rate of medication errors was identified by Kaushal et al. (2001) to be similar in both adult and paediatric patients. However, the rate of potentially harmful errors was three times higher in paediatric than adult patients (9).

Many factors should be taken into consideration when calculating a dose for children, including their age, weight, body surface area and illness (67). Paediatric patients are more vulnerable to errors than adults because most doses must be calculated on an individual basis (67). The dose must be calculated depending on the patient's age

(sometimes gestational age), weight or surface area (9). When treating paediatric patients, it is also necessary to consider the differences in their pharmacokinetics and pharmacodynamics (9). Furthermore, small children cannot communicate effectively and, consequently, cannot complain about side effects (68).

Sometimes medications designed for adults must be used for children due to a lack of suitable alternatives. These may need manipulation or to be diluted before being given to children, which may lead to errors (9). Since 2007, in accordance with the European regulation for paediatric medications; all applications for licenses for new paediatric medications must include suitable formulations for children and involve studies that prove efficacy and safety of these medications in paediatric patients (69). Following these regulations may eventually provide effective treatment for children using safe medications and dosage forms which may subsequently reduce paediatric medication errors.

1.6. Neonatal patients and medication errors

Neonates may suffer from greater medication error rates than other patients because, in addition to the paediatric challenges, their organs responsible for absorption or excretion are not yet mature (70). Moreover, their weight and renal function can change quickly, and doses must be regularly recalculated accordingly (70).

1.7. Prevalence of medication errors in paediatric patients

The IOM stated in one report published in 1999 that medication errors are responsible annually for 7,000 deaths in the US for patients of all ages (3). Because of the various denominators used, the results for medication errors from different studies are difficult to compare (20). The incidence of medication errors in children differs widely from one study to another, depending on the methods, definitions and classifications used (17, 20, 71).

1.7.1. Types of medication errors mostly associated with paediatric patients

Wrong dose has been suggested to be the most common type of error (17). Other types of errors involve wrong drug, route of administration, documentation, date, frequency of administration, patients, not considering patients' allergy, drug interaction, not considering intravenous compatibility, omission and wrong rate of infusion (17).

1.7.2. Drugs mostly associated with medication errors in paediatric patients

Antibiotics and sedatives have been noted as the drug groups most associated with medication errors (17). The reason why these groups of drugs are associated with more errors may be because these drug groups are more commonly prescribed (17). The most common route of administration associated with error is the intravenous route (17). In general, errors associated with intravenous administration are

considered to be serious by healthcare providers and it may be that, these errors are reported more often (17).

Narrow therapeutic index medications are more associated with harm from medication errors than other medications (17). LASA errors were less frequent than other types of medication errors in a study conducted by Basco et al. (2010) from paediatric emergency departments in the US (72).

1.7.3. The time of day most commonly associated with medication errors in paediatric patients

Studies by Selbst et al. 1999 in a specialist children's hospital in the US and by Kozer et al. 2002 in a paediatric emergency department in Canada identified a higher percentage of errors during the evening and at night, as compared to daytime (73, 74). However, one study conducted by Lerner et al. (2008) in a neonatal intensive care unit in Brazil found that 64% of all errors occur during the daytime (75). In another US study by Miller et al. (2010) in a tertiary care paediatric hospital aiming to identify the rate of medication errors in an inpatient setting, found the rate was higher at night and at weekends (76).

1.8. Consequences of medication errors

Medication errors lead to increased mortality and morbidity rates (77). In addition; if medication errors are not intercepted before causing harm, the cost of healthcare increases (77, 78). This may include increasing length of hospitalisation, the need for more diagnostic examinations and different types of treatment for treating adverse reactions and toxicity, and an increasing mortality rate (79-81). Medication errors

have an adverse impact not only on patients and their families but also on healthcare providers, including a loss of confidence in healthcare providers and, therefore, in the whole of healthcare services (82).

1.9. Interventional tools to decrease medication errors in paediatric patients

A number of interventions have been used to attempt to reduce medication errors such as:

- Electronic prescribing systems (Computerised Prescriber/Physician Order Entry (CPOE) and computer-assisted prescribing) (11, 83, 84).
- Ward-based clinical pharmacists (84-86).
- Educational and training programs (87-89).
- Barcode technology (e.g. dispensed medications) (90).
- Electronic medical records (84).
- Risk management programmes (91).
- Web-based (or computerised) calculators (92, 93).
- Unit dose dispensing system (individual doses are dispensed for each patient) (84, 94).
- Intelligent infusion pump systems (smart pumps) (95).
- Robots in pharmacy (84).
- Enhancing communication between healthcare providers (84).
- Automated bedside dispensing devices (84).
- Pre-printed orders (96).
- Double check (97).

Conroy et al. (2007) conducted a systematic literature review to identify interventions used in previous studies to reduce dosing errors in children (98). Electronic prescribing systems (CPOE and computer-assisted prescribing) were mostly used; followed by unit dose dispensing systems, educational programmes, risk management programmes and intelligent infusion pump systems (smart pumps). These store drug doses and pre-programmed concentrations, and calculate all required infusion rates based on patient weight (98).

The most effective interventional tools to decrease the error rate found by Fortescue et al. (2003) in the US were CPOE plus clinical decision support systems (CDSS), ward-based clinical pharmacists and communication enhancement among healthcare providers (84).

Another tool used to decrease the rate of medication dosing error is the Broselow-Luten Emergency Tape (which indicates the right dose of medications depending on the children's height) (99). Volume/weight based dose reformulation has also been used as a tool to decrease medication dosing error (100). The latter does not require converting the dose from (mg) to (ml), and only the patient's weight is needed (unlike the Broselow tape, which requires doing calculations to convert the required doses from (mg) to (ml)) (99, 100).

1.9.1. Electronic prescribing systems (CPOE and computer-assisted prescribing)

Electronic prescribing systems may reduce some problems associated with prescribing, including unclear handwriting and the omission of important information, such as doses, frequency, routes of administration, allergy and dose units (101).

CPOE may also reduce transcription errors (25). Not many UK hospitals use CPOE, however, even though it is thought to decrease the incidence of non-intercepted medication errors (102). It has been estimated that up to 20% of all hospitals in high income countries use CPOE (103). CPOE, in combination with a decision support system, is an effective tool in decreasing the incidence of prescribing errors, but many hospitals do not have access to it because it is expensive and represents a huge logistical change (84, 104). Using CPOE is clearly valuable with regard to adult patients, but there is still a need to determine whether it decreases the incidence of medication errors in children (105). Drawbacks of CPOE are decreasing the time that nurses have available to take care of patients (as they need to spend more time entering data into a computer), it does not detect administration errors and the chance of selecting the wrong medications (25, 98, 106).

Clinical decision supporting systems (CDSSs) are usually used alongside CPOE to help prescribers to check patients' allergies, drug interactions and to detect wrong doses (105). It is still not clear whether the use of CDSSs decrease the prevalence of prescribing errors in paediatric patients (105). Carefully designed CDSSs may be helpful in detecting inappropriate doses, as most CPOE systems alone do not alert prescribers to such errors as long as the dose is within the adult range (105).

The use of a paediatric decision support tool in conjunction with CPOE was found to be effective in decreasing prescribing errors for children (from 18.3 to 1.9 errors per 100 orders) in a paediatric emergency department in the US (107). It was also found to decrease the rate of incidents reported by 40% in a paediatric hospital in Canada (108). CPOE was found to be effective in reducing both the number of medication errors (from 46 to 26) and also potential adverse drug events (from 94 to 35) in a study in paediatric intensive and general care units in the US (109). CPOE decreased the required time for administering medication by 27%, as compared with handwritten orders in a simulated study by Sowan et al. (2010) in a US paediatric intensive care unit (110). In a systematic review, Conroy et al. (2007) (98) found that there was a large reduction of medication errors identified in some studies that used CPOE, however in one study error rates increased after implementation of CPOE (111).

1.9.2. Ward-based clinical pharmacists

Clinical pharmacists were found to decrease the rate of medication error (in paediatric and adult patients) by 66% in intensive care units in a general hospital in one study conducted in the US by Leape et al. (1999) in an urban teaching hospital (85). Kaushal et al. (2001) in the US judged that clinical pharmacists could have prevented 94% of potential errors in paediatric patients (9). In another study conducted in paediatric settings by Fortescue et al. (2003) in the US, it was judged that a clinical pharmacist intervention could have decreased medication errors and potential errors in paediatric patients by 58% and 72%, respectively (84). It was found by Kaushal et al. (2008) in a study in the US that having full time clinical pharmacists decreased the rate of serious medication errors in a paediatric intensive care unit from 29 to 6 per 1000 patients days, while part time clinical pharmacists did not decrease the rate of error in a paediatric general medical unit and in a paediatric surgical unit (86).

1.9.3. Educational and training programs

According to the systematic literature review by Conroy et al. (2007), educational and training strategies are considered to decrease the incidence of paediatric dosing errors, and errors may be prevented if error reports are reviewed and solutions discussed and considered (98). Educational interventions were also found to be a helpful tool in decreasing errors in a neonatal intensive care unit in the UK by Simpson et al. (2004) (89). Nonetheless, the incidence of prescribing errors amongst trainees in another study by Kozer et al. (2006) in a tertiary care paediatric hospital in Canada was almost the same before and after a short-term educational intervention (112).

Kozer et al. had done a study in the same setting previously in 2002. This showed of all prescribing errors made by doctors, trainees were responsible for the highest number (74). Medication errors committed by trainees reduced by the end of their academic training (74). This underscores the importance of experience and training in decreasing errors.

1.10. Summary

Medication errors are a very important topic, deserving of being addressed and studied in more depth. It is important to take into consideration the effect of study designs, prospective and retrospective identification of errors, and direct observation of healthcare providers on the identified rate of errors. Rates of medication errors are also presented using different definitions and denominators, and this variation makes it difficult to compare results from different studies.

1.11. The aims of this thesis

The aims of this thesis are:

1. To conduct a systematic review of paediatric medication error studies in order to explore:
    - Factors influencing the reported error rate **(Chapter 2)**.
    - Factors responsible for wide variations in error rate **(Chapter 3)**.
    - Any relationship between methods of data collection and results **(Chapter 3)**.
    - Any relationship between the clarity of definitions and results **(Chapter 3)**.
    - Interventional tools used to minimise medication errors **(Chapter 3)**.
2. To conduct a systematic review of the role of the paediatric clinical pharmacist in reducing the rate of medication errors **(Chapter 4)** in order to:
    - Identify contributions and interventions made by clinical pharmacists to minimise or prevent medication errors in neonatal and paediatric patients.
    - Use this knowledge to inform the development of my own project of direct observation of clinical pharmacist in local hospitals.
3. To conduct an observational study of the role of the paediatric clinical pharmacist **(Chapter 5)** in order to:
    - Document and describe their contributions to patient care and safety.
    - Identify errors that are being prevented by their presence.

Chapter 2: Systematic literature review of paediatric medication error studies

2.1. Introduction

Ghaleb et al (2006) published a systematic literature review including all studies identifying the rate of medication errors in paediatric patients and their methods until the end of March 2006 (17). They found 32 relevant articles of which 14 used chart review, 10 used review of medication error incident reports and eight used observations of drug administration.

The first part of my work takes this study further to identify all studies identifying paediatric medication errors published from April 2006 onwards, as it has been noticed that the literature on the subject has increased significantly since then. To this end six databases were searched to identify all relevant studies, and to extract relevant information.

2.2. Aims

- To identify and explore all studies which determined the rate and/or the number of medication errors in neonates and children published from April 2006.

2.3. Methods

Databases searched were British Nursing Index and Archive (BNI), EMBASE, International Pharmaceutical Abstracts (IPA), Ovid MEDLINE(R), Allied and Complementary Medicine (AMED) and CINAHL (Cumulative Index to Nursing and Allied Health Literature). The search was limited to studies published between April 2006 and March 2011. Hand search of bibliographies was done to include relevant articles that were not identified from searching the databases.

2.3.1. Search strategy

BNI, EMBASE, IPA, MEDLINE and AMED databases were searched separately and then combined together to remove duplication. CINAHL could not be combined with the other databases; hence, it was searched alone and manually reviewed to remove duplication and to identify relevant articles.

2.3.2. Keywords

Forty three keywords were used from the search by Ghaleb et al. 2006 (17) in order to update this work. Fifteen keywords were added to strengthen the search strategy. These were: prescribing mishap OR prescribing mishaps OR incorrect drugs OR incorrect doses OR incorrect routes of administration OR error reduction OR medical error OR medical errors OR calculation error OR calculation errors OR calculation mistake OR calculation mistakes OR error rate AND children OR baby.

The total 58 keywords used and the combining strategy for the search were as follows:

medication error OR medication errors OR administration error OR administration errors OR prescribing error OR prescribing errors OR dispensing error OR dispensing errors OR drug error OR drug errors OR drug mistake OR drug mistakes OR prescribing mishap OR prescribing mishaps OR drug mishap OR drug mishaps OR medication mistake OR medication mistakes OR medication mishap OR medication mishaps OR administration mistake OR administration mistakes OR dispensing mistake OR dispensing mistakes OR prescribing mistake OR prescribing mistakes OR wrong drug OR wrong drugs OR wrong dose OR wrong doses OR incorrect drug OR incorrect drugs OR incorrect dose OR incorrect doses OR incorrect route of administration OR incorrect routes of administration OR error reduction OR medical error OR medical errors OR calculation error OR calculation errors OR calculation mistake OR calculation mistakes OR error rate
AND
pediatric OR pediatrics OR paediatric OR paediatrics OR child OR children OR infant OR infants OR neonate OR neonates OR neonatal OR adolescent OR adolescents OR baby

2.3.3. Inclusion criteria

- Original research studies identifying the rate or number of medication errors in neonatal and paediatric settings or in the general population where neonatal and paediatric data were separately identified.

2.3.4. Exclusion criteria

1. Studies identifying the rate or number of medication errors in adult patients only.
2. Studies identifying the rate or number of medication errors in the general population where paediatric data are not separately identified.
3. Studies identifying drug toxicity and not medication errors.
4. Review articles, short surveys, adverse drug reactions and case reports.
5. Comment, audit, reply and editorial articles.

2.3.5. Quality assessment of studies

All studies which matched the inclusion criteria were assessed to determine their quality. The assessment was made using ten criteria adapted from Ghaleb's 2006 study (17) and Allan's 1990 (113) study to make these clearer and increase relevance. The criteria applied to each study were:

1. Aims/objectives of the study clearly stated.
2. Errors to be studied specified.
3. Errors to be studied defined.
4. Presence of a clearly defined denominator.
5. Data collection method described clearly.
6. Setting in which study conducted described.
7. Sampling described.
8. Reliability of methods used.
9. Limitations of study listed.
10. Ethical approval mentioned.

Only studies available as full articles with quality ratings six or more were included.

2.3.6. Extraction of data

All included studies that provided the rate of medication errors were analysed using tables according to the methods of data collection, the type of errors identified and the denominator used. Data extracted included country, setting, age and drugs studied.

2.4. Results

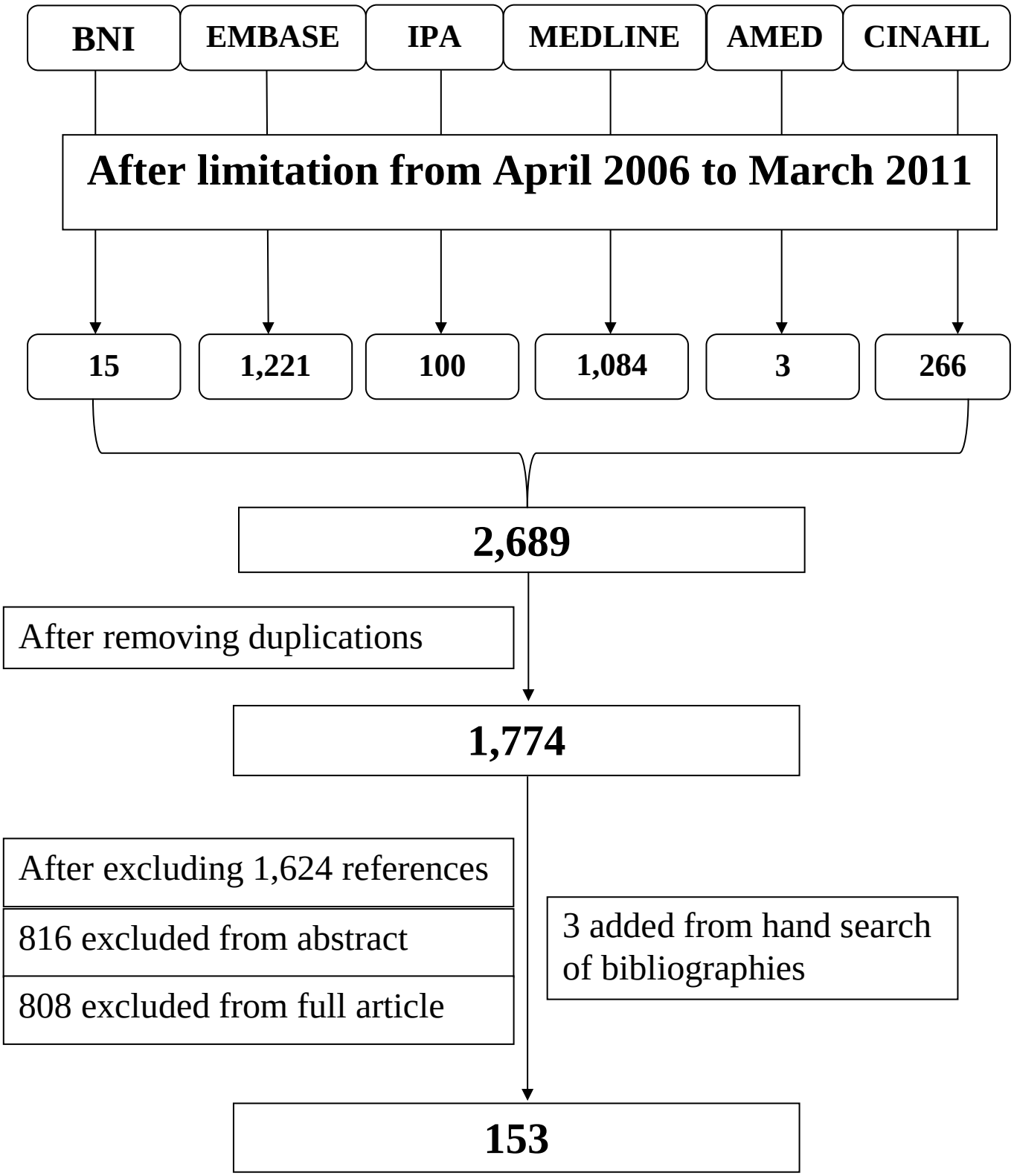
The total number of references identified after searching the six databases was 2,689 after limitation (April 2006 - March 2011). After removing duplication 1,774 abstracts were identified. These were reviewed against the inclusion and exclusion criteria. Ninety four (5.3%) abstracts (where it was not completely clear) were independently reviewed by my supervisor as to whether they should be included. Of these 30 were excluded from the abstract and 64 required access to the full articles to judge whether to exclude or include, of which 16 studies were included.

Of the reviewed references; 150 were relevant and three studies were added following hand search of bibliographies. Of the 153 included studies; eight were conference abstracts. Table 2.1 illustrates reasons for exclusion and Figure 2.1 illustrates the search strategy and its results.

Table 2.1: Reasons for excluding articles from review

Reason for exclusion	Number of papers
Not relevant	1,225
Not original research	227
Adverse drug reactions	81
Case reports	36
Literature review	26
Medication reconciliation	13
Editorial article	8
Short survey	5
Insufficient information in the abstract+ no translation	3
Total	1,624

Figure 2.1: Summary of search and review process



2.4.1. Non-English studies

Thirteen non-English studies were identified. Eight of these were included (six after full translation of the studies and for two data was extracted from the English abstract). Three studies were excluded because no translation was available. Two studies were not relevant following translation (one not in paediatric patients and the other not separating the paediatric data from the general population) (details are listed in Table 2.2).

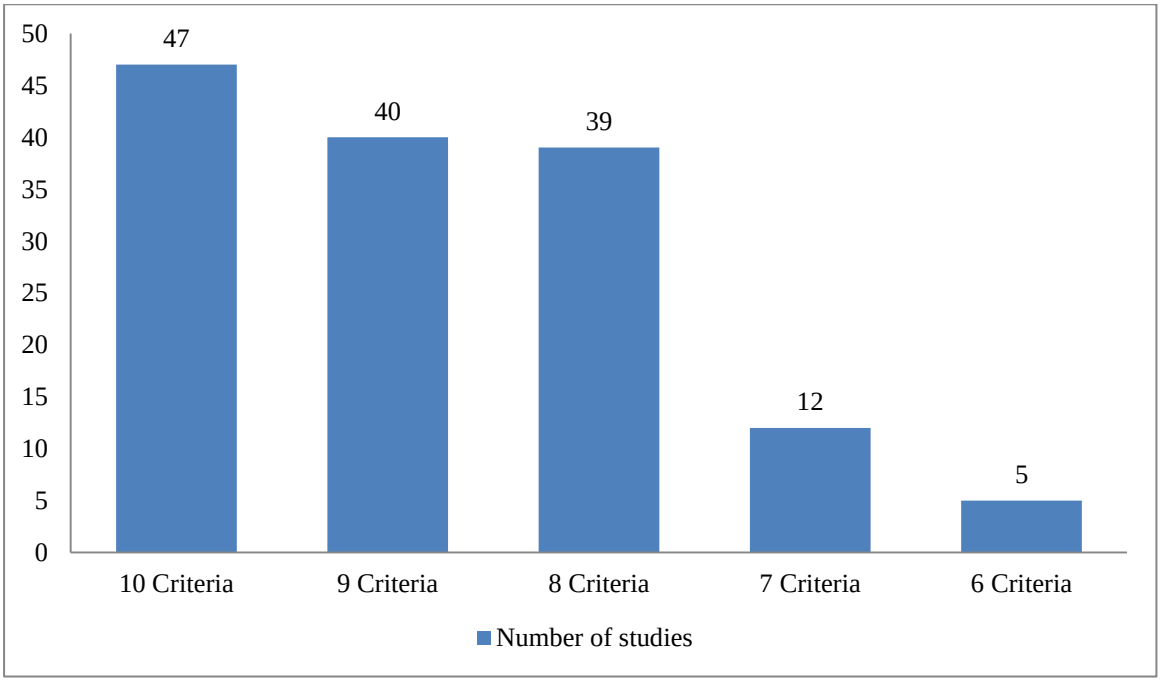
Table 2.2: Non-English studies

Number	Reference	Author	Country	Language	English Abstract	Translated	Included	Explanation	Translator
1	(114)	Diez et al. 2009	Spanish	Spanish	✔	✔	✔	Information taken from full article	Imti Choonara
2	(115)	Campino et al. 2006	Spanish	Spanish	✔	✔	✔	Information taken from full article	Imti Choonara
3	(116)	Rivas et al. 2010	Chile	Spanish	✔	✔	✔	Information taken from full article	Imti Choonara
4	(117)	Kjeldby et al. 2009	Norway	Norwegian	✔	✔	✔	Information taken from full article	Hanne Brummenaes Cathrine Kjeldby
5	(118)	Valizadeh et al. 2008	Iran	Persian	✔	✔	✔	Information taken from full article	Natasha- Vafadar-Isfahani
6	(119)	Festini et al. 2008	Italy	Italian	✖	✔	✔	Information taken from full article	Francesca-Raffi
9	(120)	Camara et al. 2011	Senegal	French	✔	✖	✔	Information taken from abstract	✖
10	(121)	Trotter et al. 2009	Germany	German	✔	✖	✔	Information taken from abstract	✖
7	(122)	Panknin 2008	Germany	German	✖	✔	✖	Not relevant (not paediatric)	Francesca-Raffi
8	(123)	Teigen et al. 2009	Norway	Norwegian	✖	✔	✖	Not relevant (paediatric data not separately identified)	Ingrid Gronlie
11	(124)	Jirapraphusak et al. 2009	Thailand	Thai	✔	✖	✖	No translation available & not enough information in the abstract	✖
12	(125)	Berghäuser et al. 2010	Germany	German	✔	✖	✖	No translation available & not enough information in the abstract	✖
13	(126)	Yamanaka et al. 2007	France	French	✔	✖	✖	No translation available & not enough information in the abstract	✖

2.4.2. Quality assessment of studies

The quality assessment was done on all studies that were in English or when full translation was available (in total 143 studies). The quality assessment was not made for studies where the data was taken only from abstracts (two studies with no full translation of the papers and eight conference abstracts). From the 143 studies; 47 studies met 10 of the quality criteria, 40 met nine criteria and 39 met eight criteria. All studies met more than five of the 10 quality criteria and therefore were included in the analysis. The results of the quality assessment can be seen in Figure 2.2.

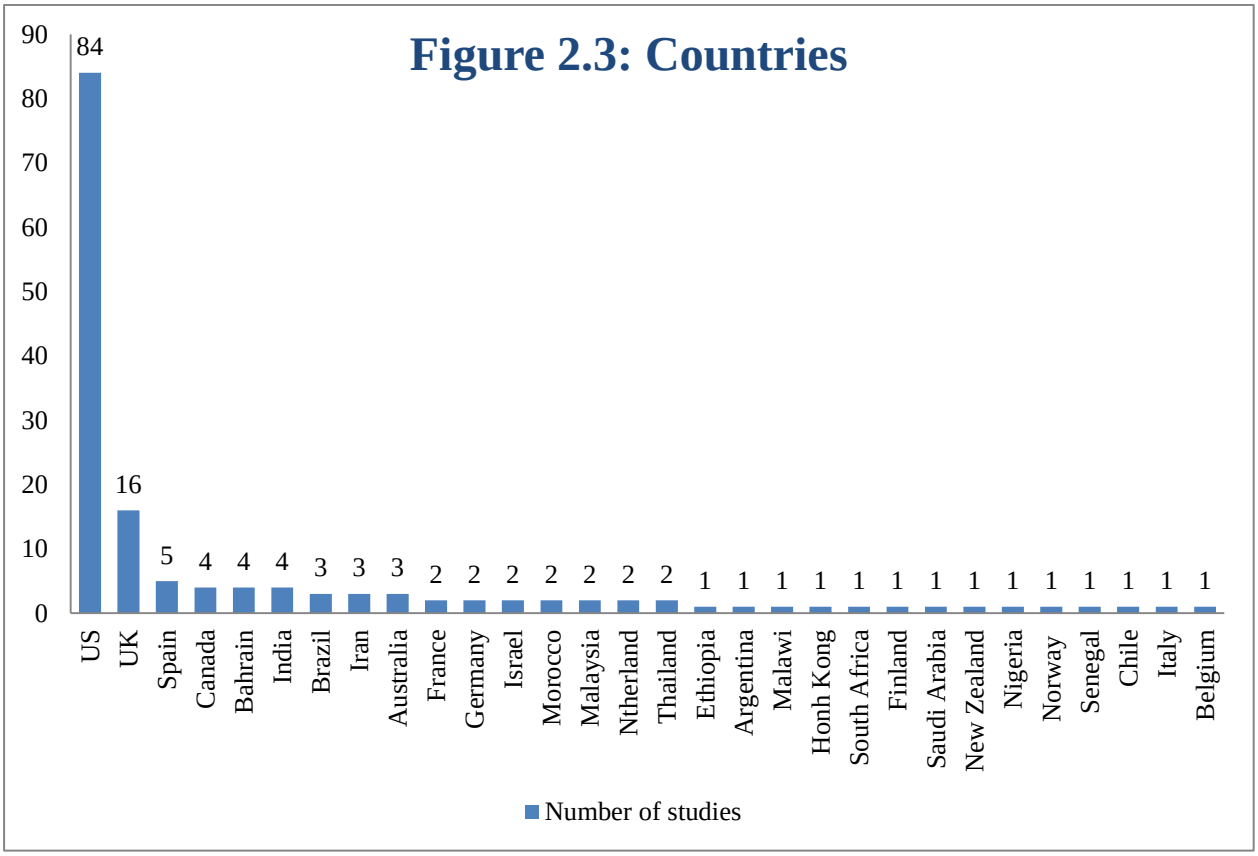
Figure 2.2: Quality Assessment of Studies



2.4.3. Countries

The 153 studies were conducted in 30 different countries of which 18 are high income countries (according to the World Bank) (127). One study was conducted in both the US and Canada (reference (128)). Of all studies; 131 (85%) were conducted in high income countries. Figure 2.3 represents the different countries where the studies were conducted.

The majority (84, 55%) of studies were conducted in the US followed by 16 studies (10.5%) conducted in the UK.



2.4.4. Settings

The 153 studies involved a variety of settings. These included specialist children's hospitals (30), neonatal units (22), paediatric units in general hospitals (16), intensive care units (13), simulation studies (12), emergency departments (12), national incident reporting systems (12), outpatients (11), poison control centres (nine), primary care centres (seven), paediatric oncology (five), neonatal and paediatric units in general hospital (five), paediatric surgical services (two), paediatric neurology ward (one), and a trauma centre (one) . Nine studies were conducted in two settings and one was conducted in four settings.

2.4.5. Age classification

According to the International Conference on Harmonisation (129); children's ages should be classified according to the following:

1. Premature baby: less than 37 weeks gestation
2. Neonates: 0-27 days
3. Infants: 28 days- 23 months
4. Child: 2-11 years
5. Adolescent: 12- 16 (or 18) years

53 studies did not mention the age of the patients studied, 25 included children of all ages, 23 included neonates, infants, children and adolescents, 19 included neonates only, 7 included preterm babies, neonates, infants and children, 5 included infants, 3 included children and adolescents, 3 included infants, children and adolescents and 3 included infants and children. Twelve studies were simulation studies.

2.4.6. Types of medication errors

Forty-four studies identified prescribing errors and 42 studies identified different types of medication errors (i.e. prescribing errors, administration errors, medication errors in general, transcribing errors, monitoring errors or dispensing errors). These will be described in more detail in the relevant sections in the following results. Thirty-six studies identified administration errors, 29 studies identified "medication errors in general". The type of error (e.g. prescribing errors) was not specified, one study identified dispensing errors and one study identified monitoring errors (i.e. therapeutic drug monitoring).

2.4.7. Types of medications studied

Forty-eight different medications or groups of medications were studied. Seventy three studies identified the error rate from all medications. Seven studies identified errors with chemotherapy, seven studied errors involving specific medications on a list, five studied errors using intravenous medications and four studies identified errors with antimicrobials. Section 1 in Appendix 1 illustrates all medications, or groups of medications studied.

2.4.8. Denominators

Twenty six different denominators were used 198 times by 109 studies (Table 2.3).

Table 2.3: All denominators identified by 109 studies

Denominators	Number of studies using this denominator
Of all errors	51
Of all orders	50
Of all patients	16
Of all administrations	13
Per 1000 patient days	13
Of all admissions	11
Of all medications	7
Mean errors	5
Per 1000 orders	5
Of all patient visits	4
Of all participants	3
Of all medication days	3
Of all doses	2
Per 1000 administrations	2
Of all possible errors	2
Median errors	1
Visits per 10,000 individuals per year	1
Per 100 patient days	1
Of all preparations	1
Of all samples	1
Per hospitalisation days	1
Per 1000 doses	1
Of all transcriptions	1
Of all charts	1
Of all ADEs	1
Per bed day	1

2.4.9. Study methods

Information (Section 2 in Appendix 1) was extracted according to the methodology used in each study to identify the rate of errors. All studies that identified the error rate (109) using 26 different denominators were analysed according to the methods of data collection, the type of medication errors and the denominator used.

Sixty studies used chart/medical record review, 50 studies used review of incident reports, 23 studies used mixed methods, (i.e. more than one method e.g. chart review plus review of incident reports), 12 studies used simulation and eight studies used direct observation.

Not all studies identified the rate of error. Forty four studies just identified the number of errors without providing denominators. These studies were excluded from analysis in the following chapters as they cannot be compared with others. Many studies identified their results using more than one denominator, hence the number of studies does not always match the number of denominators listed in the following tables.

Many studies identified more than one type of error. These studies are included in the relevant section (i.e. prescribing errors, administration errors, etc.). This is another reason for the differences in the number of studies identifying the rate of errors in each section.

2.4.9.1. Studies using chart/medical record review

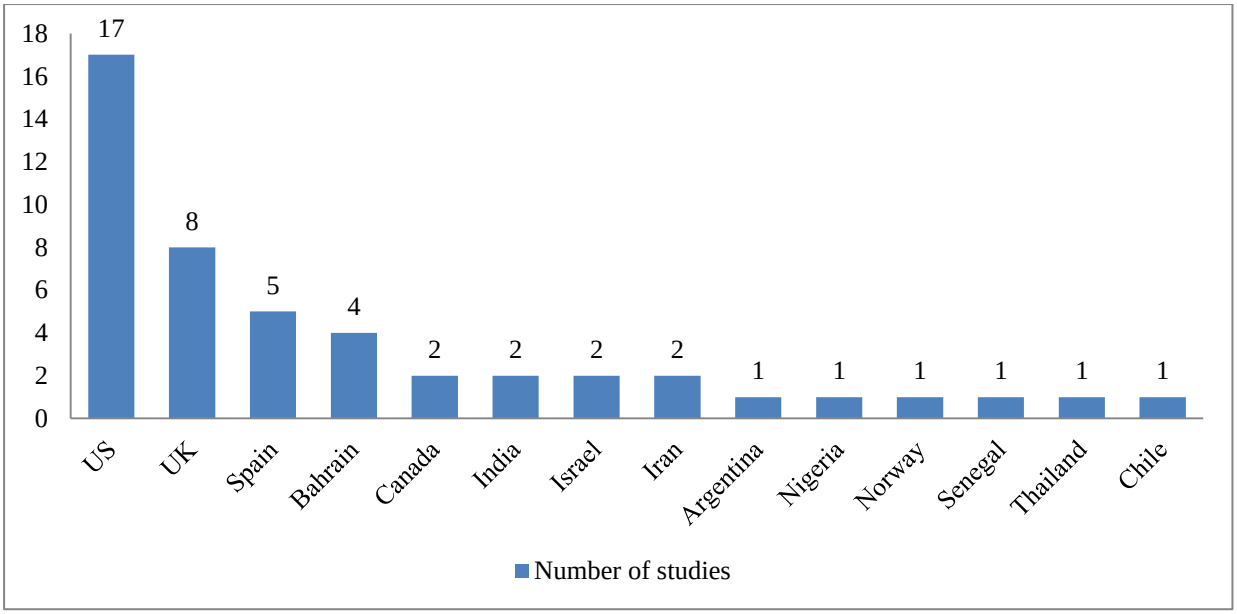
Sixty studies used chart and/or medical record review as the method of data collection:

- 34 identified prescribing errors, two identified administration errors, one identified dispensing errors, six identified medication errors in general, one identified monitoring errors and 16 identified a mixture of different types of medication errors.

2.4.9.1.1. Studies identifying prescribing errors

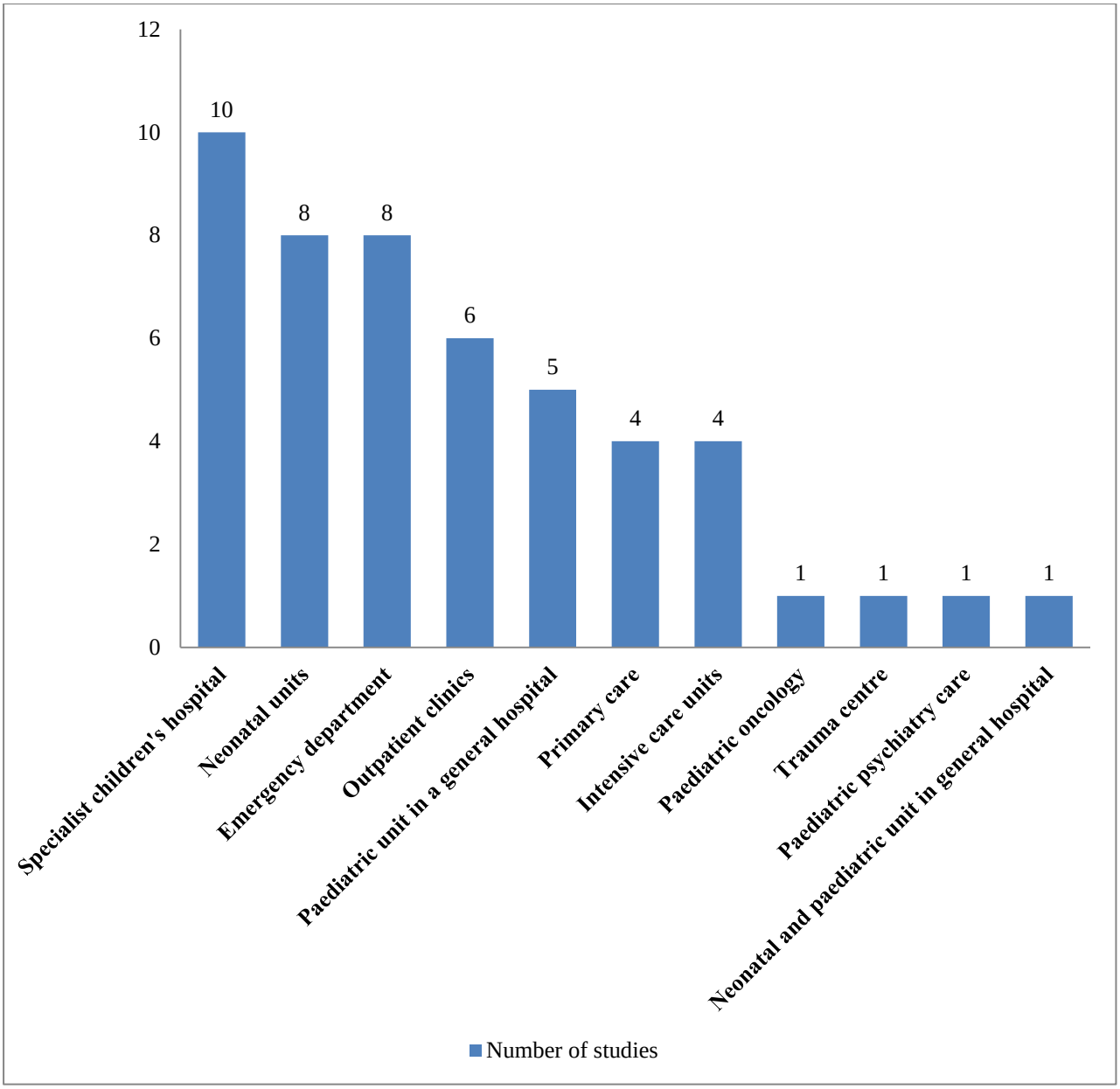
Forty eight studies in total used chart/medical record review to identify prescribing errors: 45 identified the rate and the number of prescribing errors and three studies only identified the number of errors. The majority were conducted in the US (17 studies), the UK (eight studies), Spain (five studies) and Bahrain (four studies). Figure 2.4 illustrates the different countries.

Figure 2.4: Countries in studies identifying the rate of prescribing errors using chart/medical record review



Studies were conducted in specialist children's hospitals (10), neonatal units (eight), emergency departments (eight) and outpatients (four studies in outpatient clinics, one study in a community pharmacy and one study at both a clinic and home). One study was conducted in two settings (neonatal unit and emergency department) (Figure 2.5).

Figure 2.5: Settings for studies identifying the rate of prescribing errors using chart/medical record review



The rate of prescribing errors was given using different denominators as shown in Table 2.4. “Of all orders”, “of all errors”, “of all patients” and “of all medications” are explored further in Chapter 3 as they are associated with a wide range of results.

Table 2.4: Denominators used by studies identifying the rate of prescribing errors using chart/medical record review

Denominator	Number of studies	Range of reported errors	Comment
Of all orders	27	0-90.5%	-
Of all errors	6	0.7-89%	-
Mean errors	4	0.1±0.3-14.8	-
Of all patients	3	4.8-74%	-
Of all medications	3	4.6-77.4%	-
Of all patient visits	2	13-32.6%	-
Of all medication days	1	(33)-52%	Before and (after) intervention.
Of all admissions	1	(21)-47%	Before and (after) intervention.
Per 1000 patient days	1	5	-
Per 1000 administrations	1	0.09	-
Median errors	1	1	-

2.4.9.1.2. Studies identifying administration errors

Eight studies used chart/medical record review to identify the rate of administration errors. Five studies were conducted in the US, one in the UK, one in Canada and one in Argentina. Three studies were conducted in specialist children’s hospitals, one in a paediatric unit in a general hospital, one in a neonatal and paediatric unit in a general hospital, one involved paramedics, one in an emergency department, one in a trauma centre and one in an outpatient clinic. One study was conducted in two settings (specialist children’s hospital and paediatric unit in a general hospital).

Table 2.5 illustrates the rate of administration errors identified in these studies and the denominators used. The studies using the denominator "of all patients" showed error rates varying widely from 22.7 to 87.5%. These will be explored further in Chapter 3.

Table 2.5: Denominators used by studies identifying the rate of administration errors using chart/medical record review

Denominator	Number of studies	Range of reported errors	Comment
Of all patients	2	22.7-87.5%	-
Of all errors	2	0-27%	-
Of all charts	1	15-25%	Two different settings
Of all orders	1	(3)-6%	Before and (after) intervention.
Of all possible errors	1	(1.7)-14.8%	Before and (after) intervention.
Of all administrations	1	(5.9)-8.4%	Before and (after) intervention.

2.4.9.1.3. Studies identifying dispensing errors

Six studies used chart/medical record review to identify the rate of dispensing errors. Three studies were conducted in the US, one in India, one in Thailand and one in Brazil.

Two studies were conducted in specialist children's hospitals, one paediatric unit in a general hospital, one outpatient clinic, one paediatric psychiatric care, one emergency department and one neonatal unit. One study was conducted in two settings (emergency department and neonatal unit).

Table 2.6 illustrates the rate of dispensing errors identified in these studies and the denominators used. "Of all errors" was the most widely used denominator (used by four studies) with dispensing error rates ranging from 0-21%.

Table 2.6: Denominators used by studies identifying the rate of dispensing errors using chart/medical record review

Denominator	Number of studies	Range of reported errors	Comment
Of all errors	4	0-21%	-
Of all admissions	1	(0.33)-3.01%	Before and (after) intervention.
Of all doses	1	11.5%	-

2.4.9.1.4 Studies identifying medication errors in general

Sixteen studies used chart/medical record review to identify medication errors in general. Of all studies; 14 identified the rate and the number of medication errors in general and two only identified the number of errors. Of the 16 studies, seven were conducted in the US, two in the UK, two in Iran, one in the US and Canada, one in India, one in Israel, one in Thailand and one in Brazil.

Five studies were conducted in neonatal units, three in emergency departments, three in intensive care units, two in paediatric units in general hospitals, two in specialist children's hospitals, one was in otolaryngology, one paediatric psychiatric care and one was in outpatient (clinic and home). Two studies were each conducted in two settings (neonatal unit and emergency department for one study and specialist children's hospital and paediatric unit in general hospital for the other study).

Table 2.7 illustrates the rate of errors identified in these studies and the denominators used. "Of all orders" was used in five studies and varied from 2.42-23%, and "of all patients" was used in three studies and ranged between 26.4-55%.

Table 2.7: Denominators used by studies identifying the rate of medication errors in general using chart/medical record review

Denominator	Number of studies	Range of reported errors	Comment
Of all orders	5	2.42-23%	-
Of all patients	3	26.4-55%	-
Per 1000 patient days	1	(2.4)-9.3	Before and (after) intervention.
Of all admissions	1	(2.2)-7.9%	Before and (after) intervention.
Of all medication days	1	(34)-53%	Before and (after) intervention.
Of all medications	1	7.6- 12.8%	In two groups of participants.
Of all patient visits	1	18.8%	-
Per 1000 orders	1	24.1	-
Of all adverse drug events	1	56%	-
Per 3.9 hospitalisation days	1	1	-
Per 100 patient days	1	2.1	-
Per bed day	1	(1.1)-1.8	Before and (after) intervention.

2.4.9.1.5. Studies identifying transcribing errors

A transcribing error was defined by Kazemi et al. in 2010 (102) as "An error that occurred after the prescription stage." The same authors in 2011 (130) defined a transcribing error as: "A medication that was registered with an erroneous dose in the paper-based nursing report while the prescribed order was correct". No other studies provided a definition of transcribing errors.

Six studies used chart/medical record review to identify the rate of transcribing errors. Two were conducted in Iran, two in Spain, one in the US and one in Chile. Five studies were conducted in neonatal units, one in a paediatric unit in a general hospital, one in an intensive care unit, one in paediatric surgery and one was conducted in a specialist children's hospital. One study was conducted in four settings (paediatric unit in general hospital, neonatal unit, paediatric surgery and intensive care unit).

Table 2.8 illustrates the rate of transcribing errors identified in these studies and the denominators used. “Of all orders” was used by two studies and ranged between 15.9-21.3%. Of these Campino et al. 2006 (115) identified the transcribing errors in a neonatal unit in Spain which was 21.3% of all orders. Campino et al. in 2008 (131) identified the transcribing error rate in the same country and setting and this was 20.5% of all orders at baseline and 15.9% after doctors and nurses were informed that their performance would be reviewed. They identified the following transcribing errors: omission of dose, incorrect dose, omission of units, incorrect units, omissions of interval, incorrect interval, omission of route and incorrect route.

Rivas et al. 2010 (116) did a cross sectional analysis of prescriptions in four settings: a paediatric unit in a general hospital, a neonatal unit, paediatric surgery and an intensive care unit. They found that the rate of transcribing errors was 6% of all transcriptions. They identified the following: illegible transcriptions, not transcribing all indicated medications and transcription of medications that were not prescribed.

Table 2.8: Denominators used by studies identifying the rate of transcribing errors using chart/medical record review

Denominator	Number of studies	Range of reported errors	Comment
Of all orders	2	15.9- 21.3%	-
Of all transcriptions	1	6%	-
Of all medications	1	2.5-3%	In two groups of participants
Of all medication days	1	1-(1)%	Before and (after) intervention
Of all errors	1	0%	-

2.4.9.1.6. Studies identifying monitoring errors

Three studies used chart/medical record review to identify the rate of monitoring errors. All studies were conducted in the US (two in specialist children's hospitals and one in outpatients (clinic and home)). Two studies just identified the rate of different types of errors without mentioning the medications associated with these. One study was conducted by Takata et al. 2008 (132) in 12 children's hospitals in the US. They reviewed 960 randomly selected charts and identified 62.5% of all medication errors to be monitoring errors. They defined a monitoring error to be "failure to review a prescribed regimen for appropriateness and detection of problems or failure to use appropriate clinical or laboratory data for adequate assessment of patient response to prescribed therapy". The remaining were prescribing and dispensing errors. The second study by Walsh et al. 2009 (27) was done in an outpatient clinic and home in the US. The monitoring error rate was 5% of all medication errors after reviewing all patients' charts for children with cancer treated with chemotherapy. The remaining were prescribing, administration and dispensing errors. This will be explored further in Chapter 3 because of the wide range of error rates reported in these studies (5-62.5% of all medication errors). No examples were given by either of the studies regarding the nature of the monitoring errors.

The third study was conducted by Abboud et al. 2006 (133) who reviewed the effects of implementing a corollary order screen (in which prescribers are asked via a screen regarding the need for checking the blood level and the time for the next blood sample) for three aminoglycoside medications (gentamicin, tobramycin and amikacin). The rate of toxic and subtherapeutic levels identified increased from 9.8% to 12.8% of all samples after the intervention (not statistically significant). The author

suggests that the reason for the increase in these rates was due to an increase in the rate of monitoring after the implementation of the corollary order screen.

Summary of studies using chart review

Most studies using chart review identified prescribing errors. The majority of studies were conducted in the US and the UK. Most studies were conducted in specialist children's hospitals followed by neonatal units. Twenty two different denominators were used with "of all orders" being the most common followed by "of all errors".

Eleven denominators were used to describe prescribing errors and four denominators showed a wide variation in results. Administration errors were described using six denominators with one showing wide variation. Dispensing errors were reported by six studies most of which showed a rate of 0-21% of all errors. Medication errors in general were reported in 16 studies using 12 different denominators, most commonly "of all orders" where rates varied from 2.4-23%. Transcribing errors were studied in six studies using five different denominators and showed 16-21% orders contained such errors.

2.4.9.2. Studies using direct observation

Eight studies used direct observation: one identified prescribing errors and seven identified administration errors.

2.4.9.2.1. Studies identifying prescribing errors

A study was conducted by Osterholt et al. 2006 (134) in an outpatient clinic in Malawi in which doctors' consultations were observed by the authors to assess the suitability of the prescribed antimicrobial drugs. The rate of prescribing errors was 29.1% of all patients.

2.4.9.2.2. Studies identifying administration errors

Two studies were conducted in the US, two in Malaysia, one in Germany, one in Canada and one in Ethiopia. Two studies were conducted in neonatal units, two in paediatric units in general hospitals, one in paediatric neurology, one in an intensive care unit and one in paediatric oncology. All studies used "of all administrations" as the denominator and error rates varied between studies from 5.6%-96.6%. These will be explored in more detail in Chapter 3.

Summary of studies using direct observation

Most studies using direct observation identified administration errors. Two denominators were used, with "of all administrations" being the most common.

2.4.9.3. Studies using review of medication error incident reports

Fifty studies used review of medication error incident reports: six identified prescribing errors, 12 identified administration errors, 17 identified medication errors in general and 15 identified a mixture of different types of medication errors.

2.4.9.3.1. Studies identifying prescribing errors

Nineteen studies used review of incident reports to identify prescribing errors. Ten studies identified the rate and the number of errors whereas nine studies only identified the number. Twelve studies were conducted in the US, three in the UK, one in Canada, one in Belgium, one in Australia and one in France.

The 19 studies were conducted in a variety of settings. They included five in specialist children's hospitals, two in neonatal units, one in a paediatric surgical service, one in a paediatric pain team, one in paediatric oncology, one in a paediatric unit in a general hospital, one in outpatient setting (using Medicaid Paid Claim data), one in a paediatric gastroenterology and nutrition ward and one in a neonatal and paediatric unit in a general hospital. Several used data from a national incident reporting system.

Table 2.9 illustrates the rate of prescribing errors identified and the denominators used. Seven studies used "of all errors" as the denominator and error rates varied between 1.1% (in a US neonatal unit) -24.4% (in a French neonatal unit).

Table 2.9: Denominators used by studies identifying the rate of prescribing errors using review of medication error incident reports

Denominator	Number of studies	Range of reported errors
Of all errors	7	1.1-24.4%
Per 1000 orders	3	0.03-5.93
Per 1000 patient days	1	2.67

Per 1000 orders was used by three studies to identify the prescribing error rate using review of incident reports. Takata et al. 2008 (135) had done a study in four children's hospitals in the US and identified a prescribing error rate of 0.82 per 1000 orders (or 2.67 per 1000 patient days). They only involved pharmacy interventions on prescribing errors with potential significant patient harm. Another US study by Bsaco et al. 2010 (72) identified 0.03 per 1000 orders to involve prescribing errors in an outpatient setting. Smith et al. 2011 (136) identified 5.93 prescribing errors per 1000 orders in a paediatric unit in a general hospital in the US. They only involved analgesic medications.

Each of the three studies mentioned above involved specific types of medications or prescribing errors (e.g. analgesic prescribing errors) and this is likely to be the cause for the low error rates identified by these studies.

2.4.9.3.2. Studies identifying administration errors

Twenty four studies used review of medication error incident reports to identify administration errors. Nine studies identified the rate and the number of administration errors while 15 studies only identified the number. Fifteen studies were conducted in the US, two in the UK, one in France, one in Australia, one in South Africa, one in Hong Kong, one in Thailand, one in Canada and one in Saudi Arabia.

The 24 studies were conducted in different settings. These included poison control centres (4), specialist children's hospitals (4), neonatal units (3), national incident reporting systems (5), primary care centres (2), and anaesthetics (1). Several used data from a national incident reporting system.

Table 2.10 illustrates the rate of administration errors identified in the studies and the denominators used. Seven studies used "of all errors" as the denominator and error rates varied between 30-93.2% (three in neonatal units, one in a specialist children's hospital, one in paediatric oncology, one in paediatric gastroenterology and nutrition and one used a national incident reporting system to identify antidepressant medication errors). These will be explored further in Chapter 3.

Table 2.10: Denominators used by studies identifying the rate of administration errors using review of medication error incident reports

Denominator	Number of studies	Range of reported errors	Comment
Of all errors	7	30-93.2%	-
Tenfold errors (per 1000 administrations)	1	0.595-0.718	For each individual year in five years.
Of all patient visits	1	8%	-
Visits per 10,000 individuals per year	1	0.7	-

2.4.9.3.3. Studies identifying medication errors in general

Thirty two studies used review of medication error incident reports to identify medication errors in general where the type of error was not specified. Of all studies; six identified the rate and the number of medication errors in general and 26 only identified the number. Nineteen studies were conducted in the US, four in the UK, two in France, one in the Netherlands, one in Finland, one in Morocco, one in Italy, one in Germany, one in Australia and one in Canada.

The 32 studies were conducted in different settings. These included specialist children's hospitals (seven), poison control centres (five), neonatal units (four) and intensive care units (two). Several used data from a national incident reporting system.

Table 2.11 illustrates the rate of medication errors in general identified in the studies and the denominators used. Two studies used "of all patients" denominator and error rates were between 4.9-34.3%. One of these was conducted by Hayes et al. in 2008 (137) using review of incident reports retrieved from a poison control centre in the US. The aim was to identify the rate of errors that are associated with intravenous acetylcysteine and this was found to be 34.3% of all patients. The other study was conducted by Ligi et al. 2010 (15) in a neonatal unit in France. The rate of errors was 4.9% of all patients before starting safety initiatives and iatrogenic events prevention strategies and 7% after the intervention. According to authors; this increase was because of the increase in the rate of reporting.

Table 2.11: Denominators used by studies identifying the rate of medication errors in general using review of medication error incident reports

Denominator	Number of studies	Range of reported errors	Comment
Of all patients	2	4.9-34.3%	-
Of all orders	2	0.21- 0.24%	-
Of all admissions	1	4.9%	-
Of all medications	1	(0.02)-3.3%	Before and (after) intervention.

The two studies using "of all orders" denominator have similar rate of errors. One was conducted by Burny et al. 2006 (138) in an intensive care unit in the US whereas the other was conducted by Narula et al. 2010 (139) in a paediatric gastroenterology and nutrition ward in the UK, looking only for medication errors associated with parenteral nutrition.

2.4.9.3.4. Studies identifying dispensing errors

Ten studies used review of incident reports to identify dispensing errors. Five identified the rate and the number of dispensing errors and five only identified the number. Seven studies were conducted in the US, two in the UK and one in Canada.

The ten studies were conducted in different settings. These included specialist children's hospitals (three), paediatric gastroenterology and nutrition ward (one) and neonatal and paediatric unit in general hospital (one). Several used data from a national incident reporting system.

All the five studies identifying an error rate used one denominator "of all errors" and ranged between 11.8-35.7%. Rinke et al. 2007 (140) identified a dispensing error rate of 30.3% of all errors. This was associated with chemotherapy using paediatric oncology data from a national incident reporting system in the US. Stavroudis et al. 2010 (141) identified a dispensing error rate of 11.8% of all errors and used neonatal

data from a national incident reporting system in the US, whereas Miller et al.'s 2010 study (76) was conducted in a specialist children's hospital in the US and found 35.7% of errors to be dispensing errors. One study which was conducted in a paediatric gastroenterology and nutrition ward in the UK and identified the dispensing error rate with parenteral nutrition which was 24% of all errors. Rinke et al. 2010 (66) identified 30% of all errors with antidepressant drugs were dispensing errors when also using a national incident reporting system data.

2.4.9.3.5. Studies identifying monitoring errors

Six studies used review of incident reports to identify monitoring errors. Of all studies; three identified the rate and the number of monitoring errors and the other three only identified the number. Five studies were conducted in the US and one in Canada. No examples were given by any of these studies.

One study was conducted in a specialist children's hospital and the other five studies used data from a national incident reporting system.

All three studies identifying the error rate were conducted in the US and used one denominator "of all errors". Rates of errors ranged between 0.6-1.4%. These studies did not mention the methodology of detecting the monitoring errors or medications associated with these errors and only provided the rate of monitoring errors. The first study was conducted by Rinke et al. 2007 (140) in paediatric oncology using a national incident reporting system to identify medication errors associated with chemotherapy. The monitoring error rate was 0.6% of all errors.

A second study also conducted by Rinke et al. in 2010 (66) and showed that the rate of monitoring errors was 0.7% of all errors for antidepressant medications and used a national incident reporting system, yet Stavroudis et al. 2010 (141) found that the rate

of monitoring errors was 1.4% of all errors using neonatal data from a national incident reporting system.

2.4.9.3.6. Studies identifying transcribing errors

Nine studies used review of incident reports to identify transcribing errors. Of all studies; five identified the rate and the number of transcribing errors and the other four only identified the number. Seven studies were conducted in the US and two in the UK.

Two studies were conducted in specialist children's hospitals and one in a paediatric gastroenterology and nutrition ward. Six studies used data from a national incident reporting system.

All five studies that identified the rate of transcribing errors used the same denominator. The rate of transcribing errors ranged between 7.1 and 28% of all errors. Rinke et al. 2007 (140) identified a transcribing errors rate of 7.1% of all errors associated with chemotherapy in paediatric oncology using a national incident reporting system in the US whereas Stavroudis et al. 2010 (141) identified a transcribing error rate of 18.4% of all errors for their neonatal data. Neither provided specific examples of the types of errors.

One study which was conducted in a paediatric gastroenterology and nutrition ward in the UK by Narula et al. in 2010 (139) identified the transcribing error rate with parenteral nutrition which was 20% of all errors. They identified the following types of transcribing errors: incorrect patient identification, surname, date of birth, rate or inadequate amount of medication.

Miller et al.'s 2010 study (76) was conducted in a specialist children's hospital in the US and found 24.2% of errors as transcribing errors. Rinke et al. 2010 (66) used

national incident reporting system data to identify transcribing errors with antidepressant drugs and found the highest rate of 28% of all errors.

Summary of studies using review of medication error incident reports

Most studies using review of medication error incident reports identified medication errors in general followed by administration errors. The majority were conducted in the US followed by the UK. Most studies were conducted using national incident reporting systems followed by studies in specialist children's hospitals. Ten different denominators were used with "of all errors" being the most common.

2.4.9.4. Studies using mixed methods

This section includes studies that used more than one method to collect the data to identify medication errors, for example, studies that used chart review and review of incident reports to identify the rate of medication errors.

Twenty three studies used mixed methods: two identified prescribing errors, four identified administration errors, six identified medication errors in general and 11 identified a mixture of different types of medication errors.

2.4.9.4.1. Studies identifying prescribing errors

Thirteen studies used mixed methods to identify prescribing errors. Of all studies; eight identified the rate and the number of prescribing errors and five only identified the number. Eight studies were conducted in the US, two in the UK, one in New Zealand, one in Iran and one in India.

The 13 studies were conducted in different settings. These included a paediatric unit in a general hospital (three), specialist children's hospitals (three), emergency department (one), outpatient clinic (one) and paediatric oncology unit (one).

Table 2.12 illustrates the rate of prescribing errors identified in the studies and the denominators used. "Of all orders" was used by four studies and ranged between 1.06-27%. The studies using "of all patients" denominator identified a wide range of error rates from 40-189% and therefore will be explored further in Chapter 3 to determine the reasons for this.

Table 2.12: Denominators used by studies identifying the rate of prescribing errors using mixed methods

Denominator	Number of studies	Range of reported errors	Comment
Of all orders	4	1.06-27%	-
Of all errors	2	26-54%	-
Of all patients	2	40-(189)%	(More than one error per patient)
Per 1000 patient days	1	74	-
Of all admissions	1	43%	-

2.4.9.4.2. Studies identifying administration errors

Thirteen studies used mixed methods to identify administration errors. Of all studies; seven identified the rate and the number of administration errors and six only identified the number. Seven studies were conducted in the US, two in the UK, one in New Zealand, one in the Netherlands, one in Iran and one in Brazil.

The 13 studies were conducted in different settings. These included two in specialist children's hospitals, two in paediatric units in general hospitals, two in an outpatient clinic and one in a paediatric oncology unit.

Table 2.13 illustrates the rate of administration errors identified in the studies and the denominators used. "Of all administrations" and "of all errors" were each used twice

and ranged respectively between 1.2-63.8% and 12-70%. Conroy et al. 2007 (142) identified administration errors separately after using direct observation of nurses (1.2% of all administrations). This result will be explored with results identified for the seven studies in Section 4.9.2.2. (Page 56) with a wide range of administration errors (1.2-96.6% of all administrations) in Chapter 3. The "of all errors" denominator will also be explored further in Chapter 3 as the two studies using this denominator identified a wide range of error rates (12-70%).

Table 2.13: Denominators used by studies identifying the rate of administration errors using mixed methods

Denominator	Number of studies	Range of reported errors
Of all administrations	2	1.2- 63.8%
Of all errors	2	12- 70%
Of all patients	1	75%
Per 1000 patient days	1	54
Of all admissions	1	32%
Of all orders	1	5.2%
Of all possible errors	1	19.1%

2.4.9.4.3. Studies identifying medication errors in general

Twelve studies used mixed methods to identify medication errors in general. Ten identified the rate and the number of medication errors in general and two only identified the number. Nine studies were conducted in the US, one in Morocco, one in India and one in New Zealand. The 12 studies were conducted in different settings. These included three in neonatal and paediatric units in general hospitals, two in paediatric units in general hospitals, two in specialist children's hospitals, one in a neonatal unit and one in an outpatient clinic.

Table 2.14 illustrates the rate of medication errors in general identified in these studies and the denominators used. "Per 1000 patient days" was the most commonly used denominator being used in six studies with a wide range of results from 4-167. "Of all admissions" denominator was used by three studies and with error rate of 29.5-127%. The studies using these two denominators will be explored further in Chapter 3.

Table 2.14: Denominators used by studies identifying the rate of medication errors in general using mixed methods

Denominator	Number of studies	Range of reported errors	Comment
Per 1000 patient days	6	4-167	-
Of all orders	3	1.29-11.6%	-
Of all admissions	3	29.5-127%	-
Of all patients	2	3-7.8%	-
Per 1000 doses	1	69.5-79.7	Before and after an intervention
Of all medications	1	9.9%	-
Per 1000 orders	1	15	-

2.4.9.4.4. Studies identifying dispensing errors

Six studies used mixed methods to identify dispensing errors. Of all studies; four identified the rate and the number of dispensing errors and two only identified the number. Five studies were conducted in the US and one in New Zealand.

One study was conducted in a specialist children's hospital, one in a paediatric unit in a general hospital, one in a neonatal and paediatric unit in general hospital, one in outpatient clinic, one in paediatric oncology and one in an intensive care unit. Table 2.15 illustrates the rate of dispensing errors identified in the studies and the denominators used. Two studies used "of all errors" and the result ranged between 0.2-3%.

Table 2.15: Denominators used by studies identifying the rate of dispensing errors using mixed methods

Denominator	Number of studies	Range of reported errors
Of all errors	2	0.2-3%
Per 1000 patient days	1	11
Of all admissions	1	7%
Of all orders	1	1.1%
Of all preparations	1	0%

2.4.9.4.5. Studies identifying transcribing errors

Three studies used mixed methods to identify transcribing errors. Two studies identified the rate and the number of transcribing errors and one only identified the number. All studies were conducted in the US. One study was conducted in an outpatient clinic, one in an intensive care unit and one in a neonatal and paediatric unit in a general hospital. The only example of specific transcribing errors was provided by Buckley et al. 2007 (143) who did not identify the rate of error, but identified the following types of errors: wrong dose, omission and wrong drug. The two studies identifying the rate of transcribing errors used "of all errors" denominator and the error rates varied between 2-32%. One study was conducted by Kaushal et al. 2007 (144) in an outpatient clinic using review of medication charts and telephone interview with parents. The transcribing error rate was 2% of all errors. The second study by Wang et al. 2007 (106) in neonatal and paediatric units in a general hospital used review of medical records and review of medication error incident reports. The rate of transcribing errors was 32% of all errors.

2.4.9.4.6. Studies identifying monitoring errors

Two studies used mixed methods to identify the rate of monitoring errors. One study was conducted in the US and the other in New Zealand. "Of all errors" denominator

was used in a neonatal and paediatric unit in a general hospital in the US and was 1.3%, reviewing all medication records and incident reports (106). The other study by Kunac et al. 2008 (145) was conducted in a paediatric unit in a general hospital in New Zealand. The rate of monitoring errors from reviewing incident reports and reviewing charts showed the error rates to be 18 per 1000 patient days, 11% of all admissions and 1.7% of all orders. Neither of the studies provided examples of monitoring errors.

Summary of studies using mixed methods

Most studies using mixed methods identified prescribing and administration errors followed by medication errors in general. Most were conducted in the US, then the UK and India. Most studies were conducted in specialist children's hospitals followed by paediatric units in general hospitals. Eleven different denominators were used with "of all orders" and "per 1000 patient days" being the most common.

2.4.9.5. Simulation studies

Twelve studies used simulation to explore medication errors: one study examined prescribing errors and 11 studies examined administration errors

2.4.9.5.1. Studies identifying prescribing errors

A study was conducted in the US by Vaidya et al. 2006 (146) to assess the effect of CPOE. The prescribing error rate of continuous medication infusions decreased from 73% to 4.3% of all orders after the intervention.

2.4.9.5.2. Studies identifying administration errors

Ten studies identified the rate and the number of administration errors and one only identified the number. Ten studies were conducted in the US and one in Australia. Table 2.16 illustrates the rate of administration errors identified in the studies and the denominators used.

Table 2.16: Denominators used by studies identifying the rate of administration errors using simulation studies

Denominator	Number of studies	Range of reported errors	Comment
Of all participants	3	21-86%	-
Of all administrations	3	0-100%	-
Of all orders	2	0.63-35.6%	-
Mean errors	1	(0.7)-1.8	(with) and without intervention.
Of all doses	1	(0-21) and 12-28%	Before and (after) intervention.

"Of all participants" denominator was used by three studies conducted in the US. Wheeler et al. 2008 (147) identified dosing errors by doctors using mass concentration (e.g. 1 mg in 1 ml) or ratio concentration (e.g. 1 ml of 1:1000) labels. The error rate was higher with ratio concentration labels (86% of all doctors) than with mass concentration labels (21%). The second study, by Sobhani et al. 2008 (148), assessed the measurement of 5 ml acetaminophen suspension by participants using a dosing cup (associated with 85.4% errors) or oral syringe (33.3% errors). The third study was conducted by Yin et al. 2011 (149) to assess parents' measurement of acetaminophen using a dropper. The error rate was 59% of all participants when written instructions about the administration of paracetamol were provided and 43.9% of all participants when pictogram instructions were provided.

As can be seen from Table 16; three studies used “of all administrations” as the denominator with a wide range of results from 0-100%. All studies were conducted in the US. The first study was conducted by Sowan et al. 2010 (110) and identified errors by nurses for setting infusion pumps. The error rate was 39% with handwritten orders and 37% with CPOE.

The second study was conducted by Yin et al. 2010 (48) to identify the error rate by parents administering 5 ml of acetaminophen to their children using six different instruments. Errors were mostly associated with dosing cups with printed calibration marking (69.5%) followed by dosing cups with etched calibration marking (50%). The instrument associated with the lowest rate of administration errors was an oral syringe (9%) followed by a dosing spoon (14%).

The third study by Pauly O’Neil 2009 (150) identified administration errors by nurses before and after an educational session followed by an exam. Administration errors involved wrong medication, wrong patient, wrong time, wrong route of administration, wrong dose, wrong dilution and not assessing patients’ allergy status. The error ranged from 5-100% before the intervention and 0-53% after the intervention. All types of administration errors were reduced apart from wrong dose which slightly increased from 12 to 16.7%.

Summary of studies using simulation studies

Most studies using simulation identified administration errors. Most studies were conducted in the US. Five different denominators were used with “of all administrations” and “of all orders” being the most common which was each used by three studies to identify the rate of administration errors.

2.4.9.6. Summary of all studies

Table 2.17 summarises all results identified and illustrates the number of studies using each denominator to identify each type of errors categorised according to the methods of data collection.

Table 2.17: Number of studies providing error rates by denominators and methods

Denominator	Chart/medical record review						Direct observation		Medication error incident report review						Mixed methods						Simulation		Total number of studies
	MPEs	MAEs	MEs	MTEs	MMEs	MDEs	MPEs	MAEs	MPEs	MAEs	MEs	MTEs	MMEs	MDEs	MPEs	MAEs	MEs	MTEs	MMEs	MDEs	MPEs	MAEs	
Of all errors	6	2		1	2	4			7	7		5	3	5	2	2		2	1	2			51
Of all orders	27	1	5	2							2				4	1	3		1	1	1	2	50
Of all patients	3	2	3				1				2				2	1	2						16
Of all administrations		1						8								1						3	13
Per 1000 patient days	1		1						1						1	1	6		1	1			13
Of all admissions	1		1			1					1				1	1	3		1	1			11
Of all medications	3		1	1							1						1						7
Mean errors	4																					1	5
Per 1000 orders			1						3								1						5
Of all patient visits	2		1							1													4
Of all participants																						3	3
Of all medication days	1		1	1																			3
Of all doses						1																1	2
Per 1000 administrations	1									1													2
Of all possible errors		1														1							2
Median errors	1																						1
Visits per 10,000 individuals per year										1													1
Per 100 patient days			1																				1
Of all preparations																				1			1
Of all samples					1																		1
Per 3.9 hospitalisation days			1																				1
Per 1000 doses																	1						1
Of all transcriptions				1																			1
Of all charts		1																					1
Of all ADEs			1																				1
Per bed day			1																				1
Total number of studies	50	8	18	6	3	6	1	8	11	10	6	5	3	5	10	8	17	2	4	6	1	10	198

Legend: Bold underlined numbers are studies with wide variations (> 50%) in results. These studies will be explored further in Chapter 3.

2.5. Discussion

Ghaleb et al's (2006) systematic review identified 32 relevant studies of medication errors in children from 1966 to March 2006. In my project, 153 studies have been identified from the five years April 2006 - March 2011. This suggests that the literature on the subject is increasing very quickly.

Many factors in study design can affect the rate of errors determined. These factors make comparing the rates of errors in different studies difficult and often impossible. The following summary of my findings illustrates this:

1. Two hundred and thirty six different definitions of medication errors were used by 78 studies.
2. Many studies did not identify the rate of medication errors (44 studies only identified the number of errors).
3. Five different methods were used to identify errors (chart/medical record review (39.2%), review of incident reports (32.7%), mixed methods (15.1%), simulation (7.8%) and direct observation (5.2%). Lots of US studies seem to rely on reviewing medication error incident reports.
4. The rate of error identified in some studies was for specific types of medication errors and in others was general: prescribing errors (28.8%), several specific types of errors (27.5%), administration errors (23.5%), medication errors in general (18.9%), dispensing errors (0.65%) and monitoring errors (0.65%).
5. Twenty six different denominators were used. The commonest denominators used were respectively "of all errors", "of all orders" and "of all patients".

6. Twenty two different settings were used (mostly specialist children's hospitals followed respectively by neonatal units and paediatric units in general hospitals).
7. Studies were conducted in 30 different countries often using different healthcare systems (mostly the US followed by the UK).
8. Some studies investigated medication errors with all medications (73 studies) while some studies only investigated errors with specific medications such as chemotherapy (seven studies) and antimicrobials (four studies).
9. Some studies investigated errors with only a particular route of administration, e.g. intravenous.
10. Studies used different designs, e.g. prospective or retrospective chart review.
11. Some studies identified the rate of errors in the whole paediatric population and some identified the rate of errors in specific ages.
12. Some studies focused only on medication errors, while others focused on medical errors in general or adverse drug events (which include medication errors).
13. Fifty-nine out of 153 studies used 65 interventional tools which affected the error rates.
14. Many settings used routine strategies for decreasing the rate of medication error (e.g. electronic prescribing or clinical pharmacy services); therefore, the rate of medication errors may be altered by these strategies.
15. Some studies used simulation rather than collecting data from clinical settings.
16. Chart /medical record review was used to identify prescribing errors more than other types of errors.
17. Direct observation was mainly used to identify administration errors.

18. Review of medication error incident reports was used mostly to identify medication errors in general.
19. Prescribing and administration errors followed by medication errors in general were the commonest errors identified using mixed methods.
20. Simulation studies mostly focused on administration errors.
21. The ranges reported for specific types of errors identified by the same methods are very wide in many cases.

McLeod et al. 2013 (151) identified quantitative observational studies exploring administration error rates in the UK. They aimed to measure the effect of variations in methods on the rate of administration errors identified. They identified 44 administration errors subcategories from 16 UK studies using four different denominators. Different factors were identified to be responsible for the variation in the administration error rates found. These factors include: methods of data collection, route of administration, patients' age, definitions used including explicit inclusion and exclusion criteria, subtypes of errors and denominators. McLeod only studied observational methods measuring administration errors. In my own systematic review of the factors influencing the rate of all medication errors in paediatric patients; the above factors identified by McLeod plus 15 other factors were identified.

All of these factors make it very challenging to compare studies and therefore the plan is to study the following in more depth in the next chapter of my thesis:

a) The reasons for the wide variation in reported error rates in studies which used the same methods, the same denominators and identified the same types of medication error.
b) The relationship between the methods used for data collection and the results; i.e. how did specific types of error rates vary between studies using different methods of data collection.
c) The relationship between the clarity of definitions used in studies and their results.
d) The effect of different interventional tools in reducing the rate of medication errors.
e) Studies conducted in the UK identifying the rate of medication errors and different methods used to prevent these errors.
f) Studies describing the time of the day and days of the week mostly associated with errors.

Chapter 3: Detailed analysis of papers from Chapter 2

3.1. Introduction

From reviewing the studies in Chapter 2 it has been noticed that the reported error rates for studies of the same types of errors using the same methods of data collection are very wide. It has been also noticed that different studies used different methods of data collection to identify the same type of medication errors using the same denominators. Moreover, different studies used different definitions of medication errors and different interventional tools. Few studies identified the time of the day and/or the days of the week mostly associated with errors. The UK studies represented 10.5% of all studies. Because my project is based in the UK, these studies were explored in more detail in this chapter in order to establish what has already been done and what gaps in knowledge exist.

3.2. Aim

1. To identify factors responsible for wide variations in error rate
2. To identify the relationship between methods of data collection and results
3. To identify the relationship between the clarity of definitions and results
4. To identify interventional tools used to minimise medication errors
5. To explore the UK studies
6. To identify the time of day and days of the week mostly associated with errors

3.3. Methods

3.1. To identify factors responsible for wide variations in error rate; comparable studies must have identified the rate of the same type of medication errors, used the same denominator, used the same methods of data collection and conducted in the same setting. To compare studies, one has to identify studies with wide variation **and this was defined as a difference between the highest and the lowest error rate of more than 50%**. This was chosen as this was felt to be a significant difference unlikely to be explained by variation, for example times of year that the study was done. Simulation studies were not included in the analysis as they do not reflect the true error rate in real-life.

3.2. To identify the relationship between methods of data collection and results; comparable studies must have identified the rate of the same type of medication errors, used the same denominator and used different methods of data collection.

Simulation studies were not used in comparisons as they do not reflect the true error rate in the real-life. Tables containing details of the relevant studies can be found in Appendix 2 for further reference.

3.3. To identify the relationship between the clarity of definitions and results; comparable studies must have identified the rate of the same type of medication errors, used the same denominator, used the same methods of data collection and used different clarity rating of definitions.

All studies which provided an error rate and used one or more definitions for medication errors were assessed in terms of the clarity of the definitions they used and whether this matched the aim of each study.

Clarity of definitions was judged according to the following rating:

1. Definitions not clear enough to meet study aims.
2. Definitions clear enough to meet some of study aims.
3. Definitions very clear and will meet all study aims.

Each definition in relation to the stated aims of each study was rated by both my supervisors and myself independently. These ratings of the clarity of the definitions were then compared, and a discussion between the three of us was conducted to agree on final ratings.

3.4. Studies with intervention were separately identified in order to explore the types of interventions used and their effects on the rate of medication errors in children.

3.5. The UK studies were separately identified to identify the rate of medication errors and the different methods used either to identify or prevent these errors.

3.6. Studies which identified the time of the day and days of the week mostly associated with errors were separately identified.

3.4. Results

3.4.1. Identifying factors responsible for wide variations in error rate

Four groups of studies with a wide variation in error rates (which were conducted in the same setting) were identified.

Table 3.1: Studies using the same denominators showing wide variation in error rates classified according to methodology and type of errors

Method	Type of medication errors	Denominator	Number of studies	Range of reported errors	Number of different settings	
						with wide variation
Chart/medical record review	MPEs	Of all orders	27	0-90.5%	10	3
		Of all errors	6	0.7-89%	6	1
Direct observation	MAEs	Of all administrations	8	1.2-96.6%	5	1
Mixed methods	MEs	Per 1000 patient days	6	4-167 *	4	2

* Wang et al. 2007 (106) identified more than one error per admission.

3.4.1.1. Studies using **"of all orders"** as the denominator and identified **prescribing errors** using **chart/medical record review**

Studies in three different settings (specialist children's hospital, primary care centres and outpatients) were associated with a wide variation in error rate.

Four studies in specialist children's hospitals showed error rates of 1.2-82% of all orders (68). Two of these studies used interventions. The rate of error was very high in only one study looking at controlled substances such as opiate drugs and was 82%

of all orders. The authors of this study suggested that the cause for the high error rate was because the drugs studied were high risk medications. Another study (96) just looking at sedation medication found the next highest error rate of 25%. The remaining studies looked at all medications. The Senegal study (120) showed a relatively high rate of 17% compared to a UK study (152) that identified a very low error rate both before and after the intervention (introduction of CPOE). The authors of this study suggested that this is because the study only identified dosing prescribing errors.

Four studies were conducted by the same authors in primary care centres in Bahrain. The overall error rate range was between 2.5-90.5% of all orders. In each study specific subsets of prescribing errors were studied with specific types of medications and this accounts for much of the variation. One study (153) identified a very high rate of errors (90.5% of all orders) and involved all medications, unlike the other three studies (154-156) which identified errors with particular drug groups. The authors identified three types of prescribing errors for the study involving all medications, omission, commission and integration errors. They define each type as following:

- Minor omission errors: "absence of prescription components such as date of prescription, any parameter of patient's personal identifiers, physician's stamp, and/or direction for use". Major omission errors: "absence, vague, incomplete and/or illegibility of any component of body of the prescription".
- Commission errors: "incorrectly written component(s) of body of the prescription".
- Errors of integration or knowledge-based errors in prescribing: "include potential drug-drug interactions or drug allergies which may reflect a failure of the prescriber to integrate information about the patient or drug history".

According to the study authors; the reason for high error rate is because of the lack of a national drug policy and irrational drug use in primary care centres.

Two studies (157) (57) were conducted in outpatients (error rate between 9.7-62.2% of all orders). Neither study used an intervention and both involved all medications. The Nigerian study (157) relates its high rate of error (62.2%) to irrational prescribing. Under-dosing (38% of all medications) and overdosing (19% of all medications) were identified as common errors as well as inadequate treatment courses (28% of all medications). They emphasised the urgent need for a prescribing monitoring committee. The other study conducted in the US found a far lower error rate of 9.7% (57).

3.4.1.2.Studies using **"of all errors"** as the denominator and identified **prescribing errors** using **chart/medical record review**

One study showed wide variation in error rate. Jain et al. 2009 (70) from India explained most of the wide variation with an error rate seen. This study identified only prescribing and dispensing errors of which 43 prescribing errors were in the emergency department and 24 prescribing errors in the neonatal unit. Of all medication errors in the emergency department; 79% were prescribing errors (70% of all errors by senior doctors and 9% by junior doctors). Eighty-nine percent of all errors in the neonatal unit were related to prescribing errors by senior doctors. The authors suggested that environmental issues in emergency departments (e.g. stress, noise and crowding caused by patients' carers), verbal orders and a shortage of healthcare professionals could be causes of the high rate of prescribing errors. The reason why senior doctors were involved in more prescribing errors than junior doctors is not explained. However, as this study only identified two types of

medication errors (prescribing and dispensing) it is clearly an important reason for the high prescribing error rates identified.

3.4.1.3.Studies using **"of all administrations"** as the denominator and identified **administration errors** using **direct observation**

Three studies in paediatric units in general hospitals showed a wide variation in error rates. The error rate was very high (89.9%) in the study (158) in Ethiopia which identified administration errors by nurses and parents. A wrong time error (delay in administration by more than one hour) was responsible for the highest portion of errors (28%). Conroy, in the UK, showed a very low error rate of 1.2% of all administrations (142) and Chua, in Malaysia, showed 11.7% of all administrations (67). Only doctors and/or nurses were involved in administration in these studies.

3.4.1.4.Studies using **"per 1000 patient days"** and identified **medication errors in general** and using **mixed methods**

Studies in two different settings (neonatal and paediatric units in general hospitals and paediatric units in general hospitals) showed wide variation in error rates.

Two studies (106, 159) identified the error rate in neonatal and paediatric units in general hospitals in the US. One (159) only identified serious medication errors and therefore had a much lower number of errors identified.

For the two studies (145, 160) that were conducted in paediatric units in general hospitals; the study by Walsh (160) was retrospective and only identified errors related to electronic order entry which is likely to explain the much lower error rate than the prospective study from New Zealand (145).

3.4.2. Identifying the relationship between methods of data collection and results

All denominators that were used by the different studies are presented in Tables 2-7 according to the type of errors identified.

3.4.2.1. Prescribing errors

Table 3.2 shows the 12 different denominators used by studies that identified the rate of prescribing errors. Studies using "of all orders", "of all errors", "of all patients", "per 1000 patient days" and "of all admissions" denominators will be discussed in more detail as each of these denominators was used by studies using different methodologies.

Table 3.2: Denominators used in prescribing error studies

Denominator	Range of reported errors / Number of studies	Chart/medical record review	Direct observation	Medication error incident report review	Mixed methods
Of all orders	Range of reported errors	0-90.5%	×	×	1.06-27%
	Number of studies	**27**	×	×	**4**
Of all errors	Range of reported errors	0.7-89%	×	1.1-24.4%	26-54%
	Number of studies	**6**	×	**7**	**2**
Mean errors	Range of reported errors	0.1±0.3-14.8	×	×	×
	Number of studies	4	×	×	×
Of all patients	Range of reported errors	4.8-74%	29.1%	×	40-189%
	Number of studies	**3**	**1**	×	**2**
Of all medication days	Range of reported errors	33-52%	×	×	×
	Number of studies	1	×	×	×
Of all patient visits	Range of reported errors	13-32.6%	×	×	×
	Number of studies	2	×	×	×
Per 1000 orders	Range of reported errors	×	×	0.03-5.93	×
	Number of studies	×	×	3	×
Median errors	Range of reported errors	1	×	×	×
	Number of studies	1	×	×	×
Per 1000 patient days	Range of reported errors	5	×	2.67	74
	Number of studies	**1**	×	**1**	**1**
Per 1000 administrations	Range of reported errors	0.09	×	×	×
	Number of studies	1	×	×	×
Of all admissions	Range of reported errors	47%	×	×	43%
	Number of studies	**1**	×	×	**1**
Of all medications	Range of reported errors	4.6-77.4%	×	×	×
	Number of studies	3	×	×	×
Total number of studies		50	1	11	10

3.4.2.1.1. Studies using "of all orders" to identify prescribing errors

"Of all orders" denominator was used by 27 studies (Table 1 in Appendix 2) that used chart/medical record review. This denominator was used also by four studies (Table 2 in Appendix 2) that used mixed methods. Two of the four studies using mixed methods identified the error rate separately for each method (24, 93). They identified the prescribing error rates separately after chart review and other types of errors using different methods. Therefore there are 29 studies used the same method (i.e. chart/medical record review) and so they offer no information on differences in data collection methods and results. They can be compared with the two further studies that used mixed methods and provided prescribing error rates from the combined methods (145, 161).

Landrigan et al. 2008 (161) found prescribing errors in 1.06% of all orders in a specialist children's hospital in the US using chart review plus review of incident reports. This was similar to the error rate of 2.2% found by Jani et al. 2010 (152) in the same setting in the UK using chart review alone.

Kunac et al. 2008 (145) found a prescribing error rate of 7.1% in a paediatric unit in a general hospital in New Zealand using chart review plus incident reporting. This was much lower than the rates of 30.5% found by Davey et al. 2008 (104) in the same setting in the UK and 26.8% found by Kjeldby et al. 2009 (117) in Norway.

Review of incident reports in addition to chart review does not seem to have a major effect on the results.

3.4.2.1.2. Studies using "of all errors" to identify prescribing errors

Six studies used chart/medical record review (Table 3 in Appendix 2) and seven studies used review of incident reports (Table 4 in Appendix 2) and the "of all errors" denominator to identify the rate of prescribing errors.

Only two studies were conducted in the same setting, i.e. a specialist children's hospital. Takata et al. 2008 (132) identified prescribing errors as 50% of all errors via chart review (other types of errors were administration, dispensing, transcribing and monitoring errors) while Miller et al. 2010 (76) identified 12.8% of all errors as prescribing errors via reviewing of incident reports (other types of errors were administration, dispensing and transcribing errors).

Overall studies using chart/medical record review identified a wide range of results from 0.7% to 89% of all errors being prescribing errors. Most studies gave results of 28% and above. The studies using incident reporting as the method of data collection gave much smaller figures ranging from 1.1 to 13.9%.

As can be seen from this comparison; chart review seems to identify a higher proportion of all errors as prescribing errors than review of incident reports.

Two US studies each used two methods without separating the error rates. Kaushal et al. 2007 (144) used chart review and patients (or parents) telephone interview after patients' discharge from the hospital. Wang et al. 2007 (106) used medical record review and review of medication error incident reports and was conducted in a neonatal and paediatric unit in a general hospital.

Kaushal et al. study was conducted in an outpatient department and identified 26% of all errors to be prescribing errors (other types were administration, dispensing and transcribing). Walsh et al. 2009 (27) (Table 3 Appendix 2) also studied US outpatient department and identified 64% of all chemotherapy errors as prescribing errors

(others were administration, dispensing and monitoring) using chart review. The mixed methods study by Kaushal et al. identified far less prescribing errors (for all medications) than Walsh et al. The different drugs studied is however likely to influence the variation in prescribing error rates between these two studies. Adding parental telephone interview to chart review methods did not seem to increase the errors detected however, but the differences in medications studied makes this difficult to compare.

Wang et al. study was conducted in a neonatal and paediatric unit in a general hospital and identified 54% of all errors as prescribing errors (others were administration, dispensing, monitoring and transcribing). This was a higher rate of error therefore using both methods may have increased error detection in this study, however no other study was conducted in this setting to compare it to.

3.4.2.1.3. Studies using "of all patients" to identify prescribing errors

Three studies used chart/medical record review (Table 5 in Appendix 2) and one study (detailed below) used direct observation and "of all patients" denominator to identify the rate of prescribing errors.

Osterholt et al. 2006 (134) used direct observation to identify prescribing errors in outpatients in Malawi. The study involved infants and children and found 29.1% of patients with antimalarial drug prescribing errors. This study cannot helpfully be compared with the three studies using chart review because they were conducted in different settings (an emergency department, an intensive care unit and a specialist children's hospital) and each involved different types of drugs (all drugs, resuscitation drugs and aciclovir).

Two studies used mixed methods. Pote et al. 2007 (162) conducted a study in India in a paediatric unit in a general hospital. They reviewed patients' charts prospectively

and interviewed patients or their parents. They identified errors in 40% patients. Porter et al. 2008 (163) was conducted in two US emergency departments and used questionnaire, telephone interview and chart review. More than one error per patient was identified in one emergency department for both the control and the intervention groups (parents using a mobile kiosk to enter symptoms, patient's allergy and medication history). The rate of error did not decrease significantly between both control and intervention groups (173% vs. 134% of all patients; p=0.35). Marcin et al.'s study in 2007 (164) (Table 5 in Appendix 2) also in an emergency department in the US identified 11.9% of all patients to involve prescribing errors using chart review. Using mixed methods (i.e. questionnaire, telephone interview and chart review) seemed to identify a higher rate of prescribing errors than using chart review alone.

3.4.2.1.4. Studies using "per 1000 patient days" to identify prescribing errors

Three studies identified the prescribing error rates using "per 1000 patient days" denominator. Two were conducted in the same setting. Di Pentima et al. 2009 (165) was conducted in a specialist children's hospital in the US using chart review for antimicrobials. They did not provide the prescribing error rate before their intervention (using CPOE and an antimicrobial stewardship program) and identified a prescribing error rate of 5 per 1000 patient days after the intervention for 13 antimicrobials. The second study by Takata et al. 2008 (135), also in a specialist children's hospital in the US, identified a prescribing error rate of 2.67 per 1000 patient days after reviewing incident reports for all medications. Again chart review seems able to identify a higher rate of prescribing errors compared to review of incident reports, however this is very limited by only being able to compare two

studies and this will be influenced by the fact that Di Pentima only studied antimicrobials. Error rates seem low in both studies.

Mixed methods (chart review and review of incident reports) were used by Kunac et al. 2008 (145) in a paediatric unit in a general hospital in New Zealand and identified 74 errors per 1000 patient days for all medications. Using these two methods together resulted in a much higher prescribing error rate being identified compared with the studies detailed above. The setting was different but the difference in results suggests that combining methods in the study may have increased error detection.

3.4.2.1.5. Studies using "of all admissions" to identify prescribing errors

"Of all admissions" denominator was used by two studies. A UK study by Eisenhut et al. 2011 (166) identified 47% of all admissions to be associated with prescribing errors using chart review. Kunac et al. 2008 (145) from the New Zealand identified 43% of all admissions to involve prescribing errors using chart review and review of incident reports. Both studies included all medications and were conducted in paediatric units in general hospitals. The study using mixed methods identified similar error rate to the study using chart review alone but care needs to be taken as before as they are only two studies so firm conclusions are difficult to make.

3.4.2.2.Administration errors

Table 3.3 shows the 11 different denominators that were used by studies that identified the rate of administration errors. Studies using "of all orders", "of all possible errors", "of all administrations", "of all errors" and "of all patients" denominators will be discussed in more detail as these studies used different methods.

Table 3.3: Results from administration error studies

Denominator	Range of reported errors / Number of studies	Chart/medical record review	Direct observation	Medication error incident report review	Mixed/ other methods
Of all charts	Range of reported errors	15-25%	×	×	×
	Number of studies	1	×	×	×
Of all orders	Range of reported errors	3-6%	×	×	5.2%
	Number of studies	**1**	×	×	**1**
Of all possible errors	Range of reported errors	14.8%	×	×	19.1%
	Number of studies	**1**	×	×	**1**
Of all administrations	Range of reported errors	5.9-8.4%	1.2- 96.6%	×	20.5- 63.8%
	Number of studies	**1**	**8**	×	**1**
Of all errors	Range of reported errors	0-5%	×	30-93.2%	12- 70%
	Number of studies	**2**	×	**7**	**2**
Of all patient visits	Range of reported errors	×	×	8%	×
	Number of studies	×	×	1	×
Per 1000 patient days	Range of reported errors	×	×	×	54
	Number of studies	×	×	×	1
Visits per 10,000 individuals per year	Range of reported errors	×	×	0.7	×
	Number of studies	×	×	1	×
Tenfold errors (per 1000 administrations)	Range of reported errors	×	×	0.595-0.718	×
	Number of studies	×	×	1	×
Of all patients	Range of reported errors	22.7-87.5%	×	×	75%
	Number of studies	**2**	×	×	**1**
Of all admissions	Range of reported errors	×	×	×	32%
	Number of studies	×	×	×	1
Total number of studies		8	8	10	8

3.4.2.2.1. Studies using "of all orders" to identify administration errors

Two studies identified the administration error rate using "of all orders" denominator. Larose et al. 2008 (167) used chart review and identified 6% of all orders before using a standard order form and 3% after. This study was conducted in an emergency department in Canada and only involved IV medications and fluids. Kunac et al. 2008

(145) used chart review and review of incident reports and identified 5.2% of all orders (for all medications) to involve administration errors in a paediatric unit in a general hospital in New Zealand. Both studies identified similar error rates and may suggest that using chart review plus review of incident reports does not increase administration error rates identified.

3.4.2.2.2. Studies using "of all possible errors" to identify administration errors

Sullivan et al. 2010 (168) used chart review and identified 14.8% of all insulin administration to be associated with errors in a specialist children's hospital in the US. Ghaleb et al. 2010 (24) used direct observation of nurses and review of incident reports in UK specialist children's hospitals and paediatric units in general hospitals, and identified administration errors as 19.1% of all possible errors for all medications (except parenteral nutrition). No administration errors were reported on incident reports. As the two studies involved different drugs the effect of each method on identifying administration errors is unclear for this denominator.

3.4.2.2.3. Studies using "of all administrations" to identify administration errors

Eight studies used direct observation (Table 6 in Appendix 2). Error rates varied between 1.2-42% of all administrations when healthcare professionals were studied. Rates were much higher when parents were included.

Otero et al. 2008 (29) used chart/medical record review with the "of all administrations" denominator to identify the rate of administration errors in a neonatal and paediatric unit in a general hospital in Argentina. They identified 8.4% of all administrations by nurses to involve an error before an educational programme and 5.9% after the education. This study involved neonates, infants, children and

adolescents. Administration error rate detection therefore seems generally lower with chart review than direct observation though rates vary and only one study could be compared.

From the studies using direct observation the highest rate of administration errors was seen when parents administered medications to their children (96.6% of all administrations) in a paediatric neurology unit in Germany by Bertsche et al. 2010 (169). The lowest error rate was found by Conroy et al. 2007 (142) in a UK paediatric unit in a general hospital when only nurses were involved in the administration process (1.2% of all administrations). When the rate was identified for administration errors by both doctors and nurses the rate was 11.7% in a Malaysian study by Chua et al. 2010 (67) in a paediatric unit in a general hospital. This may suggest that administration error rates are high by parents and low by nurses, the number of comparable studies are few and cannot be generalised.

Van Den Bemt et al. 2007 (47) in Netherlands used direct observation of parents' preparation and administration of medication in addition to review of incident reports. During the study period no administration error was documented through the reporting system. They observed errors in 63.8% of all administrations in one intellectual disability unit and 20.5% in another. Comparing this study to Bertsche et al. 2010 (169) which identified the rate of administration errors separately by nurses and by parents using direct observation; more administration errors were identified (96.6%) by parents in a paediatric neurology department in Germany. Both studies identified high administration error rates and the difference may be related to the setting (paediatric neurology is a high risk area) and/or the country. Incident reporting did not contribute any additional information.

3.4.2.2.4. Studies using "of all errors" to identify administration errors

Seven studies used review of medication error incident reports (Table 7 in Appendix 2). Administration errors were identified as 48-63% of all errors where all drugs were studied. Two studies using chart/medical record review (Table 8 in Appendix 2) identified the rate of administration errors to be 0% (Takata et al. 2008 (132)) and 5% (Walsh et al. 2009 (27)) "of all errors". Incident reporting schemes found a much higher proportion of errors to be administration errors than chart review.

Comparing two of these studies which took place in the same setting and country; Miller et al. 2010 (76) used review of incident reports and identified administration errors to be 56.4% of all errors (other types of errors were prescribing, dispensing and transcribing errors) in a specialist children's hospital in the US. In the same setting and country Takata et al. 2008 (132) identified no administration errors via chart review (other types of errors were prescribing, monitoring, transcribing and dispensing errors).

Two studies used mixed methods. Kaushal et al. 2007 (144) from an outpatient department in the US identified 70% of all errors as administration errors (other types included prescribing, dispensing and transcribing) using chart review and parents' interview. Wang et al. 2007 (106) identified 12% of all errors as administration errors (others included prescribing, dispensing, transcribing and monitoring) in a neonatal and paediatric unit in a general hospital in the US. They used chart review and review of incident reports. This may suggest that using parental' interview resulted in more administration errors being detected than using incident reports, however the settings and participants involved were quite different and probably more influential on the results than the methods used.

Comparing the two studies conducted in outpatients, the study mentioned above by Kaushal et al. 2007 identified far more administration errors (70% of all errors) compared with the study by Walsh et al. 2009 (27) (5% of all errors) which only identified chemotherapy administration errors using chart review, though again the drugs and participants involved were very different.

3.4.2.2.5. Studies using "of all patients" to identify administration errors

Two studies used chart review and one used mixed methods. Kaji et al. 2006 (170) used chart review and identified 72% of all patients to be associated with administration errors by paramedics in the US before using the Broselow tape was compulsory and 43% after. Using the same method Sullivan et al. 2010 (168) from the US identified errors in 87.5% of all patients before education of nurses and 22.7% after in a specialist children's hospital. Alves et al. 2007 (171) from a primary care unit in Brazil used questionnaires to study administration errors by parents using two antipyretics (acetaminophen and dipyrone) that were given just less than 24 hours prior to their arrival to emergency department. They identified 75% of all patients to be involved in administration errors. Similar administration error rates were found in the two studies using chart review with the study using questionnaires even though different participants were involved in each study. Participants involved in the administration process may be more responsible for the high error rate errors found rather than the methods used.

3.4.2.3.Medication errors in general

Table 3.4 shows the 13 different denominators used by studies that identified the rate of medication errors in general. Studies using "of all orders", "of all patients", "per 1000 patient days", "of all admissions", "per 1000 orders" and "of all medications" denominators will be discussed in more detail because these used different methods of data collection.

Table 3.4: Results from medication errors in general studies

Denominator	Range of reported errors / Number of studies	Chart/medical record review	Direct observation	Medication error incident report review	Mixed methods
Of all orders	Range of reported errors	2.42-23%	×	0.21-0.24%	1.29-11.6%
	Number of studies	**5**	×	**1**	**3**
Of all patients	Range of reported errors	26.4-55%	×	4.9-34.3%	3-7.8%
	Number of studies	**3**	×	**2**	**2**
Per 1000 patient days	Range of reported errors	3.4- 4.5	×	×	4-167
	Number of studies	**1**	×	×	**6**
Of all admissions	Range of reported errors	2.2- 7.9%	×	4.9%	29.5-127%
	Number of studies	**1**	×	**1**	**3**
Of all medication days	Range of reported errors	34-53%	×	×	×
	Number of studies	1	×	×	×
Per 1000 orders	Range of reported errors	24.1	×	×	15
	Number of studies	**1**	×	×	**1**
Of all medications	Range of reported errors	7.6- 12.8%	×	0.02-3.3%	9.9%
	Number of studies	**1**	×	**1**	**1**
Per 3.9 hospitalisation days	Range of reported errors	1	×	×	×
	Number of studies	1	×	×	×
Of all patient visits	Range of reported errors	18.8%	×	×	×
	Number of studies	1	×	×	×
Of all adverse drug events	Range of reported errors	56%	×	×	×
	Number of studies	1	×	×	×
Per 100 patient days	Range of reported errors	2.1	×	×	×
	Number of studies	1	×	×	×
Per 1000 doses	Range of reported errors	×	×	×	69.5-79.7
	Number of studies	×	×	×	1
Per bed day	Range of reported errors	1.1-1.8	×	×	×
	Number of studies	1	×	×	×
Total number of studies		18	0	5	17

3.4.2.3.1. Studies using "of all orders" to identify medication errors in general

Five studies using chart/medical record review (Table 9 in Appendix 2) and one study using review of incident reports used "of all orders" denominator to identify the rate of medication errors in general.

Two studies were in the same setting of a paediatric intensive care unit. Burny et al. 2006 (138) identified a 0.21% error rate of all orders in a US intensive care unit using review of incident reports. Kadmon et al. 2009 (105) conducted a study in Israel in the same setting and identified 8.2% of all orders to have medication errors by using chart review. Both studies involved all medications. Chart review seems more sensitive in identifying medication errors in general compared to review of incident reports from these two studies. This is supported by the studies in Table 9 using chart/medical record review where error rates ranged from 2.4% of all orders in psychiatric care to 23% in a paediatric unit in a general hospital.

Three studies used mixed methods. All used chart review and review of incident reports and involved all medications. Landrigan et al. 2008 (161) conducted a study in a specialist children's hospital in the US. They identified errors in 1.29% of all orders before implementation of Accreditation Council for Graduate Medical Education and 1.5% errors of all orders after. From a paediatric unit in New Zealand, Kunac et al. 2008 (145) identified 11.6% of all orders as medication errors. Wang et al. 2007 (106) from a neonatal and paediatric unit in general hospital in the US identified 5.2% of all orders.

The higher error rate was identified by studies using chart review followed by studies using chart review and review of incident reports. However, all studies identified error rates less than 23% (the most found by chart review alone) of all orders, therefore it is difficult to judge one method above the other in their ability in detecting medication

errors in general, but incident reporting does not seem to improve detected error rates over chart review alone.

3.4.2.3.2. Studies using "of all patients" to identify medication errors in general

Three studies used chart/medical records review (Table 10 in Appendix 2) and two studies used review of incident reports (Table 11 in Appendix 2) to identify the rate of medication errors in general using "of all patients" denominator.

Lerner et al. 2008 (75) and Ligi et al. 2010 (15) studies were both conducted in neonatal units. Lerner et al. 2008 identified 55% of patients in Brazil to be associated with medication errors by using chart review whereas Ligi et al. 2010 identified only 4.9% of all patients in France to be associated with medication errors using a review of incident reports. This may be influenced by the country but suggests that chart review again is more sensitive in identifying medication errors in general than review of incident reports. Similar error rates of 26% and 39% were found in US emergency departments by chart review.

Two studies used mixed methods. Benkirane et al. 2009 (172) from a Moroccan intensive care unit and a neonatal unit used direct observation and review of incident reports. They identified 7.8% of all patients to involve medication errors. Kaushal et al. 2007 (144) from a US outpatient department identified 3% of all patients to involve medication errors after chart review and parents' interview. Setting probably had more influence than methods here though error rates were similar.

3.4.2.3.3. Studies using "per 1000 patient days" to identify medication errors in general

Holdsworth et al. 2007 (109) used chart review and identified 4.5 per 1000 patient days errors before using electronic prescribing and 3.4 after in a paediatric unit in a general hospital in the US.

Six studies used mixed methods and identified error rates between 4-167 errors per 1000 patient days (Table 12 in Appendix 2). Two studies using chart review and review of medication error incident reports were conducted in paediatric units in general hospitals. Walsh et al. 2006 (160) from the US identified 53.9 per 1000 patient days and Kunac et al. 2008 (145) from New Zealand identified 121 errors per 1000 patient days. When only chart review was used as above in the same setting in the US far less errors were identified by Holdsworth et al (109). This suggests that chart review together with review of incident reports is better at detecting medication errors. There was however an approximately two fold difference in the errors detected by Walsh (53.9 per 1000 days) and Kunac (121 errors per 1000 patient days) using the same methods.

This wide variation is also seen between the results of two US studies (106, 159) that were conducted in neonatal and paediatric units in general hospitals and used both chart review and review of incident reports. Walsh et al. 2008 (159) only identified serious medication errors however and identified 7.9 per 1000 patient days before CPOE and 6.5 after CPOE. Wang et al. 2007 (106) identified 167 per 1000 patient days to be associated with errors of all severities and therefore the definition of errors seems the most important factor here.

3.4.2.3.4. Studies using "of all admissions" to identify medication errors in general

Holdsworth et al.'s 2007 (109) study was conducted in a paediatric unit in a general hospital in the US using chart review and identified 3.8% of all admissions to be associated with medication errors (before starting electronic prescribing) and 2.2% after. Children's ages were not mentioned. Ligi et al. 2010 (15) used review of medication error incident reports and found 4.9% of all neonatal admissions to be associated with medication errors in France. Similar error rates were therefore found despite the different settings and data collection methods.

Three studies used mixed methods. Walsh et al. 2006 (160) as mentioned before used chart review and review of incident reports and identified 29.5% of all admissions to be associated with medication errors, whereas Kunac et al. 2008 (145) found 71% of all admissions to involve errors using chart review and parents' interview. Wang et al. 2007 (106) from a neonatal and paediatric unit in a general hospital in the US identified 127% of all admissions to involve errors. They used medical record review and review of medication error incident reports. Using chart review and review of incident reports resulted in more medication errors being identified in a neonatal and paediatric unit in a general hospital but less in a paediatric unit in a general hospital. However, using both methods resulted in more medication errors detected than using chart review alone. When chart review was combined with parents' interview more medication errors were identified. The diversity of these studies makes it difficult to draw conclusions here.

3.4.2.3.5. Studies using "per 1000 orders" to identify medication errors in general

Walsh et al. 2009 (27) identified 24.1 errors per 1000 orders in an outpatient department in the US using chart review, they only studied chemotherapy. Walsh et al. 2006 (160) in their paediatric unit in a general hospital however identified 15

errors per 1000 orders using chart review and review of incident reports. This difference is likely to be because the first study only included chemotherapy (high risk) while the second study included all medications.

3.4.2.3.6. Studies using "of all medications" to identify medication errors in general

Kazemi et al. 2010 (102) used chart review and found 12.8% of all medications in POE (Physician Order Entry) and 7.6% of all medications in NOE (Nurse Order Entry) to be associated with errors, in a neonatal unit in Iran. All orders entered by physicians were reviewed by nurses and vice versa to identify MPEs and MTEs. Trotter et al. 2009 (121) used review of incident reports and identified 3.3% of all medications before and 0.02% of all medications to involve errors after electronic prescribing. This study was conducted in a specialist children's hospital in Germany and did not mention the children's ages. Chart review again detected higher rates of errors than incident reporting however the results may also have been influenced by the neonatal setting in Iran.

One study used mixed methods (medical record review and direct observation of parents administering medications to their children). Taylor et al. 2006 (173) from the US identified 9.9% of all medications to involve errors (prescribing or administration) in an outpatient department and paediatric oncology department. Similar error rates were identified by Kazemi et al and by Taylor et al., however the different errors studied and settings are more likely to have influenced the results than the data collection methods.

3.4.2.4.Transcribing errors

Table 3.5 shows the five different denominators used by studies that identified the rate of transcribing errors. Studies using "of all errors" denominator will be discussed in more detail as different methodologies were used.

Table 3.5: Results from transcribing error studies

Denominator	Range of reported errors / Number of studies	Chart/medical record review	Direct observation	Medication error incident report review	Mixed methods
Of all orders	Range of reported errors	15.9- 21.3%	×	×	×
	Number of studies	2	×	×	×
Of all medication days	Range of reported errors	1-1%	×	×	×
	Number of studies	1	×	×	×
Of all medications	Range of reported errors	2.5-3%	×	×	×
	Number of studies	1	×	×	×
Of all errors	Range of reported errors	0%	×	7.1- 28%	2-32%
	Number of studies	**1**	×	**5**	**2**
Of all transcriptions	Range of reported errors	6%	×	×	×
	Number of studies	1	×	×	×
Total number of studies		6	0	5	2

3.4.2.4.1. Studies using "of all errors" to identify transcribing errors

Five studies used review of incident reports (Table 13 in Appendix 2) and one study used chart review to identify the rate of transcribing errors. The chart review study (132) found transcribing errors to be 0% of all errors. Other types of errors were administration, dispensing, prescribing and monitoring errors. This study by Takata et al. 2008 (132) in a specialist children's hospital in the US can be compared with Miller et al.'s 2010 (76) study, which was conducted in the same setting, and identified 24.2% of all errors to be transcribing errors using review of medication error incident reports (other types of errors were administration, dispensing and

prescribing). Review of incident reports, as can be seen from this comparison, resulted in more transcribing errors being identified compared to chart review. Incident reporting identified similar rates of transcribing errors ranging from 7.1% of all errors with chemotherapy to 28% with antidepressants. Most studies using incident reporting were conducted in the US.

Two US studies each used two methods and didn't separate the error rate. Kaushal et al. 2007 (144) used chart review and patients (or parents) telephone interview after patients' discharge from hospital. Wang et al. 2007 (106) used medical record review and review of medication error incident reports. Kaushal et al. study was conducted in outpatients and identified 2% of all errors to be transcribing errors whereas Wang et al. study was conducted in a neonatal and paediatric unit in a general hospital and identified 32% of all errors as transcribing errors. Chart review plus review of incident reports by Wang et al identified slightly more transcribing errors than studies that either used chart review or review of incident reports alone.

3.4.2.5.Monitoring errors

Table 3.6 shows the five different denominators that were used by studies that identified the rate of monitoring errors. Studies using "of all errors" denominator will be discussed in more detail as they were the only group to use more than one method.

Table 3.6: Results from monitoring errors studies

Denominator	Range of reported errors / Number of studies	Chart/medical record review	Direct observation	Medication error incident report review	Mixed methods
Of all errors	Range of reported errors	5-62.5%	×	0.6- 1.4%	1.3%
	Number of studies	**2**	×	**3**	**1**
Per 1000 patient days	Range of reported errors	×	×	×	18
	Number of studies	×	×	×	1
Of all admissions	Range of reported errors	×	×	×	11%
	Number of studies	×	×	×	1
Of all orders	Range of reported errors	×	×	×	1.7%
	Number of studies	×	×	×	1
Of all samples	Range of reported errors	9.8-12.8%	×	×	×
	Number of studies	1	×	×	×
Total number of studies		3	0	3	4

3.4.2.5.1. Studies using "of all errors" to identify monitoring errors

Three studies used review of incident reports and two used chart review with the "of all errors" denominator. Tables 14 and 15 in Appendix 2 illustrate these studies.

The rates of monitoring errors (as a % of all errors) varied between 0.6% with chemotherapy (140) to 0.7% with antidepressants (66) in two US studies using review of incident reports. When assessed by chart review in a specialist children's hospital (Takata et al. 2008 (132)) also in the US this rose to 62.5% of all errors. They defined a monitoring error to be "failure to review a prescribed regimen for appropriateness and detection of problems or failure to use appropriate clinical or laboratory data for adequate assessment of patient response to prescribed therapy" (132). Chemotherapy monitoring errors detected by chart review were more similar to those detected by incident reports at 5% (27).

Wang et al. 2007 (106) from a neonatal and paediatric unit in a general hospital in the US used mixed methods (medical record review and review of medication error incident reports). They involved all medications and identified 1.3% of all errors as monitoring errors. Using mixed methods resulted in similar monitoring errors being identified compared with studies that used review of incident reports. This may be because both Rinke et al. 2007 and Rinke et al. 2010 identified monitoring errors for high-risk medications. Only one study (132) provided a definition of a monitoring error and therefore this may have also influenced the results obtained.

3.4.2.6.Dispensing errors

Table 3.7 shows the six different denominators that were used by studies that identified the rate of dispensing errors. Studies using "of all admissions" denominator and "of all errors" denominator will be discussed in more detail as they used different methodologies.

Table 3.7: Results from dispensing error studies

Denominator	Range of reported errors / Number of studies	Chart/medical record review	Direct observation	Medication error incident report review	Mixed methods
Of all admissions	Range of reported errors	0.33-3.01%	×	×	7%
	Number of studies	**1**	×	×	**1**
Of all errors	Range of reported errors	0-21%	×	11.8-35.7%	0.2-3%
	Number of studies	**4**	×	**5**	**2**
Of all doses	Range of reported errors	11.5%	×	×	×
	Number of studies	1	×	×	×
Per 1000 patient days	Range of reported errors	×	×	×	11
	Number of studies	×	×	×	1
Of all orders	Range of reported errors	×	×	×	1.1%
	Number of studies	×	×	×	1
Of all preparations	Range of reported errors	×	×	×	0%
	Number of studies	×	×	×	1
Total number of studies		6	0	5	6

3.4.2.6.1. Studies using "of all admissions" to identify dispensing errors

A US study in a paediatric unit in a general hospital by Holdsworth et al. 2007 (109) used chart review and identified 3.01% of all admissions to involve dispensing errors before using CPOE and 0.33% after CPOE. Kunac et al. 2008 (145) from New Zealand conducted a study in the same setting and identified 7% of all admissions to involve dispensing errors after using chart review and review of incident reports. Review of incident reports in addition to chart review may therefore increase the errors detected however the rates were quite low in both studies.

3.4.2.6.2. Studies using "of all errors" to identify dispensing errors

Five studies used review of incident reports and four used chart review to identify the rate of dispensing errors using "of all errors" denominator. Tables 16 and 17 in Appendix 2 illustrate all of these studies.

The studies by Miller et al. 2010 (76) and Takata et al. 2008 (132) were conducted in specialist children's hospitals. Miller et al. 2010 identified 35.7% of all errors to be dispensing errors by reviewing incident reports (other types of errors were administration, transcribing and prescribing errors). Takata et al. 2008 identified just 9% of all errors to be dispensing errors after chart review (other types of errors were administration, prescribing, transcribing and monitoring errors). Review of incident reports seems to detect more dispensing errors than chart review.

Looking at the studies overall supports this despite them being conducted in different settings. Dispensing error rates ranging from 11.8% in US neonatal units nationally to 36% in a specialist children's hospital were identified by incident reporting systems whereas chart review detected rates from 0 (US chemotherapy outpatients) to 21% in an Indian emergency department.

Two US studies each used two methods. Kaushal et al. 2007 (144) used chart review and telephone interview after patients' discharge from the hospital. Wang et al. 2007 (106) used medical record review and review of medication error incident reports. Kaushal et al. study was conducted in outpatients and identified 3% of all errors to be dispensing errors. Wang et al.'s study was conducted in a neonatal and paediatric unit in a general hospital and identified 0.2% of all errors as dispensing errors. Using chart review plus review of incident reports identified less dispensing errors compared with studies that either used chart review or review of incident reports separately. An

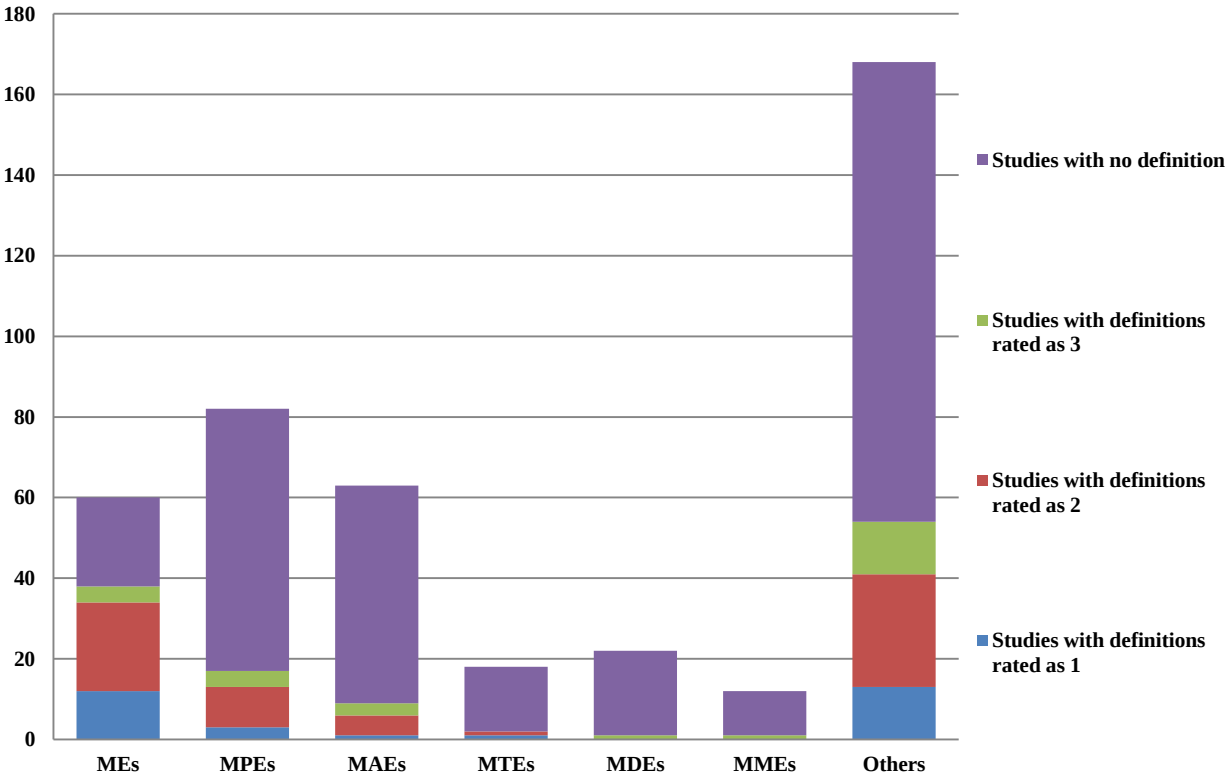
exception of this is a study by Walsh et al. 2009 who identified 0% chemotherapy dispensing errors using chart review alone.

3.4.3. Identifying the relationship between clarity of definitions and results

Only 78 of the 153 studies (51%) identified in Chapter 2 used a definition or definitions (Figure 3.1). In total 236 definitions for medication errors were found as some studies explored more than one type of error and used more than one definition. Definitions were provided in:

- Thirty eight out of 60 studies (63.3%) exploring medication errors in general
- Seventeen out of 82 studies (20.7%) exploring prescribing errors
- Nine out of 63 studies (14.3%) exploring administration errors
- Two out of 18 studies (11%) exploring transcription errors
- One out of 11 studies (9%) exploring monitoring errors
- One out of 22 studies (4.5%) exploring dispensing errors
- Fifty four studies used 168 other definitions (e.g. omission errors, near miss and harmless medication errors)

Figure 3.1: Number of studies and their definition clarity ratings



3.4.3.1. Rating the clarity of the definitions used

The definitions from 65 out of 78 (83%) studies were given the same rating by all three independent scorers and for only thirteen studies there were discrepancies. These were resolved by discussion.

- ❖ Of the 78 studies with definitions:
  - 22 (28.2%) were rated as 1 (definition not clear enough to meet study aims).
  - 42 (53.8%) were rated as 2 (definition clear enough to meet some of study aims)
  - 14 (18%) were rated as 3 (definition very clear and will meet all study aims)

Seventeen of these 78 studies did not identify the error rate, therefore 61 studies will be discussed further.

The most common definition used was the National Coordinating Council for Medication Error Reporting and Prevention's (NCC-MERP) definition:

> "Any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. Such events may be related to professional practice, health care products, procedures, and systems, including prescribing; order communication; product labelling, packaging, and nomenclature; compounding; dispensing; distribution; administration; education; monitoring; and use" (18).

The NCC-MERP definition (from the US) was used by 13 of the 78 (16.7%) studies that used a definition. Based on their aims; studies in my literature review using the NCC-MERP definition had this rated in five as clarity level 1, seven as clarity level 2

and one as clarity level 3. The definition was more relevant to some studies than others, depending on the aims and nature of the study.

An example of studies with the NCC-MERP definition rated as 1 is Campino et al. 2006 (115). Because their aim was to identify prescribing errors in a neonatal unit in Spain, and because no clear explanation of prescribing errors is provided by this definition, the study definition clarity was rated as 1. The NCC-MERP definition was rated as 2 in a study by Shah et al. 2009 (a US study in an otolaryngology ward) (14) who aimed to identify medication errors in general. The definition listed most possible different types of medication errors but without detailed explanation, and because the aim was to identify different types of medication errors; this study was rated as 2. However, a UK study, in an intensive care unit by Burmester et al. 2008 (10), used the NCC-MERP definition together with ten other definitions of prescribing errors (detailing different types of prescribing errors). Because the aim was to identify prescribing errors; definitions used by this study were rated as 3 as they were given in great detail.

3.4.3.2. Comparing studies with different ratings of definitions

Only one set of five studies used the same denominator (i.e. of all administrations) to identify the same type of errors (administration) and used the same method (direct observation) with definitions rating 1, 2 and 3 (Table 3.8).

Table 3.8: Comparable studies with the three different rating scores of clarity of definitions

Study	Definition clarity score	Setting	Age classification	Country	Intervention	Rate of errors	
						Before intervention	After intervention
Chua et al. 2010 (67)	3	Paediatric unit in general hospital	All ages	Malaysia	-	11.7% by doctors and nurses	-
Taylor et al. 2008 (174)	3	Neonatal unit	Neonates	US	CPOE	19.8% by nurses	11.6% by nurses
Raja lope et al. 2009 (88)	2	Neonatal unit	Neonates	Malaysia	CPOE	31% by nurses	15.4% by nurses
Feleke et al. 2010 (158)	2	Paediatric unit in general hospital	Neonates+ infants+ children+ adolescent	Ethiopia	-	89.9% by nurses and parents	-
Bertsche et al. 2010 (169)	1	Paediatric neurology	Not mentioned	Germany	Education + practical session	40.4% by nurses	7.9% by nurses
						96.6% by parents	5.6% by parents

From Table 3.8 it is clear that it is impossible compare these studies as the one study that was rated as 1 was conducted in a completely different setting with different participants to the other studies. Two studies (88) and (174) with different definition clarity levels identified a similar reduction in error rates after using the same intervention (electronic prescribing) in the same setting (neonatal unit). This may emphasise the importance of the effect of the intervention rather than the definition clarity rate. Pre-intervention error rates were lower in the US study (19.8%) with the definition clarity rating of 3 than the Malaysian study (31%) with the definition clarity rating of 2. This may reflect the error differences in the individual units or countries or it may be that the definition clarity meant that more specific and therefore less errors were identified in the US study.

Two other studies (67, 158) with different definition clarity rates were conducted in the same setting, i.e. a paediatric unit in a general hospital. The error rates are most likely so different, not because of the clarity rate of definitions but rather the participants involved, with one study involving parental administration and the other only healthcare professionals.

3.4.4. Interventional tools used to minimise medication errors

Fifty nine out of 153 studies (38.6%) used 65 interventional tools. Interventional studies were categorised as follows:

Dosing supporting tools –interventions to assist in dose calculation (17), electronic prescribing (15), educational interventions (7), health and safety strategies (2), clinical pharmacist services (2), pre-printed forms (2), more than one of the above interventions (6) and other interventional tools (8)

Four studies provided error results only after the intervention. Four studies provided the number of errors but not the rate of error either before and/or after the intervention. Two studies provided the overall percentage decrease in error rate rather than providing the error rate before and after interventions. Ten studies compared several different interventions, and one identified the error rate between two groups of participants (one with intervention and one without intervention).

3.4.4.1. Dosing supporting tools

Seventeen studies used dosing supporting tools, e.g. barcode medication administration systems, oral syringes and computerised automatic dosage calculation, as an intervention. The majority of studies (nine) focused on administration errors followed by prescribing errors (seven studies), with one study identifying medication errors in general.

Some studies compared the effectiveness of one dosing supporting tool over others. Three studies used the Broselow tape "which is used during paediatric emergencies to quickly estimate a child's weight, determine weight-based drug doses, and select the correct size emergency or resuscitation equipment" (175). Two studies compared it with other dosing tools (i.e. a colour coded tool on medication administration and standard volume/weight dose reformulation). The Broselow tape was found to be an effective tool in reducing the rate of administration errors from 72% to 43% of all patients receiving epinephrine in an arrest situation (170). However, a colour coded tool was shown to be more effective by Hohenhaus et al. 2008 (176) as the rate of administration errors for five out of six medications was lower when the colour coded tool was used compared to the Broselow tape. Moreover, the Broselow tape was less effective when compared to a standard volume/weight dose reformulation in a simulation study by Fineberg et al. 2008 (100). No administration errors were identified when standard volume/weight dose reformulation was used but eight errors were identified using the Broselow tape.

Two simulation studies (Sobhani et al. 2008 (148) and Yin et al. 2010 (48)) compared a dosing cup with other instruments, such as oral syringes/droppers. The dosing cup was associated with a higher error rate when used by parents. Yin et al. 2011 (149) also measured the effect of giving pictogram instructions in conjunction with written instructions on the use of a dropper device, which was found to be more effective than written instructions alone in reducing the rate of administration errors by parents.

Three studies that used dosing supporting tools to reduce prescribing errors used computerised weight based calculators. These studies found a weight based calculator to be effective in reducing continuous infusion medication prescribing errors (93), all

neonatal medications errors (177) and acetaminophen and ibuprofen outpatient prescribing errors (178).

All the above studies used dosing supporting tools to reduce the rate of errors to alert doctors when doses exceed minimum or maximum limits, reduce time needed to administer drugs, detect specific types of errors (e.g. wrong time error) or improve the quality of prescribing.

Brown et al. 2007 (179) used parenteral nutrition worksheet to aid prescribing. Senner et al. 2010 (180) used care guideline card for 10 antibiotics to be used by doctors. Both interventions were found to be effective in reducing prescribing error rate.

Hennings et al. 2010 (181) used an automated infusion device which was effective as it alerted doctors when doses exceeded the limit. Morriss et al. 2009 (90) used a barcode medication administration system which was able to detect wrong time errors and Zimmer et al. 2008 (182) used computerised prescription writers plus decision support for narcotics which alerted doctors when they prescribed a high dose. All of these interventions were effective according to the authors' conclusions even though error rates detected were increased in several cases.

Eight studies that used dosing supporting tools were simulation and identified administration errors by nurses (4), parents (3) and doctors (1). All the three studies involving parents used comparison methods. Two studies compared dosing cups with other instruments and found that more administration errors were identified when cups are used (48, 148). One study found less administration errors by parents when pictogram instructions were provided to parents in addition to the written instructions (149). Two of the four studies involving nurses concluded that the Broselow tape is less effective than other interventions (Colour Coding Kids Hospital System (176)

and volume/weight dose reformulation (100)). The other two studies with nurse participants did not use comparison methods but instead they separately measured the effectiveness of two different interventions. One study identified less administration errors after using a colour coded medication safety system (183) whereas the other study identified less administration errors after using a computer to calculate doses (184). One study measured the administration error rates by doctors and found less errors when mass concentration labels were provided compared to ratio concentration labels (147).

3.4.4.2. Electronic prescribing

Fifteen studies used electronic prescribing as an intervention. The majority of studies (nine) focused on prescribing errors. CPOE was used alone in 11 studies of which six identified prescribing errors (107, 146, 152, 185-187), two administration errors (110, 174), two medication errors in general (159) (121) and one medication errors in general and dispensing errors (109). Walsh et al. 2008 (159) stated that there is no effect of using CPOE alone on reducing the rate of serious medication errors in general and Sowan et al. 2010 (110) stated that there is no effect of using CPOE alone on reducing infusion pump programming errors. The other nine studies stated that CPOE alone was an effective intervention.

CPOE was used in conjunction with CDSS in four studies (101, 105, 130, 188); three identified prescribing errors and one identified medication errors in general, prescribing errors and transcribing errors. These four studies found a significant reduction in the rate of prescribing errors and medication errors in general after adding CDSS to CPOE (but not on transcribing errors).

Use of electronic prescribing was found by studies to be effective in reducing the rate of medication errors (101, 105, 107, 109, 130, 152, 174, 185, 187, 188), improving

the safety and efficiency of prescribing (121, 146), reducing the time needed for completing order forms (188) and increasing the completeness and legibility of prescriptions (101). CPOE saved the nurses' time and decreased the administration errors in a US simulation study by Sowan et al. 2010 (110) but did not decrease the identification of infusion pumps programming errors. In many of the studies however error rates identified even prior to the intervention were low ((105, 109, 121, 152, 159, 185, 188)). It is therefore difficult to decide the real clinical effectiveness of this intervention in terms of error reduction.

3.4.4.3. Educational interventions

Seven studies used education as an intervention. Of the seven studies, four identified administration errors and three identified prescribing errors. Educational interventions were used to address prescribing errors by doctors and administration errors by nurses (or parents). Three studies identified the effect of education on prescribing error rates. Kozer et al. 2006 (112) used a short tutorial (30 minutes) for doctors followed by a test and concluded that this intervention was not effective in reducing prescribing errors (12% of all orders by doctors whether educated or not). Campino et al. 2009 (189) provided 15 informative sessions about medication errors for doctors and the prescribing error (not including TPN) rate decreased from 20.7% to 3% of all orders. Eisenhut et al. 2011 (166) used an assessment of doctors followed by feedback and another assessment two months later which was stated to decrease the prescribing errors from 47% to 21% of all admissions.

Three studies used educational interventions to reduce the administration error rates by nurses. Raja Lope et al. 2009 (88) provided feedback, lectures and an educational poster; Pauly-O'Neill 2009 (150) provided an intensive training programme about safety in preparation and administration of medication and Sullivan et al. 2010 (168)

used compulsory online education for nurses about insulin. Bertsche et al. 2010 (169) used a 30-minutes lecture followed by 90-minutes practical session to identify administration errors by both nurses and parents (169). Less administration errors were identified after educating nurses and parents (error rate decreased from 42.8% to 7.8% of all administrations). From the above studies it is clear that the educational interventions were effective in most studies apart from one (Kozer et al.). Studies stated that educational interventions improved nurses' compliance with administration steps, reduced medication prescribing and administration errors and resulted in more accurate administration by nurses.

3.4.4.4.Health and safety strategies

Two studies used health and safety strategies as an intervention. Robinson et al. 2006 (190) in the US identified chemotherapy prescribing, dispensing and administration errors using review of charts and incident reports. They used failure mode and effects analysis (FMEA). The FMEA team consisted of a haematology/oncology doctor, nurses, pharmacists and a quality improvement consultant. Their job involved providing strategies for decreasing medication errors, ensuring the safety of medication administration and identifying risks associated with the administration process. Actual error rates detected in this study were however very low before the intervention and reduced after it (potential prescribing errors decreased from 23% to 14% of all orders after the intervention).

Ligi et al. 2010 (15) used safety initiatives (e.g. continuous reporting medication errors) and iatrogenic events prevention strategies e.g. education in a neonatal unit in France. Even though the rate of errors increased after the intervention; the author stated that the intervention was effective and the reason for the error rate increasing was because of an increase in the rate of reporting.

3.4.4.5.Clinical pharmacists

Two studies used clinical pharmacists as an intervention. One study was conducted in the US and identified only the rate of serious errors using review of charts and incident reports (86). The other was conducted in Norway and identified the prescribing error rate using chart review (117) .

Clinical pharmacy was an effective intervention according to these studies. However, Kaushal et al. 2008 (86) US study stated that clinical pharmacy is only effective in reducing the rate of serious medication errors when available full time. The effectiveness of clinical pharmacy services was also measured by its ability to detect medication errors that would otherwise be missed as in Kjeldby et al.'s 2009 study (117).

3.4.4.6.Pre-printed order forms

Two studies used pre-printed forms as an intervention. Larose et al. 2008 (167) identified IV medications and fluids prescribing and administration error rates in an emergency department in Canada. Broussard et al.'s study in 2009 (96) was conducted in a specialist children's hospital in the US and identified the prescribing error rate for sedation medications. Both studies used chart review and concluded that this intervention led to an increase in the documentation and completeness of medication orders.

3.4.4.7.Studies using more than one intervention

Six studies each used two interventions in combination (10, 29, 104, 165, 191, 192). Three studies were conducted in the US, two in the UK and one in Australia. Most studies did not separately evaluate the relative contributions of the different interventions to the error reductions. Intervention use by the studies included clinical pharmacy services, safety strategies (e.g. effective communication, safety

environment and following important steps regarding prescribing and administration), new reporting form, educational, pre-printed form, bedside prescribing guidelines, CPOE, antimicrobial stewardship program and multidisciplinary practice (involving paediatric hospitalist, paediatric care coordinator, paediatric nurse, pharmacist and the trauma service).

All the above studies used combinations of interventions stated to be effective apart from Davey et al. 2008 (104), who separately identified the effectiveness of education of doctors about good prescribing and after implementation of bedside prescribing guidelines. According to the authors the educational intervention was effective in reducing the rate of prescribing errors whereas the bedside prescribing guidelines intervention was not.

Prescribing errors were shown to be reduced by the implementation of pre-printed order forms, education of doctors, following safety strategies, using electronic prescribing in conjunction with supporting programmes and implementation of multidisciplinary practice. Administration errors were shown to be decreased by education of healthcare professionals, following safety strategies and implementation of multidisciplinary practice. Medication errors in general found to be reduced following introduction of clinical pharmacy services and the rate of reporting medication errors was increased.

The effectiveness of these studies was measured according to different parameters, i.e. the rate of errors identified, the severity of errors, rate of reporting and completeness of order forms. However, all interventions used were effective according to these parameters and the authors' conclusions.

3.4.4.8.Miscellaneous interventions

Eight studies used miscellaneous interventions. Five interventions, which were considered effective, were an anonymous error reporting system which decreased the rate of medication errors in general (58), an integrated care pathway which decreased the prescribing error rate (193), observation of doctors and nurses decreased the prescribing but not transcribing error rate (131), responding of doctors and nurses to alerts generated by CPOE decreased prescribing but not transcribing error rates (102) and consultant review and rewriting medication orders with errors decreased the medication error rates in general (194). Using an anonymous reporting system according to Taylor et al. 2007 (58) was effective even though the rate of error increased. The authors explained that the increase in reporting rate after the intervention showed it had worked.

Three of the eight studies showed no effect of their interventions. These less effective interventions were: corollary order screen to decrease monitoring error rate (133), using a mobile kiosk by parents to enter symptoms, patient's allergy and medication history to decrease prescribing error rate (163) and changing doctors' hours to decrease prescribing error rate (161).

3.4.5. Studies conducted in the UK

Sixteen studies were conducted in the UK. Thirteen studies identified the error rate. The majority (14 studies) identified prescribing errors. In addition, five identified medication errors in general, five administration errors, two dispensing errors and one transcribing errors.

According to the quality assessment (Section 3.5. Chapter 2); six studies met 10 criteria, four met nine, two met eight and one met seven. The quality for three studies could not be assessed as these studies were only available as conference abstracts. Ages of patients were not provided in 12 studies. Two of the remaining studies involved neonates, infants, children and adolescents; one involved infants, children and adolescents; and one involved only children and adolescents.

Eleven different denominators were used by 13 studies while the remaining studies purely provided numbers of errors. Eleven out of the 14 studies that identified the prescribing errors used six denominators. The most commonly used was "of all orders", used by five studies, and results were between 2.2% of all orders in a specialist children's hospital and 30.5% of all orders in a paediatric unit of a general hospital before interventions. "Of all patients" denominator was used by two studies and ranged between 16.8% of all patients in an intensive care unit only looking at resuscitation drugs and 74% of all patients in a specialist children's hospital looking only at intravenous aciclovir. One study each used "mean errors per patient", "of all admissions", "of all medications" and "of all errors".

Administration errors were identified by five studies. One study did not identify the error rate whereas the other four studies used different denominators, and showed; 1.2% of all administration in a paediatric unit in a general hospital, 15-25% of all charts in a specialist children's hospital and a paediatric unit respectively, 19.1% of

all possible errors in specialist and general paediatric units and 30% of all medication errors in gastroenterology ward.

Medication errors in general were identified by five studies of which only two identified the rate using denominators (1.8 errors per bed day occupancy in ICU and 0.24% of all parenteral nutrition days in a gastroenterology ward). Only one denominator, "of all medication errors", was used to identify dispensing (24%) and transcribing (20%) errors in a gastroenterology ward.

The studies were conducted in the following settings:

Specialist children's hospitals (3), paediatric units in general hospitals (3), intensive care units (3), specialist children's hospital and in a paediatric unit of a general hospital (2), outpatient clinic (1), paediatric gastroenterology and nutrition ward (1), paediatric pain team (1), neonatal and paediatric unit in a general hospital (1) and one study used the national incident reporting system to identify medication errors with aseptic products.

The studies used chart/medical record review (10 studies), review of medication error incident reports (4), chart review and direct observation of nurses when administering drugs plus review of interventions (1) and chart review and incident reports (1).

Eight studies used seven different interventions. Six interventions were used in seven studies to reduce prescribing error rates. These included electronic prescribing in nephrology outpatients (101), where prescribing errors reduced from 77% of all medications to 4.8% with CPOE+CDSS. Positive results were also seen in a specialist children's hospital where errors reduced from 2.2% of all orders to 1.2% after CPOE alone was introduced (152); and an intensive care unit where errors reduced from 8.8% to 4.6% of all orders (187). Chart review was used in all studies to measure errors.

Educational sessions (10, 104), pre-printed post-cardiac surgery order forms (10), bedside prescribing guidelines (104), an integrated care pathway (ICP) (193) and assessment of doctors and giving them feedback (166) were also studied. One intervention (daily consultant review of prescriptions and mandatory rewriting any prescriptions with errors) was used to reduce the rate of both prescribing and administration errors in an intensive care unit (194). All interventions were effective according to authors apart from using bedside prescribing guidelines by Davey et al. 2008 (104) which was not found to be effective in reducing prescribing errors.

3.4.6. Time of the day and days of the week mostly associated with errors

Eight studies identified the time and/or the day involved in errors. Three studies using chart review were from the UK, Brazil and Argentina. Four studies identified the time, three identified the time of the day and the days of the week and one identified the days of the week mostly associated with errors.

Only eight studies (5%) looked at the time of the day or days of the week where errors are more likely. Three studies (Burmester et al. 2008 (10), Lerner et al. 2008 (75) and Engum et al. 2008 (4)) found that the day shift was associated with more errors than other shifts. None of these studies suggested a reason for the high error rate in the daytime compared with other times of the day. Two of these studies (4, 75) did not mention the shifts' hours time whereas one study (10) considered the time between 07.00 to 19.00 as the day shift.

Most authors do not concentrate on the time of medication errors or the days associated with more errors. For example; Rinke et al. 2007 (140) only mentioned that

82.9% of all errors occurred in weekdays without any further explanation. Another example is Engum et al. 2008 study which only provided the rate of errors in the daytime (57% of all errors).

Miller et al. 2010 (76) specifically examined the time and the days mostly associated with medication errors. They clearly defined the day shift and the difference between weekdays and weekends. Nursing and pharmacy shifts were separately defined. These involved two nursing shifts: 07.00 to 18.59 and 19.00 to 06.59 and three pharmacy shifts: 07.00 to 14.59, 15.00 to 21.59 and 22.00 to 06.59. They considered weekdays to start from 07.00 on Monday to 18.59 on Friday, and weekends from 19.00 on Friday to 06.59 on Monday. In nursing shifts, fewer errors were identified in the first shift compared with the second shift (1.17 vs. 2.12 errors per 1000 doses, p=0.005). In contrast, in pharmacy more errors occurred in the second shift compared to the first and the third shifts (2.24 vs. 1.01 and 1.88 errors per 1000 doses, p=0.0019). They identified more errors at weekends compared with weekdays (2.55 vs. 1.9 per 1000 doses, p=0.181). Miller et al. 2010 emphasised the importance of clinical pharmacy services in reducing the rate of errors as the rate was highest at the time when no, or few, pharmacists are available. Rinke et al. 2007 (140) study was conducted in a paediatric oncology unit in the US. They showed a high error rate at weekdays but did not give further details or provide an explanation for their findings.

Hicks et al. 2007 (195) and Chuo et al. 2007 (196) found more Intralipid® prescribing and administration errors between 18.00 and 24.00. Both of these studies suggested that this is because new infusions are supplied and set up during this time. Chuo et al. 2007 found no significant difference in the rate of error between shift change hours (the time of change ± 2 hours) and non-shift change hours. However, they found more

errors on the 2nd shift change hours (between 17.00 to 21.00) compared with the 1st shift change hours (between 05.00 to 09.00).

Otero et al. 2008 (29) identified prescribing and administration errors in three shifts: morning shifts (07.00 to 13.59), afternoon shifts (14.00 to 20.59) and night shifts (21.00 to 06.59). They identified the error rate before and after the introduction of an intervention of education and safety strategies. Prescribing errors were highest before the intervention in the afternoon (67.6% of all orders) and after the intervention at night (30% of all orders). Administration errors were highest in the afternoon and decreased from 11.1% to 6.3% of all administrations after the intervention. Otero et al. 2008 (29) found a similar error rate between weekdays and weekends. They did not suggest reasons for these results.

Hicks et al. 2007 (195) conducted a study at a neonatal unit in the US searching MEDMARX to identify administration medication errors by nurses associated with fat emulsion. They found more errors on Mondays and Fridays compared with other days. They suggested that this is because staff usually change on Monday and they are therefore not familiar with the care plan provided for patients at weekends. Another possibility is that management plans change after the ward round on Monday especially for infants who may have been reweighed requiring dose changes to be made accordingly.

None of the studies identified a relation between the time of errors and patient harm making it difficult to measure the consequence of the higher error rates on patients at a particular time of the day or day of the week.

3.5. Discussion

3.5.1. Clarity of definitions

Most studies which examined transcribing, dispensing and monitoring errors did not provide a definition. Some studies and their definitions focused purely on specific indications or medications (e.g. insulin administration (168)). With brief and vague definitions (rating 1) it is possible that many types of errors (especially small errors) may be missed. For example, Kazemi et al. 2010 (102) conducted a study in a neonatal unit in Iran and provided a definition of prescribing errors, which simply stated, "An error that occurred during the prescription stage." They found that 10.3% of all medications involved prescribing errors in physician order entry and 4.6% in nurse order entry. On the other hand such a simple definition may actually result in more errors being identified than a more specific definition.

It is clear that no definition has been globally agreed upon for medication errors. Of all definitions used, the most common one used was the NCC-MERP definition. This was used by 13 of the 78 (16.7%) studies that used a definition. Ghaleb in 2006 stated that a difference in definitions is an important factor of variation in reported medication error rates. This group however did not attempt to test the clarity of definitions and its effect (17).

Lisby et al (2010) (20) found that 17 studies (adult and paediatric) used the NCC-MERP definition, and in my search, which only involved paediatric patients, 13 studies were identified. This may reflect the satisfaction of many researchers with this definition compared with others or it may purely be the one most cited and therefore well known. Even this one definition however received different clarity ratings as it was more relevant to some studies than others.

Studies using clear definitions were lowest in number. This may indicate that most authors did not think carefully enough about appropriate definitions when starting their studies. The majority of studies however used definitions rated as clear enough to meet some of the study aims. Since the effect on the results is not possible to assess it is difficult to know the significance of this. It may emphasise the need to provide clearer definitions when starting a study to ensure that the study aims are met and the results are reliable. The number of studies without definitions or with definitions not clear enough to meet all of the study aims is of concern. I would therefore encourage researchers to use very clear and carefully considered definitions in order to meet all the aims of their studies as this may influence the results. Information found by studies may then reflect more accurately the actual epidemiology of medication errors in the intended settings and populations.

Lisby et al. in 2010 also did a systematic review aiming to identify studies that used definitions of medication errors and to identify the effect of these definitions on the rate of errors. Their judgments on the clarity of definitions depended only on the terminology (e.g. medication errors, prescribing errors, medication failure or medication deviations) used to create definitions. Differently; in my systematic review; the judgment on the clarity of definitions was done according to the aims of each study and whether definitions used by each study linked properly with these aims or not. Lisby et al found that 45 definitions used for medication errors appeared in 203 studies (adult or paediatric). They found no relationship between the definitions used and prevalence of medication errors in studies identified from their systematic literature review.

3.5.2. Interventional tools

Unfortunately ten out of 59 studies (17%) using interventions did not identify the error rate before and after using the intervention. Despite this all studies stated that the intervention was effective. It is helpful if studies identify the rate of errors before and after an intervention in order to estimate it's efficacy in terms of error reduction. Many of the studies only identifying the rate of errors after the intervention concluded by mentioning that the intervention was effective because it was able to detect many errors, for example, Zimmer et al. 2008 (182) who identified the number of alerts generated from the use of the web based controlled substance writer. Kjeldby et al. 2009 (117) found around a quarter of all orders had a prescribing error which would not be identified and addressed if the clinical pharmacist service was not provided. Therefore they considered this as an effective intervention.

Some studies identified more errors after the intervention and the authors of these studies stated that the intervention was effective. For example; an increase in the rate of reporting was suggested to be a cause of the higher error rate after patient safety initiatives and iatrogenic events prevention strategies by Ligi et al. 2010 (15). Moreover, the error rate was increased in the study by Morriss et al. 2009 (90) after using a barcode administration system. The authors concluded that the rate of error increased because the system detected and addressed wrong time errors.

Some studies did not provide the prescribing error rate either before or after the intervention. Van De Velde et al. 2009 (186) compared the effect of CPOE and pre-printed order forms on the rate of chemotherapy prescribing errors. They only identified the number of prescribing errors without giving the rate of errors. They concluded that the CPOE was more effective because it decreased prescription writing errors. Costello et al. 2007 (191) who conducted a study in an intensive care unit in

the US did not identify the error rate but only the number of errors after the intervention (109 medication errors). They did not provide the number of errors before the intervention but stated that the clinical pharmacist and education was effective because the reporting rate was increased by six fold and because the number of serious errors was decreased from 46% to 0% of all reported errors.

Studies did not only measure the effect of interventions on reducing the error rate but also looked at other parameters. For example, Fineberg et al. 2008 (100) identified the effect of using a standardised volume-weight dose reformulation of resuscitation drugs (reformulated to 0.1 ml/kg to give an identical volume of medication per kilogram of body weight for each drug) and critical care medications instead of using the Broselow tape on both administration dosing errors and time needed to deliver medications to patients. They found that using the weight dose formulation was associated with less dosing errors and led to delivering medications to patients faster.

Thirteen out of the 17 studies using dosing support tools suggested that all interventions were effective. Most of these studies (nine) identified administration errors. The most commonly used dosing supporting tool was an automatic weight based dosing calculator. The remaining four studies compared different dosing tools of which two studies concluded that oral syringes were associated with less dosing errors than cups (48, 148). One study by Yin et al. 2011 (149) found that providing pictogram instructions helped the parent to give more accurate doses to their children (149). Wheeler et al. 2008 found that calculating doses by doctors using mass concentration labels was associated with less errors than using ratio concentration labels (147).

Our review suggests that adding clinical decision supporting systems (CDSS) to CPOE results in more medication errors being prevented compared to CPOE alone.

Two studies (105, 130) identified prescribing errors when CPOE was used alone and in conjunction with CDSS. Both studies found that the rate of prescribing errors significantly decreased when CDSS was used together with CPOE.

Authors of most studies using educational interventions concluded that education was an effective method to decrease the rate of administration and prescribing errors. An exception was one study by Kozer et al. 2006 (112) which identified the rate of prescribing errors in groups of doctors who attended or did not attend a tutorial. They stated that the rate of prescribing errors did not improve in the group of doctors who attended the educational session. The authors suggested that this might be because doctors who did not attend the session may have had better knowledge, experience or confidence than those who agreed to attend the session. The authors also suggested that the intervention was short (30 minutes) and this might be another cause for its poor effect.

Even though the same intervention, e.g. education, was used by more than one study; it is important to notice that different factors can alter the results following such interventions. For instance; as before Kozer et al. 2006 (112) used a short and single education session and found no effect on reducing prescribing errors. On the other hand Campino et al. 2009 (189) used a programme of 15 informative sessions and found a clear effect of the education on reducing the prescribing error rate (from 20.7% to 3% of all orders after the intervention).

Other successful educational interventions were also much more intensive than Kozer's. For example Bertsche et al. 2010 (169) used a 90 minute practical session after a 30 minute lecture for all healthcare professionals and Eisenhut et al. 2011 (166) who evaluated the effect of five prescribing tasks for doctors on the rate of prescribing errors followed by two assessments (the second assessment two months

after the first). The reduction in error rates in the latter study may also have been influenced by doctors learning on the job in the two months between assessments.

The most common interventions used for prescribing errors were electronic prescribing followed by dosing supporting tools (e.g. computerised automatic dosage calculation), education and pre-printed order forms. Administration errors were mostly addressed by using dosing supporting tools (e.g. barcode medication administration systems and oral syringes) followed by electronic prescribing and education.

Safety strategies were used by two studies (in the US and France), clinical pharmacy services were used by two studies (in the US and Norway) and pre-printed order forms were used by two studies (in the US and Canada). According to the authors of these studies all of these interventions were effective. However, clinical pharmacists were effective only when a full time service was provided according to Kaushal et al. 2008 (86).

The period between starting the intervention and examining the results may be important. This is because estimating the efficacy of an intervention directly after introducing it may not reflect its real effect, which may need lead time before starting to assess results. This was clear from Neal et al.'s 2010 (187) study which identified the rate of prescribing errors before and after using CPOE. The error rate did not improve after one week of electronic prescribing (decreased from 8.8% to 8.1% of all orders), but after six months the rate of error decreased significantly to 4.6% of all orders.

Making interventions may be associated with new possibilities for errors. For example, using electronic prescribing will eliminate the problem of clarity associated with poorly handwritten order forms but has been associated with wrong selection

from the drop-down menu, e.g. selecting the wrong dose or medicine (152). Therefore, when developing a new system to be used to minimise the rate of medication errors, it is important to keep in mind any drawbacks that may be associated with this system.

Campino et al. 2008 (131) found that observation alone was effective in decreasing the rate of prescribing errors by doctors but not transcribing errors by nurses. This is called the "Hawthorne effect", i.e. the effect of being observed improving practice. This finding is supported by a Tanzanian study by Leonard et al. 2006 (197) who found that the effect of observing doctors resulted in a 13% increase in the quality of care provided to patients, however, this effect reduced with time. In contrast a UK study by Dean et al. 2001 (198) found no effect of observing nurses in decreasing the rate of administration errors.

The majority of studies (12, 75%) used chart/medical record review to collect data. Only 60 studies (39%) from the full literature review used chart/medical record review. This method was however still the most common used method of data collection in both the UK and non-UK studies. All the UK studies that used chart review identified prescribing errors. Three other studies used review of medication error incident reports to identify prescribing errors in addition to other types of errors (i.e. medication errors in general, administration errors, dispensing errors and transcribing errors).

3.5.3. Comparing UK to all other studies

UK studies identified all types of medication errors except monitoring errors. This is similar to the non-UK studies included in my systematic review (Chapter 2) with only 11 studies (overall 7%) looking at monitoring errors. Even though some non-UK studies identified the rate of monitoring error; only one study provided a definition of

it and most studies identified the proportion of this error among other types of errors e.g. prescribing and administration errors. This may reflect the low interest of researchers in identifying this type of error in children or lack of awareness that monitoring errors can and do occur.

Comparing the clarity rating of definitions used by UK studies (nine studies) with all studies (78 studies); 44%, 44% and 11% of the UK studies with definitions were rated respectively as 1, 2 and 3. All studies (UK and non-UK) with definitions were similarly rated respectively as 28%, 53% and 18%. Both the UK and non-UK studies used mainly unclear definitions when identifying the rate of errors. This reflects the need for using clear definitions by researchers from any country.

Comparing the quality assessment of the UK studies with other studies (UK and non-UK); 15%, 31% and 46% of the UK studies with quality assessment (13 studies) respectively met 8, 9 and 10 criteria. From the total 143 studies with their quality assessed; 27%, 28% and 33% respectively met 8, 9 and 10 criteria. The methodological quality of UK studies therefore seems to be slightly higher compared to the studies overall.

3.6. Limitation

1. Few numbers of comparable studies with wide variation in error rate were identified from my literature review due to the number of different denominators and methods used.
2. There is no standard definition for the term “wide variation” and therefore it was considered to occur when the difference between the highest and lowest error rate was more than 50%.

3. Some studies used “of all errors” as the denominator which does not reflect the actual rate of each type of medication error but rather provides the proportion of each type of error amongst others.
4. No guidance on writing a good definition of an error exists therefore my supervisors and I agreed our own rating scale.
5. Because of the low number of studies that can be compared due to different denominators being used; the rate of specific types of errors in particular settings cannot be generalised to the UK children’s population.

3.7. Conclusion

The reasons for the wide variation in error rates found in studies using the same methods and denominators were identified in many cases. Different settings are a significant reason for wide variations in error rates in some studies. Other important causes of variation are the use of interventions, country, identifying subtypes of errors, identifying errors with specific medications, different inclusion criteria, environment, study designs and difference in participants’ level of education, training and experience. Neonates are involved in a number of the studies and showed a high rate of errors.

Despite the challenges of the current literature base the main messages to be taken from this review of the methods of data collection on the identified rate of medication errors are:-

- Prescribing errors are more likely to be detected using chart review though the addition of incident reporting, questionnaires and/or parental interview may improve error detection rates in some settings.

- Administration errors may be best studied using direct observational techniques though incident reporting seems to be useful here. The Hawthorne effect may however be important and affect results so study design and awareness of this is very important.
- Chart review seems to identify more medication errors in general than other methods and incident reporting in combination with this may improve the results.
- Transcribing, monitoring and dispensing errors have been less well studied than other error types. Incident reporting schemes may be better to detect transcribing and dispensing errors whereas chart review may be better for monitoring errors. Definitions of such errors are very important as the current literature is unclear.

There is no globally agreed definition for medication errors. Many studies used definitions which were unlikely to adequately meet their study aims. It is unfortunately not possible to decide what influence the definition has on the results of these studies as they cannot be compared adequately. Future researchers are however advised to give careful consideration to the definitions they use, to ensure that they will meet the aims of their study and where possible to use previously used definitions in order to be able to compare their results with those of others.

It is important not only to identify the rate of errors in paediatric patients but rather to find out solutions for these errors. Using electronic prescribing has been found to be a good intervention to reduce prescribing errors. Moreover, use of dosing supporting tools, such as computerised automatic dosage calculation, were found to be useful to reduce administration errors. It seems that measuring the effect of some interventions may need time before making a judgment as to their effect as healthcare professionals sometimes need time to adapt to such interventions.

The rates of medication errors from the UK studies identified in this systematic review cannot be generalised due to the low number of studies that were conducted in the same setting, using the same methodology and the same denominators to identify the rate of the same type of errors. However, the data suggests that the rate of prescribing and administration errors is higher in paediatric units in general hospitals compared to specialist children's hospitals. This trend should be explored in future work. The authors of the UK studies however focused mainly on identifying and reducing the rate of prescribing errors more than any other types of errors. Further investigations regarding the incidence and causes of medication errors in children in the UK are required to develop interventions to reduce risk. I recommend that UK researchers should consider the following when starting new studies:

- More studies investigating the reasons for medication errors happening in children need to be done.
- Choose appropriate denominators to identify each type of error so that results can be compared to previous studies and lessons learned if possible.
- Studies should include different types of medication errors (e.g. prescribing and administration errors).
- Use clear definitions which are designed to meet the study aims.
- Examine the effect of other types of interventions such as clinical pharmacy services.
- Focus separately on neonates and other children's age classifications.

There are few studies that identified errors in different time frames. These were often different as some studies divided the day time to two shifts whereas others to three shifts. Even though some studies identified the error rate in the same number of shifts; the start and the end times of these shifts often differed. These differences make it difficult to draw conclusions.

Chapter 4: Systematic literature review of the role of the paediatric clinical pharmacist in reducing the rate of medication errors

4.1. Introduction

The American College of Clinical Pharmacy (ACCP) defined clinical pharmacy as "that area of pharmacy concerned with the science and practice of rational medication use" (199). The term "Pharmaceutical Care" was firstly introduced by Hepler and Strand in 1990 and was defined as "The responsible provision of drug therapy for the purpose of achieving definite outcomes that improve a patient's quality of life" (200). Compliance with standards (e.g. cooperating with other healthcare professionals) that should be followed to protect patients from unsafe use of medications, as detailed in regulation 13 of the Health and Social Care Act 2008, can only be achieved by providing an effective clinical pharmacy service (201).

Clinical pharmacy was started in the University of Michigan in the US in the early 1960s by students studying in the pharmacy school (202). After graduation of these students; three of them, David Burkholder, Paul Parker, and Charles Walton, made a strong effort to initiate clinical pharmacy services (202). The first university that started offering a clinical pharmacy degree was the University of Kentucky in the late 1960s (202). In the US, the board of pharmacy specialties provides clinical pharmacy in eight specialities; ambulatory care, critical care, nuclear, nutrition support, oncology, paediatrics, pharmacotherapy and psychiatry (203).

Pharmacy practice in the UK changed from being product oriented to patient oriented in the mid-1960s and increased after the 1970s (204). Postgraduate courses started in Bradford, London and Manchester universities in the 1970s (205-207). The "clinical pharmacy" term was formally used in the UK by the Nuffield report in 1986 (204).

Prescriptions and medication charts are reviewed by pharmacists to identify errors, drug interactions, and appropriateness of prescribing in terms of choice of drug and compliance with local policies. Patients may be asked by pharmacists to give details of e.g. medication history, allergy status, side effects and adverse drug reactions. Pharmacists provide advice to other healthcare professionals including choice of medication, correct dose, suitable administration routes, drug interactions and side effects. They monitor and provide advice on use of drugs with a narrow therapeutic index e.g. aminoglycosides and anticonvulsants. They also play important roles with anticoagulant medications to advise on keeping the international normalisation ratio within the therapeutic range (208).

Pharmacists may practice in many different areas including; ambulatory care, critical care, drug information, geriatric and long-term care, internal medicine and subspecialties, cardiology, endocrinology, gastroenterology, infectious disease, neurology, nephrology, obstetrics and gynaecology, pulmonary disease, psychiatry, rheumatology, nuclear pharmacy, nutrition, neonatal intensive care, paediatrics, pharmacokinetics and surgery (209). There is currently limited formal specialist training in such areas for UK pharmacists however.

Clinical pharmacists are involved before, during and after writing the prescription (210). Before prescriptions are written; clinical pharmacists' roles include the decision of which products should be purchased, which medications should be included in hospital formularies and which management guidelines should be

implemented (210). During prescription writing; their role involves advising doctors around the best medications and dose regimen to use including cost (210). After writing prescriptions; they ensure the suitability and accuracy of medications prescribed and monitoring process are in place (210).

Clinical pharmacists are a primary source for providing information and advice, based on scientific evidence, to ensure delivery of the correct, safest and most effective medication to patients (199). In order for them to work effectively they need to have a good background knowledge about diseases, therapeutics, medications and their mechanism of actions, drug monitoring, good therapeutic planning skills, the ability to do a risk assessment and interpret their findings, the effect of the body on drugs and the effect of drugs on the body, adverse drug events, the economic and effective impact of using some medications over others and good communication skills (211).

The goals of clinical pharmacy involve (211, 212):

1. Using suitable medications according to the individual patient's situation to obtain the desired effects.
2. Minimising adverse drug events, drug interactions and other medication-related problems as far as possible.
3. Monitoring the medication effectiveness for each patient.
4. Monitoring medication adherence by patients.
5. Providing effective alternative medications to decrease cost where possible.
6. Simplifying dosing regimens.
7. Making sure that all medications are used according to national or local guidelines.
8. Avoid waste of medications and ensure all currently prescribed medications are required.
9. Counselling and education of patients, parents and other healthcare professionals.
10. Assessing patients' ability to take medications.
11. Encouraging patient adherence and providing compliance aids when required.

As identified in Chapter 2, the literature on medication errors in paediatric patients has increased since 2006. It is important to know what different paediatric clinical pharmacists' activities are being used to improve healthcare services and their

effectiveness in reducing medication errors. Therefore a systematic review of the literature to explore the effect of clinical pharmacists' activities in reducing paediatric medication errors was conducted.

4.2. Aims

1. To identify contributions and interventions made by clinical pharmacists to minimise or prevent medication errors in neonatal and paediatric patients.
2. To use this knowledge to inform development of my own study involving directly observing clinical pharmacists locally to identify their role in decreasing the rate of medication errors and improving care provided to paediatric patients.

4.3. Methods

Five databases were searched to identify relevant studies:

- EMBASE 1974-July 2013
- International Pharmaceutical Abstracts (IPA) 1970- July 2013
- Ovid MEDLINE(R) 1946- July 2013
- Allied and Complementary Medicine (AMED) 1985- July 2013
- CINAHL (Cumulative Index to Nursing and Allied Health Literature) 1982-July 2013

There were no limitations for the search.

4.3.1. Search strategy

EMBASE, IPA, MEDLINE and AMED databases were searched separately and then combined together to remove duplication. CINAHL could not be combined with the other databases; hence, it was searched alone and manually reviewed to remove

duplication and to identify relevant articles. A hand search of bibliographies was done to include relevant articles that were not identified from the databases.

4.3.2. Keywords

Forty-four keywords were used from Ghaleb et al. 2006 (17) who had previously conducted a well-recognised systematic review of medication errors in children.

Sixteen keywords were added to strengthen their strategy. These were: prescribing mishap OR prescribing mishaps OR incorrect drugs OR incorrect doses OR incorrect routes of administration OR error reduction OR medical error OR medical errors OR calculation error OR calculation errors OR calculation mistake OR calculation mistakes OR error rate OR dose error OR dosing error AND baby.

The most sensitive and specific keywords for neonatal and paediatric patients according to a validated age specific search strategy by the Hedges Team (213) are as follows: children or infant or pe*diatric* or neonate or adolescence or adolescences or adolescent (213). Therefore three keywords were added: children OR adolescence OR adolescences.

Eleven keywords used by five previous systematic review studies (214-218) exploring the role of pharmacists were included: pharmacist OR pharmacists OR pharmacy OR clinical pharmacy OR pharmaceutical care OR pharmacy services OR clinical pharmacist OR clinical pharmacists OR pharmaceutical services OR ward-based pharmacists OR pharmacists interventions

The combined strategy for the search was therefore:

medication error OR medication errors OR administration error OR administration errors OR prescribing error OR prescribing errors OR dispensing error OR dispensing errors OR drug error OR drug errors OR drug mistake OR drug mistakes OR prescribing mishap OR prescribing mishaps OR drug mishap OR drug mishaps OR medication mistake OR medication mistakes OR medication mishap OR medication mishaps OR administration mistake OR administration mistakes OR dispensing mistake OR dispensing mistakes OR prescribing mistake OR prescribing mistakes OR wrong drug OR wrong drugs OR wrong dose OR wrong doses OR incorrect drug OR incorrect drugs OR incorrect dose OR incorrect doses OR incorrect route of administration OR incorrect routes of administration OR error reduction OR medical error OR medical errors OR calculation error OR calculation errors OR calculation mistake OR calculation mistakes OR error rate OR drug death OR dose error OR dosing error
AND
pediatric OR pediatrics OR paediatric OR paediatrics OR child OR children OR infant OR infants OR neonate OR neonates OR neonatal OR adolescent OR adolescents OR adolescence OR adolescences OR baby
AND
pharmacist OR pharmacists OR pharmacy OR clinical pharmacy OR pharmaceutical care OR pharmacy services OR clinical pharmacist OR clinical pharmacists OR pharmaceutical services OR ward-based pharmacists OR pharmacists interventions

A paediatric patient was defined according to the International Conference on Harmonisation (129) to be 18 years or less.

4.3.3. Inclusion criteria

Original research studies identifying the effect of pharmacists' activities on reducing or detecting medication errors either in neonatal or paediatric patients or in the general population, where the neonatal or paediatric data are separately identified.

4.3.4. Exclusion criteria

- Studies identifying the effect of pharmacists' activities on reducing errors in adults only.
- Studies identifying the effect of pharmacists' activities on reducing errors in the general population where paediatric data are not separately identified.
- Studies identifying drug toxicity and not errors.

- Review articles.
- Editorial article, reply, comment, letter, news, notes and case reports.

A random 10% of all papers identified, and all those where it was not immediately obvious whether it should be excluded or included from the abstract, were independently reviewed by my supervisor (Dr Conroy) to confirm whether the study met the inclusion/exclusion criteria or not.

4.3.5. Quality assessment of studies

All included studies were assessed to determine the quality of each study. The assessment was made using ten criteria adapted from Ghaleb's 2006 study (17) and Allan's 1990 study (113):

1. Aims/objectives of the study clearly stated.
2. Errors to be studied specified.
3. Errors to be studied defined.
4. Presence of a clearly defined denominator.
5. Data collection method described clearly.
6. Setting in which study conducted described.
7. Sampling described.
8. Reliability of methods used.
9. Limitations of study listed.
10. Ethical approval mentioned.

Only studies available as full articles (or conference abstracts) with quality ratings six or more were included. A research nurse and I scored the quality assessments independently. Any disagreement was resolved by discussion.

4.3.6. Extraction of data and analysis

All data was entered into three tables according to their methodology: authors, country, setting, aim, type of error, period of study, sample, method, type of contributions, error rate, sub-types of errors, medications associated with error, other significant results and quality rating. Data was analysed descriptively.

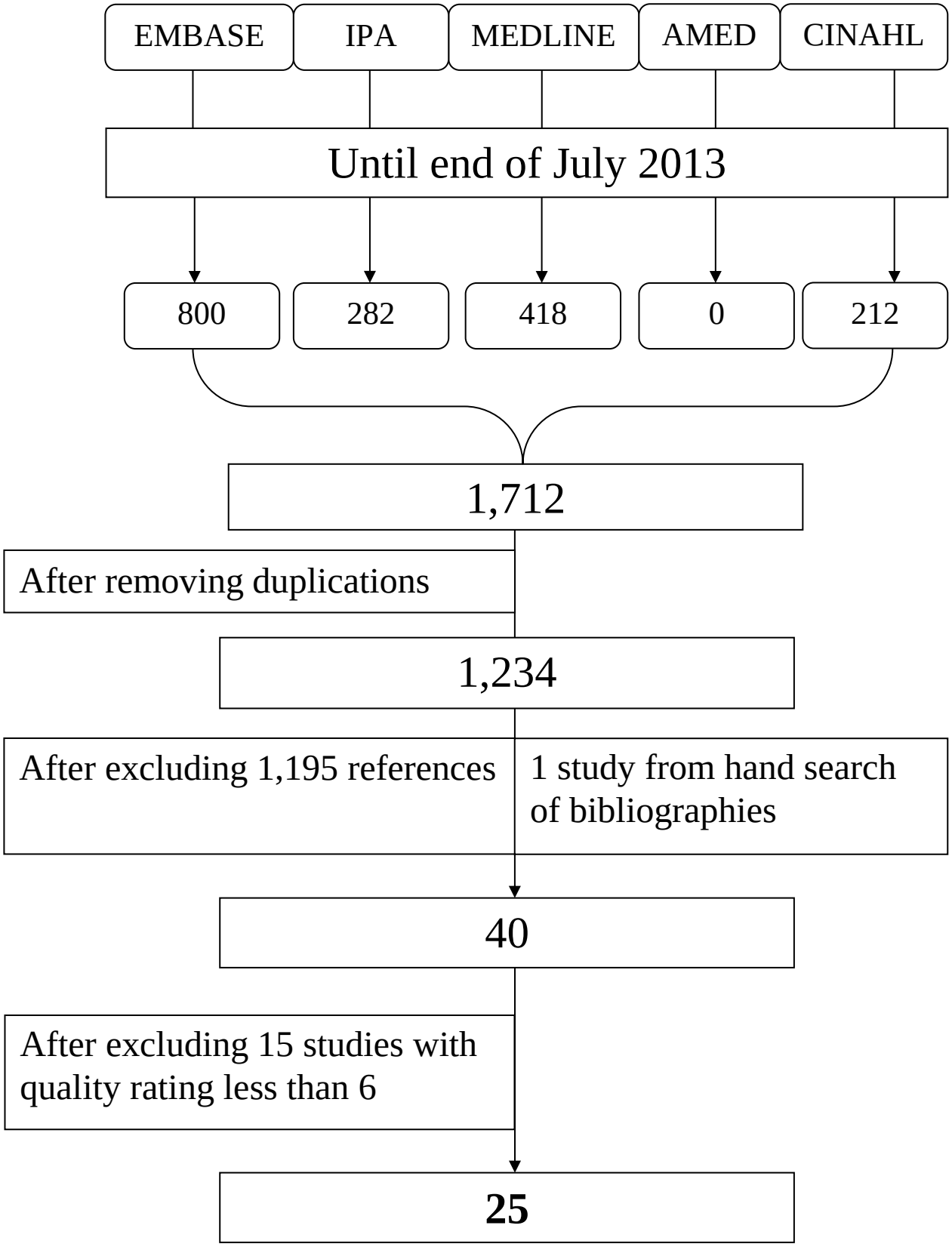
4.4. Results

The total number of references identified was 1,712. After removing duplication; 1,234 abstracts remained. All were reviewed against the inclusion and exclusion criteria. Of these, 39 were relevant and one study was added following hand search of bibliographies. Fifteen studies (two full articles and 13 abstracts) were excluded because they had a quality assessment score of less than six and therefore 25 studies remained (18 full articles and seven abstracts). Table 4.1 illustrates reasons for exclusion and Figure 4.1 illustrates the search strategy and results.

Table 4.1: Reasons for excluding articles from review

Reason for exclusion	Number of papers
Not relevant	727
Not original research	126
Literature review	121
Editorial article, reply, comment, letter, news, notes	107
Case reports	67
Studies not separating paediatric results from adult results	32
Quality rating less than six	15
Adverse drug events not involving medication errors	12
Insufficient information from abstract (full article not available)	3
Total number of studies	1,210

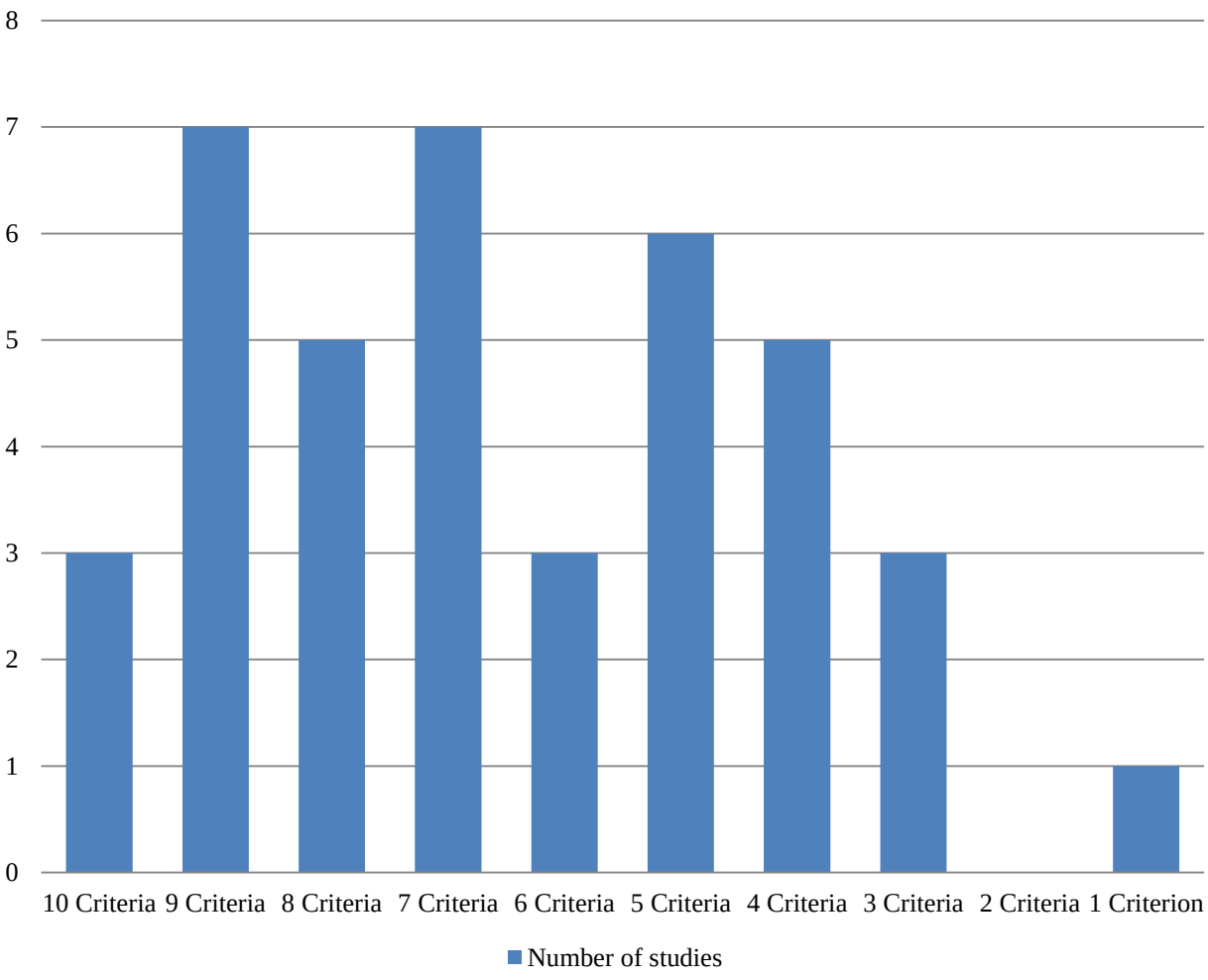
Figure 4.1: Summary of search and review process



4.4.1. Quality assessment

Quality assessment was completed on all studies with full articles available (20) and on those only available as conference abstracts (20). Quality assessment (by myself and the research nurse had R-value for agreement before discussion of 0.975%. Only one study needed discussing. The results can be seen in Figure 4.2. Two full articles and 13 abstracts had a score of less than 6 and therefore were excluded.

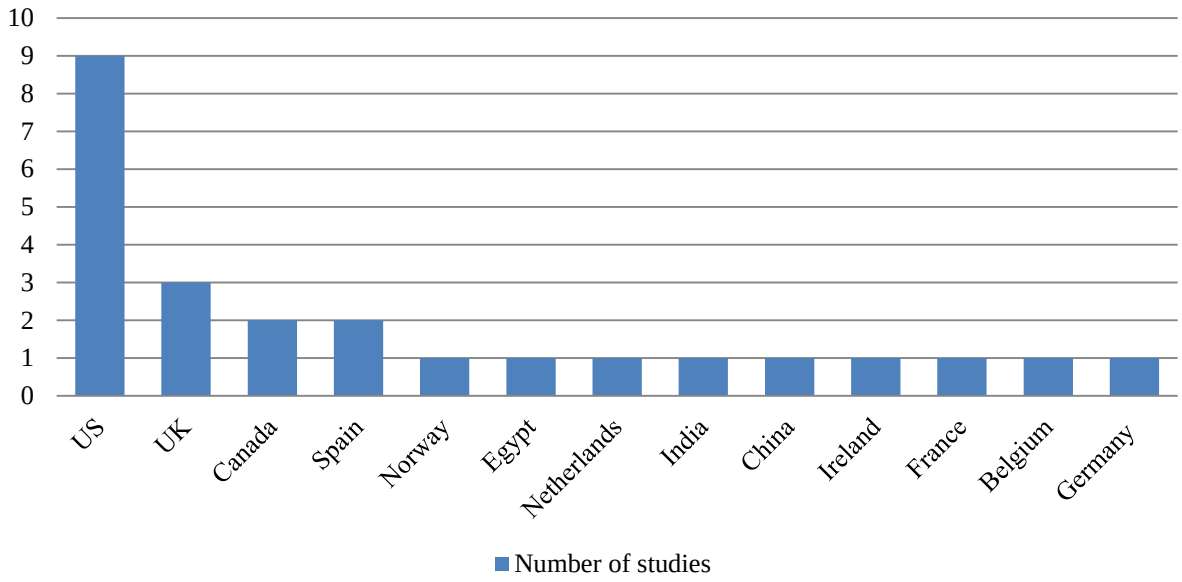
Figure 4.2: Quality assessment of studies



4.4.2. Countries

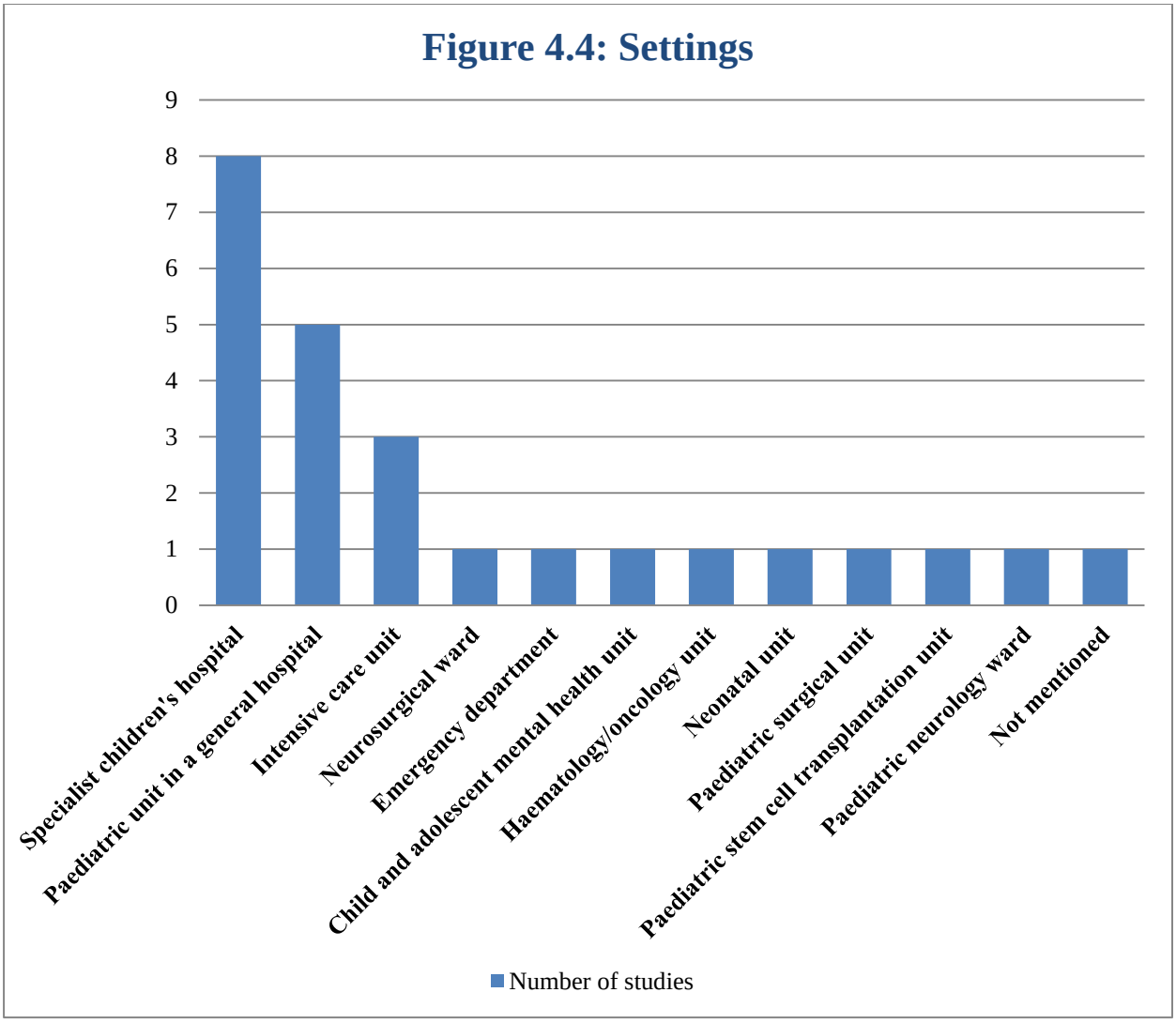
The 25 remaining studies were conducted in 13 different countries of which nine were in the US, three in the UK, two in Canada and two in Spain (Figure 4.3).

Figure 4.3: Countries



4.4.3. Settings

The studies were conducted in 12 different settings (Figure 4.4), of which the majority were in specialist children's hospitals (8), paediatric units in general hospitals (5) and intensive care units (3). The setting for one study (a conference abstract) was not provided. The remaining eight studies were each conducted in different settings.



4.4.4. Methods of data collection

Three different methods of data collection were used:

Nineteen used chart review, four used review of incident reports, one used direct observation of parents and nurses administering medications and one used a mixed method and identified the rate of prescribing errors (using chart review) and administration errors (using direct observation of parents) separately and therefore will be included twice in the analysis.

The following sections illustrate the 25 included studies according to the methodology used for data collection.

4.4.4.1. Studies using chart review

Twenty studies used chart review. Seventeen studies identified prescribing errors and three identified medication errors in general. Error rates varied greatly and five studies just provided a number with no denominator.

Most studies looked at the introduction of clinical pharmacy services (chart review, medication reconciliation, annotating prescriptions with administration information, provision of information, answering queries, quiz and feedback for doctors, participation in doctors' rounds, developing clinical guidelines, identifying opportunities for cost saving and education of healthcare providers, patients and parents) and the effects they have.

Antibiotics were the most common class of drug where errors were found. Six studies identified the medications most often associated with errors that were intercepted by clinical pharmacists. Five studies (117, 219-222) identified antibiotics as the group of medications mostly associated with errors and one study (223) identified central nervous system drugs. Two studies identified single medications mostly associated with errors of which the most common medication was omeprazole (224) in a Spanish ICU and paracetamol in a French paediatric surgical unit (225). Wrong doses (especially overdoses) were the commonest errors intercepted.

Two studies (226, 227) showed that discharge prescriptions are best checked by pharmacists on the ward rather than in the dispensary as they are familiar with the patients' medications and history and have access to charts and medical notes.

Only one study was a randomised controlled trial (221) in a Chinese paediatric unit. This study showed error prevention, cost savings and reduced length of stay after pharmacists' contribution (answering healthcare professionals' questions, suggestions of treatment and educating patient). Doctors' acceptance rate of interventions was

high where stated except in a US emergency department (227) and a Dutch specialist children's hospital (222).

Three studies found that clinical pharmacists were effective in reducing the cost. Chan et al. 1990 (226) saved $263 per month following a decrease in discharge medications wasting. This was because patients were given the medications issued during hospitalisation to be taken home at discharge. Two studies found clinical pharmacists effective in saving the cost of medications; $1,977 was saved in a US ICU by reducing drug acquisition costs (228) and $5485.80 was saved in a Canadian child and adolescent mental health unit by reducing total drug costs (229).

Table 4.2 illustrates the 20 studies using chart review as a method of data collection.

Table 4.2: Studies using chart review

Reference number Authors Country Setting	Aim Type of error Period Sample	Method Types of contributions	Rate of errors	Sub-types of errors	Medications associated with errors	Other results	Quality rating
(219) Folli et al. 1987 US Two specialist children's hospitals	To assess prospectively the impact of clinical pharmacists at two hospital pharmacies on detecting and preventing prescribing errors before dispensing medications MPEs 6 months (February- July 1985) 57,394 orders at the first hospital and 43,628 orders at the second hospital	Prescriptions with errors were detected prospectively by clinical pharmacists before dispensing and passed to a doctor and two clinical pharmacists for confirmation Not mentioned	1.35 per 100 patient days (4.9 per 1000 orders) in the 1st hospital & 1.77 per 100 patient days (4.5 per 1000 orders) in the 2nd hospital	Over-dose (55.1%), under-dose (26.9%), wrong medication (5.6%), IV incompatibility (2.7%), wrong route of administration (1.9%), drug interaction (1.9%), drug allergy (0.4%) and others (5.4%)	Most errors were associated with antibiotics (28.1% of all errors at the 1st hospital and 47% at the 2nd hospital) followed by theophylline at the first hospital (16.4% of all errors) and analgesics (14.6% of all errors)	100% agreement was identified between the doctor and the two clinical pharmacists. 49.7% of all errors occurred on NICU compared with 23.2% on PICU and 27.1% at other paediatric units.	8
(226) Chan et al. 1990 US Paediatric unit in a general hospital	To assess the effect of reviewing discharge prescriptions by pharmacists (on paediatric ward) rather than by pharmacists in outpatient pharmacies MPEs August 1988 to May 1989 An average of 154 prescriptions per month	Pharmacists on paediatric ward reviewed discharge medications instead of pharmacists at outpatient pharmacies and compared the discharge medications with the patients' inpatient medications Not mentioned	18% of all orders	Omissions errors (17%), incomplete prescriptions (13 %), wrong dose (10%), wrong dosage form (15%), wrong direction (3%), wrong drugs (3%) and others (39%).	Not mentioned	Pharmacists decreased the cost (decreased waste of medication). Doctors and nurses' time saved because pharmacists are familiar with the patients' medications and history. $263 per month saved	7

Reference number Authors Country Setting	Aim Type of error Period Sample	Method Types of contributions	Rate of errors	Sub-types of errors	Medications associated with errors	Other results	Quality rating
(230) Koren et al. 1991 Canada Specialist children's hospital	To assess the effect of paediatric clinical pharmacists on reducing the rate of prescribing errors MPEs One month retrospectively (March 1989) and another month (June 1989) prospectively Not mentioned	Two methods 1. Prospective chart review by clinical pharmacists 2. Retrospective prescriptions review (from the hospital pharmacy) by a quality assurance pharmacist Suggestions and recommendations of treatment	516 interventions identified retrospectively. Prospectively 390 interventions were identified	Wrong dose, omission of dose, omission of frequency, wrong length of therapy, prescribing medication to allergic patients, ADRs, not adherence to guideline, wrong formulation	Not mentioned	Major cause for dosage error was miscalculation resulting from misplacing of decimal point	7
(220) Grinder et al. 1991 US Not mentioned	To identify the effect of pharmacists on preventing prescribing dosing errors MPEs (dosing errors) 4 months (period not mentioned) 69,282 prescriptions	Four months study. Pharmacist reviewed prospectively all prescribed doses for appropriateness according to mg/kg basis. Not mentioned	80 dosing errors	60% were overdose and 40% were under dose	Antibiotics were associated with 49% of all dosing errors.	Doctors accepted 97.5% of all pharmacists' recommendations.	6

Reference number Authors Country Setting	Aim Type of error Period Sample	Method Types of contributions	Rate of errors	Sub-types of errors	Medications associated with errors	Other results	Quality rating
(231) Zangwill et al. 2000 US Paediatric unit in a general hospital	To assess the effect of using quiz program followed by feedback (once monthly for 11 months) on reducing the rate of prescribing errors MPEs Two weeks (period not mentioned) after the intervention Not mentioned	Prescribing errors were identified and reviewed by two pharmacists and one doctor before and after the intervention. The rate of prescribing errors was compared before and after the intervention using chart review Quiz +feedback for doctors	Prescribing errors decreased from 6.2% to 4.1% of all orders	Not mentioned	Not mentioned	Not mentioned	6
(228) Krupicka et al. 2002 US Intensive care unit	To identify the types and numbers of clinical pharmacists interventions. MEs in general 19th November 1996 to 6th May 1997 215 patient admissions (493 patient days)	Pharmacist reviewed medication charts prospectively Participation in doctors' round, answering healthcare providers' queries and educating healthcare professionals.	35 recommendations per 100 patient days (28% dosage changes, 26% drug information)	Wrong medication, wrong route of administration, wrong dose, omission of medications, unnecessary medication, TDM and ADRs	Not mentioned	$1,977 was saved (from drug acquisition costs)	8

Reference number Authors Country Setting	Aim Type of error Period Sample	Method Types of contributions	Rate of errors	Sub-types of errors	Medications associated with errors	Other results	Quality rating
(229) Virani et al. 2003 Child and adolescent mental health unit Canada	To identify the effect of clinical pharmacists on reducing the medication error rate and on reducing the financial cost MPEs 4 week interval (June 4 to June 29, 2001) for prospective review 12 months (September 1998-August 1999) before and 12 months after the intervention (September 1999-August 2000) for retrospective review Not mentioned	Pharmacists collected all pharmacists' interventions prospectively by chart review. A retrospective cost analysis was done (not mentioned by whom). Pharmacists participated in doctors' rounds, provided consultation to healthcare professionals and answering their queries, preventing medication errors, cost saving and provide interdisciplinary staff support.	48 interventions in 4 weeks	32 errors were identified. These involved adverse drug reactions (38%), under-dose (19%), drug not indicated (19%), wrong medication (6%), over-dose (3%), drug indicated but not prescribed (3%) and others (12%).	Not mentioned	98% were accepted by doctors $5485.80 was saved (21% decrease in total drug cost).	7
(232) Angalakuditi et al. 2003 India Specialist children's' hospital	To measure the accuracy of doses measurement by parents and the accuracy of prescribing by doctors. MPEs One-week study. 175 patients in Group 1 and 162 patients in Group 2	Doctors received feedback from the Group 1 prescribing errors results and given a paediatric dosing chart for paracetamol to calculate doses according to patients' weight. Feedback to doctors+dosing chart	% recommended doses prescribed by doctors in group 1 was 38.2% and 98.7% in group 2.	Dosing errors	Not mentioned	Not mentioned	9

Reference number	Aim	Method	Rate of errors	Sub-types of errors	Medications associated with errors	Other results	Quality rating
Authors	Type of error						
Country	Period	Types of contributions					
Setting	Sample						
(86)	To assess the effect of clinical pharmacists services on the rate of serious medication errors	Data from medication orders, incident reports, MARs and patients' charts were reviewed prospectively by trained nurses. All suspected medication errors were passed to two doctors for confirmation	Serious MEs rate decreased in ICUs from 29 to 6 per 1000 patient days after the intervention but did not decrease in the general medical unit (from 8 to 9 per 1000 patient days after the intervention) or in the general surgical unit (from 7 to 9 per 1000 patient days after intervention)	Not mentioned	Not mentioned	79% of all pharmacists' interventions occurred during prescribing stage.	10
Kaushal et al. 2008	Serious MEs in general						
US	6-8 weeks in three paediatric unit (PICU, medical unit and surgical unit) for 6 months between March- August 2000 and for 3 months in each unit between June-November 2000	Introduction of clinical pharmacy					
Specialist children's hospital	1249 admissions in the PICU, 1690 admissions in the paediatric medical unit and 1924 admissions in the paediatric surgical unit.						

Reference number Authors Country Setting	Aim Type of error Period Sample	Method Types of contributions	Rate of errors	Sub-types of errors	Medications associated with errors	Other results	Quality rating
(117) Kjeldby et al. 2009 Norway Paediatric unit in a general hospital	To assess the effect of clinical pharmacist services on the quality assurance of drug management MPEs February 2006- March 2007 384 orders	Chart review was done by pharmacists six months after starting the clinical pharmacy services Participation in doctors' round, discussing errors with doctors and nurses, answering queries from healthcare professionals, education, cost saving and developing clinical guidelines	103 orders (26.8%) involved 137 MPEs	48 (35%) related to dosage, 35 (26%) drug choice, 32 (23%) related to monitoring, 18 (13%) illegible writing, 3 (2%) interaction and 1 (0.7%) ADR.	Most prescribing errors were associated with antibiotics, followed by diuretics	Not mentioned	9
(233) Terry et al. 2010 UK Neurosurgical ward	To identify the effect of medication reconciliation by pharmacists on reducing MPEs MPEs September 200- March 2007 100 patients	Prospective observational study of medication reconciliation by one clinical pharmacist to compare medications prescribed on admission with medications from before admission Medication reconciliation	39% of initial medication orders differed from pre-admission medication orders.	Not mentioned	Not mentioned	Not mentioned	9

Reference number	Aim	Method	Rate of errors	Sub-types of errors	Medications associated with errors	Other results	Quality rating
Authors	Type of error						
Country	Period	Types of contributions					
Setting	Sample						
(223)	To identify the effect of different interventions by pharmacists on the rate of prescribing errors	Charts were reviewed by one pharmacist before and after an intervention	78.1% of all orders before the intervention involved prescribing errors and 35.2% of all orders after the intervention.	Unclear orders, incomplete orders, wrong instructions for nurses (most types of errors after intervention), wrong selection, wrong frequency, wrong concentration, wrong rate of administration (most type of error before intervention) and wrong dose	Most groups associated with prescribing errors before intervention: cardiovascular drugs and central nervous system drugs. Most groups associated with prescribing errors after intervention: central nervous system drugs and respiratory drugs.	Most route of administration associated with errors before the intervention was IV and after the intervention was inhalation	9
Alagha et al. 2011	MPEs						
Egypt	October 2008- March 2009 (pre-intervention) and October 2009- March 2010 (post-intervention)	Starting new charts, educating doctors, assisting with dosing and provide feedback for doctors regarding their performance.					
Intensive care unit	1,417 orders for 139 patients (pre-intervention) and 1,097 orders for 101 patients (post-intervention)						
(225)	To identify the effect of clinical pharmacists activities on reducing the rate of prescribing errors	Pharmacists identified prescribing errors by chart review.	558 recommendations in 2007, 223 in 2008 and 387 in 2009	13% of medication orders: 50.9% about overdose, 20% wrong route or wrong administration, 11.6% under-dose	Acetaminophen (23.2% of all recommendation), ondansetron (19.7%), nalbuphin (15.6%) codeine (12.8%)	61.9% accepted in 2007, 75.9% accepted in 2008 and 69.1% accepted in 2009 by doctors	6
Maire et al. 2011	MPEs						
France	2007- 2009	Provide recommendations					
Paediatric surgical unit	Not mentioned						

Reference number Authors Country Setting	Aim Type of error Period Sample	Method Types of contributions	Rate of errors	Sub-types of errors	Medications associated with errors	Other results	Quality rating
(224) Echarri-Martínez et al. 2011 Spain Intensive care unit	To identify the effect of clinical pharmacists activities on reducing the rate of prescribing errors MPEs October- December 2009 Not mentioned	Prospective review of charts by pharmacists. Any intervention or contribution was recorded prospectively and stored on database Financial saving and annotate prescription with administration information.	40 interventions and contributions (4 per 100 patient days).	1. Documentation of allergy status 2. Clarification of prescriptions 3.Preventing medication errors: duplication, wrong dose, illegible writing, non-adherence to guideline, incomplete information, interaction, wrong dosage interval, unnecessary medication, omission of medication, ADR and wrong route of administration.	Most drugs associated with recommendations were omeprazole followed by acetylcysteine.	95% of pharmacists recommendations were accepted by doctors	9
(234) Fernandez-Llamazares et al. 2012 Spain Specialist children's hospital	To assess the effect of clinical pharmacist intervention on reducing prescribing errors. MPEs 2007-2009 61,458 prescriptions	Prospective review of charts by pharmacists. All interventions activities were recorded prospectively and stored on database Financial saving and annotate prescription with administration information.	1,475 contributions and interventions (0.019 per bed day or 2.4% of all orders)	As above (same research group)	Not mentioned	Not mentioned	10

Reference number Authors Country Setting	Aim Type of error Period Sample	Method Types of contributions	Rate of errors	Sub-types of errors	Medications associated with errors	Other results	Quality rating
(235) Patel et al. 2012 UK Haematology/ oncology ward	To assess the effect of clinical pharmacy services on reducing MPEs MPEs November 2010- November 2011 Not mentioned	Prescribing error rate compared one year before intervention and one year after the intervention (not mentioned by whom it was reviewed) The intervention involved pharmacist daily review of prescriptions, taking medication history within 24 hours of admissions and discuss any errors with the prescribers.	Prescribing errors decreased from 20 to 9. Pharmacists' intervention decreased from 4.05 to 2.09 per 100 medications prescribed.	Not mentioned	Not mentioned	Not mentioned	8
(221) Zhang et al. 2012 China Paediatric unit in a general hospital	To investigate the effect of clinical pharmacists on reducing medication errors and to identify the different types of intervention made by pharmacists MEs in general December 2010 to March 2011 80 patients in the interventional group and 80 patients in the control group	Randomised controlled trial. The interventional group involved clinical pharmacists care and the other group was a control group. All clinical pharmacists' interventions were reviewed (not mentioned by whom) Answering healthcare professionals' questions, suggestions of treatment, patient education and prevention of medication errors (by review of medication charts).	109 interventions (31 prevention of medication errors)	Prescribing errors, dosage errors, preparation errors, technology errors and compliance errors	42.2% of all interventions were associated with antibiotics	Length of stay at the hospital was less in intervention group compared to the control group (6.45 days vs. 10.83 days)	8

Reference number	Aim	Method	Rate of errors	Sub-types of errors	Medications associated with errors	Other results	Quality rating
Authors	Type of error						
Country	Period	Types of contributions					
Setting	Sample						
(236)	To identify the effect of clinical pharmacy services on prescribing process	Interventions and activities of clinical pharmacists were collected and reviewed by one pharmacist by review of medication charts.	73 interventions made (5.4 per 100 patients care days and 9.1 % of all prescriptions).	47.9% was dosing errors	Not mentioned	Doctors accepted 91.8% of all interventions	8
Conway et al. 2012	MPEs						
Ireland	Three months (period not mentioned)	Not mentioned					
Neonatal unit	110 patients						
(222)	To identify the types and numbers of interventions prevented by clinical pharmacist intervention on prescribing errors.	Prospective cohort study. All electronic medication prescriptions for paediatric inpatients were verified prospectively (not mentioned by whom).	2282 interventions for 1577 orders (1.1% of all orders).	18.9% related to completion and 81.1% related to corrections of prescriptions. Most completions were absence of body weight (55.7%) followed by absence of dosage form (17.9%) and absence of strength/concentration (16.2%). Most corrections were wrong dose (45%) followed by wrong drug formulation (9.4%).	15.6% of all interventions were about antibacterial agents.	Risk of intervention was higher in children younger than two years old. Doctors accepted 57.5% of all interventions. 31.1% of all interventions were in immunology/haematology unit, 20.3% in neurology unit and 17.5% in internal medicine unit. More interventions were identified on oral dosage form and oral administration route.	10
Maat et al. 2013	MPEs						
Netherlands	1st March 2004- 1st January 2008	Not mentioned					
Specialist children's hospital (excluding ICU)	138,449 orders						

Reference number	Aim	Method	Rate of errors	Sub-types of errors	Medications associated with errors	Other results	Quality rating
Authors	Type of error						
Country	Period	Types of contributions					
Setting	Sample						
(227)	To identify the rate of pharmacists' intervention for discharge prescriptions	Pharmacists reviewed discharge prescriptions prospectively. One pharmacist reviewed and analysed all interventions.	17 interventions (23.6% of all orders).	Wrong patient, drug, drug omission, drug or class duplication, drug interaction, allergy, contraindication, dosage form, strength, route of administration, dose, frequency, duration, monitoring, quantity, refills and non-formulary medications.	Not mentioned	24% of all recommendation were accepted by doctors	9
Cesarz et al. 2013	MPEs						
US	Three weeks in 2010.	Chart review					
Emergency department	72						

4.4.4.2. Studies using review of incident reports

Four studies used review of incident reports. Two studies identified prescribing errors and two studies identified medication errors in general. None of the four studies identified the error rate (i.e. they all identified the error number without using a denominator). Only one study by Bauters et al. 2010 (237) identified the group of medications mostly associated with errors which was antibiotics. Two studies (237, 238) identified the acceptance rate of pharmacists' recommendations by doctors which was between 91-92%. Pharmacists' activities were provided by three studies and involved provision of information, educating and answering of healthcare professionals' queries, medication reconciliation, annotating prescriptions with administration information and introduction of a new reporting form. Wrong doses were the commonest errors intercepted.

Table 4.3 illustrates the four studies using review of incident reports as a method of data collection.

Table 4.3: Studies using review of incident reports

Reference number Authors Country Setting	Aim Type of error Period Sample	Method Types of contributions	Rate of errors	Sub-types of errors	Medications associated with errors	Other results	Quality rating
(238) Condren et al. 2004 US Paediatric unit in a general hospital	To investigate the different types of contributions made by paediatric pharmacists to prevent medication errors MEs in general 2002 3978 patients	Interventions were recorded by paediatric pharmacists on an incidents' database and were then reviewed by another pharmacist. Answer healthcare professionals' queries, medication reconciliation and annotating prescription with administration information	4605 interventions	Drug therapy change (mostly dosing errors) and pharmacokinetic monitoring	Not mentioned	91% of all interventions were accepted by doctors	9

Reference number	Aim	Method	Rate of errors	Sub-types of errors	Medications associated with errors	Other results	Quality rating
Authors	Type of error						
Country	Period	Types of contributions					
Setting	Sample						
(191)	To identify the effect of pharmacists on the rate of medication errors reporting	Phase 1: retrospective collection of medication error reports Phase 2: prospective collection of medication error reports. Phase 3: after pharmacist led paediatric medication safety team (including paediatric critical care nurse, paediatric intensivist). At the end of each month, one pharmacist and one nurse review medication error incident reports and then the pharmacists entered the incidents to the incidents' database.	109 MEs were identified. MEs reporting increased between phase1 and 2 to two fold, between phase 2 and 3 to three fold and between phase 1 and 3 to six fold. Reporting of nurses errors increased from 9% in phase 1 to 38% in phase 2 and 51% in phase 3	Omission error, wrong medicine, wrong dosage, wrong patient, incomplete prescription, transcribing error, wrong rate and unauthorized medicine.	Not mentioned	Not mentioned	7
Costello et al. 2007	MEs in general						
Specialist children's hospital	Phase 1: (September- December 2004) Phase 2: (February- May 2005) Phase 3: (June- September 2005)	Implementing new reporting form and educational forum					
US	Not mentioned						

Reference number	Aim	Method	Rate of errors	Sub-types of errors	Medications associated with errors	Other results	Quality rating
Authors	Type of error						
Country	Period	Types of contributions					
Setting	Sample						
(237)	To identify different interventions made by clinical pharmacists	Interventions made by clinical pharmacists were collected (not mentioned by whom)	142 interventions	26.8% of all interventions were related to change of therapy, 55.4% increased drug monitoring, 16.1% start drug therapy, 1.7% clarification of order	Antibiotics were associated with 28.9% of all interventions, antineoplastic and immunomodulating agents (28.9%)	92% of all interventions were accepted by doctors	7
Bauters et al. 2010	MPEs						
Belgium	10 weeks (non-consecutive days).	Answer healthcare professionals' queries					
Paediatric stem cell transplantation unit	Not mentioned						
(239)	To identify the effect of pharmacists on reducing prescribing errors	Paediatric pharmacists' interventions were retrieved from the hospital database to identify prescribing errors (not mentioned who collected and analyse them).	489 interventions.	Wrong dose, wrong frequency, interventions regarding wrong calculations, decimal point or unit of mass errors, wrong or cheaper formulation, altered drug handling e.g. renal impairment, illegible prescribing, incorrect or incomplete history on admission.	Not mentioned	Not mentioned	7
Isaac et al. 2012	MPEs						
UK	Not mentioned	Not mentioned					
Specialist children's hospital	500 prescriptions						

4.4.4.3. Studies using direct observation

Two studies used direct observation of parents and/or nurses to identify administration dosing errors. High error rates were identified with both parents and nurses before education. After pharmacists' education a significant reduction in dosing errors were identified in both studies.

Angalakuditi et al. 2003 (232) identified paracetamol suspension administration errors by parents. They divided parents into two groups (the 1st group were educated by hospital staff other than pharmacists and used a cup, whereas the 2nd group were educated by a pharmacist and used a marked syringe). The percentage of recommended doses measured by parents in group 1 was 48.6% and in group 2 was 98.7%. Bertsche et al. 2010 (240) identified administration errors by nurses and parents before and after education. Medication administration errors decreased by nurses from 40.4% to 7.9% of all administrations and by parents from 96.6% to 5.6% of all administrations. This study identified anticonvulsants as the most common group of medications associated with errors. It also identified an annual cost saving of €532.90 per patient.

Table 4.4 illustrates the two studies using direct observation as a method of data collection.

Table 4.4: Studies using direct observation of parents and/or nurses

Reference number Authors Country Setting	Aim Type of error Period Sample	Method Types of contributions	Rate of errors	Sub-types of errors	Medications associated with errors	Other results	Quality rating
(232) Angalakuditi et al. 2003 India Specialist children's' hospital	To measure the accuracy of doses measurement by parents MAEs One-week study. 175 patients in Group 1 and 162 patients in Group 2	Direct observation of parents: Group 1 parents asked to measure the dose of paracetamol suspension using a cup after verbal instructions by the hospital staff other than pharmacists. Group 2 parents asked to measure the dose of antipyretic suspension using a marked syringe and were educated by a pharmacist. Education for parents	The percentage of recommended doses measured by parents in group 1 was 48.6% and in group 2 was 98.7%.	Dosing errors	Not mentioned	Not mentioned	9
(240) Bertsche et al. 2010 Germany Paediatric neurology ward	To identify MAEs by parents and nurses MAEs Not mentioned Not mentioned	Prospective two-period observational study. Clinical pharmacists observe administrations made by parents and nurses and identified administration errors. The intervention included teaching of nurses and parents and providing information pamphlets.	Medication administration errors decreased by nurses from 40.4% to 7.9% of all administrations and by parents from 96.6% to 5.6% of all administrations.	Dosing errors	Most errors were associated with anticonvulsants	Annual saving of €532.90 per patient	7

4.4.5. Rate of medication errors

All of the 25 included studies found that clinical pharmacists were effective, according to their authors, in either reducing or preventing medication errors. Nine studies (191, 220, 221, 225, 229, 230, 237-239) did not provide the rate but only the number of medication errors that received an intervention by pharmacists. The remaining 16 studies identified the error rate using seven different denominators.

Of the 16 studies that identified the error rate; ten identified the rate of errors only after intervention by pharmacists (117, 219, 222, 224, 226-228, 233, 234, 236). The remaining six studies (86, 223, 231, 232, 235, 240) identified the rate before and after starting clinical pharmacy services. All of these six studies resulted in a decrease in medication error rate after starting this service. This ranged from 6.2-78.1% of all orders before to 1.1-35.2% of all orders after intervention.

Table 4.5 illustrates the rate of different types of medication errors identified by pharmacists categorised according to the denominators and the methods used. Three studies (219, 234, 236) each provided the prescribing error rate using two different denominators. One study identified prescribing errors and administration errors (232).

Table 4.5: Rate of medication errors identified before and/or after clinical pharmacists' services

Denominator	Methodology	Type of error	Country	Setting	Error rate		Reference	Range	Median
					Before	After			
Of all orders	Chart review	Prescribing errors	US	Paediatric unit in a general hospital	Not provided	18%	(226)	6.2-78.1% before and 1.1-35.2% after intervention	61.8% before and 14% of all orders after intervention
			US	Paediatric unit in a general hospital	6.2%	4.1%	(231)		
			Norway	Paediatric unit in a general hospital	Not provided	26.8%	(117)		
			UK	Neurosurgical ward	Not provided	39%	(233)		
			Egypt	Intensive care unit	78.1%	35.2%	(223)		
			Spain	Specialist children's hospital	Not provided	2.4%	(234)		
			Ireland	Neonatal unit	Not provided	9.1%	(236)		
			Netherlands	Specialist children's hospital (excluding ICU)	Not provided	1.1%	(222)		
			US	Emergency department	Not provided	23.6%	(227)		
			India	Specialist children's hospital	61.8%	1.3%	(232)		
Per 100 patient days	Chart review	Prescribing errors	US	Two specialist children's hospitals	Not provided	1.35-1.77 (in two different hospitals)	(219)	1.3-5.4 after intervention	2.8 per 100 patient days
			Spain	Intensive care unit	Not provided	4	(224)		
			Ireland	Neonatal unit	Not provided	5.4	(236)		
		Medication errors in general	US	Intensive care unit	Not provided	35	(228)		
Per 1000 orders	Chart review	Prescribing errors	US	Two specialist children's hospitals	Not provided	4.9-4.5 (in two different hospitals)	(219)	4.5-4.9 after intervention	4.7 per 1000 orders
Per 1000 patient days	Chart review	Medication errors in general (serious)	US	Specialist children's hospital	29	6	(86)		
Per bed day	Chart review	Prescribing errors	Spain	Specialist children's hospital	Not provided	0.019	(234)		
Per 100 medications	Chart review	Prescribing errors	UK	Haematology/ oncology ward	4.05	2.09	(235)		
Of all administrations	Direct observation	Administration errors by nurses	Germany	Paediatric neurology ward	40.4%	7.9%	(240)		
		Administration errors by parents			96.6%	5.6%			
		Administration errors by parents	India	Specialist children's hospital	51.4%	1.3%	(232)		

4.4.6. Types of interventions identified

Twenty-one studies identified 29 different subtypes of medication errors. Table 4.6 illustrates the different types of medication errors that needed intervention by pharmacists. Wrong dose followed by wrong drug were identified by most studies.

Table 4.6: Subtypes of medication errors intercepted by pharmacists.

	Type of error	Explanation/example	Number of studies identified in	References
1	Wrong dose	Either over- or under-dose	21	(117, 191, 219-230, 232, 234, 236-240)
2	Wrong drug	Prescribing drug not according to guidelines	11	(117, 191, 219, 222, 223, 226-229, 237, 238)
3	Wrong route of administration	IV instead of oral	8	(219, 222, 224, 225, 227, 228, 234, 238)
4	Incomplete prescription	Not writing the dose	8	(117, 191, 222, 224, 226, 234, 238, 239)
5	Omission of medication	Not prescribing salbutamol inhaler on admission for patients with asthma	8	(191, 224, 226-229, 234, 237)
6	Drug interaction	Prescribing morphine and codeine together	7	(117, 219, 222, 224, 227, 234, 238)
7	Non formulary medicine	Using an adult only drug for treating a child	7	(191, 222, 224, 227, 230, 234, 238)
8	Identification of actual or potential adverse drug reactions	Harmful reactions resulting from administration of a medication	7	(117, 224, 228-230, 234, 238)
9	Unclear prescription	Not writing the dose clearly	7	(117, 223, 224, 234, 237-239)
10	Wrong dosage form	Capsule instead of liquid	6	(222, 226, 227, 230, 234, 238)
11	Wrong frequency/interval	8 hourly instead of 6 hourly	5	(222, 223, 227, 238, 239)
12	Therapeutic drug monitoring	Adjusting interval	5	(117, 227, 228, 237, 238)
13	Duplication	Prescribing pseudoephedrine twice	5	(222, 224, 227, 234, 238)
14	Drug prescribed to which patient is allergic	Prescribing amoxicillin to patients with known allergy toward penicillin	4	(219, 227, 230, 238)
15	Changing the length of therapy	For five days instead of seven days	4	(222, 227, 230, 238)
16	Wrong concentration/strength	0.45% NaCL instead of 0.9%	4	(222, 223, 227, 238)
17	Wrong patient	Prescribing a drug to the wrong patient	4	(191, 222, 227, 238)
18	Medicine not indicated	Prescribing ineffective drug for indication	3	(224, 229, 234)
19	Wrong direction/instruction	Wrong administration instruction for nurses	3	(223, 226, 238)
20	Omission of dose	Not writing amoxicillin dose	3	(191, 230, 238)
21	Omission of frequency/interval	Not writing how many times the drug should be taken	3	(224, 230, 234)
22	Wrong rate of IV administration	Wrong rate of IV gentamicin administration	3	(191, 223, 238)
23	IV drug incompatibility		2	(219, 238)
24	Wrong administration technique by nurses	Crushing tablets which should not be crushed	2	(225, 238)

	Type of error	Explanation/example	Number of studies identified in	References
25	Wrong patient's weight/BSA on drug chart		2	(222, 238)
26	Compliance of patients (by phone interview of patients after discharge)	Taking drug twice daily instead of three times daily	1	(221)
27	Wrong preparation		1	(221)
28	Contraindication		1	(227)
29	Wrong quantity		1	(227)

4.4.7. Types of contributions

Eight studies (86, 219, 220, 222, 226, 227, 236, 239) did not mention the types of pharmacists' contributions. The remaining 17 studies highlighted 15 different types of contributions (Table 4.7). Answering queries about drug use, education of other healthcare professionals and making cost savings were most commonly documented.

Table 4.7: Pharmacists' contributions

	Type of contribution	Explanation/example	Number of studies seen in	References
1	Reactive information giving in response to other healthcare professionals' queries	Information about drug usage	7	(117, 221, 228, 229, 235, 237, 238)
2	Education of healthcare professionals	About different formulation	6	(117, 191, 223, 228, 229, 240)
3	Cost saving	Change drug to a cheaper one	5	(117, 224, 228, 229, 234)
4	Medication reconciliation	Take history of all medications patient taking regularly before admission	3	(233, 235, 238)
5	Education of patients or parents	About side effects	3	(221, 232, 240)
6	Participating in doctors' round	To provide information and recommendations to doctors	3	(117, 228, 229)
7	Recommendations and suggestions	Using combination of drugs	3	(221, 225, 230)
8	Annotating prescriptions with administration information	With food/milk	3	(224, 234, 238)
9	Providing feedback+ dosing chart to doctors	To help prescribing the correct dose	2	(223, 232)
10	Introduction of new prescribing chart form	Using a clearer drug chart	1	(223)
11	Developing internal clinical guidelines		1	(117)
12	Assessment+ feedback of doctors		1	(231)
13	Staff support		1	(229)
14	Providing dosing supporting tools	To help nurses and parents measuring the correct dose	1	(240)
15	Implementing new reporting form		1	(191)

4.4.8. Acceptance of recommendations by doctors

Nine studies (220, 222, 224, 225, 227, 229, 236-238) identified the percentage of doctors' acceptance of all pharmacists' recommendations. The acceptance rate ranged between 24-98%. None of the 25 studies identified the acceptance rate by healthcare professionals other than doctors. All studies identified a more than 50% acceptance of pharmacists' recommendations apart from a US study by Cesarz et al. 2013 (227). They identified only 24% of all recommendations were accepted by doctors in an emergency department and did not explain the reason for the low rate. Maat et al. 2013 (222) also identified a slightly low rate of acceptance (57.5%) in a specialist children's hospital in Netherlands. The authors stated that the reason for this was because many patients were either discharged or transferred to other units, received once only medications or because doctors had no time.

4.5. Discussion

Healthcare professionals should take particular care when treating paediatric patients because they are more vulnerable to medication errors than adults. Different strategies have been applied; including clinical pharmacy services to try to prevent this. Clinical pharmacists work in various healthcare specialities, including paediatric wards, to not only prevent medication errors but also to provide other contributions that lead directly to improving healthcare services for patients.

Many studies note the effects of clinical pharmacists on reducing the rate of medication errors, but this review only identified 25 studies that directly researched the effects of clinical pharmacists in paediatric patients. Sixteen of these studies (64%) identified an error rate. The first step in measuring the effects of clinical pharmacists on reducing error rates would logically be to identify the rate of errors

using a specific denominator. The second step is to identify the rate of errors before and after starting clinical pharmacy services or a specific intervention from them. However, only six studies (24%) identified the error rate before and after the implementation of clinical pharmacists' services. This ranged from 6.2-78.1% of all orders before to 1.1-35.2% of all orders after intervention. All of these studies showed that clinical pharmacists were able to reduce error rates.

The most common contributions identified in this review were related to interactions of the clinical pharmacist with other healthcare professionals, i.e., educating them and answering their queries. A previous systematic review of the different types of contributions by clinical pharmacists was conducted in general emergency departments by Cohen et al. (2009) (214). Similar to my research, 17 studies were included and the most common types of contributions were related to educating, consulting, and answering healthcare professionals' questions. This supports the information provided by the American College of Clinical Pharmacy (199), which states that clinical pharmacists are considered important sources of knowledge by healthcare professionals.

Another systematic review by Kaboli et al. (2006) (218), of all peer-reviewed English-language articles published January 1985 to April 2005, identified different activities by clinical pharmacists in relation to adult patients only. They found 36 relevant articles and identified three types of activities: medication reconciliation, participating in doctors' rounds, and drug-class-specific pharmacist services, e.g., providing inpatient anticoagulation services. The last type of pharmacists' activities was not identified in my review in children. Similar to my review, medication reconciliation and participating in doctors' rounds were identified by Kaboli et al. The current thesis also identified a further 13 types of activities. These pharmacists'

contributions such as education of healthcare professionals and patients, are not specific for children, but were not considered by Kaboli et al.

Even though two thirds (64%) of all studies only identified the rate of medication errors after starting clinical pharmacy services, they all stated that clinical pharmacists were effective either in reducing the rate of errors or in detecting errors. However, some studies also included the effects of clinical pharmacists on other important measures. For example, Chan et al. (1990) (226) found that the rate of waste of medications was decreased after implementing clinical pharmacist services, as they stopped supplying medications for discharged patients who already had enough of the medicine from their admission. Moreover, for doctors and nurses, a saving of time was seen, as they were less frequently consulted regarding medications at discharge, since the pharmacists already knew patients' diagnoses and medications from their visits to the paediatric ward.

Some studies identified the causes of errors. For example, Koren et al. (1991) (230) found that most dosage errors occurred as a result of miscalculation when a decimal point was misplaced. This might lead to interventions to improve the performance of healthcare professionals through discussing and providing feedback about errors to them. Providing feedback is an effective method of reducing the rate of errors, as demonstrated by Angalakuditi et al. (2003) (232) who found that prescribing the correct dose by doctors increased from 38.2% to 98.7% after feedback by pharmacists.

The types of errors needing intervention by pharmacists were identified in 21 out of 25 studies. The most common type was wrong dose. This was followed respectively by wrong drug, wrong route of administration, incomplete prescriptions, and omission of medications. Similar to this review, a previous systematic review found that wrong dose was the most common type of error in children (17).

The rate of acceptance of pharmacists' recommendations by doctors was only measured in a third of studies (nine studies) and the acceptance rate varied from 24 to 98%. It is important to measure the rate of acceptance by all healthcare professionals who are involved in medication errors and monitor why feedback is not accepted.

Similarly to my systematic review of all studies of errors in paediatric patients **(Chapter 2)**, the majority of clinical pharmacists' studies were conducted in the US, followed by the UK, and in specialised paediatric hospitals. This illustrates the interest of these two countries in identifying and preventing medication errors and their implementation of clinical pharmacy services, especially in children's hospitals. Most studies (nine) were conducted in the US where the medicines management system is completely different from the UK. Three studies were conducted in the UK but in three different settings (neurosurgical ward, haematology/oncology ward and specialist children's hospital). These three studies do not provide much information about pharmacists' contributions and mentioned only medication reconciliation and reviewing of prescriptions. Clinical pharmacy is an expensive resource in the UK and only three studies were identified which assessed their efficacy on reducing errors in paediatric patients but no other measures, such as cost saving.

Only two studies were conducted in Asia (8%) and one study was conducted in Africa (4%). The North American and European studies were conducted in high-income countries whereas the Asian and Africa countries were middle-income countries. This shows the high interest of high-income countries in identifying the pharmacists' efficacy on reducing the error rate in paediatric patients unlike other countries which may have no clinical pharmacy services. This also shows the narrow spread of countries. Only one Middle East country (Egypt) was identified with no studies identified from my country (Saudi Arabia) to show the effect of pharmacists on

reducing paediatric medication errors, even though there are clinical pharmacy services in some hospitals there. Therefore more work is needed to assess the effect of clinical pharmacy services on reducing error rates particularly in paediatric settings in Saudi Arabia.

This review provided the rate/number of errors prevented or decreased after the implementation of paediatric clinical pharmacy services in the literature. It also provided me with knowledge of pharmacists' activities and the different types of errors in which they intervene. This information was used in the methodology for my own study **(Chapter 5)** to create data collection lists of pharmacists' contributions and interventions, adapted from this systematic review and other important sources.

Three different methods of data collection were identified in this review. Chart review and review of incident reports were mainly used by pharmacists to identify prescribing errors and medication errors in general. Direct observation of nurses and/or parents was the primary method used to identify administration errors. However, none of the included studies were found to have used direct observation of paediatric pharmacists. Pharmacists make many interventions on a regular basis, but these are often not documented or reported due to time and workload constraints (241). The method of direct observation of clinical pharmacists allows the pharmacists to focus on their daily jobs while the researcher records their activities. With direct observation many problems related to self-reporting or incident reporting, such as, under reporting can be avoided (242, 243).

This review has a number of limitations. Few studies were identified. Moreover, many included studies do not contain enough information, especially regarding the types of contributions. Different methodologies and denominators make comparison between studies difficult. Even though some studies used the same methods of data

collection to identify the same type of error rate, they used different denominators which makes comparison impossible. Fifteen out of 40 studies (37.5%) were excluded as they had a quality rating of less than 6. This indicates that many studies that identified the effect of pharmacists' activities on reducing errors had low methodological quality or they did not report all the information required for the assessment of quality. Twenty studies were available as full papers and 20 others were only available as conference abstracts. Unsurprisingly less full articles, compared to abstracts, were excluded because of low quality rating (2 vs. 13) as the chance to identify the 10 criteria used for quality assessment was more likely. It is a shame that the conference abstracts were not written up as full papers, to fully demonstrate their methods and results.

4.6. Conclusion

Only 25 studies were identified describing the ability of clinical pharmacists to reduce medication errors in paediatric patients. It is important to have more literature on this topic to compare the percentages of different types of medication errors prevented by clinical pharmacists. It is also important to link the different clinical pharmacists' contributions with different types of medication errors prevented by each type of contribution.

Chapter 5: An observational study of the role of the paediatric clinical pharmacist

5.1. Introduction

My systematic literature review to identify what is known already about the effect of paediatric clinical pharmacy services on reducing the rate of medication errors **(Chapter 4)** showed that there had been no study that used direct observation of paediatric pharmacists to assess their contributions and interventions in the healthcare services provided to patients. Twenty-five relevant studies were identified of which 19 used chart review, four review of error incident reports, one used direct observation of nurses and parents and the last one used both chart review and direct observation of parents.

Direct observation allows the pharmacists to focus on their job while the researcher records their contributions and interventions. It also allows the researcher to be involved in the event in its natural setting e.g. conversations between the pharmacist and other healthcare professionals and patients/families. This allows them to have a better understanding of the situation and to collect and document more accurate data e.g. document potential as well as actual medication errors. With direct observation many problems related to self-reporting or incident reporting (such as under reporting) can be avoided. It also helps the observer to document the outcome and the response of healthcare professionals, i.e. either to accept proposed interventions or not (242, 243).

Pharmacists are known to make many interventions on a regular basis, but these are often not documented due to time and workload constraints (241). Direct observation

was therefore hypothesised to be the most robust method of data collection in order to get a more accurate picture of the role of the paediatric clinical pharmacist.

5.2. Aim

The aim was to observe paediatric pharmacists doing their day to day work in order to describe their role, to document their contributions to patient care and safety and to identify errors that are being prevented by their presence. I was not able to do a before and after study as clinical pharmacy services are already established.

5.3. Methods

5.3.1. Setting

Because contributions and interventions made by pharmacists can vary in different circumstances; I decided to collect data from several paediatric specialties in three different hospitals to gain a broad overview.

5.3.1.1. Derbyshire Children's Hospital (DCH) at the Royal Derby Hospital

The Derbyshire Children's Hospital (DCH) at the Royal Derby Hospital includes five paediatric wards classified according to patient ages and conditions (244, 245):

1. Neonatal Intensive Care Unit (NICU): babies born with any health condition (or prematurity) admitted directly from the labour wards.
2. Dolphin ward (Paediatric High Dependency Unit (PHDU)): children with a critical illness or requiring one to one care.
3. Ladybird ward (LBW): children under 2 years of age with acute medical or surgical conditions.
4. Puffin ward (PW): children older than 2 years with acute medical or surgical conditions.
5. Sunflower ward (SFW): children undergoing elective surgery.

Four specialist clinical pharmacists and one shift working pharmacist were shadowed.

The aim was to shadow pharmacists to document interventions and contributions made for at least 1000 patients in DCH. This number of patients was chosen because during a pilot study it was anticipated that around 25 patients would be a realistic number to be seen per visit. Therefore I decided to aim for at least 40 visits which was possible in the time available.

5.3.1.2. Nottingham Children's Hospital (NCH) at Queen's Medical Centre in Nottingham

This hospital is a tertiary referral children's hospital with 116 beds, which admits 40,000 patients each year. Data was collected from ten wards with different specialities (246):

1. NICU (Neonatal Intensive Care Unit (medical and surgical))
2. PICU (Paediatric Intensive Care Unit)
3. Paediatric High Dependency Unit (PHDU)
4. Ward D33 (cystic fibrosis and gastroenterology related diseases)
5. Ward D34 (surgical unit including: orthopaedics; spinal; ear, nose and throat; cleft lip and plate; ophthalmic and maxillofacial).
6. Ward D35 (general surgery)
7. Ward E17 (renal and urological conditions)
8. Ward E39 (oncology ward)
9. Ward E40 (neuroscience including neurosurgery, neuro-oncology and neurology)
10. Ward E37 (medical short stay unit)

Eight pharmacists were shadowed: (five specialist pharmacists (in PICU, nephrology, neonatology, oncology, parenteral nutrition and cystic fibrosis), two senior clinical pharmacists and one junior clinical pharmacist).

5.3.1.3. NICU at Nottingham City Hospital

Visits to a neonatal unit at the City Hospital on five consecutive days were arranged with one specialist clinical pharmacist. Data collected from this unit were combined with the data collected from NCH because they are part of the same NHS Trust.

The aim was to shadow clinical pharmacists during a 6-week period in Nottingham. This was the time the Chief Pharmacist at NCH agreed and would give the opportunity to accompany pharmacists to wards with different specialities.

5.3.2. Ethics

According to the UK National Research Ethics Service the project was classified as service evaluation and therefore it was not necessary to obtain formal ethical or Research and Development department approval (247). I was required to follow the clinical governance procedures of the NHS trusts where the study took place. This included Criminal Records Bureau clearance, obtaining honorary contracts and undergoing induction procedures. Permission was obtained from the Chief Pharmacists, Chief Nurses and clinical governance leads in each hospital.

In accordance with the requirements of the UK National Information Governance Board for Health and Social Care (248), consent was required to look at any child's prescriptions and/or medical notes from his/her carer. Consent was taken from patients themselves only if they were 16 years old or more and understood an explanation of the project. A consent form was designed in accordance with those used by the National Research Ethics Service (Figure 1 in Appendix 3). I was supervised taking consent on the wards of the DCH during a pilot study with my supervisor until I was judged competent.

Reasons for not obtaining permission from patients/carers included their refusing for any reason, carers not being available or special precautions being in place (such as not being able to enter the patient's room due to infection control measures). If I could not obtain consent, data was not seen or recorded.

5.3.3. Data collection form

After reviewing each relevant study from the clinical pharmacists systematic literature review **(Chapter 4)** in detail, and discussion with my two supervisors (a paediatric clinical pharmacist and a consultant paediatrician), none of the studies were felt to provide a comprehensive list of contributions and interventions. A preliminary data collection list was therefore written as described below. It was spilt into two sections:

1. Interventions: where a medication error was identified by the pharmacist who intervened to prevent further doses of the medication reaching the patient. These interventions (Table 5.1) were adapted from the American Society of Hospital Pharmacists (82), the Pharmaceutical Care Network Europe Foundation (249) and a list of interventions adapted from 21 studies in **Chapter 4** (117, 191, 219-230, 232, 234, 236-240).

Table 5.1: Medication errors identified and addressed by pharmacists.

I	Type of medication error
1	Omission error
2	Wrong dose (including dose amendment for accuracy of administration)
3	Illegible prescribing
4	Wrong frequency/duration/interval
5	Wrong ward documented on drug chart
6	Monitoring errors (including drug level not monitored appropriately & providing recommendations to adjust dose or interval)
7	Wrong medication prescribed
8	Wrong route of administration prescribed
9	Unnecessary medication prescribed
10	Duplication of medication
11	Wrong formulation prescribed
12	Wrong time of administration selected/ written on drug chart
13	Wrong concentration/strength prescribed
14	Wrong weight documented on drug chart
15	Wrong rate of administration prescribed
16	Drug interaction
17	Contraindication
18	Allergy error (prescribing to a patient allergic to that medication)

19	Adherence error by patient or carer
20	Wrong date on drug chart

2. Contributions to care: made by the pharmacist to enhance the care provided to patients (Table 5.2). These were adapted from the Royal Derby Hospital medicines code (250), the NHS careers website (working as a hospital pharmacist) (251) and from a list of contributions from 17 studies in **Chapter 4** (117, 191, 221, 223-225, 228-235, 237, 238, 240).

Table 5.2: Different types of contributions made by pharmacists.

Code	Type of contribution
A	Drug history checked
B	Allergy status checked
C	Answering queries/educating nurses and doctors
D	Supplying medications
E	Annotating prescriptions with information e.g. administration instructions
F	Education and providing of information to patient/carer
G	Therapeutic drug monitoring (record blood level/ document on prescription when levels are due to be taken/ advice to doctors or nurses)
H	Miscellaneous

Using this preliminary data collection list I conducted a pilot study for five days (one day every week for five consecutive weeks) with my supervisor (Dr Conroy) in the paediatric wards in DCH. The aim of this pilot study was to assess the preliminary list and to create a comprehensive list and data collection system before starting my study. Another aim was to practice taking consent from parents or children aged 16 years or older under supervision. Three interventions were added to the list (wrong ward, date and weight documented on drug chart) after the pilot study.

5.3.4. Data entry

All data was entered into a password protected Excel spread sheet according to the following: pharmacists' code, date, ward, patient number, age, sex, number of prescriptions, type of contributions, type of intervention, explanation and response of

healthcare professionals to identified medication errors (accepted and corrected, not measured or not accepted). Each prescribed drug was considered to be one prescription. All data from Derby and Nottingham hospitals were separately analysed.

Data entries from 10-day visits (220 patients (16%)) were reviewed by an independent person to ensure that the data was entered and categorised correctly.

5.4. Results

Only one mistake out of 671 data entries (0.15%) was identified independently by my colleague. This mistake was duplication of an entry.

5.4.1. Results from DCH

Five pharmacists were shadowed on 61 separate days (total 150 ward visits) on the five paediatric wards for the period between the 7-6-2012 and 18-4-2013. During these visits 4,204 prescriptions for 1,039 patients were checked by pharmacists (472 patients (45%) were new admissions). There was at least one intervention or contribution for 785 patients (75.6%). In total 2,637 contributions (62.7% of all prescriptions) and 366 interventions on medication errors (8.7% of all prescriptions) were observed.

5.4.2. Results from NCH

Nine pharmacists were shadowed on 30 separate days (total 47 ward visits) over the period between the 8-5-2013 to 4-7-2013 on ten paediatric wards. During these visits 1,830 prescriptions for 332 patients were checked by pharmacists (86 patients (26%) were new admissions). There was at least one intervention or contribution for 210 patients (63.3%). In total 674 contributions (36.8% of all prescriptions) and 139 interventions on medication errors (7.6% of all prescriptions) were observed.

5.4.3. Summary of all pharmacists' visits

All patients were aged 17 years or less. More new patients were identified in DCH compared with NCH (45% vs. 26% of all patients). Similar range of prescriptions per patient was identified in both hospitals (range: 0-18 vs. 0-17; median: 5 vs. 3). Similar rates of interventions were identified in DCH and NCH (8.7% vs. 7.6% of all prescriptions) while more pharmacists' contributions were identified in DCH compared with NCH (62.7% vs. 36.8% of all prescriptions).

Table 5.3: Summary of visits to paediatric and neonatal wards

	DCH	NCH	Total
Age range	1 day- 17 years		
Number of patients (boys vs. girls)	1,039 patients (561 boys & 478 girls)	332 patients (191 boys & 141 girls)	1,371
Number of new admissions (% of all patients)	472 (45%)	86 (26%)	558 (40.7%)
Number of prescriptions (Range/Mean/Median) per patient	4,204 prescriptions (0-18/5.5/5)	1,830 prescriptions (0-17/4/3)	6,034
Number of pharmacists' shadowed	5	9	14
Number of paediatric wards	5	10	15
Number of separate day visits	61	30	91
Number of ward visits	150	47	197
Number of patients with intervention or contribution (% of all patients)	785 (75.6%)	210 (63.3%)	995 (72.6%)
Number of contributions (% of all prescriptions)	2,637 (62.7%)	674 (36.8%)	3,311 (54.8%)
Number of interventions (% of all prescriptions)	366 (8.7%)	139 (7.6%)	505 (8.4%)

5.4.4. Interventions

During the study period; 505 medication errors were identified and interventions made (366 interventions in DCH and 139 interventions in NCH). These errors were grouped into 20 different categories (I1-20) (Table 5.4).

Table 5.4: Interventions made in DCH and NCH

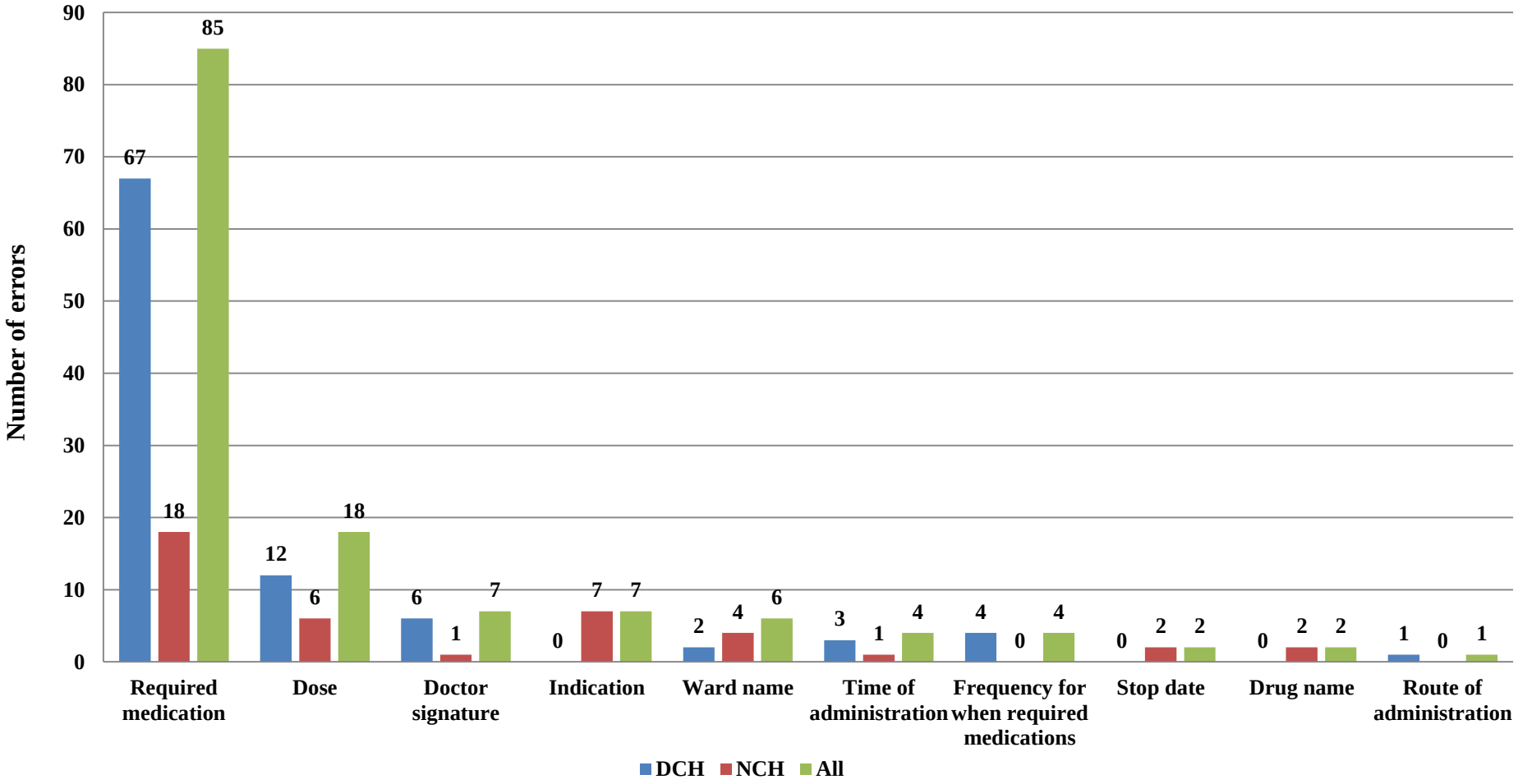
Code	Type of medication errors	DCH 4,204 prescriptions for 1,039 patients	NCH 1,830 prescriptions for 332 patients	All (% of all errors)
I		Number of interventions (% of all prescriptions)		
1	Omission error	96 (2.3%)	45 (2.5%)	141 (27.9%)
2	Wrong dose	94 (2.2%)	27 (1.5%)	121 (24%)
3	Illegible prescribing	85 (2%)	12 (0.7%)	97 (19.2%)
4	Wrong frequency	23 (0.5%)	6 (0.3%)	29 (5.7%)
5	Wrong ward	19 (0.4%)	7 (0.4%)	26 (5%)
6	Monitoring error	9 (0.2%)	9 (0.5%)	18 (3.6%)
7	Wrong medication prescribed	10 (0.2%)	3 (0.2%)	13 (2.6%)
8	Wrong route of administration	7 (0.2%)	6 (0.3%)	13 (2.6%)
9	Unnecessary medication	2 (0.04%)	10 (0.5%)	12 (2.4%)
10	Duplication	6 (0.1%)	3 (0.2%)	9 (1.8%)
11	Wrong formulation	1 (0.02%)	6 (0.3%)	7 (1.4%)
12	Wrong time of administration	6 (0.1%)	0	6 (1.2%)
13	Wrong concentration/strength	1 (0.02%)	3 (0.2%)	4 (0.8%)
14	Wrong weight documented on drug chart	1 (0.02%)	1 (0.1%)	2 (0.4%)
15	Wrong rate of administration	1 (0.02%)	1 (0.1%)	2 (0.4%)
16	Drug interaction	1 (0.02%)	0	1 (0.2%)
17	Contraindication	1 (0.02%)	0	1 (0.2%)
18	Allergy error (prescribing a medication to a patient who is allergic to that medication)	1 (0.02%)	0	1 (0.2%)
19	Compliance error by patient/carer	1 (0.02%)	0	1 (0.2%)
20	Wrong date documented on drug chart	1 (0.02%)	0	1 (0.2%)
Total (% of all prescriptions)		366 (8.7%)	139 (7.6%)	505 (8.4%)

The most common type of pharmacists' intervention was for an omission error followed by wrong dose, illegible prescribing and wrong frequency. These are discussed in more detail in the following sections.

5.4.4.1. Omission error (2.3% of all prescriptions)

This was the most common type of error (involving 15 different sub-categories) identified in 141 cases (27.9% of all errors). Similar error rates were identified in DCH and NCH (2.3 vs. 2.5% of all prescriptions). The most common sub-types of omission error were omission of medications on admission (60.3% of all omission errors or 15.2% of all new patients) followed by omission of dose (12.8% of all omission errors). No omission errors were considered serious. Figure 5.1 illustrates the top ten types of omission errors.

Figure 5.1: Top ten types of omission errors



5.4.4.2. Dosing error (2% of all prescriptions)

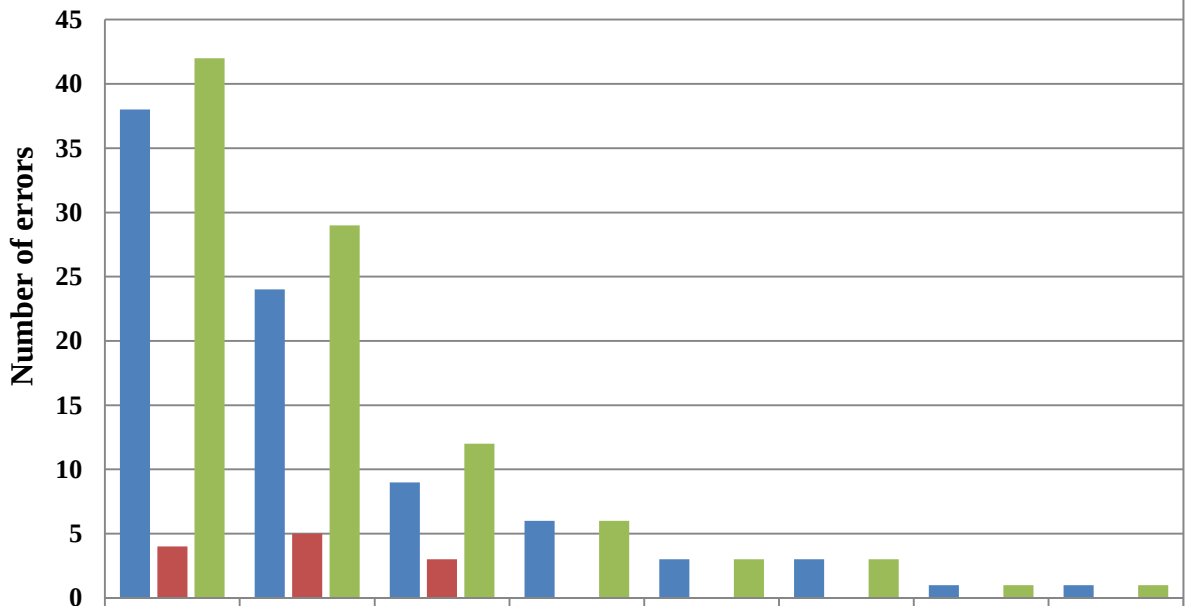
The second most common errors were dosing errors identified in 121 cases (24% of all errors). Dosing errors included:

1. Dose amended for accuracy of administration (63, 52%). Pharmacists changed the dose to be measurable by nurses.
2. Overdose (28, 23.1%). These included: three double doses, two doses calculated according to actual weight for overweight patients, one tenfold dose error (diazepam), one misplacing of numbers (gentamicin 210 mg instead of 120 mg), one adding a zero (1400 mg cefuroxime instead of 140 mg) causing a tenfold error and one was wrong unit (co-amoxiclav 600g instead of 600mg).
3. Under-dose (28, 23.1%). The cause for under-dose was identified in one case and was because the patient previously had impaired renal function which improved and therefore the dose of cotrimoxazole was required to be increased. In three cases doctors were asked to increase the dose because the patients had gained weight. In two cases pharmacists advised doctors to double the dose of antibiotics because of severe infection.
4. Side effect of a medicine (1, 0.9%) (advised doctor to decrease the dose of Modigraf® because of side effect (diarrhoea)).
5. Dose of morphine was written for heparin and vice versa (1, 0.9%) for a one day old boy in the intensive care unit.

5.4.4.3. Illegible prescribing (1.6% of all prescriptions)

Illegible prescribing was the third most common type of error identified in 97 cases (19.2% of all errors). The illegible prescribing rate was higher in DCH compared to NCH (2% vs. 0.7% of all prescriptions). The most common examples of illegible prescribing were unclear drug name (43.3%) followed by unclear dose (29.9%) and unclear time of administration (12.4%). Figure 5.2 illustrates all types of illegible prescribing.

Figure 5.2: Types of illegible prescribing



	Drug name	Dose	Time of administration	Strength	Frequency	Route of administration	Rate of administration	Ward name
DCH	38	24	9	6	3	3	1	1
NCH	4	5	3	0	0	0	0	0
All	42	29	12	6	3	3	1	1

5.4.4.4. Wrong frequency, duration or interval (0.5% of all prescriptions)

This type of error was identified in 29 cases (5.7% of all errors). An example was prescribing paracetamol five times a day instead of four times a day.

5.4.4.5. Wrong ward documented on drug chart (0.4% of all prescriptions)

Twenty-six charts were identified with the wrong ward documented on the drug chart (5% of all errors). All of these cases were because of patients transferring from one ward (mostly from ICU or PHDU) to other units without changing the ward name.

5.4.4.6. Monitoring error (0.3% of all prescriptions)

Monitoring errors were identified in 18 cases (3.6% of all errors) and included:

1. Pharmacist documenting blood level if it was not recorded by other healthcare professionals (nine cases).
2. Pharmacists advising dose or interval adjustment to doctors when blood levels were outside the therapeutic range (nine cases).

5.4.4.7. Wrong medication prescribed (0.2% of all prescriptions)

Thirteen medications (2.6% of all errors) were found inappropriate by pharmacists because:

1. Not according to hospital guideline (six cases) mostly when treating babies with sepsis using combination of antibiotics which changes after the age of three months.
2. More potent drug/strength needed (two cases): nicotine patch and diuretic (furosemide)
3. Similarity in concentration in one case (0.45% dextrose was prescribed instead of 0.45% sodium chloride)
4. Not suitable for indication in one case: cefotaxime was recommended to be used instead of cefuroxime for management of meningitis
5. Not recommended in children in one case: prochlorperazine

6. Not recommended for children less than 12 months old in one case: chlorphenamine
7. Not recommended for children less than 12 years old in one case: codeine

5.4.4.8. Wrong route of administration (0.2% of all prescriptions)

Thirteen medications were prescribed with wrong route of administration (2.6% of all errors):

1. Nine medications were prescribed IV or IM even though patients could take orally
2. One medicine was prescribed orally for a patient who was not able to eat or drink.
3. Salbutamol was prescribed IV/Nebuliser for a patient and changed to nebuliser.
4. Buccastem was prescribed sublingually (should be buccal).
5. IV/oral to NG (one case)

5.4.4.9. Unnecessary medication (0.2% of all prescriptions)

Twelve cases (2.4% of all errors) involved prescribing unnecessary medications:

- Ten because courses of antibiotics were complete and should be discontinued
- One to stop prophylaxis (IV ceftriaxone and IV aciclovir) for a 14 year old child with stroke
- To stop domperidone because the patient started to eat and drink

5.4.4.10. Duplication (0.1% of all prescriptions)

Medications (e.g. ondansetron, paracetamol and ibuprofen) were written both as required and regularly in nine cases (1.8% of all errors).

5.4.4.11. Wrong formulation (0.1% of all prescriptions)

Seven cases (1.4% of all errors) were associated with prescribing the wrong formulation e.g. capsule instead of liquid.

5.4.4.12. Wrong time of administration (0.1% of all prescriptions)

Six cases (1.2% of all errors) of medications in DCH were prescribed at the wrong time, e.g. 16.00 instead of 18.00.

5.4.4.13. Wrong concentration/ strength (0.07% of all prescriptions)

Four cases (0.8% of all errors) of wrong concentration/ strength, e.g. 0.45% sodium chloride to 0.9%, were identified.

5.4.4.14. Wrong patient weight documented (0.03% of all prescriptions)

Two cases (0.4% of all errors) were identified in which the patients' weight on the drug chart was not the same as in the medical notes. This also required doctors to change all doses calculated according to the wrong weight.

5.4.4.15. Wrong rate of administration (0.03% of all prescriptions)

Two cases (0.4% of all errors) were identified in which wrong rate of IV fluid was identified in one case and of morphine IV in another case.

5.4.4.16. Drug interaction (0.02% of all prescriptions)

One case (0.2% of all errors) was identified in DCH. Both codeine and morphine were prescribed regularly for a patient.

5.4.4.17. Contraindication (0.02% of all prescriptions)

One case (0.2% of all errors) was identified in DCH. Non-recommended medication in children (sodium chloride 0.18% and glucose 4% solution) was prescribed.

5.4.4.18. Allergy error (0.02% of all prescriptions)

One case (0.2% of all errors) was identified in DCH. Patient with penicillin allergy was prescribed amoxicillin.

5.4.4.19. Compliance error by patient/carer (0.02% of all prescriptions)

One case (0.2% of all errors) was identified in DCH. The mum was applying Fucidin® cream on the child's skin only once daily but the label and the BNF both say twice daily therefore advice given to mum.

5.4.4.20. Wrong date documented on drug chart (0.02% of all prescriptions)

One case (0.2% of all errors) was identified in DCH of which the date on the drug chart was not correct.

5.4.5. Contributions

3,311 pharmacists' contributions to healthcare were recorded (2,637 contributions in DCH and 674 contributions in NCH). These contributions were grouped into eight categories (A-H) (Table 5.5).

Table 5.5: Contributions made in DCH and in NCH

Code	Type of contribution	DCH (4,204 prescriptions for 1,039 patients for 150 ward visits)	NCH (1,830 prescriptions for 332 patients for 47 ward visits)	Total (6,034 prescriptions for 1,371 patients for 197 ward visits)
		Number of contributions		
A	Drug history checked (% of all new patients)	620 (97.7%)	80 (93%)	700 (97%)
B	Allergy status checked (of all new patients)	550 (100%)	86 (100%)	636 (100%)
C	Answering queries/educating nurses and doctors (of all ward visits)	91 (60.7%)	19 (40.4%)	110 (55.8%)
D	Supplying medications (of all prescriptions)	435 (10.3%)	177 (9.7%)	612 (10.1%)
E	Annotating prescriptions with information e.g. administration instructions (of all prescriptions)	907 (21.6%)	253 (13.8%)	1160 (19.2%)
F	Education and providing of information to patient/carer (of all patients)	20 (1.9%)	6 (1.8%)	26 (1.9%)
G	Therapeutic drug monitoring (record blood level + document on prescription when levels are due to be taken) (of all ward visits)	8 (5.3%)	47 (100%)	55 (27.9%)
H	Miscellaneous (of all ward visits)	6 (4%)	6 (12.8%)	12 (6%)
Total number of contributions (of all prescriptions)		2,637 (62.7%)	674 (36.8%)	3311 (54.8%)

As can be seen; the most common pharmacists' contribution was annotating prescriptions with information followed respectively by checking drug history, checking allergy status and supplying medications. The overall contribution rate was 54.8% of all prescriptions. More contributions (mainly annotating prescriptions and answering queries) were identified in DCH compared to NCH (62.7 vs. 36.8% of all prescriptions). Unlike DCH, NCH provides bedside guidelines which doctors and

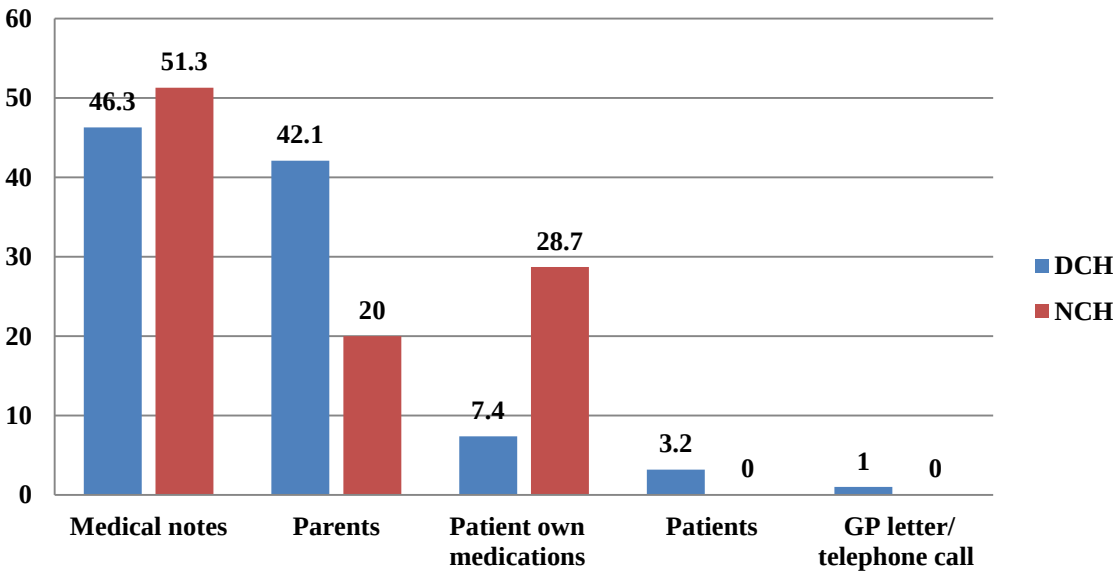
nurses can use to find out information required on some medications, which was thought to be the reason for the lower level seen.

Contributions are explained in more detail in the following sections.

5.4.5.1. Drug history

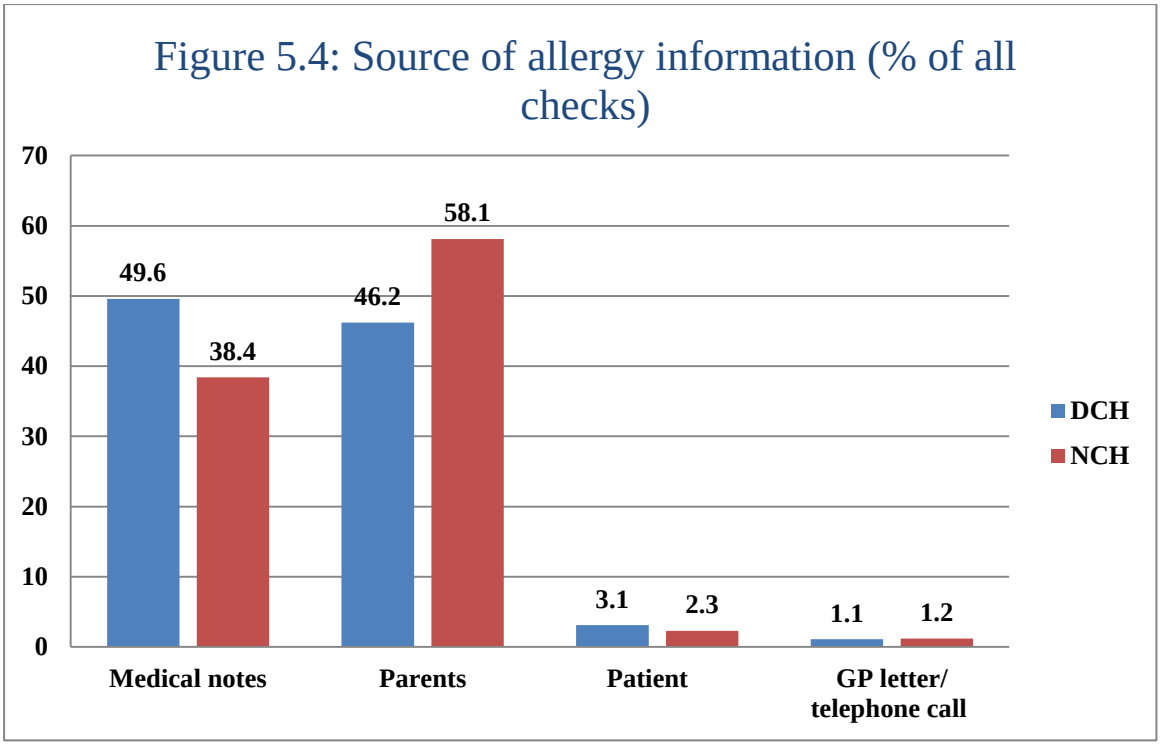
Drug history (i.e. history of all medications used regularly prior to admission) was checked for 461 new patients (97.7% of all new patients) in DCH and for 80 new patients (93% of all new patients) in NCH. This was mostly checked from information from the medical notes and parents (Figure 5.3).

Figure 5.3: Source of drug history (% of all checks)



5.4.5.2. Allergy checked

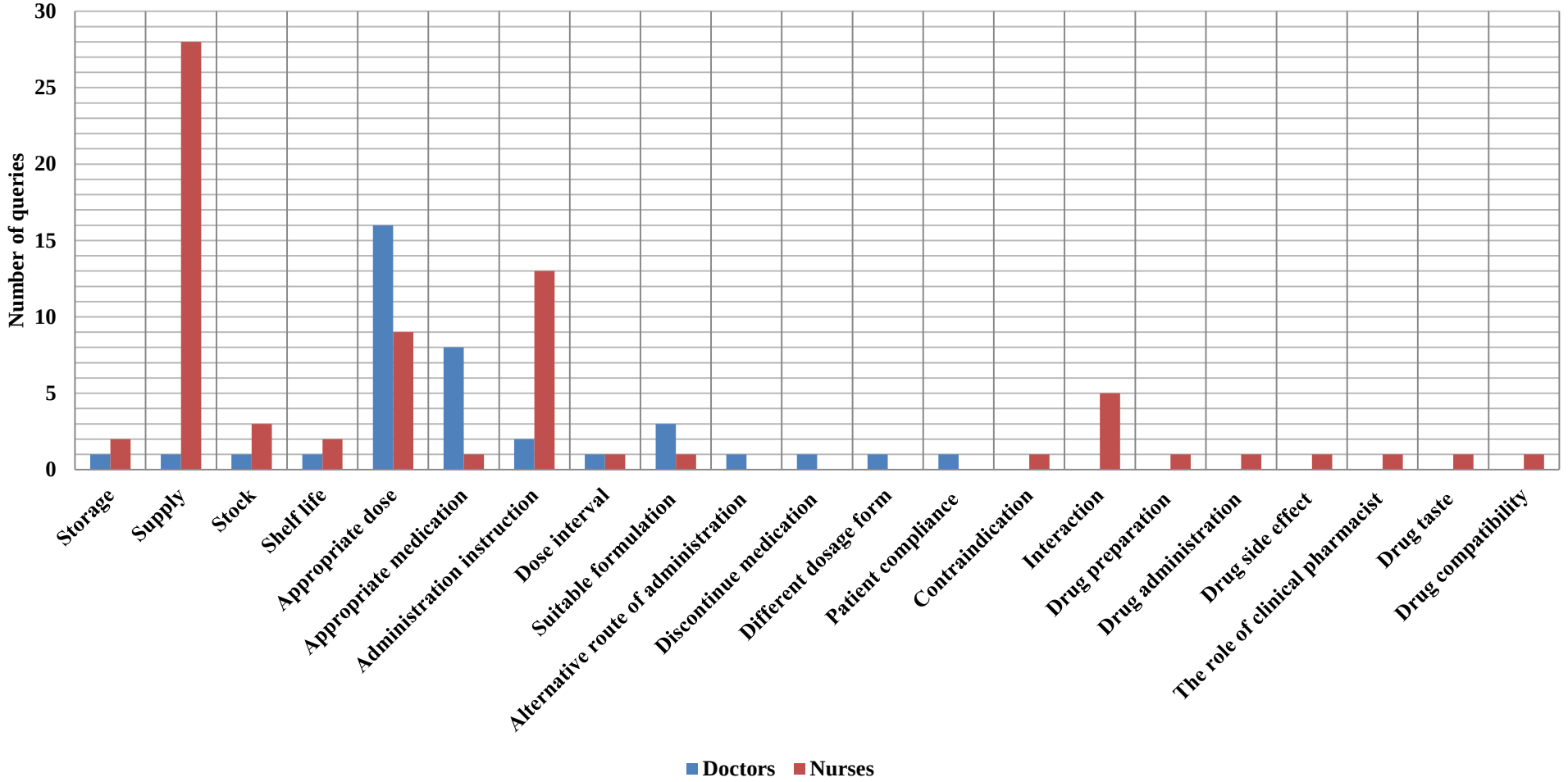
Allergy status was checked for all new patients in DCH and in NCH. Again this was mostly obtained from medical notes and parents (Figure 5.4).



5.4.5.3. Answering queries/educating nurses and doctors

Pharmacists answered 21 types of queries from doctors and nurses (Figure 5.5). Ninety one queries were answered by pharmacists in DCH and 19 queries in NCH. The most common queries asked by doctors involved choice of doses and medications. The most common queries by nurses were regarding drug supply and administration instructions.

Figure 5.5: Queries asked by doctors and/or nurses

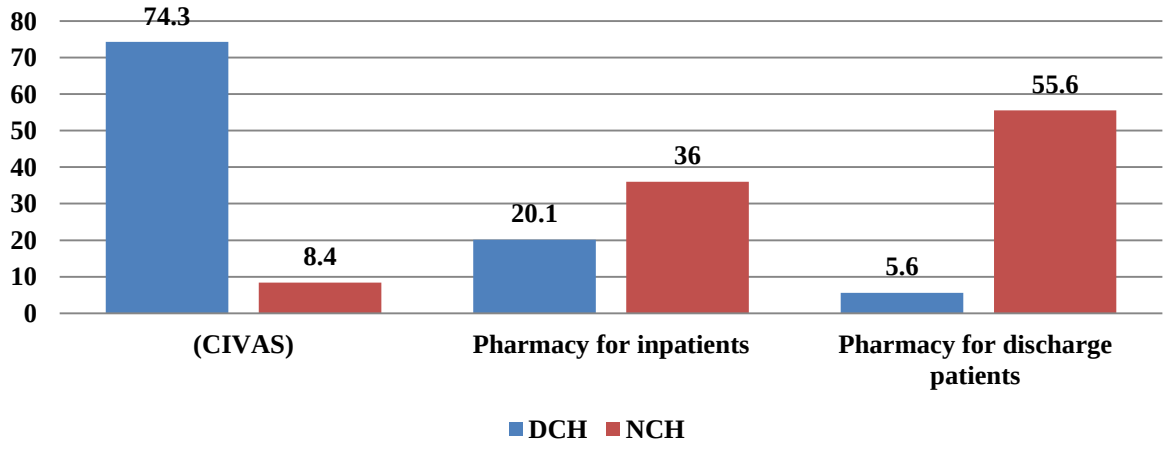


5.4.5.4. Supplying medications

Pharmacists are required to supply medications prescribed to patients which are not available as ward stock. These come from pharmacy for inpatients and discharges or from the central intravenous additive service (CIVAS) for pre-prepared IV doses for inpatients where stability data allows.

Pharmacists requested new labels for medications on six occasions (three in DCH and three in NCH) due to the lack of clarity of the label on a patient's own medicine, a change in dose or to add additional instructions. Pharmacists were also involved in disposing of expired or no longer needed medications. No medication was disposed of from DCH whereas seven medications were disposed of by pharmacists from NCH. Figure 5.6 illustrates the percentage of medications supplied from the aseptic units and from pharmacy (for either inpatient or discharge patient). Most medications requested by pharmacists in DCH were from the aseptic unit and in NCH were from the pharmacy. This is because DCH provide a comprehensive CIVAS services and NCH has a more limited service.

Figure 5.6: Sources of medications supplied (% of all supplied medications)



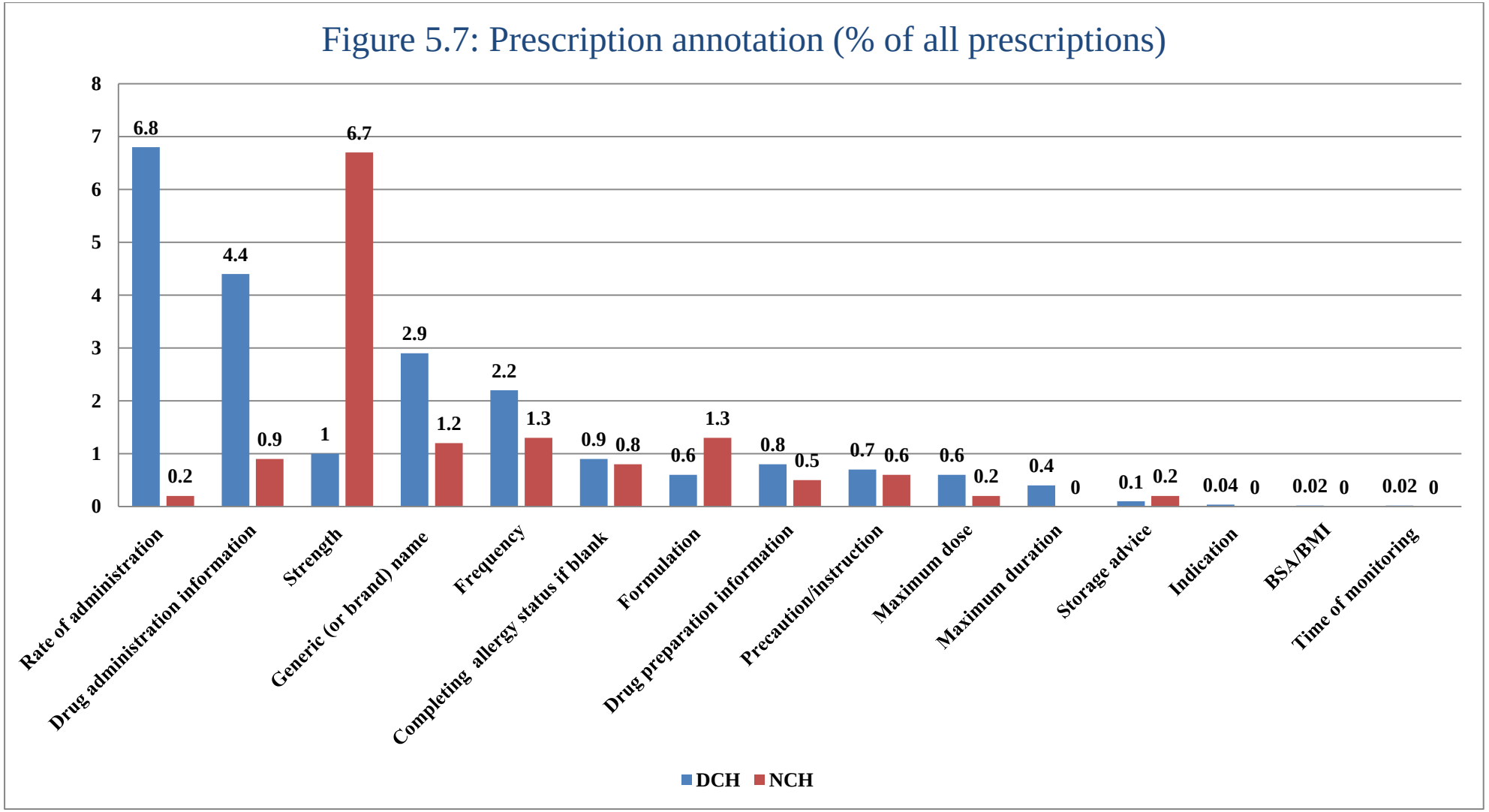
5.4.5.5. Annotating prescriptions

Pharmacists annotate prescriptions when important information is missing or when clarification/completion of the prescription is required. Prescriptions were annotated with 15 types of different information. The most common five were:

1. Rate of administration of IV medications e.g. vancomycin "infuse over 60 minutes"
2. Administration information, e.g. Tacrolimus 2 hours after food or one hour before food
3. Strength of formulations e.g. 2 puffs of ipratropium inhaler = 40mcg
4. Generic name (or brand name for drugs where it is important that the same brand is always used) e.g. amoxicillin/clavulanate instead of augmentin®
5. Frequency of medication administration on "as required" e.g. paracetamol QID

Pharmacists made 907 prescription annotations in DCH and 253 annotations in NCH (Figure 5.7).

Figure 5.7: Prescription annotation (% of all prescriptions)



More pharmacists' annotations were made in DCH than NCH, particularly about the rate of administration (6.8% vs. 0.2% of all prescriptions) and drug administration information (4.4% vs. 0.9% of all prescriptions). This may be because bedside guidelines are available in NCH but not in DCH. However, there were more prescriptions annotations with strength in NCH compared to DCH (6.7% vs. 1% of all prescriptions). This might be because more unlicensed medications were used in NCH compared to DCH, due to the more specialist patients treated there.

5.4.5.6. Education and provision of information to patient/carer

Information and education was provided to patients and parents 20 times in DCH and six times in NCH. This aimed to increase patients' adherence when using inhalers and to provide instructions about using discharge medications. Other education by pharmacists was related to educating parents on how to reconstitute antibiotic powders after the first bottle has finished and about the clinical effect of medications.

5.4.5.7. Therapeutic drug monitoring (TDM)

TDM is usually done for medications with a low therapeutic index or for patients with specific circumstances, e.g. renal impairment. Pharmacists' contributions involved recording the blood level of drugs and advising when the next blood level monitoring should be done. Pharmacists' activities regarding TDM were identified in 55 cases (eight in DCH and 47 in NCH). They also provide advice on dose adjustment when levels are not in the therapeutic range (e.g. gentamicin blood level). Most cases where patients were on low therapeutic index medications occurred on intensive care units, high dependency unit and specialised units. As NCH has more such speciality units this is likely to be the cause for more pharmacists' TDM activities in NCH compared to DCH.

5.4.5.8. Miscellaneous

Pharmacists also made ten other types of contributions on six occasions in DCH and six occasions in NCH. Examples of these include advising doctors to prescribe medications regularly instead of when required, doing a second check for medication administration with a nurse and changing one drug to a cheaper one.

5.4.6. Comparing the rate of contributions and interventions made by pharmacists in the same wards in different hospitals

Fifteen different paediatric wards were visited in Derby and Nottingham. Because data was collected from three different hospitals; I wished to compare activities in the same type of ward. Two wards can be compared: the NICUs and PHDUs (Table 5.6).

Table 5.6: Contributions and interventions identified in NICU and PHDU

Hospital	% of contributions (of all prescriptions)	% of interventions (of all prescriptions)	Number of visits	Number of pharmacists
NICU				
DCH	29.6	4.2	18	3
NCH	20.6	9.1	10	5
PHDU				
DCH	51.4	12.8	32	5
NCH	47.5	6.3	3	1

As can be seen; the highest rate of contributions in NICU and PHDU was identified in DCH. Higher interventions rates were identified in NICU at NCH compared with DCH. However, more interventions were identified in PHDU at DCH compared with NCH. The results cannot be generalised as only three visits by one pharmacist to PHDU were in NCH compared to 32 visits by five pharmacists in DCH.

5.4.7. Recommendations accepted by doctors

Some errors were corrected by pharmacists without asking doctors. These were related to illegible prescribing (clarity issues), omissions (ward name, time of administration, weight, date, age and hospital number), wrong paediatric wards, adherence errors by patients/ parents and accuracy of measurement. In total 138 errors were corrected by pharmacists (27.3% of all errors). Of 367 errors highlighted to doctors 365 (99.5%) errors were acknowledged and corrected. One doctor refused to correct an error and therefore an incident report was written. This doctor increased the dose of vancomycin regardless of a high blood level measured after the last dose. The other error was a recommendation from the pharmacist to change one diuretic to a more potent one. However, the doctor did not change the medication and preferred to discuss other options with other doctors. Therefore the response could not be measured.

5.4.8. Other activities

Paediatric pharmacists are involved in many activities other than those on ward visits. These include writing and keeping drug monographs up to date, participating in the Hospital's Guidelines Committee, the Trust Medicines Management Committee and the Paediatric, Obstetric and Neonatal Governance Groups.

Paediatric pharmacists in Nottingham have a monthly meeting with doctors and nurses to discuss current issues and to answer their queries. In both cities they are involved in teaching pharmacy, nursing and medical staff and medical students and supervising pre-registration and junior pharmacists. They are also involved in the development of prescription charts, and in Derby the development of the electronic prescribing system which is to be introduced soon.

5.5. Discussion

Medication errors occur on all paediatric wards **(Chapter 2)**. Different interventions have been implemented in order to reduce the rate of errors **(Chapter 3)**. One of the most effective interventions was a paediatric clinical pharmacist **(Chapter 4)**. To our knowledge this study is the first to use direct observation of pharmacists on paediatric wards and suggests that pharmacists improve healthcare services provided to paediatric patients and are an effective tool in identifying and preventing medication errors.

An Australian observational study by Stuchberg et al. 2007 (252) of six clinical pharmacists in adult medical and surgical wards (in two general hospitals) was carried out for six separate days during March and April 2004. They used a preliminary list of pharmacists' activities adapted from literature review and the experience of researchers. They divided the pharmacists' activities into four main groups involving 28 sub-groups and did not separate contributions from interventions. They identified 807 different activities for 195 patients. Most activities were related to review of medication charts, annotating prescriptions with information and checking drug history. In our study the pharmacists' activities were separately divided into contributions (eight types) and interventions (20 types) with a total of 3,816 different activities for 1,371 patients identified during 91 day visits. Similar to Stuchberg et al., annotating prescriptions with information was the most common contribution followed by drug history check. I did not define reviewing of medication charts as a contribution.

Basger et al.'s 2014 systematic literature review (253) identified English-language studies (in both adults and children) published from January 2000 to July 2013 that

used a classification system and identified drug-related problems, including medication errors. From the 268 studies reviewed, these authors identified 20 classification systems; most studies modified existing systems or devised their own. They concluded that no ideal classification system exists. For my current study I adapted two lists, one for contributions, the other for interventions, from studies in the systematic review of paediatric clinical pharmacy **(Chapter 4)**, as well as other sources. This aimed to provide a comprehensive list for paediatric pharmacists.

5.5.1. Results from DCH and NCH

DCH and NCH involve different specialities and therefore results identified from both hospitals cannot be directly compared. Similar overall intervention rates were identified in DCH and NCH (8.7 vs. 7.6% of all prescriptions). However, where there was a clear difference in the rate of contributions or interventions possible causes were explored.

The contribution rate was higher in DCH compared to NCH (62.7% vs. 36.8% of all prescriptions). This is likely to be due to the higher percentage of new admissions at DCH compared to NCH (45% vs. 26% of all patients). Pharmacists made more contributions for newly admitted patients by taking drug and allergy status history. When the pharmacists' contributions were re-calculated without considering drug history and allergy status check for new patients; the contribution rate was found to be similar between DCH and NCH (34.9% vs. 27.8%). NCH also provides bedside guidelines which may be another explanation for the lower contribution rate (especially answering queries from healthcare professionals) compared with DCH. This suggests that even though the study was conducted in different settings;

pharmacists' activities (contributions and interventions) are similar overall between the two sites.

The higher new admission rate in DCH compared to NCH may be because of the time of the year. Many visits to DCH were in winter which is often associated with more admissions, especially for paediatric patients due to causes such as bronchiolitis. Reasons for the lower admission rate in NCH might be because DCH is a general medical hospital with only one PHDU and one NICU unlike NCH which involves two NICUs, one PICU, one PHDU and different specialist units. Patients usually have a longer stay in specialist wards and intensive care units compared to patients on the general wards.

5.5.2. Medication reconciliation

Pharmacists spend a great deal of time checking and recording the drug history and allergy status of newly admitted patients. Doing so is clearly important, since it can reduce the chance of anaphylaxis and improve the quality of care. The NHS's mandatory requirement for medication reconciliation concerns adults, but not paediatric patients (254). In our study, the most common error was omission error (2.3% of all prescriptions and 27.9% of all errors). The most common omission was missing medication upon admission (60.3% of all omission errors and 15.2% of all new patients). Previous studies have identified higher rates. Terry et al. 2010 (233) found that in 39% of paediatric patients receiving medication on a UK neurosurgical ward this differed from that prescribed prior to admission. This finding emphasises the importance of medication reconciliation for paediatric patients.

5.5.3. Methods of data collection

Franklin et al. 2009 (255) identified prescription errors in adult surgical wards in the UK using four different methods of data collection: prospective collection by pharmacists, retrospective trigger tools, retrospective chart review, and spontaneous reporting. They found that prospective data collection by pharmacists was better in detecting prescribing errors than using retrospective trigger tools and spontaneous reporting but less effective than retrospective chart review. Using these four methods the error rate was 10.7% of all prescriptions before using CPOE and 7.9% after.

Our study found in three UK hospitals from June 2006–July 2007, the rate of prescription errors was 8.4% of all prescriptions. The effect of directly observing paediatric pharmacists to investigate medication errors had not previously been assessed to the best of my knowledge. To compare the effectiveness of this method of data collection requires comparing our study with previous studies that identified prescription errors by pharmacists in paediatric patients using "of all prescriptions" as a denominator. Of 25 identified studies in my systematic literature review **(Chapter 4)**, only ten (all using chart review) identified prescription errors using the denominator "of all prescriptions" and therefore are comparable.

Two studies identified similar rates of prescription errors associated with discharge prescriptions. Chan et al. 1990 (226) identified that 18% of all discharge prescriptions from a US paediatric unit were associated with errors. In a US emergency department, Cesarz et al. 2013 (227) identified that 23.6% of all orders involved prescription errors. By comparing prescribed medications with medications regularly taken before admission in a UK neurosurgical department, Terry et al. 2010 (233) identified that 39% of all prescriptions were associated with errors. These three studies identified higher prescription error rates than found in my observational study, perhaps because

these studies focused only on medication reconciliation or occurred in different paediatric settings, not because of any difference in methods used for data collection.

Kjeldby et al. 2009 (117) conducted a study in a Norwegian paediatric unit and identified that 26.8% of all prescriptions were associated with prescription errors. Zangwill et al.'s 2000 study conducted in a similar setting in the US (231) identified a lower error rate of 6.2% of all prescriptions, while in an Egyptian paediatric ICU, Alagha et al. 2011 (223) identified a much higher error rate (35.2%). In a specialist children's hospital (excluding the ICU) in the Netherlands, Maat et al. 2013 (222) identified that only 1.1% of all prescriptions were associated with prescription errors. The above four studies suggested that more errors may be identified in paediatric ICUs. In NICUs, as in Conway et al. 2012 (236), 9.1% of all prescriptions involved errors, which though lower than the error rate identified by studies conducted in paediatric ICUs, is nevertheless similar to the rate identified in my observational study of 9.1% of all prescriptions in NICU in NCH.

Similar to my study, two studies have been done in paediatric wards only. In a Spanish ward, Fernández–Llamazares et al. 2012 (234) identified a prescription error rate of 2.4% of all prescriptions, while in India, Angalakuditi et al. 2003 (232) identified a prescription error of 61.8% of all prescriptions. The latter study identified only prescription dosage errors, which might have inflated the error rate beyond that found by Fernández–Llamazares et al.

From all of the above studies, it is clear that different error rates were identified in different settings and therefore comparing the effect of direct observation of paediatric clinical pharmacists with other methods of data collection cannot be done. Only one study (Fernández–Llamazares et al. 2012 (234)) was identified to be comparable with my study as this study identified prescribing errors in general,

conducted in the same setting as in my study and used the same denominator. From this comparison it seems that using direct observation of paediatric clinical pharmacists may be more effective in detecting prescribing errors than using chart review as the error rate found was higher. However, due to the low number of comparable studies, this conclusion cannot be generalised.

5.5.4. Significance of some of interventions

In my observational study many potentially serious errors were identified. These included omission of medications, omission of doses, omission of the route of administration; wrong doses, illegible prescribing, wrong frequency, wrong medications, duplication of medications, wrong weight, wrong rate of administration, drug interaction, contraindication and prescribing medications to patients with allergy. I was unfortunately not able to identify the outcome of the medication errors identified however, this is an important area for future studies.

Pharmacists are required to not only detect prescription errors, but also encourage doctors to adhere to national and hospital-specific guidelines. Doing both is crucial in treating paediatric patients, since the rate of potentially harmful medication errors may be three times higher in paediatric than adult patients (9). Among 20 types of errors, I identified wrong dosage as the second most common type of medication error. Similar to my findings, two systematic literature reviews by Ghaleb et al. 2006 (17) and Wong et al. 2004 (71) found dosage errors to be the most common type of medication error.

5.5.5. Doctors' acceptance rate of recommendations

My systematic review of studies addressing paediatric clinical pharmacists' activities **(Chapter 4)** identified nine studies reporting doctors' acceptance rates (220, 222, 224, 225, 227, 229, 236-238). Acceptance rates ranged from 24–98%. In my observational study, the acceptance rate of doctors was very high (99.5% of all recommendations), which indicates that paediatric pharmacists are trusted and respected members of the paediatric team in these hospitals. It also suggests that there is no barrier to doctors' acceptance of pharmacists' recommendations in these hospitals.

5.5.6. Study implications

This study identified the presence of clinical pharmacists as an effective method for averting prescription errors. Since clinical pharmacy services were not provided at night or weekends, these periods may face greater risks of medication errors. Future research is needed to investigate this. In addition most of the studies identified in this thesis were conducted in the US followed by the UK. The use of clinical pharmacists in other countries is therefore unclear. Their benefits may be being missed in many hospitals treating children across the world. A future study would be needed to clarify this and its effects.

5.5.7. Limitations

The severity and consequences of the errors identified and the medications associated with errors were not always recorded, due to time constraints, since I was required to shadow pharmacists to observe their activities at all times. As such, future studies could investigate this further.

I visited DCH and NCH at different times of the year, which may have affected the number of pharmacists' contributions, since pharmacists perform more activities

related to checking drug history and allergy status with influxes of new patients. It might have also affected admission rates, which might in turn have affected the total error rate (i.e., the chance that pharmacists' contributions and interventions increase when more new patients are admitted). Different paediatric ward specialties at DCH and NCH made comparing the two hospitals less reliable, apart from the two common wards (i.e., NICU and PHDU).

Observing pharmacists doing their daily jobs may have been associated with the Hawthorne effect, i.e. the effect of being observed improving the shadowed paediatric pharmacists practice. It is very difficult to know how this may have affected the results.

5.5.8. Strengths

To the best of my knowledge, this study is the first to involve the direct observation of pharmacists in children's wards. It was multi-centred and involved various specialities. The data collection form used in my observational study was adapted from studies included in my previous systematic literature review **(Chapter 4)** and so was evidence-based. The study identified two types of information: contributions and interventions by pharmacists regarding improving paediatric healthcare and intercepting medication errors. It provided detailed subtypes of errors that had not previously been reported.

5.6. Conclusion

The key finding of this study is that clinical pharmacists play a very important role in preventing medication errors and contributing to the safe and effective use of drugs. Pharmacists intercepted medication errors in 8.4% of all prescriptions. The most common type of pharmacists' contribution was annotating prescriptions with

important information. At the same time, the most common type of medication error intercepted by pharmacists was omission errors, especially the omission of medications and doses at admission; the second most common was wrong dosage. Doctors' acceptance rate of pharmacists' recommendations was high, and though similar error and intervention rates occurred in DCH and NCH, DCH reported a higher contribution rate than NCH.

Chapter 6: Conclusion

6.1. Introduction

Literature on paediatric medication errors has increased dramatically in the last few years. Through detailed analysis of the current literature base it was hoped to learn some important lessons to inform and improve the use of medicines in children by identifying means of reducing errors. Some of these lessons were used to inform my own study of the role of the paediatric clinical pharmacist in their everyday practise.

By directly observing pharmacists, I aimed to provide evidence regarding their ability to reduce or prevent medication errors and contributions to paediatric health care services.

6.2. Key findings

The systematic review of literature **(Chapter 2)** from the 5-year period from April 2006 to March 2011 identified 153 studies, mainly conducted in the US. Most studies used chart review, while the second greatest number reviewed incident reports. Studies identified prescription and administration errors as the first and second most common type of medication errors, respectively. Twenty-six different denominators

were used, the most common being “of all errors”, followed by “of all orders”. Error rates could not be compared for most studies and nine factors were identified which influenced the error rates. These factors are the use of 26 different denominators, study of six types of medication errors, use of five different methods of data collection, use of 236 definitions, inclusion of patients from five different age categories, inclusion of 30 different countries, investigation of 48 different groups of medications, in 22 different settings, and the use of 65 interventional tools. Of these, the most important factor was felt to be a difference in denominator, which generally precluded meaningful comparison of studies as their results were presented in such diverse ways.

The wide ranges of error rates seen in these studies **(Chapter 3)** stemmed from studies using interventional tools and reporting pre and post intervention error rates, identifying subtypes of errors (e.g., prescription dosage errors), studying different specific or groups of medications, implementing different inclusion criteria, and using different study designs. Neonatal unit setting, work environment, and differences in participants’ level of education, training, and experience were associated with high error rates.

I tried to study the relationship between methods of data collection and results **(Chapter 3)** in order to establish which methods are best used to study which types of error. Results suggest that prescription errors are best studied using chart review, administration errors by using direct observational techniques, and transcription and dispensing errors by reviewing incident reports. Monitoring and documentation errors are rarely studied and their importance should probably be better recognised.

I also studied the relationship between clarity of definitions used in studies and results **(Chapter 3)**. Many studies used definitions that were unlikely to adequately meet the

study's aims. It was unfortunately not possible to determine how clarity of definition influenced results of studies as few could be adequately compared.

In all, 59 studies used interventional tools and assessed their benefits **(Chapter 3)**. Forty-nine studies (83%) identified the error rate before and after the intervention. Forty-six of these concluded that their interventions were effective. The two most common types of intervention were dosing support tools, mostly used to reduce administration errors, and electronic prescription systems, mostly used to reduce prescription errors.

Of the 16 UK studies, 13 used 11 different denominators, while the other three did not use any denominator but provided only numbers of errors **(Chapter 3)**. Most studies identified prescription errors. The rates of errors cannot be generalised to characterise the rate of medication errors in children across the UK, because too few studies occurred in the same setting and used the same methodology and denominators to identify the rate of the same type of medication errors. The findings however suggest that prescribing and administration errors may be more prevalent in paediatric units in general hospitals than in specialist children's hospitals.

Eight studies identified the time and/or day of errors **(Chapter 3)**. Four studies identified the time most associated with errors, three the time of day and days of the week most associated with errors, and one the days of the week most associated with errors. However, these studies used various definitions of times of day, shifts, and weekdays. It was impossible to draw conclusions about the time or day of errors because of the low number of studies and because different studies used different definitions of times of day, shifts and weekdays.

The second systematic review **(Chapter 4)** examined the role of paediatric clinical pharmacists in reducing the rate of medication errors. The review included 25 studies, all of which reported that pharmacists were effective in either reducing or preventing medication errors and highlighted their many activities. From this I developed two lists, one of pharmacists' interventions which involved 29 different subtypes of errors identified and addressed by pharmacists. The second list involved 15 different types of contributions where pharmacists made additional contributions to patient care. Though clinical pharmacy services in the UK began in the mid-1960s, only three UK studies were found which assessed the effectiveness of clinical pharmacy services in reducing the error rate of medication errors in paediatric patients. Of these, two used chart review, while another reviewed incident reports.

I conducted an observational study of the role of paediatric clinical pharmacists in two NHS Trusts in the UK **(Chapter 5)**. This study showed that paediatric clinical pharmacists identified medication errors in 8.4% of all prescriptions and made contributions to 54.8% of all prescriptions. Most types of medication errors identified by pharmacists were omission errors, followed by incorrect dosage and illegible prescriptions, respectively. Pharmacists' contributions mainly included annotating prescriptions with administration advice, checking drug history and allergy status, respectively. Doctors' acceptance rate of pharmacists' recommendations was high (99.5%).

6.3. Limitations

The systematic review of paediatric medication error studies had some limitations:

1. There is no standard definition for "wide variation" in terms of rates of errors reported. I therefore considered such variation to occur when the difference between the highest and lowest error rate exceeded 50%. This would be unlikely to occur as a result of chance or seasonal variation.
2. No guidance on writing a good definition of an error exists therefore my supervisors and I agreed our own rating scale.

The systematic review of the effect of clinical pharmacists on reducing medication errors in paediatric patients also had limitations. Few studies examined the effect of paediatric clinical pharmacists' activities on reducing error rates, while many studies lacked sufficient information regarding the types of contributions. I excluded studies that identified pharmacists' contributions without providing a rate or number of medication errors.

The observational study of paediatric clinical pharmacists had some limitations. I did not record the severity and consequences of medication errors identified by the pharmacists or which medications were associated with the errors. Being required to shadow pharmacists at all times in order to observe their activities; I was unable to leave their sides to search for other information in medical notes or medication charts. Also the studies at DCH and NCH were conducted at different times of the year, which might have affected the number of pharmacists' contributions and interventions, since pharmacists conduct more activities involved with checking drug history and allergy status when new patients are admitted.

6.4. Challenges

A large number of relevant papers (153) was identified in the first systematic review and generated a large amount of data which I was required to manage and analyse. The aim of this review was not only to identify the error rate but to look in more depth at each of the 153 studies to find out similarities and differences between studies in order to draw conclusions about factors influencing the error rates.

Firstly I identified studies that used each single denominator. Secondly I combined studies that used the same denominator to identify the same type of errors. Thirdly I separated these studies according to their methods of data collection. Doing this I was able to explore the reasons for the wide variations in error rate, the relationship between methods and results and the relationship between definitions and results.

I also searched the 153 included studies to identify different interventional tools used to minimise errors and to identify their effectiveness; the UK studies to identify similarity and differences between these studies and to identify the time and/or day of errors. Doing all this analysis meant that I was required to search the relevant papers many times and to make sense of a huge amount of information.

When I started my observational study I faced the challenges of taking consent from each individual patient (or carer). This was time consuming and I had to explain to each patient/carer the aim of my study and ask for their permission. Moreover, since pharmacists need to work very quickly and since I was required to shadow them without interrupting, I could not always capture all required information (e.g., medications associated with errors). In addition given the lack of a recognised classification system, I had to develop a list of interventions and contributions from different studies and sources.

6.5. Recommendations for future studies

It is important that future studies consider all factors in their study design when exploring the rate of medication errors in paediatric patients, especially clear denominators, definitions, and appropriate methods of data collection. Doing so should make future studies comparable with each other so that lessons can be learned from their finding to improve patient safety.

In my opinion it is better to detect prescribing errors using direct observation of clinical pharmacists and administration errors using direct observation of nurses and parents. Dispensing, monitoring and transcribing errors are probably better studied using a mixed method (e.g. chart review and review of incident reports). I think identifying medication errors from only incident reports does not reflect the actual error rate. This is because incident reports are associated with many drawbacks such as under-reporting.

Future researchers should give particularly careful consideration to the definitions they use to ensure that they will meet the aims of their study, and use established definitions when possible in order to facilitate the comparison of different studies results. In my opinion the best approach seems to be using a brief definition of each type of medication error, along with detailed explanations of subtypes of errors, including examples.

In my opinion it is better to identify interventions used to reduce the error rate and to assess their effectiveness rather than just identifying the error rate. Studies should measure the rate of errors before and after interventions in order to estimate the intervention's efficacy in terms of error reduction using an appropriate and robust method of data collection.

Future research should examine the influence of time of day and days of the week, subtypes of medication errors and drugs most associated with medication errors, as little is known in these areas. Future studies should also further investigate the consequences of medication errors, including harm, prolonged hospitalisation, and increased cost of care.

6.6. Lessons learned and future plans

The systematic reviews of studies of paediatric medication errors and the role of paediatric clinical pharmacists provided me with a good picture of the incidence and nature of medication errors in paediatric patients and factors influencing the error rate. Shadowing pharmacists in Derby and Nottingham provided me with knowledge and experience of different clinical pharmacists' activities in the UK. In Saudi Arabia, by contrast, clinical pharmacy services are relatively new, especially in paediatric wards. In fact, no study has yet identified the effect of paediatric clinical pharmacists on reducing the rate of medication errors in Saudi Arabia.

The experience gained from the work for this thesis will help me to initiate paediatric clinical pharmacy services in Saudi Arabia that can hopefully also improve health care services and minimise the risk of medication errors in paediatric patients in my country. I plan to investigate the error rate in different paediatric wards in Saudi Arabia and assess the effectiveness of paediatric clinical pharmacy services there in both reducing the error rate and improving the health care services provided.

6.7. Conclusion

The heterogeneity of studies reviewed precludes useful comparison of the rate of medication errors in different settings or countries. Instead of conducting additional studies, purely measuring error rates researchers should perhaps concentrate on identifying interventions that will decrease errors. Careful measurement of error rates

before and after interventions is essential to assess their efficacy and should be done using reproducible and appropriate methods that include clear definitions, a well-defined patient population, and appropriate denominators.

This research confirms my hypothesis, since I found that paediatric clinical pharmacists do effectively reduce errors, as well as improve paediatric health care services. Moreover, this research is the first to directly observe paediatric clinical pharmacists, and clarify the different types of their activities performed in paediatric wards.

Appendix 1

Section 1: Types of medications studied

Medication studied	Chart/medical record review	Direct observation	Review of medication error incident reports	Mixed methods	Simulation	Total
All medications	32	3	24	14		73
Chemotherapy	2	1	2	2		7
Specific medications on a list	3	1			3	7
Intravenous medications	2	1			2	5
Antimicrobials	2	1	1			4
Resuscitation medications	2				2	4
Controlled analgesic	2		1			3
Acetaminophen					3	3
Parenteral nutrition	1		1			2
Surgical medications	1		1			2
All except parenteral nutrition	1			1		2
Opioids			2			2
Medications with serious errors				2		2
Harmful medications			1		1	2
Epinephrine	1				1	2
Topical corticosteroids	1					1
Asthma medications	1					1
Nephrotic medications	1					1
Acetaminophen & ibuprofen	1					1
Sedation	1					1
Ambulatory medications	1					1
Iron preparations	1					1
Antimicrobials & analgesics	1					1
Aciclovir	1					1
Insulin	1					1
Aminoglycosides	1					1
Intravenous methotrexate		1				1
All except oral fluids and nutrition		1				1
Medication with pharmacist intervention			1			1
22 look-alike sound-alike medications			1			1
Analgesics			1			1
Escitalopram			1			1
Fat emulsion			1			1
Cough and cold medications			1			1
Anaesthetics			1			1
Medications with 10-fold exposure			1			1
Oseltamivir			1			1
Post-anaesthesia medications			1			1
Intravenous acetylcysteine			1			1
Intralipid medications			1			1
Medications for patients with attention deficit hyperactivity disorder			1			1
Cardiovascular medications			1			1
Antidepressants			1			1
Aseptic products			1			1
Medications for patients with severe injury or death			1			1
Medications for patients with fever, asthma, head trauma, otalgia and dysuria				1		1
Dipyrone & acetaminophen				1		1
Naloxone & insulin				1		1
Total	60	9	50	22	12	153

Section 2: Tables of studies identifying the rate of medication errors according to the methodology used

1. Studies using chart/medical record review (60 studies)

Studies identifying prescribing errors (34 studies)									
(112) [Kozer et al. 2006]	(185) [Kim et al. 2006]	(154) [Al khaja et al. 2006]	(153) [Al Khaja et al. 2007]	(155) [Al Khaja et al. 2007]	(179) [Brown et al. 2007]	(188) [Vardi et al. 2007]	(157) [Oshikoya et. 2007]	(256) [Rinke et al. 2008]	(182) [Zimmer et al. 2008]
(10) [Burmester et al. 2008]	(107) [Sard et al. 2008]	(104) [Davey et al. 2008]	(193) [Cunningham et al. 2008]	(177) [Pallas et al. 2008]	(101) [Jani et al. 2008]	(117) [Kjeldby et al. 2009]	(114) [Diez et al. 2009]	(68) [Lee et al. 2009]	(178) [Ginzburg et al. 2009]
(165) [Di Pentima et al. 2009]	(189) [Campino et al. 2009]	(96) [Broussard et al. 2009]	(257) [Neuner et al. 2009]	(156) [Al Khaja et al. 2010]	(258) [Miller et al. 2010]	(181) [Hennings et al. 2010]	(57) [Condren et al. 2010]	(259) [Pandey et al. 2010]	(260) [Kneen et al. 2010]
(152) [Jani et al. 2010]	(187) [Neal et al. 2010]	(120) [Camara et al. 2011]	(166) [Eisenhut et al. 2011]						
Studies identifying administration errors (2 studies)									
(170) [Kaji et al. 2006]		(168) [Sullivan et al. 2010]							
Studies identifying dispensing errors (one study)									
(42) [Costa et al. 2008]									
Studies identifying medication errors in general (6 studies)									
(128) [Sharek et al. 2006]	(261) [Dharmar et al. 2007]	(75) [Lerner et al. 2008]	(14) [Shah et al. 2009]	(262) [Agarwal et al, 2010]	(194) [Booth et al. 2010]				
Studies identifying medication monitoring errors (one study)									
(133) [Abboud et al. 2006]									

Studies identifying different types of errors (16 studies)								
(115) [Campino et al. 2006]	(164) [Marcin et al. 2007]	(109) [Holdsworth et al. 2007]	(167) [Larose et al. 2008]	(131) [Campino et al. 2008]	(29) [Otero et al. 2008]	(132) [Takata et al. 2008]	(263) [Sirithongthavorn et al. 2009]	(27) [Walsh et al. 2009]	(192) [Kalina et al. 2009]
(105) [Kadmon et al. 2009]	(70) [Jain et al. 2009]	(116) [Rivas et al. 2010]	(102) [Kazemi et al. 2010]	(264) [Simons et al. 2010]	(130) [Kazemi et al. 2011]				

2. Studies using direct observation (8 studies)

Studies identifying prescribing errors (one study)								
(134) [Osterholt et al. 2006]								
Studies identifying administration errors (7 studies)								
(265) [Parshuram et al. 2006]	(174) [Taylor et al. 2008]	(88) [Raja Lope et al. 2009]	(158) [Feleke et al. 2010]	(67) [Chua et al. 2010]	(169) [Bertsche et al. 2010]	(266) [Russell et al. 2010]			

3. Studies using review of medication error incident reports (50 studies)

Studies identifying prescribing errors (6 studies)									
(135) [Takata et al. 2008]	(4) [Engum et al. 2008]	(186) [Van De Velde et al. 2009]	(72) [Basco et al. 2010]	(180) [Senner et al. 2010]	(136) [Smith et al. 2011]				
Studies identifying administration errors (12 studies)									
(267) [Jirapaet et al. 2006]	(268) [Forrester. 2007]	(195) [Hicks et al. 2007]	(269) [Schaefer et al. 2008]	(8) [Ferranti et al. 2008]	(270) [Llewellyn et al. 2009]	(271) [Taylor et al. 2009]	(272) [Schillie et al. 2009]	(7) [Crouch et al. 2009]	(273) [Forrester. 2010]
(274) [Sadat-Ali et al. 2010]	(275) [Yip et al. 2011]								
Studies identifying medication errors in general (17 studies)									
(138) [Burny et al. 2006]	(276) [Hicks et al. 2006]	(277) [Hain et al. 2007]	(58) [Taylor et al. 2007]	(191) [Costello et al. 2007]	(40) [Payne et al. 2007]	(278) [Alj et al. 2007]	(137) [Hayes et al. 2008]	(36) [Kuitunen et al. 2008]	(6) [Hicks et al. 2008]
(119) [Festini et al. 2008]	(121) [Trotter et al. 2009]	(279) [Tzimenatos et al. 2009]	(280) [Shah et al. 2009]	(281) [Snijders et al. 2009]	(282) [Skapik et al. 2009]	(283) [Lillis et al. 2010]			
Studies identifying different types of errors (15 studies)									
(284) [Miller et al. 2006]	(196) [Chuo et al. 2007]	(140) [Rinke et al. 2007]	(63) [Ligi et al. 2008]	(285) [Bundy et al. 2008]	(286) [Alexander et al. 2009]	(141) [Stavroudis et al. 2010]	(139) [Narula et al. 2010]	(76) [Miller et al. 2010]	(15) [Ligi et al. 2010]
(66) [Rinke et al. 2010]	(287) [Bateman et al. 2010]	(288) [Morton et al. 2010]	(37) [Conroy. 2011]	(289) [Mc Donnell et al. 2011]					

4. Studies using mixed methods (23 studies)

Studies identifying prescribing errors (2 studies)									
(162) [Pote et al. 2007]	(163) [Porter et al. 2008]								
Studies identifying administration errors (4 studies)									
(47) [Van Den Bemt et al. 2007]	(171) [Alves et al. 2007]	(290) [Lemer et al. 2009]	(291) [Muething et al. 2010]						
Studies identifying medication errors in general (6 studies)									
(160) [Walsh et al. 2006]	(159) [Walsh et al. 2008]	(292) [Parihar et al. 2008]	(86) [Kaushal et al. 2008]	(172) [Benkirane et al. 2009]	(90) [Morriss et al. 2009]				
Studies identifying different types of errors (11 studies)									
(93) [Lehmann et al. 2006]	(173) [Taylor et al. 2006]	(190) [Robinson et al. 2006]	(142) [Conroy et al. 2007]	(143) [Buckley et al. 2007]	(144) [Kaushal et al. 2007]	(106) [Wang et al. 2007]	(161) [Landrigan et al. 2008]	(118) [Valizadeh et al. 2008]	(145) [Kunac et al. 2008]
(24) [Ghaleb et al. 2010]									

5. Studies using simulation studies (12 studies)

Studies identifying prescribing errors (one study)									
(146)[Vaidya et al. 2006]									
Studies identifying administration errors (11 studies)									
(99) [Morgan et al. 2006]	(147) [Wheeler et al. 2008]	(100) [Fineberg et al. 2008]	(176) [Hohenhaus et al. 2008]	(148) [Sobhani et al. 2008]	(183) [Feleke et al. 2009]	(150) [Pauly-O'Neil. 2009]	(184) [Yamamoto et al. 2010]	(110) [Sowan et al. 2010]	(48) [Yin et al. 2010]
(149) [Yin et al. 2011]									

Appendix 2: Comparison of studies using the same denominator to identify the same type of errors but using different methods

Table 1: Studies identifying prescribing error rates using chart/medical record review and "of all orders" as a denominator

Reference	Study	Country	Setting	Age classification	Medications studied	Intervention	Rate of prescribing errors "of all orders"	
							Before intervention	After intervention
(115)	Campino et al. 2006	Spain	Neonatal unit	Neonates	All	-	35.2%	
(179)	Brown et al. 2007	US	Neonatal unit	Neonates	Parenteral nutrition	Computerised parenteral nutrition worksheet	14.5%	6.8%
(131)	Campino et al. 2008	Spain	Neonatal unit	Neonates	All	Physicians and nurses were informed that prescriptions will be reviewed to identify prescribing errors (by physicians) and transcribing errors (by nurses) to measure the effect of observation.	32.8%	19.2%
(177)	Pallas et al. 2008	Spain	Neonatal unit	Neonates	All	Computerised automatic dosage calculation	39.5%	11.9%
(189)	Campino et al. 2009	Spain	Neonatal unit	Neonates	All medication except parenteral nutrition	Education about medication errors by a pharmacist	20.7%	3%

Reference	Study	Country	Setting	Age classification	Medications studied	Intervention	Rate of prescribing errors "of all orders"	
							Before intervention	After intervention
(112)	Kozer et al. 2006	Canada	Emergency department	Not mentioned	All	Education of doctors by one author (30 minutes tutorial followed by test)	12.4% by trainees who attended tutorial	
							12.7% by trainees who did not attend tutorial	
(256)	Rinke et al. 2008	US	Emergency department	Not mentioned	All	-	12.5% from in-house	
							4.3% from ambulatory	
(167)	Larose et al. 2008	Canada	Emergency department	Not mentioned	Intravenous medications and fluids	Pre-printed order form	9%	2%
(107)	Sard et al. 2008	US	Emergency department	Neonates+ infants+ children+ adolescent	All	CPOE	31%	14%
(114)	Diez et al. 2009	Spain	Emergency department	Not mentioned	All	-	43%	
(96)	Broussard et al. 2009	US	Specialist children hospital	Neonates+ infants+ children+ adolescent	Sedation medication	Pre-printed order from	25%	9%
(68)	Lee et al. 2009	US	Specialist children hospital	Neonates+ infants+ children+ adolescent	Controlled substances (e.g. opiates)	-	82%	
(152)	Jani et al. 2010	UK	Specialist children hospital	Not mentioned	All	CPOE	2.2%	1.2%
(120)	Camara et al. 2011	Senegal	Specialist children hospital	-	All	-	17%	
(154)	Al Khaja et al. 2006	Bahrain	Primary care	Infants	Antimicrobials	-	22% subtherapeutic doses	
							5.2% supratherapeutic doses	
(155)	Al Khaja et al. 2007	Bahrain	Primary care	Infants	Topical corticosteroid	-	21.6% omission errors related to dosing frequency	
							43.6% omission errors related to length of therapy	

Reference	Study	Country	Setting	Age classification	Medications studied	Intervention	Rate of prescribing errors "of all orders"	
							Before intervention	After intervention
(153)	Al Khaja et al. 2007	Bahrain	Primary care	Infants	All	-	90.5% (omission, commission and integration errors)	
(156)	Al Khaja et al. 2010	Bahrain	Primary care	Infants	Iron preparations	-	9.4% unclear or incomplete names of iron preparations	
							2.5% no daily dosages	
							26.4% no dosage form	
							8.8% no duration of therapy	
							6.9% unavailable trade names	
(104)	Davey et al. 2008	UK	Paediatric unit in general hospital	Not mentioned	All	Education of doctors by a pharmacist (about good prescribing)	30.5% before first intervention	16.5% after first intervention
						Bedside prescribing guidelines	18.4% before second intervention	17% after second intervention
(117)	Kjeldby et al. 2009	Norway	Paediatric unit in general hospital	Infant+ children+ adolescent	All	Clinical pharmacist	No rate measured	26.8%
(188)	Vardi et al. 2007	Israel	Intensive care unit	Not mentioned	Resuscitation medications	CPOE+CDSS	0.02%	0%
(187)	Neal et al. 2010	UK	Intensive care unit	Not mentioned	All	CPOE	8.8%	8.1% after one week
								4.6% after 6 months
(157)	Oshikoya et al. 2007	Nigeria	Outpatients	Preterm baby+ neonates+ infants+ children	All	-	62.2%	
(57)	Condren et al. 2010	US	Outpatients	Not mentioned	All	-	9.7%	

Reference	Study	Country	Setting	Age classification	Medications studied	Intervention	Rate of prescribing errors "of all orders"	
							Before intervention	After intervention
(185)	Kim et al. 2006	US	Paediatric oncology	Not mentioned	Chemotherapy	CPOE	5.8% calculation errors	0.54% calculation errors
							2.3% improper dosing	0.06% improper dosing
							18% missing cumulative dose	5.7% missing cumulative dose
							4.8% incomplete nursing checklist	2.5% incomplete nursing checklist
(29)	Otero et al. 2008	Argentina	Neonatal and paediatric unit	Neonates+ infants+ children+ adolescent	All	Education of all healthcare professionals (by the Patient Safety Committee) about the patient safety+ safety strategy	17.3%	9.2%
(116)	Rivas et al. 2010	Chile	Paediatric unit in general hospital+ neonatal unit +intensive care unit+ paediatric surgical service	Not mentioned	Intravenous prescriptions	-	21%	

Table 2: Studies identifying prescribing error rates using mixed methods and "of all orders" as a denominator

Reference	Study	Country	Setting	Methods	Age classification	Intervention	Medications studied	Type of errors	Rate of prescribing errors "of all orders"	
									Rate before intervention	Rate after intervention
(93)	Lehmann et al. 2006	US	Specialist children's hospital	Chart review	Not mentioned	Calculator generated orders	Continuous infusion medication	MPEs	27% of all handwritten orders	6% of all calculator generated orders
				Direct observation of all pharmacy preparation and dispensing		-		MDEs	0% of all orders	
(161)	Landrigan et al. 2008	US	Specialist children's hospital	Chart review & review of medication error incident reports	Not mentioned	Accreditation Council for Graduate Medical Education (ACGME) (doctor is not working for more than 30 continuous hours or more than 88 hours weekly).	All	MPEs	1.06% of all orders	1.38% of all orders
								MEs	1.29% of all orders	1.5% of all orders
(145)	Kunac et al. 2008	New Zealand	Paediatric unit in general hospital	Chart review & review of medication error incident reports	Neonates+ infants+ children+ adolescent	-	All	MPEs	7.1%	
								MDEs	1.1%	
								MAEs	5.2%	
								MMEs	1.7%	

(24)	Ghaleb et al. 2010	UK	Specialist children's hospital and paediatric units in general hospital	Chart review	Not mentioned	-	All except parenteral and enteral nutrition	MPEs	13.2% of all orders
				Direct observation of preparations and administrations made by nurses				MAEs	19.1% of all possible errors
				Review of medication error incident reporting.				MPEs & MAEs	None

Table 3: Studies identifying prescribing error rates using chart/medical record review and "of all errors" as a denominator

Reference	Study	Country	Setting	Age classification	Intervention	Medications studied	Rate of prescribing errors "of all errors"		Other errors identified
							Rate before intervention	Rate after intervention	
(164)	Marcin et al. 2007	US	Emergency department	Neonates+ infants+ children+ adolescent	-	All	28.6%		Not specified
(132)	Takata et al. 2008	US	Specialist children's hospital	Not mentioned	-	All	50%		MAEs, MDEs, MTEs & MMEs
(105)	Kadmon et al. 2009	Israel	Intensive care unit	Not mentioned	CPOE	All	5.5%	5.3%	Not specified
					CDSS		5.3%	3.8%	
					Preventing nurses from signing orders instead of doctors		3.8%	0.7%	
(70)	Jain et al. 2009	India	Neonatal intensive care unit+ emergency department	Neonates	-	All	70% of all errors in the emergency department were prescribing errors by senior doctors & 9% by junior doctors		MDEs
							89% in neonatal intensive care unit were prescribing errors by senior doctors		
(27)	Walsh et al. 2009	US	Outpatient	Not mentioned	-	Chemotherapy	64%		MAEs, MDEs & MMEs
(263)	Sirithongthavorn et al. 2009	Thailand	Paediatric psychiatry care	Not mentioned	-	All	37.8%		MDEs & MTEs

Table 4: Studies identifying prescribing error rates using review of medication error incident reports and "of all errors" as a denominator

Reference	Study	Country	Settings	Age classification	Medications studied	Intervention	Rate of prescribing errors of all errors"		Other errors identified
							Rate before intervention	Rate after intervention	
(196)	Chuo et al. 2007	US	Neonatal unit	Neonates	Intralipid	-	1.1%		MAEs
(15)	Ligi et al. 2010	France	Neonatal unit	Neonates	All	Safety initiatives and iatrogenic events prevention strategies	10.5%	24.4%	Not specified
(140)	Rinke et al. 2007	US	Paediatric oncology and national incident reporting system	All ages	Chemotherapy	-	10.3%		MAEs, MDEs, MTEs & MMEs
(141)	Stavroudis et al. 2010	US	Neonatal unit and national incident reporting system	Neonates	All	-	13.9%		MTEs, MDEs, MAEs & MMEs
(139)	Narula et al. 2010	UK	Paediatric gastroenterology and nutrition ward	Not mentioned	Parenteral nutrition	-	11%		MTEs, MDEs, MAEs & others
(76)	Miller et al. 2010	US	Specialist children's hospital	Not mentioned	All	-	12.8%		MTEs, MDEs & MAEs
(66)	Rinke et al. 2010	US	National incident reporting system	All ages	Antidepressants	-	7.8%		MAEs, MTEs, MMEs & MDEs

Table 5: Studies identifying prescribing error rates using chart/medical record review and "of all patients" as a denominator.

Reference	Study	Country	Setting	Age classification	Intervention	Medications studied	Rate of prescribing errors "of all patients"	
							Rate before intervention	Rate after intervention
(164)	Marcin et al. 2007	US	Emergency department	Neonates+ infants+ children+ adolescent	-	All	11.9%	
(10)	Burmester et al. 2008	UK	Intensive care unit	Not mentioned	Pre-printed order form+ education for doctors	Resuscitation medications	16.8%	4.8%
(260)	Kneen et al. 2010	UK	Specialist children's hospital l	Neonates+ infants+ children+ adolescent	-	Intravenous aciclovir	74% (38 out of 51 patients, in 20 needed re-calculation	

Table 6: Studies identifying administration error rates using direct observation and "of all administrations" as a denominator.

Reference	Study	Country	Setting	Age classification	Intervention	Medications studied	Rate of administration errors "of all administrations"		Notes
							Rate before intervention	Rate after intervention	
(265)	Parshuram et al. 2006	Canada	Paediatric oncology	All	-	Methotrexate	23%		Administrations by nurses
(174)	Taylor et al. 2008	US	Neonatal unit	Neonates	CPOE	All except fluids and nutrition	19.8%	11.6%	Administrations by nurses
(88)	Raja lope et al. 2009	Malaysia	Neonatal unit	Neonates	Education for nurses	All	31%	15.4%	Administrations by nurses
(142)	Conroy et al. 2007	UK	Paediatric unit in a general hospital	Not mentioned	-	All	1.2%		Administrations by nurses
(158)	Feleke et al. 2010	Ethiopia	Paediatric unit in general hospital	Neonates+ infants+ children+ adolescent	-	All	89.9%		Administrations by nurses and parents
(67)	Chua et al. 2010	Malaysia	Paediatric unit in general hospital	All	-	All	11.7%		Administrations by doctors and nurses
(169)	Bertsche et al. 2010	Germany	Paediatric neurology unit	Not mentioned	Education for nurses and parents	All	40.4%	7.9%	By nurses
							96.6%	5.6%	By parents
(266)	Russell et al. 2010	US	Intensive care unit	Neonates+ infants+ children+ adolescent	-	Infusion medications and fluids	24% of all medication infusions		Administrations by nurses
							42% of all fluid infusions		

Table 7: Studies identifying administration error rates using review of medication error incident reports and "of all errors" as a denominator.

Reference	Study	Country	Setting	Age classification	Medications studied	Rate of administration errors "of all errors"	Other errors identified
(140)	Rinke et al. 2007	US	Paediatric oncology and national incident reporting system	All	Chemotherapy	48.1%	MPEs, MDEs, MTEs & MMEs
(196)	Chuo et al. 2007	US	Neonatal unit	Neonates	Intralipid	93.2%	MPEs
(63)	Ligi et al. 2008	France	Neonatal unit	Neonates	All	63%	Not specified
(141)	Stavroudis et al. 2010	US	Neonatal unit and national incident reporting system	Neonates	All	48.2%	MPEs, MDEs, MTEs & MMEs
(76)	Miller et al. 2010	US	Specialist children's hospital	Not mentioned	All	56.4%	MPEs, MDEs & MTEs
(66)	Rinke et al. 2010	US	National incident reporting system	All	Antidepressants	33%	MPEs, MDEs, MTEs & MMEs
(139)	Narula et al. 2010	UK	Paediatric gastroenterology and nutrition ward	Not mentioned	Parenteral nutrition	30%	MPEs, MDEs & MTEs

Table 8: Studies identifying administration error rates using chart/medical record review and "of all errors" as a denominator.

Reference	Study	Country	Setting	Age classification	Medications studied	Rate of administration errors "of all errors"		Other errors
						Rate before intervention	Rate after intervention	
(132)	Takata et al. 2008	US	Specialist children's hospital	Not mentioned	All	0%		MPEs, MMEs, MDEs & MTEs
(27)	Walsh et al. 2009	US	Outpatients	Not mentioned	Chemotherapy	5%		MPEs, MMEs & MDEs

Table 9: Studies identifying medication error rates in general using chart/medical record review and "of all orders" as a denominator.

Reference	Study	Country	Setting	Age classification	Intervention	Medications studied	Rate of medication errors in general "of all orders"	
							Rate before intervention	Rate after intervention
(263)	Sirithongthavorn et al. 2009	Thailand	Paediatric psychiatry care	Not mentioned	-	All	2.42%	
(105)	Kadmon et al. 2009	Israel	Intensive care unit	Not mentioned	CPOE	All	8.2%	7.8%
					CDSS		7.8%	4.4%
					Preventing nurses from signing orders instead of doctors		4.4%	1.4%
(70)	Jain et al. 2009	India	Neonatal intensive care unit+ emergency department	Neonates	-	All	9.6%	
(102)	Kazemi et al. 2010	Iran	Neonatal unit	Neonates	CPOE	All	22.7% in physician order entry	
							14.5% in nurse order entry	
(264)	Simons et al. 2010	UK	Specialist children's hospital & paediatric unit in a general hospital	Infants+ children+ adolescents	-	All	14% in specialist children's hospital	
							23% in paediatric unit in general hospital	

Table 10: Studies identifying medication error rates in general using chart/medical record review and "of all patients" as a denominator.

Reference	Study	Country	Setting	Age classification	Medications studied	Rate of medication errors in general "of all patients"	
						Rate before intervention	Rate after intervention
(261)	Dharmer et al. 2007	US	Emergency department	Neonates+ infants+ children+ adolescent	All	26.4%	
(164)	Marcin et al. 2007	US	Emergency department	Neonates+ infants_ children+ adolescent	All	39%	
(75)	Lerner et al. 2008	Brazil	Neonatal unit	Neonates	All	55%	

Table 11: Studies identifying medication error rates in general using review of medication error incident reports and "of all patients" as a denominator.

Reference	Study	Country	Setting	Age classification	Intervention	Medications studied	Rate of medication errors in general "of all patients"	
							Rate before intervention	Rate after intervention
(137)	Hayes et al. 2008	US	Poison control centre	All ages	-	IV acetylcysteine	34.3%	
(15)	Ligi et al. 2010	France	Neonatal unit	Neonates	Safety initiatives and iatrogenic events prevention strategies.	All	4.9%	7%

Table 12: Studies identifying medication error rates in general using mixed methods and "per 1000 patient days" as a denominator.

Reference	Study	Country	Methods	Setting	Intervention	Age classification	Medications studied	Rate of medication errors in general "per 1000 patient days"	
								Rate before intervention	Rate after intervention
(160)	Walsh et al. 2006	US	Chart review and review of incident reports	Paediatric unit in general hospital	-	Not mentioned	All	53.9	
(145)	Kunac et al. 2008	New Zealand	Chart review and review of incident reports	Paediatric unit in a general hospital	-	Neonates+ infants+ children+ adolescent	All	121	
(106)	Wang et al. 2007	US	Chart review and review of incident reports	Neonatal and paediatric unit in a general hospital	-	Not mentioned	All	167	
(159)	Walsh et al. 2008	US	Chart review and review of incident reports	Neonatal and paediatric units in general hospital	CPOE	Not mentioned	All	7.9 (serious errors)	6.5 (serious errors)
(86)	Kaushal et al. 2008	US	Chart review and review of incident reports	Specialist children's hospital	Clinical pharmacists' services		All	29 (serious errors) in ICUs	6 (serious errors) in ICUs
								8 (serious errors) in general medical unit	9 (serious errors) in general medical unit
								7 (serious errors) in general surgical unit	9 (serious errors) in general surgical unit
(172)	Benkirane et al. 2009	Morocco	Direct observation of ordering and transcribing and review of incident reports	Intensive care unit and neonatal unit	-	Not mentioned	All	9.1 in an intensive care unit	
								4 in a neonatal unit	

Table 13: Studies identifying transcribing errors rates using review of incident reports and "of all errors" as a denominator

Reference	Study	Country	Setting	Age classification	Medications studied	Rate of transcribing errors "of all errors"		Other errors identified
						Rate before intervention	Rate after intervention	
(140)	Rinke et al. 2007	US	Paediatric oncology and national incident reporting system	All ages	Chemotherapy	7.1%		MAEs, MDEs, MPEs & MMEs
(141)	Stavroudis et al. 2010	US	Neonatal unit and national incident reporting system	Neonates	All	18.4%		MPEs, MDEs, MAEs & MMEs
(139)	Narula et al. 2010	UK	Paediatric gastroenterology and nutrition ward	Not mentioned	Parenteral nutrition	20%		MPEs, MDEs, MAEs & other
(76)	Miller et al. 2010	US	Specialist children's hospital	Not mentioned	All	24.2%		MPEs, MDEs & MAEs
(66)	Rinke et al. 2010	US	National incident reporting system	All ages	Antidepressants	28%		MAEs, MDEs, MPEs & MMEs

Table 14: Studies identifying monitoring errors rates using review of incident reports and "of all errors" as a denominator

Reference	Study	Country	Setting	Age classification	Medications studied	Rate of monitoring errors "of all errors"		Other errors identified
						Rate before intervention	Rate after intervention	
(140)	Rinke et al. 2007	US	Paediatric oncology and national incident reporting system	All ages	Chemotherapy	0.6%		MAEs, MDEs, MPEs & MTEs
(141)	Stavroudis et al. 2010	US	Neonatal unit and national incident reporting system	Neonates	All	1.4%		MPEs, MDEs, MAEs & MTEs
(66)	Rinke et al. 2010	US	National incident reporting system	All ages	Antidepressants	0.7%		MAEs, MDEs, MPEs & MTEs

Table 15: Studies identifying monitoring errors rates using chart/medical record review and "of all errors" as a denominator

Reference	Study	Country	Setting	Age classification	Medications studied	Rate of monitoring errors "of all errors"		Other errors identified
						Rate before intervention	Rate after intervention	
(132)	Takata et al. 2008	US	Specialist children's hospital	Not mentioned	All	62.5%		MAEs, MDEs, MPEs & MTEs
(27)	Walsh et al. 2009	US	Outpatients	Not mentioned	Chemotherapy	5%		MAEs, MDEs & MPEs

Table 16: Studies identifying dispensing error rates using review of incident reports and "of all errors" as a denominator

Reference	Study	Country	Setting	Age classification	Medications studied	Rate of dispensing errors "of all errors"		Other errors identified
						Rate before intervention	Rate after intervention	
(140)	Rinke et al. 2007	US	Paediatric oncology and national incident reporting system	All ages	Chemotherapy	30.3%		MAEs, MTEs, MPEs & MMEs
(139)	Narula et al. 2010	UK	Paediatric gastroenterology and nutrition ward	Not mentioned	Parenteral nutrition	20%		MPEs, MTEs, MAEs & other
(76)	Miller et al. 2010	US	Specialist children's hospital	Not mentioned	All	35.7%		MPEs, MTEs & MAEs
(141)	Stavroudis et al. 2010	US	Neonatal unit and national incident reporting system	Neonates	All	11.8%		MPEs, MTEs, MAEs & MMEs
(66)	Rinke et al. 2010	US	National incident reporting system	All ages	Antidepressants	30%		MAEs, MTEs, MPEs & MMEs

Table 17: Studies identifying dispensing error rates using chart/medical record review and "of all errors" as a denominator

Reference	Study	Country	Setting	Age classification	Medications studied	Rate of dispensing errors "of all errors"		Other errors identified
						Rate before intervention	Rate after intervention	
(132)	Takata et al. 2008	US	Specialist children's hospital	Not mentioned	All	9%		MAEs, MMEs, MPEs & MTEs
(70)	Jain et al. 2009	India	Neonatal unit and emergency department	Neonates	All	21% in emergency department 11% in neonatal unit		MPEs
(263)	Sirithongthavorn et al. 2009	Thailand	Paediatric psychiatry care	Not mentioned	All	9.4%		MPEs & MTEs
(27)	Walsh et al. 2009	US	Outpatients	Not mentioned	Chemotherapy	0%		MAEs, MTEs & MPEs

Appendix 3

Figure 1: Consent form

I give permission for Ahmed Alsenani, PhD student to record the hospital pharmacist's work in relation to my child. I understand that this may involve him having sight of my child's treatment chart and notes. I understand that no personal information regarding my child will be documented and that this will not affect my child's care in any way.

Hospital name:…….

Ward name:…… Date ……/…../……..

Bed number	Patient initials	Parent signature

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