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Drug Safety Decision Support Model
to reduce Medication Errors

Sanaa Henni

**A thesis submitted in fulfilment of the
requirements for a PhD in Health Informatics**

Centre for Health Informatics

City University

September 2009

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Declaration

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Abstract

The steps involved in the medication process for instance prescribing, dispensing and administering medicines (the "medication process") have always posed some risk to individual patient health. Such "medication errors" were sufficiently common in

developed countries by the 1960s to warrant formal research. Moreover, the frequency of errors appears not to have declined with the introduction of electronic systems.

Several technological approaches have been used to reduce medication errors such as Computerized Physician Order Entry (CPOE), Electronic Patient Record (EPR), drug record system in Denmark and PRESQUID project in France, based on models and theories of errors in healthcare and electronic systems that were drawn from different countries including the UK. Examples of the systems and their evaluation methodology are examined, some of them have already been implemented and others are still being assessed. Consequently, an addition of Clinical Decision Support Systems in current prescribing systems (CDSSs) is necessary. The research considers the development of a medication management model including all the steps of the medication process that involves a clinical decision support system starting from medication prescribing to administration. A necessary preliminary step is to understand the types and contexts of the risks involved. The design of the model was based on the systematic review and meta-analysis outcomes that analysed journal papers, addressing individual themes from definitions, the source of risks and the consequences of errors to comparisons of the medication errors rates between simple prescribing systems and electronic prescribing systems that include CDSSs. The English National Programme For IT is also given prominence as it is a test case for many developed countries and the context for much of my practical work.

The new model demonstrates a notable reduction in the frequency of medication errors and the number of patients with Adverse Drug Events. A system dynamics methodology is used to design the model; the first step is the development of Causal Loop Diagrams (CLDs) which are used as an alternative summary of systematic review findings. They show connections between human and technological factors in the medication process and suggest points for support and intervention potentially addressed by the model that includes CDSSs. The second step is the development of system dynamic models of hospital medication flow in order to detect the effect of CDSSs in reducing the rate of patients with medication errors and application of the effect data of CDSSs to one large hospital to identify the consequence of the model with CDSSs on patient's rate. An evaluation is performed based on focus groups and discussions with clinical pharmacists to demonstrate how the drug safety model can be used. Furthermore an exploitation of pharmacist's opinions on CLDs and drug

safety model by using a short survey has been presented to improve the consequences of medication errors.

Chapter 1

Introduction

1.1 Introduction

This opening chapter, explains why this is a valid research topic and outlines how this report fits with the aims and objectives of my broader research programme.

The content of subsequent chapters is summarised in the final section.

1.2 Background and motivation

The use of prescribed drugs within healthcare systems in developed countries is not as safe as it should be. The problem may have received its first formal attention in the 1960s when Barker and McConnel published a paper in American Journal of Hospital Pharmacy named “The problems of detecting medication errors in hospitals” [1, 2].

In England , 1.8 million prescriptions are issued daily by general practitioners (GPs) and 0.5 million in hospitals [3]. Error reporting is low, which make the patients complain against GPs in the UK, for example in 1996 there were 1000 complains from patients reported to the medical protection society that included 193 errors in prescribing. [4, 5]

Similarly in the United States, approximately 1-2% of patients admitted to hospitals are harmed by medication errors almost all of them are in prescribing [6], a research study estimated that 7,000 deaths occur in this way each year and it is still increasing and the number of deaths increased from 2876 in 1983 to 7391 in 1993. [7]

Medication errors have promoted policy initiatives from the English Department of Health and the American Institute Of Medicine (IOM). They suggested reducing errors by 40% and 50% respectively by 2005 [6, 8, 9]. A prominent feature of these initiatives has been greater use of IT support.

England provides the largest example of IT support in healthcare anywhere in the world. The National Programme For IT (NPFIT) includes electronic records and prescriptions among various local and national components. Moreover a logical place for support to reduce medication errors is as a component of electronic records called Clinical Decision Support Systems (CDSS).

Despite the promise of IT, research suggested that support from electronic systems is not reducing errors [10]. Computerised physician order entry (CPOE) is still associated with errors in data entry and display screen errors and abbreviations [10].

In summary, there seemed to be a good case for studying medication errors. Error reductions should inevitably lead to better health for individual patients and more effective and efficient healthcare systems overall. Improvements are expected through IT. But systems and related national policies are so far not delivering on their promise.

1.3 Fundamentals

This section presents the general area of “medical error” and a general theory of errors in healthcare to put medication errors into a wider context including their definitions. It provides the fundamental information to understand what “medication error” means in theory and practice.

1.3.1 Medical error

Medical error was defined by the US Institute Of Medicine as a failure action to assure patients needs ^[6]. Including adverse drug events, wrong blood transfusion, surgical injury, wrong-place surgery, falls, burns, mistaken identity of patients and names of born babies.

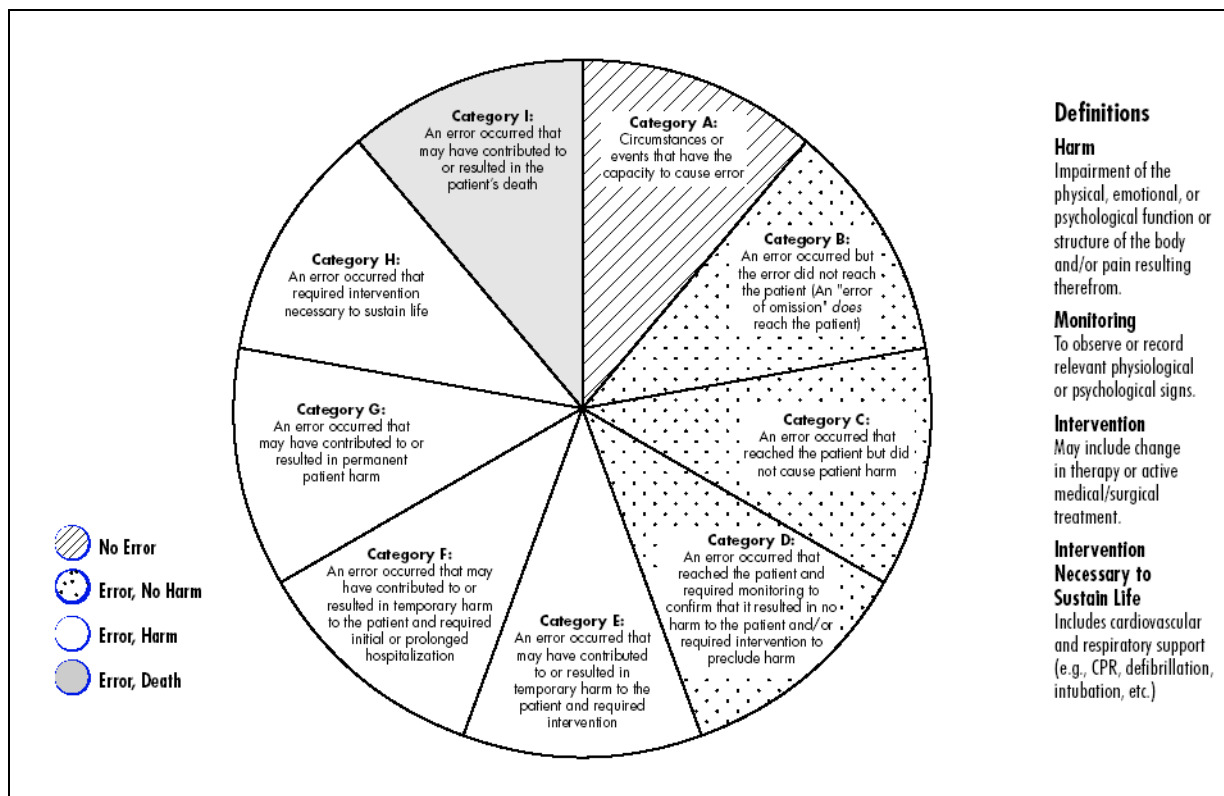
A research group from Virginia Commonwealth University defined it as “All form of improper, delayed, or omitted care that unnecessarily injures patients by either worsening health outcomes or causing physical or emotional distress” [11].

Thus, by those definitions, a medical error is every mistake that happens in hospital or any health department concerning patients related to drugs, surgery, intensive care, and emergencies.

1.3.2. Medication error

Medication errors are a subset of medical errors and it has been defined by several researchers. In 1982, Barker suggested that “A medication error constituted a dose administered to a patient that deviated from the physician’s order such as omission, wrong dose or unauthorized drug” [12]. The American Society of Hospital Pharmacists (ASHP) addressed medications errors in 1992 as “Episodes in drug misadventuring, that should be preventable through effective systems control involving pharmacists, physicians and other prescribers, nurses, risk management personnel, legal counsel, administrators, patients and others in the organizational settings as well as regulatory agencies and the pharmaceutical industry” [13]. In 1993 Bates et al gave a precise definition of medication errors: “Any error in the process of prescribing, dispensing, administration, monitoring drug therapy regardless of whether an injury occurred or the potential for an injury was present”. [14]

In 1997, the US National Co-ordinating Council for Medication Error Reporting and Prevention has defined the subset as [15]:



“A medication error is any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of health professional, patient or consumer. Such events maybe related to professional practice, healthcare products, procedures and systems including prescribing, order communication, product labelling, packaging and nomenclature, compounding, dispensing, distribution, administration, education, monitoring and use”. Finally, the ASHP and the UK National Patient Safety Agency (NPSA) has used this definition.

1.3.3 Classification of medication errors

In order to identify medication errors and find sources of errors, it was important to use an appropriate classification. We have chosen three main classifications: the classification from the US council, the contextual classification and the psychological classification which was based on Reason’s human error model applied in healthcare which was further explained in chapter 3.

The US National Co-ordinating Council for Medication Error Reporting and Prevention proposed a standardized categorisation in July 1996; a Medication Error Index that classified errors according to the severity of the outcome. The index was divided into nine categories from no error to error causing death as shown in Figure 1.1 [15].

Figure 1.1: Index for categorization of Medication Errors [15]

Category A: Events that can cause error

Category B: An error happened but did not reach the patient

Category C: An error happened and reaches the patient but did not cause any harm

Category D: An error happened, reach the patient and require intervention to prevent harm

Category E: An error happened that resulted in temporary patient harm and required intervention

Category F: An error happened that resulted in temporary patient harm and required initial or prolonged hospitalisation

Category G: An error happened that has resulted in permanent patient harm

Category H: An error happened that required intervention to survive

Category I: An error happened that contributed or resulted in the patient's death

The second classification chosen was the contextual classification, which was classified according to where the error occurred in the medication distribution process or use cycle ^[16]. This method can be used by type of medication errors and practitioner group in order to improve the performance of pharmacists and prescribers[17].

The diagram below shows the process and steps involved in the management and use of drugs in healthcare. It should be noted, however, that this model refers mainly to the hospital setting which was used to design the simulation model of the hospital medication process in chapter 5.

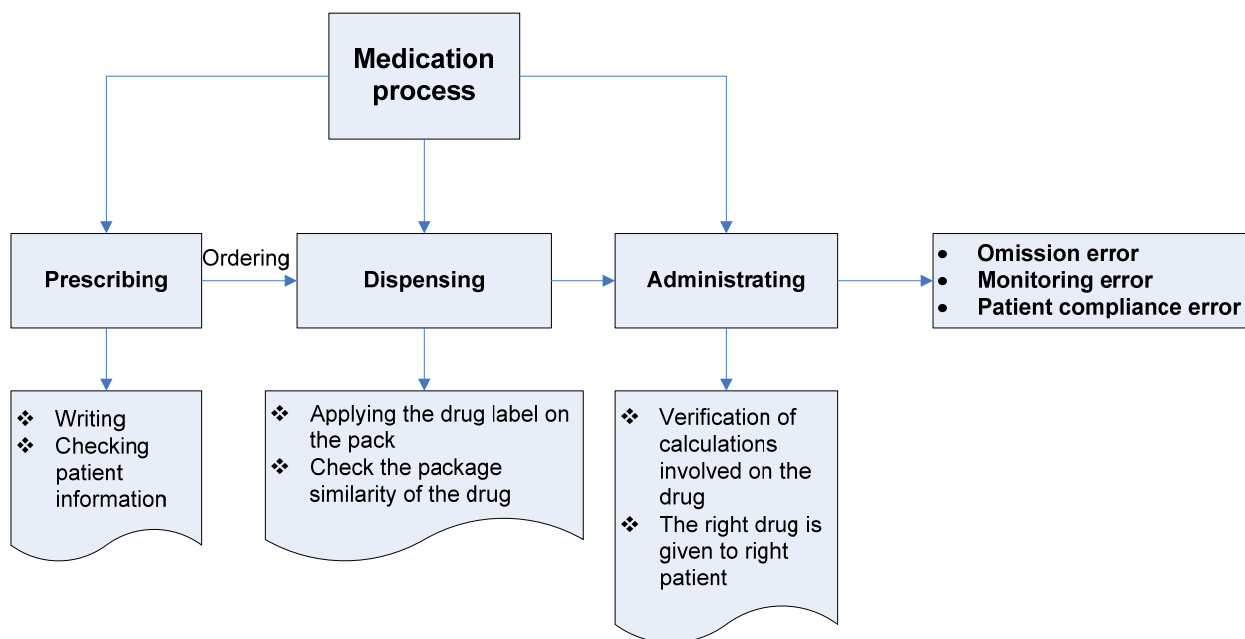


Figure 1.2: Processes involved in the use of drugs in healthcare (mainly in a hospital setting).

The following are the steps in the overall medication process:

Prescribing: To write a drug on a prescription, with the dose of the drug and guidance on how to use it.

Ordering: To order a drug in a hospital pharmacy department or local pharmacy for patients.

Dispensing: To prepare a drug and apply a label on the medicine package, then show the drug to the pharmacist to check if the right drug with the right dose and the right patient's name is written on the label of the medicine package.

Administration of the drug: Medicines are administered to patients by patients or by a doctor or nurse. Drugs are introduced into the body by a number of ways for example; orally by mouth, inhalation, intravenously or intramuscularly, transdermal route, ocular route.

Monitoring: Some medicines have to be monitored in order to maintain a constant concentration of the drug in the bloodstream and each patient will metabolize and eliminate the drug at a different rate. Usually drugs that are taken for a long time are monitored such as drugs for; cardiovascular diseases, thyroid diseases, HIV/AIDS.

Patient involvement/compliance: Schedule medications for patients to follow certain rules on how to take their medicines.

The third classification was the psychological approach based on Reason’s accident causation model (Figure 1.3) to identify, quantify categories of errors which are divided into mistakes, slips and lapses. These categories are explained in detail in the literature review [18].

As explained in the English Department of Health’s consultation document on data quality [3]:

“Error is a failure of a planned sequence of events to achieve an intended outcome when the failure cannot be attributed to chance”. The classification used in ‘Organisation with a Memory’ [3] helpfully divides the causes of errors following the logic behind Reason’s model of accident causation in healthcare which has been widely adopted [18, 19].

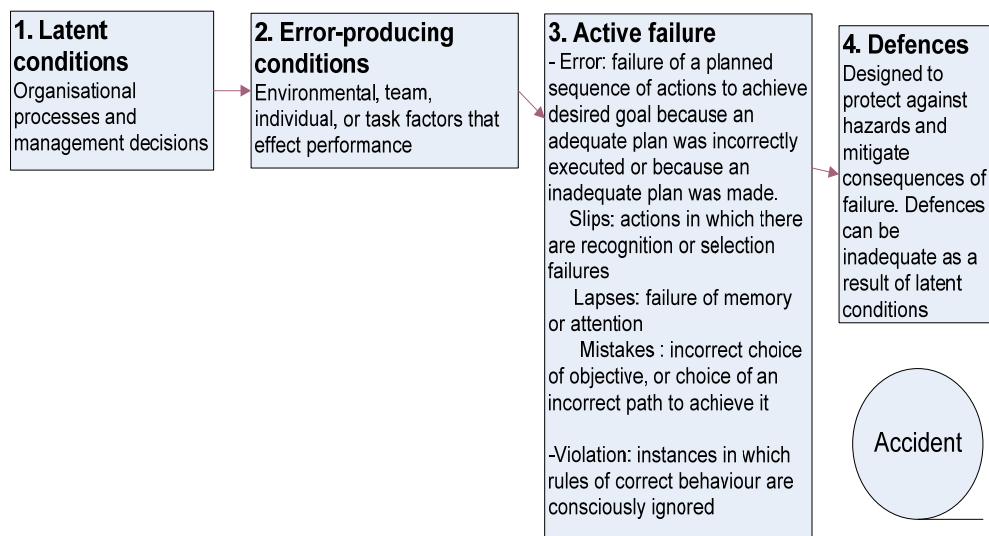


Figure 1.3: Reason’s four stage model of human error [18]

In this section, we looked in detail at each type of errors mapping to the process model given in Figure 1.2. The definitions and evidence for the causes, frequency and consequences/severity of the various error types and the methods used to detect medication errors are explained in the results of the systematic review.

1.4 Aim and objectives

Medication errors continue to occur because of an inadequate understanding of the processes and practices involved. By understanding the general theory and models of medication errors in healthcare, and the identification of current approaches used to reduce those errors; the aim of our research was to develop a new approach which was a system dynamics model of the hospital medication process incorporated with Clinical Decision Support components (CDS Components) with the potential to reduce the frequency and consequence of patients harmed by drug mismanagement.

The aim implied a programme of research that was defined by the following objectives:

- Identification of the settings, needs and components for a drug safety CDSS based on a literature review.
- To carry out a systematic review with meta-analysis to explain definitions and causes of errors and to identify the main variables of the CDS components.
- Design and development of a hospital medication process model with or without a clinical decision support component.
- A simulation of the designed models to analyse the impact of CDS components in reducing medication errors.
- A brief evaluation: Assessment of the performance of the CDS components on the medication process stages and their application, a qualitative evaluation by verifying some elements and flow of the model and finally a summative evaluation by collecting feedbacks from clinical pharmacists on the medication process model.

1.5 Structure of the thesis

1. Introduction

This chapter introduced the history, the background, and the processes involved in drug management with definitions and classification of medication errors and explains the research aims and objectives.

2. Methodology

Chapter describes of the methodology that was used to achieve the aims and objectives of the research.

3. A Literature review

Chapter 3 provides a description of the context of the research by describing the models involved in healthcare to reduce errors and it states the relevant national and international organisations with special interests in medication errors. The chapter also explores the specific systems from various countries with related research, and illustrates the context of the English system.

4. Systematic review with meta-analysis

A systematic review was performed, while it was not possible to do an observational study in a real hospital to collect clinical data on rates and frequencies of errors.

The chapter starts with an explanation of the sources, terms and inclusion/exclusion criteria used to select studies that have investigated the incidence of medication errors and the identification of methods used to detect and classify medication errors. The meta-analysis was carried out in order to compare a simple prescribing system (paper-based or simple computer) with a computer prescribing system that includes CDSSs and to analyse the effect of a computer system on reducing medication errors.

5. Model development

Chapter 5 contains the expected components and standards for the model, and concentrates the findings from the literature and meta-analysis into Causal Loop Diagrams (CLDs) as the basis for the drug safety model. Then a development of system dynamic models of hospital medication flow in order to detect the effect of CDSSs in reducing the rate of patients with medication errors. Finally we applied the effect data of CDS components to hospital to identify the consequence of the model with CDS components on patients rate.

6. Evaluation chapter

We have completed a brief evaluation by following three steps a model consistency check, where we have evaluated the impact of CDS components in a hospital. We have discussed and verified the meaning and flow of the variables with colleagues. We have also presented opinions from clinical pharmacists on CLDs, the initial step of the model.

7. Discussion and conclusion chapter:

The chapter has discussed the main achievements based on the aim and objectives of the research. It has presented outcomes of the research by discussing constructive improvement of the current interventions and the results of the research based on the new approach. The final chapter includes a summary of the research contributions, the weaknesses and suggestions to improve them. Finally, directions for the current project and other opportunities related to medication errors and patient safety.

Chapter 2

Methodology

2.1 Introduction

This chapter consists of the methodology that was used to achieve the aim and objectives of the research. The aim of the project was to design a drug safety model incorporated with CDS components in order to reduce the rate of patients harmed by medication errors. The first chapter of the thesis explained the validity of the research subject by presenting the background of the problem “medication errors” and its general idea and a comprehensive classification of medication errors in healthcare.

2.2 Literature review

The aim of the literature review was to understand the meaning of medication errors and the identification of possible solutions; by investigating types of past and current information technologies that have been involved in this area.

It was important to understand the significance of medication errors by exploring models and examples to explain the term “medication errors” such as Reason’s model explaining different circumstances leading to error; followed with a model of the medication process related to the different types of errors identified.

A summary of relevant national and international organisations with special interests in medication errors that are working specifically in the field has provided us with background and reports on large scale initiatives.

An investigation of the available information technologies such as CPOR, EPR, drug record system in Denmark and PRESQUID project in France and their implication in reducing medication errors from various countries with related research to categorize different systems design and types of medication errors induced by those technologies to use them as a guide to progress in the research.

A review of the English context was essential to consider where the new approach might fit into the current system. Therefore, the official structure for electronic records and electronic prescribing has been viewed, at least for a hospital setting, also to note the standards for the model and the missing elements.

The literature review was conducted using journals, books and web based sources.

2.3 Systematic review with meta-analysis

The general approach was based on methods detailed by “systematic reviews to Support Evidence-based Medicine” [20]. A systematic review is a scientific method to identify relevant studies, and summarise the quality of the results, and a meta-analysis is a part of the review which is a statistical technique for combining the results of the studies into a summary result [20]. This method has been used in several studies; to investigate the incidence of medication errors in paediatrics [21], and to analyse the effect of CDSSs on practitioner performance and patient outcomes [22]. Therefore, it was a reasonable method from which to develop the drug safety model.

The systematic review described the sources, key words and the methodology used in the search strategy. The aim of the meta-analysis was to identify the difference between the number medication errors using a paper system or simple computer and those using an electronic system that includes CDSSs. The analysis was performed to understand the effect of electronic prescribing systems in healthcare compared with a simple prescribing system.

The results of the systematic review were the preliminary step to set up the necessary elements of the model, since it has summarised the findings of the papers and compared the rate of medication errors by using a simple prescribing system with e-prescribing and CDSSs.

2.4 Model design and development

The approach that was used to design the model was system dynamics modelling which is a methodology to study and manage complex systems that has its own principles to predict possible solutions to the problem as it was defined by Roberts et al as “The system dynamics approach to modelling and computer simulation is a problem-solving tool. To evaluate possible solutions to a problem, the problem itself must be clearly stated” [23].

It has been used previously in healthcare to analyse health systems performance [24] a use of national medicines and health policy and the dynamic of hospital medication errors in Australia [25, 26]. Almost all of the studies have used this method to evaluate new clinical systems in their hospital.

Our new approach was to apply the systematic review outcomes to build the model flows, variables and elements in order to assess the impact of CDS components in reducing medication errors. The review has confirmed that electronic systems including CDSSs reduce medication errors; however, some errors are still occurring from the computer system itself. Therefore we have chosen a simulation method to provide descriptive results using system dynamics. The first step was a design of CLDs to express types and causes of medication errors by using a simple prescribing system and computer system that includes CDSSs which is only a description of the system. The second step was the development of a hospital medication process model using a simple prescribing system, and then CDS components were added to the structure to investigate their effect in reducing the rate of patients with medication errors and the rate of harmed patients.

2.5 Model evaluation

The evaluation was an important step in describing the developed model, to validate its structure and usability and to establish how the new approach will improve the outcomes of patient safety.

The methodology required to test the model was found by detecting the appropriate techniques available that can be applied to the model. Several studies have evaluated the e-prescribing tools related to the hospital ward and demonstrated the challenges to evaluating e-prescribing system. The methods that have been used to perform the evaluation were observational studies of past and current prescribing systems, and the introduction of a prospective intervention to examine the effect [27].

We have chosen three methodologies to demonstrate the validity of the model starting with a model consistency check to assess the impact of CDS components in reducing the rate of patients harmed by medication errors. A qualitative evaluation to examine the flows and variables of the model, and a formative or summative study to identify the benefits and limitations of the model with some feedback.

Chapter 3

Literature review

3.1 Introduction

A literature review was the starting point for our research. It would justify "medication errors" as a legitimate area for study and provide relevant background for later development and evaluation of the model. A general theory of medication errors and their classification was explained in the introduction chapter.

The literature review chapter consists of four main sections, starting with models of errors in healthcare, relevant National and International organisations with special interests in medication errors, current electronic systems used to reduce medication errors in USA and Europe and the final section is about the English system. Every section includes an introduction and a summary.

3.2 Objectives

Specifically the review was intended to:

- Provide models and examples to explain the term "medication errors".

- Provide studies of errors occurring under existing paper systems.
- Place my research in the context of national and international organisations with relevant interests, particularly the context of England's National Programme For IT.
- Identify electronic systems and components, with related research, as a guide to progress in the field.
- Identify any special methods used in system development and evaluation.

3.3. Models and theory of errors in healthcare generally

3.3.1. Introduction

Several researchers have proposed models and theories of errors applied in healthcare and their management because a patient can be harmed by human error.

Reason had divided the problem of human error into two approaches [19, 28]: the person approach and the system approach. The person approach problem came from errors made by individuals, such as nurses, physicians, surgeons and pharmacists, which can be forgetfulness, inattention, poor motivation, carelessness and negligence. The system approach problem was defined as a result of the conditions under which those individuals are working; where errors were seen as consequences of a poor design of an organisation. The first step of the simulation model was CLDs (see chapter five), that included some variables that were based on Reason's concept of human errors.

3.3.2. Swiss cheese model

Reason has proposed the model to explain the defenses, barriers and safeguards that occupy a key position in the system approach. It can be described as a number of layers or defensive barriers that protect potential victims from hazards. In an ideal world each defensive layer would be intact; however, in a real world, the slices are more like a Swiss cheese with many holes. The holes in the model are continually opening, closing and changing their locations, when the holes in several layers line up to form a trajectory of accident; therefore the hazards reach the patient and cause harm. There are two reasons influencing the defenses in the holes; active failures and latent conditions which are explained in detail in the section below [19].

The Swiss cheese model as presented in figure 3.1 was widely accepted by patient safety professionals, an evaluation of the understanding of the model was demonstrated by Perneger [16].

The researcher analysed questionnaires given to health professionals who believed that they knew and understood the model, he tackled the familiarity of the respondent with the model and the understanding of various aspects of it; such as the meaning of the slice, the hole, the arrow and active failures.

The interpretation of the model elements varied between quality and safety of the professionals, consequently, more work needs to be performed in the concepts and requirements of patient safety [16].

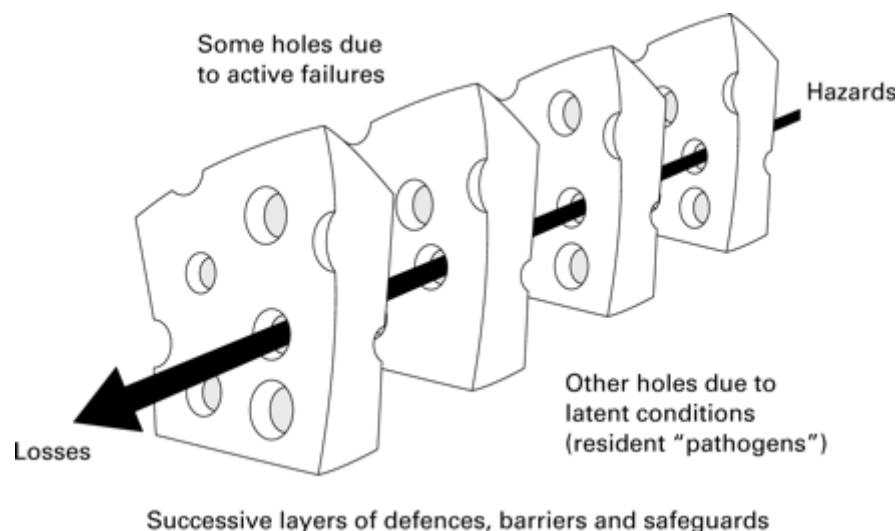


Figure 3.1: Reason's Swiss cheese model [16]

3.3.3. Reason's accident causation model

The structure of the model was explained in chapter 1 in the medication errors classification in Figure 1.3. The details of each part are explained in the following sections, those sections represent the building blocks for developing CLDs as an initial step of the simulation model. The model is divided into four parts: latent conditions, error-producing conditions, active failure and defenses.

3.3.3.1 Latent conditions

Latent conditions are the inevitable “resident pathogens” within the system. They arise from decisions made by designers, builders, procedure writers, and top level management[28].

Latent conditions can also stem from the environment the staff working in. They often reflect elements such as poor design or installations, limited training, an unsuitable environment for the task and may impact at any time. Those conditions pose the greatest problem. They are harder to detect, harder to correct and will affect a wider range of people [29].

Significantly:

“Many active failures and virtually every latent condition can be attributed to management failures, faulty systems, unhelpful processes and poor training and guidance for staff. People are set up to fail” [29].

3.3.3.2 Error-producing conditions

Error-producing conditions are those that lead to errors but are different from latent conditions because they are down to the health professionals not following the hospital policy. Examples of errors producing conditions are shown in Figure 3.2; those errors can be related to the work environment such as less time for heavy work, it can also be related to team or individual when there is no communication between hospital staff or lack of knowledge or experience particularly for junior doctors. Lack of work organization or complex patient health can result in medication errors [18].

The latent conditions and error producing conditions could be the result of uncontrolled actions of prescribers towards the design and use of technology [30].

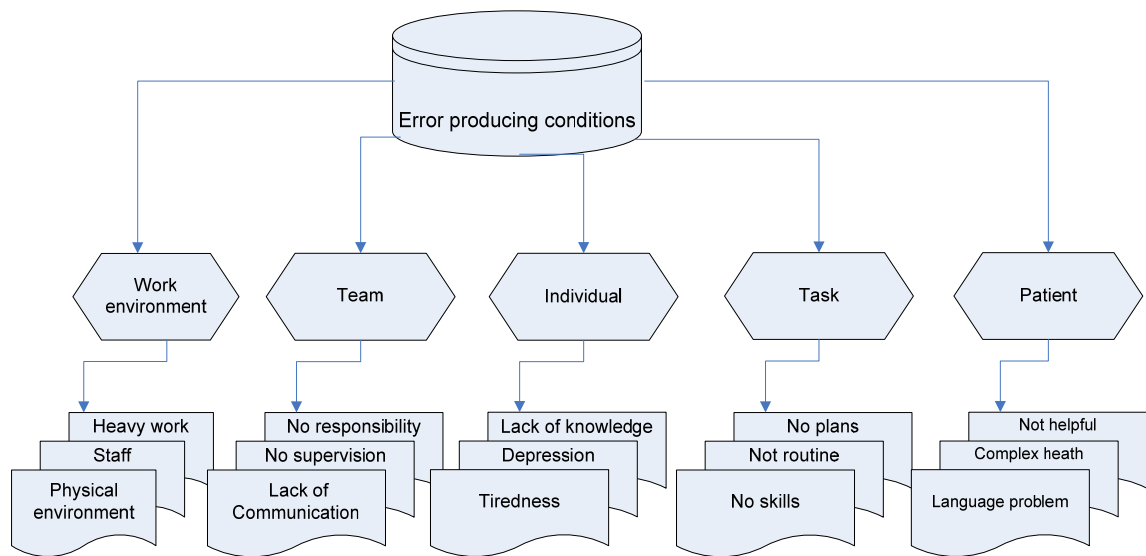


Figure 3.2: Examples of error producing conditions

3.3.3.3 Active failure

Active failure errors cover errors and violations and are one of the causes of prescribing errors. They take a variety of forms: slips, lapses, fumbles, mistakes and procedural violations [28]. Those errors can be violations such as ignorance of the hospital or pharmacy rules when there is no guidance [18]. They are the unsafe acts committed by people who are in direct contact with the patient [28]. Those failures are due to health professionals and often have an immediate impact [29]. (See Figure 3.3)

In the UK almost all of the prescribers are doctors, but there is still a lack of teaching on prescribing and assessment. They might only follow the instruction by their team or by the British National Formulary or the hospital prescribing guide [30]. Therefore junior doctors are the most responsible for these errors based on their individual competence. Recently, a prospective cohort study has focused on medication errors caused by junior doctors who have depression or are burnt- out in three pediatric centres in the US, to determine the levels of depression related to make an unintentional mistake [31, 32].

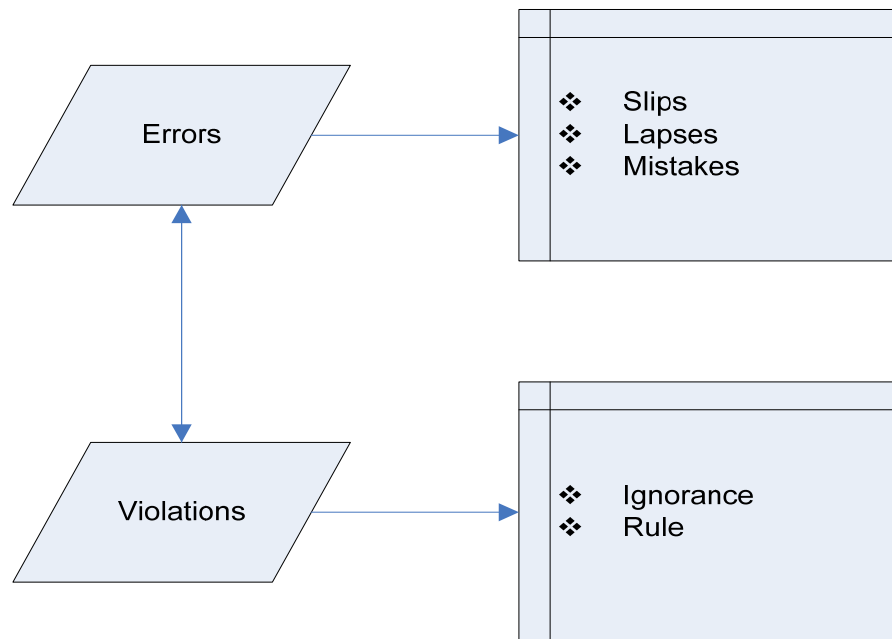


Figure 3.3: Active failure error

Defenses: actions/behaviours to reduce the impact for the professional once an error has occurred [32].

3.3.4 Section summary:

This section of the literature review has presented a general model of errors in healthcare where medication errors were identified as a subset.

The important point was to note the two main categories of error that are observable in the management of drugs and which are commonly associated with errors in healthcare more widely. Identification of Active Failures and Latent Conditions highlighted that the research must develop systems for identifying types of errors and their inter-relationships within the whole medication process. Above all, the research must produce a model that reduces the associated risks.

3.4. Relevant national and international organisations with special interests in medication errors

3.4.1. Introduction

Major organisations around the world have focused on "medication errors" as a special issue. In this section, those organizations have been identified by geographic area, explaining their significant reports and other contributions to the field.

In terms of our research, these organisations represent the response to medication errors on a national and international scale as well as points for monitoring progress. For quick reference, Table 1 in the appendix identified the main reports by organisations which are discussed below.

The identification of national and international organisations with special interests in medications errors was from general knowledge, consultation with research colleagues and through review of the literature cited in other reports and papers

uncovered by other searches. Most organisations and related documents have identifiable online sources.

3.4.2. Worldwide organisations

The World Health Organisation (WHO) [33]

The organisation is a United Nations agency for health, which was established in 1948. One of the organisation's objectives was patient safety, in 2004 WHO launched the world alliance for patient safety. The association organises programmes on patient safety including areas on medication errors. The report from the organisation focused on patient safety and medication safety.

3.4.3. US organisations.

The Institute Of Medicine (IOM) in USA [34]

The institute was chartered in 1970 as a component of the National Academy of Science. IOM has focused on medication errors and human error since 1999 when “to error is human: building a safer health system”, the report included that 44,000 to 98,000 people die in American hospitals each year because of medication errors [6].

The institute suggested reducing errors by 40% in five years and make healthcare safer. In 2005 five years after that report healthcare institutions made some changes based on the Institute implications such as communication between staff and training programmes in using information technologies.

Another report from the institute on preventing medication errors was published in July 2006 (www.iom.edu). It indicated that medication errors are still common and costly and new approaches should be considered (including multiple stakeholders) from medical staff to FDA, government agencies and even patients.

The US National Co-ordinating Council for Medication Error Reporting and Prevention [35]

The aim of the council is to maximise the safe use of medicines and increase awareness of medication errors with preventive strategies and reporting. The association also evaluated the causes of medication errors, and gained the understanding of errors by sponsoring research. The recommendations of the council

were given to colleges, schools and pharmacy, nursing, national professional associations and state associations of medicines.

3.4.4. European organisations

European Commission [36]

The section that deals with government programmes, including healthcare and IT to reduce medication errors; it is called the IDABC (Interoperable Delivery of European eGovernment Services to public Administration, Business and Citizens). It is a programme that delivers information and communication technologies to the public.

3.4.5. English and UK organisations

The English Department of Health (DoH) [37]

The purpose of the department is to improve the health and social care for people in England. The services are delivered by the NHS, local authorities, arm's length bodies and other public and private sector organisations. Since devolution in 1999, the English DoH has had a leading role in health issues within the UK but individual countries actually have overall control in their geographic areas.

Objectives from DoH reports related to medication errors were:

- Reducing medication errors by 50%
- Supporting people with long-term conditions

Connecting For Health NHS [38]

NHS Connecting for Health was formed as an agency of the Department of Health in April 2005 to deliver the National Programme for IT (NPfIT). It replaced the organisation responsible for information and IT issues up to that point (the NHS Information Authority). More details on CFH and the English context were given in section 4 of the literature review.

National Patient Safety Agency (NPSA) [39]

The National Patient Safety Agency is a health authority created for patient safety and incidents happening in the NHS. The agency is responsible for: safety aspects in hospitals, food safety, research safety, assuring performance of doctors and dentists for patient safety.

Medical defence union (MDU) [40]

The organisation was established in 1885 as the world 1st organisation to defend a reputation of doctors based in UK. The MDU is owned by doctors, dentists and other healthcare professionals. Some of the union aims were to introduce risk management services including medication errors caused by doctors and to assist members and to introduce legal teams. Reports from the organisation were on patient safety and particularly medication errors which is one of the causes of patient safety incidents.

Medical protection society [41]

The society is a world leader of health professionals based in UK. The society runs risk management and education programmes to reduce adverse incidents and promote safer practice. The society helps with clinical negligence claims, complaints procedures and disciplinary procedures

Prescription Pricing Authority [42]

The organisation is part of the NHS and Department of Health. It contains everything about prescription price changes and payment for pharmacists. The organisation provides guidance on drugs prices and prescription endorsement. The organisation was included in the flow of prescription data between community pharmacists and payment authorities.

3.4.6. Section summary

This section has reviewed some of the most important national and international organizations with an interest in medication errors. The focus on their main reports in recent years has identified some of the major programmes to reduce medication errors worldwide and specified the sources of statistics for monitoring progress in areas relevant to my area of research.

3.5 Electronic systems

3.5.1 Introduction

This section turns to specific electronic systems used to reduce medication errors. Examples are drawn from the US and two European countries. English examples were left until the next section.

It is important to note that these are only examples. Specific terms and principles behind technologies are not restricted to the identified countries or systems. However, the examples do suggest technological approaches which might be incorporated in our model such as CDSSs as well as methods for evaluation.

3.5.2. United States systems

3.5.2.1. Hospital Computerised Physician Order Entry (CPOE)

An implementation of CPOE may prevent some types of errors such as the written prescription that is misinterpreted while dispensing or administering the wrong drug to patients. CPOE included alerts of potential error to the doctor before the order is made using elements of artificial intelligence [43].

CPOE is basically an electronic prescribing system that stops the error from happening at the ordering time, includes warnings of allergies and drug interactions, contains information concerning new drugs introduced into the market, can improve communication between the physician and the pharmacist, and reduces healthcare costs.

In 2000 the Leapfrog group in the USA promoted the use of CPOE in government hospitals to prevent serious medication errors, in November of that year the group introduced the importance of the system and educated employees, retirees, and families about it.

The evaluation was conducted in five steps:

- Hospital staff were registered on the web with a user name and a security code
- Hospital representative entered the test orders into the CPOE system against the test patients
- When the evaluation was done each hospital recorded the responses of each test order on the website, and the results were evaluated and scored
- Feedbacks from the performance of the CPOE system were received in the hospital
- A composite score was used for public reporting

A recent version of the system required a drug liquid specification on intravenous drugs, and the system provided feedback on drug allergies. On one hand CPOE has advantages, on the other hand it could facilitate up to twenty two types of medication error risks, some of advantages and disadvantages are shown in table 3.1 [10].

Table 3.1. Advantages and disadvantages of CPOE [43, 44]

Advantages of CPOE	Disadvantages of CPOE
--------------------	-----------------------

• Free of handwriting • Faster to reach the pharmacy • Easily integrated into medical records and decision-support systems • More likely to identify the prescribing physician • Reduce incorrect drug choices	• Failure to provide medication after surgery • Antibiotics renewal placed on a paper chart rather than CPOE • Incorrect ordering formats that results on the wrong drug order • Wrong medication selection in the screen of the computer • Increased 19% of pediatric medication errors related to computer
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3.5.2.1.1 Case studies that demonstrated medication errors from CPOE

1. A system was evaluated in New York-Presbyterian Hospital [45], where a case study was demonstrated concerning computer-based ordering of Potassium Chloride (KCl). The examination of KCl orders was carried out over a three day period, it was based on the providers names, starting time, stopping time of the order, and routes of administration in comparison to IV medication injections or fluids. An error was made for an elderly patient during that time, the patient was given a high dose of KCl with different providers and system users, therefore the patient was severely hyperkalemic (an abnormally high concentration of Potassium ions in the blood which can cause renal failure), but he was treated straight away. The error was in the use of the clinical information system when the previous order of KCl did not appear on the screen, and users did not use the options of activation and discontinuation of the order.

Changes were discussed in the evaluation step; some of them are listed below:

- Screens with active list of medication orders should list IV drip orders
- Recent laboratory results should appear on the screen as a snap shot when the same product is re-ordered.
- An alert should be added to inform users for any previous active order of KCl

- Another alert should be added where there is no order of KCl recorded to inform that patient might be hyperkalemic

2. An evaluation study was carried out between October 2001 and March 2003 in a paediatrics referral centre in Children's Hospital of Pittsburgh (CHP) [46]. Before the implementation of CPOE, employees were trained for at least three hours a week with tutorials on the system usability, then the installation was in October 29th 2002. The results of this study totally opposed the judgement of CPOE reduced medication errors, after the implementation of the system, the hospital had a significant increase in child mortality. The implementation of CPOE in hospitals was simultaneously implemented with its application platform; the problem might have been a fault with the application and not the actual clinical system. Or, using an adult based clinical application platform in a children's hospital was not appropriate. Or the problem could have developed from the existing system in the hospital which were not well received from the staff so the implementation of CPOE made it worst. Therefore, CPOE should be well assessed in its applications linked to users. However, in 2006 another paper was published which denied the association of CPOE with increased mortality rates as the analysis was not statistically significant to confirm that, but it suggested that it was important to be aware of the design and implementation of a new system in a pediatric intensive care unit[47].

3. Several studies suggested that CPOE was good in preventing medication errors, but the cost of the software and its implementation was very high. The cost of the first year installation can go up to 4.1 million US dollars, plus the annual maintenance cost can be up to 470,000 dollars which was quite high. Before installing CPOE, the IT infrastructure of the hospital should be checked, and the new system should adapt with the existing clinical information system in the hospital. It was very difficult to implement such a system in small hospitals because of the financial impact of CPOE, the system should be improved [48]. In addition, the time to enter data into CPOE will increase the doctor's work week hours by 5% [49].

3.5.2.1.2 Other types of medication errors from CPOE [50, 51]

CPOE induced medication errors have been evaluated by Ash et al who have viewed the problems and consequences of using the new system, some of these types of errors have been used as variables in the initial step of the model which was CLDs. Those errors are summarized below:

- Juxtaposition error in the computer screen (wrong option is easily clicked)
- Order entry errors (medicines nomenclature)
- Code of data entry (inappropriate text entries)
- Human computer interaction interface (problems on the screen's design and overview)
- Cognitive problems (record a maximum amount of information in the minimum amount of time)
- Communication and coordination errors (misinterpretation of information and comments)
- Lack of flexibility (problems with urgent medication orders and doctor authorization)
- Enter new information; therefore difficult to respond to excessive warnings
- System changes (implementation issues and upgrade of the applications)

3.5.2.2. Computerised clinical decision support systems (CDSSs).

CDSSs are information systems designed to improve decision making. There are several types of systems such as alerts and reminders for drug orders which can be through a feedback on the screen or by instant email, it can also be used to check drug-drug interactions, contraindication and doses [52].

Patient's data are entered into a computerised knowledge base, and software algorithms generate the patient's recommendation. The system was also used for the diagnosis of chest pain the treatment of infertility, and the administration of immunization [22].

These systems were made for clinical decision therefore, they included advice for drug prescribing, alerts for wrong doses and suggestions for various decisions making. A systematic review [22] was published in March 2005 assessing the effects of computerised CDSSs on practitioner performance and patient outcomes.

One of the review question was “Do CDSSs improve practitioner performance or patient outcomes”. The results of the review showed that the CDSS system improved practitioners’ performance in 62% of the assessed outcomes.

The paper described the use of CDSSs that can help doctors in medical areas. One of the studies assessed the drug dosing or prescribing systems; the results showed that CDSSs have a good effect on avoiding some intravenous drug errors.

3.5.2.3. Computer alert system to prevent incidence from adverse drug events and smart infusion technology to prevent IV medication errors:

In 1997 in a community teaching hospital in Phoenix, Arizona, a pilot tested computer programme was developed to generate alerts for specific adverse drug events. The computerized alert system can be used to reduce medication errors, specifically errors from adverse drugs events by giving recommendation to prescribers, and by identifying the error and preventing it.

For example a patient with a haemorrhage was receiving the normal dose of a drug to reduce major bleeding, but with poor indicators of normal drug metabolism (creatinine clearance), the alert appeared with the recommendation to reduce the dose of the drug for the patient [53].

Software has been designed to prevent errors by programming aspecial infusion device for intravenous drugs, the implementation of the system has proven to prevent heparin intravenous medication errors in Vanderbilt Medical Centre in the USA [54].

3.5.3 European systems

3.5.3.1. Drug record system in Denmark

In 2000 a Danish hospital implemented a drug prescribing sheet that allowed medical staff to use it for a particular study and observed the consequences, the results were that medical staff differed in their knowledge of using a new system, the system forced the team to change the drug procedure [55].

The staff that used the system faced some major problems that are cited below:

1. Lack of knowledge
2. Ignorance of the sources of error

3. Lack of responsibilities
4. Low team work
5. Less communication between the staff
6. Staff could not accept the change to their working system
7. Strong professional identity that prevent to use the system

3.5.3.2. PRESGUID project in France

The PRESGUID project (PREScriptioN and GUIDelines) was organized in France, the aim of the project was to improve the assistance of clinical practice guidelines (CPGs). The objective of the project was to create an online system to facilitate the combination between computerised CPGs and drug databases [56].

CPGs were only guidelines produced by ANAES (Agence Nationale d'Accreditation et d'Evaluation en Sante: the agency tasked by the French government with the production of medical references and clinical practice guidelines), the guidelines included the appropriate drugs, but it was insufficient so a link to a drug database was designed to complete the system. Physicians should know the specific classes of the drugs used, regular updates on drug prescription, and which new drugs are available including prices, pharmaceutical data, contraindications and marketing authorizations. PRESGUID is an online service where doctors can access computerized CPGs linked to a drug database which is Vidal in France BNF (British National Formulary) in the UK and PDR (Prescription Drug Reference) in the USA.

Basically, the text of CPGs was reformatted into a computer-interpretable format, and linked with the Vidal drug database. The researchers used the GLIF model which is the evolution of a guideline representation format. The model was to represent the project and the architectural design which is shown in figure 3.4 [56].

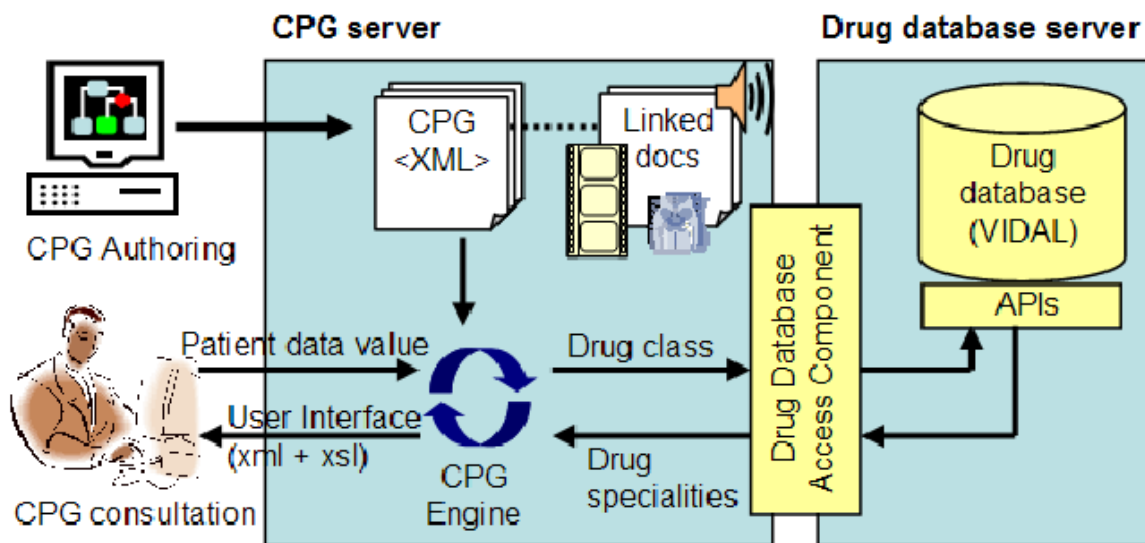


Figure 3.4. Architecture of the PRESGUID project [56]

The figure shows that the project is divided into two servers, the first one is CPG development and distribution platform which contains the following steps;

Step one: Textual CPG was represented in a computer-interpretable format as an XML (eXtensible Markup Language) document merged with other documents, the XML was designed for documents containing structured information (words, pictures, etc) where it can be stored and exchanged.

Step two: This step is the action step where patient data are collected and the values are assigned, then a recommendation or decision message will be displayed for example the drug class or the diet used by the patient.

Step three: This is also an action step where the message is sent to the drug database Vidal to get the appropriate drug speciality.

Step four: It is the guideline and decision step, for example if the patient has to follow any special diet, or should practice physical activity.

Step five: It is the display step of the project, where CPGs are fully stored into the web server, the output is related with the patient data and sent to the user interface which is a dynamically generated web page. The recommendation and results are represented in XML format, even eXtensible Style sheets (XSL) are used to format the document.

3.5.3.3. The French electronic shared medical file

The project was designed to enable health professionals to access patient care records electronically from any location. The programme was presented in May 2004 as a single medical file, the Dossier Medical Personnel (DMP) for each French individual aged 16 and above. The file contained patient data and was accessible online by doctors and the patient via a secure internet connection, or by telephone. The system was designed by the santenergie consortium which is founded by Siemens, Bull, and EDS.

Doctors are already using the computerised patient records, for example in Normandy, the Pays-de-La-Loire, Midi-Pyrenees and Limousin [36].

3.5.4. Section summary

This section has introduced various electronic systems from the US and two European countries. It has provided an international perspective on the uses of IT to tackle medication errors, as well as specific elements for the examination and potential use in the development of my model.

It has viewed three systems in the USA; the CPOE which is an electronic prescribing system that stops errors from happening, the CDSS is a computerised knowledge base and software algorithm to generate patient recommendations with a good effect on avoiding intravenous drug errors, and finally a pilot tested computer programme to generate alerts for specific adverse drug events. Problems, consequences and medication errors induced by the system have been cited.

For Europe we have included the drug record system in Denmark that organises prescribed and dispensed drugs in the hospital, which also gave us an important outcome regarding the hospital staff and their ability to use the new system. The French PRESGUID is also an interesting online system that facilitated the access between computerised prescription and guidelines and the drug data database to avoid medication errors. The French electronic shared medical file is a single file for each French individual that included diagnosis, diseases, treatment and medicines.

3.6 The English context

3.6.1 Introduction

The section begins by looking at the role of electronic records in direct care (Electronic Patient Records- EPR) are playing in IT initiatives in many countries including England. It also includes an overview of the National Programme For IT (NPFIT) under the direction of NHS Connecting For Health (CFH) and we have placed electronic records in the context of wider eHealth components and identify the mechanisms and companies involved in delivery. Finally, we looked at the English approaches to IT related to medicines in hospitals and the community (ePrescribing and Electronic Transfer of Prescriptions).

3.6.2. Electronic patient records: definitions and international significance.

At the heart of electronic developments in healthcare in virtually all developed countries are electronic records. In 1997 the Institute of Medicine report included the definition of patient record system which is similar to EPR [34].

“A patient record system is a type of clinical information system, which is dedicated to collecting, storing, manipulating and making available clinical information important to the delivery of patient care. The central focus of such systems is clinical data. Such systems may be limited in their scope to a single area of clinical information (e.g., dedicated to laboratory data), or they may be comprehensive and cover virtually every fact of clinical information pertinent to patient care (e.g., computer-based patient record systems)”.

This form of record is often called the Electronic Patient Record (EPR). The aim was to inform medical user, to monitor patient medication, to provide computer aided diagnosis, and hospital management. EPR will offer new methods of medical communication between patient and doctor, where information will be stored safely, including text, images, and it is more secure than paper based information [3].

3.6.3. Electronic patient record development in the NHS.

3.6.3.1. Early developments.

In 1988, NHS started a programme on hospital information support systems (HISS), where the NHS spent £48 million in financial support to 16 projects at 25 hospitals. In 1992, more programmes were introduced, systems were integrated and information was secured and confidential. Between 1994 and 1997 the EPR programme was

demonstrated in Queen’s Hospital Burton and Arrowe Park Hospital, Wirral Hospital, it was implemented successfully with good management [57].

After the introduction of the EPR in some hospitals, a report on “Information for Health” was written to give more information on the system and future development on the EPR [57].

Another programme was introduced in 2000-2003 which was the Electronic Record Development and Implementation Programme (ERDIP). The objectives of the project were to create an easy access to patient and electronic health record (EHR), integration between primary and community care, with direct booking, and information technology support to the NHS.

3.6.3.2 EPR and Integrated Care Record Service (ICRS) in England

The last part of the EPR evolution was an integrated service. In December 2003 the health secretary announced that by 2010, every patient in England should have an individual electronic NHS care record, which contains the treatment and care in health service of social care. The NHS record service will connect more than 30,000 GPs and 270 acute, community and mental health NHS trusts in a single national system [38].

This facility is discussed further in section 3.6.3.3.

3.6.3.3. Proposed structure of EPR in England.

EPR in hospitals was divided into six levels (Table 3.2). Significantly, levels 4 and 6 include CDSS and therefore were the targets for our research.

Table 3.2. Main levels of EPR [39, 58]

EPR Levels	Content
Level 1	Clinical support (laboratory, pharmacy), and all administrative support
Level 2	Diagnosis and treatment support integrated with other departments and GP's
Level 3	Electronic prescribing and results reporting
Level 4	Decision support systems, rules and diagnosis
Level 5	Each medical area is incorporated with the EPR
Level 6	Support to doctors, including medical images, X-rays, and telemedicine

Standards which are mandatory for the design and implementation of EPR, include:

Web standards and the extensible markup language (XML)

These have requirements across the whole public sector since the first publication of the eGovernment Inter-operability Framework [59].

Choose and book system (CAB)

It is an electronic-booking service that allows patients to choose their hospital and book appointment with specialists. It was introduced in the summer 2004, and entered to all hospitals, from January 2006; patients were able to choose from four hospitals, book the date and time of the appointment [58]. Patients can book their appointment electronically from the GP, or call the hospital and choose the suitable date and time for them. The system gives patients the right to choose an appointment which is suitable for them.

SNOMED Clinical Terms

SNOMED CT is the Systematised Nomenclature of Medicine Clinical Terms, it is a clinical terminology, clinical computerised language used in the NHS and is a collaboration between NHS and the College of American Pathologists that is more

efficient than the Read codes. The SNOMED CT terms included illnesses, diagnosis, treatment and data that are stored in the patient record and communicated between healthcare departments. SNOMED CT is the global language of the NHS care record to improve patient safety and reduce medical errors [58].

Dictionary of medicines and devices (dm+d)

The NHS dictionary is a unique identifier for medicines and devices. It contains the drug name, strength, ingredients, forms and routes of administration, dose range, contraindications, drug-drug interaction [60]. It is integrated with SCNOMEDCT.

The current version of the dm+d contains almost all prescribed items in primary and secondary care. The contents continue to be updated.

3.6.4 The National Programme For IT (NPFIT)

NPFIT was anticipated by the National Strategic plan [58] and effectively launched with contracts in late 2003. It is now under the overall control of the agency Connecting For Health.

3.6.4.1. The Care Records Service

A key NPFIT component relevant to managing drug information for individual patients was the NHS Care Records Service (CRS- formerly the Integrated CRS). The architecture is shown in figure 3.5.

The strategy of the EPR and its wider uses and integrations in England was divided into three main parts. The first part was the active part, which included all the clinical support systems such as prescribing, pharmacy, radiology and ordering of medicines. The second part was the passive part which was the results or outcome of the active part showed as electronic data. The final part was the secondary analysis data which included information [58].

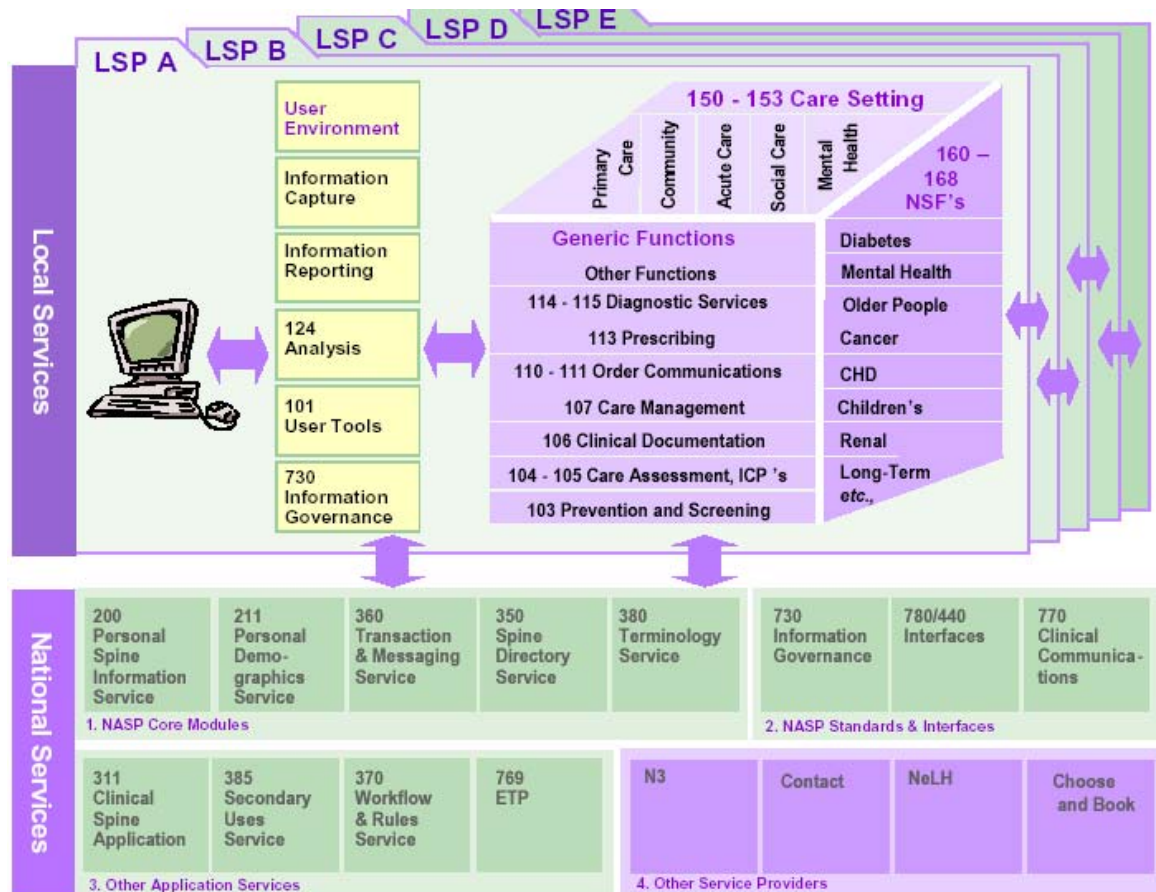


Figure 3.5. Logical architecture of the NHS care records service [38]

The figure above shows that the structure of the NHS care records; was divided into care settings such as primary and acute care, and disease types such as diabetes, mental health and children's health.

The application itself was divided into sections such as choose and book, electronic transfer, quality management and analysis system, and picture archiving and communications system [38].

3.6.4.2. National delivery.

When NPFIT began, the NHS had to select companies to develop the software and the geography for each computerised system.

The NPfIT will be delivered by organisational structures called clusters, there were five clusters for the NHS in England [57, 58] (**Table 3.3**)

Table 3.3: The structure of the NPfIT (Connecting for health) project and its clusters

Regions	Clusters
• London • North East, Yorkshire, and Humberside • South East and South West • East of England and East Midlands • North West and West Midlands	• BT with IDX • Accenture with iSOFT • Fujitsu and IDX • Accenture with iSOFT • CSC with iSOFT

Some of the companies have been recently changed because of financial and delivery problems.

London: Is the smallest cluster in England, The Capital Care Alliance chose BT (British Telecommunication) to be responsible of the London area. IDX will supply to Guy's, King's, St Thomas hospitals, and the new UCLH hospital.

North East cluster: The second smallest cluster, the local service provider is Accenture which is the world leading provider of management and technology, consulting services and solutions, and the main partner is iSOFT (a Manchester based company). The site of this cluster will be the Darlington Memorial hospital.

South East and South West cluster: The southern area is the largest cluster, it includes Oxford's John Radcliffe Hospital, and Bristol's Southmead, and teaching hospitals in Southampton, Exeter, Portsmouth, Brighton, Salisbury, and some other towns. Fujitsu will be the main provider with their partners IDX.

East of England and East Midlands cluster: includes Addenbrookes Hospital in Cambridge, and teaching hospitals in Nottingham, Leicester and Derby. It will be provided by Accenture with their partners iSOFT.

North West and West of Midlands: merges Liverpool, Manchester, Birmingham, and Coventry areas. Some other places such as Burton and Wirral hospitals, it is the second largest cluster. It is lead by CSC (Computer Science Corporation) which is a global services company, and partners with iSOFT.

3.6.5. Electronic prescribing and prescription transfers within the NHS

In 1998, a decision was made by the NHS to all hospitals to implement electronic prescribing [61]. Ideas for Electronic Transmission of Prescriptions (ETP) followed with the focus on primary care which was launched on the 1st October 2007. The current delivery target date for secondary care is 2010 [62].

Some features are common to both approaches and relevant to my research on reducing medication errors.

3.6.5.1. The dictionary of medicines and devices (dm+d) model and integration into care records

The dm+d is part of the UK Care Patient Record system and an important part of the NHS systems handling drug information. (See Figure 3.6).

Project history [60]

The original project started with a primary care drug dictionary (PCDD) which was developed in July 2001 and released in December 2002, in October 2001 a secondary care drug dictionary (SCDD) and medical devices dictionary were developed. The model of the NHS dm+d combines the primary care and secondary dictionaries and the medical devices dictionary which is integrated with SNOMED CT. The NHS dictionary for drugs is the unique identifier for medicines and devices.

Description of the dm+d model

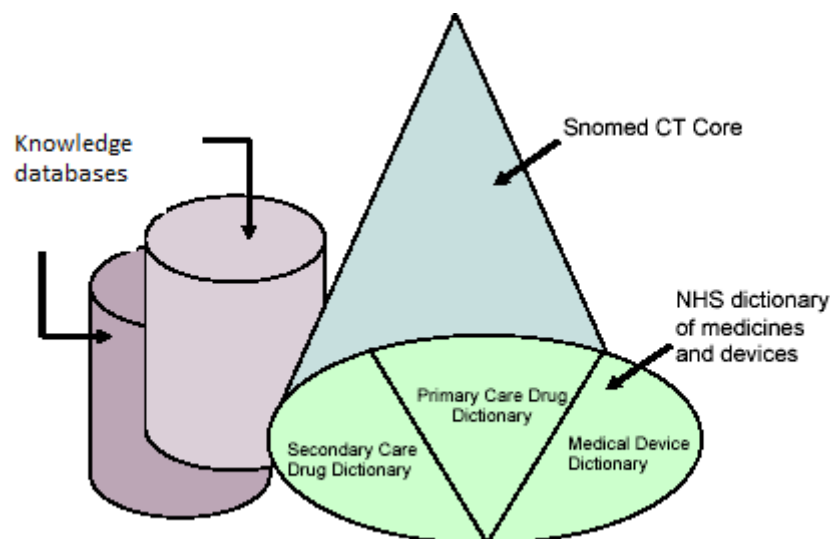


Figure 3.6: The UKCPRS Federal Model for dm+d [60]

Figure 3.6 shows that dm+d is connected to SNOMED CT, by allowing the coding in SNOMED CT to identify the category of the drug and hence to classify the drug product. The dictionary is divided into two sections the virtual and actual sections, and into four sub-sections [41, 59].

1. Virtual therapeutic moiety:

It is the name of the substance in medical nomenclature which is authorised for use in the NHS to treat patients for example Fluoruracil (a chemotherapy drug) or Paracetamol.

2. Virtual medicinal product:

It is the name of the drug with the dose on the pack and the form. For example Panadol 500 mg (Paracetamol) tablets. This part is related with the dose form, active ingredients, and route of administration.

3. Actual medicinal product:

Is the actual name of the drug with the dose and the form, including the name of the supplier. It is connected with product excipients, availability and the supplier name. Panadol 500mg (Paracetamol) from GSK.

4. Virtual medicinal product pack:

It is the name of the drug with the dose form on the pack, and the number of tablets or patches or solution injections. Panadol 500mg (Paracetamol) from GSK, take two tablets every four hours for adults do not exceed eight tablets in 24 hours, and half to one tablet every four hours for children and do not exceed four tablets in 24 hours.

3.6.5.2. British National Formulary (BNF)

It is an information book on prescribing, dispensing and administering of medications. Also with pharmacology, side effects and costs of the prescription and all drugs available on the NHS. The book is used by physicians, pharmacists, nurses and other health-care professionals in the UK [63].

3.6.5.3. Delivering E-prescribing and prescribing transfers

3.6.5.3.1. E-prescribing

Within the Care Records Services is a subset of features known as electronic prescribing. This is simply a computer-based system, responsible for the creation, transmission, dispensing, and monitoring of pharmacological therapies [58].

e-Prescribing is created and implemented, and integrated with the NHS health service record. The system includes the prescribing and dispensing of drugs. But “controlled drugs” are excluded (those currently covered by misuse of drugs legislation). There has been experience of e-Prescribing in some UK centres [64], such as the Wirral Hospitals [9] and Burton-upon Trent [65].

3.6.5.3.2. Electronic Transfer of Prescriptions

Apart from hospitals, Connecting for Health has also introduced e-Prescribing in every GP surgery and community pharmacies nationally, it is part of the Electronic Transmission of Prescription (ETP), as foreseen by a report published in 2000 to improve pharmacies in the future [38].

The system in community settings is also linked to the Prescription Pricing Authority that is covered by a special programme called electronic prescribing and financial information for practices (e-PFIP).

The project consisted of two stages. In the first stage a doctor has to prescribe and printout the prescription with a barcode, then the patient takes the prescription to a local pharmacist, where the bar code will be scanned, so the details of the drugs are downloaded into the system. In the second stage of the project; prescriptions are sent to the pharmacy system automatically [58].

3.6.5.3.3. Strengths and weaknesses of e-Prescribing.

According to the literature some of e-Prescribing strengths are [38, 64, 66, 67, 68]:

- A drug database is already in the system such as BNF, therefore prescribers do not check the paper book each time they need to verify a dose or a drug, and it will save time for patients.
- Electronic Prescribing should include warnings about specific dose, drugs interaction, and adverse drug events.

- Using electronic prescribing will facilitate the communication between medical staff, information will be sent easily.
- Prescribers can add or remove drugs for a particular patient in the system.
- New medications enter the market everyday, so a computerised system can update the drug databases by including or excluding a particular drug in the system.
- Electronic prescribing can be more accurate than written prescription.
- Availability of prescribing history.
- Improvement in completing and the quality of prescriptions to avoid prescribing errors.
- Availability of electronic decision support tools when prescribing, and the inclusion of ordering and monitoring tools along with e-Prescribing could reduce medication errors associated with ADEs.
- The addition of an audit trail to the e-Prescribing, will be useful to track a reported medication error.
- The system encourages the staff to work as a team by increasing communication between them.
- Reduction of work duplication in GP's practice.
- Improvement in patient care by introducing specific interventions for a particular disease.
- Improvement in the quality of prescription writing and reduction of administration errors in an orthopaedic ward.

On the other hand, weaknesses of e-prescribing might be [61]:

- Teaching staff to use new system, it takes time to learn new information specially for certain age practitioners
- Technical problems, one of the causes is the knowledge base and development process of the system such as design and implementation plans
- Complications in compatibility issues; connecting electronic prescribing with other medical systems for example; patient information, laboratory results, pharmacy and decision support

3.6.6. Examples of medication errors in the UK:

Almost all General Practices in the UK are computerised, of the 30,000 GP's only 30 of them do not use computers. There are different suppliers, but not all of them have the appropriate functions to satisfy the user, such as drugs interactions. A project was carried out for the NPSA in 2003 to evaluate the patient record system used in general practices in the UK. To test the system in contraindication, doses and patient information, some examples were used such as [69]:

- Aspirin was entered into the system for an eight years old child, there was a fault because the system did not detect the age, and Aspirin should not be prescribed for children under sixteen years old
- In some cases, doctors entered only the first four letters of the drug for example: PENI for Penicillin, so on the screen the drug Penicillamine appeared which is very toxic and is used for patients with rheumatoid arthritis problem and can lead to death, this fault is due to a lack of training on the system
- Some systems contain the allergy code, but others do not, therefore it is a big problem for patient safety

A retrospective overview of two London hospitals has shown a significant rate of ADEs, 10.8% of patients admitted to hospital experience ADEs, and half of them were preventable. The highest number was in general surgery and orthopaedics. However the study was small and only covered two hospitals. There was an estimation of 5% of patients with ADEs of the 8.5 million patients admitted to hospitals in England and Wales each year [70]. The overview of medication errors in the UK was important and proved that there is an urgent need for system change and improvement. Table 2 in the appendix section represents the types of medications in the UK that were at high risk of errors.

3.6.7 Section summary

The section has reviewed the English programme for IT including ePrescribing, the integration between GPs and community pharmacies. We have identified the central role of Electronic Patient Records in the programme; the role of e-Prescribing; and also the place for CDSS at level 4 and 6 of EPR development. In addition, we have

presented the scale of the IT initiative in English healthcare and the structures and companies responsible for delivery.

These were important observations for the research. Any additional components which we developed for the model must conform to existing standards and should also anticipate changes in delivery of eHealthcare in the foreseeable future.

3.7 Chapter conclusion

The literature review concluded by presenting results using the objectives for the review starting with models and examples to explain the term “medication errors”.

3.7.1. Models, theories of errors in healthcare and types of organisations with special interests in medication errors.

The section has covered Reason’s two models; the Swiss cheese model and the accident causation model where errors were broadly classified as active failures and latent conditions. The second section highlighted the major national and international organisation that focused on medication errors.

3.7.2. Computerised systems used to reduce medication errors.

The second section of the literature has reviewed the main features of existing electronic systems in the US and two European countries, the systems illustrated some benefits in the structure such as the French PRESQUID project that is linked to a drug database, the CPOE system in USA which was mainly designed to reduce prescribing errors and it was connected with the hospital pharmacy and integrated into the patient medical record. However, the CPOE system has introduced new computer medication errors that it was explained at the end of section two of the literature review.

3.7.3 The English system.

The review of the English context, in the third section of the literature review has identified electronic prescribing linked to electronic patient records as part of the bigger National Programme For IT. The official overall structure for electronic records, at least for hospitals, identified six main levels. In particular, CDSSs were identified as an area to assist with medication errors from Level 4 and above. The

important standards for the English system were identified such as: the electronic prescribing, SNOMED Clinical Terms, Dictionary for medicines and devices and the BNF.

In summary the outcome of the literature review was valuable as we could look at medication errors from four aspects. Firstly from the human side including pharmaceutical and medical knowledge errors, process involved and cognitive errors. Secondly, there was the aspect of the human computer link such as system design, interface and system help and guidelines. The third aspect was the computer system including the changes, stability, flexibility and implementation issues. Finally, the computer to user or paper to user side that tackles the delivery of information to the proper user which can be a doctor, a pharmacist, a dispenser or a nurse, inclusion of several types of CDSSs and guidelines.

Chapter 4

Systematic review and Meta-analysis

4.1. Introduction

1.5% of hospital prescriptions in the UK have a medication error, and a quarter of these could result in potentially serious effects [18]. A prominent feature of these initiatives has been greater use of IT support.

We have chosen the approach of a systematic review to identify a common problem between the papers reviewed. The selected papers were divided into three main categories, the first one was papers that included medication errors by errors type for example in prescribing, dispensing and administration using only a paper prescribing system, after that we compared the rate of medication errors in every error type.

The second category included articles selected for a meta-analysis, which contained a rate of medication errors using a paper or simple prescribing system versus prescribing computer system with CDSSs, the results are shown in section 4.4.2. The rest of the papers included some articles that were selected for the literature review also papers that included definitions and causes of medication errors.

4.1.1 Definition of systematic review including a meta-analysis

A systematic review as defined by Altman et al [71] is “a review that has been prepared using a systematic approach to minimise biases and random errors which are documented in a materials and methods section. A systematic review may, or may not contain a meta-analysis which is a statistical analysis of the results from independent studies, which generally aim to produce a single estimate of a treatment effect. A meta-analysis is a tool that helps in understanding the results of intervention in medicine”.

4.2. Aim and objectives of the review

The purpose of carrying out a systematic review was to identify common problems in the chosen articles by comparing the error rate between medication error type, and analyse the efficacy of computerised systems with CDSSs to reduce medication errors compared to a simple prescribing system.

The objectives are cited below:

- Search for themes in scientific databases to collect all possible definitions, causes and sources of “medication errors”
- Provide studies of errors occurring under existing paper systems
- Detect the types of medication errors and find a common error type
- Comparison of error rates in medication error types (prescribing, dispensing and administration)
- Identify types of error reporting methods
- Benefits of electronic systems used to reduce medication errors
- Classify type of errors that electronic systems might reduce compared to paper system

4.3. Methods

4.3.1 Questions for the systematic review

1. What are medication errors?
2. What are the sources of error?
3. What are the types of errors?
4. What are the causes of errors?
5. How can I classify the incidence of medication error?
6. What are the factors contributing to medication error?
7. Were there any solutions to reduce medication error?
8. If yes, what were they?
9. How do computer systems reduce medication errors compared to a paper system?
10. What are the types of errors that electronic systems might reduce?

4.3.2 Search strategy

1. Search sources and criteria

Table 4.1 lists the scientific electronic database and journals used and Table 4.2 lists the selected papers used in the systematic review and meta-analysis. No restrictions were placed on the publication date but only documents in English were considered.

Papers with keywords were available in the listed databases. The search was performed on the first few months of my research from October 2004 to March 2005; afterwards more papers were searched and included through my research. Almost all of the selected papers are available on hard copies for further analysis.

Search words and phrases are specified in Table 4.3, the keywords chosen were based on the review and research objectives. Documents were marked for examination if at least one of the keywords or phrases appeared in the title, abstract or body of the text.

Table 4.1: Databases and journals searched

Name of databases	Number of Articles
Cochrane collaboration (Abstracts of systematic reviews)	3
Journals from Medscape	541
The lancet	122
Journals from Science direct	100
Journal of American Medical Association	80
Journal of American Medical Informatics Association	10

Table 4.2: list of the final papers selected

Name of databases and journals	Number of selected articles
1. MEDLINE (PubMed)	27
2. JAMA (Journal of American Medical Association)	6
3. BMJ	11
4. JAMIA (Journal of American Medical Informatics Association)	12
5. Pharmaceutical journal	2
6. Science direct	8
7. International journal of clinical pharmacy and pharmaceutical care	1

8. Archive of internal medicine (American Medical Association)	3
9. Pharmacy World and Science	1
10. Journal of Perinatology (Nature)	1
11. Advanced of Patient Safety	1
12. The New England Journal of Medicine	1

Table 4.3: Search words and phrases

Words and phrases used for the search
Prescribing medications
Medical error
Prescribing error
Drug mismanagement
Medication error in hospital
Medication error in pharmacy
Mistaken dosage of medication
Role of practitioners and pharmacists in prescribing
Patient safety
Electronic patient record
Computerised prescribing
Implementation, design of systems in healthcare
Prevention of medication error

2. Inclusion and exclusion criteria

The selection of 75 papers (hand searched and papers from the databases) from 858 was based on the following points, The diagram of selection is shown in figure 4.1:

1. The exclusion of 758 citations after screening titles and abstracts This selection was only based on keywords we have used, such as medication errors, prescribing errors, drug mismanagement and so on the title or abstract did not contain any of my keywords.

2. The exclusion of 25 papers from 100 was based on screening titles, abstracts, introduction, and discussion. The excluded articles had nothing to do with the research topics, because its merge the medication suicide, and medical errors such as surgery, or accidents.
3. At the end we have selected only 75 articles, those articles answered almost all of my review questions. The papers included definitions of medication errors, incidence of medication errors (prescribing, dispensing, administration, Adverse Drug Events) and papers on electronics systems used to reduce medication errors.
4. The selection of 75 papers, was based on reading the whole paper and only categorizing the papers with a significant rate of medication errors. The first selection contains 30 articles that discussed medication errors using a paper system including definitions and causes of errors and three of them were reports from organisations, where 13 of them included the rates of errors. The second category contained 23 articles that discussed the problem of medication errors along with types of systems used to reduce those errors. The third one contained 22 articles on error rates comparing electronic system with CDSSs and simple prescribing system, the meta-analysis of those articles is shown section 4.4.2.

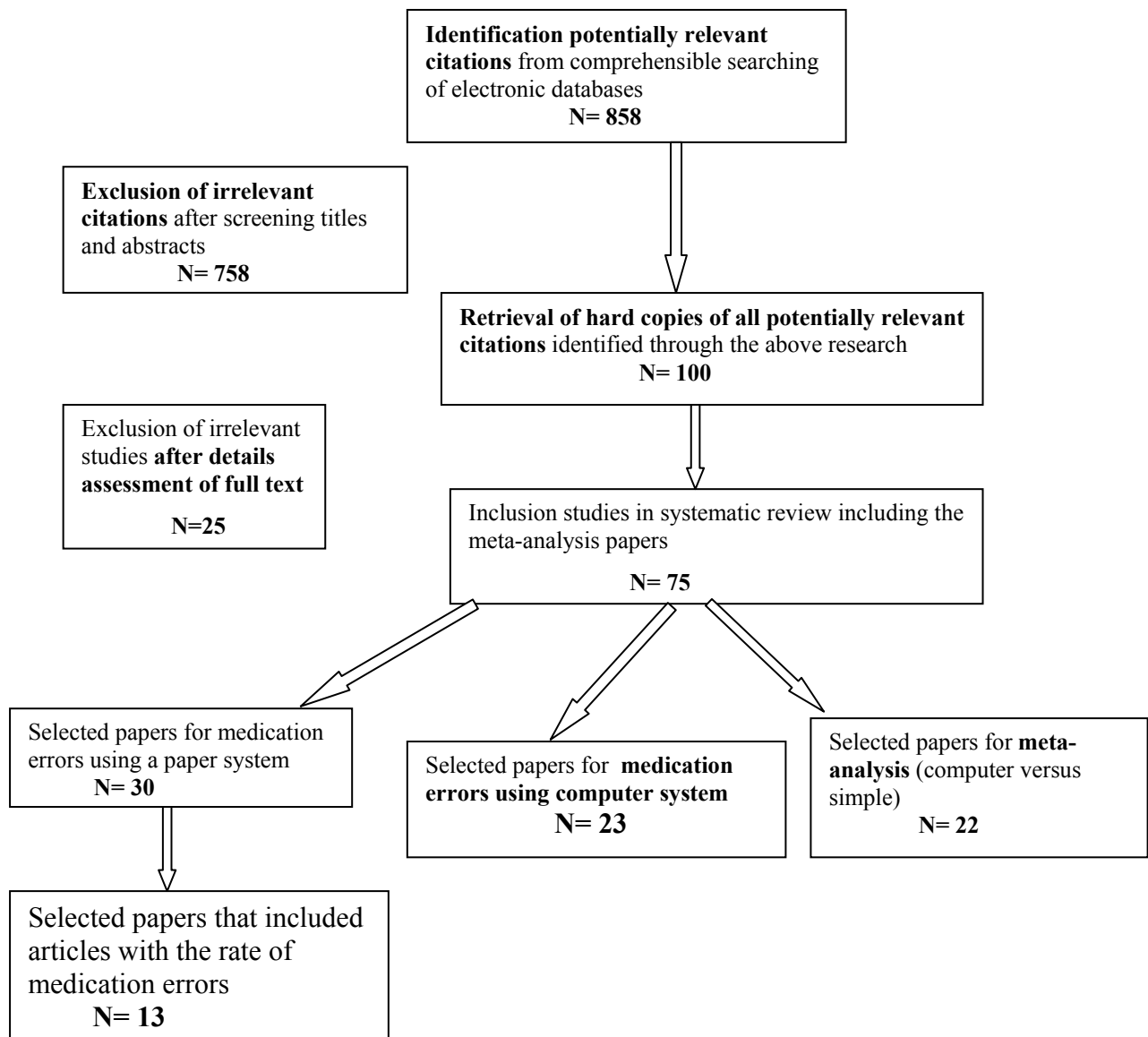


Figure 4.1: Flow chart summarizing the process of identifying relevant journal literature

Table 4.4: Criteria selection

Question component	Inclusion criteria	Exclusion criteria
• The population	Patients, doctors, nurses, pharmacists	Other medical problems
• The interventions	Computerized prescribing compared to written one	Other medication errors
• The outcome	Patient harm due to medication errors	No patient harm (poisoning, suicide)
• The study design	Literature studies on evidence and patient safety	Studies without any evidence

4.3.3. Review procedure

1 Quality of the papers

There was a lack of literature that gave an indefinite rate of errors per studies conducted in hospitals. The first category of articles (thirty articles) discussed medication errors while using a paper system, including definitions and causes of errors according to their classification. This category covered thirteen papers that included the rate of errors; seven articles for prescribing [72-77] , two articles for dispensing errors [78,79] and three articles included the rate of administration errors [80,81,82] .

The second category of articles (twenty three articles) discussed medication errors using computerized systems. The articles selected did not contain the rate of errors. However, it has useful information for the research such as the types electronic systems used to reduce errors in several countries, their structure, benefits and disadvantages. Most of the articles were discussed in the literature review chapter.

The articles were analyzed based on the number of errors in each case over the number of medication orders in prescribing, dispensing and the administration errors category. The contents of both categories of articles are summarized in Tables 3,4,5 and 6 in the appendixes section.

The selection of the appropriate overall papers was based on the following criteria:

1. Aims, objectives and questions of the study which are stated
2. Definitions of medication errors and identification of causes and factors of medication errors
3. Categorizations of the medication process
4. A clear definition of data collection
5. Methods used for data measurement

The third category was the twenty two selected papers for the meta-analysis that compared the rates of medication errors by using a simple prescribing system that could be a paper system or a simple computer prescription with the rate of medication errors using computer system with CDSSs. Details of these articles are described in the meta-analysis section. We could not access to the full text of three papers [83, 84, 85] for the meta-analysis, however we could have enough information to enter their data into the meta-analysis software.

4.4. Results and discussion

At the start we identified seventy five papers that answered almost all of our review questions. However, not all the papers had enough data to do a statistical analysis on them. Following the quality assessment data, thirteen papers were analyzed for the rate of medication errors in every stages of the process.

The articles for drug administration errors reported a significant rate of errors compared with prescribing and dispensing errors. There was a lack of data that reported the rate of medication errors using handwritten prescribing.

4.4.1 Results of papers on prescribing, dispensing and administration errors

4.4.1.1 Definitions and causes of medication errors

4.4.1.1.1 Prescription error

One group has worked to find a clear definition for “prescribing error” [86], their resulting definition is now widely used in the UK for recording/monitoring prescribing incidents.

“A clinically meaningful prescribing error occurs when, as a result of a prescribing decision or prescription writing process, there is an unintentional significant (1) reduction in the probability of treatment being timely and effective or (2) increase in the risk of harm when compared with generally accepted practice”.

Causes of prescription errors

One study in 1999 [18], looked closely at a UK hospital with the purpose of detecting the causes of prescribing errors made by doctors for inpatients at a teaching hospital. The results were presented following Reason’s four stages model of human error, the data was collected in the form of questionnaires and interviews.

From that study they concluded that two main categories caused prescribing errors, the first one was errors producing conditions, such as lack of knowledge in a particular direction or a misunderstanding of hospital guidelines. Problem occurred when doctors have to deal with another doctor’s patient without knowing the patient’s medical history, and another cause when it was too busy in the hospital and patients were waiting to be seen. Some errors occurred in emergency departments where there is a lack of staff and extra workload for doctors.

The study also found several examples of active failures. One of the examples of slips in attention occurs when a doctor has a choice between two drugs, he prescribes one but with the second drug’s dose which is different, the main cause was a lack of concentration.

Another cause was lapses for example if the medication dose was increased or decreased, doctors should add it to the patient’s drug chart but forgot to delete the previous dose which can lead to an overdose, the information system was not good enough to alert the doctor about erasing the first dose of the same medicine.

A further cause that was a simple mistake mostly in long-term medication occurs when the drug’s dose is reduced which depends on the disease stage, it was lack of knowledge as well as the indication for the drug applied.

4.4.1.1.2 Ordering medication error

This error may happen when doctors order medicines from a pharmacy in the hospital; it can be a wrong drug dose, wrong chemical substance for intravenous medications or ordering a drug for the wrong patient [87].

Causes of ordering error

As [10] has observed in a study of the role of computerized physician order entry systems in facilitating medication error, the results of the study showed that CPOE could facilitate twenty two types of errors and some of them were related to ordering errors are often related to:

- Verbal order in a busy work place
- Spelling mistake of the medication
- Mistake in a computer entry order by forgetting to cancel previous orders, patient will end up with an overdose

4.4.1.1.3 Dispensing error

The dispensing error was defined as a “discrepancy between the prescriber’s interpretable written order and the filled prescription (including written modifications made by pharmacist pursuant to contact with the prescriber or in compliance with pharmacy policy)” [78].

Causes of dispensing error

According to studies like [9], dispensing errors can be caused by: prescribing errors, such as unclear prescription’s write up or the error in the prescription with the wrong drug, dose, and even the number of tablets given to the patient. Other causes which were not related to prescribing include inexperienced staff, and similar sounding drug names or packaging for different diseases. Errors in the dispensing label specifically in the drug transcription, applying the drug dose from electronic patient record and not the actual prescription so the dose can be changed by the doctor.

The job environment conditions were associated with the risk of dispensing errors such as the prescription volume, staff training and experience of pharmacists [79].

4.4.1.1.4 Administration error

Drug administration errors can be the result of a prescribing error in a wrong handwritten prescription, or a result of a dispensing error in labelling and packaging, or when the dose is missed or delayed on time, and even the administration of an expired drug.

Some errors, more directly related to administration, are in the dose, route and rate of administration, even administration of expired drug to the patient without checking

the date and more particularly for intravenous drugs. An intravenous (IV) drug error was defined as “A deviation in preparation or administration of a drug from a doctor’s prescription, the hospital’s intravenous policy, or the manufacturer’s instructions”[83].

An observational study was carried out in Royal Belfast Hospital for sick children over a four week period out of a total of one hundred and seventy nine IV doses 40% were on a wrong administration time. Another error was when nurses used the intramuscular rather than IV administration; one dose was given twice and the wrong diluent was used in the drug [88]. Cousins et al also mentioned that almost all of intravenous errors are made by junior doctors [89].

The rate of administration error is about 5% on hospital wards [9]. During the year 2000, 184 American healthcare organisations reported 37,994 medication errors, where 42% were errors in administration [87].

Causes of administration error

Frequent causes are prescription errors like poor handwriting, or wrong medication or dose, and dispensing errors like an incorrect medication label. Other factors include stress and tiredness. Other causes include lack of performance and distractions by new doctors or nurses [90].

According to the NHS Clinical Resource and Audit Group, administration errors can occur in the medication preparation process for example [91]:

- Incorrect drug calculation
- Selection of the wrong drug or chemical substance
- Mislabelling syringes
- Incorrect method of preparation
- Suspension of the continuous infusion that can lead to high blood pressure
- Microbial contamination

Omission error as a special case of administration error

This error happens, when a patient does not have the scheduled dose of medication, it means that the prescribed drug is not administered. Almost of all those errors are made by nurses and are followed by giving the wrong dose to patients [90].

Causes of omission errors are often [87]

- Lack of communication between staff and patient
- Unclear prescription

4.4.1.1.5 Monitoring error

When the patient is not monitored properly before or after receiving the drug. Error can be made by a practitioner or a pharmacist by giving a drug without checking the patient history that can result in a drug interaction [92].

Causes of monitoring error

According to [92], these are commonly:

- Lack of knowledge
- Disorganisation of the patient data

4.4.1.1.6 Patient compliance error/ issues

Patient compliance is when patients comply on doctors directions on how to use their medicines. In some cases patients do not follow the doctor's advice; therefore a medication error might occur.

This error is made by the patient when the drug is misused, because the patient does not have the complete knowledge about the drugs, or the patient does not want to take the drug.

Causes of patient error and related research

The Royal Pharmaceutical Society of Great Britain has noted problems with compliance in particular [93]. They note that:

- No concordance between doctors and patients`
- Patients do not have enough information about their medications

4.4.1.1.7 Related errors

Two additional categories of “medication errors” are also worth noting. They can be seen as errors in their own right, but are more commonly viewed as potentially unpredictable incidents which should be specially recorded and monitored (eg- by national monitoring agencies).

4.4.1.1.7.1 Adverse drug reactions (ADRs)

There are many definitions for ADRs. Many overlap with earlier definitions for “medication error” more generally. Nevertheless, two definitions are presented for information.

The first one is from the US FDA (Food and Drug Administration) [92].

“Any adverse event associated with the use of a drug in humans, whether or not considered drug related, including the following: in the course of the use of a drug product in professional practice; an adverse event occurring from drug overdose, whether accidental or unintentional; drug abuse; drug withdrawal; and any significant failure of expected pharmacologic action”.

The second definition is from the World Health Organisation (WHO) [3]:

“Any noxious or unintended response to a drug that occurs at doses usually used for prophylaxis, diagnosis, or therapy of disease or for the modification of psychological function.”

4.4.1.1.7.2 Adverse drug events (ADEs)

It is a combination between adverse drug reactions such as allergies or drug interactions, and error in medication prescription or administration.

It was defined by the Institute Of Medicine as “An injury resulting from medical intervention related to a drug” which explained any damage caused by the drug such as overdose or anything caused by the use of the drug such as reduction or increase of the dose or discontinuation of the treatment. Therefore, the difference between medication errors and ADEs is that medication errors are the inappropriate use of a drug that may or may not result in patient harm [94]. ADEs could be associated with medication errors and others could be independent, a study has showed that ADEs can be 20% associated with medication errors that almost all of them were preventable[95].

4.4.1.2. Detection methods of Medication Errors [21, 96, 97, 98]

The review included a few methods to measure medication errors:

a. Paper or simple prescribing system

- Spontaneous reporting after the discovery of an error. There were four papers from prescribing errors [72, 73, 76, 77]. One from dispensing [76] and one from administration errors category [90] that have used spontaneous reporting for their studies.
- Chart review is a check of prescriptions and prescribing charts to identify medication errors. The review included only two papers [74, 99] in the prescribing errors category that have used the chart review method to detect prescribing errors.

- Observational study is a surveillance of health professionals while they are prescribing, dispensing and administering medications. The review included four articles for prescribing errors [75, 72, 100, 101], two for dispensing errors [78, 79] and six for administration errors [80, 88, 81, 82, 89, 102] .

Those methods are processed-based methods and the figure of medication process involved in the use of drugs in healthcare was explained in the introduction and literature chapters.

b. Computer system

- Spontaneous reporting was used less in this category as almost all of the papers have evaluated the impact of new systems in reducing medication errors. There were only two studies that used a spontaneous report of medication errors while using bar coding intervention [103, 104].
- Medication order charts review was used in one article only [105].
- Four articles have used observational studies to detect medication errors using prescribing tools [53, 106, 107, 108].
- Almost all of the meta-analysis papers have evaluated a prescribing system, their methods were based on observation and interviews. One article used a web-based supervision of the use of computerised prescribing with decision support systems [109].

4.4.2 Results of the selected papers for the meta-analysis

4.4.2.1 The program

The meta-analysis was performed using the program META [110], it is Windows based. It contains a database which is easy to enter and elaborate the data statistically. The program was designed to produce an analytical and graphical outcome of the statistical analysis. It can also save a large number of studies organized in one or more databases and allows the user to modify the data already entered [110].

4.4.2.2 Meta-analysis methodology

The meta-analysis methodology was part of the systematic review in order to extract papers that assessed the systematic review questions by including the keywords selected. The aim of the meta-analysis was to compare the rate of medication errors between two prescribing systems; a simple prescribing system which was handwritten or simple printed prescription and a computer system that included CDSSs. The presentation of meta-analysis data was given by tables and graphics.

The subsequent steps of the methodology were as follows [110]:

- **The number of trials in the meta-analysis**

The of studies chosen for the meta-analysis are shown in Table 4.9, these showed the rate of drug entries and the rate of medication errors as observed events both in control and intervention groups.

- **The test for heterogeneity**

The test was performed to know if the chosen trials or studies belong to same distribution. The presence of heterogeneity should be explained by factors influencing the effect. The funnel and Galbraith plots were used to represent heterogeneity.

- **Publication bias assessment (PBA)**

A tool that assessed the number of unpublished studies which were similar to those published and analysed, from the results we could identify if the meta-analysis was statistically or not statistically significant.

- **Number needed to treat (NNT) odds ratio or risk difference**

The data was reported by numbers with their confidence interval, more details were explained through the analysis.

- **Graphic representation**

A selection of the most instructive plots was used such as the standard and forest plot. The Galbraith plot was the most complete graphic representation, that showed the effect of medication errors of each single trial included in the meta-analysis, it also provided information on heterogeneity between the trials analysed.

- **Sub-group analysis**

The meta-analysis results indicated a divergence between studies; therefore, we had to look at the differences between studies, such as the types of intervention or population differences.

4.4.2.3 Assessment of study quality

The quality of the papers was examined with the systematic review, though with the meta-analysis studies; more validation questions were added to assess the papers such as:

1. Did the papers describe the questions to be answered by the meta-analysis?
2. Did they include a control group and intervention group?
3. Did they give results on comparisons between the two groups?
4. Did they contain a specific type of intervention?
5. Did they give a clear outcome of the interventions?

The assessment of included studies of the meta-analysis was done by using the “Newcastle-Ottawa Scale” [111]. The “CONSORT checklist” [112] was only used to specifically score randomized controlled trials, as all the studies were controlled trials but not all of them selected patients randomly, some of them selected the whole patient population was chosen and assessed as control and intervention.

➤ The “Newcastle-Ottawa Scale” (NOS) [111]:

The methodology was scored by awarding stars to key steps; the highest score of the best methodology was seven stars, and studies that scored less than four stars were considered weak. The assessment scale was based on the following criteria:

Table 4.5: The “Newcastle-Ottawa Scale” assessment criteria

Assessed criteria	Questions based on the criteria	Number of stars for the scoring
Cohort selection	1. Representation of the rate of medication errors 2. Clear identification of the types of intervention used? 3. Demonstration of the outcome interests	* * *
Cohort comparability	Comparison of the difference between studies, such as the type of intervention used	**
Outcome from the studies	1. Measurement of the assessed outcomes 2. The period of the reported study	* *

➤ The “CONSORT Checklist” [112]:

The scoring system was only used for randomized control trials based on the following assessment:

Table 4.6: The CONSORT checklist

Section and topic	Item No	Description
Title and abstract	1	How participants were allocated to interventions for example random allocation, randomized, or randomly assigned.
Introduction	2	Scientific background and explanation of rationale
Methods: Participants	3	Criteria of participants and location of settings
Interventions	4	Precise details of interventions intended for each group
Objectives	5	Specific objectives and hypothesis
Outcomes	6	Methods of outcome measurements such as observations or spontaneous reporting
Sample size	7	Determination and analysis of sample size
Randomization: Sequence generation	8	Methods used to generate the random allocation
Allocation concealment	9	Methods used to implement the random allocation
Implementation	10	Who generated the allocation sequence and enrollment of participants
Blinding	11	If participants were blinded to group assignment, and how the success of blinding was evaluated
Statistical methods	12	Methods to compare groups for analysis
Results:	13	Number of participants in each stage of

Participant flow		study and for each group
Recruitment	14	Dates and periods of recruitment
Baseline data	15	Characteristics of each group
Numbers analyzed	16	Number of participants
Outcomes and estimation	17	A summary of results for each group
Ancillary analyses	18	Other analysis such as sub-group analyses
Adverse events	19	Important side effects in each intervention group
Comment: Interpretation	20	Interpretation of the results including hypotheses and imprecision
Generalizability	21	External validity of the trials findings
Overall evidence	22	Interpretation of the results in the context of current evidence

Table 4.7: Non randomised comparative studies

Study Number	year	Author	Journal	NOS (Max=7)
2	1998	K D Evans	Critical Care	5
3	1998	R S Evans	N Engl J Med	7
4	1999	Bates	JAMIA	7
5	2000	Teich	Arch Intern Med	6
6	2001	Mullet	Pediatrics	5
7	2001	Bizovi	Acad Emerg Med	3
8	2001	Chertow	JAMA	7
9	2002	Gandhi	JAMIA	4
10	2003	King	Pediatrics	6
12	2004	Fontan	Pharm World & Science	3
13	2004	Potts	Pediatrics	7

14	2004	Cordero	Journal of Perinatology	3
15	2005	Shulman	Critical Care	7
16	2005	Gandhi	J Gen Intern Med	5
17	2005	Peterson	Arch Intern Med	6
18	2005	Rudman	Adv Intern Med	4
19	2005	Oliven	Intern J Med Inform	5
22	2007	Donyai	BJCP	7

Table 4.8: Randomised control trials

Study Number	Year	Author	Journal	NOS (Max=7)	CONSORT (Max=22)
1	1998	Bates	JAMA	7	18
11	2003	Tamblyn	CMAJ	5	19
20	2006	Feldstein	Arch Intern Med	5	17
21	2006	Colpaert	Critical Care	7	17

4.4.2.4 Hypothesis

To show that “computer prescribing system with CDSSs reduces medication errors”.

4.4.2.5 Analytical representation

1. The number of trials in the meta-analysis

The analysis has been performed with twenty two trials, with a total of 410754 prescribed drugs; with 223653 prescribed drugs or prescriptions using a computer system with CDSSs and 187101 using a simple system as shown in Table 4.9. The studies were ordered by year of publication. Studies 7, 12 and 14 were based on reading their abstracts only; it was not possible to access the full paper.

Table 4.9: The 22 papers selected for the meta-analysis

ORIGINAL DATA							
Author	Journal	Score	Year	Control Ent.	Obs.	Intervention Ent.	Obs.
1 Bates	JAMA	0	1998	12218	127	24539	134
2 KD Evans	Crit Care	0	1998	1184	290	1225	372
3 RS Evans	N Engl J Med	0	1998	3650	785	942	138
4 Bates	JAMIA	0	1999	10070	242	14352	50
5 Teich	Arch Intern Med	0	2000	26354	552	64594	363
6 Mullet	Pediatrics	0	2001	1262	630	1309	500
7 Bizovi	Acad Emerg Med	0	2001	2326	54	1594	11
8 Chertow	JAMA	0	2001	58160	6298	38399	2714
9 Gandhi	JAMIA	0	2002	1868	159	1868	81
10 King	Pediatrics	0	2003	6674	173	5786	120
11 Tamblyn	CMAJ	0	2003	6276	909	6284	755
12 Fontan	Pharm World & Science	0	2004	589	518	3943	419
13 Potts	Pediatrics	0	2004	6803	2196	7025	100
14 Cordero	Journal of Perinatology	0	2004	31	2	28	0
15 Shulman	Crit Care	0	2005	1036	69	2429	117
16 Gandhi	J Gen Intern Med	0	2005	940	141	939	64
17 Peterson	Arch Intern Med	0	2005	3908	195	3525	99
18 Rudman	Adv Patient Saft	0	2005	25713	416	26490	959
19 Oliven	Intern J Med Inform	0	2005	4365	622	4743	220
20 Feldstein	Arch Intern Med	0	2006	10000	3294	10000	2804
21 Colpaert	Crit Care	0	2006	1224	331	1286	44
22 Donyai	BJCP	0	2007	2450	94	2353	48

Fixed effect model		
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Measure	Difference of percentage	LOG Odds Ratio Mantel Haenzel
ϕ	-0.015	-0.617
SE (ϕ)	0.001	0.014
z	-28.481	-45.224
P(z)	0.000	0.000
Q	6813.018	4130.601
P(Q)	0.000	0.000
df	21	21

I^2	99.7	99.5
95 % CI	99.5-99.8	99.1-99.7

Odds Ratio		0.540
95 % CI	-0.016/-0.014	0.525-0.554

Random Effect Model		
Measure	Difference of percentage	LOG Odds Ratio (DerSimonian-Laird)
ϕ	- 0.086	- 0.973
SE (ϕ)	0.010	0.183
z	- 8.325	- 5.321
P(z)	0.000	0.000

Odds Ratio		0.378
95 % CI	- 0.107/-0.066	0.264-0.541

Φ Mean effect

SE (ϕ) Standard error of natural of odds ratio

z Significance

P(z) Specific test for statistical significance

Q Test for heterogeneity

P(Q) Specific test for statistical significance

df Degree of freedom

I^2 Percentage of total variation across studies due to heterogeneity

Publication bias assessment (number of void or negative trials necessary to render meaningless the meta-analysis): 6802

Number Needed to Treat (95 % CI): - 68(-73/-64)

Number Needed to Treat (95 % CI): -12 (-15/ -9) (REM)

Test of funnel plot asymmetry: $\alpha = -6.56$ 95 % CI= -13.75/ 0.63 $p(z) = 0.07$

Table 4.10: The meta-analysis table

2. Explanation of the meta-analysis table

The table was the output from the software; it was divided into four parts: fixed effect model, quantifying the heterogeneity, the Random effect model and publication bias, the Number Needed to Treat and the test for funnel plot asymmetry.

2.1 Results of the Fixed Effect Model

The first part of the table shows the analysis performed by the Fixed Effect Model. The model required that the estimates of treatment effect obtained from all trials belong to the same distribution. It was verified by the Galbraith plot described in section 4.4.2.5.

The first line of the column difference percentage indicated the mean effect, or the pooled Odds Ratio (ϕ).

A meta-analysis was a process that allowed aggregation of the results of multiple studies. It was a procedure that weighted the results of each study according to their variance where the weight of each study i was given by the inverse of the variance as shown in the formula below:

$Wi = 1/Vi$ (1) where the variable Wi was the weight and Vi the variance of the outcome of the study.

Therefore, once the studies were individually weighted, the global effect or the pooled effect indicated the general formula of the meta-analysis in terms of a weighted mean:

$$D \equiv \frac{\sum wi di}{\sum wi} \quad (2) \text{ where the variable } di \text{ was the odds ratio.}$$

The mean difference in efficacy of the rate of medication errors between using a simple prescribing system and using a computer system with CDSSs was only 1.5 %

by using a simple system, because we are looking at a negative event, with a 95% confidence interval of (-0.016/-0.014). The effect was significant as shown by both CI (which did not cross 0) and the specific test of statistical significance whose p was reported in the fourth row by (0.000).

The other columns showed the Odds Ratio calculated using Peto, Gart and Mantel Haenszel. We have chosen the Mantel Haenszel formula which was according the table below:

Table 4.11: Example on how to use Odds Ratio to compare between simple system and computer system

	Medication errors		Total
	Yes	No	
Computer	10112 (A)	213541 (B)	223653 (E)
Simple	18097 (C)	169004 (D)	187101 (F)
Total	28209	382545	

$$OR = \frac{A/B}{C/D} = \frac{A \times D}{B \times C} \quad (3)$$

$$CI(95\%) = \exp[LnOR \pm 1.96 \times SE(LnOR)] \quad (4)$$

The Logarithm of OR has a standard error given by:

$$SE(\log OR) = \sqrt{\frac{1}{A} + \frac{1}{B} + \frac{1}{C} + \frac{1}{D}} \quad (5)$$

Moving from the first to the last row of the meta-analysis table, the variables represented are the natural Logarithm of the Odds Ratio (ϕ) for each test, its standard error SE (ϕ), the significance (z) and its relative p value.

2.2 Test for heterogeneity

The other procedure was related to the formal test of statistical heterogeneity, which was more precise. The results of the test were indicated by Q which was the chi-squared with the degree of freedom df which is shown below it. The statistical significance was also shown in the same section indicated by $p(Q)$.

The Cochran Q value showed a high level of heterogeneity of 6813.018, which was calculated using the equation:

$$Q = \sum [W_i(d_i - D)^2] \quad (6)$$

Where D was the pooled effect

d_i = the percentage difference

W_i = weight of the j-n study

The second part of the table was **quantifying the heterogeneity** as follows:

The I^2 values expressed the percentage of the total variation across the studies due to heterogeneity. An I^2 value of 95% CI showed a high heterogeneity as shown in the second part of the table. Due to high heterogeneity as explained, the hypothesis that the trials under study had the same distribution was rejected.

The test for statistical heterogeneity was significant, so we have used the results of the random effect model; which mean that the trials did not belong to the same distribution. Therefore, we have searched for possible causes of heterogeneity and evaluation of the outlier trials of the funnel plot, by developing a sub-group analysis shown in section 4.5.

2.3 Results of the Random Effect Model

The model did not require the assumption that each study was derived from the same population and the n studies were considered separately, each one with their own mean. The trials under study did not have the same distribution, because of high heterogeneity; therefore, we have decided to use the Random Effect Model.

The Odds Ratio were calculated using the following **DerSimonian-Laird** formulae:

$$\text{Ln OR}_{\text{dl}} = \frac{\sum (w_i \times \text{LnOR}_i)}{\sum w_i} \quad (7)$$

Where

$$wi^* = \frac{1}{\left[D + \left(\frac{1}{wi} \right) \right]}$$

$$D = \frac{[Q - (S - 1)] \times \sum wi}{[(\sum wi)^2 - \sum wi^2]}$$

Where S was the number of studies

$$Q = \sum wi (\ln OR_i - \ln OR_{MH}) \quad (8)$$

where Q has a chi-square distribution with the degrees of freedom equal to n-1 studies.

By reading the first column of the Random effect model of the difference percentage, the first line indicated the mean effect of medication errors by using a computer system with CDSSs and a simple prescribing system, there was a mean difference in efficacy of **8.6%** with a 95% confidence interval of (-0.107/-0.066). As we were looking at a **negative event** which was medication errors in healthcare using a computer system with CDSSs versus a simple prescribing system (paper or simple computer), the value was towards the medication errors when using a simple prescribing system when looking at the graphical results of the data); that means that there was **8.6%** more medication errors in a simple system compared to a computer system with decision support systems.

This effect was significant by reading the *p* value of the test of statistical significance which was (0.000). These results are also explained in the graphical representation (forest plot of the risk difference (fig 4.6) and the Galbraith plot (fig 4.8)).

2.4 Odds Ratio

The measure of the effect size, defined as the ratio of the odds of medication errors using a simple system compared to medication errors using a computer system with CDSSs.

The other column of the table showed the Odds Ratio calculated using the **DerSimonian-Laird** formula for the Random effect model and **Mantel Haenszel** for the fixed effect model. Those results are also shown in the standard plot of the Odds Ratio (fig 4.4) and the forest plot (fig 4.5).

2.5 Tests for publication bias

The method was applied when the result of the meta-analysis was statistically significant. The publication bias using the *Klein formulae* which answered the question if there was a publication bias, how many negative studies are needed to influence the findings of the meta-analysis.

However, the funnel plot and the test for funnel plot asymmetry explained if publication bias was present or not as shown and explained in figures 4.2 and 4.3.

Klein formulae:

$$\left(\frac{k \ln OR}{1.96} \right)^2 \bar{w} - k \quad (9)$$

$\bar{w}$ was the mean of the weights of k trials per $1/V_i$

In this case the test demonstrates that 6802 studies with negative results were needed to make the meta-analysis show no difference between the computer system and the paper system. Therefore our results were reliable, because the number of studies was quite high. The data were obtained automatically from the software.

2.6 Number Needed to Treat

The aim of the meta-analysis was to evaluate the efficacy of a computer prescribing system with CDSSs versus a simple prescribing system; the NNT indicated how many drugs were to be prescribed to see the one-unit difference between the two ways of prescribing.

The value was NNT= 12 (REM) which meant that one doctor need to prescribe 12 drugs or prescriptions using the computer system to use one additional drug compared to the simple prescribing system. It was an evaluation of using a new prescribing system, those results concluded if the computer system was more significantly effective than a simple prescribing system. The number was calculated as a reverse of the pooled risk difference $[1/\theta]$; which was the difference of the proportion of the events, so two different values were produced depending on the fixed effect model or the random effect model which were shown in the meta-analysis table.

The number needed to treat can be calculated from the software from the summary OR (odds ratio) according to the following formulae:

$$NNT = \frac{1 - p_c(1 - OR)}{p_c(1 - p_c)(1 - OR)} \quad (10)$$

Where P_c was the typical event rate without any treatment and in our case it was the rate of medication errors using the simple prescribing system.

2.7 The value of the Funnel plot asymmetry

The results of the α value, where the line on the test for funnel plot asymmetry crossed the y axis, was $\alpha = -6.56$, with an 95% confidence interval of $(-13.75/0.63)$. The fact that it crosses the zero meaning there was no significant publication bias (see explanation of funnel plot and funnel plot asymmetry). The equation (15) was shown in section 4.4.2.5.

3. Other significant calculations

The software did not include the results of the effect of the new prescribing system in reducing medication errors as the question searched was identification of the rate of medication errors using two systems but not looking at the impact of the intervention in reducing errors.

Difference proportions

The difference of the proportion of the events observed in the two groups.

$$d = \frac{A}{E} - \frac{B}{F} \quad (11)$$

A was the observed events (Medication errors) by using a computer system with CDSSs

B was the observed events (Medication errors) by using a simple prescribing system

E was the number of subjects included in the study that have used computer system with CDSSs (total number of prescriptions),

F was the number of subjects included in the study that have used a simple prescribing system

The 95% confidence interval was calculated by:

$$CI(95\%) = d \pm 1.96 \times SE(d) \quad (12)$$

Where d was the percentage difference and $SE(d)$ was the standard error of the difference calculated according to the following equation:

$$SE(d) = \sqrt{\frac{B \times (F - B)}{F^3} - \frac{A \times (E - A)}{A^3}} \quad (13)$$

According to the example in table 4.11 we could use the following formulas:

Medication error ratio for the Computer system = $A/E = 10112/223653 = 0.045 = 4.5\%$ probability of errors using a computer system with CDSSs

Medication error ratio for the Simple system = $C/F = 18097/187101 = 0.096 = 9.6\%$ probability of errors using a simple system

The proportion of the Difference percentage or Risk Difference (RD), or the absolute risk reduction (AAR) between the computer and the simple system was:

$$0.045 - 0.096 = -0.051 = -5.1\%$$

Calculation of the effect of a computer system with CDSSs in reducing medication errors:

Medication error ratio proportion or relative risk:

The frequency of medication errors, which can vary between the two prescribing systems

Medication error ratio for the Computer system = $A/E = 10112/223653 = 0.045$, while the risk reduction of medication errors using a computer system was 95.5 % ($100 (1 - 0.045)$).

Ratio for the Simple system = $C/F = 18097/187101 = 0.096$, the risk reduction of medication errors using a simple prescribing system was 90.5 % ($100 (1 - 0.096)$)

The ratio proportion or relative risk was calculated by the following formula:

$$RR = \frac{A/E}{C/F} \quad (14)$$

Ratio of errors using a computer system with CDSSs/Ratio of errors using a simple system: $0.045/0.096 = 0.47$

In our study we were looking at a negative event which was medication errors that we have compared their rate using the two prescribing systems. In order to identify the effect of the new system or intervention (computer with CDSSs) in reducing the negative event or medication errors we have to calculate the relative risk reduction of the ratio proportion.

The relative risk reduction, obtained by subtracting the ratio of relative risk from 1 and expressing the results as a percentage, was 53% ($100 (1 - 0.47)$). However, if we considered Mantel-Haenszel results from the meta-analysis table, the reduction in the Odds Ratios of medication errors by using a computer system and a simple system was 62.2% ($100 (1 - 0.378)$), around 10 % more of the size. According to our results, Odds and risks are very different; we had to consider the reduced risk as a benefit because of the 53% improvement in using a computer system with CDSSs and it should not be assumed that the benefit of the intervention was larger than was truly the case. However the reduction of the ORs was 62.2% very close to the relative risk reduction, therefore events in both groups (control and interventions) were also similar, if the events rates (medication errors) increased suddenly when comparing control and intervention then the OR and RR will have diverged.

4.4.2.6 Graphical representation

1. Funnel plot and the test of funnel plot asymmetry

The funnel plot is the graphic method proposed by Light and Pillemer^[71], which was calculated by using the intervention size and the control size of every trial. The X axis represented the Odds ratio with a log scale and the Y axis was the sample size with a log scale. The trials are distributed quite symmetrically around the axis represented by the pooled odds ratio.

The funnel plot is actually a visual assessment of the data and is not precise from the graph.

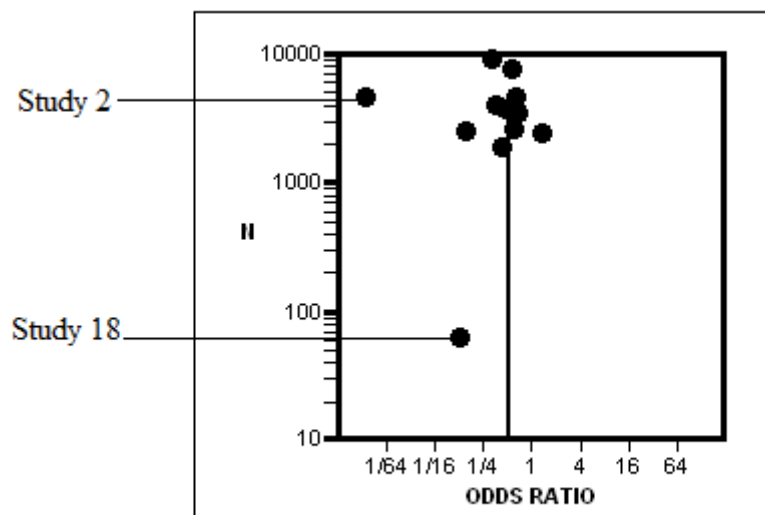


Figure 4.2: Funnel plot

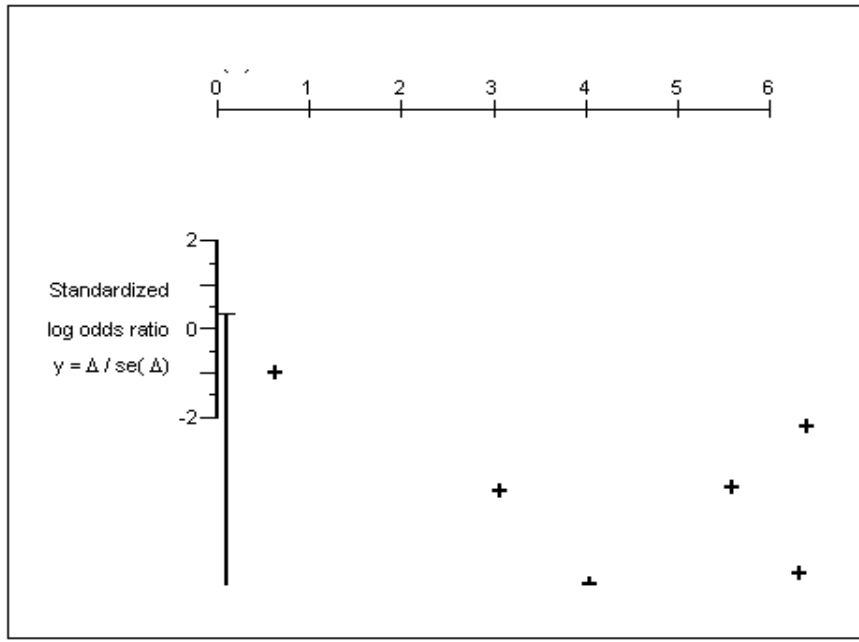


Figure 4.3: Test for asymmetry in Funnel plot

The value was (– 6.56) which was the line on the test for funnel plot asymmetry crossed the y axis.

The formulae used to calculate the α value is: $\alpha = \sum_{i=1}^n \frac{y_i}{n} - \beta \sum_{i=1}^n \frac{x_i}{n}$ where (15)

$$\beta = \frac{\sum_{i=1}^n (x_i - \bar{x})(y_i - \bar{y})}{\sum_{i=1}^n (x_i - \bar{x})^2} \quad \text{for} \quad x = 1/\text{se}(\Delta) \text{ and } y = \Delta/\text{se}(\Delta)$$

Each study was labeled using + in the test for funnel plot asymmetry. The x axis represented the odds ratio and the y axis represented the trial size. The CI line crossed the zero line on the y axis, therefore there was no significant publication bias. The 95% CI was (-13.75/ 0.63).

2. The standard forest plots

There was a high heterogeneity; therefore, only graphical results of the Random Effect Model were explained.

2.1 The standard plot of the Odds Ratio data

Figure 4.4 shows the standard plot; with the pooled OR and 95%CI 0.378(0.264/0.541) which was shown at the bottom line outside the rectangle. The OR and the CI were represented by a box with two lines on either side, for each single study. Study number 14 by Cordero [84] crossed the vertical line of unity; the data of that study was not statistically significant. On the left handside of the rectangle the number for each trial is shown from 1 to 22.

As we were looking at a **negative event** which was medication errors; from the standard plot below, all the trials showed a tendency towards the papering system. It has proven that medication errors occurred more when using an old system is a paper system or simple computer prescription.

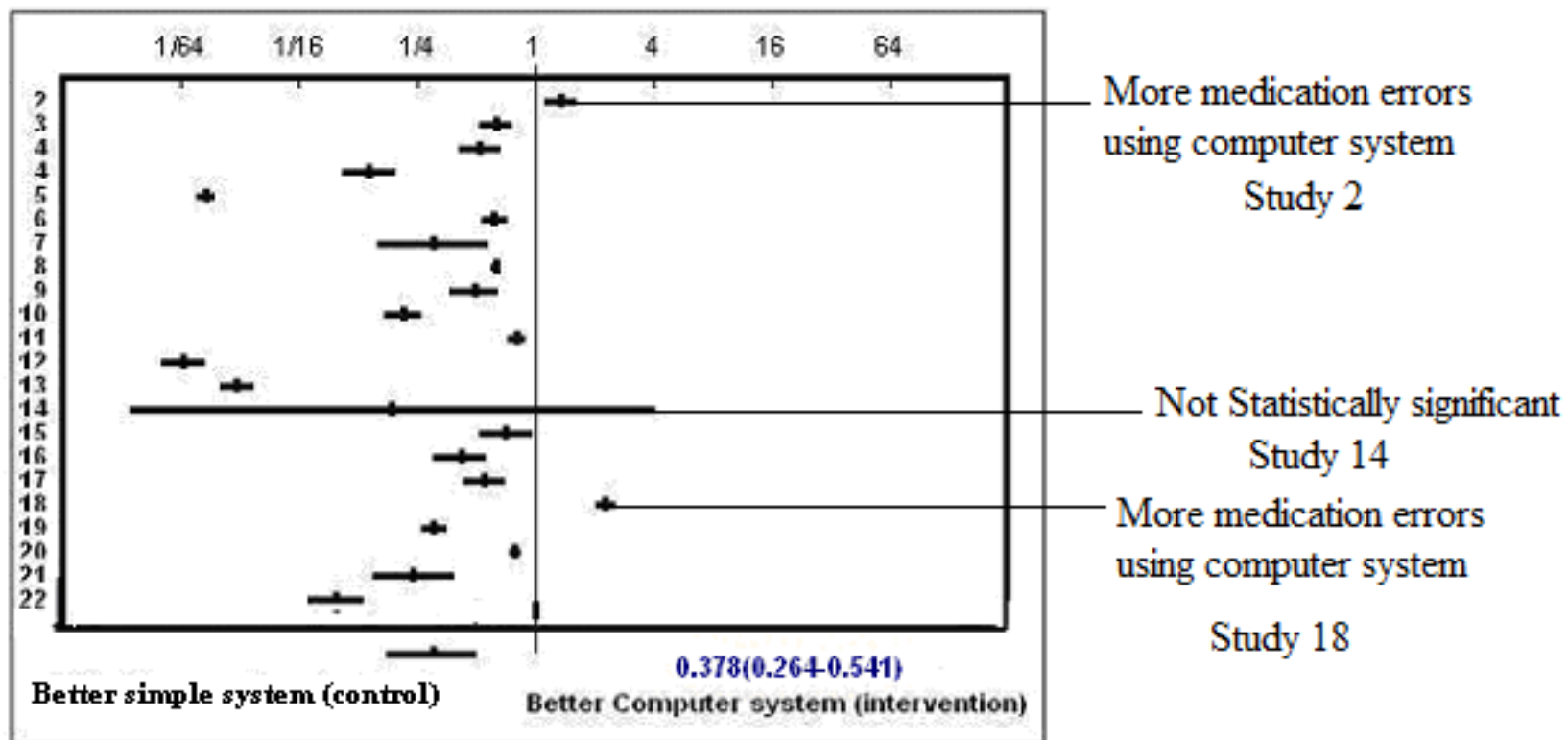


Figure 4.4: Standard plot of the OR

2.2 The standard Forest plot of the OR data

The forest plot gave a more detailed representation of the data. The graphic part was identical to the one in the standard plot, further information was added on the left side of the graph such as: author, year of study, number of medication errors (number of events) and the number of prescribed drugs or prescription (number of subjects) included in the study of the simple system and the computer system. It was represented using the OR related data 0.378 (0.264/0.541). The graph showed that two studies stated an increase for the risk of medication errors by 24% for study number 2 [113] and more than 100% of risk of errors in study 18 [114].

Rudman et al (study 18) used the number of medication errors reported for the paper system but the number of reported errors using a computer system; that was the reason why more medication errors were reported when using an automatic web-based reporting system. (See Figure 4.5)

2.3 The Forest plot of the difference percentage

The graph was quite similar to the previous one, the only difference was using the difference percentage instead of the OR, it was represented using the difference percentage data which is - 0.086(- 0.107/ - 0.066). There were approximately 8.6 % more medication errors when using a simple system, because the results were towards the simple system as explained before in the meta-analysis table. (See Figure 4.6)

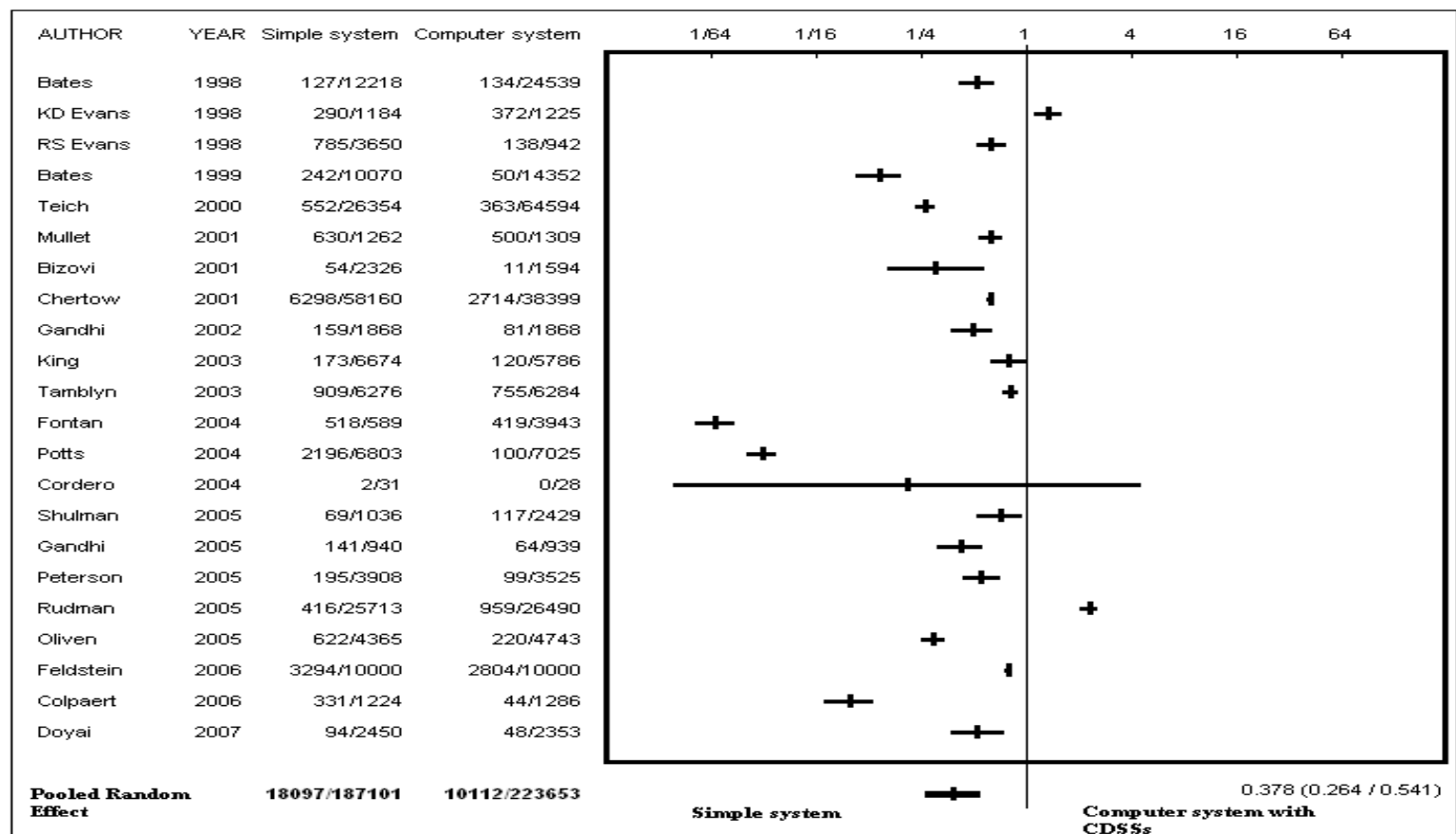


Figure 4.5: The standard forest plot of the OR

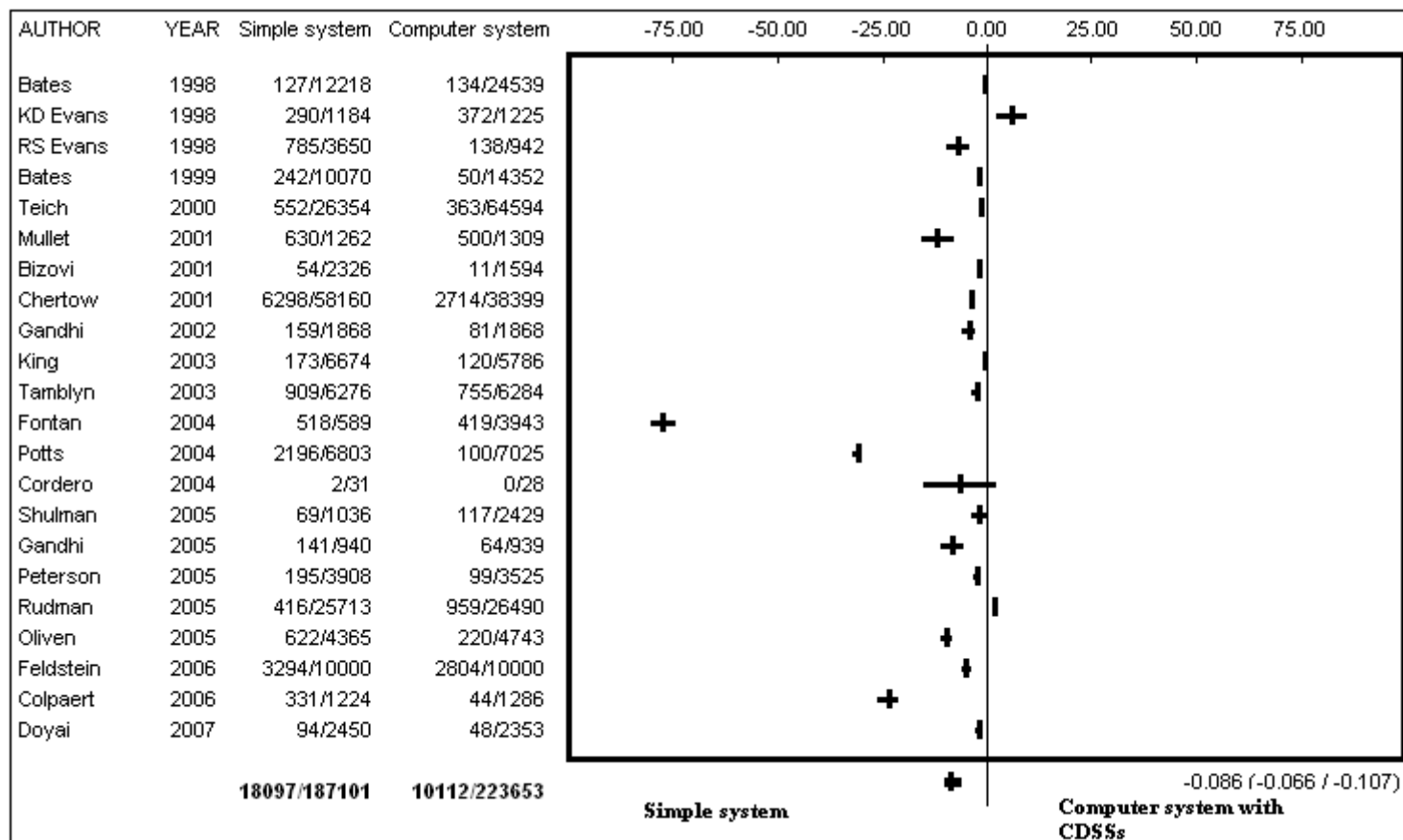


Figure 4.6: The standard Forest plot of difference percentage

2.4 The standard cumulative plot of the OR

The trials were listed in chronological order. The first OR referred to the first trial in time order; the second was the results of a pooled OR between the first and the second and so on. The last OR was the one resulting from a meta-analysis of all studies. The first three studies from 1998 indicated that less medication errors that occurred when using a simple prescribing system. The results were confirmed over the following years (1999-2007). (See Figure 4.7)

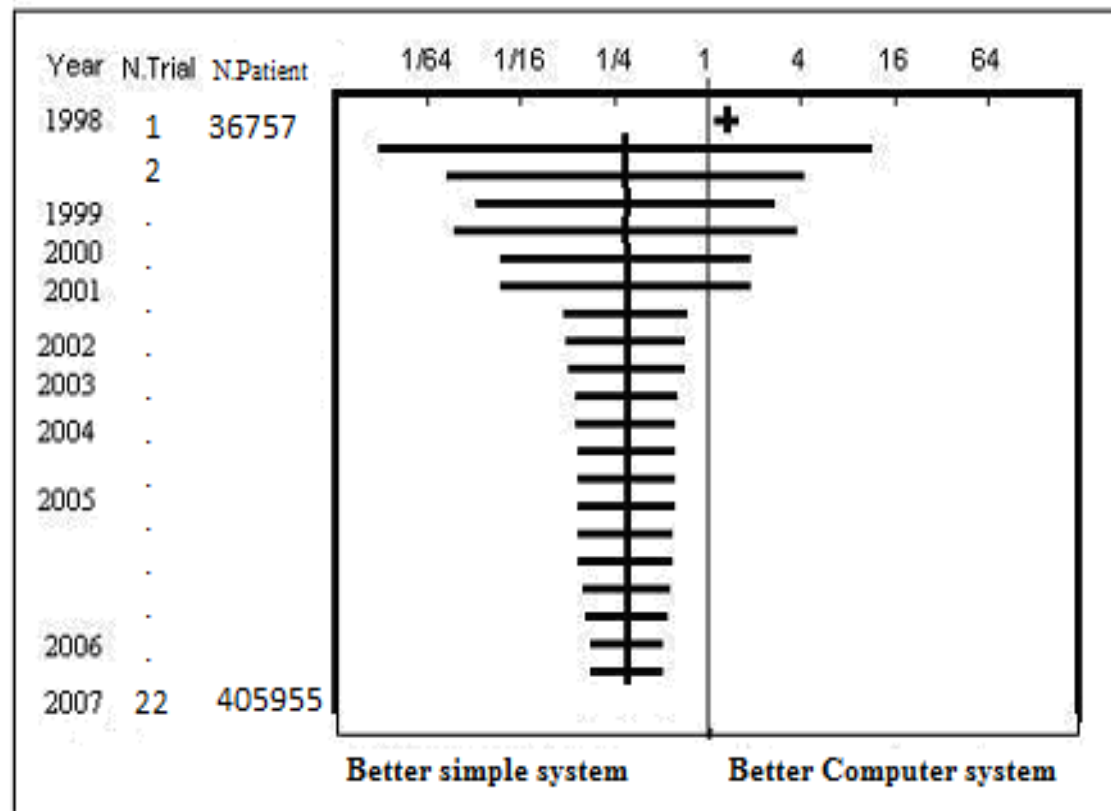


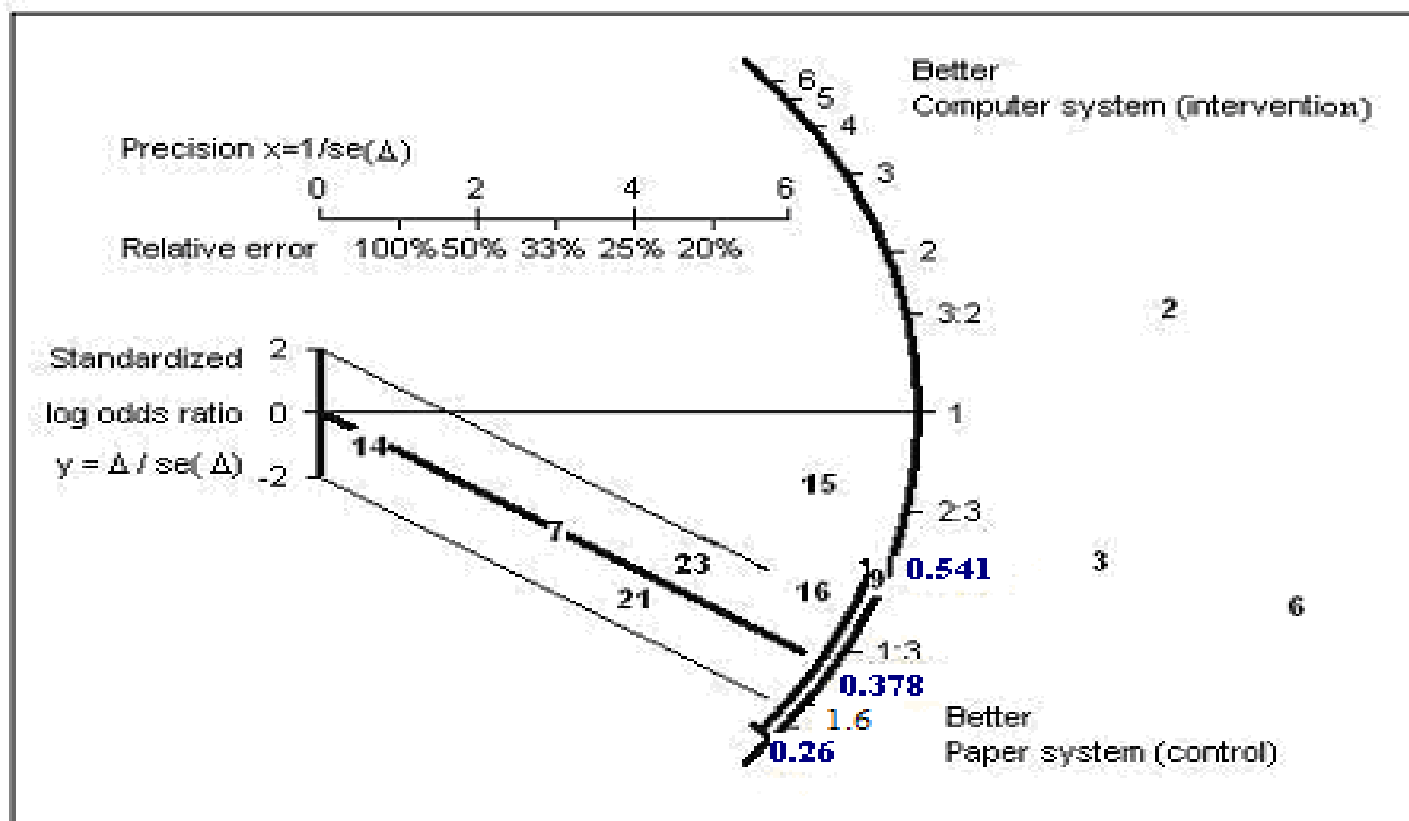
Figure 4.7: The standard cumulative plot of the OR

3. The Galbraith plot

The Galbraith plot was more informative. Every trial was represented by a number. The graph axes had two different characteristics; on the **X** axis was the precision of the study as the inverse of the standard error of the OR, or the inverse of the dispersion ($x = 1/SE(\Delta)$), and the **Y** axis was the standard OR logarithm ($y = \Delta/SE(\Delta)$), where

$$\Delta = \text{LnOR}.$$

The plot had three continuous parallel lines; the central one in bold indicates the pooled OR in the scale which was 0.378 and its 95% confidence interval was indicated by the segment of arc parallel to the scale which was (0.264/0.541). The other parallel lines represented the homogeneity area within their limits. The studies 2[11], 3[115], 6^l116] and 15[117] were outside the homogeneity area, therefore, they are heterogeneous. The studies were on the lower part of the graph, all in favor of using a simple prescribing system. Consequently, that confirmed the results from the standard and forest plot.



4. The l'Abbe plot

The L'abbe plot (See Figure 4.9) has several features, including the explicit display of the range of variation in event rates in treatment and control groups. The plot represented the observed treatment group risk against the observed control group risk to explore possible heterogeneity [71].

Each trial was represented by a number; the **X** axes represented the proportions of the observed rates of the control group and the **Y** axes were the proportions of the observed rates of the intervention group. The parallel lines of the square represented the points where the event rate in the two groups was identical. The other lines were the points where a difference of 25% and 50% occurred between the groups.

Trials in the graph were represented by circles, larger circles were trials that contained more information or larger data; the size of the circle containing the number of the trials was proportional to the sample size of the trial. The results of our trials showed a large deviation between the trials, which would indicate a possible heterogeneity.

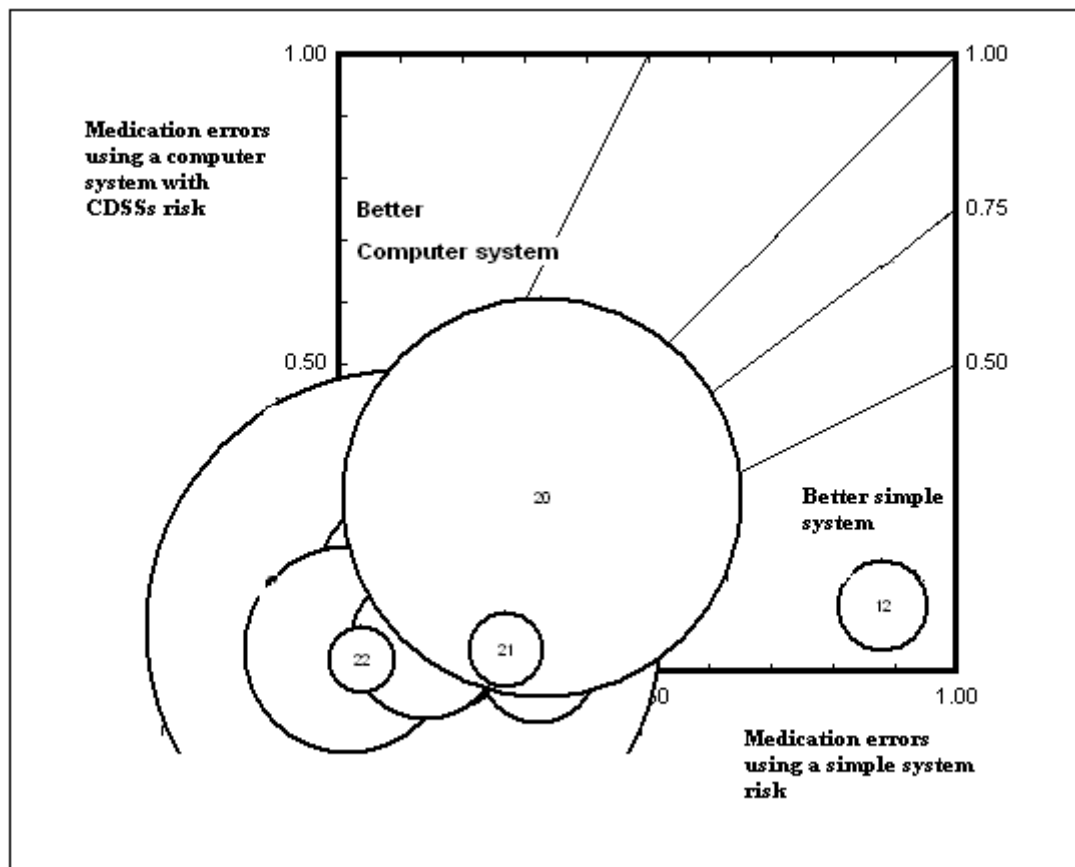


Figure 4.9: The L'abbe plot

4.5. The sub-group analysis

The main aim of the meta-analysis was to estimate the average effect seen in trials comparing beneficial approaches. Some of the trials have specific characteristics, or the approaches used are slightly different, therefore, the effect was different from one group to another.

The meta-analysis of the trials showed a significant heterogeneity and the great variability of efficacy observed in the trials explained that there was something in the trial design or treatment that could have caused the difference.

The exploration of these differences can be facilitated by constructing a summary (table 7 in the appendixes section) that explained the differences in effects based on types of interventions. Hence, based on the table we could stratify the studies into subgroups according to populations, interventions and outcomes.

We have performed a meta-analysis of subgroups of studies in order to examine if the effects were consistent within the subgroups; four subgroups were distinguished; the first one included trials that have used paediatrics CPOE, the second one was trials that have used CPOE for adults, the third group included trials with prescribing systems for specific type of medication, and the fourth group included all other types of prescribing systems. The purpose of those particular selections was to determine types of CDSSs used in every step of the medication process in order to develop the system dynamic model.

4.5.1 Comparison of Pediatrics CPOE and adults CPOE

The standard forest plot in figure 4.10 shows the difference in the rate of medication errors between using paediatrics CPOE and CPOE for adults. The grouped ORs for both paediatric and adult prescribing system demonstrated that the rate of errors was higher when using the simple system (REM 0.303 95% CI 0.172-0.534, FEM 0.429 95 % CI 0.414-0.444). The paediatrics CPOE group OR was lower than the adult CPOE group, however it was not statistically significant (0.240 95% CI 0.038-1.517) as the 95% CI crossed the OR line of 1 on the REM.

In addition, we have calculated the relative risk reduction to measure the effect of both systems in reducing medication errors. The relative risk reduction of paediatrics CPOE was 75 % ($100 \times (1-0.25)$) and the OR reduction was 76 % ($100 \times (1-0.24)$) from the forest plot.

Table 4.12: Calculation of RRR of pediatric CPOE

Medication errors in pediatrics CPOE			Total
	Yes	No	
Intervention	720 (A)	13420 (B)	14148 (E)
Control	3001 (C)	11769 (D)	14770 (F)
Total	3721	25189	

$RR = \frac{720}{14148} / \frac{3001}{14770} = 0.25$, and the relative risk reduction was 75% ($100 \times (1 - 0.25)$)

Table 4.13: Calculation of RRR of adult CPOE

Medication errors in adults CPOE			Total
	Yes	No	
Intervention	3521 (A)	145603 (B)	149124 (E)
Control	7814 (C)	105156 (D)	112970 (F)
Total	11335	250759	

$RR = \frac{3521}{149124} / \frac{7814}{112970} = 0.34$, and the relative risk reduction was 66% ($100 \times (1 - 0.34)$).

The relative risk reduction of adults CPOE was 66% ($100 \times (1 - 0.34)$) and the OR reduction from the plot was also 66% ($100 \times (1 - 0.34)$). The pediatrics CPOE reduced more medication errors than the adults CPOE.

4.5.2 Comparison of CPOE systems and prescribing systems for specific type of medication

The standard forest plot in figure 4.11 shows the difference in the rate of medication errors between paediatrics and adult CPOEs and other prescribing systems that are designed for specific types of medications such as R Evans et al [115] for antibiotics, Teich et al [118] for H₂-blockers, Chertow et al [119] for renal insufficiency medications and Peterson for psychotropic medications. The grouped ORs for the three sub-groups demonstrated that the rate of errors was higher when using the simple system (REM 0.350 95% CI 0.235-0.523, FEM 0.504 95 % CI 0.490-0.520). The other types of prescribing systems group OR was higher then CPOE systems (REM 0.540 95% CI 0.397-0.734, FEM 0.644 95% CI 0.623-0.666).

The relative risk reduction of prescribing system for specific drugs was 53 % (100 x (1-0.47)), which was the effects of specific system groups in reducing medication errors. The OR reduction was 46% (100 x (1-0.540)).

Table 4.14: Calculation of RRR of prescribing systems for specific medication

	Medication errors using specific systems		Total
	Yes	No	
Intervention	6118 (A)	111342 (B)	117460 (E)
Control	1124 (C)	100948 (D)	102072 (F)
Total	7242	212290	

$$RR = \frac{6118}{117460} \div \frac{1124}{102072} = 0.47, \text{ and the relative risk reduction was } 53 \%$$

$$(100 \times (1-0.47))$$

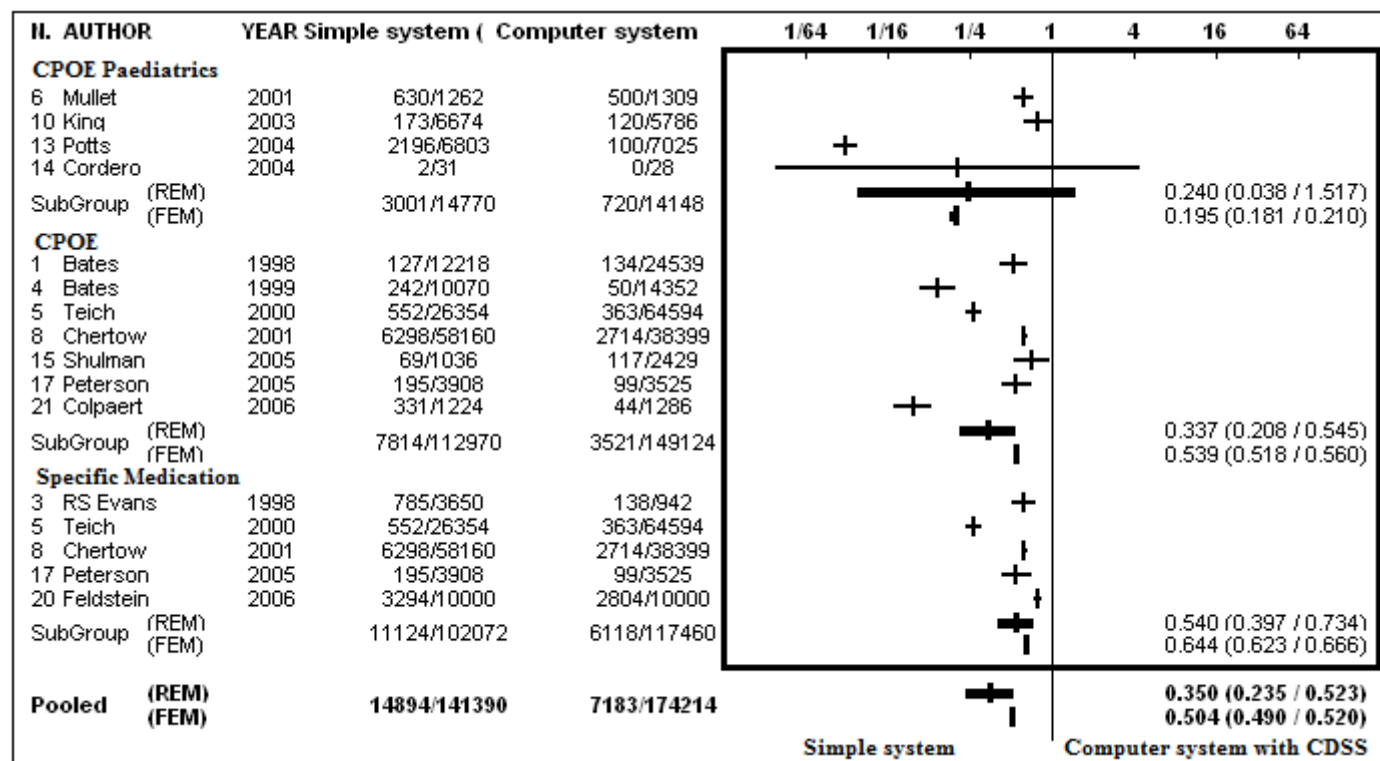


Figure 4.11: Standard forest plot of sub-group analysis 2 (Odds ratio)

4.5.3 Comparison of CPOE systems, systems for specific medications and all other types of systems

The standard forest plot in figure 4.12 shows the difference in the rate of medication errors between pediatrics and adult CPOEs, other prescribing systems that are designed for specific types of medication, and all other types of prescribing systems. The grouped ORs for the four sub-groups demonstrated that the rate of medication errors was higher when using the simple system (REM 0.378 95% CI 0.264-0.541, FEM 0.536 95 % CI 0.522-0.550). The fourth sub-group results of OR was higher than CPOE systems and lower than systems for specific drugs (REM 0.419 95% CI 0.185-0.952, FEM 0.663 95 % CI 0.627-0.701).

The relative risk reduction of the other types of prescribing systems was only 16% ($100(1-0.84)$). Therefore, other types of prescribing systems only reduced medication errors by 16%, because it included two studies (Study 2 and 18) that showed an increased risk of errors when using their systems as shown in figure 4.6.

Table 4.15: Calculation of RRR of other types of prescribing systems

	Medication errors using other systems		Total
	Yes	No	
Intervention	2929 (A)	46510 (B)	49439 (E)
Control	3203 (C)	42508 (D)	75711 (F)
Total	6132	89018	

$$RR = \frac{2929}{49439} \div \frac{3203}{45711} = 0.84, \text{ and the relative risk reduction was } 16\% (100 \times (1-0.84))$$

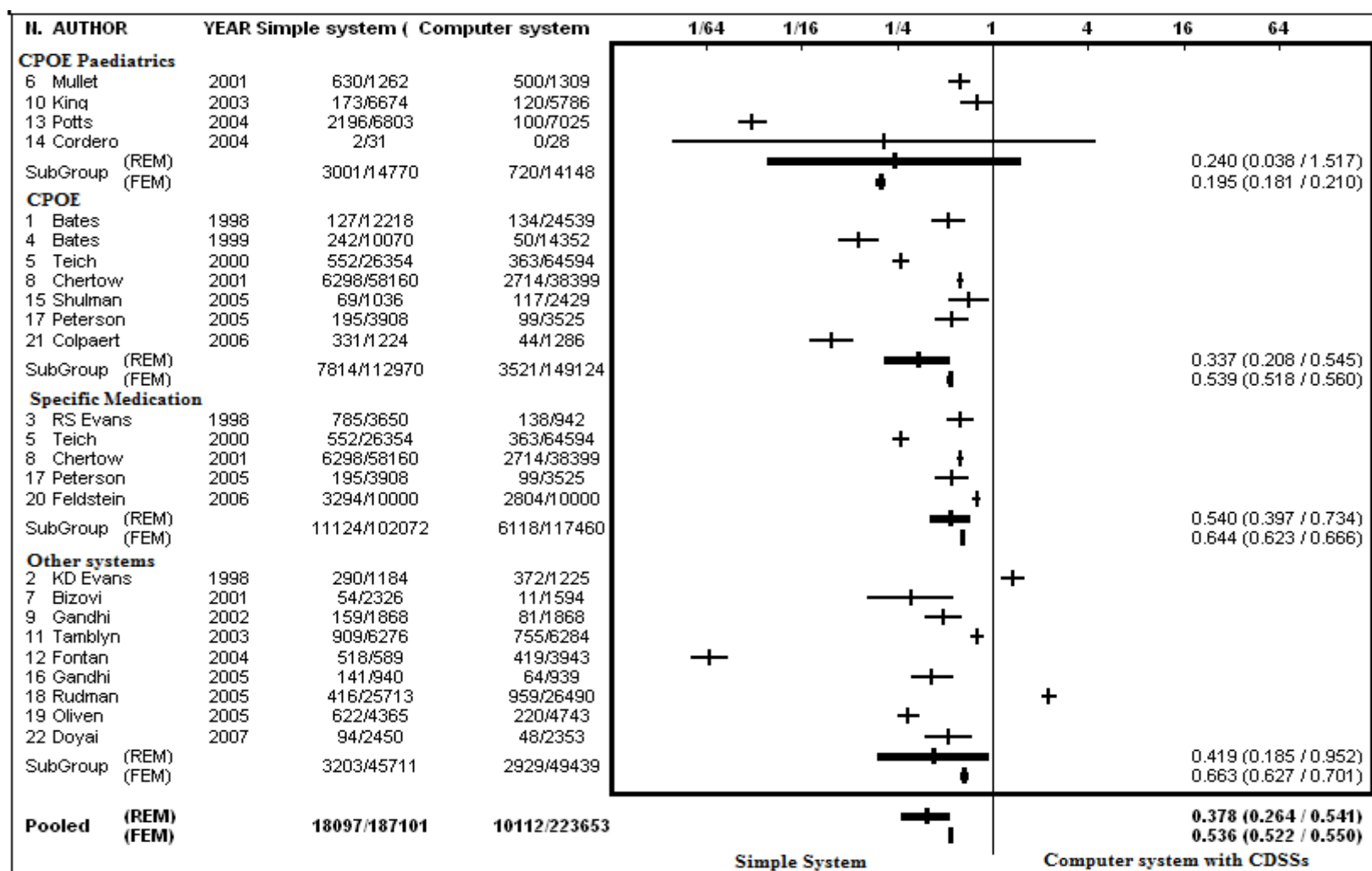


Figure 4.12: Standard forest plot of sub-group analysis 3 (odds ratio)

4.6 Summary of the sub-group analysis results

The meta-analysis has given us results of the effectiveness of different types of CDSSs compared to a simple system. A classification of those CDSSs could be identified from the selected papers, in order to include them in a system dynamic model to reduce the rate of patients harmed by medication errors. In addition, the results of the sub-group analysis were useful so that we could categorize prescribing systems by their effectiveness in reducing medication errors as shown in table 7 of the appendixes. The paediatric prescribing system showed a higher reduction in medication errors than other types of prescribing systems.

4.6.1 Prescribing systems to reduce medication errors

4.6.1.1 Computer physician order entry (CPOE)

CPOE was mentioned previously in the literature review chapter, with the analysis of its structure, features, strengths and weaknesses. The meta-analysis has extracted the effect of CPOE (adults or paediatrics) in reducing medication errors.

The first category was CPOE in paediatrics which compared handwritten prescribing system and CPOE systems. The benefits of CPOE for children has included antibiotic DSSs from Mullet et al [116] that reduced antibiotic medication errors by 23% compared to a CPOE prescribing system without the antibiotic DSSs tool. King et al's [120] study was the first that evaluated the impact of a CPOE on medication errors and ADEs in paediatrics compared with a handwritten prescribing system, CPOE has reduced errors by 20% but there were limitations on reported errors and further evaluation of the benefits has to be done. The CPOE paediatric evaluation from Potts et al [121] has improved communication between staff and there were no reported errors from the system and decreased medication errors compared with a handwritten system by 95%. However more features should be added on patient data such as age and weight and incorporation of dosing and calculation guidelines for children. Results from the study [84] showed a significant reduction in Gentamicin medication errors, there were no errors when the new system was added.

The second category was CPOE in adult patients that included several comparisons such as comparing handwritten prescribing system and initial CPOE system (Studies: 1, 4, 5, 15, 17, 21), then by comparing the initial CPOE system with their recent version that included CDSSs. The benefits of CPOE were reduction of medication errors and ADEs by 48% and 85% respectively from Bates et al [97, 43] , but there were problems in multiple routes and multiple sedating drugs, the system needed inclusion of CDSSs, guided drug algorithms, drug-laboratory checking, drug-patients characteristics and strategies for missed doses and problems such as bar coding.

Teich et al's [118] (Study 5) evaluation has demonstrated reduction of medication errors by 23.5%, the benefits were highlighted for multiple doses and easy access to the system from any hospital clinic. It was only assessed for H2 blocker drugs such as nizatidine and intravenous ranitidine. The system did not include any warning to stop a wrong entry and users became dependent on the computer.

Shulman et al [117] (Study 15) showed a reduction of 36% for medication errors. The system reduced errors in dose, units and frequency, however it required other tools such as drugs with multiple doses, incomplete prescriptions such as missing doctor's signature. Their data also showed that some serious errors occurred when using the CPOE system [122].

Peterson et al's [123] study has mentioned the benefit of using guidelines on renal impairment disorders with the interactions of psychotropic medications, and decreased errors by 44%. Colpaert et al's [124] study showed a good improvement in reducing medication errors and adverse drug events by 28%, because the system included warnings on double prescriptions.

4.6.1.2 Prescribing systems that are specific for some medications or diseases

The category of prescribing systems included decision support systems specific for some types of medications or diseases such as RS Evans et al's [115] study that evaluated a computer assisted management program for antibiotics that reduced allergy and dosage errors by 32%, but the program did not include information for specific recommendation for the prescriber and it took a long time to order drugs.

Chertow et al [119] group was also part of the CPOE; the study assessed the system in reducing medication errors for patients with renal problems, post implementation results showed a reduction of errors by 35%. Peterson et al's [123] study included CPOE for psychotropic medication orders and Feldstein et al's [125] study assessed

EPR alerts in Warfarin, which has reduced the frequency of medication interaction.

4.6.1.3 Other types of prescribing systems

The third category in the sub-group analysis included all other types of prescribing systems that were chosen from the meta-analysis table. Almost all of these systems were designed for prescribing, for instance the computer assisted prescribing system from KD Evans et al [113] , where most of error reduction was due to using an intravenous decision support system that reduced those errors by almost 90%. However, the system itself actually increased medication errors by 24%.

Tamblyn et al's [126] study looked at the medication error rate by using a simple computer system versus clinical decision support system. After the introduction of the CDSS, medication errors were reduced by 17%, however, the system has some problems in patient data and relocation of prescribed drugs by different doctors. Fontan et al's [83] study included more errors in drug administration; after the introduction of the distribution system, the errors decreased by 88%. Rudman et al's [114] group evaluated medication errors using a web-based reporting system, which seemed to have more medication errors reported when using an electronic system.

Oliven et al [109] reported errors in drug-laboratory interactions, after the surveillance of the system the errors were reduced by 67.5 %, and finally Donyai et al's [127] research group reported a 47% reduction in the rate of medication errors after the introduction of computer drug entry system . Ghandi et al's [128, 129] groups had no significant rate difference on ADE between control and intervention and antibiotics and nonstreoidal anti-inflammatory drugs were not reduced by a basic computerized prescribing system.

4.7 Chapter summary

The systematic review comprised two sections. The first section was a qualitative analysis of fifty-three articles that included classification, definitions and causes of medication errors by classification, also the types of methods used to detect and report errors. The second section was a meta-analysis that included twenty two studies to view types of prescribing systems involved in reducing medication errors and categorized them into sub-groups. We have compared the odds ratios and risk ratios reduction of medication errors by using a simple prescribing system with an electronic prescribing system that included CDSSs. Computer systems with CDSSs reduced medication errors by 53%, and from the sub-group analysis we identified that paediatric CPOEs have a higher reduction of medication errors by 76% compared to other types of prescribing systems.

The review included four randomized control trials, although in one of the studies (Bates 1998) [97] only the intervention part which was randomized. The rest of the studies were non-randomized but were comparative controlled studies that included a control and intervention data to assess the difference between two prescribing systems. Consequently, we could select the types of CDSSs to apply into the drug safety simulation model. Eight types of clinical decision support components were chosen to be added to the simulation model such as the drug order entry antibiotic DSSs, and drug reminders in the prescribing stage, unit dosing in the dispensing stage, intravenous DSSs and bar coding in the administration stage, and guidance or surveillance of the system in the total rate of patients with adverse drug events.

The systematic review had some limitations such as a lack of studies that had a quantitative measurement between using an old and a new prescribing system, almost all of the studies were conducted in US hospitals. Only a few studies were RCTs, more research should be done in this area to improve the evidence and the impact of prescribing systems.

Chapter 5

Model Design and Development

5.1 Introduction

The first section of this chapter exemplifies the integration of the medication process with key information on error-causing conditions and different types and frequencies/consequences using Causal Loop Diagrams (CLDs). The diagrams summarised many of the practical issues raised by the literature review. Moreover, they form the basis or initial steps of model development. Real life examples were used to illustrate the diagrams.

The second section of the chapter discusses the development and simulation of hospital medication process systems which are either simple systems (handwritten or simple computer) or computer systems that include CDS components using system dynamics modelling and also using the data of medication errors from the meta-analysis papers. The simulation was run for a fourteen week period.

The aim of the model was to assess the impact of both systems on medication errors and ADEs, and to measure the percentage reduction of the number of patients with medication errors for the simple system and for the electronic system with CDS components. Subsequently, the effect percentages data which is the measurement subtraction between two prescribing systems; for example the number of patients when using a simple prescribing system was 13.2 and the number of patients when using the prescribing system with intervention was 8, therefore the intervention reduced the number of patients with prescribing errors by almost 42% (100-58) of the comparison was applied to the simple system to evaluate the effectiveness of CDS components in reducing medication errors.

5.2 Methodology of system dynamics

The system dynamics approach was simply defined by the System Dynamics Society[130] as “a methodology for studying and managing complex feedback systems, such as are found in business or other social systems. In fact it has been used to address practically every sort of feedback system. While the word System has been applied to all sorts of situations, feedback is the differentiating descriptor here. Feedback refers to the situation of X affecting Y and Y in turn affecting X perhaps through a chain of causes and effects. One cannot study the link between X and Y and, independently, the link between Y and X predicts how the system will behave. Only the study of the whole system as a feedback system will lead to correct results”.

The methodology and principles of the approach was based on the following points[131] :

- 1.** Identification of the problem and its background by using the key words searched in the systematic review
- 2.** Formulation of a dynamic hypothesis explaining the causes and consequences of the problem; the purpose of the research was to develop a new model of a hospital prescribing system that included CDSSs to reduce medication errors based on the principles of system dynamics. A development of CLDs to map the causal structure of the problem.
- 3.** Development of a computer simulation model of the system at the root of the problem: the problem of medication errors started from prescribing errors, dispensing errors and administration errors up to patient harm involving doctors, nurses, pharmacists and patients.
- 4.** The model should be integrated into a project from the start:

The problem that had to be solved was reducing the rate of patients with different types of medication errors. Accordingly, the proposed simulation model has reduced the rate of patients with medication errors.

- 5.** The use of other methods along with system dynamics:

The hospital prescribing system was based on figure 1.2 in the introduction chapter that represented the process and steps involved in the management and use of medication in healthcare. Also the data and types of CDS elements were collected from the meta-analysis papers and used the simulation model.

- 6.** Validation of the model:

Testing and building confidence in the model by comparing results with real world systems and verification of the model sensitivity by checking the model behaviour under different data.

- 7.** Evaluation of the model.

Design of the model based on real world environment, results of the model were compatible with the prescribing system in the hospital.

5.3 Types and causes of error expressed as Causal Loop Diagrams

The system dynamics approach has been considered after carefully reviewing the literature on techniques used to reduce medication errors. Examples of simulation models were already used to demonstrate medication errors related to some events such as the medication complexity and the knowledge of staff [25]. Also system dynamics was used in hospital safety systems and health policy [26].

Anderson et al [132, 133] group has evaluated the capability of information technology to prevent ADEs using a computer simulation methodology. However, the study did not include any CLDs.

Another type of simulation of the hospital drug distribution system has been constructed in a London teaching hospital, to explore the effect of different changes to the system in reducing administration errors using observational study before and after the introduction of the drug distribution system [134].

CLDs are often a first step in structuring concepts and building simulation models.

In the subsections below, is an explanation of how the Causal Loop Diagrams were developed and . Then the findings were presented as a series of such diagrams, making special cross-references to Reason's model of error-causing conditions. The CLDs were constructed using VENSIM [135] software for system dynamics.

5.3.1. Principles of CLD construction and interpretation [131, 136]

- **Defining a system/process in terms of components and variables.** A “system” or process of interest is summarised as a set of defining variables. Each variable represents a stage or activity in the system that can vary over time. The variable may be important enough to be a component in its own right. More commonly, the higher component is usually used as the label or name. The sum of the components (and variables) defines the system/process under study, but it is a static or tabular summary.
- **Causation versus correlation:** Every link between two variables should signify a causal relationship between variables that must behave in the same way as the real system would. The components/variables are arranged on the page and linked by arrows of influence. The arrows show which variable is influencing another variable. The whole represents a graphic summary of

variables and influences representing the system/process of interest and now containing a dynamic feature. The correlation between variables will appear from the simulation model behaviour; therefore the connection between variables should be understandable and not confusing.

- **Assigning the nature of influence or a labelling link polarity.** A sign is attached to each arrow to show the direction of change. A “+” on the arrow between variables A and B indicates that a change in A will cause a change in B in the same direction. A “-” shows that a change in A will cause a change in B in the opposite direction. Now we have a full specification of the system/process, with defining components/variables and dynamic arrows of influence and signs for the nature of change. Labelling the polarity is important for the loops feedback.
- **Determination of the loop polarity.** There are two ways to determine if the loop is positive or negative. The fast way is to count the number of negative links in the loop. If the number of negative links is even then the loop is positive which is also called a reinforcing loop and if the number is odd the loop is negative. The second method is to trace the effect of a change around the loop; if the feedback effect reinforces the original change, it is a positive loop; and if it opposes then it is a negative loop. An example of that was shown in figure 5.1, where heavy work increases tiredness, when the medical professional is tired it lead to lapses and human error will enhance disorganisation in work place, so professionals will end up with an increase workload.

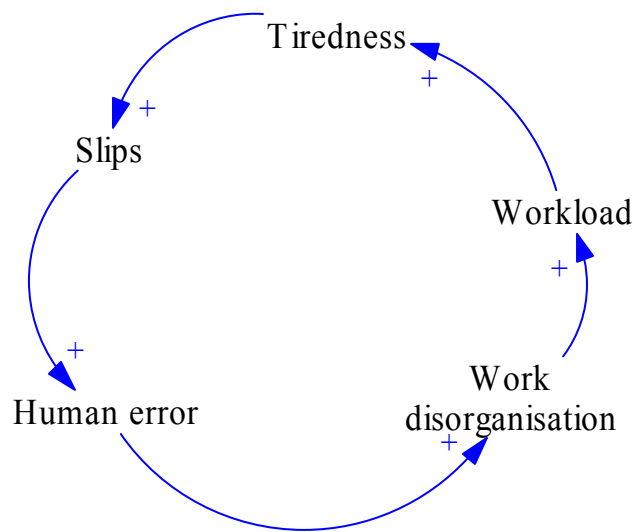


Figure 5.1: Example of reinforcing loop

However if two variable is added to the loop with a negative link on the arrow the loop will be balanced, such as adding the use of paper based guidelines as shown in figure 5.2.

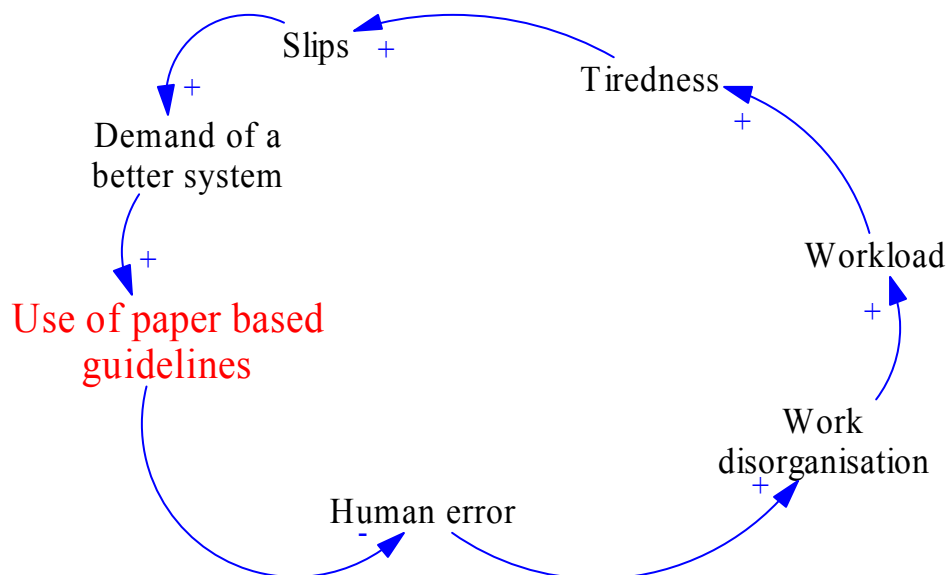


Figure 5.2: An example of a balanced loop

Two aspects are particularly important when analysing and interpreting CLDs. First we look for loops in the system. This is a continuous set of arrows, starting and returning to the same variable but also tracing a cycle through another variable. This shows how influences between variables can combine or integrate to form the basis of feedback/feedforward mechanisms.

Secondly we look at the balance of signs on identified loops. More “-” than “+” on the loop suggests a stable loop or a feedback mechanism within the system. An excess of “+” over “-” suggests an unstable or self-enhancing loop in the system and evidence of feedforward mechanism.

Examination of a CLD and the constituent loops is one approach that indicates the nature of an error and its causes in a real setting.

5.3.2 Causal Loop Diagram 1: Mismanagement of medication process

Figure 5.3 reproduces the medication process model from chapter 1. It was presented as a continuous cycle of activities for the long-term management of drugs for a patient in hospital. Moreover, the stages names have been replaced by variables relevant to my research. For example, “Prescribing” has been replaced by “Prescribing errors”.

Clearly the diagram was a continuous loop for a hospital inpatient. Errors in different stages of the medication process impact on each other and lead to an uncontrolled or augmenting loop of errors. The diagram also included factors influencing the loops presented in the text boxes.

The loop started with the first step in the medication process which is prescribing; errors in prescribing lead to the incorrect drug name which increases the risk at an incorrect dose and the incorrect form of the drug, therefore the dispenser or pharmacist could select the wrong drug package and the wrong drug label, those errors resulted in a dispensing error.

Dispensing a drug is the second step in medication management; when a dispensing error occurred, an unsuitable diluent was selected for a specific drug if it was an intravenous drug or paediatric medication; this would lead to the wrong drug strength that increased calculation errors then a drug-drug interaction that can harm the patients. However, if the prescription was checked before administration it will decrease administration errors.

Drug administration is the third step; when an administration error resulted from a dispensing error; this might happen whether patients were taking their own

medications or it was given to the patient in hospital which also might result in harm. Therefore the mismanagement of medication errors demands the use of a better system which implies less error.

CLD1 includes some factors influencing the loop; some of them were solutions to medication errors such as: A clearly written prescription that decreased prescribing errors, accurate patient data that decreased dosing errors, good supervision that prevented applying the wrong label on the drug, availability and utilisation of dose and calculation guidelines that reduced the wrong selection of the drug strength and prevented calculation error, and warnings on particular drugs also avoided drug interactions. Those solutions could be applied to any prescribing system; more technological approaches are described in CLD2.

The loop was dominated by three major circles, the first one starting from writing a prescription via a wrong drug label then an administration error to the demand for the better system. The second circle started from wrong drug label that increased dispensing error and leads to administration error. The third circle began from the wrong drug strength that increased drug interactions up to patients harm.

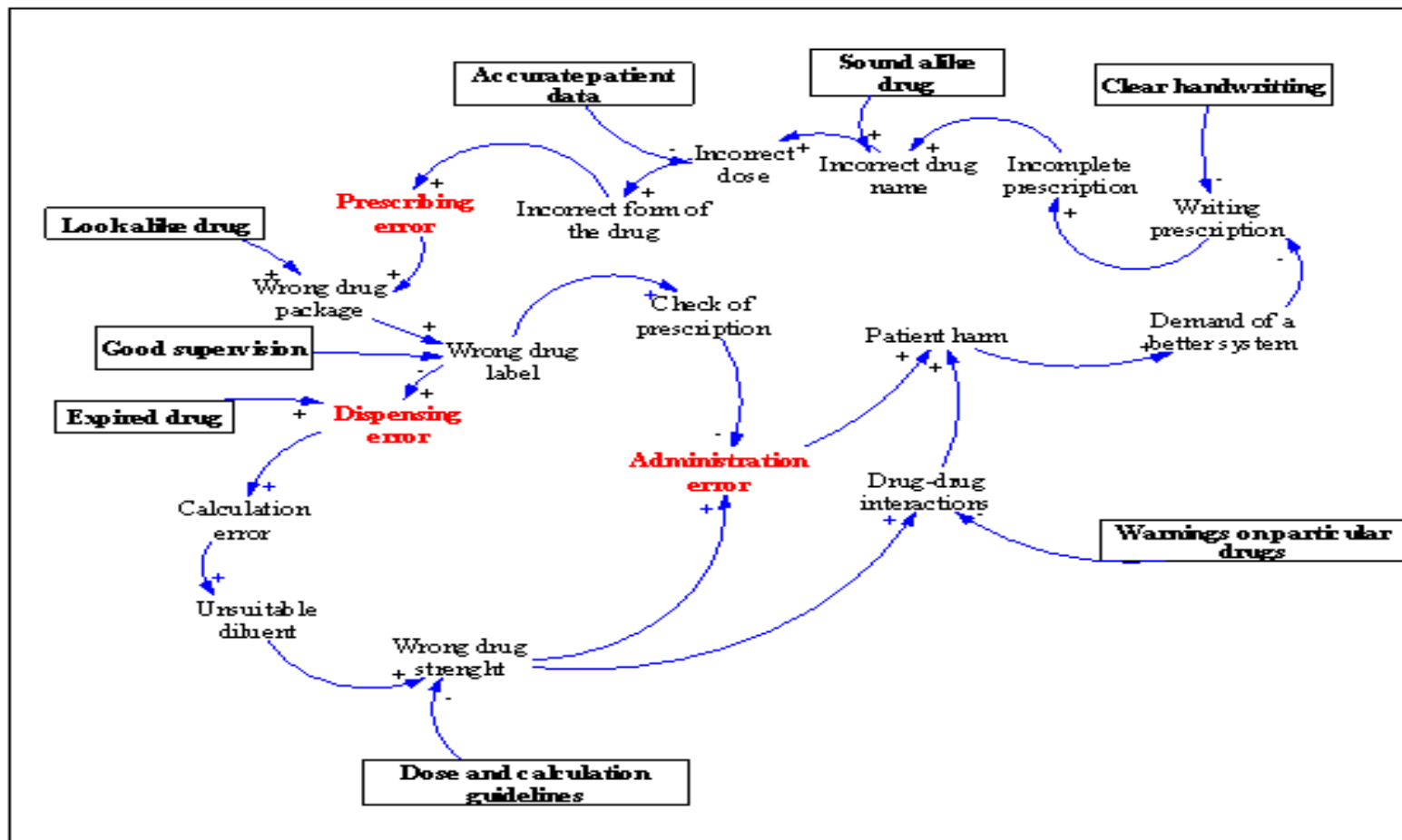


Figure 5.3: Causal Loop Diagram 1 showing the mismanagement of a medication process

5.3.2.1. Explanation of CLD1 variables

Prescribing error: any mistake that can happen when a doctor or nurse are writing or filling in a prescription.

Incomplete prescription: Any filled prescription with the wrong name or with incomplete patient details such as the age, sex and date of birth or if the doctor forgot to sign the prescription, which is double checked of it.

Incorrect drug name: If the wrong drug name was written in the prescription, it will lead to the pharmacist giving the wrong drug. Even if the prescription was written correctly the pharmacist could still give the wrong drug due to many factors.

Incorrect dose: A dose is a specific quantity of medication every medication has different dosage and all depend on a patient criteria. If an error occurred in the drug name an error might happen in the drug dose or even if there was no error in the drug name a wrong dose might be prescribed or given to the patient.

Incorrect form of the drug: The form a medication can be prescribed includes; capsules, tablets, drops, liquids, powders, inhalants or spray, skin preparation or suppositories. For example capsules and tablets are not given for paediatric patients, so an error might happen if the age of the patient was missed in the prescription or the incorrect dose was prescribed, hence the wrong form of the drug is given.

Wrong drug package: a box or any other type of package where the drug is stored, a mistaken drug package is selected because it looks like the correct medication.

Wrong drug label: an incorrect label is applied to the medication box. It can happen because of a prescribing error or it can be a dispenser's mistake.

Dispensing error: Dispensing was defined as a preparation of the prescribed drug and application of a label on the medicine package, then the label is checked by the pharmacist. An error happens because of the drug name or is due to bad handwritten prescription.

Calculation error: an error in calculating the dosage of the drug before administration to patients.

Unsuitable diluent: a diluent is a chemical substance chosen for some types of medication such as syrups for children or medication taken intravenously or intramuscularly. A mistaken substance can be mixed with the prescribed drug, or the incorrect drug is prescribed with the appropriate diluent will be given.

Incorrect drug strength: the incorrect indication of the active ingredients in the drug, if two medications have the same ingredients, then the strength expressed is the one of the equivalent (see Duplication in drug-drug interactions).

Administration error: This is an error that can be the result of a prescribing or a dispensing error or it can be in the dose, the route or the rate of administration.

Check of prescription: the prescription should be checked twice by the doctor; also it should be verified by the pharmacist.

Drug-drug interactions [137]: it can involve a prescription and over the counter drugs; there are three types of interactions such as duplication, opposition and alteration of body reaction.

Duplication is when two drugs with the same effect are taken or have the same active ingredient; their side effects are more severe. For example cold tablets and sleeping tablets can be taken at the same time and both of them contain diphenhydramine, or a painkiller containing opiod and cold tablets with acetaminophen, can both be taken together resulting in patient's toxicity.

Opposition is when two drugs with opposing actions can interact and reduce the effectiveness of one or both. For example nonsteroidal anti-inflammatory drugs (NSAID) such as ibuprofen may cause the body to retain salt and fluid when taken with diuretics such as furosemide that help the body to clear out excess salt and fluid, If the NSAID may reduce the effectiveness of the diuretic.

The third type of interaction is alteration where a drug may alter how the body absorbs, distributes, metabolizes and excretes another drug. For example if the patient takes the acid blocking drug, histamine-2 blockers which may raise the ph of the stomach, then this will decrease the absorption of drugs such as ketoconazole, a drug for fungal infection.

Interactions may also happen with nutrients such as food. Medication taken by mouth must be absorbed through the lining of the stomach or the intestine. When food is present in the digestive tract it may reduce the absorption of a drug. Dietary supplements like herbal medicines and vitamins can interact with prescription or over the counter drugs and alcohol can also affect body processes and interact with medication.

Doctors should be aware of drug disease interactions because some drugs are effective in one disease and harmful in another one.

Patient harm: when the incorrect prescribed drug or the wrong dose reaches the patient it could have severe side effects.

Demand for a better system: when adverse drug events are reported due to medication errors, then a demand for a better medication management system is required.

5.3.3 Causal Loop Diagram 2: Medication process mismanagement using a computer system

Figure 5.4 adds variables representing the causes of medication errors when using a computer system. Starting with the same principle of the medication pathway which is prescribing. In the computer case prescribers use an order application to order or prescribe a drug, a clear order application could decrease order entry error and this could enhance juxtaposition error which leads to duplicate drug orders and errors in multiple drug orders that was influenced by drug interactions and drug contraindications that cause side effects, therefore it will increase the demand for a better system.

A better system is suggested as an e-health system that encourages the designer to include sufficient information on specific drug or system recommendations; it will influence the user to use the appropriate guidelines that decrease error in multiple drug orders.

The loop was dominated by three major circles; the first one starting from clear order that minimised order entry errors which could help to reduce the error in multiple drug orders that required a better system with sufficient information and recommendations. The second circle began with an error in multiple drug orders through drug contraindication and again it was closed with the use of guidelines and DSSs. The third circle starting from an error in multiple drug orders passing through the inclusion of sufficient information that influenced the utilisation of the system where the circle was closed at the same starting point.

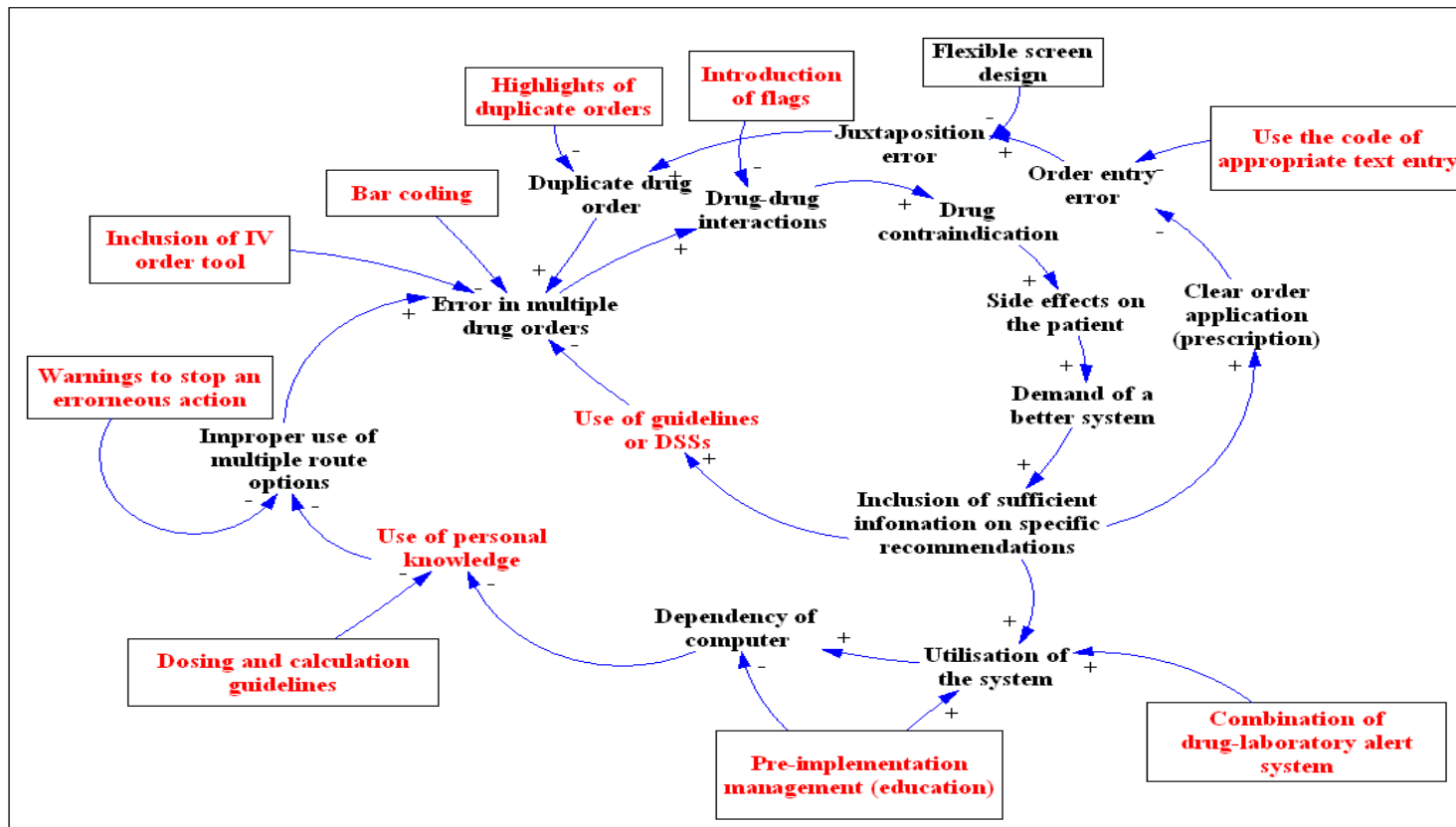


Figure 5.4 Causal Loop Diagram 2 showing mismanagement of medication process using a computer system with CDSSs

5.3.3.1 Explanation of CLD2 variables

Clear order application or prescription: The computer order application or the prescription should be well designed in order to avoid any entry mistake.

Order entry error: A mistake in the usability of entering an order [136]

Juxtaposition error: A mismatch between interface and use context, the incorrect option is chosen when it is close to another one on the computer screen [51]

Duplicate drug order: The same drug or diluent is prescribed twice, such as the case of prescribing potassium chloride twice for a patient by ignoring the first order or the no warning for the first order dose [45].

Error in multiple drug orders: A mistake in ordering the same medication more than once or in prescribing several drugs at the same time.

Improper use of multiple route options: The incorrect chosen drug will lead to an incorrect route. In particular when a patient is having complex medication, the prescribers could be confused with the number of drugs and doses.

Use of personal knowledge: Use of medical and pharmaceutical information learnt previously in the particular qualification and experience or the use of information gained during the training given by the hospital when introducing a new prescribing system.

Dependency of computer: Practitioners become dependent on the use of computers without using any paper guidelines or personal knowledge.

Drug contraindication: When the drug might have severe side effects on the patients, it is contraindicated to be given to the patients, it might cause allergies.

Side effects of the patients: Problems that occur when the treatment is not suitable for the patient.

Inclusion of sufficient information on specific recommendations: A good prescribing system should include enough information and should be user friendly. For example alerts on contraindication and possible side effects of the treatment and inclusion of information on the patient's past treatment.

Utilisation of the system: A good prescribing system that includes all the appropriate features will attract the user to utilise it.

Use of guidelines or CDSSs: Use of paper guidelines and computer CDSSs in order to avoid all types of errors.

5.3.4 Causal Loop Diagram 3: factors attributed to latent conditions (working environment)

Figure 5.5 looked at the first two diagrams in terms of the working environment and management practices. It showed that good/bad practices, in training and supervision for example, have related impacts on error rates across all stages of the medication process. This figure added human factors to the previous diagram. It illustrated how tiredness, slips in attention or limited knowledge may increase error rates across all process stages

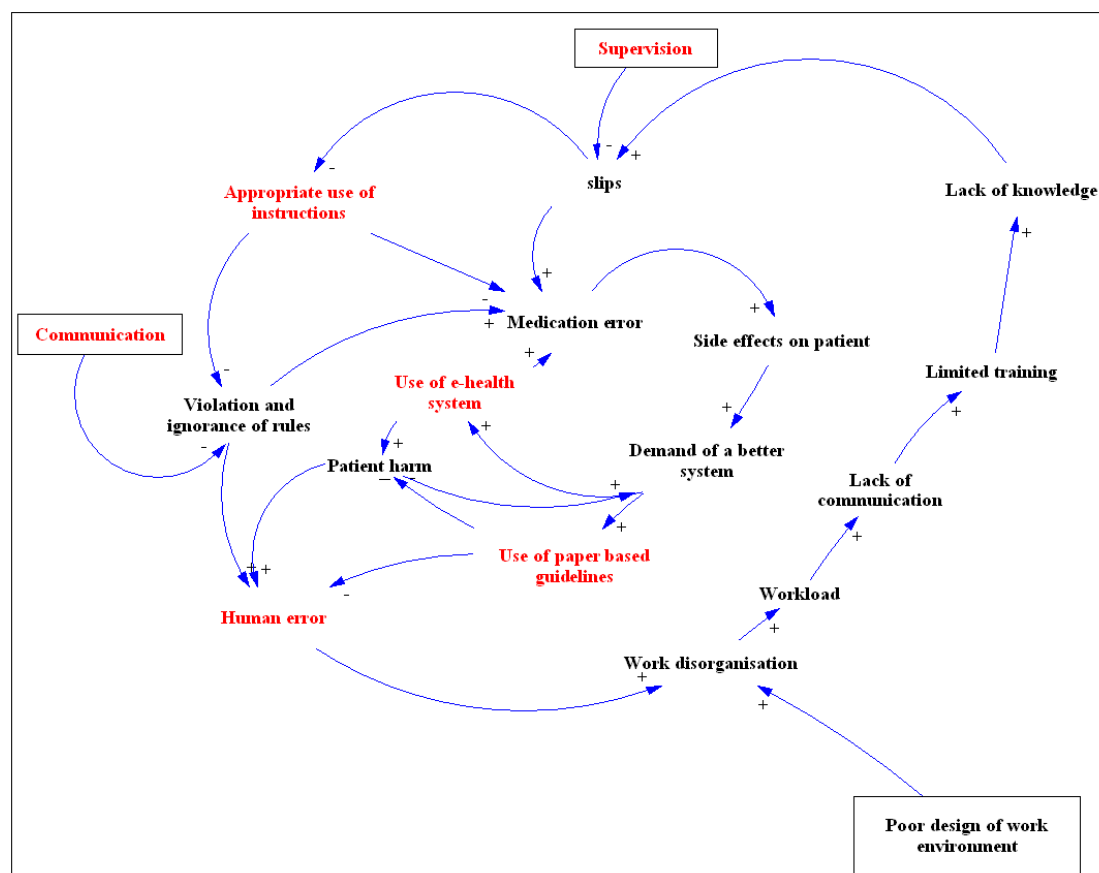


Figure 5.5 Causal Loop Diagram 3: factors attributed to latent conditions and active failure (human error).

5.3.4.1 Explanation of CLD3 variables

Human error: It has been defined by Reason as “ Error will be taken as a generic term to encompass all those occasions in which a planned sequence of mental or physical activities fails to achieve its intended outcome, and when these failures cannot be attributed to the intervention of some chance agency” [28].

Work disorganisation: Poor plan of working conditions, which is designed by human. If there is an error in the design it will lead to work disorganisation.

Workload: High amount of work assigned to prescribers.

Lack of communication: High amount of work will lead to no communication between medical professionals.

Limited training: If the medical professionals do not complain or communicate, no further training will be provided to them to improve the situation.

Lack of knowledge: When not enough training is provided it will be a problem in the personal knowledge of the new professionals.

Slips: Errors that result from some failure in the execution and/or storage stage of an action sequence, regardless of whether or not the plan which guided it was adequate to achieve its objective [28]

Appropriate use of instructions: The prescriber should be well supervised not to make any mistake then it will improve the use of the work instructions.

Violation and ignorance of the rules: A failure to apply a good rule [139] and can be deviations from safe operating procedures, standards or rules [140]

5.3.5. Examples of medication errors applied on CLDs

1. A patient hospitalised for chemotherapeutic treatment for a malign tumour was prescribed vincristine (oncovine) to treat her breast cancer, which is an intravenous drug, it is usually given weekly $1.4\text{mg}/\text{m}^2$. However the patient was given vincristine intravenously at the higher dose of vinblastine (Velban) which is also an anticancer drug but with a different dosage. It is an administration error which is part of the CLD1, with the wrong drug name leading to an incorrect dosage. Even when using a computer to enter the drug information, errors may happen; therefore a dose warning system should be installed to alert staff on specific sound-alike drugs to avoid confusion.
2. Another example is slips in attention, when there is a lapse in concentration, a patient is prescribed Amaryl (Glimepiride) instead of Reminyl (Galantamine hydrobromide). Amaryl is used for type II diabetes, by lowering blood sugar levels and stimulating the production of insulin from the pancreas with a dosage of 1-2 mg daily. Reminyl is prescribed to treat symptoms of Alzheimer's disease, the starting dose is 4mg twice daily for four weeks. In this case the doctor has Reminyl in mind but by mistake wrote or entered Amaryl, the patient is not diabetic so his blood glucose is not monitored which is very dangerous. This error is classified in the CLD3 because it is a product of a slip in attention error influenced by human error. In this case an alarming system should also appear with the patient's medical history explaining that this patient never had diabetes.

5.4. Computer simulation models of the hospital medication process

5.4.1 Method

The methodology was based on the development of two simulation models. The first simulation was built to model of a hospital medication flow system using a hand written prescription or a simple computer (figure 5.7), the second one was to model a hospital medication process using a computer system with CDSSs components (Figure 5.8). The software that was used to build the model was Stella iThink 8.1 for continuous simulation modelling.

5.4.2 Explanation of the model features

A system dynamics model consists of diagrams which are stocks and flows. The stocks are represented by rectangles, inflows are presented by an arrow pointing into the stock and outflow is pointing out of the stock and the valve controls the flows[129] as shown in figure 5.6.

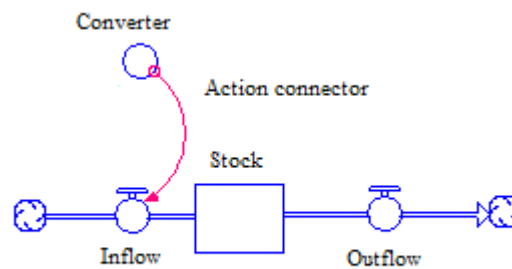


Figure 5.6: A diagram of the model features

The stocks and flows principle was based on the hydraulic metaphor of the water flow into and out of reservoirs from Forester in 1961. The stock represented a bath or reservoir where the accumulation of water flowing from the tap is less than the water flowing out through the drain. The same principle was followed in our model where the quantity of patients with medication orders or prescriptions is the accumulation of the flows of patients in less the flow of patients out. The stock is also influenced by the converters or auxiliaries that can be constant or exogenous inputs. The mathematical equation used for the stock is:

$$Stock(t) = \int_{t_0}^t [Inflow(s) - Outflow(s)]ds + Stock(t_0)$$

Where Inflows is the value of the inflow at any time s between the initial time t_0 and the current time t .

5.4.3 Data collection

The models included data from the 22 papers of the meta-analysis that compared the rate of errors using a simple system and a computer CDSS . The rate of total admissions and the rate of total patients selected for the studies were also concluded from the papers (table 4 appendixes); a total of 14930 admissions per week and a total of 13491 patients for the simple model and 20165 admissions and 18435 selected patients for the computer decision support system model. The rates used in the models are calculated by number of patients, such as the number of patients with medication errors and the number of patients with prescribing errors. The collected variables are summarised in tables 8, 9 and 10 in the appendix section.

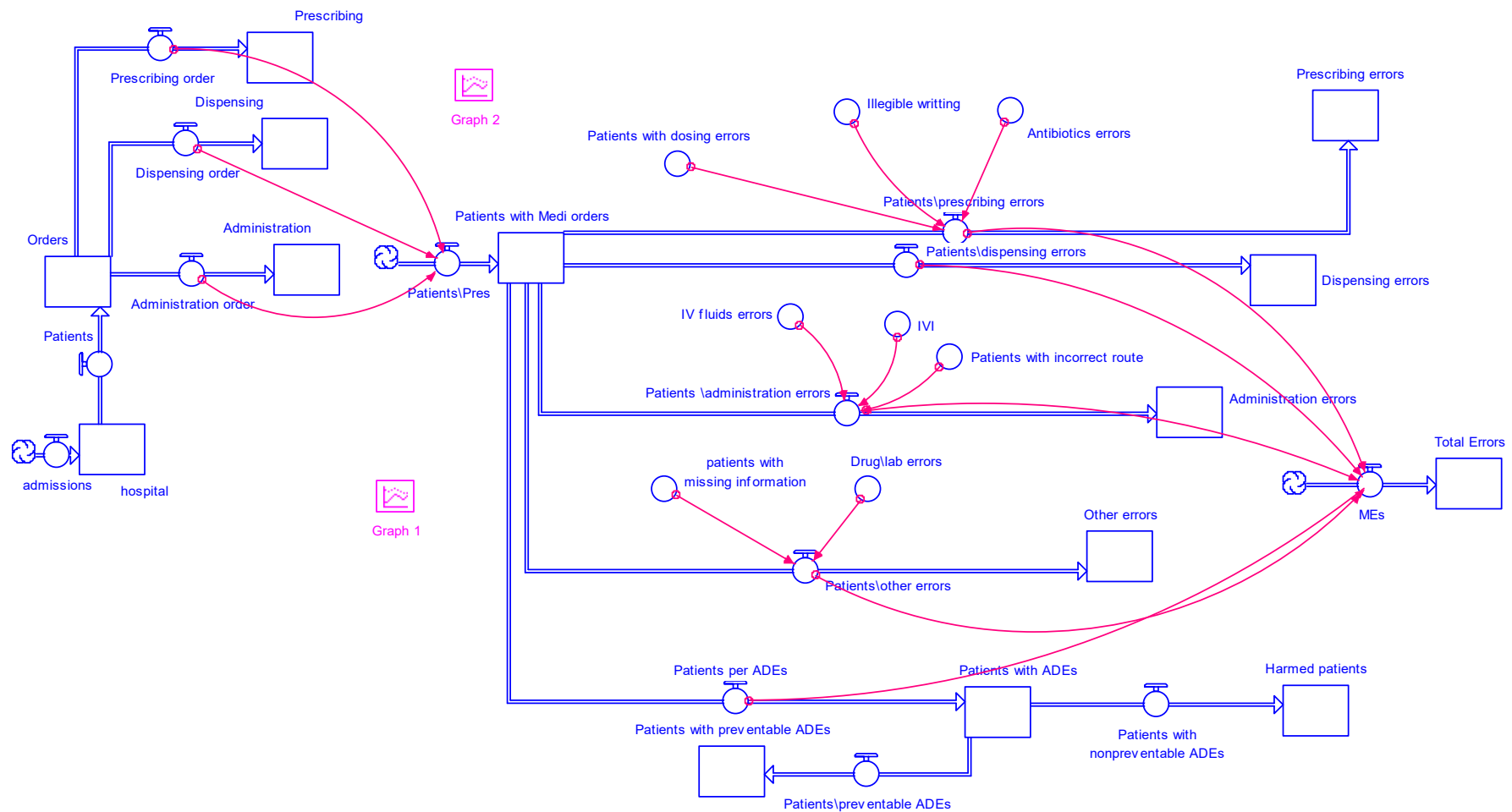


Figure 5.7: A system dynamics model of a hospital medication process using a simple medication prescribing system (model 1)

5.4.4 Analysis

The hospital medication process was simulated, by using error rates obtained from the meta-analysis published papers.

Model 1: A simulation model of hospital medication process errors using a simple system (figure 5.7)

The results of patients with medication errors at every stage were shown in figure 5.9 that described a continuous simulation of the rates of patients with prescribing errors, dispensing errors, administration errors and harmed patients from adverse drug events. The rates are also shown in numbers by using a bar chart (figure 5.9).

The results showed that the rate of patients with prescribing errors was significant compared with patients with other types of errors which was 70 % of total patients population. The rate of patients with administration errors was less significant 5 % of the total patients and the rate of patients with dispensing errors was even smaller only 0.04 % which was 5 patients only out of 13491 patients. However, the rate of patients with other types of errors such as missing information or errors with drug-laboratory interaction was 14 % out of the total population of patients. The total number of harmed patients from adverse drug events was 204 patients and the total number of patients with medication errors was 12517 patients out of 13491 patients.

Model 2: A simulation model of hospital medication errors using a computer system with CDSSs. (figure 5.8)

The results of patients with medication errors at every stage were described by a bar chart in figure 5.10.

The results showed that the rate of patients with prescribing errors was significant at 28.7% of the total compared with patients with other errors. The rate of patients with administration errors was less significant at 3% of the total patients, the rate of patients with dispensing errors was even smaller only 0.05% which was only 10 patients out of 18435 patients. The number of patients with other types of errors such as missing information or errors with a drug-laboratory interaction was 2.63 % of the total population of patients. The total number of harmed patients from adverse drug events was 187 patients and the total number of patients with medication errors was 6746 patients out of 18435 total patients.

The comparison between the control model which was the simple prescribing system and the intervention model that was the new prescribing system showed that there

were less medication errors and fewer patients were harmed with the intervention system. Therefore, in order to explore the impact of CDSSs components, we applied the effect of every component on the simple model, the results are described in the following section.

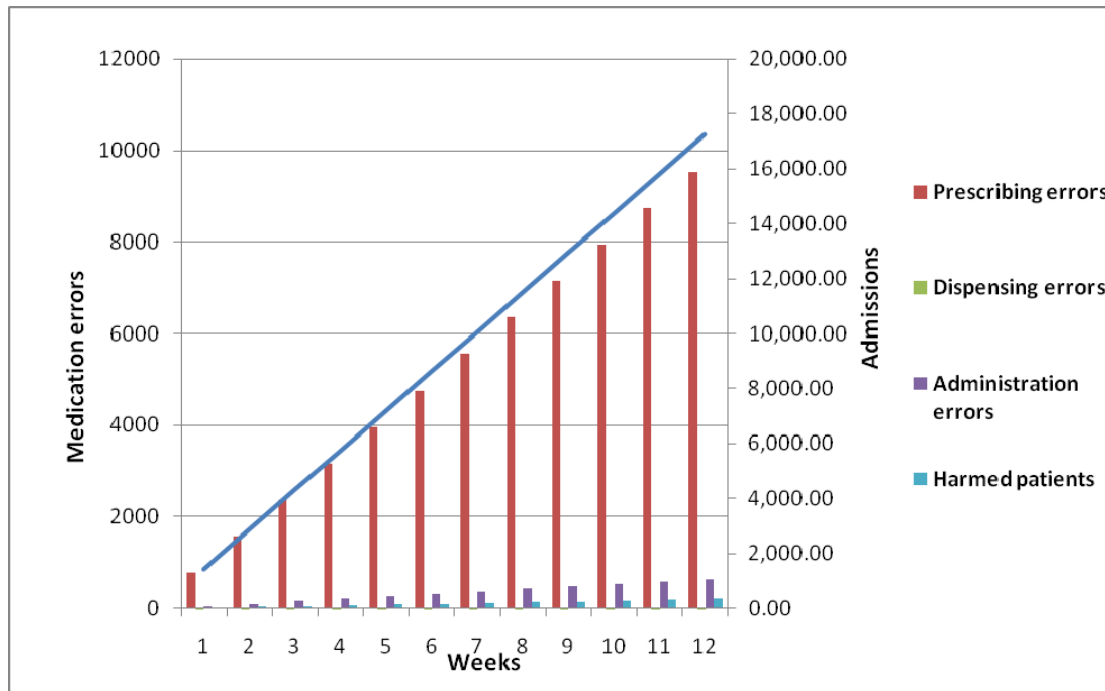


Figure 5.9: A bar chart of patients with medication errors in hospital using a simple medication process system

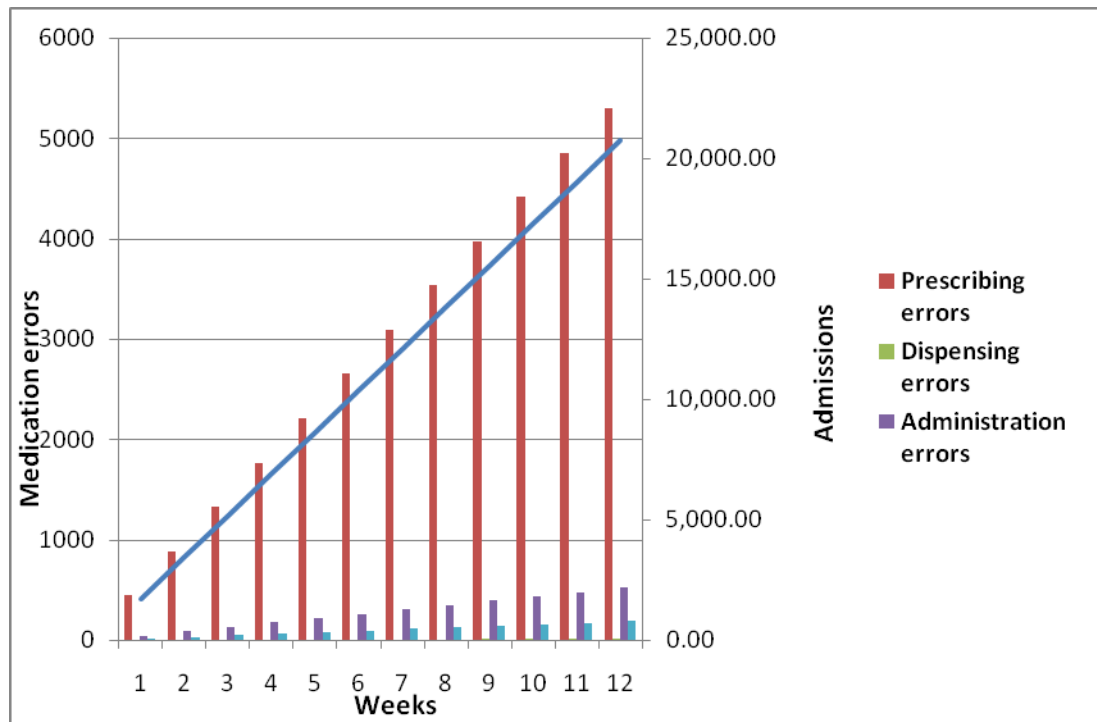


Figure 5.10: A bar chart of patients with medication errors in hospital using a computer with decision support systems

5.5 Application of CDS components on the simple prescribing system

Model 3:

The data collected for this model was the measurement of the effect percentage between the simple system and a computer system with CDSSs. Subsequently, the effect percentage results of the comparison were applied to the simple system to explore the effectiveness of CDSSs on reducing medication errors (figure 5.11).

The effect rates:

- The inclusion of Order entry has reduced the rate of patients with written prescribing errors by 42 % from Donyai et al
- Antibiotics decision support system has an impact of 5 % reduction in patients with antibiotics errors from Mullet et al
- Intravenous infusion DSSs has caused 80% reduction in patients with administration errors according to KD Evans et al
- CPOE surveillance has reduced the number of patients with drug-laboratory problems by 49 % from Oliven et al

- CPOE and DSSs has decreased the rate of patients with non-preventable ADEs by 8 % from total rate of the data

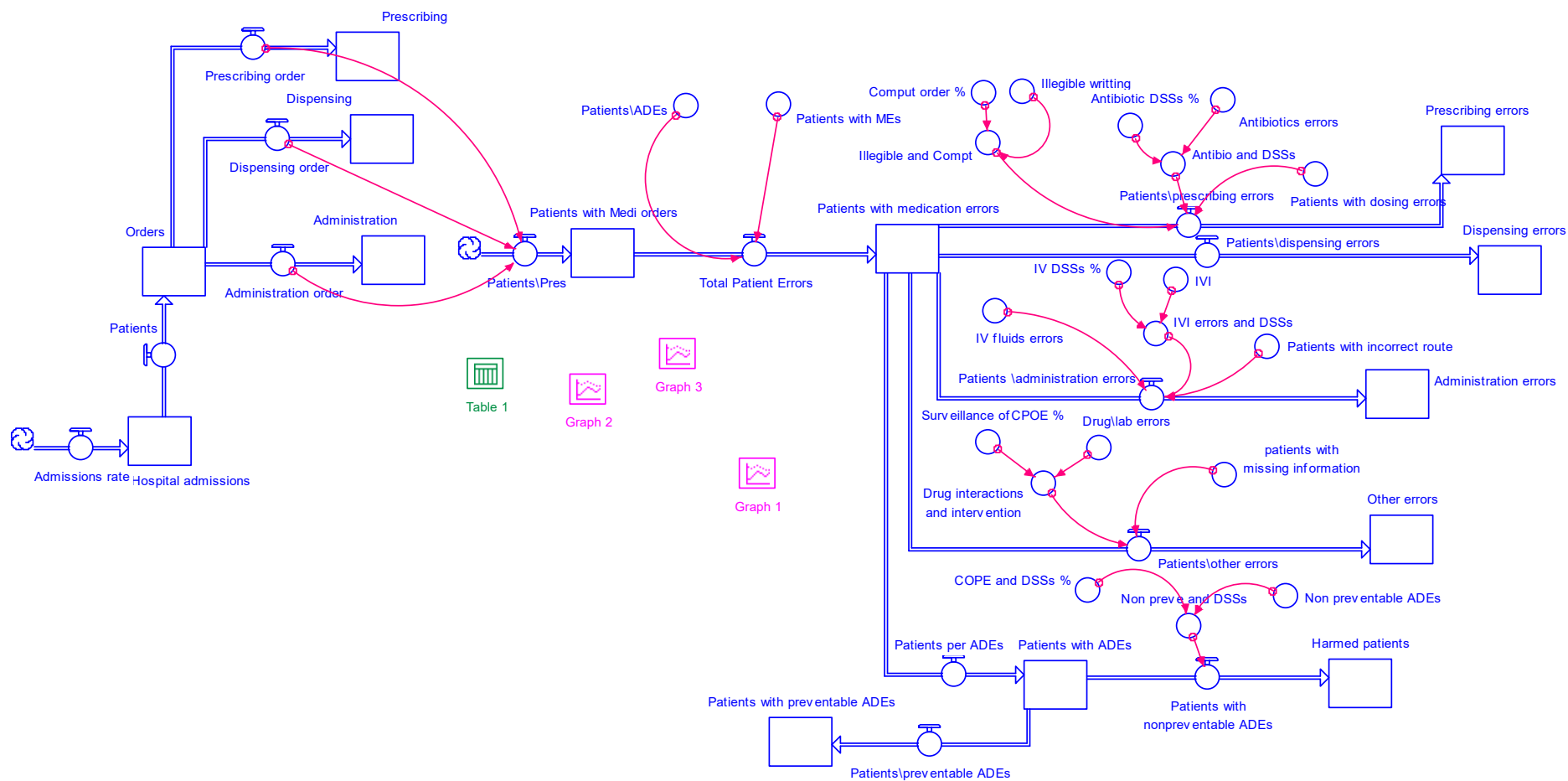


Figure 5.11: A system dynamic model of hospital medication process system using CDSSs (model 3)

5.5.1 Results and analysis

5.5.1.1 Prescribing stage

The first stage of the medication process is prescribing; the first intervention applied to the simple model was an order entry computer application that showed a 1% reduction of patients with prescribing errors; from 9524 to 9433.

The second intervention of this stage was the inclusion of an antibiotics decision support system. After that inclusion the rate of patients with prescribing errors decreased further by 2.6% reduction; from 9524 to 9279.

Figure 5.12 shows a clear drop of patients with prescribing errors after the introduction of the order entry element, and the rate dropped again after the inclusion of the antibiotics DS element. The number of patients was increased by the number of admissions through the twelve week period of simulation.

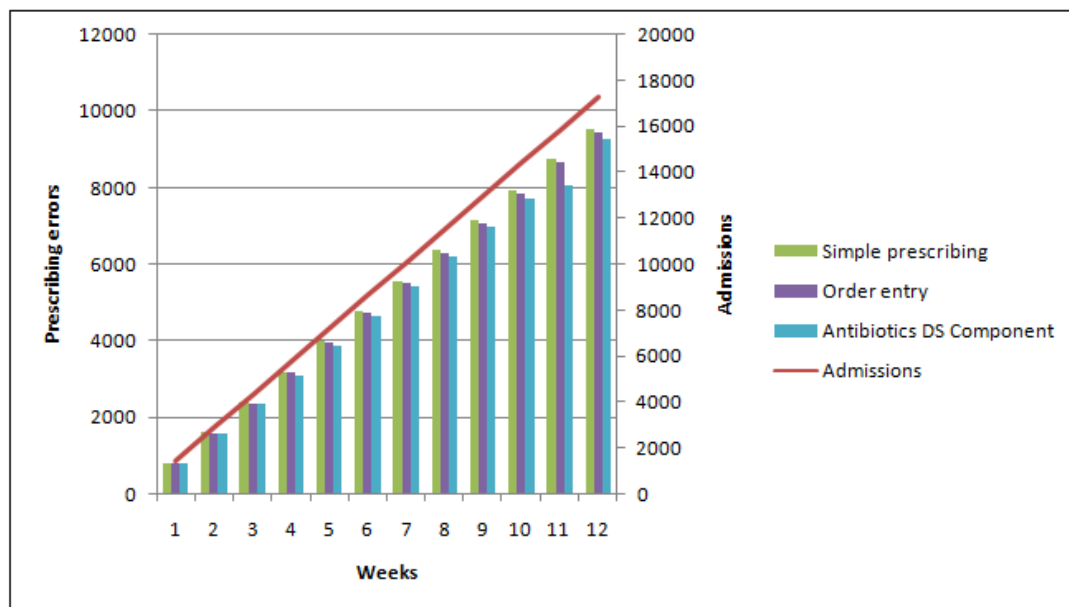


Figure 5.12: A graph showing the rates of patients with prescribing errors after the inclusion of interventions.

5.5.1.2 Administration stage

Drug administration is the third stage of the medication process. The intervention involved was an intravenous infusion decision support component, which showed a noteworthy effect in reducing the rate of patients with administration errors by 10.5%; from 655 to 586 patients after using an IVI intervention.

Figure 5.13 shows the reduction of the number of patients with administration errors after the addition of the intravenous decision support element, it also shows the number of admissions.

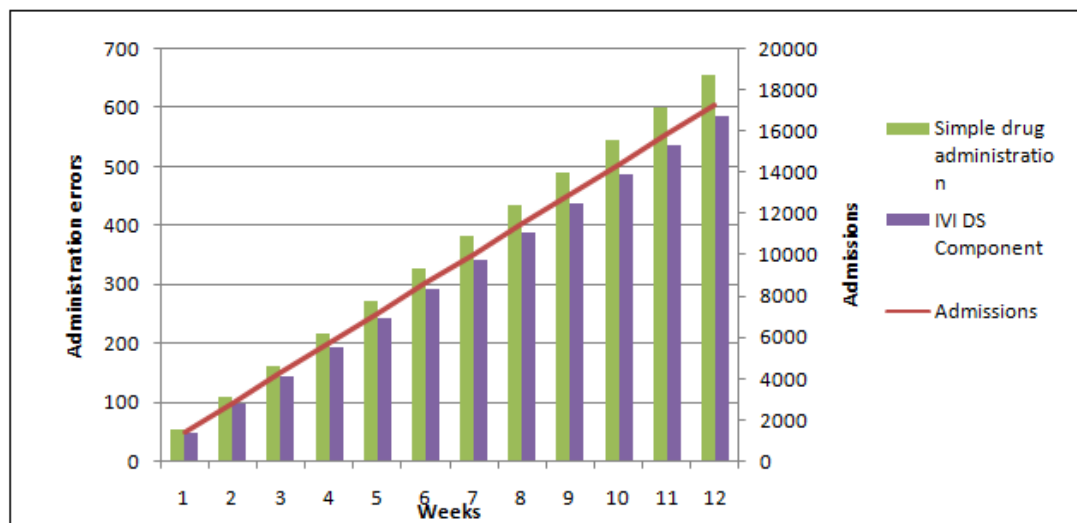


Figure 5.13: A graph showing the rate of patients with administration errors after the inclusion of intervention

5.5.1.3 Other types of medication errors

This part shows the rate of patients with other types of patients with medication errors such as the rate of patients with missing information which was almost 1% of the total patients and patients with drug-laboratory interaction which was 0.05% of the total patients. Also present were other errors that were not clear from the papers. However, after the application of a web-based surveillance on the computerised prescribing system the rate of patients with those types of errors decreased by 2.17 %; from 1886 to 1845 patients after the surveillance of CPOE. The results are shown in figure 5.14.

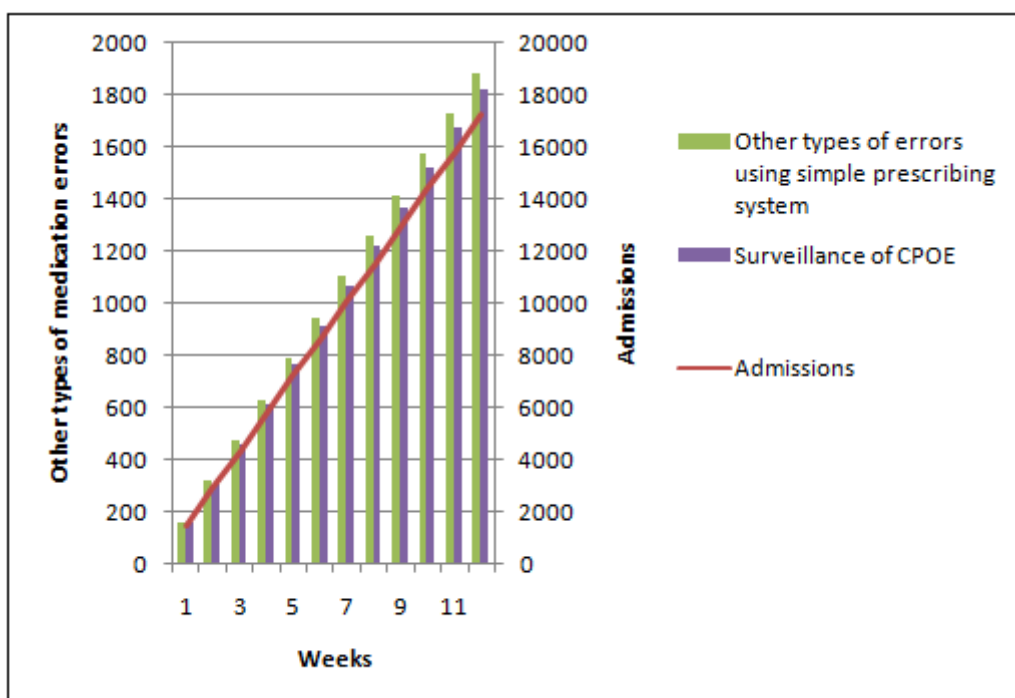


Figure 5.14: A graph showing the number of patients with other types of medication errors after the surveillance of the prescribing system

5.5.1.4 Number of harmed patients

The number of patients harmed by adverse drug events after the addition of the decision support systems showed a significant reduction by 7.8 %; from 204 to 188 patients (figure 5.15).

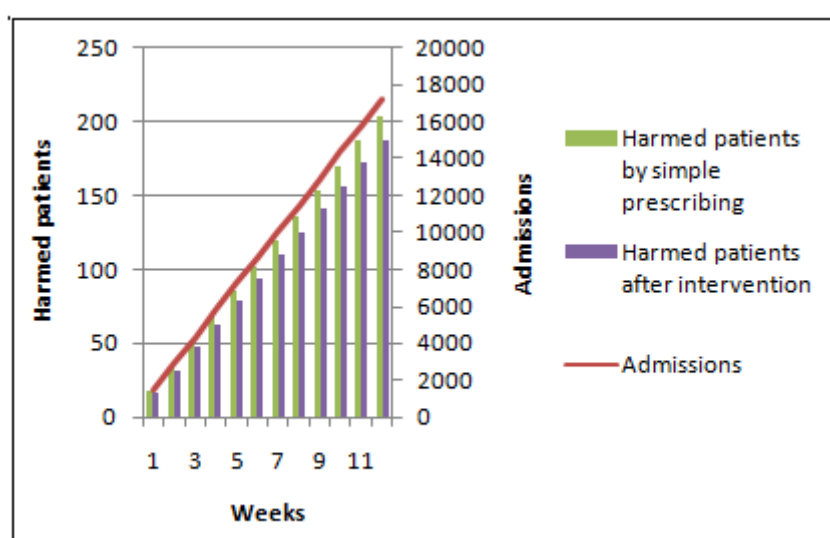


Figure 5.15: A graph showing the number of harmed patients after interventions

5.6 Chapter summary

In this chapter a number of simulation models were constructed to assess the consequences of medication errors on patient safety. Three models have been developed; the first one represented the hospital medication process using a simple prescribing system with estimated figures from the control group of the meta-analysis articles, the second one characterized the hospital medication process using a computer prescribing system with CDS components with estimated data from the intervention group of the meta-analysis papers.

The third model was developed to explore the effect of different types of CDS elements in reducing the rate of patients with medication errors, the parameters were taken by estimating the effect percentage between control model and intervention.

The structure of the models was based on the process involved in the use of drugs in healthcare at hospital setting in the UK as explained in Chapter 1 figure 1.2.

The first two models confirmed that the rate of patients with prescribing errors was higher than other types of errors, because almost all of the available data were focused on prescribing errors, even though patients with dispensing and administration errors and other categories of medication errors showed a high risk to patient health. The rate of patients with medication errors when using the computer with CDSSs was much lower than the rate of patients when using the simple prescribing system.

Therefore, the results of model three has shown the importance of every element of CDS in every stage of the medication process. Order entry application and antibiotic decision support elements had reduced the number of patients with prescribing errors by 2.6%. An intravenous decision component has decreased the rate of patients with administration errors by 10.5%, as well a web based surveillance of the prescribing system had an impact in decreasing the number of patients with other types of medication errors by 2.2% and the total reduction in harmed patients after interventions was 7.8%. More components could have been tested, but unfortunately the chosen articles only included data from a few CDSSs.

Chapter 6

Evaluation

6.1 Introduction

By developing a medication safety model, it was essential to validate the flow of the simulation models and the CLDs. The assessment was based on three methods; a model consistency check, a qualitative and formative evaluation and testing of the model in a paediatric setting.

6.2 Aim and reasons for performing the evaluation

The purpose of the evaluation was to describe the developed approach; we evaluated how well the solutions fit to research key objectives, by considering feedback from medical professionals and potential users [141].

The main reasons for carrying out this evaluation were; first to encourage the use of information systems with knowledge bases and decision support systems in medicine. Doctors should be comfortable and confident in using a safe system that benefits healthcare professionals and patients. Second, a consideration of the impact of the model structure and its function on the user including the change of the CLDs features for the pharmacist's advantage. Finally, users require evaluation results in order to accept the use of new approaches.

Other aspects should be considered to complete an evaluation such as:

- Structure of the healthcare system
- Processes that take place during health care activity
- Outcomes of healthcare for both individual patients and community

6.3 Methodology

The methodology has involved three steps:

1. Initial model development consistency check; by applying the results of the effect percentage in Brigham and Women hospital based on their patients' admission rate data.
2. Qualitative evaluation: verification of CLDs with colleagues to look at the flow variables and their relations and clinical professionals to validate the process and signification of variables.
3. Formative evaluation: pharmacists to assess the relation between the CLDs variables. Output analysis of the model by pharmacists by applying the benefits of clinical decision support systems on a paediatrics hospital.

6.4 Consistency check of the model

This section demonstrates the development of a simulation model that was built to model a medication process system in Brigham and Women's Hospital in Boston with an admission rate of 44000 a year, a rate of 846 per week. The hospital was chosen because of the availability of the data and almost all of the research studies were done in this hospital.

The model was divided into two models; a basic one that included data of a simple prescribing system and an intervention model that included the first type of interventions that were collected from the meta-analysis papers, and the second types which were collected from other published papers such as computer reminders, unit dose and bar coding. The model was run for a twelve week period.

6.4.1 A model of a simple prescribing system

The structure of the simple prescribing system model was the same as the previously designed models, however the rates included in the model were based on the number of admissions in the hospital.

The rates of the rest of the variables were estimated from model 3 in chapter 5 as effect percentage; for example the rate of admitted patients was estimated to be 90% of the 846 admitted patients and also it was estimated that there was almost 2 prescriptions or drug entries per patient based on the results of model 3.

The effect of CDSSs was measured from model 3 but based on the number of admissions on this hospital, for example there was a 2.4% reduction of patients with

prescribing errors when order entry application was added to the prescribing stage, the effect percentage in the evaluation models was different because the number of admissions was different.

The number of patients with prescribing errors was significantly higher than other types of errors which was 70.9 % of total patients. The number of patients with administration errors was significantly less 5.25 %, and patients with dispensing errors 0.035 % was lower. The rate of patients with other types of errors such as missing information or errors with drug-laboratory interaction was 14.45 % out of the total population of patients. The total number of harmed patients from adverse drug events was 11 out of 761.5 total patients which was 1.45%. The results are shown in figure 6.1.

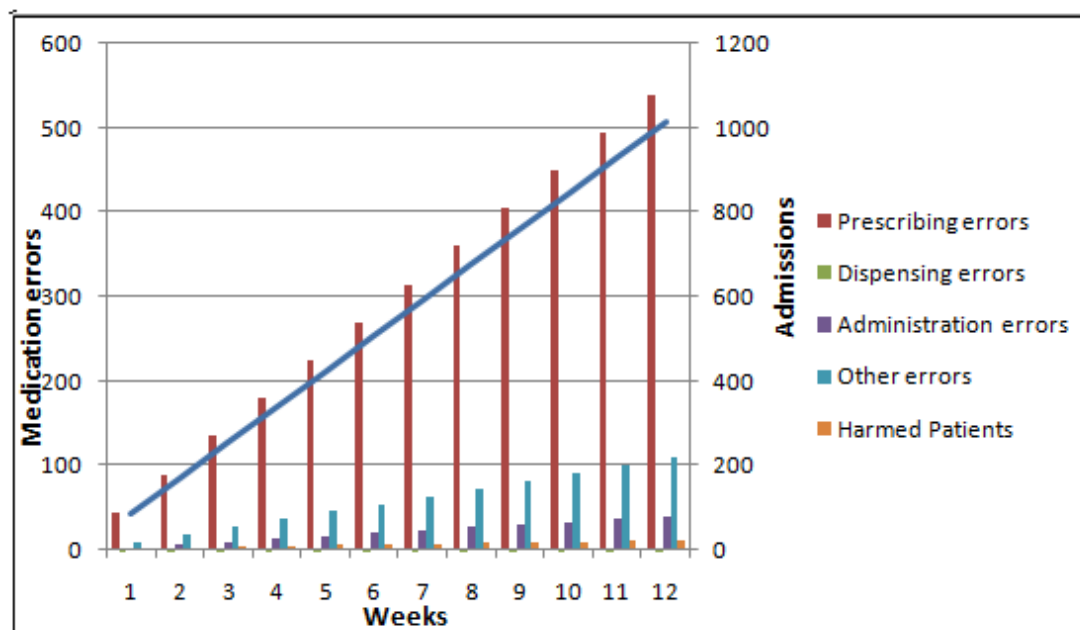


Figure 6.1: A bar chart of the rate of patients with medication errors for the evaluation model

6.4.2 Intervention models

Model 6.1: First interventions

The interventions applied were the same CDS components applied in the previous chapter. The purpose of the addition of the CDS elements was to measure their effect in reducing the rate of medication errors. The results after the addition of intervention were summarised in figure 6.2.

- Order entry application resulted in a 2.4 % reduction of patient with prescribing errors. The intervention was chosen from the Donyai et al paper from the meta-analysis as an order entry application has shown great impact in reducing prescribing error.
- Antibiotics DS component gave a 0.3 % reduction in patients with prescribing errors, it was chosen from Mullet et al
- Intravenous infusion DS component gave a 4.51 % reduction in patients with administration errors from KD Evans et al
- CPOE surveillance gave a reduction of 2.75 % reduction in patients with drug-laboratory medication errors from Oliven et al
- CPOE and DSSs gave a 0.5 % reduction from taken the effect percentage of harmed patients by using a simple prescribing system and harmed patients by using the intervention system

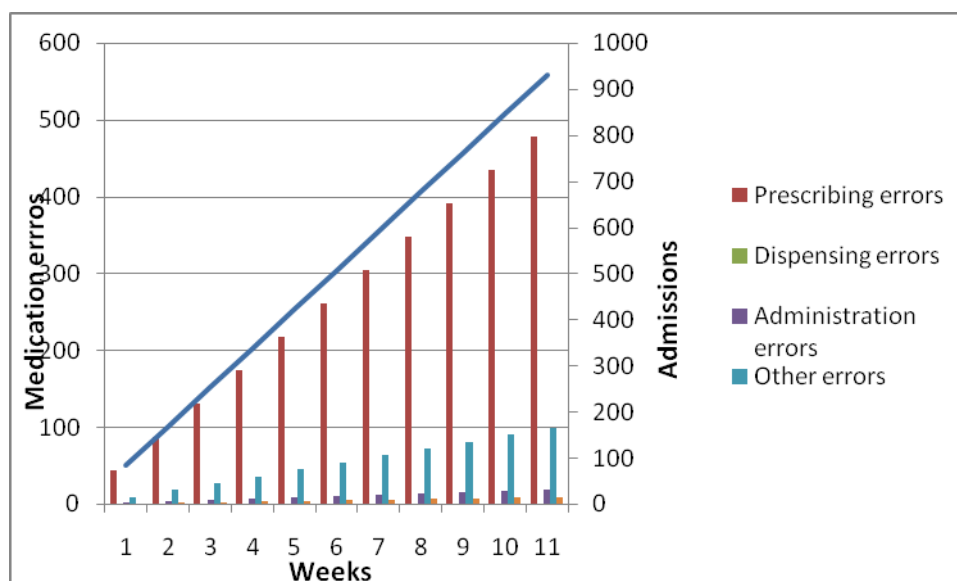


Figure 6.2: A bar chart of the rate of patients with medication errors after the first interventions

Model 6.2: Second interventions

For the purpose of the evaluation, the following model (figure 6.3) included additional interventions that were not applied to the previous models which illustrated data from the meta-analysis.

- Unit dosing DS component that reduced patients with dispensing errors by 20%, the effect was chosen according to Anderson et al 2003 [133], that showed a 80% reduction of medication errors, when using a unit dose at the dispensing stage.

The Institute Of Medicine [6] has estimated reduction of medication errors when using an automated dispensing system by 78%. Many UK hospitals have introduced the system along with bar coding; the implementation of the system in King's College Hospital in London had shown a reduction of dispensing errors by 65 % [142].

- Bar coding system that reduced patients with administration errors by 41.14%, the effect was taken from Anderson et al 2002 [132], which showed a reduction of administration errors by 60% by using their own rate of patients.

The tool has great potential to improve hospital administration system in the UK, as a closed-loop prescribing and medication administration system has been evaluated and showed a reduction in administration errors by almost 50%[142]. Implementing the application of bar-code technology in Northern Michigan Regional Health System has eliminated the missed doses and the system recorded the actual medication administration [144].

- Computer reminders DSSs used to inform a doctor for medication shortage which can be related to human error and reduced the error by 55% according to Bogucki et al, 2004 [145]. The new intervention has reduced the rate of patients with prescribing errors by 50%.

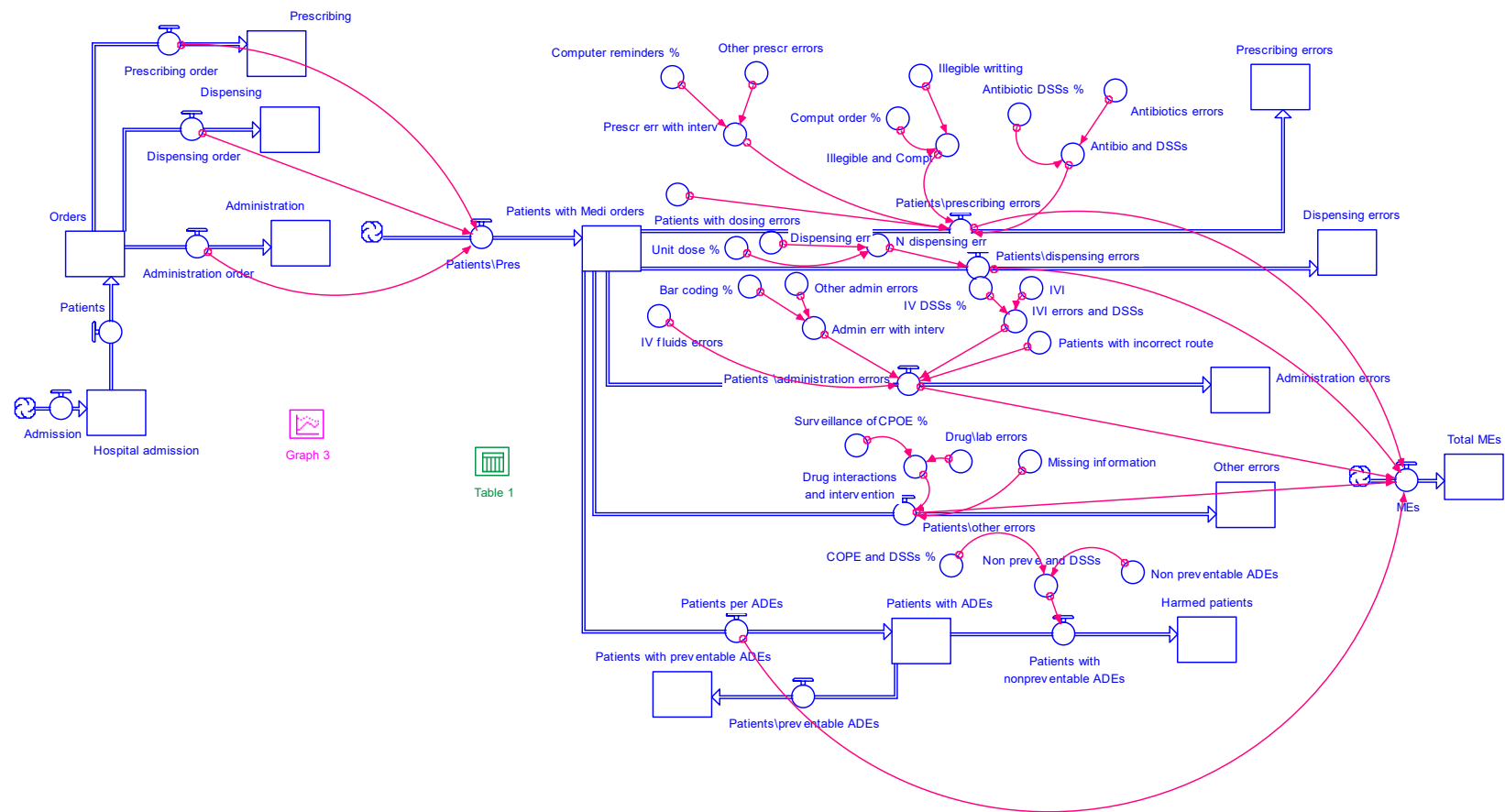


Figure 6.3: A system dynamic model of a medication process system at the Boston hospital with second intervention

6.4.3 Results Analysis

6.4.3.1 Prescribing stage

The first intervention applied to the simple model was an order entry computer application that showed a notable reduction of patients with prescribing errors, a 9.8% reduction compared to the rate of patients with prescribing errors in the simple model; from 540 to 487 patients with prescribing errors after using a computer application order entry.

The second intervention of this stage was the inclusion of an antibiotics decision support component. After this addition the rate of patients with prescribing errors dropped further by 11.5%; from 540 patients with prescribing errors using a simple system to 478 patients using two types of interventions order entry and an antibiotics DS component.

The third new intervention at this stage was the addition of computer reminders which aim to and supposedly reduce prescribing errors by 50% [145]. After the inclusion of computer reminders, the rate of patients with prescribing errors decreased further more by 31%: from the initial rate of 540 to 373 patients with prescribing errors. The results were shown in figure 6.4.

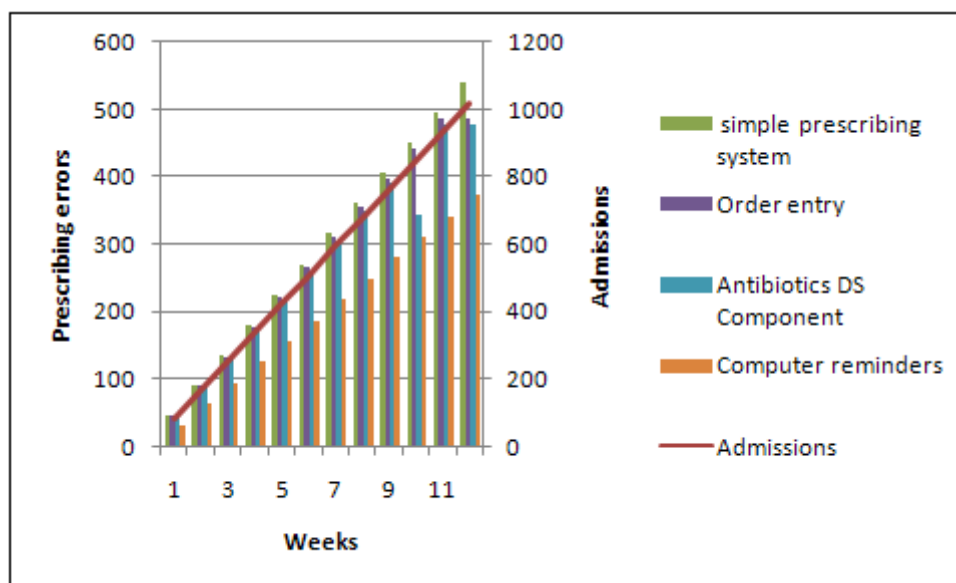


Figure 6.4: A graph showing rates of patients with prescribing errors after inclusion of interventions

6.4.3.2 Dispensing stage

The second stage of the medication process is dispensing medication. A unit dose DS component was added to the dispensing stage in order to detect the effect in reducing the rate of patients with dispensing errors, as estimated by Anderson that unit dose reduced dispensing errors by 80% [133], and 20% reduction when it was applied to the rate of admissions in Brigham and Women's Hospital. After the addition of a unit dose element the rate of patient with dispensing errors decreased by 18.51%. See figure 6.5

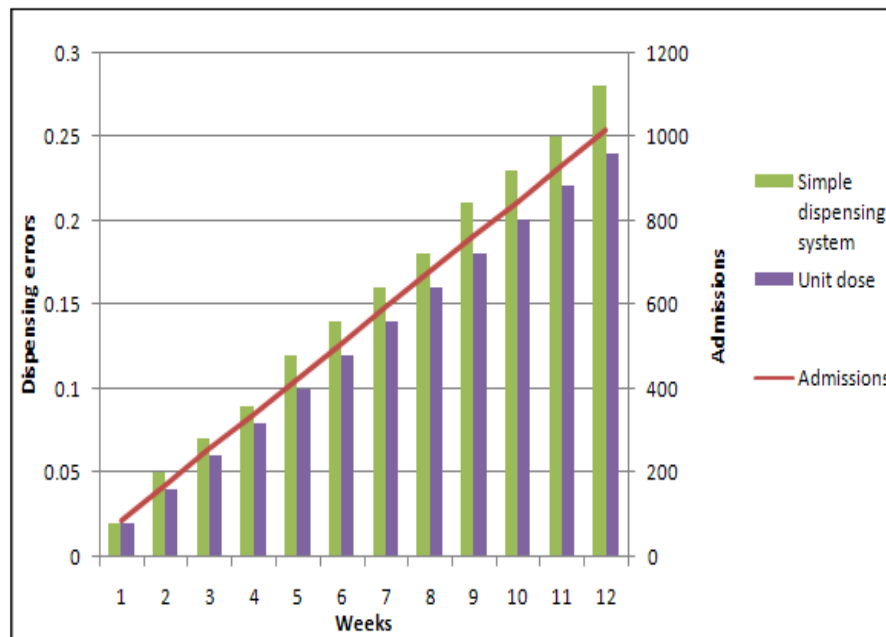


Figure 6.5: A graph showing the rates of patients with Dispensing errors after the inclusion of the unit dose element.

6.4.3.3 Administration stage

The first intervention involved in the administration stage was an intravenous infusion decision support component, which also showed an important effect in reducing the rate of patients with administration errors by 52.5%; from 40 to 19 patients after using an IVI intervention.

The second new intervention applied was a bar coding system that was estimated by Anderson to reduce administration errors by 60% [132], and by 40% when it was applied to the intervention model. A number of patients with administration errors has been reduced by 21%; from 19 to 15 patients with administration errors. See figure 6.6.

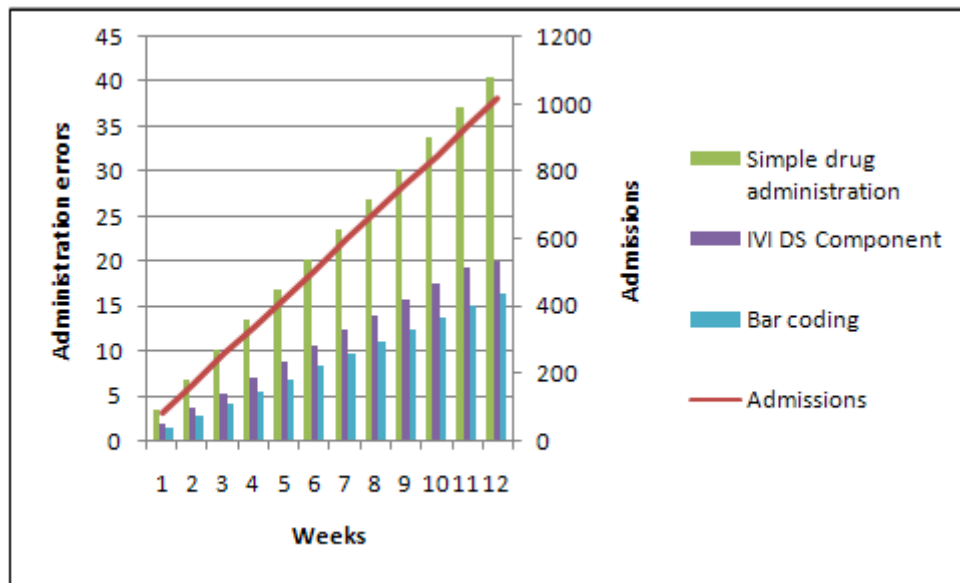


Figure 6.6: A graph showing the number of patients with administration errors after the inclusion of interventions.

6.4.3.4 Other types of medication errors

The intervention was the addition of web-based surveillance of the use of a computerised prescribing system. The rate of patients with those types of errors decreased by 10%; from 110 to 99 patients after the surveillance of CPOE. See figure 6.7.

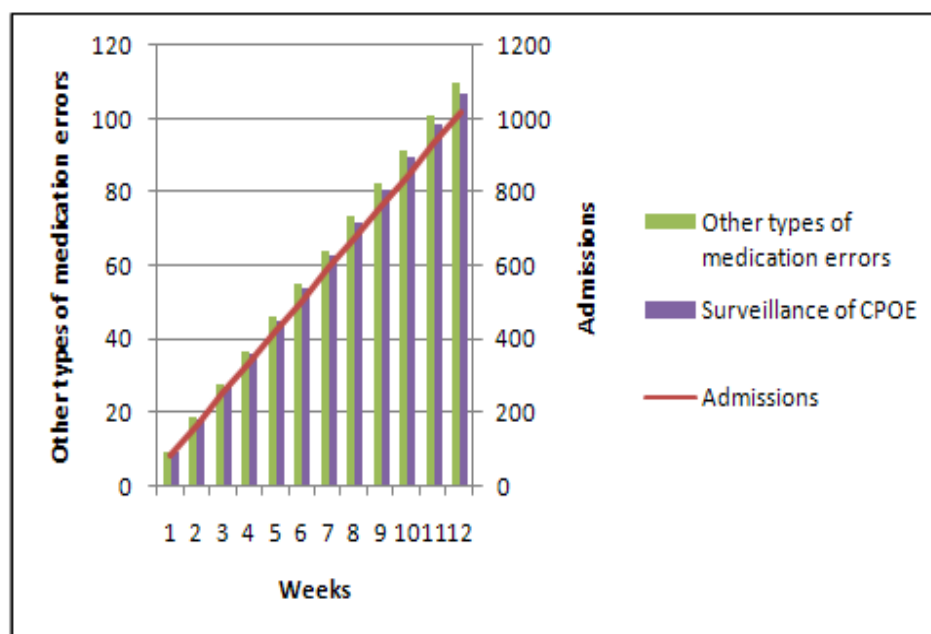


Figure 6.7: A graph showing the number of patients with other types of medication errors

6.4.3.5 Harmed patients

The number of patients harmed by adverse drug events was reduced by the addition of CPOE and DSSs by 9%; from 11 to 10 patients. See figure 6.8.

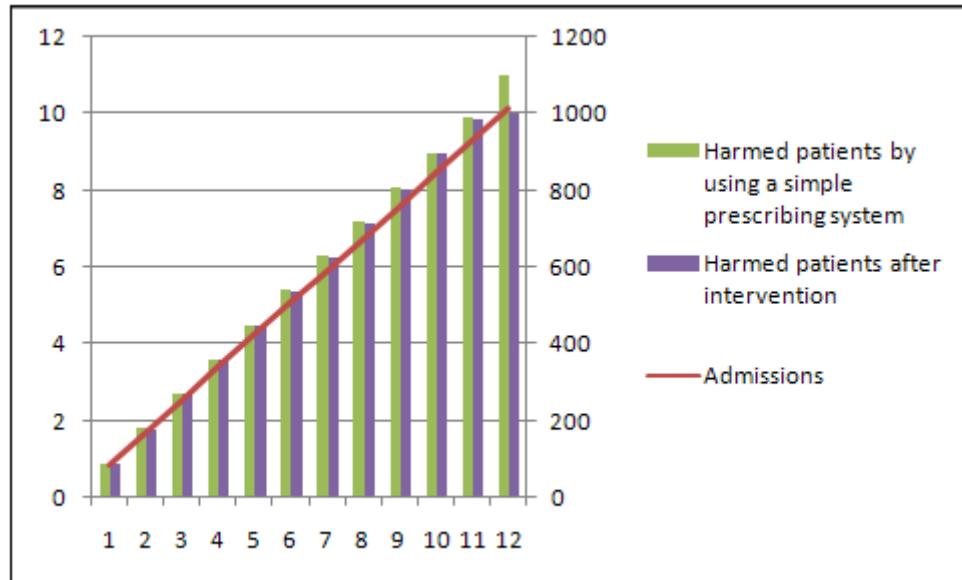


Figure 6.8: A graph showing the number of harmed patients after inclusion of intervention.

6.5 Qualitative evaluation

The feedback from the group meeting that consisted of three researchers had a valuable implication on the flow of the loops and definitions of variables; also the group has suggested looking at other factors that might influence the development of a new prescribing system with CDSSs such as the cost.

The colleagues have proposed the following suggestions:

- **Addition of measurements** into the variables such as sources of variables including Reason’s model of error-causing conditions and the Delphi technique that was used to develop a definition for the term “medication error” and its likely causes [86], which is a technique is a method to collect information and judgment from participants in order to help researchers to solve their problems and decision making [146]. The principles and methods behind the Delphi Technique are shown in table 11 in the appendix section.

- **Consideration of the cost of medication errors and the cost of the development of a new information system.** The purpose of the research project was to change an old prescribing system, as we have already justified the benefit of the inclusion of CDSSs based on the clinical improvement of the patients. At that stage of the research cost variables were not added to the model, to evaluate the effect of the cost, a new model should be developed as part of future recommendation of the research.

The cost of medication errors that harm patients was already high; moreover the cost of system development and renovation is higher. Some of the cost examples of existing systems were reviewed. As has been mentioned before, one of the inconveniences of CPOE was the cost of the installation and the maintenance, plus the cost of health professionals' education [48]. An experience of e-prescribing in Massachusetts has stated that the cost of the initial investment of collaboration between two companies to install the system has cost them three million dollars. There was a problem in the long term cost such as the cost of technology sophistication, practice management system capabilities, internet connection, patient data loading, project management, training effort, devices, license, and wireless access and cost to implement and use the system per doctor up to ten thousand US dollars in the first year and up to three thousand in the second year [147].

6.6 Formative evaluation from clinical pharmacists

6.6.1 Suggested changes of CLDs

Clinical pharmacists (Four pharmacists) have suggested dividing the CLD of mismanagement of medication process into three stages; prescribing, dispensing and administration. The reason to divide the loop was because a source of error can be from a doctor in writing a prescription so the nurse and pharmacist will follow the doctor's prescription whether it has the incorrect or correct drug for the particular patient. Therefore, a doctor can make a mistake at the prescribing stage, a pharmacist or dispenser at the dispensing stage and a nurse at the administration stage, if we assume that medication process was for inpatients.

6.6.1.1 CLD of a prescribing error

The loop described an error while writing a prescription in a busy work environment, if the prescription is incomplete that increased an error in patients information, both variables are influenced by a missing signature and no time to check the appropriate information. If the age of the patient was wrong or missing, it lead to a different drug name, at this stage the dose was correct for the wrong given drug, and ended up in patient harm, because the wrong medication was prescribed to the right patient.

Consequently, a new prescribing system was required to reduce a mistake at the prescribing stage such as an order entry application with additional antibiotics DSS and computer reminders and warnings on specific patient information. The loop is shown in figure 6.9.

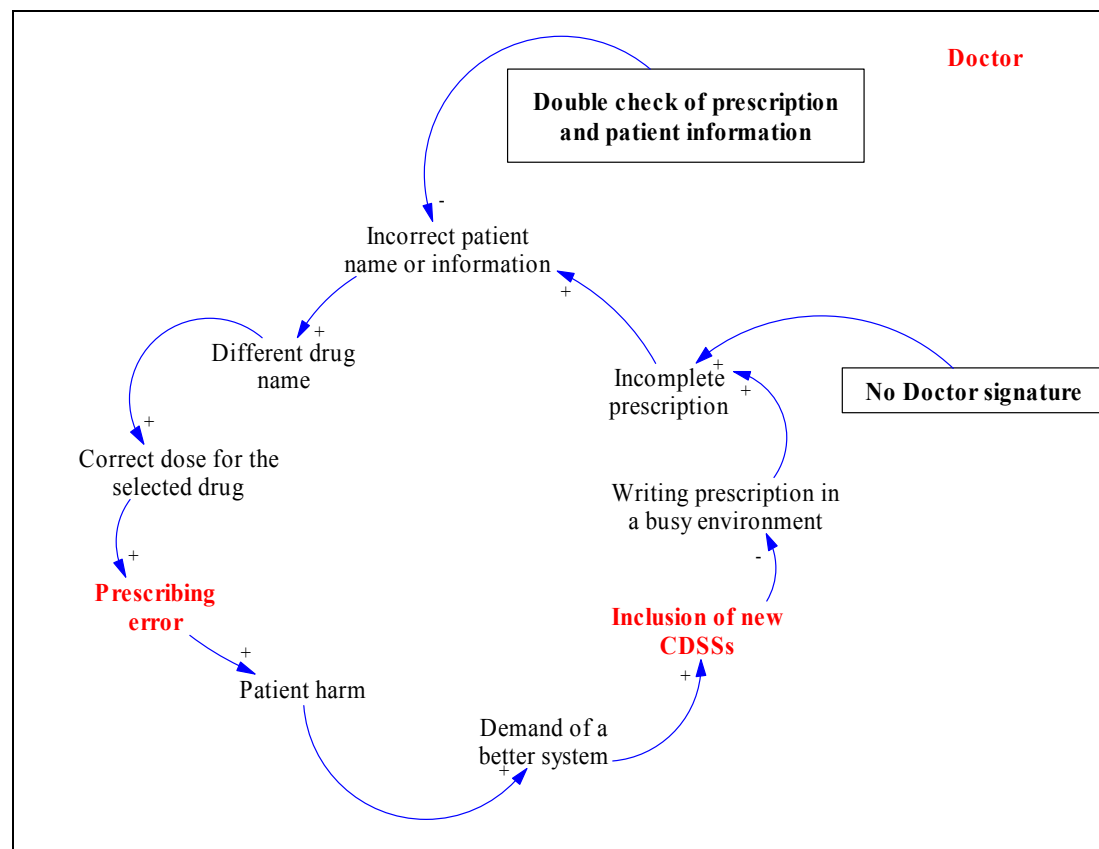


Figure 6.9: Causal Loop Diagram showing an example of prescribing error

6.6.1.2 Causal Loop Diagram of a dispensing error

The source of dispensing error can happen at the pharmacy ward while dispensing the medication. An error might have occurred in the form of the drug and the package, when the dispenser is preparing the drug without any supervision and lack of communication between doctor, pharmacist and dispenser; the problem increased the risk of a dispensing error. An inclusion of a unit dose could prevent the problem. The loop is shown in figure 6.10.

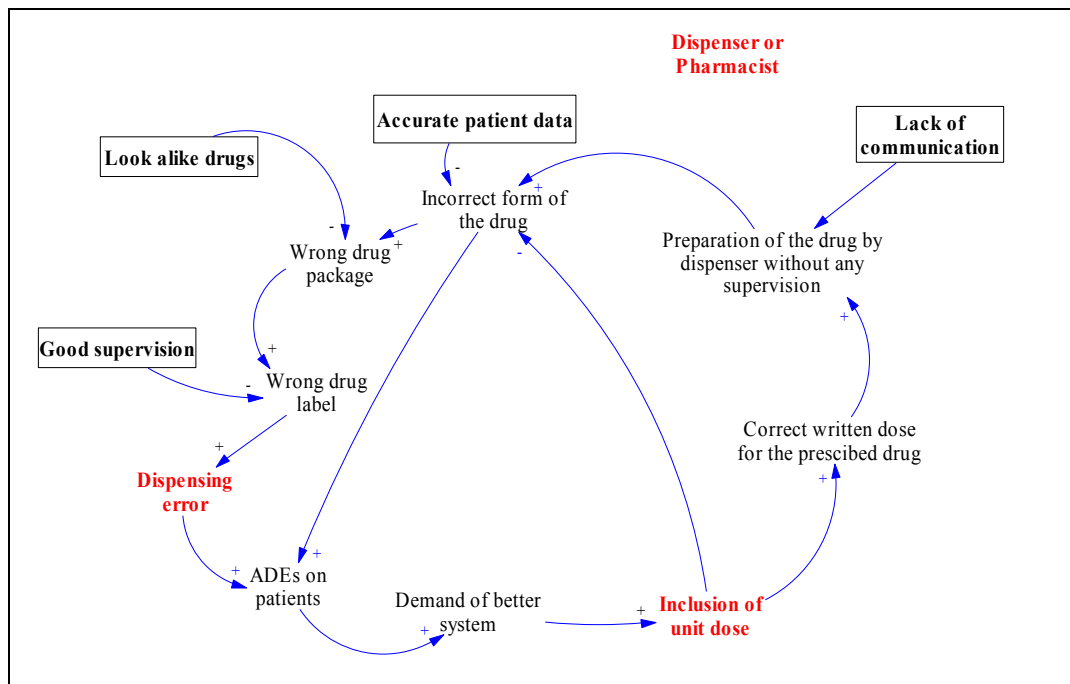


Figure 6.10: Causal Loop Diagram describing an example of dispensing error

6.6.1.3 Causal Loop Diagram of an administration error

An administration error can happen even if the drug is correctly prescribed and dispensed with the right patient name. While the nurse was preparing a drug in a disorganised work place, it influenced slips in attention, therefore the wrong diluent or calculation errors happened, and an overdose or the incorrect diluents was given to patients that ended up in side effects or harm. An addition of bar coding along with other CDSSs reduced the risk of patients with administration errors as it was proven with simulation models.

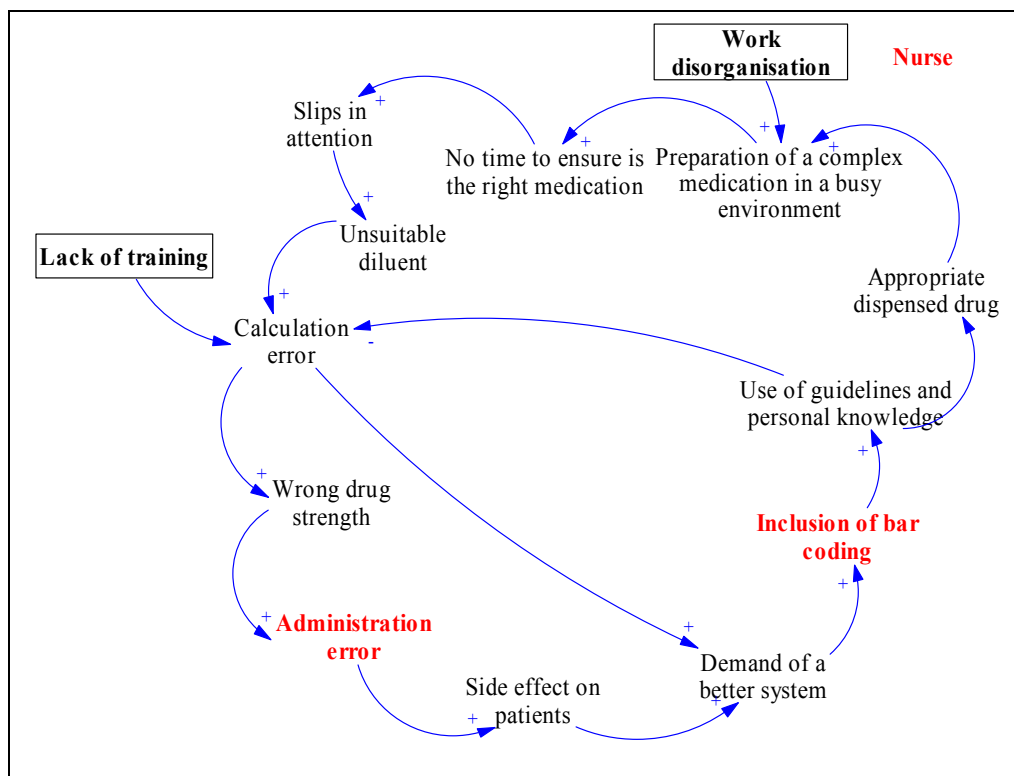


Figure 6.11: Causal Loop Diagram describing an example of administration error

6.6.2 Addition of paediatric CDS Components

Clinical pharmacists have recommended designing a specific model for paediatric patients that includes interventions to reduce the risk of medication errors in children. Almost all of the research into errors and their preventions has been carried out for adult patients, several factors have influenced the risk of errors in paediatrics because of the variation in body mass, that involve the right calculation of medication doses based on the patient age, weight or body surface area including the clinical condition of the patients [21] . An error is likely to happen in the preparation of the drug, because dosage formulation for children are prepared in small compounds to meet the need for small doses, there is a lack of guidelines and information on paediatric doses instructions [148]. Due to the lack of sources in paediatrics, we were unable to add specific variables for paediatrics.

We have applied the same model to Great Ormond Street hospital intensive care unit, with 941 patients admitted per week. The model resulted in a reduction of medication errors at each stage of the medication process. Prescribing errors have been reduced by 48%, dispensing errors by 90% and administration errors by 30%. The results are shown in figures 3 and 4 in the appendix section.

6.7 Chapter Summary

This chapter has described the steps followed in the evaluation to confirm the effectiveness of CDSSs in reducing medication errors. We have carried out three types of evaluations; the first one was to check the model consistency in order to validate the functions of the model in a hospital medication process. The results have confirmed that the model structure and features were adequate to use in another set of data or hospital setting, by adding the suitable components to each appropriate patients group, such as adding a warning on patient weight for a paediatric type of model.

The second evaluation was a qualitative one to verify the flow and signification of CLDs, the definitions of the CLDs variables were added and some of loops directions were changed based on colleagues suggestions.

The third method was a formative evaluation that included feedbacks from clinical pharmacists. The opinions evolved to divide the first CLD of the mismanagement of medication errors into three stages of medication process; prescribing, dispensing and administration.

Chapter 7

Discussion, Conclusion and Future work

7.1 Introduction

This thesis has discussed research to solve the problem of medication errors. Many approaches have been suggested to reduce medication errors in a hospital setting, almost all of them have focused on prescribing errors. Therefore the approach that we have used was system dynamics modelling of a hospital medication process; the aim of the model was to estimate and explore the impact of the frequency and consequence of patients harmed by drug mismanagement, when introducing several types of CDS components. The causal loops diagrams have considered some non-technological solutions to reduce medication errors; however, we could not imply those solutions into the model because of the inaccessibility of data.

The thesis investigated the sources of medication errors using a simple prescribing system and electronic prescribing with CDS components by looking at evidence based studies. We have also explored the effectiveness of these new information technologies in reducing the risk of patients harmed by medication errors. As information systems continue their development and gain an important place within all aspects of healthcare, the need of designing a new strategy to help medical professionals decrease the risk of medication errors.

We have identified at the start of the thesis in order to achieve effective results; the classification of medication errors, the processes involved in the management of medication in a hospital setting, and the causes of errors based on their classification. Those findings were categorized in the literature review and a systematic review. In addition, we have demonstrated the effect of CDSSs in reducing medication errors, as we have assessed each element of CDS specific to every step of the medication process using a system dynamics simulation modelling.

7.2 Achievements based on the aim and objectives of the research

The research was based on four main objectives that we have achieved effectively.

The first objective of the research was to identify settings, needs and elements to develop a simulation model of the drug safety incorporated with CDS elements. This part has been completed by covering findings of the literature review, starting by the classification of errors, definitions, their sources and causes by looking at Reason's human error models. Then, identification of needs and components of the model by looking at the suggested solutions to reduce errors which were technology based and

non-technology based, hence we could assess the missing part by mapping the findings into CLDs and design the simulation model.

The second objective was to carry out a systematic review along with meta-analysis which was completed successfully, as the results of the systematic review were very helpful to categorize the causes of errors in medication mismanagement with their definitions and to identify common errors in the papers.

The meta-analysis was useful in comparing the rate of medication errors by using a simple prescribing system with electronic prescribing that includes CDSSs. The variables of the model were collected from the meta-analysis results as it included the number of admissions, the number of selected inpatients, and the number of medication errors in each step. Evidently, more medication errors occurred when using a simple prescribing system and electronic systems with interventions reduced errors by 53%. However, we found out that some electronic prescribing systems with CDSSs increased the rate of medication errors by 24%. [111]

The third objective was to design and develop a simulation model to assess the impact of CDS components in medication errors. The model was designed based on system dynamics methodology for continuous flow models. The results were efficient, in particular when new components were introduced into the model to reduce the risk of patients with medication errors.

The fourth objective was to conduct CLDs and model evaluation based on medical professionals opinions; the evaluation of the CLDs and the simulation model was productive and confirmed the intended results of the research.

7.3 Research review and outcomes

Electronic prescribing was known to reduce errors, along with bar coding screening and automated dispensing that reduced dispensing and administration medication errors [143]. A number of studies have demonstrated the impact of e-prescribing and CDSSs in reducing medication errors in the USA, but only few studies evaluated the effectiveness of CDSSs in the UK.

A study in a US hospital has evaluated the capability of information technology to prevent ADEs using a simulation approach; we have used their estimated data of bar coding and unit dose in reducing medication errors in our evaluation model. It has suggested that information technology systems were a cost-effective means of

preventing ADEs in hospitals [132, 133]. It has been cited that CPOE along with CDSSs has been promoted as having great potential for reducing medication errors and ADEs and almost all of those studies have been conducted in hospital settings, where full description and training on the new system has been provided [149, 150].

Instructions for effective CDSSs have been proposed by Bates et al such as; speed for decision support to appear on the screen, provide information for the user at the time needed, alerts and guidelines should fit into the user's workflow, the designer should make it easy for the user as little things could make a difference, alternative suggestions should be available in case if the user ignores the first one, changing some of the features by using personal medical knowledge, accessibility of guidelines on the screen, providing space for extra data to be entered into the computer such as the weight of the patient, user's feedback is important in the design of a new system, and for maintaining and managing the knowledge-based system [151] .

Several studies in the UK evaluated the use and cost of e-prescribing, as it achieved a good improvement in time savings by replacing the handwritten prescriptions. However doctors did not pay attention to warnings because of the frequency, therefore there is a need for potential instructive CDSS [67, 152].

A qualitative evaluation has been carried out of an integrated e-prescribing and administration system designed to improve patient safety; the system has shown positive feedback by users as it was shown to reduce prescribing and drug administration errors. The prescriptions were more legible and the preparation for a drug conduct was well structured for nurses, also there was more attention to patient identification with bar coding and pharmacists detected and corrected errors before reaching the patients [143].

Our approach was to use the outcomes of evidence based studies on medication errors and the impact of information technology in reducing errors, in particular CDSSs that has not been implemented yet in the UK. We had constructive outcomes from performing a meta-analysis that showed us the difference between using a simple prescribing system and using a prescribing system that included CDSSs. As well as the impact of different CDSSs used in reducing prescribing, dispensing and drug administration errors.

The structure of the model has followed the medication process in a UK hospital setting, and the idea of the flow was based on Reason's Swiss Cheese model of human error or system failure; every step in the process has the potential for failure,

each layer represents a step in the medication management. The holes were considered as chances for the process to fail.

Starting with setting when the drug is ordered, therefore the number of patients with prescriptions was identified, from that point if the work environment was well organised it means there was no error that allowed the problem to pass through the hole in the next layer. As we can see in figure 7.1; from prescriber slice to dispenser slice the holes were not aligned, a dispenser slice was like a defence to the arrow by introducing an automated unit dose to the dispensing stage that blocked the hole and prevent the error from occurring. As we have previously explained in the literature review, if the layers are set up with all the holes lined up, where the problem has started from the start to the end for patient harm, the addition of CDS elements has given a defence to prevent medication errors. See figure 7.1.

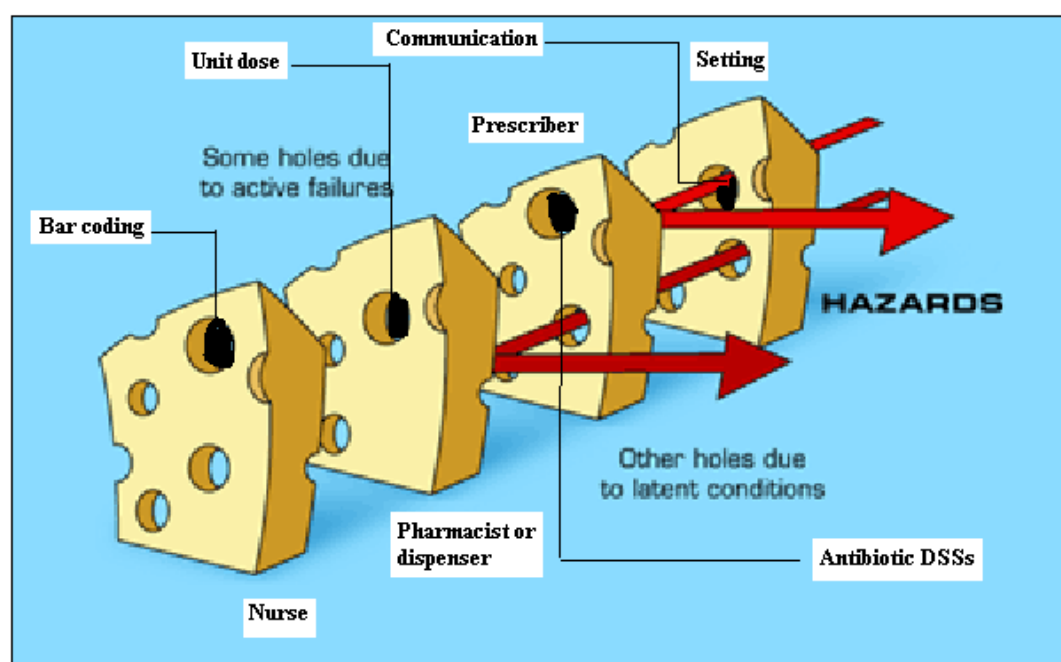


Figure 7.1: Swiss Cheese Model with CDS components

The simulation model results after the inclusion of CDS components has shown potential in medication safety by decreasing the rate of patients with prescribing, dispensing and administration drug errors, and has even reduced the rate of harmed patients with ADEs. However, the research did not have enough data about other

types of suggestions to reduce the risk of errors. Some of these approaches were described in the following points:

1. Improvement of medical professional's knowledge:

- Training and education of medical students on therapeutics, in particular prescribing was a concern in the UK, house officers should be taught more about drug doses and all sort of prescribers should be assessed on their prescribing competency [30]. As well as some risk factors that could interfere such as skills, lack of knowledge and experience [18, 153].
- The pharmacists play an important role in patient safety by improving the quality of prescribing, the Department of Health considered improvements since 2000 [154]. The NHS is providing more training to newly registered pharmacists by providing guidance and additional resources. Pharmacists have to work alongside other professionals and help patients get the most of their medicines.
- Training and guidelines to nurses for calculation errors and the use of measurement systems such as the infusion pumps [21].

2. Improvement of the hospital system:

- Standardisation of new systems, the drug charts should be the same between trusts that would reduce errors caused by the unfamiliarity of the charts [30]. This part was essential in the NHS Connecting for Health along with SNOMED CT terms that included medicines nomenclature, also the dictionary for medicines and devices which is an important tool in the medication process with CDSSs; hence doctors, pharmacists and nurses have to work closely with patients using the same language to avoid abbreviations and incomplete prescriptions, and inclusion of drug database such as the example of the French project in France see figure 3.4
- Healthcare professionals should learn to report medication errors, a good reporting system will allow collecting the source of errors or failure of a system [21].

3. Patient involvement:

- Patients should be involved in improving healthcare quality [155]

- They should be able to access their record, and discuss the appropriate treatment
- They should learn more from doctors and pharmacists and healthcare system about their disease, treatment and drug interactions and side effects

7.4 Summary of contributions

In addition to the research review of understanding the idea of medication errors, their sources, classification and solutions to reduce them. The thesis has contributed to the patient safety management of medication in conjunction with information technology in the following aspects:

- The ability to justify the term “medication errors” as a legitimate area for study, and to provide the general theory of errors and their classification, also models and examples to explain the term.
- The description of relevant background of current information technologies to reduce medication errors.
- A presentation of a comprehensive systematic review to explore the definitions, sources and causes of errors based on their classification, we have conducted a meta-analysis to compare the rate of medication errors by using a simple prescribing system that was either handwritten or a simple computer application, with computer system that included CDSSs. We have concluded that the effect of CDSSs in reducing medication errors and ADEs was 53%. In addition a sub-group analysis of the papers was performed to detect the difference between several CDSSs and the difference between paediatrics and adults hospital settings. We found out that a paediatric prescribing system was the most competent and reduced the rate of medication errors by 76%.
- The drug safety model has looked at the extent of the impact of CDS elements in reducing medication errors. The model started with CLDs that illustrated the general theory of errors. The components of the system dynamic model has conformed to existing standards of UK hospital inpatients settings, it should be incorporated with current e-prescribing with the same nomenclature of SNOMED CT and the dictionary of medicines and devices.

7.5 Limitations of the research and possible suggestions

The work carried out presents some weaknesses; some actions were suggested to rectify those downsides.

- Lack of literature review on the rate of medication errors in UK hospitals, it was difficult to do an observational study to check doctors and nurses on their medication management skills; this point could be corrected by conducting an observational study in a of London hospital in order to collect real world data to use in the model.
- Few studies in the UK have evaluated the impact of e-prescribing with CDSSs. Therefore, there is a need to do more evaluation studies to assess the effectiveness of e-prescribing and the performance of users, also the involvement of patients in the delivery of better eHealthcare.
- We could have designed a model specific for paediatric patients, but unfortunately we did not have available data to design it. For the reason that CDSSs used in prescribing a drug to children could be different than that for adults.
- A systematic review was published recently in October 2008 [156], that evaluated the effect of electronic prescribing which was similar to the research meta-analysis but we were looking at diverse outcomes such as types of CDSSs involved in medication errors and the basis of the sub-groups selection.

7.6 Opportunities for further research

The research conducted covers a wide range of areas. There are several prospect opportunities to consider which are suggested below:

Directions for the current project:

- Observational study in a London hospital in order to assess doctors, pharmacists or nurses conducting the prescribing process as a randomised control study in order to improve the drug safety model.
- Carrying out questionnaires and interviews with the range of staff involved in medication management by the suggesting the research solutions.

- Review of the IT division within the hospital to determine how closely it matches national standards and level of availability as expected under the English NPFIT. Key issues will be the degree of integration between systems in different areas of the hospital and use by relevant staff. Also consideration of CDSSs and their integration with EPR. This step defines the operating IT environment for developing a drug safety system.
- Estimation of the cost effectiveness of installing a new system and also an evaluation of the cost of e-prescribing in the UK.
- Development of a drug safety system based on the results of the observational study and feedback of healthcare professionals using a system dynamic modelling approach as an initial step for the program.

Other opportunities:

- Conducting individual research for each step of the medication process such as looking at concerns with the prescribing step with doctors, dispensing stage with pharmacists and dispensers and the drug administration step with nurses and patients.
- Selection of a specific group of patients such as paediatrics, elderly patients or patients with long term and complex treatment. Other research could be carried out on errors on medications that are at high risk of errors, or by choosing a particular type of disease.

7.7 Chapter Summary

This chapter has discussed the findings of the research, starting with the thesis achievements based on objectives. The outcomes of the research have been studied such as the model structure that followed the initial idea of Reason's system failure and the medication process in the UK hospital setting, the results of the drug safety simulation model that inserted the CDS component in every step of the process. Also suggestion of solutions for an effective new prescribing system that includes technological and theoretical CDSSs. Finally, we concluded with summary of contributions and opportunities for future work.

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Appendixes:

Table 1. Main reports by health organisations.

Name of the organisations	Reports by the organisations
• World health organization • Medical defense union • Medical protection society • The institute of medicine • European commission • Department of Health	• The importance of medication errors and the role of the pharmacist (2005) • Claims on medication errors (2004) • Medication errors are common cause of patient safety (2005) • A response to the health commission report on medication errors (2006) • Claims on medication errors (2004) • Medication errors in acute trusts (2006) • “To error is human” report (1999) • Five years after error is human report (2005) • Preventing medication errors (2006) • French electronic medical file (2004) • Building a safer NHS for patients; improving medication safety (2004) • Delivering 21st century IT support for the NHS; National strategic programme (2002) • The prevention of intrathecal

Table 2: Group of drugs that can be at high risk of errors. (NHS report)

Drugs	Risk of error
1. Drugs in anaesthetic practice: Midazolam and suxamethonium (short acting muscle relaxant) 2. Anticoagulants: Warfarin (can be adjusted for each patient from 1 to 5 mg) 3. Cytotoxic drugs: These drugs are used to treat cancer chemotherapeutically. Carboplatin it is a chemotherapy drug for breast cancer 4. Opiate analgesics: Used for severe pain, such as morphine (8 to 20mg every four hours orally) There are many other drugs that are at risk of errors such as: intravenous infusion, potassium chloride which is for the deficiency of potassium in the blood called hypokalaemia a fast administration of it can cause cardiac arrest, methotrexate which can block the metabolism of the cell used for cancer treatment and for rheumatoid	1. Packaging and ampoule size of both drugs are identical. (difficult breathing) 2. Sometimes doctors prescribe warfarin and the patient is already taking over the counter medicines such as anti-inflammatory drugs, that can lead to haemorrhage and death 3. Errors are due to complex calculations of the drug. For example Carboplatin was prescribed based on renal function, and the body weight. Wrong calculation results on renal failure 4. Errors happened usually in overdose, for example high dose was given to the wrong patient, and died from pneumonia

Studies included in the systematic review:

Table 3. Prescribing errors

Reference	Year and country	Study duration	Study location	Type of study	Rate of errors or findings
Lesar et al (1990)	1990 (USA)	1 year	Tertiary care teaching hospital New York	Reported errors from doctors	905/289411 orders
Dean et al (2002)	2002 (UK)	4 weeks	Teaching hospital (Ward pharmacy service)	Hand writing medication orders	135/36200 medication orders (each week)
Lesar et al (1997)	1994-1995 (USA)	1 year	Tertiary care teaching hospital	Prescribing errors detected by pharmacists	3.99/1000 medication order
Dean et al (2002)	1999 (UK)	2 months	Teaching hospital	Errors reporting by doctors	88 serious prescribing errors
Dean et al (2007)	2005 (UK)	4 months	London teaching trust	Recording of prescribing errors by pharmacists, examination of medication incidents	474/4995 medication orders
Mack et al (2000)	1999 (UK)	8 weeks	British Epilepsy Association	Patients responses to BEA on carbamazepine dosage errors	3/30 prescribed drugs
Lesar et al (1997)	1987-1995 (USA)	9 years	Teaching hospital in	Prescribing errors detected	11186 prescribing errors

			NY	by pharmacists	
Rubin et al (2005)	2002 (UK)	2 weeks	10 general practices in the North East of England	Anonymous self-report	397/940 prescriptions
Kozer et al (2004)	2001-2002 (Canada)	9 months	Emergency department in Tertiary pediatric hospital	Observational study on pediatric resuscitation in emergency depart	9 dosing errors orders/125 orders
Stheneur et al (2006)	2006 (France)	2 months	9 pediatric units in teaching hospitals	Observational study of medical staff	21 prescribing errors
Dean et al (2000)	(UK)	Not mentioned	Doctors working in London hospitals	Develop a definition of prescribing errors	A general definition of prescribing error has been identified
Ghaleb and Wong (2005)	UK	Not mentioned	Not specified	A general view of medication errors in children	Suggestions to reduce MEs in children
Allan and Barker (1990)	(USA)	Not applicable	Not applicable	A view of medication error research by observational studies	The use of new techniques to identify errors
Ghaleb et al (2006)	UK	Not applicable	Not applicable	A systematic review of medication	Methods for detecting medication errors

Manasse (1989)	(USA)	Not applicable	Not applicable	errors A general view of medication use	Solutions of drug misadventure problem
Morimoto et al (2004)	USA	Not applicable	Not applicable	Detection and classification of medication errors	Methods for detecting medication errors
Marinker et al (2003)	UK	Not applicable	Not applicable	Medicine and practice	Problems in compliance and concordance with patients

Table 4: Dispensing errors

References	Year and country	Study duration	Study location	Type of study	Rate of errors
Flynn et al (2003)	2000-2001 (USA)	10 months	50 pharmacies in 6 cities of USA	Detection of dispensing errors by observational study	77 errors per 4481 prescription
Bond et al (2001)	1998 (USA)	10 months	7298 Texas pharmacists	Assessment of pharmacists in dispensing errors	793 pharmacists out of 535 reported that there is at least one patient a week at risk of error
Mack et al (2000)	1999 (UK)	8 weeks	British Epilepsy Association	Patients responses to BEA on carbamazepine dosage errors	17/30 dispensing errors

Table 5: Administration errors

References	Year and country	Study duration	Study location	Type of study	Rate of errors
O'Hare et al (1995)	1995 (Belfast)	4 weeks	Royal Belfast Hospital for Sick Children	Observational study of nurses	291 errors in 168 observed doses
Taxis and Barber (2003)	1999 (UK)	7 months	10 wards in a teaching and non-teaching hospitals	Observational study of nurses	249/430 IV drug doses
Dean and Barber (2001)	1998 (UK)	6 months	UK teaching hospital	Observational study of nurses	257 administration errors
Stheneur et al (2006)	2006 (France)	2 months	9 pediatric units in teaching hospitals	Observational study of medical staff	45 administration errors
Flynn et al (2002)	1997	Not mentioned	36 hospitals in Colorado and Georgia	Observational study	300 pharmacists made errors on 2556 doses
Wolf et al (2006)	1999-2003 (USA)	4 years	La Salle university school of nursing	Retrospective study; voluntary report of errors by student nurses	1305 errors and 2 errors only resulted in patient harm
Cousins et al (2005)	2001-2002 UK France Germany	1 year	6 hospitals	Prospective observational study of IV medication errors	171/534 administred drugs

Table 6: Electronic systems and medication errors

References	Year and country	Study duration	Study location	Type of study	Rate of errors/results
Koppel et al (2005)	2002 (USA)	2 years	Tertiary-care teaching hospital	Qualitative and quantitative study of medical staff using CPOE	22 types of medication errors risks
Shulman et al (2005)	2001 (UK)	70 weeks	2 Tertiary-care hospitals (UCL)	Prospective study; chart review and assessment by pharmacists	117/2429 prescription errors
Horksy et al (2005)	2005 (USA)	Not mentioned	New York-Presbyterian hospital; intensive care unit	Visual and cognitive evaluation of the order screen of CPOE	Over dose error of Potassium Chloride
Han et al (2005)	2003 (USA)	18 months	Tertiary-care children hospital	Analysis of clinical and mortality data of CPOE implementation	75 dead children/ 1942 examined children
C.J.Macdonald (2006)	2005 (USA)	Not mentioned	US large hospital	Spontaneous reporting	Bar coding error with CPOE
Walsh et al (2006)	2002 (USA)	3 to 12 months	Teaching hospital in Boston	Retrospective study; recording and data collection of medication orders	104/6916 medication errors
Patterson et al	Not mentioned	1 week to 3	Veterans	Observational	5 negative side effects

(2002)	(USA)	13 months	Health Administration hospitals	study of nurses using bar coding	on bar coding/ 67 nurses
Del Beccaro et al (2006)	2002 (USA)	2 years	Tertiary care PICU	Retrospective study; verification of admission database	Non-significant difference of mortality between pre-implementation and post-implementation
Tamblyn et al (2006)	2003 (Canada)	20 months	28 primary cares in Quebec	Analysis of the usability of the drug management system	Re-prescribing was faster using electronic system
Van Der Meijden et al (2001)	2001 (Netherland)	3 years	Maastricht University Hospital	Measurement of EPR usability by medical staff using questionnaires and interviews	26/40 staff did not have enough experience using the computer
Kushniruk et al (2005)	Not mentioned (Canada)	Not mentioned	Canada	Experimental evaluation of handled prescription writing tool	27 errors/10 physicians using the system
Raschke et al (1998)	1997 (USA)	6 months	Teaching hospital in Phoenix	Evaluation of computer alert system to reduce ADEs	Alerts prevented patient's harm at 64 times per 1000 admissions
Ohsfeldt et al (2005)	2002 (USA)	Not mentioned	General medical/ surgical hospitals in Iowa	Evaluation of the financial and feasible impact of CPOE	The cost of the implementation, installation and annual maintenance was high
Galanter et al (2005)	Not mentioned (USA)	14 months	University of Illinois hospital and Medical centre	Evaluation of automated alerts and creatinine clearance	Alerts decreased contraindicated drugs from 89% to 47%
Berger and	Not applicable	Not		Advantages and	CPOE could increase

Kichak (2004)		applicable	Not applicable	disadvantages of CPOE	ADEs
Pace et al (2003)	USA	Not mentioned	Not mentioned	Design of database to locate anonymous and confidential reports of MEs by Applied Strategies for Improving Patient Safety (ASIPS)	The ASIPS resulted with 500 reports of MEs
Wilson and Sullivan (2004)	USA	Not mentioned	Vanderbilt University Medical Centre	Evaluation of infusion device to prevent IV medication errors	The system prevents errors that involved heparin drug
Fowlie et al (2000)	1998 (UK)	17 months	Orthopaedic ward in a British hospital	Evaluation of electronic prescribing and administration system and prescription assessment	Errors were decreased by the system but the rate is still significant
S E Andersen (2002)	2000 (Denmark)	9 months	Two general internal medicine wards in Copenhagen	Qualitative interview study on difficulties using a computerized drug record	The staff that used the system faced nine problems
Miller et al (2005)	Not applicable	Not applicable	Not applicable	Assessment of factors related to electronic prescribing	Improve the guidelines and evaluation of the system
Nelson et al (2005)	2001 (USA)	12 weeks	Two surgical units in tertiary care hospital	Analysis of the usability of real-time and bedside charting by nurses	Computerised medication charting is good to decrease MEs

Table 7. Studies included in the meta-analysis

Reference	Year , country and length of study	Location , number of beds and number of admissions	Rate of MEs per prescription or per drug entry in handwritten compared to computer system		Rate of other medication errors or deaths		Type and number of medical professionals	Type of intervention	Benefits	Problems	Suggestions
			Control/intervention		Control/intervention						
Bates (1998)	2002, (USA), 15 months, randomized trials	Brigham and Women's hospital, 726 beds, 2491 admissions in 26 weeks and 4220 in 39 weeks	Total: 127/12218 (per day) 889/85526 (per 7 days)	Total: 134/24539	Non-intercepted potential ADEs: 72/12218 Preventable ADEs: 55/12218	Non-intercepted potential ADEs: 32/24539 Preventable ADEs: 102/24539	Nurses and pharmacists	CPOE	- MEs decreased from 10.7 to 4.86 per admission - Reduction of the length of stay for patients	- Issue with multiple sedating drug orders - Some errors in ADEs	- Inclusion of decision support system - Guided drug algorithms - Drug-laboratory checking - Drug-patient characteristic - Information on reactions that occur in hospital with patients
K D Evans (1998)	1996, (UK), 3 weeks per study	John Radcliffe Hospital, ICU, 128 in control and 110 in intervention charts treated (assumed this is the number of patients entered in this study)	290/1184	372/1225			25 Doctors	Computer-assisted prescribing	- Computerised prescriptions were more complete than handwritten. - Legibility of the text - Full identification of the patient and any allergies	- Errors were in IV prescriptions - Drug duplicates entry - Longer to record the data and make an order	- Include a facility for IV prescriptions - Highlights of duplicate studies - A facility to make changes to the prescription without rewriting the full prescription - Including a decision support system - Improving the safety of drug therapy by flagging the interactions and incompatibilities of drugs

R S Evans (1998)	1995, (USA), 3 years (104 weeks in control and 52 weeks in intervention)	Private hospital in UTAH (520- bed), test in 12-bed ICU, total number of admitted patients (1136 in control and 545 in intervention), Number of patients selected for the study (766 in control and 398 in intervention)	785/3650	138/942	ADEs: 28/3650 Deaths 172/1136	ADEs: 4/942 Deaths 88/545	Doctors	A Computer- assisted manageme nt program for antibiotics	- 70 % reduction of ADEs - Less mismatch alerts - Less allergy and dosage alerts	- Insufficient information for specific recommendat ions for the doctors - Longer time to order drugs	
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Bates (1999)	1997, (USA), 9 weeks control and 9 weeks intervention	Brigham and Women's Hospital 700 beds, 379 patients in control and 475 patients in intervention	242/10070	50/14352	25/10070	18/14352	Doctors	CPOE	- Missed-dose error rate decreased by 64% after introducing the last version of CPOE	- Improper use of multiple routes options	- Include the guided dose algorithms for renal insufficiency - Add another algorithm for multiple sedating drugs - System strategies for missed-dose errors such as bar coding
Teich (2000)	1993, (USA), 26 weeks in control and 4 weeks intervention	Brigham and Women's Hospital 720 beds, assumed that number of admissions is the number of orders: 26354 in control and 64594 in intervention	5528/263549	363/64594			Doctors	CPOE used for Nizatidine and intravenous ranitidine (H2-blocker)	- List of suggested doses as decision support system tool and highlights of the recommended dose - Changes in ordering behavior - Decrease of the cost of prescribing - Easy access of the order entry from	- Implementation of warning to stop an action or a wrong entry - Dependency on computer use	- Consideration of the pre-implementation management and education - Consideration of the post-implementation

									any clinical work station - Computer interventions increase compliance with recommendations and guidelines at the right time		
Mullet (2001)	1999, (USA), 26 weeks for each period	Primary children medical centre (Utah), 232-beds, 1758 admissions (809 in control and 949 in intervention)	630/1262	500/1309	18/809 deaths	20/949 deaths	Clinician	Computerized pediatric anti-infective decision support system	- The rate of pharmacy drug doses errors decreased by 59 % - The number of orders per by anti-infective dose decreased by 11.5% - The cost benefit of the program	- Incorrect dosage calculation - No change in the rate of adverse drug events	- The system should be combined with a clinical physician order entry

Bizovi (2001)	2000, (USA), 4.3 weeks for each period	Emergency department in Portland, 1459 patients in control and 1056 in intervention	54/2326	11/1594	3/2326	1/2326	Prescriptions written by doctors and pharmacists	Computer-assisted prescription	-Significant reduction in errors without pharmacists clarification - Improvement of the pharmacy and emergency department	- Missing or incorrect information	
Chertow (CPOE versus DSSs) (2001)	1998, (USA), 7 weeks for each period	Brigham and Women's hospital, 720-beds, total of 19982 admission for 2 periods: 9941 patients in control and 7887 in intervention	6298/58160	2714/38399	142/7887 deaths	189/9941 deaths	Prescriptions written by doctors	Real-time computerized decision support system for prescribing drugs in patients with renal insufficiency	- Significant decrease in the frequency of severe renal dysfunction	- 49% of inappropriate orders for drug dosing - The intervention and control periods were not analogous	- Period of study and number of patients or prescriptions should be equal in control and intervention
Gandhi (2002)	1999-2000, (USA), 6 weeks per study	Brigham and Women's hospital, 720-bed, total 661 patients	159/1868	81/1868	81/1868 ADEs	81/1868 ADEs	Prescriptions written by doctors	Basic computerized prescribing	- Lower rate of rule violation errors	- No significant rate difference on ADE between control and intervention	- Prescribing system with decision support system, and include monitoring and communication tools

King (2003)	1999, (Canada), 3 years per study (312 weeks in total)	Children's hospital of Eastern Ontario, 6000 admissions	173/6674	120/5786	6/6674	1/5786	Doctors	CPOE in pediatrics patients	- 40% decrease in medication errors rate	- Limitation of reported errors	- Further evaluation of the benefit and cost
Tamblyn (basic computer versus comp with DSSs) (2003)	1998, Canada, 13 months (52 weeks), randomized	Data obtained randomly from primary care physicians in Quebec, 6276 in control and 6284 in intervention	909/6276	755/6284	470/6272 ADEs	396/6284 ADEs	Physicians	Computerized decision making support system	- Lower cost - 18 % decrease of inappropriate prescriptions after the introduction of CDS	- Limited alert system - Absence of patient data - Relocation of drugs prescribed by other doctors	- A better developed information technology system
Fontan (2004)	1999, France, 8 weeks,	Hopital Robert Debre, pediatric neurology ward, 511 prescription assumed 511 patients	518/589	419/3943	Administrative errors: 189/589	Administrative errors: 888/3943	Doctors	Computerized dispensing system	- The prescription and administrative errors decreased significantly		

Potts (2004)	2001, USA, 2 months in each study (8.7 weeks for each period)	Vanderbilt children hospital, 20-bed Pediatric critical care unit, 514 pediatric patients (268 in control and 246 in intervention)	2196/6803	100/7025	ADEs: 147/6803	ADEs: 88/7025	Medical staff	CPOE in pediatrics	- No reports of orders being entered on the wrong patient - No errors caused by the system - Communication between medical staff	- Incorrect or missing information by staff - Limited data on errors rate on pediatric orders	- Include more features on patient data (age, weight) - Incorporation of pediatric specific dosing and calculating guidelines -
Cordero (2004)	2002, USA, 1 year (52 weeks)	The Ohio state medical centre, neonatal ICU, 111 in control and 100 in intervention	2/31	0/28			Orders from nurses and doctors	CPOE in pediatrics	- Significant reduction in Gentamicin errors		

Shulman (2005)	2001, UK, 28 weeks in control and 74 weeks in intervention	Two tertiary care hospitals (UCLH), 22-bed ICU, number of prescriptions: 1036 (control) and 2429 (prevention)	69/1036	117/2429	Omission error: 22/1036 Incorrect route: 5/1036	Omission error: 1/2429 Incorrect route: 8/2429	Charts review and assessment by pharmacists	CPOE	- The system reduced error in dose, units and frequency	- Lack of features related with drugs with variable doses - Prescribers prescribe quickly with computers - No doctor signature in the CPOE system, therefore nurses administered medication without a valid doctor order - Different types of errors occur with CPOE	- The CPOE should include more decision support system -
Gandhi (2005)	1997, USA, 6 months, random (26 weeks)	4 adult primary care practices in Boston, 1202 patients	141/940 prescribing: 103/940	64/939 Prescribing: 40/939	ADEs: 38/940	ADEs: 24/939	Physicians	Computerized prescribing	- The basic computerized prescribing system reduced only few errors, therefore there were not a significant difference	- Antibiotics and nonsteroidal anti-inflammatory drugs were not reduced by basic computerized prescribing - Errors in	- Including more decision support system into the computerized prescribing

									between handwritten and computer prescription	rule violation and missing route	
Peterson (2005)	2002, USA, 8 months (35 weeks)	Brigham's and Women hospital in Boston, 720-bed, 1925 patients in control and 1793 in intervention	195/3908	99/3525			Physicians	CPOE and evaluation of psychotropic medication orders	- Reduction of dosing errors - Benefit of the guidelines on renal impairment	- Doctors were not willing to accept some dosing guidelines - No verification of the actual administration of the medication order	- Provision of guidance and expert advice at the point of decision making
Oliven (2005)	2004, Israel, 26 weeks for each study	Bnai-Zion medical center, 44-bed, 641 patients in control and 709 patients in intervention	622/4365	220/4743	Drug-laboratory interactions: 320/4365	Drug-laboratory interactions: 128/4743	Doctors	Online surveillance of computer drug order entry (CDOE)	- Elimination of potential drug interactions	- Some errors were associated with drug-laboratory interaction	- Combining the system with drug-laboratory alert system

Rudman (web-based reporting) (2005)	2003, USA, 6 years (1994-2000) control and 1 year (2003) intervention	University of Mississippi medical center, 25713 patients in control and 26490 in intervention per year	Rate of reported errors: 416/25713	Rate of reported errors: 959/26490	ADEs: 118/25713	ADEs: 103/26490	Doctors, nurses and pharmacists	Web based reporting system	- Easy to report errors using a web-based system		
Feldstein (2006)	2002-2003, USA, 12 months	15 primary care clinic in Boston, 9910 patients	3294/10000	2804/10000			172 physicians, 27 nurse practitioners and 37 physician assistants	EPR alerts in Warfarin	- The implementation of the alerts reduced errors by 15 % - Reduction of the frequency of coprescribing interacting medications	- Academic detailing did not improve the effectiveness of the alerts	- A good alert should provide the just in time warnings, it is the best tool to improve prescribing - Improvement of medication interaction alerts in outpatients
Colpaert (2006)	2004, USA, 5 weeks	Tertiary care hospital, 22-bed, first paper on moderate CDSS in ICU, 80 patient-days	331/1224	44/1286	ADEs: 48/1224	ADEs: 21/1286	Doctors	CPOE in ICU	- The system decreased serious errors by 67 %	- Double prescription occurred by the system - Complexity of medication prescriptions that increased the occurrence of MEs	- To evaluate a system, it is better to have a standardized way of error classification and detection

Donyai et al (2007)	2004, UK, 4 Weeks	28-bed General surgery ward in London Hospital	94/2450	48/2353				Electronic prescribing and the quality of prescribing	- Order entry decreased prescribing error by 1.8%	- New error type such as selection of new product or dose type	Further work is needed to evaluate different types of prescribing systems
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Table 8: Number of admissions and medication errors for simple system

References	Rate of admissions per week	Total rate of MEs/prescription or drug entry per week	Rate of ADEs/prescription per week (% errors)
Bates 1998	96	5/470 (0.43%) Writing: 2 (0.42%) Prescription: 0.6 (0.13%) Dispensing: 0.4 (0.02%) Administration: 2 (0.42%)	ADEs from MEs: 3/470 (11.5%) Preventable from MEs: 2/470 (0.42%)
K D Evans (1998)	43	97/395 (25%) Intravenous : 23/395 (6%) Intravenous infusion: 51/395 (13%) Other drugs: 23/395 (6%)	NA
R S Evans (1998)	Total number of admissions: 11 Number of patients for the study: 7.4	7.6/35 (22%)	0.3/35 (1%)
Bates (1999)	42	Total : 60.4/1119 Non-missed dose MEs: 27 (2.41%) Missed-dose MEs: 32 (3%) Non-intercepted serious MEs : 1.4 (0.13%)	ADEs: 3/1119 (0.3%) Preventable: 0.6 (0.05%) Non-preventable: 2 (0.2%)
Teich (2000)	10136	213/10136 (2.10%)	
Mullet (2001)	31	24/49 (49%)	
Bizovi (2001)	340	13/541 (2.4%)	
Chertow (2001)	Total number of admission: 2855 Patients for the study: 1420	900/8308	
Gandhi (2002)	110	26.5/331 (8%)	13.5/331 (4%)
King (2003)	19	1.10/43 Prescribing: 0.05 (0.11%) Dispensing: 0.019 (0.04 %) Administration: 0.87 (2%) Others: 0.16	0.04/43 (0.09%)

Tamblyn (2003)	112	16/112 (14.3%) Drug disease contraindication: 8.4/112 (7.5%) Drug-age contraindication: 6.7/112 (5.9%) Excessive duration of therapy: 8.9/112 (7.9%) Therapeutic duplication: 3.8/112 (3.4%) Drug interaction: 0.9/112 (0.8%)	Excessive duration of therapy: 8.9/112 (7.9%) Therapeutic duplication: 3.8/112 (3.4%) Drug interaction: 0.9/112 (0.8%)
Fontan (2004)	69	65/74 (88%) Administration errors: 18.85 (29%) Other errors: 46.2	
Potts (2004)	31	252.4/782 (32.3%) Illegible: 5.5/ 782 (0.70%) Missing information: 227.5/782 (29%) Other errors: 2.4	17/782 (2.17%) Inappropriate dose: 6/782 (0.8%) Wrong drug: 0.7/782 (0.09%)
Cordero (2004)	2.13	0.038/0.6 (6%)	
Shulman (2005)	37	2.5/37 (7%) Omission error: 0.8/37 (2%) Incorrect route: 0.2/37 (0.5%) Other errors: 1.5	
Gandhi (2005)	46	5.4/36.2 (15%) Prescribing error: 4/36.2 (11%) Other errors: 1.4	1.5/36.2 (4.2%)
Peterson (2005)	55	5.6/112 (5%)	
Rudman (2005)	82	1.5/82 (2%)	0.4/82 (0.5%)
Oliven (2005)	25	24/168 (14%) Drug-lab interactions: 12/168 (7.2%) Other errors: 12	
Feldstein (2006)	191	63/192 (33%)	
Walsh (2006)	9	2.2/177 (1.2 %)	
Colpaert (2006)	560	66/245 (27%)	10/245 (4%)
Donyai (2007)	28	23/612 (4%) Prescribing decision: 7 (1.1%) Writing medication order: 16 (2.7%)	

Table 9: Number of admissions and medication errors per week for computer system that includes CDSSs

References	Rate of admissions per week	Total rate of MEs/prescription or drug entry per week	Rate of ADEs/prescription per week (% errors)
Bates 1998	108	3.4/629 (0.54 %) Order entry: 1.6 (0.25%) Prescriptions: 0.13 (0.02 %) Dispensing: 0.18 (0.03%)	ADEs: 0.8/629 (0.13 %) Preventable ADEs: 2.6/629 (0.41%)
K D Evans (1998)	37	124/408 Intravenous fluids and entail: 44/408 (11%) Intravenous infusion: 5/408 (4 %) Other drugs: 27/408 (22 %)	NA
R S Evans (1998)	Total number of admissions: 10.5 Number of patients for the study: 7.7	2.7/18.2 (15 %)	0.08/18.2 (0.5 %)
Bates (1999)	53	Total : 75/1595 Non-missed dose MEs: 6 (0.4%) Missed-dose MEs: 69 (4.3%) Non-intercepted serious MEs: 0.2 (0.03%)	ADEs: 2/1595 (0.13%) Preventable ADEs: 0.2 (0.03%) Non-preventable ADEs: 1.8 (0.12%)
Teich (2000)	15022	84.5/15022 (0.6%)	
Mullet (2001)	37	19/50 (38%)	
Bizovi (2001)	246	3/371 (0.8%)	
Chertow (2001)	Total number of admission: 2854 Patients for the study: 1127	388/5486	
Gandhi (2002)	110	0/331 (0%)	13.5/331 (4%)
King (2003)	19	1/37 (2.7%) Prescribing: 0.03 (0.08%) Administration: 0.51 (1.37%) Others: 0.5	Not significant

Tamblyn (2003)	112.3	13.5/112.3 (12%) Drug disease contraindication: 7 (6.2%) Drug-age contraindication: 5 (4.5%)	Total: 10.5/112.3 Excessive duration of therapy: 6.5 (5.8%) Therapeutic duplication: 3.2 (2.8%) Drug interaction: 0.8 (0.7%)
Fontan (2003)	69	52.4/493 (11%) Administration errors: 43 (22.5%) Other drugs: 9.4	
Potts (2004)	28	11.5/807.5 (1.42%) Missing information: 1.4/807.5 (0.17%) Other errors: 10	10/807.5 (1.24%) Inappropriate dose: 6.8/807.5 (0.84%) Wrong drug: 0.11/807.5 (0.014%)
Cordero (2005)	2	No error	
Shulman (2005)	33	1.6/33 Incorrect route: 0.1/33 (6.25%) Other errors: 1.5	
Gandhi (2005)	46	2.5/36 (7%) Prescribing error: 1.6/36 (4.4%) Other errors: 0.9	1/36 (2.8%)
Peterson (2005)	51	3/101 (3%)	
Rudman (2005)	509	18/509 (3.5%)	2/509 (0.4%)
Oliven (2005)	27	8.5/183 (5%) Drug-lab interactions: 5/128 (4%) Other errors: 3.5	
Feldestein (2006)	191	54/192 (28%)	
Walsh (2006)	9	0.5/177 (0.3%)	
Colpaert (2006)	560	9/257 (3.5%)	4/257 (1.6%)
Donyai (2007)	31	12/588 (2%) Prescribing decision: 3.25 (0.6%) Writing medication order: 8.75 (1.5%)	

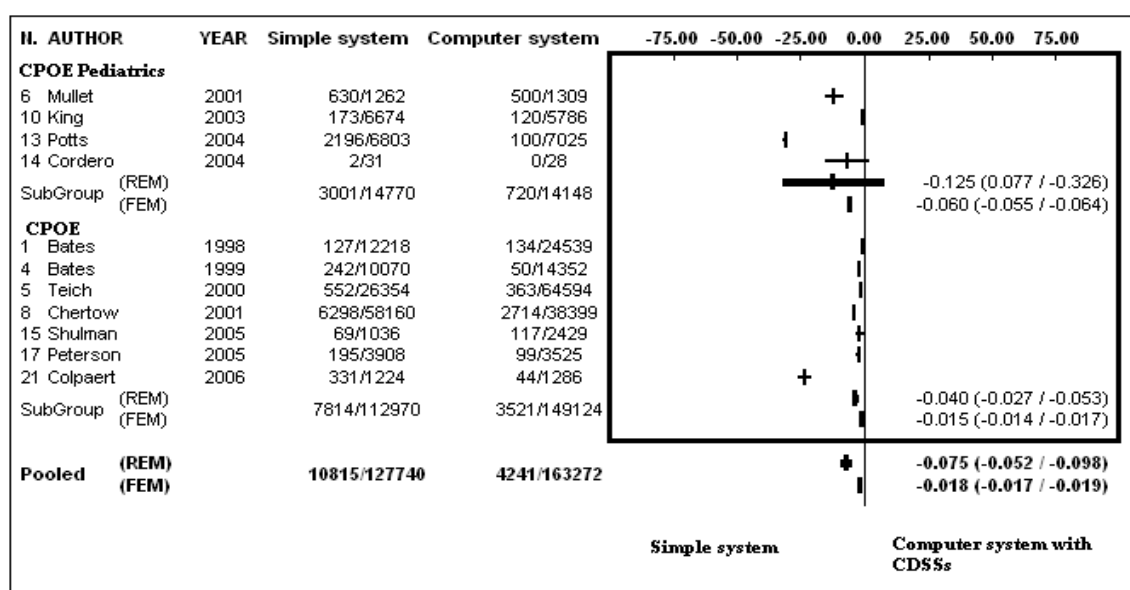


Figure 1: Standard plot of the sub-group analysis (Difference percentage)

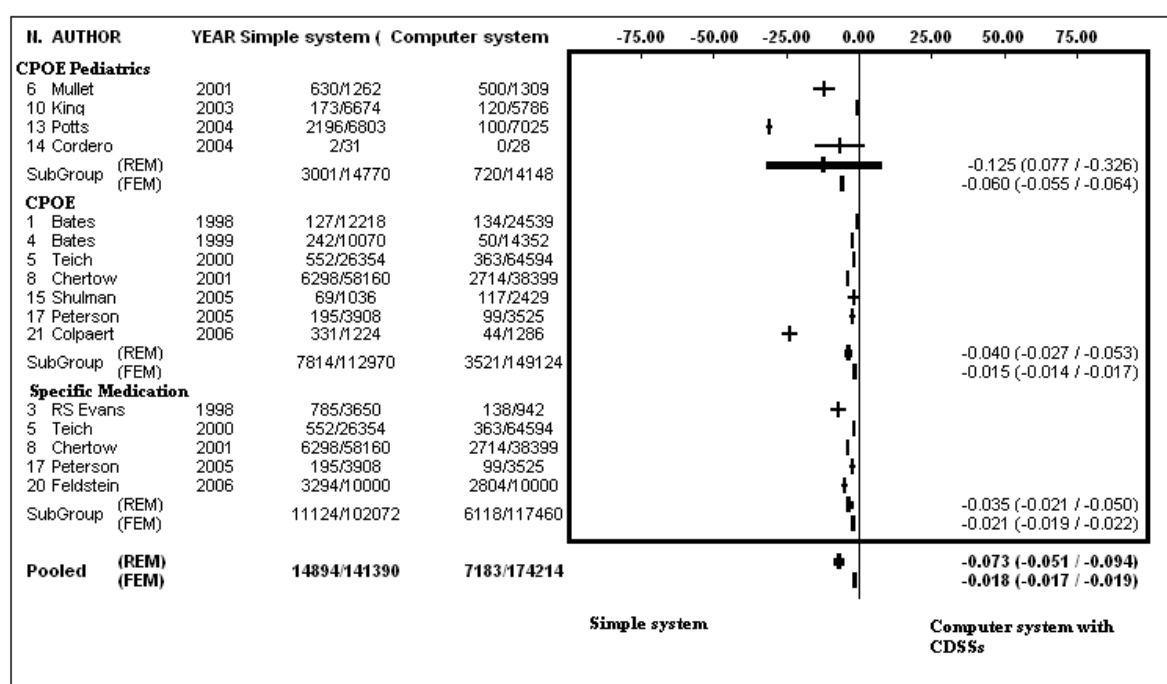


Figure 2: Standard plot of sub-group analysis 2 (difference percentage)

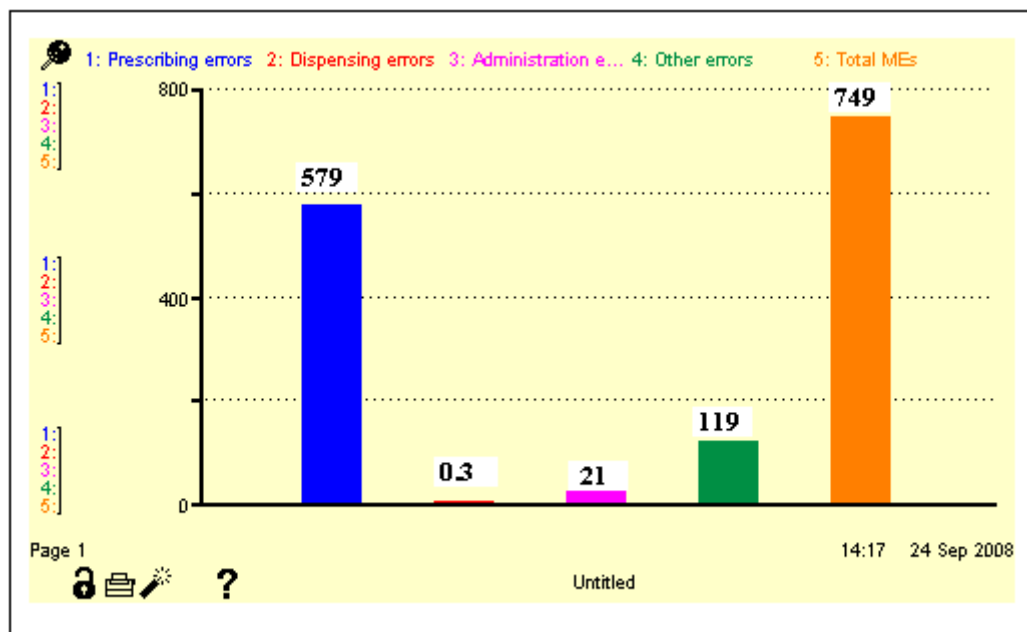


Figure 3: Great Ormond street Hospital results. Before interventions.

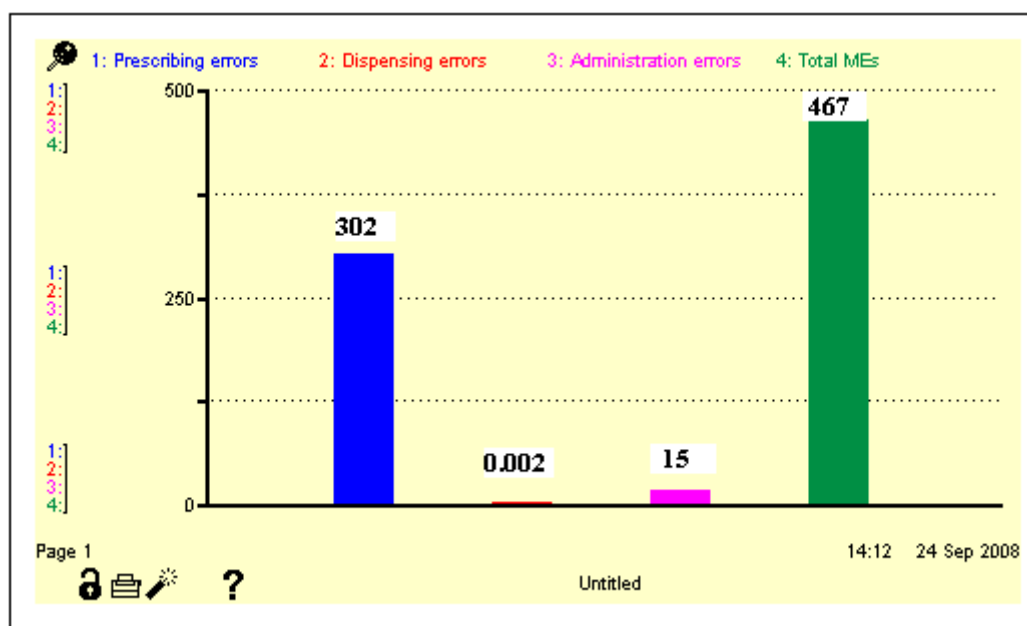


Figure 4: Great Ormond Street Hospital. After interventions

Table 10: Calculated data for patients with prescribing errors:

	Admission s	Number of patients	Number of prescription s	Number of medication errors	Number of Adverse Drug Events	Number of patients with medication errors	Number of patients with ADEs
Model 1 (Simple prescribing)	14930.13	13491.53	24056.8	1874.24	66.34	1051.1	37.2
Model 2 (Computer prescribing with CDSCs	20165	18435	27436.6	887	53.8	595	36.1
Model 3 (Intervention s on the simple system)	14930.13	13491.53	24056.8	1874.24	66.34	1051.1	37.2
Model 4 (Evaluation model of Boston hospital)	846.15	761.5	135779.8	105.78	3.74	60.92	2.3

1. Table 11: Principles and methods behind the Delphi Technique

Principles of the Delphi technique	Process of the Delphi technique
• Anonymity • Iteration • Controlled feedback • Statistical group response	Part 1: • Individuals give their opinions about the subject based on their knowledge and experience • The Delphi organisers give their opinion and select a group of experts to participate Part 2: • Participants rank their agreement with each statement in the questionnaire • The rankings are summarised and included in a repeat version of the questionnaire Part 3: • Participants rerank their agreement with each statement in the questionnaire and can change scores with a group • The rerankings are summarised and assessed for degree of consensus • If the result is obtained will end, if not the third part is repeated

Questions of the survey with Pharmacists:

- Do you think that the variables used for the Causal Loops Diagrams are correct?
- Are the variables in the right order?
- Are there additional variables that I can include in the loops?
- Is the order of the loops match with the UK prescribing process?
- What do you think if I will include practitioners?
- Is the structure of the model correct based on the UK prescribing system?
- Are there any additional CDSSs that I have missed in my model?
- What are the paediatric CDSSs?
- Do you have any data for paediatrics?
- Will you use the CDSSs added in the model?
- What do you think that it may be missing to improve the medication management systems overall?