A prospective hazard and improvement analysis of medication errors in a UK secondary care setting

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Executive summary

Background

It is estimated that around 10 per cent (900,000) of patients admitted to NHS hospitals every year are unintentionally harmed in some way, and that half of these incidents may be preventable. Medication errors are likely to be a key contributor to this total impact, though UK-specific research on the health impacts of medication errors is sparse. This means that it is difficult to target finite research budgets at prospective solutions aimed at reducing the impact of medication errors. Limited, and often contradictory, research results on the effectiveness of alternative interventions have been reported, and these are mainly US-based studies.

The aim of this study is to inform research priorities into reducing the impact of medication errors in secondary care through a prospective hazard and improvement analysis (PHIA) that identifies interventions with the greatest potential for the cost-effective reduction of the impact of medication errors on costs and health outcomes from the perspective of the NHS.

Definitions

The definition of medication errors specified in the current study “include prescriptions that have never been considered appropriate for the diagnosed condition, and preventable events that cause a deviation in the medication received by an inpatient from an appropriate prescription intended by the prescriber, excluding patient non-compliance.” The main impact of medication errors is the subsequent experience of adverse drug events (ADEs), which are defined as “an unwanted or harmful effect that occurs as a result of a medication error”.

Methods

The following paragraphs describe the main methodological elements of the PHIA, which include the modelling approach and the development of medication pathways; the systematic review; expert elicitation; model calibration; and the main model analysis.
A PHIA describes a series of error points within a defined system (in this study, the system is a secondary care hospital). At each error point, the PHIA describes the types of errors that can occur, the causes of the errors, and lists possible solutions. Detailed medication pathways are developed for the management of moderate and severe depression, which inform the specification of a simpler generic model structure that is populated with quantitative estimates to predict the cost and health impacts of medication errors in a secondary care setting. The effectiveness of potential interventions is estimated by describing the impact of the interventions on the baseline medication errors pathway.

A systematic review identifies a range of data informing the frequency of medication errors, though the definitions of error types and stages in medication pathways are not consistent, and not directly comparable. Data describing error detection rates, the health impacts of medication errors, and the effectiveness of potential interventions, are not well covered.

A two-day workshop was convened to elicit missing input parameter values from a group of experts, though the workshop was only partially successful, and many input parameters could not be estimated by the assembled group.

The model is calibrated to calculated values for preventable ADE rates by type and stage of origination in the medication pathway. Cost values are estimated for three interventions (computerised physician order entry systems; additional ward pharmacists; and bar coding systems at the administration stage of the medication pathway), including potential efficiency savings from the deployment of CPOE. Resource requirements for the additional treatment of ADEs, and monetary valuations of the health effects of ADEs on patients are also included in the analysis.

Estimates of the effectiveness of the three interventions are implicitly informed by the reviewed literature and workshops as no direct evidence of the impact of the interventions at different stages of the medication pathway are identified.

Results

The model analyses the potential cost-effectiveness of three interventions: CPOE; additional ward pharmacists; and bar coding systems at medication administration. Probability distributions describe a decrease in the range of the annual number of preventable ADEs that are predicted to occur in a 400-bed hospital from the base case.
(200 – 700 preventable ADEs per year) to 100 – 500 with a CPOE system or employing additional ward pharmacists; and 250 – 650 with a bar coding system in use at administration.

Including only the effects on direct health care costs, the net benefit calculations show that assumptions about the costs of the respective interventions, in particular CPOE, have a significant impact on the predicted results. The net benefits over a 5 year time horizon for CPOE are between £0 and £5 million if the low intervention costs are assumed, and between -£8 and -£3 million in the high cost scenario. If the monetary valuations of the health effects are included, the net benefits increase by an order of magnitude to a median value of around £30 million and an upper interquartile range approaching £50 million, regardless of implementation costs. The distribution of net benefits from employing additional ward pharmacists is slightly lower if minimum intervention costs are assumed and slightly higher is maximum intervention costs are assumed. Bar coding is predicted to produce a smaller range of potential net benefits.

Conclusions

The results show that there is very large uncertainty around the estimated net benefits of the interventions included in the analysis, which is due to uncertainty in the rate of medication errors as well as around the effectiveness of the interventions. Much of this uncertainty is due to the heterogeneity in the medication errors literature and the need to incorporate data based on the US health care system. Few UK studies were identified, and most reported findings based on incident reports, which have been shown to identify only a fraction of the errors identified by observation or detection techniques.

The majority of the reviewed studies specified the number of medication errors occurring as the primary outcome measure. An assumption of similar extrapolated effects of medication errors, even if sub-divided into error type and stage of origination in the medication pathway, is a weak assumption. There are almost infinite types of medication errors, each of which will have different probabilities of detection prior to administration, of causing harm, and of causing different levels of severity of harm and these effects should inform decision makers. This may mean that interventions aimed at reducing the impact of medication errors cannot be definitively evaluated within the framework of a decision modelling approach, and that it is imperative that primary studies report rates of ADEs rather than just medication errors.
However, the objective of the PHIA was not to inform resource allocation decisions, but rather research allocation decisions. The broad-brush analysis presented in this report may inform research allocation decisions by identifying those interventions with the largest potential for reducing the impact of medication errors and providing net benefits to the health service. The analysis suggests that CPOE systems and the provision of additional ward pharmacists have a greater potential for net benefits than bar coding systems. The variation in the reported effectiveness of the few identified studies of medication error interventions, particularly in studies of CPOE, illustrates the need for extreme attention to detail in the development of interventions, but also in their evaluation and may justify the evaluation of more than one specification of evaluated interventions.

(Executive summary word count: 1,000)
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Glossary

ADE - adverse drug event
ADM - automated dispensing machine
ADR - adverse drug reaction
AHRQ - Agency for Healthcare Research and Quality (USA)
CABG – coronary artery bypass graft
CI - confidence interval
CMAR - computerised medication administration record
CPOE - computerised physician order entry
DRG - diagnosis-related group
DSS – decision support system
FDA - Food and Drug Administration (USA)
GP - general practitioner
ICU - intensive care unit
ITU – intensive therapy unit
JCAHO - Joint Commission on Accreditation of Healthcare Organisations (USA)
LAN - local area network
LoS - length of stay
MCA - Medical Control Agency (UK)
NCC MERP - National Coordinating Council for Medication Error Reporting and Prevention
NHS - National Health Service (UK)
NHSLA - NHS Litigation Authority (UK)
NICE - National Institute for Clinical Excellence (UK)
OAE - opportunity for administration error
PCICU - paediatric cardiology intensive care unit
PCW - paediatric cardiology ward
PHA - prospective hazard analysis
PHIA - prospective hazard and improvement analysis
PPP - purchasing power parity
PRA - probabilistic risk assessment
QALY - quality adjusted life year
RCA - root cause analysis
RCT - randomised controlled trial
RFID - radio frequency identification
RHH - Royal Hallamshire Hospital (Sheffield, UK)
RR - relative risk
SSRI – selective serotonin reuptake inhibitor
WHO - World Health Organisation
WTP - willing(ness) to pay
Chapter 1 Introduction

1.1 Background

It is estimated that around 10 per cent of patients (900,000) admitted to NHS hospitals every year are unintentionally harmed in some way, and that half of these incidents may be preventable. Medication errors are likely to be a significant contributor to the aggregate number of adverse events, though no reliable evidence of the direct impact of medication errors on health outcomes is currently available in the UK.

Primary and secondary research on medication errors, particularly from the US and from Australia, has identified safety critical points in the patient journey (particularly in hospitals), causes and potential solutions for reducing error rates. Although the patient journey models in the literature are mainly generic across hospitals rather than site specific (such as in ITU) they do provide a useful starting point for modelling out the patient journey from primary to secondary care. Much of the recent work on clinical guidelines in the UK has taken similar approaches to patient care flows across primary and secondary care to provide a basis for developing whole system models.

Understanding the causes of error gives some indication as to the possible options for solutions. Thus, for example, common causes of medication errors include:

- Hand written prescriptions that are difficult to read
- Incorrect selection of strength or drug dosage
- Medication packages that look alike
- Administration to the wrong patient

Lesar and colleagues were able to classify prescribing errors (with potential for causing an adverse drug event (ADE)) in such a way as to identify some important steps in the ‘prescribing pathway’ of a hospitalised patient, enabling some element of prediction to be made about the possible rates of error in patients who required particular classes of drugs. A review of the Australian literature also identified particular strategies that have been shown to reduce medication errors, from which the following solutions are suggested, though the evidence base for many of the strategies is of variable quality, mainly relating to US hospitals:

- Use of computerised prescribing with decision support systems
- Computerised adverse drug event alerts in electronic patient records
- Individual patient medication supply in hospitals
- Pharmacists working with clinical teams
- Information transfer between hospital and community settings
- Medication reconciliation practices.

One of the most useful syntheses of the evidence on patient safety practices is that published by the Agency for Healthcare Research and Quality (AHRQ) in late 2001\textsuperscript{6}. The AHRQ report covered all interventions whose application reduces the probability of adverse events resulting from exposure to the health care system across a range of diseases and procedures, including Computerised Order Entry Systems\textsuperscript{7}, the pharmacist’s role in preventing ADEs\textsuperscript{8}, computerised adverse drug event detection\textsuperscript{9}, and of the usefulness of high-risk drug protocols\textsuperscript{10}, that are relevant to reducing the impact of medication errors. The appraisal placed each of the reviewed interventions into one of five categories that reflected their impact and/or strength of evidence regarding their impact and effectiveness\textsuperscript{11}. Table 1.1 describes the five categories, and level of evidence of the included interventions aimed specifically at medication errors.

Table 1.1  
Levels of evidence identified for medication error interventions by the AHRQ Critical Analysis of Patient Safety Practices

<table>
<thead>
<tr>
<th>Level of evidence</th>
<th>Medication error interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Greatest strength of evidence</td>
<td>-</td>
</tr>
<tr>
<td>High strength of evidence</td>
<td>Computer monitoring for the detection of ADEs related to targeted classes (analgesics, KCl, antibiotics, heparin)</td>
</tr>
<tr>
<td>Medium strength of evidence</td>
<td>Computerised physician order entry (CPOE) and clinical decision support (CDSS)</td>
</tr>
<tr>
<td></td>
<td>Clinical pharmacist consultation services</td>
</tr>
<tr>
<td>Lower impact and/or strength of evidence</td>
<td>Automated medication dispensing devices</td>
</tr>
<tr>
<td></td>
<td>Bar coding</td>
</tr>
<tr>
<td></td>
<td>Unit-dosing distribution systems</td>
</tr>
<tr>
<td>Lowest impact and/or strength of evidence</td>
<td>-</td>
</tr>
</tbody>
</table>
It is clear that further evidence is required to inform the prioritisation of interventions aimed at reducing medication errors, particularly as the AHRQ review was undertaken from a US perspective and did not analyse the potential cost-effectiveness of the interventions, other than to categorise the ‘Implementation Cost/Complexity’ of the interventions as being low, medium, or high.

Ideally, alternative specifications of all potential interventions aimed at reducing medication errors would be evaluated as part of multi-centred randomised controlled trials (RCTs). This would be an expensive undertaking and there is a finite research budget, which means that priorities for research in this area must be identified.

1.2  Aim and objectives

The aim of the study is to inform the setting of priorities for research into interventions aimed at reducing the impact of medication errors on costs and health outcomes from the perspective of the NHS.

The objectives are to:

- undertake a prospective hazard and improvement analysis (PHIA) of potential interventions that identifies the range and likelihood of medication errors at different stages of the medication pathway

- describe the impact of interventions aimed at reducing incidence of medication errors as a function of their impact on the occurrence and detection of medication errors at different stages in the medication pathway

- undertake a systematic literature review of the incidence of medication errors and ADEs, and the effectiveness of interventions aimed at reducing medication errors, to inform the model

- use expert elicitation techniques to interpret and supplement the data derived from the literature review based on the views of experts from a range of relevant disciplines.

1.3  Analysis boundaries

The potential boundary for an evaluation of medication errors is very large, covering the full patient journey from initial contact with a general practitioner in primary care, through secondary care and beyond into nursing homes and other long-term institutions. However, the impact of most interventions is restricted to broad stages of the patient
journey, for example, interventions are generally defined within the primary care or secondary care setting. As separate models would need to be developed and populated to evaluate interventions in the primary and secondary care settings, it is considered feasible only to evaluate interventions in one of the two main settings. The analysis presented in this report is restricted to the secondary care sector, and medication pathways describing the route between the specification of a prescription order for an inpatient and the point at which a medication is administered to an inpatient. Secondary care is chosen due to the concentration of error frequency and intervention studies in this setting.

The definition of medication errors and ADEs is an important aspect informing the boundaries of the analysis. Medication errors have been defined by the US National Coordinating Council for Medication Error and Prevention as: “any preventable event that may cause or lead to inappropriate medication use or patient harm, while the medication is in the control of the health care professional, patient, or consumer”. Such events may be related to professional practice, health care products, procedures, and systems including: prescribing; order communication; product labelling, packaging and nomenclature; compounding; dispensing; distribution; administration; education; monitoring; and use”.

The definition of medication errors used in this study is:

“Medication errors include prescriptions that have never been considered appropriate for the diagnosed condition, and preventable events that cause a deviation in the medication received by an inpatient from an appropriate prescription intended by the prescriber, excluding patient non-compliance.”

This definition excludes what may be defined as errors outside of the medication process (e.g. misdiagnosis) and more subjective errors (e.g. the prescription of medications that have been prescribed for the diagnosed condition but that are now considered inappropriate due to the emergence of new interventions). The definition does include prescription orders that have never been considered appropriate for the diagnosed condition. Such errors may occur as a result of errors in the prescribers decision making, or due to an error translating the prescribers intentions onto a prescription.
The key assumption in the above definition is that the prescriber always intends to prescribe an appropriate medication. This assumption is not made because it is likely to be true, rather it puts a boundary around the type of errors considered in the model that excludes misjudgements in the diagnosis of patients, and the prescription of medications that have been prescribed for the diagnosed condition but that are now considered inappropriate due to the emergence of new interventions. Both of these instances may be defined as medication errors, though they are subject to greater degree of subjectivity in their identification than other errors that occur further down the medication pathway.

The main purpose of preventing medication errors is to avoid ADEs, which impact on costs to the health service, as well as potentially affecting the health of the patient. A wide range of definitions for ADEs is identified in the literature, a selection of which is presented:

An injury resulting from medical intervention related to a drug\textsuperscript{13}.

Injury caused by medical management resulting in prolonged hospitalisation or disability at discharge\textsuperscript{14}.

Unintended injury caused by medical management resulting in measurable disability or prolonged hospitalisation\textsuperscript{15}.

Any noxious and unintended effect of drug that occurs at doses used in humans for prophylaxis, diagnosis, or treatment\textsuperscript{16}.

Any illness resulting from diagnostic procedure or from any form of treatment\textsuperscript{17}.

It is apparent that some definitions of ADEs include events that occur as a result of the intended medication being administered, which are sometimes referred to as adverse drug reactions (ADRs), which have been defined by the World Health Organisation (WHO) as:

A response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function\textsuperscript{18}.

There is some disagreement as to the precise definition of an ADR, with the Medical Control Agency (MCA) in the UK including reactions that are known side effects of the drug and new previously unrecognised reactions, whilst the Food and Drug Administration (FDA) in the US consider an ADR that is unexpected in intensity or in kind.
as distinct from expected side effects. From the perspective of the current study, all medication side effects resulting from the administration of an intended medication are outside the boundaries of the PHIA as they are not due to medication errors. The Venn diagram presented in Figure 1 describes the relationship between medication errors and ADEs, identifying a subset of ADEs that occur as a result of medication errors, which has been referred to as preventable ADEs. The term preventable ADEs is used in the current analysis and is defined as:

“An unwanted or harmful effect that occurs as a result of a medication error”

Figure 1.1 Venn diagram of the relationship between medication errors and adverse drug events

1.4 Methodological framework

The framework for the prospective hazard and improvement analysis (PHIA) comprises the methods used to quantify the impact of potential interventions, which include decision modelling, a systematic literature review, and expert elicitation. The following sections describe the structure of the report in the context of setting out the rationale and general approaches behind the main elements of the PHIA: the modelling approach and the development of medication pathways; the systematic review; expert elicitation; model calibration; and the main model analysis.

1.4.1 The modelling approach

The PHIA is an intermediary stage in the evaluative process of new interventions aimed at reducing the impact of medication errors, which involves the development of pathways describing potential error points within a defined system. Possible detection points are
defined for each error point, and the sum of the error points and detection points can be combined to develop potential pathways through the system. This model structure can be implemented as a computerised model, to which quantitative estimates of the probabilities describing the likelihood of error, and of error detection, at different points within the system can be defined. The model can then be solved mathematically to estimate relevant outputs, such as the number of errors that remain undetected.

The modelling approach requires the synthesis of data from disparate sources, which requires consideration of the comparability of the data used to populate a model, though a key element of the modelling approach is the representation of the uncertainty in the model’s output. The main benefit of the modelling approach is that it allows for the estimation of full effects of interventions in the absence of primary research with the necessary sample size and follow-up period (i.e. identify significant differences in the occurrence of preventable ADEs).

The estimation of the proportion of errors that are identified at different stages in the pathway between error occurrence and the error reaching the patient informs the prospective importance of identifying errors at different stages. It also enables the prediction of the value of improving the detection rate at different points in the medication pathway in terms of prevented ADEs.

The process for defining the model structure that was based on the development of medication pathways is described in Chapter 2. Having defined the model structure, the subsequent stage involves the estimation of input parameters values that describe the likelihood of the represented events occurring (e.g. error frequencies and detection rates). A general hierarchy of data sources for the direct estimation of input parameters may be defined in which primary ‘patient-level’ data is the preferred data source, followed by secondary data, with expert opinion acting as a ‘back-up’. If experts are unable to provide reliable input parameter estimates, then the technique of calibration is sometimes used to populate a model. The application of these population sources and methods to the medication errors model is described in the following sections.

1.4.2 **Systematic literature review**

A systematic review of the literature covering medication error rates, preventable ADE rates, and interventions that may impact upon error rates is presented in Appendix 2. The purpose of the review is to inform the population of the medication errors model,
though the review is also presented as a standalone exercise. In some cases, papers that are excluded from the literature review are included in the modelling analysis, as they contain information that informs elements of the medication errors model that are not informed by any of the papers included in the literature review. The reasons for exclusion of the papers from the literature review are incorporated in their use in the model, for example, by the specification of wider ranges of uncertainty.

Initially it was envisaged that only an update of the recent AHRQ report would be undertaken\(^6\); however, it soon became apparent that this would not be sufficient, either in scope or method. The aims of the systematic review were firstly to identify medication error rates and secondly to assess the evidence on effectiveness of different interventions on medication error rates. The following review objectives address these aims.

**Error rates**

What medication error rates are reported for different settings?

What error rates are reported for different types of medication error?

What error rates are reported for different points on the medication pathway?

**Interventions**

What interventions have an effect on medication error rates in different settings?

What interventions have an effect on different types of medication errors?

What interventions have an effect on medication error rates at different points on the medication pathway?

Details of the search and review strategies are described in Appendix 2. It is worth mentioning that studies were not limited by country, type of setting/facility, type of health care professionals or patients involved, length of study, number of participants, though only English language papers were retrieved.

The review of error frequencies include disguised observational, undisguised observation, RCTs, controlled trials, cohort studies (prospective and retrospective), case controlled studies, case studies, surveys, record reviews, and audits. The selection criteria for intervention studies are concerned primarily with study designs that allowed confidence in being able to show the impact of the intervention was due to the intervention, i.e. the presence of controls. RCTs, controlled trials, cohort studies
(prospective and retrospective), case controlled studies, case studies were included, though simple before and after studies in one setting with no comparative group are excluded.

One of the main difficulties in this review is the very disparate nature of the evidence. The definitions of error types and stages in medication pathways are not consistent, in most cases they are not directly comparable, which may contribute to the considerable variation found between studies. The data are arranged in groupings that allow as much comparison as possible. Figure 1.2 describes the categorisation of the data, which combines studies by setting, study methods and type of medication error.

The error frequency papers that inform the medication errors model are described in Chapter 3, along with the methods used to synthesise data across studies. The review of studies evaluating the effectiveness of interventions does not directly inform the modelled analysis as the model describes separate error and detection points (as described in Chapter 2), for which separate estimates of effectiveness for the interventions are required. The intervention studies do not present such data and the results of the review of interventions inform the interpretation of the main analysis.

A separate stage of the model population process involves the estimation of the cost values attached to the interventions, and to the outcomes described in the model, i.e. cost savings and the value of the health benefits gained from avoiding preventable ADEs. The respective cost estimates are based on data extracted from the literature, though some additional assumptions and analyses are required to estimate the monetary value of the health benefits gained from avoiding ADEs. The full details of the costing methods are described in Chapter 4.
Figure 1.2 Categorisation of error frequency data derived from the systematic literature review

United Kingdom

Primary care

observation
- wrong drug
  - prescription
  - dispensing
  - administration

- wrong dose
  - prescription
  - dispensing
  - administration

- wrong route
  - prescription
  - dispensing
  - administration

- timing (freq/omission)
  - prescription
  - dispensing
  - administration

record review
- wrong drug
  - prescription
  - dispensing
  - administration

- wrong dose
  - prescription
  - dispensing
  - administration

- wrong route
  - prescription
  - dispensing
  - administration

- timing (freq/omission)
  - prescription
  - dispensing
  - administration

other
- wrong drug
  - prescription
  - dispensing
  - administration

- wrong dose
  - prescription
  - dispensing
  - administration

- wrong route
  - prescription
  - dispensing
  - administration

- timing (freq/omission)
  - prescription
  - dispensing
  - administration

Secondary care

observation
- wrong drug
  - prescription
  - dispensing
  - administration

- wrong dose
  - prescription
  - dispensing
  - administration

- wrong route
  - prescription
  - dispensing
  - administration

- timing (freq/omission)
  - prescription
  - dispensing
  - administration

record review
- wrong drug
  - prescription
  - dispensing
  - administration

- wrong dose
  - prescription
  - dispensing
  - administration

- wrong route
  - prescription
  - dispensing
  - administration

- timing (freq/omission)
  - prescription
  - dispensing
  - administration

other
- wrong drug
  - prescription
  - dispensing
  - administration

- wrong dose
  - prescription
  - dispensing
  - administration

- wrong route
  - prescription
  - dispensing
  - administration

- timing (freq/omission)
  - prescription
  - dispensing
  - administration

Primary care

observation
- wrong drug
  - prescription
  - dispensing
  - administration

- wrong dose
  - prescription
  - dispensing
  - administration

- wrong route
  - prescription
  - dispensing
  - administration

- timing (freq/omission)
  - prescription
  - dispensing
  - administration

record review
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- wrong route
  - prescription
  - dispensing
  - administration

- timing (freq/omission)
  - prescription
  - dispensing
  - administration

Secondary care

observation
- wrong drug
  - prescription
  - dispensing
  - administration

- wrong dose
  - prescription
  - dispensing
  - administration

- wrong route
  - prescription
  - dispensing
  - administration

- timing (freq/omission)
  - prescription
  - dispensing
  - administration

record review
- wrong drug
  - prescription
  - dispensing
  - administration

- wrong dose
  - prescription
  - dispensing
  - administration

- wrong route
  - prescription
  - dispensing
  - administration

- timing (freq/omission)
  - prescription
  - dispensing
  - administration

other
- wrong drug
  - prescription
  - dispensing
  - administration

- wrong dose
  - prescription
  - dispensing
  - administration

- wrong route
  - prescription
  - dispensing
  - administration

- timing (freq/omission)
  - prescription
  - dispensing
  - administration
1.4.3 Expert elicitation

As described in Chapter 3, the data extracted from the literature review does not inform the full range of input parameters included in the medication errors model. In such cases, it is common to use the knowledge of relevant experts to estimate uninformed parameters. The process of elicitation used in the current project was undertaken in the form of a two day workshop at which a facilitator provided an expert group of general practitioners, secondary care clinicians, a public health physician, pharmacists, a nurse, and human factors experts through a process by which the experts were asked to express prior knowledge in probabilistic form. The aim of the workshop was to estimate probability distributions that incorporate a point estimate for each parameter, as well as describing a range within which the true value for the parameter is likely to lie.

The workshop was split into two sections. The first section addressed error frequency and detection parameters, and the second section concentrated on the estimation of the effectiveness of alternative interventions. The outcomes from the workshop are described in detail in Chapter 5, which shows that the process was only partially successful as the experts found it very difficult to estimate values for both types of parameter.

The main difficulty in estimating values for the error frequency and detection rate parameters was for parameters for which the probabilities were assumed to be very small. The experts recognised that whilst the individual probabilities of error (per prescription) are small, the absolute impact of a small probability of individual error on the NHS is large. They found it difficult to differentiate between different types of errors and were only comfortable in estimating values for relatively large probabilities. In the section estimating intervention effectiveness, the participants felt unable to quantify the likely effectiveness of the interventions, preferring to specify areas in which an intervention may impact on medication errors.

1.4.4 Calibration

Preferably, model input parameters are estimated directly using primary or secondary data sources, and if not using values elicited from relevant experts. As noted above, data to populate the medication errors model are scarce, and there is great uncertainty around the values of many of the model’s input parameters. It is necessary, therefore, to
use a method of model estimation that calibrates the sum of the model's input parameters to observed values for some of the model's outputs.

Calibration is possible because the literature review identifies a range of data that enable the estimation of the rate of ADEs by the type of medication error that led to the ADE, and by the stage in the medication pathway at which the error was committed. Using the ranges defined in Chapter 3 for each of the model's input parameters the following process is undertaken to calibrate the model:

- a large number of sets of input parameter values are sampled from the defined uniform distributions (i.e. a value for every input parameter was sampled),

- each input parameter set is entered into the model, and the output parameters for which observed values are available are estimated,

- the predicted and observed estimates of the relevant model outputs are compared, and weights are estimated for every input parameter set reflecting the closeness of the predicted and observed values.

The main analysis of the medication errors model involves sampling from the same input parameter sets based on the estimated weights, i.e. sets with higher weights have a higher probability of being sampled. The calibration process is described in full in section 3.5, whilst the results of the model fitting are presented in Chapter 6, prior to the main results from the medication errors model.

1.4.5 Model analysis

The calibrated input parameter sets inform the model to the point at which a medication error reaches the patients (i.e. an unintended medication is administered), and has an ‘unwanted or harmful effect’ on a patient. The severity of the effect is not calibrated and neither are the cost effects. The analysis of the model estimates the frequency and cost of preventable ADEs using the following process:

- sample a larger number of the calibrated weight-based input parameter sets,

- for each input parameter set:

- sample probabilities describing the distribution of severities for each type of ADE,

- sample cost estimates for each severity of ADE
- solve the model to estimate the total number of ADEs by severity and the associated costs
- sample a set of relative risk (RR) estimates reflecting the impact of alternative interventions in reducing the frequency, or increasing the detection, of medication errors at different points in the medication pathway
- solve the model to estimate the total number of ADEs by severity and the associated costs with the sampled RRs applied to the relevant input parameter values.

This analysis produces linked estimates of each of the model outputs for the baseline (no intervention) scenario as well as for each of the interventions. In combination with the estimated costs of implementation and maintenance, the net benefits of each intervention are then estimated over a five and ten year time horizon. These analyses produce probability distributions describing the range of net benefits associated with each of the interventions.

The interpretation of the model’s results does not identify a point estimate for any of the model’s outputs due to the extreme uncertainty around all of these estimates; rather, the characteristics of the estimated probability distributions are described to provide an indication of the likely range within which the true effects of medication errors, and interventions aimed at reducing their impact, may lie.

1.5 Discussion

This chapter has provided a background and laid out the objectives for the PHIA that is described in this report. The boundaries for the analysis with respect to the stages of the patient journey that are assessed, and the definitions of medication errors and ADEs that are examined have also been specified. The summary of the methodological approach provides an outline of the remainder of the report, whilst the following chapter provides more detail on the development of the analytic framework, i.e. the structure of the decision model used to facilitate the explicit synthesis and analysis of data from disparate sources.
Chapter 2 The methodological framework

2.1 Introduction

This chapter describes the methodology for the prospective hazard and improvement analysis (PHIA) of medication errors. The aims include the assessment of the potential cost-effectiveness of interventions intended to reduce the incidence of medication errors, so the methodology should represent the full impact of such interventions on costs and health benefits. Preferably, data describing both the incremental costs and benefits would be collected alongside randomised controlled trials (RCTs) of the potential interventions. The systematic review of the medication errors literature identified no primary economic studies of potential improvement interventions. It is clear, therefore, that some form of modelling is required to synthesise data from disparate sources to estimate the cost-effectiveness of such interventions.

This chapter contains four main sections that provide the foundations to the modelling framework developed for the PHIA of medication errors. The first section describes the general decision modelling approach and how it fits within the context of the PHIA. The following section critiques previous approaches to estimating the cost-effectiveness of interventions aimed at reducing medication errors. The third section describes the process of expert elicitation to develop a series of medication pathways, which informed the model structure for the current analysis. The final section describes the structure of the medication errors model.

2.2 The need to model

Most primary studies of health care interventions require the extrapolation of observed results to estimate the lifetime effects of treatment, for example, the number of quality adjusted life years (QALYs) gained. Two stages of extrapolation may be required in a medication errors model. Firstly, the occurrence of medication errors should be extrapolated to estimate the incidence of adverse drug events (ADEs). Secondly, it may be necessary to describe the health impact of the ADEs, which will require extrapolation beyond the occurrence of the ADEs.

Another issue is around the transferability of the results of primary studies undertaken in a location outside the decision makers domain, to the patient population of interest to the decision maker, for example, how relevant are the results of an RCT undertaken in the US to the patient population in the UK? This issue is of particular relevance to
interventions aimed at reducing medication errors, as differences in medication pathways between countries, and even between hospitals within the same country, are likely to be even greater than differences in patient characteristics. The impact of geographical variation for a similarly defined intervention would preferably be informed by an adequately powered multi-centre clinical trial undertaken at different locations within the domain of the relevant decision maker, for example, across England and Wales. In the absence of such a trial, a model-based evaluation can be used to control for potential differences between alternative geographical locations.

Decision models describe the transition of entities through defined states to one or more endpoints. In the area of health care, decision models are generally used to describe the progression of patients (the entities) through different combination of health states related to a particular disease, for example, a breast cancer model may describe pathways between states describing alternative forms of cancer recurrence. The endpoint is normally death. Data are generally synthesised from disparate sources that describe different aspects of the modelled process, for example, a clinical trial may inform recurrence rates for breast cancer over the treatment period for an intervention of interest, but event rates following recurrence may be informed by different trials or observational datasets.

The entities in a generic model for the evaluation of medication error interventions would be medication orders that pass through a series of states that could affect whether the intended medication is given to the intended patient. The endpoint could be the point at which the impact of the administered medication is known. Data describing transition probabilities between states could be derived from a wide range of sources, including expert opinion and secondary data analyses. To evaluate the effectiveness of a medication error intervention, relevant transition probabilities would be altered to reflect the impact of an intervention, and the flow of medication orders would be re-evaluated.

A PHIA may be interpreted as a form of decision modelling. The hazard analysis component defines the relevant model structure by using a formal process involving informed participants to identify the points at which errors are most likely to occur. The improvement analysis involves the identification of potential solutions that address the error points. The estimation of the likelihood of errors occurring at each defined error point is not commonly undertaken (references?) though a process of quantification has been described under the term ‘probabilistic risk assessment’.
2.3  Review of previous approaches to modelling medication errors

Three studies were identified that have estimate the costs and benefits of interventions aimed at reducing errors\textsuperscript{20,21,22}, which are reviewed in the following sections.

2.3.1  Anderson et al, Evaluating the capability of information technology to prevent adverse drug events: a computer simulation approach\textsuperscript{20}

Anderson et al describe the development of a simulation model that predicts the number of ADEs, extra days of hospitalisation, and excess costs of hospitalisation that are attributable to medication errors occurring at different stages in the medication delivery system. The model is used to evaluate the impact of potential interventions at each stage of the medication process. The study involved the collection of primary data in a US hospital describing medication errors at the prescription, transcribing, dispensing, and administration stages. In total, 227 medication errors were identified from a sample of almost 7,000 drug orders. Each errors was categorised by severity – problem, significant, potentially serious, or potentially fatal.

The model structure describes the entry of medication orders onto the hospital information system (either directly by physicians or transcribed by ward clerks). Orders are then sent to a central pharmacy, where they are printed and checked by a pharmacist. Medications are then dispensed and transported to the ward, where they are administered by nurses.

Mean medication error rates and standard deviations are specified for the error rates at each of the four medication stages, based on the observed error data. It is not clear whether error severity varies by stage. The model assumes that orders are only liable to a single error, i.e. if a prescription error occurs then the order is not susceptible to further errors at the transcription, dispensing and administration stages. Two scenarios describing the occurrence of ADEs are defined. Firstly, it is assumed that 26% of the medication errors with the potential for serious toxic reactions or inadequate treatment would have resulted in ADEs if not detected and corrected. It is implied that serious toxic reactions incorporate potentially serious errors and inadequate treatment incorporates significant errors, which comprise 6% and 18% of all errors, respectively. Secondly, it is assumed that 8% of potentially serious or fatal errors would have resulted in ADEs. An estimate of an additional 2.2 additional days of hospitalisation per ADE, at a cost of
£2,595, is based on previous studies\textsuperscript{23,24}. It is implied that this cost is applied regardless of the severity of the potential error.

The model is analysed assuming no additional interventions; assuming separate interventions at each stage of the medication delivery system; and assuming the combination of interventions at all four stages. The interventions and their assumed effectiveness are described in Table 1. The combined intervention included the assumed error reductions at each stage of the process.

Table 2.1 Interventions modelled by Anderson et al at different stages of the medication delivery system and their assumed effectiveness\textsuperscript{20}.

<table>
<thead>
<tr>
<th>Medication stage</th>
<th>Intervention</th>
<th>Reduction in errors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prescription</td>
<td>Computer-based system providing dosing information at the time orders are written</td>
<td>20%</td>
</tr>
<tr>
<td>Transcription</td>
<td>Computerised Physician Order Entry</td>
<td>30%</td>
</tr>
<tr>
<td>Dispensing</td>
<td>Unit dosing system</td>
<td>80%</td>
</tr>
<tr>
<td>Administration</td>
<td>Bar coding</td>
<td>60%</td>
</tr>
</tbody>
</table>

The main results presented by Anderson are replicated in Table 2.2, which show the number of ADEs expected in the absence, and presence, of alternative interventions for the two ADE scenarios, and the cost savings due to the avoidance of ADEs. The cost savings are presented for a total of 195,392 drug orders, which represents the annual volume of orders in the hospital under consideration. Of the individually applied interventions, the use of CPOE at the transcription stage results in the largest reduction in ADE rates and associated costs.

An apparently counter-intuitive result is that more ADEs are predicted for the prescription stage intervention (computer-based system providing dosing information at the time orders are written), when the low estimate ADE scenario is analysed (8% of serious and fatal errors result in ADEs). This result must be due to a higher proportion of errors occurring at the later medication stages resulting in ADEs, as the 20% of errors that are prevented at the prescription stage are then susceptible to errors at the subsequent stages.
Table 2.2  ADE rates per 1,000 orders and total cost savings for a total of 195,392 drug orders by intervention

<table>
<thead>
<tr>
<th></th>
<th>Low ADE scenario</th>
<th>High ADE scenario</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Assumption: 8% serious/fatal error lead to ADEs</td>
<td>Assumption: 26% potential serious/inadequate treatment errors lead to ADEs</td>
</tr>
<tr>
<td>ADE rates</td>
<td>Costs ($000s)</td>
<td>ADE rates</td>
</tr>
<tr>
<td>Baseline</td>
<td>3.3</td>
<td>1652</td>
</tr>
<tr>
<td>Prescription intervention</td>
<td>3.4</td>
<td>1730</td>
</tr>
<tr>
<td>Transcription intervention</td>
<td>2.8</td>
<td>1439</td>
</tr>
<tr>
<td>Dispensing intervention</td>
<td>3.2</td>
<td>1601</td>
</tr>
<tr>
<td>Administration intervention</td>
<td>2.9</td>
<td>1460</td>
</tr>
<tr>
<td>Combined interventions</td>
<td>2.4</td>
<td>1251</td>
</tr>
</tbody>
</table>

Critique: Anderson uses a simple model structure to describe the occurrence of ADEs from medication errors that originate at different stages of the medication process. The model could quite easily have been implemented as a simple decision tree, rather than the seemingly complex patient-level simulation model that was used.

The inputted incidences of medication errors of different levels of severity at different stages of the process was of great relevance to the hospital for which the analysis was undertaken as they were based on a primary study undertaken at the hospital. The other key parameters in the model – the rate at which ADEs occur – were assumed, not being referenced to any existing studies. This reduces the value of the model to a what-if analysis, as the reader may only infer the likelihood of the two scenarios based on their own experience. Also, the costs of implementing the alternative interventions are not incorporated into the analysis so it is not possible to estimate the relative cost-effectiveness of the interventions.

Other limitations include the application of a constant cost effect to all ADEs, and the non-consideration of the cost of implementing the defined interventions, which precluded any estimation of their relative cost-effectiveness.

A lesser limitation concerns the assumption that errors may only occur at one point in the medication process, and that observed error rates were applied to all orders remaining free of error at each stage. This assumption led to the counter-intuitive result...
that ADEs actually increased when an effective intervention was implemented. In reality, errors that occur early in the medication process can lead to additional errors at later stages of the medication pathway. Modelling this effect would eliminate counter-intuitive results that may reduce confidence in the model.

2.3.2 Van den Bemt et al, Cost-benefit analysis of the detection of prescribing errors by hospital pharmacy staff

Van den Bemt et al aim to estimate the costs and benefits of routine activities undertaken by hospital pharmacists to detect prescribing errors, based on primary data collected in two general hospitals in Holland. Errors detected by pharmacists were recorded, and then classified into one of six categories of severity by two hospital pharmacists. The first two categories describe errors predicted to be detected prior to administration, the third category describes errors that reach the patient, but require no additional intervention. Health effects, additional monitoring and treatment, and additional time spent by nursing staff were estimated for each prevented error (presumably by the two hospital pharmacists). The time required by the pharmacists to prevent the prescribing error was recorded.

The results show that 9.9% of orders included an error, and that 37% of errors were predicted to require some form of intervention to monitor or treat the consequences of the error. The net costs of preventing errors (pharmacy costs minus costs of nurses clarifying orders in the first two severity categories) were estimated to be €285, whilst the benefits from preventing errors were estimated to be €9867, giving a net benefit figure of €9582 over a period of one week in two hospitals. Almost 80% of the benefit was derived from 4 prevented errors. These errors are described in detail to allow the reader to assess the plausibility of the assumptions made about the impact of these errors.

Critique: The evaluation of the routine practice of pharmacy staff is not of relevance in itself, though the methods may be applicable to the evaluation of new interventions. The collection of data describing the type of errors prevented, followed by the prediction of the impact of each error, is a reasonable approach to take in the absence of a comparative primary study that describes ADE rates in the presence of alternative error prevention strategies. The process is explicit, and the paper provides detailed descriptions of the assumptions made around the key observed errors.
However, the predictions regarding the impact of the observed errors raise concerns about the ability of, in this case, pharmacists to accurately predict the consequences of errors. The pharmacists predicted that 37% of the prevented prescription errors would have resulted in increased frequency of monitoring or worse, and that almost 19% could have caused harm to the patient. Of five empirical studies that have examined the relationship between medication errors and ADEs\textsuperscript{25-29}, a maximum of 3.7% of errors leading to actual ADEs was reported\textsuperscript{29}, whilst the maximum for non-intercepted potential ADEs was 7.6%\textsuperscript{27}. The highest combined total for actual and potential ADEs due to medication errors was 8.4%\textsuperscript{27}.

This analysis does not account for any of the health benefits arising from the prevention of ADEs, which should inform the benefits side of the cost benefit equation (cost savings should be subtracted from costs incurred to inform the cost side of the cost benefit equation).

2.3.3 Heisler et al, Preventing adverse drug events: an evaluation of strategies\textsuperscript{22}

Heisler et al\textsuperscript{22} report a cost benefit analysis of two strategies for the prevention of ADEs, which are compared to the status quo. The interventions are the requirement for hospitals to adopt computerised surveillance systems (including CPOE systems); and the use of federal regulations in the US to require health professionals to report ADEs to MedWatch (a US national adverse event reporting programme).

Their methodology involves estimating the number of ADEs and ADE-deaths in a 650-bed hospital, based on a study that evaluated a computer alert system designed to correct errors that might lead to ADEs and to detect ADEs before maximum injury occurs\textsuperscript{30}. The number of reported ADEs and deaths are adjusted proportionately to estimate the number of events in different size hospitals. Each ADE was assumed to require an additional 5 inpatient days to estimate the number of inpatient days avoided.

High and low implementation costs for computerised drug surveillance systems were taken from two studies\textsuperscript{23,31}. Minimum and maximum estimates of aggregate cost savings due to the prevention of ADEs from the implementation of a CPOE system were taken from Bates\textsuperscript{23}.

A US Department of Health and Human Services report is referenced as predicting that CPOE systems could prevent between 28% and 95% of hospital-based ADEs\textsuperscript{32}. The model appears to assume that computerised drug surveillance systems would prevent
all ADEs and ADE deaths resulting from different aspects of software and programmes implemented in hospitals (e.g. software controlling infusion delivery, or providing direct access to hospital practice guidelines). The impact of enforced reporting to MedWatch is assumed to be a 10% decrease in ADEs due to the increase in information available to the FDA on drug reactions and drug-drug interactions, which is based on a study of reporting surgical outcomes from CABG.

The results comprise estimates of three categories of costs: upfront implementation costs; maintenance costs; and cost savings due to fewer ADEs. For a hospital of size 300-499 beds, the computer surveillance system is estimated to cost between $0.5 and $1.43 million to implement, have $200 - $285.7 annual maintenance costs, and prevent between $2.5 and $5 million worth of health care resource expenditure through the avoidance of ADEs. The computerised surveillance system is therefore estimated to produce net benefits to the health service. Cost savings are not estimated for the MedWatch system so net benefits are not estimated.

Critique: Heisler et al do not model the relationship between medication errors and ADEs. The analysis is based on assumed estimates of the impact of interventions on observed ADE rates, which are based on a limited interpretation of the existing literature. The ADE rate is based on a single study of a computer alert system, which implicitly assumes 100% sensitivity for the alert system. The assumption of 100% effectiveness of computerised surveillance systems in preventing ADEs provides a ‘best case’ analysis for this intervention.

The analysis does not account for any of the health benefits arising from the prevention of ADEs. The cost estimates for the interventions are taken from published sources, and the cost range describing the aggregate effects of preventing ADEs is based on a single published source. In the light of the uncertainties around the clinical parameters, more detailed costings would not significantly improve the findings of this analysis.

The evaluation provides a crude estimate of the likely cost-effectiveness of two interventions for a best-case scenario regarding the effectiveness of the interventions evaluated (though the value of the health benefits arising from the prevention of ADEs is excluded). This indicates the need for extensive sensitivity analysis around any analysis of the costs and benefits of interventions aimed at reducing medication errors.
2.3.4 Summary of previous approaches

The three reviewed studies illustrate a range of methods that have been used to estimate the impact of alternative interventions aimed at reducing medication errors.

The evaluation by Heisler et al is based on direct estimates of the effectiveness of one intervention (CPOE), and a more indirect estimate of the effect of another intervention (error reporting), in reducing ADEs\textsuperscript{22}. Combined with cost estimates, this approach provides a crude estimate of cost-effectiveness. Data describing the impact of CPOE on ADE rates are preferable to less direct data, such as medication error rates (if the presented ADE rate data are relevant to the population of interest). The methodology may provide a suitable approach for the approximate evaluation of interventions for which relevant such data exist. Unfortunately, few such data are available, and the current study evaluates a range of potential interventions for which it will be necessary to extrapolate ADE rates from medication error rates.

Van den Bemt et al used primary data to estimate error detection rates, and expert opinion to predict the potential impact of the detected errors\textsuperscript{21}. The relevance of this methodology to the current analysis of aggregate medication errors is limited, as the analysis was restricted to prescription errors. Also, the validity of the expert predictions of the effects of the medication errors is questioned.

Anderson has a similar objective to the current study, as he evaluates a range of interventions that impact at different stages of the medication pathway\textsuperscript{20}. A model is used that describes the incidence of errors at different stages, though the model does not predict the number of errors that remain undetected and result in an ADE. The ADE effects are estimated outside the model according to assumptions about the proportion of errors that cause ADEs, i.e. the extrapolation of medication errors to ADEs is not based on evidence synthesis (of published data or expert opinion).

Of the three approaches, the model-based approach described by Anderson provides the most likely approach for the current study, though the model structure requires some additional complexity in order to allow the model-based extrapolation of medication errors to ADEs.
2.4 Use of evidence based medication care pathways to prospectively identify error opportunities and potential solution points

Understanding the medication pathway, from its origination as a decision to prescribe to the administration to the recipient, is as important first step in prospectively appraising hazards that lead to medication errors, and evaluating potential solutions that might reduce medication safety incidents.

The medication process is complex and usually comprises a number of contextual factors that might be seen as a barrier to deriving generic hazards and potential solutions. Nevertheless, through the use of standardised care mapping processes it is possible to identify generic medication hazard points (sometimes referred to as opportunities for error) against which error types and causes may be matched and potential solutions may be tested using available research data. For example, Leape and colleagues used a pathway approach to identify key steps in the medicines pathway in hospitals\(^3\). This was refined into a 9-step map by the Australian Council for Safety and Quality in Health Care\(^4\) [see Figure 2.1] and, in expanded form, included some generic solutions that might be used in the redesign of medication processes, such as reducing reliance on memory, simplifying and standardising processes and the use of protocols and checklists.

Figure 2.1 Pathway for medicines in hospitals. Modified from Leape et al\(^3\)
While the basic structure identified in Figure 2.1 is a valuable start to a discussion of medication error on a care pathway, it contains insufficient detail on which to establish a search for cost effective solutions to improve medication safety. Most of the solutions proposed by the Australian Council, for example, are what may be called ‘headline’ solutions, that require many layers of activity to effect the solution. In the light of research evidence on the implementation of protocols and checklists, for instance, this particular type of solution might prove difficult to implement unless supported by other decision support tools.

There are a number of ways to improve on the Figure 2.1 structure. Leape and colleagues, and the Australian Council, chose to approach this by the use of safeguards. In effect, these are design requirements for a safe medication system. An example of safeguards defined for pharmacists reviewing prescriptions (Step 3 of Figure 2.1) is presented in Figure 2.2.

**Figure 2.2 Safeguards for pharmacists reviewing prescriptions**

<table>
<thead>
<tr>
<th>Step 3 Pharmacist reviews prescription</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pharmacist must have information on which to base the review. This may include:</strong></td>
</tr>
<tr>
<td>Patient information including age, weight, height</td>
</tr>
<tr>
<td>Clinical judgement about whether the drug and dosage are appropriate</td>
</tr>
<tr>
<td>Information about possible interactions with other drugs</td>
</tr>
<tr>
<td>Any problems identified should be clarified with the prescriber.</td>
</tr>
</tbody>
</table>

This is a useful first step to understanding the needs of the health professional and the system requirements for a safe process, but there is still a lack of specificity about the opportunity for error or hazard, the error type, the possible causes and, most importantly, the possible solutions. A more detailed care map is required for such an approach, in which error opportunities, causes and solutions are inter-related and plotted onto the process of care. But this is not without its own difficulties, for the care map becomes very complicated (as it does in the reality of health care provision). In particular, it
becomes difficult for health care professionals to test out a generic map against their experience of the real world.

For this reason we decided to use an actual clinical pathway to test out the reality of hazards and solution. The clinical recommendations in the recently published national clinical practice guideline for the management of depression\textsuperscript{36} were used as the basis for a detailed care pathway to which opportunities for error could be identified, alongside error types, possible causes and potential solutions.

2.4.1 Medication pathway methods

2.4.1.1 Choice of clinical guideline

The study group decided to use the recently published national clinical guideline on the management of depression as the demonstration model for identifying opportunities for medication error. The recommendations in the guideline cross the system boundaries between primary and secondary care and the guideline is therefore a good demonstration of the complexities of medication provision. It also enabled the study group to explore and contrast different types of medication and their provision, related to differing levels of severity of depression. Two pathways were developed, representing the choices made for people with moderate depression and for those people with more severe depression.

2.4.1.2 Use of expert groups

Two expert groups were convened to develop the medication error pathways. The first group, the internal study expert group, comprising senior hospital pharmacists and the research team, met on two occasions to [1] refine the care pathway model developed from the clinical guideline and [2] identify through an iterative process the possible error types, causes and possible solutions at each opportunity for error point.

The second expert group comprised the internal study group together with 8 experts from nursing, general practice, medication safety, pharmacy practice and human factors engineering. This group reviewed the product from the internal group over a two day period, deriving the final model for the pathway and associated hazard information on medication safety.
2.4.1.3 Mapping methods

Standardised care mapping methods were used to identify decision points and processes on the care pathway\(^3\), drawn using Microsoft Visio (2005 Microsoft Corporation).

2.4.1.4 Conceptual basis and scope of the pathway

As an initial conceptual basis for the pathway, the research team used the work of Leape\(^3\) and the Australian Council\(^4\) to derive a first stage framework against which to plot the care process. As the complexity of mapping error types, causes, and solutions to each error opportunity point became clear, the study team took the decision, within resource constraints, to limit the mapping exercise in three ways.

First, the field of study was limited to hospital care and detailed consideration was not given to opportunities for error and their solutions at the primary/secondary care interface.

Second, the exploration of opportunities for error was bounded to those arising after the decision had been taken to prescribe (in part because this field includes knowledge base and decision making, in themselves very complex fields and beyond the scope of this study).

Third, the study excluded consideration of the influence on patient decision making and the role of the patient in protecting themselves from the impact of errors made at earlier points in the medication process. While acknowledging the potential importance of the role of patients in this regard, it was again considered that this was beyond the scope of what was possible in the study.

2.4.2 Medication pathway results

Guideline based medication pathways were developed and mapped for the management of moderate depression. Opportunities for error were identified, characterised and fitted to points on the pathways, demonstrating that many of the error opportunities are generic to medication care pathways. The full pathway is described across the following Figures 2.3 to 2.6.

Possible types of medication errors, causes, and potential solutions, were determined for each error opportunity, which are presented in Appendix 2. A number of solutions could work at more than one point. Some possible solutions, when applied at one point, were
seen to be possible causes of error at other points on the care pathway. A new risk may occur with the introduction of Computerised Physician Order Entry (CPOE) if by chance, or due to an event such as distraction, the prescriber highlights the wrong drug or the wrong dose on the CPOE screen and implements an order, there may be a low likelihood than that the wrong order will be picked up in pharmacy unless it is a very unusual treatment or a wrong dose (adult instead of paediatric, for example). The dose and route will be ‘correct’ and the pharmacy will not be able to tell whether or not the physician intended to prescribe the inadvertently identified medication. Similarly, the inappropriate prescription is unlikely to be picked up at administration unless the drug is very unusual for the patient (such as insulin for a person who does not have diabetes).

Bar coding at drug administration offers some valuable opportunities for reducing the frequency of ADEs, for example through better identification of the right drug for the right patient. Patterson and colleagues point out, however, that unexpected new socio-technical vulnerabilities can arise through the introduction of a complex technology such as a bar coding system. For instance, the authors found that the clinical coordination between doctors and nurses became degraded as a result of the different (and more restricted) ways in which the medications were displayed by the bar code system. Care pathway mapping can be used to highlight where some of these unexpected new vulnerabilities might be anticipated.

The following section describes how the defined medication pathway was distilled into a generic decision model structure to be used to evaluate medication error interventions.

### 2.5 Development of the model structure

In the area of medication errors, the primary model outputs are the incidence of preventable ADEs of different severity levels. The basic model structure describes the incidence of medication errors and the pathway from errors to the occurrence of ADEs. A PHIA of error points associated with a specific form of medication, such as the use of oral methotrexate tablets for the treatment of rheumatoid arthritis, would probably develop a very detailed representation of the pathways between the processes leading to the incidence of errors, and the pathways between the occurrence of an error and the incidence of ADEs. Such a model may describe specific conditions and/or actions that may increase the probability that an error occurs, or that an incident error is not detected.
The current analysis covers all medication errors that may occur across the full range of patient journeys within the health care system. The improvement analysis component also covers a wide selection of potential interventions that may either prevent errors occurring (e.g. CPOE) or increase the detection rate of errors (e.g. pharmacists participating on ward rounds). Given the broad scope of the analysis it is not feasible to describe the pathways in as much detail as might be possible for a more focussed PHIA.

The previous section described the development of medication pathways, along which potential error points are highlighted. Combining this process with the findings from the systematic literature review of medication errors and/or ADE frequencies, a simplified model structure was developed to describe the medication error pathway for a generic inpatient population. The model structure is presented in Figure 1, and incorporates the assumptions that are listed in Table 2.3. The structure describes the incidence of different medication errors at three points in the medication pathway: prescription; dispensing; and administration. The different error types have separate probabilities of being detected at different points prior to administration, and the errors that reach the patient have probabilities of not causing harm, or of causing different severities of harm.

2.6 Discussion

Prospective hazard analysis (PHA) is in general a much more open and extensive process than root cause analysis (RCA). PHA looks forward and is able to ask the ‘what if’ questions about potential hazards and solutions, including the new hazards arising from solution, while RCA is concerned with understanding the causes of an event. Prospective mapping of error opportunities onto evidence based care pathways therefore enables broad consideration of possible causes and solutions.

The applied process of care pathway mapping was embraced by the health professionals as providing a structured and explicit mechanism for the definition of opportunities for error that underlay the pathway, as well as the identification of causes and potential solutions. The process also provided the non-clinical members of the research team with a clear and intuitive introduction to the complexities of the medication process, which served as a solid foundation for the subsequent reviewing and modelling work undertaken as part of the PHIA.
Discussion of causes, to some extent evidence based, demonstrates the multifactorial nature of error causation and indicates the need for realistic expectations of the introduction of individual interventions to reduce medication error.

Use of care pathway mapping highlighted that some suggested solutions may have unexpected impacts at subsequent points on the pathway, either producing new opportunities for error or having positive impacts at more than one point.

The outputs from the defined care pathway informed the two main elements of the PHIA; the systematic literature review, and the model-based evaluation of potential improvement interventions. A key output of the care pathway was the enhanced background understanding of the review area, which the reviewers could apply to their interpretation of the literature. The medication pathway process also informed decisions on topic areas for the systematic review of the literature and on the search for solution options resourced from the commercial and grey literature.

The care pathway provided the foundation for the development of the model structure used to evaluate potential solutions. As discussed in section 2.4, the development of a model structure is sometimes an implicit and unsystematic process, but the defined care pathway underpinned a structured approach that facilitated discussion around the appropriateness of alternative model structures.

Table 2.3 Medication errors model assumptions

<table>
<thead>
<tr>
<th>Assumption</th>
<th>Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medication errors may occur at three distinct stages in the medication pathway: prescription; dispensing; and administration</td>
<td>The predominantly US medication errors literature generally describes four stages in the medication process (prescription; transcription; dispensing; and administration). Transcription describes the process by which a pharmacist transcribes a verbal order (from a nurse or doctor) into the pharmacy system. This stage is not a feature of the UK medication pathway and is not represented in the model.</td>
</tr>
<tr>
<td>Prescription errors are defined as occurring after the decision to prescribe a particular medication has been made by the prescriber</td>
<td>This assumption excludes cases where the medication prescribed is indicated for the condition being treated but the evidence base suggests that an alternative medication should be used in preference. These are knowledge-based errors that are more subjective in determination and are considered to outside the scope of the medication errors model.</td>
</tr>
<tr>
<td>At each of the three stages, four specific types of medication errors are described, which represent all errors: Prescription errors include wrong drug; wrong dose, wrong route and wrong frequency errors;</td>
<td>Specific error types are included to allow for error-specific detection and ADE severity rates, as well as possible differences in the effectiveness of potential interventions in preventing different errors. The use of four error types at each stage to represent all errors is a</td>
</tr>
<tr>
<td>Dispensing errors include wrong drug, wrong strength, wrong quantity, and wrong label errors;</td>
<td></td>
</tr>
<tr>
<td>Administration errors include wrong drug, wrong dose, wrong route and wrong frequency errors</td>
<td></td>
</tr>
</tbody>
</table>

necessary simplification to make the model manageable. The included error types at each stage are chosen on the basis of the literature review and are the most commonly reported error types at each stage that were shown to lead to ADEs. The dispensing error types include wrong strength errors, which are not explicitly defined in the literature, though they are assumed to include both wrong dose and wrong form errors.

| Medication errors may be detected at two distinct stages in the medication pathway: dispensing; and administration |

Prescription errors may be detected at the dispensing or the administration stage; dispensing errors may be detected at the administration stage; errors during the administration stage may be detected prior to administration.

| Medication errors that reach the patient may or may not cause harm; those that cause harm are categorised as: |
| Significant: resulted in temporary harm to the patient and required intervention |
| Serious: resulted in temporary harm to the patient and required initial or prolonged hospitalisation |
| Severe, life threatening, or fatal: resulted in permanent patient harm, required intervention to sustain life, or contributed to a patient’s death. |

It is necessary to differentiate between ADEs of different levels of severity to properly inform the cost-effectiveness of alternative interventions (assuming it is more valuable to prevent severe ADEs than minor ADEs). The literature presents a range of categorisations of ADEs, including the National Coordinating Council for Medication Error Reporting and Prevention’s (NCC MERP’s) index that includes 9 categories, though only five categories describes cases in which harm occurs as a result of a medication error. In the medication errors literature, a three category approach comprising significant, serious, and severe/life threatening/fatal ADEs, was common.\(^{25,27,39-42}\)
Figure 2.3 Medication errors model structure

- **Prescription order**
  - No prescription error
  - Dispensing error
    - Wrong drug
    - Wrong dose
    - Wrong route
    - Wrong quantity
    - Wrong label
    - Detected at dispensing
      - Not detected at dispensing
      - Detected at administration
        - No harm
        - Minor harm
        - Moderate harm
        - Severe/life threatening harm

- **No administration error**
  - Wrong drug
  - Wrong dose
  - Wrong route
  - Wrong frequency
    - Detected prior to administration
    - Not detected prior to administration
    - Go to Node 4
  - Go to Node 3
Chapter 3  Model population: clinical parameters

3.1  Introduction

Chapter 2 describes the structure of the decision model to be used to evaluate the potential cost-effectiveness of alternative interventions aimed at reducing medication errors. The model defines four error types at each of the three medication stages (as presented in Figure 2.1) that are assumed to cover the full range of medication errors, i.e. the sum of the four errors occurring at each stage is assumed equal to the aggregate number of medication errors occurring at each stage. Whilst it is recognised that other types of errors occur, to make the modelling tractable other error types are implicitly assimilated into one of the four defined error type categories. The object of the analysis is to model the relationship between different types of errors occurring at different stages of the medication process and the incidence of adverse drug events (ADEs).

The main parameters required to populate the medication errors model include the medication error rates, detection rates for the alternative error categories; the proportions of undetected errors that result in harm to the patient (i.e. become ADEs); and the levels of severity of the occurring ADEs. Aggregate ADE rates do not directly inform the model, though they are used to calibrate the model by comparing the sum of the predicted ADEs resulting from the different error categories to observed estimates of the frequency of ADEs. Calibration is necessary given the large uncertainty around the true values of the model’s input parameters, and the extent to which parameters are correlated. The process of calibration is described in detail in section 3.5.

This chapter describes the data and assumptions used to estimate the frequency of these errors, their subsequent pathways to detection or reaching the patient, and their impact on the patient if they remain undetected.

3.2  Medication error frequency parameters

The purpose of reviewing studies reporting error frequency rates for alternative error types at different stages of the medication process is to inform a model describing the progression of such errors to ADEs from a UK perspective. As a range of studies was identified for some error categories, a means of ranking these data in order of relevance to the modelling study is presented. The hierarchy described in Table 1 was established for the main analysis of medication error pathways in an UK adult inpatient setting. The hierarchy accounts for three main characteristics of reporting studies. The most relevant
setting is the UK, with studies located in other developed countries being placed at the same level in the hierarchy. Error frequency rates have been shown to vary considerably between adult and paediatric wards\textsuperscript{40,43}. As fewer studies have addressed paediatric medication errors, the analysis focuses on error rates in adult inpatients, and precedence is given to studies reporting error rates in exclusively adult inpatient wards. The final item in the hierarchy is the outcome measure presented. The model describes the frequency of errors as a function of the number of prescriptions ordered as this is the most commonly presented denominator. In cases where the most relevant study does not use this denominator, an adjustment is required using the ratio of prescription orders to other denominators presented in studies reporting both outcome measures.

Table 3.0 Hierarchy for aggregation of medication errors data

<table>
<thead>
<tr>
<th>Most relevant</th>
<th>Setting: UK; Patient group: adult inpatient; Outcomes: medication errors per ‘n’ (e.g. 1000) orders or opportunities for error</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Setting: North American, Western Europe, Japan, Australasia; Patient group: adult inpatient; Outcomes: medication errors per ‘n’ (e.g. 1000) orders or opportunities for error</td>
</tr>
<tr>
<td></td>
<td>Setting: UK; Patient group: general inpatient; Outcomes: medication errors per ‘n’ (e.g. 1000) orders or opportunities for error</td>
</tr>
<tr>
<td></td>
<td>Setting: North American, Western Europe, Japan, Australasia; Patient group: general inpatient; Outcomes: medication errors per ‘n’ (e.g. 1000) orders or opportunities for error</td>
</tr>
<tr>
<td></td>
<td>Setting: UK; Patient group: adult inpatient; Outcomes: medication errors per ‘n’ (e.g. 1000) admissions or patient days</td>
</tr>
<tr>
<td></td>
<td>Setting: North American, Western Europe, Japan, Australasia; Patient group: adult inpatient; Outcomes: medication errors per ‘n’ (e.g. 1000) admissions or patient days</td>
</tr>
<tr>
<td>Least relevant</td>
<td>Setting: North American, Western Europe, Japan, Australasia; Patient group: general inpatient; Outcomes: medication errors per ‘n’ (e.g. 1000) admissions or patient days</td>
</tr>
</tbody>
</table>
The hierarchy does not control for two other important study characteristics: medication error definition; and method of data collection. These factors are more difficult to categorise due to the wide range of options for both of these characteristics. The relevance of alternative studies with respect to these characteristics is discussed in the context of the identified studies in each of the error categories.

3.2.1 Prescription orders and opportunities for administration error

The model requires estimates of the number of prescription orders processed over the timeframe of the model in order to provide a relevant estimate of the cost savings due to the prevention of medication errors. The analysis is undertaken from the perspective of a single 400-bed hospital. The number of prescriptions ordered is estimated as a function of the number of prescribed items per patient and the average length of stay. A recent audit undertaken at the Royal Hallamshire Hospital (RHH) in Sheffield reported the mean number of regularly prescribed items to be 8.44 in a general hospital population. To account for additional ‘when required’ and single doses, this figure is rounded up to 9, which is taken as the average number of prescription orders received per inpatient stay. The average length of stay is reported as 8.1 days (Department of Health, Hospital Episode Statistics, 2001-2). The following equation is used to estimate the number of prescription orders per bed per year:

\[
\text{Prescription orders per bed per year} = \frac{\text{Days per year} \times 365}{\text{Average length of stay}} \times \text{Mean number of prescribed items} = 406\text{ prescription orders}
\]

For the 400-bed hospital the total number of prescription orders per year is estimated to be 400 x 406 = 162,000.

In addition to estimating the number of prescription orders, it is also necessary to describe the number of doses administered to patients (per bed), which inform the number of opportunities for administration error (OAEs). Another audit study at the RHH in 2001 identified an average of 64.5 dose administrations over the course of an inpatient stay, for which the average number of regularly prescribed medications was 7. The number of doses was uprated to reflect the above estimate of 8.44 regularly prescribed items per inpatient episode by dividing 64.5 by 7 (9.2) and multiplying up by 8.44 (77.8). ‘When required’ and single doses are not incorporated into the calculations.
as these items are assumed to add only marginally to the number of drug administrations. The mean number of OAEs per hospital bed day is estimated as:

Opportunities for error per hospital bed year = 365 multiplied by the number of dose administrations over an inpatient stay (77.8) divided by the average length of stay (8.1) = 3500.

The number of OAEs per year for a 400-bed hospital is estimated to be 400 x 3500 = 1.4 million. The ratio of OAEs to prescription orders is therefore estimated to be 1.4 million divided by 162,000 = 8.6.

Similarly, dispensing error rates are presented as a function of the total number of medications dispensed and so the same ratio of OAEs to prescription orders (8.6) is applied to estimate the number of dispensing errors. In addition, however, it is recognised that a proportion of medications received by inpatients in UK hospitals are kept on ward stock. These medications are not subject to dispensing errors as they are not dispensed to a specific patient from the pharmacy, though they may increase the rate of administration errors (relative to a system where all medications are dispensed directly to the patient). No data source describing the proportion of ward stock medications was identified, and so a wide range of between 40% and 70% was specified based on the best estimates of the UK-based health professionals on the research team.

Whilst the above adjustment to dispensing error rates reduces the estimated frequency of such errors, it is recognised that the ward stock system may result in higher rates of administration errors due to the increased requirements for nurses to identify the correct medication from the ward stock.

3.2.2 Prescription medication errors

A range of studies presented error rate frequencies for different types of prescription errors. The main error types are defined as wrong drug, wrong dose, wrong route, and wrong frequency. The error rates reported for these error types are presented in Table 1.1 to 1.4, along with the main characteristics of the reporting studies.

The range of reported error rates for all four error types is noticeable. Some of these differences may be explained by the study date and setting, error definitions, and the methods used to detect errors. The two UK studies illustrate these differences. Wilson et al report the rate of any medication errors in paediatric wards45, probably in the mid-1990s, based on the number of errors reported via an incident reporting scheme.
Hawkey et al report rates of ‘appreciable or major errors’ and ‘errors with possible impact on patients’ across inpatient care\textsuperscript{43}, probably in the mid- to late 1980s, based on the specific collection of errors by pharmacists. In addition, the error rates are presented with alternative denominators, Wilson reports errors per 1,000 patient days and per 100 admissions, whilst Hawkey presents error rates per 1,000 prescription orders.

The US studies by Lesar and colleagues report rates for ‘significant errors’\textsuperscript{39,40}, which are defined as errors with significant potential for adverse consequence and having a ‘non-negligible potential to be carried out’. Also in the US, Bobb et al use similar methods but do not include ‘non-negligible potential to be carried out’ criterion\textsuperscript{46}. Hawkey defines appreciable errors as having a 5-20% chance of noticed effect, and major errors as having >20% chance of noticed effect, >5% chance of harmful effect, or any chance of lethal effect\textsuperscript{43}. All studies were based in a general inpatient setting and errors were detected via pharmacists. The presented error rate in the UK setting is between 6 and 30 times higher than the rates reported in the US setting, for example, in Table 3.1 Hawkey reports a rate of 45.4 wrong dose prescription errors per 1,000 orders compared to rates of 1.61 and 7.5 per 1,000 orders reported by Lesar and Bobb, respectively.

Another UK-based paper is also considered to inform aggregate rates of prescription errors. Dean et al observed prescription errors in a 550-bed UK hospital over a four week period in 1999. Whilst only a limited range of error rates by error type are presented, the aggregate definition of prescription errors is similar to the current study’s definition and so the aggregate prescription error rates inform the estimation of input parameter ranges for the medication errors model. The aggregate prescription error rate is estimated to be 14.9 per 1,000 prescription orders.

Table 3.1 Identified wrong dose prescription error rates

<table>
<thead>
<tr>
<th>Author</th>
<th>Data period</th>
<th>Country</th>
<th>Inpatient setting</th>
<th>Data collection method</th>
<th>Error definition</th>
<th>Errors</th>
<th>Error rates per</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bobb\textsuperscript{46}</td>
<td>2002</td>
<td>US</td>
<td>General exc. surgical</td>
<td>Pharmacists</td>
<td>Errors with the potential to lead to extra monitoring or worse</td>
<td>134</td>
<td>7.5</td>
</tr>
<tr>
<td>Briceland\textsuperscript{101}</td>
<td>1994/5</td>
<td>US</td>
<td>All antimicrobial orders</td>
<td>Pharmacists</td>
<td>Significant/severe error</td>
<td>654</td>
<td>9.2</td>
</tr>
<tr>
<td>Dean\textsuperscript{102}</td>
<td>1999</td>
<td>UK</td>
<td>All non-obstetric</td>
<td>Pharmacists</td>
<td>Any medication error</td>
<td>211</td>
<td>8</td>
</tr>
<tr>
<td>Dean\textsuperscript{102}</td>
<td>1999</td>
<td>UK</td>
<td>All non-obstetric</td>
<td>Pharmacists</td>
<td>Serious medication error</td>
<td>78</td>
<td>2.2</td>
</tr>
<tr>
<td>Kirk\textsuperscript{103}</td>
<td>2003</td>
<td>Singapore</td>
<td>Paediatric</td>
<td>Computer analysis of database</td>
<td>Any medication error</td>
<td>534</td>
<td>282</td>
</tr>
<tr>
<td>Kozer\textsuperscript{47}</td>
<td>2000</td>
<td>Canada</td>
<td>A&amp;E</td>
<td>Chart review by medical students</td>
<td>Any medication error</td>
<td>133</td>
<td>79.3</td>
</tr>
</tbody>
</table>
### Table 3.2  Identified wrong drug prescription error rates

<table>
<thead>
<tr>
<th>Author</th>
<th>Data period</th>
<th>Country</th>
<th>Inpatient setting</th>
<th>Data collection method</th>
<th>Error definition</th>
<th>Errors</th>
<th>Error rates</th>
<th>per</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kozer</td>
<td>2000</td>
<td>Canada</td>
<td>A&amp;E</td>
<td>Chart review by medical students</td>
<td>Significant/severe error</td>
<td>68</td>
<td>40.5</td>
<td>1,000 orders</td>
</tr>
<tr>
<td>Hawkey</td>
<td>Pub 1990</td>
<td>UK</td>
<td>General Pharmacists</td>
<td>Appreciable or major errors**</td>
<td>97</td>
<td>15.7</td>
<td>1,000 orders</td>
<td></td>
</tr>
<tr>
<td>Hawkey</td>
<td>Pub 1990</td>
<td>UK</td>
<td>General Pharmacists</td>
<td>Errors with possible impact on the patient.</td>
<td>280</td>
<td>45.4</td>
<td>1,000 orders</td>
<td></td>
</tr>
<tr>
<td>Lesar</td>
<td>1987-1995</td>
<td>US</td>
<td>General Pharmacy, confirmed by physicians</td>
<td>Significant errors*</td>
<td>6272</td>
<td>1.61</td>
<td>1,000 orders</td>
<td></td>
</tr>
<tr>
<td>Lesar</td>
<td>1994/5</td>
<td>US</td>
<td>General Pharmacy, confirmed by physicians</td>
<td>Significant errors*</td>
<td>406</td>
<td>2.31</td>
<td>1,000 orders</td>
<td></td>
</tr>
<tr>
<td>Lesar</td>
<td>1995/6</td>
<td>US</td>
<td>Adult inpatient Pharmacy, confirmed by physicians</td>
<td>Significant errors*</td>
<td>61</td>
<td>0.13</td>
<td>1,000 orders</td>
<td></td>
</tr>
<tr>
<td>Lesar</td>
<td>1995/6</td>
<td>US</td>
<td>Paediatric inpatient Pharmacy, confirmed by physicians</td>
<td>Significant errors*</td>
<td>139</td>
<td>4.94</td>
<td>1,000 orders</td>
<td></td>
</tr>
<tr>
<td>Potts</td>
<td>2001</td>
<td>US</td>
<td>Paediatric CCU Pharmacists</td>
<td>Potential ADEs</td>
<td>53</td>
<td>7.8</td>
<td>1,000 orders</td>
<td></td>
</tr>
<tr>
<td>Wilson</td>
<td>Pub 1998</td>
<td>UK</td>
<td>Paediatric cardiac ICU</td>
<td>Incident reporting</td>
<td>Any medication error</td>
<td>35</td>
<td>27.9</td>
<td>1,000 patient days</td>
</tr>
<tr>
<td>Wilson</td>
<td>Pub 1998</td>
<td>UK</td>
<td>Paediatric cardiac ward</td>
<td>Incident reporting</td>
<td>Any medication error</td>
<td>33</td>
<td>8.1</td>
<td>1,000 patient days</td>
</tr>
<tr>
<td>Lesar</td>
<td>1987-1995</td>
<td>US</td>
<td>General Pharmacy, confirmed by physicians</td>
<td>Significant errors*</td>
<td>6272</td>
<td>3.66</td>
<td>1,000 patient days</td>
<td></td>
</tr>
<tr>
<td>Lesar</td>
<td>1995/6</td>
<td>US</td>
<td>Adult inpatient Pharmacy, confirmed by physicians</td>
<td>Significant errors*</td>
<td>61</td>
<td>2.6</td>
<td>1,000 patient days</td>
<td></td>
</tr>
<tr>
<td>Lesar</td>
<td>1995/6</td>
<td>US</td>
<td>Paediatric inpatient Pharmacy, confirmed by physicians</td>
<td>Significant errors*</td>
<td>139</td>
<td>43.4</td>
<td>1,000 patient days</td>
<td></td>
</tr>
<tr>
<td>Wilson</td>
<td>Pub 1998</td>
<td>UK</td>
<td>Paediatric cardiac ICU</td>
<td>Incident reporting</td>
<td>Any medication error</td>
<td>35</td>
<td>18.2</td>
<td>100 admissions</td>
</tr>
<tr>
<td>Wilson</td>
<td>Pub 1998</td>
<td>UK</td>
<td>Paediatric cardiac ward</td>
<td>Incident reporting</td>
<td>Any medication error</td>
<td>33</td>
<td>4.9</td>
<td>100 admissions</td>
</tr>
<tr>
<td>Lesar</td>
<td>1987-1995</td>
<td>US</td>
<td>General Pharmacy, confirmed by physicians</td>
<td>Significant errors*</td>
<td>6272</td>
<td>2.96</td>
<td>100 admissions</td>
<td></td>
</tr>
<tr>
<td>Lesar</td>
<td>1995/6</td>
<td>US</td>
<td>Adult inpatient Pharmacy, confirmed by physicians</td>
<td>Significant errors*</td>
<td>61</td>
<td>0.43</td>
<td>100 admissions</td>
<td></td>
</tr>
<tr>
<td>Lesar</td>
<td>1995/6</td>
<td>US</td>
<td>Paediatric inpatient Pharmacy, confirmed by physicians</td>
<td>Significant errors*</td>
<td>139</td>
<td>3.56</td>
<td>100 admissions</td>
<td></td>
</tr>
</tbody>
</table>

* Errors with ‘significant’ potential for adverse consequence and having non-negligible potential to be carried out

** Appreciable 5-20% chance of noticed effect; Major >20% chance of noticed effect, >5% chance of harmful effect, any chance of lethal effect
<table>
<thead>
<tr>
<th>Author</th>
<th>Data period</th>
<th>Country</th>
<th>Inpatient setting</th>
<th>Data collection method</th>
<th>Error definition</th>
<th>Errors</th>
<th>Error rates per</th>
<th>per</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bobb</td>
<td>2002</td>
<td>US</td>
<td>General exc. surgical</td>
<td>Pharmacists</td>
<td>Errors with the potential to lead to extra monitoring or worse</td>
<td>10</td>
<td>0.6</td>
<td>1,000 orders</td>
</tr>
<tr>
<td>Briceland</td>
<td>1994/5</td>
<td>US</td>
<td>All antimicrobial orders</td>
<td>Pharmacists</td>
<td>Significant/severe error</td>
<td>33</td>
<td>0.5</td>
<td>1,000 orders</td>
</tr>
<tr>
<td>Dean</td>
<td>1999</td>
<td>UK</td>
<td>All non-obstetric</td>
<td>Pharmacists</td>
<td>Any medication error</td>
<td>33</td>
<td>0.9</td>
<td>1,000 orders</td>
</tr>
<tr>
<td>Dean</td>
<td>1999</td>
<td>UK</td>
<td>All non-obstetric</td>
<td>Pharmacists</td>
<td>Serious medication error</td>
<td>12</td>
<td>0.3</td>
<td>1,000 orders</td>
</tr>
<tr>
<td>Hawkey</td>
<td>Pub 1990</td>
<td>UK</td>
<td>General</td>
<td>Pharmacists</td>
<td>Appreciable or major errors**</td>
<td>23</td>
<td>3.7</td>
<td>1,000 orders</td>
</tr>
<tr>
<td>Hawkey</td>
<td>Pub 1990</td>
<td>UK</td>
<td>General</td>
<td>Pharmacists</td>
<td>Errors with possible impact on the patient.</td>
<td>129</td>
<td>20.9</td>
<td>1,000 orders</td>
</tr>
<tr>
<td>Kozer</td>
<td>2000</td>
<td>Canada</td>
<td>A&amp;E</td>
<td>Chart review by medical students</td>
<td>Any medication error</td>
<td>5</td>
<td>3</td>
<td>1,000 orders</td>
</tr>
<tr>
<td>Kozer</td>
<td>2000</td>
<td>Canada</td>
<td>A&amp;E</td>
<td>Chart review by medical students</td>
<td>Significant/severe error</td>
<td>4</td>
<td>2.4</td>
<td>1,000 orders</td>
</tr>
<tr>
<td>Lesar</td>
<td>1987-1995</td>
<td>US</td>
<td>General</td>
<td>Pharmacy, confirmed by physicians</td>
<td>Significant errors*</td>
<td>463</td>
<td>0.12</td>
<td>1,000 orders</td>
</tr>
<tr>
<td>Lesar</td>
<td>1994/5</td>
<td>US</td>
<td>General</td>
<td>Pharmacy, confirmed by physicians</td>
<td>Significant errors*</td>
<td>35</td>
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<td>1,000 orders</td>
</tr>
<tr>
<td>Potts</td>
<td>2001</td>
<td>US</td>
<td>Paediatric CCU</td>
<td>Pharmacists</td>
<td>Potential ADEs</td>
<td>6</td>
<td>0.9</td>
<td>1,000 orders</td>
</tr>
<tr>
<td>Lesar</td>
<td>1987-1995</td>
<td>US</td>
<td>General</td>
<td>Pharmacy, confirmed by physicians</td>
<td>Significant errors*</td>
<td>463</td>
<td>0.27</td>
<td>1,000 patient days</td>
</tr>
<tr>
<td>Wilson</td>
<td>Pub 1998</td>
<td>UK</td>
<td>Paediatric cardiac ICU</td>
<td>Incident reporting</td>
<td>Any medication error</td>
<td>24</td>
<td>19.2</td>
<td>1,000 patient days</td>
</tr>
<tr>
<td>Wilson</td>
<td>Pub 1998</td>
<td>UK</td>
<td>Paediatric cardiac ward</td>
<td>Incident reporting</td>
<td>Any medication error</td>
<td>4</td>
<td>1</td>
<td>1,000 patient days</td>
</tr>
<tr>
<td>Lesar</td>
<td>1987-1995</td>
<td>US</td>
<td>General</td>
<td>Pharmacy, confirmed by physicians</td>
<td>Significant errors*</td>
<td>463</td>
<td>0.22</td>
<td>100 admissions</td>
</tr>
<tr>
<td>Wilson</td>
<td>Pub 1998</td>
<td>UK</td>
<td>Paediatric cardiac ICU</td>
<td>Incident reporting</td>
<td>Any medication error</td>
<td>24</td>
<td>12.5</td>
<td>100 admissions</td>
</tr>
<tr>
<td>Wilson</td>
<td>Pub 1998</td>
<td>UK</td>
<td>Paediatric cardiac ward</td>
<td>Incident reporting</td>
<td>Any medication error</td>
<td>4</td>
<td>0.6</td>
<td>100 admissions</td>
</tr>
</tbody>
</table>

* Errors with ‘significant’ potential for adverse consequence and having non-negligible potential to be carried out

** Appreciable 5-20% chance of noticed effect; Major >20% chance of noticed effect, >5% chance of harmful effect, any chance of lethal effect
<table>
<thead>
<tr>
<th>Author</th>
<th>Data period</th>
<th>Country</th>
<th>Inpatient setting</th>
<th>Data collection method</th>
<th>Error definition</th>
<th>Errors</th>
<th>Error rates</th>
<th>per</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kozer‡</td>
<td>2000</td>
<td>Canada</td>
<td>A&amp;E</td>
<td>Chart review by medical students</td>
<td>Significant/severe error</td>
<td>2</td>
<td>1.2</td>
<td>1,000 orders</td>
</tr>
<tr>
<td>Lesar†</td>
<td>1987-1995</td>
<td>US</td>
<td>General</td>
<td>Pharmacy, confirmed by physicians</td>
<td>Significant errors*</td>
<td>393</td>
<td>1</td>
<td>1,000 orders</td>
</tr>
<tr>
<td>Lesar†</td>
<td>1994/5</td>
<td>US</td>
<td>General</td>
<td>Pharmacy, confirmed by physicians</td>
<td>Significant errors*</td>
<td>23</td>
<td>0.13</td>
<td>1,000 orders</td>
</tr>
<tr>
<td>Lesar†</td>
<td>1987-1995</td>
<td>US</td>
<td>General</td>
<td>Pharmacy, confirmed by physicians</td>
<td>Significant errors*</td>
<td>393</td>
<td>0.23</td>
<td>1,000 patient days</td>
</tr>
<tr>
<td>Potts†</td>
<td>2001</td>
<td>US</td>
<td>Paediatric CCU</td>
<td>Pharmacists</td>
<td>Potential ADEs</td>
<td>6</td>
<td>0.9</td>
<td>1,000 orders</td>
</tr>
<tr>
<td>Lesar†</td>
<td>1987-1995</td>
<td>US</td>
<td>General</td>
<td>Pharmacy, confirmed by physicians</td>
<td>Significant errors*</td>
<td>393</td>
<td>0.19</td>
<td>100 admissions</td>
</tr>
<tr>
<td>Hawkey‡</td>
<td>Pub 1990</td>
<td>UK</td>
<td>General</td>
<td>Pharmacists</td>
<td>Appreciable or major errors**</td>
<td>NR</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>Hawkey‡</td>
<td>Pub 1990</td>
<td>UK</td>
<td>General</td>
<td>Pharmacists</td>
<td>Errors with possible impact on the patient.</td>
<td>NR</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>Wilson‡</td>
<td>Pub 1998</td>
<td>UK</td>
<td>Paediatric cardiac ICU</td>
<td>Incident reporting</td>
<td>Any medication error</td>
<td>NR</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>Wilson‡</td>
<td>Pub 1998</td>
<td>UK</td>
<td>Paediatric cardiac ward</td>
<td>Incident reporting</td>
<td>Any medication error</td>
<td>NR</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>Wilson‡</td>
<td>Pub 1998</td>
<td>UK</td>
<td>Paediatric cardiac ICU</td>
<td>Incident reporting</td>
<td>Any medication error</td>
<td>NR</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>Wilson‡</td>
<td>Pub 1998</td>
<td>UK</td>
<td>Paediatric cardiac ward</td>
<td>Incident reporting</td>
<td>Any medication error</td>
<td>NR</td>
<td>NR</td>
<td></td>
</tr>
</tbody>
</table>

NR – not reported
* Errors with ‘significant’ potential for adverse consequence and having non-negligible potential to be carried out
** Appreciable 5-20% chance of noticed effect; Major >20% chance of noticed effect, >5% chance of harmful effect, any chance of lethal effect

Table 3.4 Identified wrong frequency prescription error rates
<table>
<thead>
<tr>
<th>Year</th>
<th>Location</th>
<th>Setting</th>
<th>Reporting</th>
<th>Nature of Medication Error</th>
<th>Error Rate</th>
<th>Admissions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1998</td>
<td>Wilson</td>
<td>UK</td>
<td>Paediatric cardiac ward</td>
<td>Incident reporting</td>
<td>Any medication error</td>
<td>10</td>
</tr>
<tr>
<td>1990</td>
<td>Hawkey</td>
<td>UK</td>
<td>General Pharmacists</td>
<td>Appreciable or major errors**</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>1990</td>
<td>Hawkey</td>
<td>UK</td>
<td>General Pharmacists</td>
<td>Errors with possible impact on the patient</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>1987-</td>
<td>Lesar</td>
<td>US</td>
<td>General Pharmacists, confirmed by physicians</td>
<td>Significant errors*</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>1995</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1994/5</td>
<td>Lesar</td>
<td>US</td>
<td>General Pharmacists, confirmed by physicians</td>
<td>Significant errors*</td>
<td>NR</td>
<td></td>
</tr>
</tbody>
</table>

NR – not reported
* Errors with ‘significant’ potential for adverse consequence and having non-negligible potential to be carried out
** Appreciable 5-20% chance of noticed effect; Major >20% chance of noticed effect, >5% chance of harmful effect, any chance of lethal effect

Summary

The estimated parameter values for prescription medication errors are presented in Table 3.5. Hawkey et al and Dean et al present the highest ranked study in the defined hierarchy, i.e. the most relevant, though error rates are only presented for wrong drug and wrong dose errors. The medication errors definitions used in the Hawkey study less transparent than the definitions reported in by Dean et al, as well as the study being at least 10 years older. Hawkey et al also reports significantly higher rates than other studies. The mean input parameter values for wrong drug and wrong dose errors are, therefore, based on the study by Dean et al.

Error rates for wrong route and wrong frequency errors are estimated by applying the ratio of different error types observed in another study to the observed error rates in the Dean study. The ratio of wrong drug to wrong dose errors is 0.16 as reported by Bobb et al, and 0.11 by Dean et al. This is considered sufficiently close to apply the ratios of wrong drug to wrong route errors, and wrong dose to wrong route errors, estimated from Bobb et al to the error rates for wrong drug and wrong dose reported by Hawkey. The average of the two estimated rates is specified as the baseline estimate. The process is described as:

Ratio wrong drug: wrong route errors$^{46} = 1.2:0.6 = 2$

Ratio wrong dose: wrong route errors$^{46} = 7.5:0.6 = 12.5$
Wrong drug errors \(^{43}\) / Ratio wrong drug: wrong route errors \(^{46}\) = 0.9 / 2 = 0.45

Wrong dose errors \(^{43}\) / Ratio wrong dose: wrong route errors \(^{43}\) = 8 / 12.5 = 0.65

Baseline wrong route error rate = 0.55 per 1,000 orders

The lower bound was estimated using the same process applied to the presented error rates for ‘appreciable or major errors’. The upper bounds are estimated to be 50% higher than the baseline. A similar process was undertaken to estimate a baseline wrong frequency error rate of 3.6.

The aggregate prescription error rate is around 1.3%, which is slightly less than the aggregate prescription error rate observed by Dean et al, \(^{102}\) which is consistent with the more specific definition of prescription errors used in the current study. Upper ranges of double the baseline estimate are defined due to the significant uncertainty introduced by the much higher, UK-based, error rates reported by Hawkey. \(^{43}\) The lower ranges are defined as 50% of the baseline value.

Table 3.5  Model parameters for prescription errors per 1,000 orders

<table>
<thead>
<tr>
<th>Error type</th>
<th>Baseline</th>
<th>Lower bound</th>
<th>Upper bound</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wrong drug</td>
<td>0.9</td>
<td>0.45</td>
<td>1.8</td>
</tr>
<tr>
<td>Wrong dose</td>
<td>8</td>
<td>4</td>
<td>16</td>
</tr>
<tr>
<td>Wrong route</td>
<td>0.55</td>
<td>0.28</td>
<td>1.1</td>
</tr>
<tr>
<td>Wrong frequency</td>
<td>3.6</td>
<td>1.8</td>
<td>7.2</td>
</tr>
</tbody>
</table>

3.2.3  Dispensing medication errors

Tables 3.6 to 3.9 present error frequency estimates for dispensing errors of the following types: wrong drug, wrong label, wrong strength and wrong quantity. Three of the five estimates were derived from studies of community pharmacies. Chua et al investigated the feasibility of a self-reporting system for dispensing errors and near misses in primary care (community) pharmacies in the UK. \(^{48}\) Out of a total of 51,357 items dispensed during the two phases of the study, 39 dispensing errors (0.08%) and 247 near misses (0.48%) were detected. Two studies by Flynn et al used the direct observation method of error detection to record dispensing error rates for alternative error types in community pharmacies. \(^{49,50}\) The studies report similar error rates for the different error types, for
example, error rates of around 2 per 1,000 orders for wrong drug, strength, and quantity errors, and 20 to 26 per 1,000 orders for wrong label errors. The later study reports that of the 77 detected errors, 5 (6.5%) were judged to be clinically important, i.e. 0.1% of all prescriptions.

Beso et al\textsuperscript{51} report individual inpatient dispensing error rates based on incident reports for wrong drug, strength and label errors, as well as for ‘other content’ errors, of which only 1 error was identified, which is assumed to be a wrong quantity error. These data are in agreement with data presented by Roberts et al\textsuperscript{54}, who record dispensing errors reported by 43 hospitals in the UK via a secure web-site. It is not possible to estimate error rates directly as the number of prescriptions is not presented, though the distribution of the type of errors is informed by these data. Of 2,068 error reports, the single most common error type was dispensing the wrong strength of the right drug (23%). 18\% of errors involved the wrong medicine being supplied, and in 7\% the wrong quantity was supplied. This study compared results with a previous study that had presented dispensing errors reported to an unofficial error reporting scheme\textsuperscript{55}. The earlier study reported the same proportion of wrong strength errors (23\%), a higher estimate of the proportion of wrong drug errors (23\%) and wrong quantity errors (10\%). The 2002 paper also states that 10\% of errors involved the wrong directions being provided, which are likely to be a subset of wrong label errors.

Lisby et al reports much higher inpatients dispensing error rates using observation techniques in Denmark.\textsuperscript{105} Fisher et al observed one wrong label dispensing errors from 304 opportunities for error, resulting in an error rate per 1,000 orders of 2.9.\textsuperscript{106}

Table 3.6  Identified wrong drug dispensing error rates

<table>
<thead>
<tr>
<th>Author</th>
<th>Data period</th>
<th>Country</th>
<th>Setting</th>
<th>Collection method</th>
<th>Error definition</th>
<th>Errors</th>
<th>Error rates per 1,000 orders</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beso\textsuperscript{51}</td>
<td>2004</td>
<td>UK</td>
<td>Inpatient pharmacy</td>
<td>Routine reporting</td>
<td>Deviation from an interpretable order discovered after medication left pharmacy</td>
<td>4</td>
<td>0.02</td>
</tr>
<tr>
<td>Lisby\textsuperscript{105}</td>
<td>2003</td>
<td>Denmark</td>
<td>Medical/surgical wards</td>
<td>Compared dispensed &amp; prescribed orders</td>
<td>Deviation from an order discovered after medication left pharmacy</td>
<td>5</td>
<td>9.3</td>
</tr>
<tr>
<td>Flynn\textsuperscript{49}</td>
<td>1992</td>
<td>US</td>
<td>Community pharmacy</td>
<td>Direct observation</td>
<td>Event involving one or more deviations from an interpretable order</td>
<td>10</td>
<td>1.9</td>
</tr>
<tr>
<td>Flynn\textsuperscript{50}</td>
<td>2000/1</td>
<td>US</td>
<td>Community pharmacy</td>
<td>Direct observation</td>
<td>Event involving one or more deviations from a NEW order</td>
<td>4</td>
<td>2.0</td>
</tr>
<tr>
<td>Flynn\textsuperscript{50}</td>
<td>2000/1</td>
<td>US</td>
<td>Community pharmacy</td>
<td>Direct</td>
<td>Event involving one</td>
<td>2</td>
<td>1.2</td>
</tr>
<tr>
<td>Author</td>
<td>Data period</td>
<td>Country</td>
<td>Inpatient setting</td>
<td>Collection method</td>
<td>Error definition</td>
<td>Errors</td>
<td>Error rates</td>
</tr>
<tr>
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<td>-------------</td>
<td>---------</td>
<td>-------------------</td>
<td>-------------------</td>
<td>-----------------</td>
<td>--------</td>
<td>-------------</td>
</tr>
<tr>
<td>Chua**</td>
<td>2002</td>
<td>UK</td>
<td>Community pharmacy</td>
<td>Self-reported</td>
<td>Error discovered after medication given to patient</td>
<td>7</td>
<td>0.13</td>
</tr>
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</table>

Table 3.7 Identified wrong strength dispensing error rates

<table>
<thead>
<tr>
<th>Author</th>
<th>Data period</th>
<th>Country</th>
<th>Inpatient setting</th>
<th>Collection method</th>
<th>Error definition</th>
<th>Errors</th>
<th>Error rates</th>
<th>per</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beso**</td>
<td>2004</td>
<td>UK</td>
<td>Inpatient pharmacy</td>
<td>Routine reporting</td>
<td>Deviation from an interpretable order discovered after medication left pharmacy</td>
<td>13</td>
<td>0.07</td>
<td>1,000 orders</td>
</tr>
<tr>
<td>Lisby**</td>
<td>2003</td>
<td>Denmark</td>
<td>Medical/surgical wards</td>
<td>Compared dispensed &amp; prescribed orders</td>
<td>Deviation from an order discovered after medication left pharmacy</td>
<td>5</td>
<td>9.3</td>
<td>1,000 orders</td>
</tr>
<tr>
<td>Flynn**</td>
<td>1992</td>
<td>US</td>
<td>Community pharmacy</td>
<td>Direct observation</td>
<td>Event involving one or more deviations from an interpretable order</td>
<td>10</td>
<td>1.9</td>
<td>1,000 orders</td>
</tr>
<tr>
<td>Flynn**</td>
<td>2000/1</td>
<td>US</td>
<td>Community pharmacy</td>
<td>Direct observation</td>
<td>Event involving one or more deviations from a NEW order</td>
<td>4</td>
<td>2.0</td>
<td>1,000 orders</td>
</tr>
<tr>
<td>Flynn**</td>
<td>2000/1</td>
<td>US</td>
<td>Community pharmacy</td>
<td>Direct observation</td>
<td>Event involving one or more deviations from a REFILL order</td>
<td>4</td>
<td>2.4</td>
<td>1,000 orders</td>
</tr>
<tr>
<td>Chua**</td>
<td>2002</td>
<td>UK</td>
<td>Community pharmacy</td>
<td>Self-reported</td>
<td>Error discovered after medication given to patient</td>
<td>-</td>
<td>-</td>
<td>1,000 orders</td>
</tr>
</tbody>
</table>

Table 3.8 Identified wrong quantity dispensing error rates

<table>
<thead>
<tr>
<th>Author</th>
<th>Data period</th>
<th>Country</th>
<th>Inpatient setting</th>
<th>Collection method</th>
<th>Error definition</th>
<th>Errors</th>
<th>Error rates</th>
<th>per</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beso**</td>
<td>2004</td>
<td>UK</td>
<td>Inpatient pharmacy</td>
<td>Routine reporting</td>
<td>Deviation from an interpretable order discovered after medication left pharmacy</td>
<td>1</td>
<td>0.01</td>
<td>1,000 orders</td>
</tr>
<tr>
<td>Flynn**</td>
<td>1992</td>
<td>US</td>
<td>Community pharmacy</td>
<td>Direct observation</td>
<td>Event involving one or more deviations from an interpretable order</td>
<td>11</td>
<td>2.3</td>
<td>1,000 orders</td>
</tr>
<tr>
<td>Flynn**</td>
<td>2000/1</td>
<td>US</td>
<td>Community pharmacy</td>
<td>Direct observation</td>
<td>Event involving one or more deviations from a NEW order</td>
<td>5</td>
<td>2.5</td>
<td>1,000 orders</td>
</tr>
<tr>
<td>Flynn**</td>
<td>2000/1</td>
<td>US</td>
<td>Community pharmacy</td>
<td>Direct observation</td>
<td>Event involving one or more deviations from a REFILL order</td>
<td>4</td>
<td>2.4</td>
<td>1,000 orders</td>
</tr>
<tr>
<td>Chua**</td>
<td>2002</td>
<td>UK</td>
<td>Community pharmacy</td>
<td>Self-reported</td>
<td>Error discovered after medication given to patient</td>
<td>5</td>
<td>0.1</td>
<td>1,000 orders</td>
</tr>
</tbody>
</table>

Table 3.9 Identified wrong label dispensing error rates

<table>
<thead>
<tr>
<th>Author</th>
<th>Data period</th>
<th>Country</th>
<th>Inpatient setting</th>
<th>Collection method</th>
<th>Error definition</th>
<th>Errors</th>
<th>Error rates</th>
<th>per</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beso**</td>
<td>2004</td>
<td>UK</td>
<td>Inpatient pharmacy</td>
<td>Routine reporting</td>
<td>Deviation from an interpretable order discovered after medication left pharmacy</td>
<td>11</td>
<td>0.06</td>
<td>1,000 orders</td>
</tr>
<tr>
<td>Author</td>
<td>Year</td>
<td>Location</td>
<td>Pharmacy Type</td>
<td>Method</td>
<td>Event Description</td>
<td>Deviation Rate</td>
<td>Errors Detected</td>
<td>Total Orders</td>
</tr>
<tr>
<td>---------</td>
<td>------</td>
<td>----------</td>
<td>---------------</td>
<td>--------------------</td>
<td>--------------------------------------------------------</td>
<td>----------------</td>
<td>-----------------------</td>
<td>---------------</td>
</tr>
<tr>
<td>Fisher</td>
<td>2001</td>
<td>Australia</td>
<td>Surgical ward</td>
<td>Compared dispensed &amp; prescribed orders</td>
<td>Deviation from an order discovered after medication left pharmacy</td>
<td>1</td>
<td>2.9</td>
<td>1,000 orders</td>
</tr>
<tr>
<td>Lisby</td>
<td>2003</td>
<td>Denmark</td>
<td>Medical/surgical wards</td>
<td>Compared dispensed &amp; prescribed orders</td>
<td>Deviation from an order discovered after medication left pharmacy</td>
<td>12</td>
<td>22.3</td>
<td>1,000 orders</td>
</tr>
<tr>
<td>Flynn</td>
<td>1992</td>
<td>US</td>
<td>Community pharmacy</td>
<td>Direct observation</td>
<td>Event involving one or more deviations from an interpretable order</td>
<td>131</td>
<td>25.9</td>
<td>1,000 orders</td>
</tr>
<tr>
<td>Flynn</td>
<td>2000/1</td>
<td>US</td>
<td>Community pharmacy</td>
<td>Direct observation</td>
<td>Event involving one or more deviations from a NEW order</td>
<td>40</td>
<td>20.4</td>
<td>1,000 orders</td>
</tr>
<tr>
<td>Flynn</td>
<td>2000/1</td>
<td>US</td>
<td>Community pharmacy</td>
<td>Direct observation</td>
<td>Event involving one or more deviations from a REFILL order</td>
<td>0</td>
<td>0.0</td>
<td>1,000 orders</td>
</tr>
<tr>
<td>Chua</td>
<td>2002</td>
<td>UK</td>
<td>Community pharmacy</td>
<td>Self-reported</td>
<td>Error discovered after medication given to patient</td>
<td>2</td>
<td>0.04</td>
<td>1,000 orders</td>
</tr>
</tbody>
</table>

The aggregate undetected error rate in hospital has been reported as being between 16 and 18 items per 100,000 dispensed items in the UK by multiple studies\textsuperscript{51-53}, though all of these studies are based on voluntary incident reports. Poon and colleagues used direct observation techniques after completion of the dispensing process to identify aggregate dispensing errors in inpatient settings in the US. In one study the aggregate dispensing error rate was reported as 7.5 per 1,000 orders (4 if wrong quantity errors were excluded), and a 1.8 per 1,000 orders rate for potential ADEs.\textsuperscript{107} A separate study estimated an aggregate rate of 9.2 per 1,000 orders, and a 2.4 per 1,000 orders rate for potential ADEs.\textsuperscript{108} Fisher et al observed two dispensing errors from 304 opportunities for error, resulting in an aggregate error rate per 1,000 orders of 5.8.\textsuperscript{106}

Campbell and Facchinetti\textsuperscript{56} investigated whether licensed practice nurses (LPNs) had a checking-error rate for dispensed prescriptions comparable to that of pharmacists. The study was based in the US hospital pharmacy between April and July 1995 (split into seven sampling periods). 560 dispensing errors were detected from the 18,774 routine doses dispensed (2.98%). LPNs detected 413 (26.3% error missed), pharmacists detected 472 (15.7% errors missed). For the 812 artificial (planted) dispensing errors, LPNs detected 667 (17.9% missed), pharmacists detected 712 (12.3% missed). The number of dispensing errors leaving the pharmacy is estimated as the number of routine errors detected divided by the proportion of the artificial errors detected, minus the number of the errors detected:
Dispensing errors undetected in pharmacy with pharmacist checking = \( \frac{472}{0.877} - 472 = 66 \)

Dispensing errors undetected in pharmacy with nurse checking = \( \frac{413}{0.821} - 413 = 90 \)

The undetected error rates are 0.35% and 0.48% for pharmacist and nurse checking, respectively.

**Summary**

The studies describing dispensing error rates show that the dispensing process is relatively safe, with multiple studies reporting a narrow range of dispensing error rates in UK hospitals. However, the UK studies report dispensing errors detected routinely (i.e. incident reports), rather than errors detected proactively, which are likely to underestimate the true error rate. The aggregate error rate estimated using the data presented by Poon et al, Campbell and Facchinetti are an order of magnitude higher, 350 - 920 per 100,000 orders compared to 18 per 100,000 orders.

The baseline inpatient error rates presented in Table 3.10 are estimated by multiplying the aggregate error rate for pharmacists using the US data presented by Campbell and Facchinetti (0.35%) by the observed distribution of errors in the UK studies reported by Beso et al and Roberts et al. It is recognised that all medications are dispensed directly in the US, as opposed to only those medications not kept on ward supply in the UK, and that rates may be different due to much wider range of medications dispensed by US pharmacies. Therefore, a wide range was specified for dispensing errors to represent this uncertainty. The lower bound is based on an aggregate error rate of 0.18% (as reported for potential ADEs by Poon et al, and the upper bound is based on an aggregate error rate of 0.75% (as reported for potential ADEs by Poon et al).

**Table 3.10** Model parameters for dispensing errors per 1,000 orders

<table>
<thead>
<tr>
<th>Error type</th>
<th>Baseline</th>
<th>Lower bound</th>
<th>Upper bound</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wrong drug</td>
<td>0.90</td>
<td>0.46</td>
<td>1.93</td>
</tr>
<tr>
<td>Wrong strength</td>
<td>1.30</td>
<td>0.67</td>
<td>2.79</td>
</tr>
<tr>
<td>Wrong quantity</td>
<td>0.25</td>
<td>0.13</td>
<td>0.54</td>
</tr>
<tr>
<td>Wrong label</td>
<td>0.90</td>
<td>0.46</td>
<td>1.93</td>
</tr>
</tbody>
</table>
3.2.4 Administration medication errors

Eleven error frequency studies describing administration errors were identified. The reported error rates are presented in Table 3.11 to 3.14, along with the main characteristics of the reporting studies. These studies tended to describe errors as the percentage of all opportunities for administration error (OAE), which are estimated to be significantly more frequent than prescription orders (a ratio of 8.6 OAEs to orders is presented in section 3.2.1). Of the more reliable studies (that used an observation method to detect errors), only Calabrese et al report error rates per 1,000 orders. For comparability with rates per OAE, the results presented by Calabrese et al are divided by 8.6.

For wrong dose errors, other than a high estimate in one outlier group, and 2 studies based on incident reporting, the reported error rates lie within a relatively narrow range. An error rate of 1% of opportunities for errors is reported by two studies: a UK study based in a medical ward and a French study based on a surgical ward. An adapted rate of 0.3% was reported by a US-based study reporting errors per 1,000 orders that was restricted to 12 targeted drug classes. Excluding the outlier observation, the highest reported error rate is 6.7% of opportunities for error, which was reported by an earlier French study, but in a surgical ICU ward.

Four studies report wrong drug error rates, including a UK study that used the disguised observation technique in a medical ward and a US study restricted to 12 targeted drug classes. The two other studies were based on incident reporting.

All identified administration error studies report missed dose administration errors. Excluding the rates based on intravenous doses, with rates for all missed dose errors vary from 0.5% to 5.7% of all opportunities for error.

More studies report wrong rate administration errors, though the only UK studies either use incident reports or report only administration errors for intravenous drugs. The remaining studies report a relatively wide range of error rates from 0.4% on a French geriatric ward to 6.1% on a French surgical ICU.
Table 3.11 Identified wrong drug administration error rates

<table>
<thead>
<tr>
<th>Author</th>
<th>Data period</th>
<th>Country</th>
<th>Inpatient setting</th>
<th>Data collection method</th>
<th>Error definition</th>
<th>Errors</th>
<th>Error rates per</th>
<th>per</th>
</tr>
</thead>
<tbody>
<tr>
<td>Taxis</td>
<td>1997</td>
<td>UK</td>
<td>Medical ward</td>
<td>Disguised observation</td>
<td>All errors</td>
<td>5</td>
<td>0.5%</td>
<td>OE</td>
</tr>
<tr>
<td>Fisher</td>
<td>Pub 2001</td>
<td>Australia</td>
<td>Surgical ward (trolley system)</td>
<td>Observation</td>
<td>All errors</td>
<td>0/151</td>
<td>0%</td>
<td>OE</td>
</tr>
<tr>
<td>Prot</td>
<td>2002/3</td>
<td>France</td>
<td>Paediatric: general, ICU, nephrology, NICU</td>
<td>Observation</td>
<td>All errors</td>
<td>11</td>
<td>0.6%</td>
<td>OE</td>
</tr>
<tr>
<td>Wilson</td>
<td>Pub 1998</td>
<td>UK</td>
<td>Paediatric ICU</td>
<td>Incident reporting</td>
<td>All errors</td>
<td>1</td>
<td>0.5%</td>
<td>100 admissions</td>
</tr>
<tr>
<td>Little</td>
<td>1996-01</td>
<td>US</td>
<td>Labour &amp; Delivery</td>
<td>Incident reporting</td>
<td>All errors</td>
<td>10</td>
<td>0.44</td>
<td>1,000 patient days</td>
</tr>
<tr>
<td>Little</td>
<td>1996-01</td>
<td>US</td>
<td>Obstetrics</td>
<td>Incident reporting</td>
<td>All errors</td>
<td>14</td>
<td>0.28</td>
<td>1,000 patient days</td>
</tr>
<tr>
<td>Wilson</td>
<td>Pub 1998</td>
<td>UK</td>
<td>Paediatric ICU</td>
<td>Incident reporting</td>
<td>All errors</td>
<td>1</td>
<td>0.8</td>
<td>1,000 patient days</td>
</tr>
<tr>
<td>Calabrese</td>
<td>Pub 2001</td>
<td>US</td>
<td>General</td>
<td>Observation</td>
<td>Errors involving 12 targeted drug classes</td>
<td>1</td>
<td>1.2</td>
<td>1,000 orders</td>
</tr>
<tr>
<td>Husch</td>
<td>2003</td>
<td>US</td>
<td>General</td>
<td>Observation</td>
<td>All intravenous medication errors</td>
<td>14</td>
<td>2.6%</td>
<td>OE</td>
</tr>
<tr>
<td>Husch</td>
<td>2003</td>
<td>US</td>
<td>General</td>
<td>Observation</td>
<td>Potential intravenous ADEs</td>
<td>3</td>
<td>0.7%</td>
<td>OE</td>
</tr>
<tr>
<td>Rothschil</td>
<td>2002</td>
<td>US</td>
<td>Cardiac surgery ICU and step-down wards</td>
<td>Chart review, solicited reports, voluntary reports, computer ADE searches</td>
<td>Intravenous medication errors</td>
<td>0/4276</td>
<td>0</td>
<td>1,000 pump days</td>
</tr>
<tr>
<td>Barker</td>
<td>1999</td>
<td>US</td>
<td>General</td>
<td>Observation</td>
<td>Potential to cause a patient discomfort or harm</td>
<td>NR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Barker</td>
<td>1999</td>
<td>US</td>
<td>General</td>
<td>Observation</td>
<td>All errors</td>
<td>NR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lisby</td>
<td>2003</td>
<td>Denmark</td>
<td>Medical/surgical wards</td>
<td>Observation</td>
<td>All errors</td>
<td>NR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>McNally</td>
<td>Pub 1997</td>
<td>Australia</td>
<td>Medical ward</td>
<td>Disguised observation</td>
<td>All errors</td>
<td>NR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>McNally</td>
<td>Pub 1997</td>
<td>Australia</td>
<td>Surgical ward</td>
<td>Disguised observation</td>
<td>All errors</td>
<td>NR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schneider</td>
<td>Pub 1998</td>
<td>Swiss</td>
<td>Paediatric ICU</td>
<td>Undisguised observation</td>
<td>All errors</td>
<td>NR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tissot</td>
<td>Pub 1999</td>
<td>France</td>
<td>Surgical ICU</td>
<td>Undisguised observation</td>
<td>Resulting in an increase in patient monitoring or worse</td>
<td>NR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tissot</td>
<td>Pub 1999</td>
<td>France</td>
<td>Surgical ICU</td>
<td>Undisguised observation</td>
<td>All errors</td>
<td>NR</td>
<td></td>
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</tr>
<tr>
<td>Tissot</td>
<td>Pub 2003</td>
<td>France</td>
<td>Surgical ward</td>
<td>Undisguised observation</td>
<td>All errors</td>
<td>NR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tissot</td>
<td>Pub 2003</td>
<td>France</td>
<td>Geriatric ward</td>
<td>Undisguised observation</td>
<td>All errors</td>
<td>NR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>van den</td>
<td>Pub 2002</td>
<td>Holland</td>
<td>Surgical ICU</td>
<td>Disguised observation</td>
<td>All errors</td>
<td>NR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wilson</td>
<td>Pub 1998</td>
<td>UK</td>
<td>Paediatric ICU</td>
<td>Incident reporting</td>
<td>All errors</td>
<td>NR</td>
<td></td>
<td></td>
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<tr>
<td>Author</td>
<td>Data period</td>
<td>Country</td>
<td>Inpatient setting</td>
<td>Data collection method</td>
<td>Error definition</td>
<td>Errors</td>
<td>Error rates per</td>
<td>per</td>
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</tr>
<tr>
<td>Wilson</td>
<td>Pub 1998</td>
<td>UK</td>
<td>Paediatric ward</td>
<td>Incident reporting</td>
<td>All errors</td>
<td>NR</td>
<td></td>
<td></td>
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<tr>
<td>Wirtz</td>
<td>2000</td>
<td>UK</td>
<td>Surgical ward</td>
<td>Disguised observation</td>
<td>All intravenous errors</td>
<td>NR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wirtz</td>
<td>2000</td>
<td>Germany</td>
<td>TGP Surgical ward</td>
<td>Disguised observation</td>
<td>All intravenous errors</td>
<td>NR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wirtz</td>
<td>2000</td>
<td>Germany</td>
<td>GSP Surgical ward</td>
<td>Disguised observation</td>
<td>All intravenous errors</td>
<td>NR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NR – not reported</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
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</tr>
</tbody>
</table>

Table 3.12  Identified wrong dose administration error rates

<table>
<thead>
<tr>
<th>Author</th>
<th>Data period</th>
<th>Country</th>
<th>Inpatient setting</th>
<th>Data collection method</th>
<th>Error definition</th>
<th>Errors</th>
<th>Error rates per</th>
<th>per</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barker</td>
<td>1999</td>
<td>US</td>
<td>General</td>
<td>Observation</td>
<td>All errors</td>
<td>103</td>
<td>3.20%</td>
<td>OE</td>
</tr>
<tr>
<td>Barker</td>
<td>1999</td>
<td>US</td>
<td>General</td>
<td>Observation</td>
<td>Potential to cause a patient discomfort or harm</td>
<td>15</td>
<td>0.49%</td>
<td>OE</td>
</tr>
<tr>
<td>Fisher</td>
<td>Pub 2001</td>
<td>Australia</td>
<td>Surgical ward (trolley system)</td>
<td>Observation</td>
<td>All errors</td>
<td>2</td>
<td>1.3%</td>
<td>OE</td>
</tr>
<tr>
<td>McNally</td>
<td>1997</td>
<td>Australia</td>
<td>Medical ward</td>
<td>Disguised observation</td>
<td>All errors</td>
<td>13</td>
<td>5.30%</td>
<td>OE</td>
</tr>
<tr>
<td>McNally</td>
<td>1997</td>
<td>Australia</td>
<td>Surgical ward</td>
<td>Disguised observation</td>
<td>All errors</td>
<td>7</td>
<td>2.80%</td>
<td>OE</td>
</tr>
<tr>
<td>Prot</td>
<td>2002/3</td>
<td>France</td>
<td>Paediatric, general, ICU, nephrology, NICU</td>
<td>Observation</td>
<td>All errors</td>
<td>83</td>
<td>4.8%</td>
<td>OE</td>
</tr>
<tr>
<td>Schneider</td>
<td>1998</td>
<td>Swiss</td>
<td>Paediatric ICU</td>
<td>Undisguised observation</td>
<td>All errors</td>
<td>4</td>
<td>1.50%</td>
<td>OE</td>
</tr>
<tr>
<td>Taxis</td>
<td>1997</td>
<td>UK</td>
<td>Medical ward</td>
<td>Disguised observation</td>
<td>All errors</td>
<td>9</td>
<td>1.0%</td>
<td>OE</td>
</tr>
<tr>
<td>Tissot</td>
<td>1999</td>
<td>France</td>
<td>Surgical ICU</td>
<td>Undisguised observation</td>
<td>All errors</td>
<td>38</td>
<td>6.70%</td>
<td>OE</td>
</tr>
<tr>
<td>Tissot</td>
<td>2003</td>
<td>France</td>
<td>Surgical ward</td>
<td>Undisguised observation</td>
<td>All errors</td>
<td>17</td>
<td>3.0%</td>
<td>OE</td>
</tr>
<tr>
<td>Tissot</td>
<td>2003</td>
<td>France</td>
<td>Geriatric ward</td>
<td>Undisguised observation</td>
<td>All errors</td>
<td>6</td>
<td>2.6%</td>
<td>OE</td>
</tr>
<tr>
<td>Tissot</td>
<td>1999</td>
<td>France</td>
<td>Surgical ICU</td>
<td>Undisguised observation</td>
<td>Resulting in an increase in patient monitoring or worse</td>
<td>4</td>
<td>1.6%</td>
<td>100 admissi ons</td>
</tr>
<tr>
<td>van den Bernt</td>
<td>2002</td>
<td>Holland</td>
<td>Surgical ICU</td>
<td>Disguised observation</td>
<td>All errors</td>
<td>9</td>
<td>3.90%</td>
<td>OE</td>
</tr>
<tr>
<td>Wirtz</td>
<td>2000</td>
<td>UK</td>
<td>Surgical ward</td>
<td>Disguised observation</td>
<td>All intravenous errors</td>
<td>2</td>
<td>3.0%</td>
<td>OE</td>
</tr>
<tr>
<td>Wirtz</td>
<td>2000</td>
<td>Germany</td>
<td>TGP Surgical ward</td>
<td>Disguised observation</td>
<td>All intravenous errors</td>
<td>26</td>
<td>21.0%</td>
<td>OE</td>
</tr>
<tr>
<td>Wirtz</td>
<td>2000</td>
<td>Germany</td>
<td>GSP Surgical ward</td>
<td>Disguised observation</td>
<td>All intravenous errors</td>
<td>7</td>
<td>5.0%</td>
<td>OE</td>
</tr>
<tr>
<td>Wilson</td>
<td>1998</td>
<td>UK</td>
<td>Paediatric ICU</td>
<td>Incident reporting</td>
<td>All errors</td>
<td>3</td>
<td>1.6%</td>
<td>100 admissi ons</td>
</tr>
<tr>
<td>Wilson</td>
<td>1998</td>
<td>UK</td>
<td>Paediatric ICU</td>
<td>Incident reporting</td>
<td>All errors</td>
<td>2</td>
<td>0.3%</td>
<td>100 admissi ons</td>
</tr>
<tr>
<td>Little</td>
<td>1996-01</td>
<td>US</td>
<td>Obstetrics</td>
<td>Incident reporting</td>
<td>All errors</td>
<td>7</td>
<td>0.14%</td>
<td>1,000 patient days</td>
</tr>
<tr>
<td>Little</td>
<td>1996-01</td>
<td>US</td>
<td>Labour &amp; Delivery</td>
<td>Incident reporting</td>
<td>All errors</td>
<td>7</td>
<td>0.31%</td>
<td>1,000 patient days</td>
</tr>
<tr>
<td>Wilson</td>
<td>1998</td>
<td>UK</td>
<td>Paediatric ICU</td>
<td>Incident reporting</td>
<td>All errors</td>
<td>3</td>
<td>2.4%</td>
<td>1,000</td>
</tr>
<tr>
<td>Author</td>
<td>Data period</td>
<td>Country</td>
<td>Inpatient setting</td>
<td>Data collection method</td>
<td>Error definition</td>
<td>Errors</td>
<td>Error rates</td>
<td>per</td>
</tr>
<tr>
<td>--------------</td>
<td>-------------</td>
<td>------------</td>
<td>--------------------------------</td>
<td>------------------------</td>
<td>-------------------------------------------------------</td>
<td>--------</td>
<td>-------------</td>
<td>-----</td>
</tr>
<tr>
<td>Wilson</td>
<td>Pub 1998</td>
<td>UK</td>
<td>Paediatric ward</td>
<td>Incident reporting</td>
<td>All errors</td>
<td>2</td>
<td>0.5</td>
<td>1,000 patient days</td>
</tr>
<tr>
<td>Calabrese</td>
<td>Pub 2001</td>
<td>US</td>
<td>General</td>
<td>Observation</td>
<td>Errors involving targeted drug classes</td>
<td>12</td>
<td>25.9</td>
<td>1,000 orders</td>
</tr>
<tr>
<td>Rothschild</td>
<td>2002</td>
<td>US</td>
<td>Cardiac surgery ICU and step-down wards</td>
<td>Chart review, solicited reports, voluntary reports, computer ADE searches</td>
<td>Intravenous medication errors</td>
<td>81</td>
<td>18.9</td>
<td>1,000 pump days</td>
</tr>
<tr>
<td>Husch</td>
<td>2003</td>
<td>US</td>
<td>General</td>
<td>Observation</td>
<td>All intravenous medication errors</td>
<td>NR</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>Lisby</td>
<td>2003</td>
<td>Denmark</td>
<td>Medical/surgical wards</td>
<td>Observation</td>
<td>All errors</td>
<td>NR</td>
<td>NR</td>
<td></td>
</tr>
</tbody>
</table>

TGP – ward stock pharmacy service  
GSP – satellite pharmacy service

<table>
<thead>
<tr>
<th>Table 3.13 Identified missed administration error rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Author</td>
</tr>
<tr>
<td>--------------</td>
</tr>
<tr>
<td>Fisher</td>
</tr>
<tr>
<td>Prot</td>
</tr>
<tr>
<td>Tissot</td>
</tr>
<tr>
<td>Tissot</td>
</tr>
<tr>
<td>Tissot</td>
</tr>
<tr>
<td>Wirtz</td>
</tr>
<tr>
<td>Wirtz</td>
</tr>
<tr>
<td>Wirtz</td>
</tr>
<tr>
<td>Barker</td>
</tr>
<tr>
<td>McNally</td>
</tr>
<tr>
<td>McNally</td>
</tr>
<tr>
<td>Schneider</td>
</tr>
<tr>
<td>Taxis</td>
</tr>
<tr>
<td>van den Bent</td>
</tr>
<tr>
<td>Nettlemann</td>
</tr>
<tr>
<td>Barker</td>
</tr>
<tr>
<td>Tissot</td>
</tr>
<tr>
<td>Author</td>
</tr>
<tr>
<td>------------</td>
</tr>
<tr>
<td>Wilson</td>
</tr>
<tr>
<td>Wilson</td>
</tr>
<tr>
<td>Little</td>
</tr>
<tr>
<td>Wilson</td>
</tr>
<tr>
<td>Wilson</td>
</tr>
<tr>
<td>Calabrese</td>
</tr>
<tr>
<td>Rothschild</td>
</tr>
<tr>
<td>Wirtz</td>
</tr>
<tr>
<td>Wirtz</td>
</tr>
<tr>
<td>Wirtz</td>
</tr>
<tr>
<td>Wilson</td>
</tr>
<tr>
<td>Little</td>
</tr>
<tr>
<td>Little</td>
</tr>
<tr>
<td>Wilson</td>
</tr>
</tbody>
</table>

NR – not reported

Table 3.14  Identified wrong rate administration error rates
Estimated administration medication error rates are presented in Table 3.15. The administration error rates reported by Wilson et al., which were based on incident reports, are substantially lower than all of the studies using observation techniques. Wirtz reported UK administration error rates for the use of intravenous drugs. The only other UK study reports wrong dose, wrong drug, and missed dose administration error rates based on 9, 5, and 43 observed errors, respectively.

The baseline wrong drug administration error rate is based on that reported by Taxis (5 per 1,000 OAEs), whilst Prot et al report a similar error rate. The lower bound of 1 per 1,000 OAEs is based on the zero rate reported by Fisher and the only other study that was not based on incident reports, but was restricted to 12 targeted drugs. The upper rate is assumed to be 7 per 1,000 OAEs.
The wrong dose rate reported by Taxis et al for the UK (10 per 1,000 OAEs) was not used directly as the baseline estimate as this was the lowest of the 11 reported rates that covered all administration doses. The mean wrong dose error rate for the 7 studies that report non-IV drug wrong dose errors in non-ICUs (23 per 1,000 OAEs) was adjusted downwards to 15 to represent the increased weight of the only UK-based estimate. The lower bound of 10 is based on the rate reported by Taxis et al. The upper bound represents the highest non-ICU, non-outlier rate (32 per 1,000 OAEs).

Missed dose errors reported by the main UK study (50 per 1,000 OAEs, Taxis) are at the top end of the range. Other studies report error rates of between 4 and 57 missed administration errors per 1,000 OAEs. The baseline rate is assumed to be 40 per 1,000 OAEs, whilst the lower and upper bounds are set to 10 and 50.

The lower and upper bounds for wrong rate administration errors are based on a French study, which reported rates of 4 and 48 per 1,000 OAEs in non-ICU wards. The mean is taken as the midpoint between these bounds.

The reported error rates per 1,000 opportunities for administration error are uprated to error rates per 1,000 prescription orders using the estimated ratio of OAEs to prescription orders (8.64) reported in Section 3.2.1.

Table 3.15 Model parameters for administration errors per 1,000 prescription orders

<table>
<thead>
<tr>
<th>Error type</th>
<th>Baseline</th>
<th>Lower bound</th>
<th>Upper bound</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wrong drug</td>
<td>43</td>
<td>8.6</td>
<td>60</td>
</tr>
<tr>
<td>Wrong dose</td>
<td>129</td>
<td>43</td>
<td>456</td>
</tr>
<tr>
<td>Missed dose</td>
<td>43</td>
<td>9.5</td>
<td>49</td>
</tr>
<tr>
<td>Wrong rate</td>
<td>34</td>
<td>189</td>
<td>413</td>
</tr>
</tbody>
</table>

3.3 Error detection rates

A number of studies reported data that could be used to estimate detection rates for medication errors. These studies are described in Table 3.16 and below.
Table 3.16 Medication errors and ADE rates by error type in studies reporting both rates

<table>
<thead>
<tr>
<th>Author</th>
<th>Data period</th>
<th>Country</th>
<th>Inpatient setting</th>
<th>Event definition</th>
<th>Total errors</th>
<th>Wrong drug</th>
<th>Wrong dose</th>
<th>Wrong route</th>
<th>Wrong frequency per 1,000 orders</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bates²⁵</td>
<td>1993 US</td>
<td>General</td>
<td></td>
<td>Preventable ADEs</td>
<td>5</td>
<td>0.5</td>
<td>0</td>
<td>0.1</td>
<td>1,000 orders</td>
</tr>
<tr>
<td>Bates²⁵</td>
<td>1993 US</td>
<td>General</td>
<td></td>
<td>Non-intercepted potential ADEs</td>
<td>8</td>
<td>0.8</td>
<td>1</td>
<td>0.1</td>
<td>1,000 orders</td>
</tr>
<tr>
<td>Bates²⁵</td>
<td>1993 US</td>
<td>General</td>
<td></td>
<td>Intercepted potential ADEs</td>
<td>28</td>
<td>2.8</td>
<td>2</td>
<td>0.2</td>
<td>1,000 orders</td>
</tr>
<tr>
<td>Bates²⁵</td>
<td>1993 US</td>
<td>General</td>
<td></td>
<td>Non-missing dose medication errors</td>
<td>252</td>
<td>25.0</td>
<td>11</td>
<td>1.1</td>
<td>1,000 orders</td>
</tr>
<tr>
<td>Kaushal ²⁷</td>
<td>1999 US</td>
<td>Paediatric</td>
<td></td>
<td>Non-intercepted &amp; intercepted potential ADEs</td>
<td>120</td>
<td>11.1</td>
<td>6</td>
<td>0.6</td>
<td>1,000 orders</td>
</tr>
<tr>
<td>Kaushal ²⁷</td>
<td>1999 US</td>
<td>Paediatric</td>
<td></td>
<td>Medication errors</td>
<td>616</td>
<td>57.2</td>
<td>8</td>
<td>0.7</td>
<td>1,000 orders</td>
</tr>
</tbody>
</table>
3.3.1 Bates

This study estimated how often medication errors are associated with ADEs and potential ADEs on two general medical and one medical intensive care unit (ICU) at Brigham and Women’s Hospital, Boston Massachusetts, USA. Potential medication errors were detected in three ways: 1) pharmacists reported any prescribing errors identified during the dispensing process; 2) a study nurse reviewed all patient records for evidence of medication errors; 3) a trained reviewer evaluated all medication sheets received by pharmacy. Chart review included careful daily reading of progress notes in each chart, followed by more detailed investigation if a nurse identified possible medication error. Reports of incidents were also solicited from nurses through daily visits to the units by study nurse, and daily email notes to nurses on units. All potential medication errors were evaluated by a physician reviewer, who classified them as medication error, rule violation, or no error.

Results

The data from this study are presented in Table 3.16, which shows that the described relationship between medication errors and ADEs is based on very small numbers of ADEs, particularly by error type. Based on 1 ADE each, the percentages of wrong dose errors and wrong frequency errors that result in ADEs are 1.3% and 2.3%, respectively. However, given the number of errors observed, the reported 0% relationship between wrong route errors and preventable ADEs would fall within 95% confidence intervals for a mean value of 10%. Likewise, the 0% rate for wrong drug errors would fall within 95% confidence intervals for a mean value of 20%.

Detection rates for medication errors defined as not having the potential to cause harm are not presented, but detection rates for potential ADEs can be estimated. The aggregate detection rate is 68% (28/41 potential ADEs detected), within the four error categories described in the model, the detection rate varies from 50% for wrong frequency errors (2/4) to 100% for wrong route errors (3/3).

3.3.2 Kaushal

This study estimated rates of medication errors, potential ADEs, and preventable ADEs in paediatric wards at Brigham and Women’s Hospital, Boston Massachusetts, USA. Errors and ADEs were identified from voluntary and verbally solicited reports, as well as
by reviewing all medication order sheets, medication administration records and patient charts. Two physicians reviewed suspected ADEs, potential ADEs.

Results

Kaushal et al do not disaggregate preventable and potential ADE rates by the individual error types. The aggregate percentage of medication errors that result in preventable ADEs is 0.8% (5/616). Other data from this study are presented in Table 3.16, which shows that 19.5% of medication errors are defined as non-intercepted & intercepted potential ADEs (120/616). The only detection rate that can be estimated from these data is the aggregate rate at which potential ADEs are detected, which is estimated to be 57% (68/120).

3.3.3 Wilson

This study reports the findings from a medication error reporting scheme that was set up in the University Hospital of Wales. The form for each reported error listed different types of prescription, supply (dispensing), and administration errors, and asked whether the error was detected before the drug was given. The form also contained space for the clinical consequences of an event to be described.

A Medication Error committee sat every 3 months to examine the reports and to grade the errors into one of seven categories, as defined by the NCC MERP:

Level 0: error prevented by staff surveillance

Level 1: error occurred; but no patient harm

Level 2: error occurred; increased monitoring but no change in clinical status

Level 3: error occurred; change in clinical status, or need for increased laboratory monitoring, but no ultimate harm

Level 4: error occurred; extra treatment required, or increased length of stay

Level 5: error occurred; permanent patient harm resulted

Level 6: error occurred; resulting in death of patient
Results

Table 3.17 Medication error proportions presented by Wilson et al\textsuperscript{45}

<table>
<thead>
<tr>
<th>Error severity</th>
<th>No. errors</th>
<th>% errors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level 0</td>
<td>298</td>
<td>68</td>
</tr>
<tr>
<td>Level 0 exc. Wrong time</td>
<td>264</td>
<td>65</td>
</tr>
<tr>
<td>Level 1</td>
<td>134</td>
<td>30</td>
</tr>
<tr>
<td>Level 2</td>
<td>3</td>
<td>0.7</td>
</tr>
<tr>
<td>Level 3</td>
<td>5</td>
<td>1.1</td>
</tr>
<tr>
<td>Level 4</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Level 5</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Level 6</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Results were presented by year (years 1 and 2) and by ward type (paediatric cardiology ICU (PCICU) and paediatric cardiology ward (PCW)). Table 3.17 shows that 68% of all errors (65% of all non-wrong time errors) were detected prior to reaching the patient. The text reports that 26 errors involved deliberate deviations by nurses that were judged to be appropriate. If these are excluded as errors, the detection rate rises to 72% (69% of all non-wrong time errors). 93.7% (92.3% excluding appropriate deviations) of undetected errors resulted in no harm to the patient.

Error rates are presented for the different error types at the three stages of the medication process, though the error severity categories are not presented for the disaggregated error rates.

The main shortcoming of the reported data is that the error rates are based on incident reports, which are known to significantly underestimate error rates. It may be a strong assumption that the reported detection rate applies to the higher error rates that have been reported by studies using alternative error detection techniques.

It is unlikely that errors occurring at different stages of the medication process have the same detection rates; one would expect prescription errors to have the largest detection rate. The reported detection rates require adjustments across the medication stages for use in the error frequency model.
This study evaluated the impact of clinical pharmacists on medical ward prescribing errors using an intervention and control ward. The same pharmacists were assigned to both wards in rotation, where the pharmacists provided the same range of standard clinical pharmacy activities and recorded relevant details. Activities included post-admission drug histories, daily review of patient charts, and discharge prescription review. Prescription errors were identified on both wards, but only in the intervention ward were recommendations and solutions provided. Unless an error was thought to be life threatening, only theoretical recommendations were defined on the control ward. The potential outcomes of errors were defined separately by a pharmacist and a consultant (if either defined a life threatening error in the control group, the recommended solution was provided).

Results

113 patients were included in the intervention ward, and 122 in the control ward. The observed error rate per patient was 3.06 (n=346) on the intervention ward and 3.22 (n=394) on the control ward. The outcome codes estimated by the pharmacist and the consultant are presented in Table 3.18, four separate errors were defined as life threatening on the control ward.

The aggregate error detection rate was 18%, as 69 of the theoretical recommendations made on the control ward were implemented with no pharmacist intervention. Using the conservative estimate of consultant outcome predictions, 84 of the 94 ‘major’ errors on the control ward were not amended. The detection rate errors defined as ‘major’ was 11%.
Table 3.18  Outcome codes assigned by pharmacist and consultant for errors on the intervention and control wards presented by Dale et al\textsuperscript{72}

<table>
<thead>
<tr>
<th>Outcome code for recommendations</th>
<th>Pharmacist</th>
<th>Consultant</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intervention %</td>
<td>Control %</td>
</tr>
<tr>
<td>Life saving</td>
<td>0.3 (n=346)</td>
<td>0.5 (n=394)</td>
</tr>
<tr>
<td>Major</td>
<td>43.9 (n=346)</td>
<td>42.1 (n=394)</td>
</tr>
<tr>
<td>Minor</td>
<td>46 (n=346)</td>
<td>41.9 (n=394)</td>
</tr>
<tr>
<td>Neutral</td>
<td>7.8 (n=346)</td>
<td>14.7 (n=394)</td>
</tr>
<tr>
<td>Harmful\textsuperscript{*}</td>
<td>0.9 (n=346)</td>
<td>0.5 (n=394)</td>
</tr>
<tr>
<td>No code</td>
<td>1.1 (n=346)</td>
<td>0.2 (n=394)</td>
</tr>
</tbody>
</table>

\* ‘harmful’ recommendations are predicted to result in some detrimental effect to the patient.

3.3.5  Scarsi\textsuperscript{73}

Scarsi et al evaluate a similar intervention to Dale et al\textsuperscript{72} – the impact of pharmacist participation in medical rounds – though a different study design is used. An intervention ward is identified for which pharmacists accompany ward prescription rounds. Control patients were matched to the patients in the intervention ward by age, sex, length of stay, number of orders, and nursing unit. Three pharmacists, with previous experience of chart review, retrospectively reviewed all selected patients’ charts to identify medication errors.

Results

Table 3.19 presents the results reported by Scarsi et al, which shows that only 17\% of all errors were detected. Of most relevance to the baseline error frequency model, only 7.5\% of errors in the control group were detected; 12.5\% of prescription errors and 4\% of administration errors\textsuperscript{74}. The errors that occurred in the intervention group typically occurred during off shifts - evenings/weekends - and were corrected when the rounding pharmacist returned the next day (as evidenced by a shorter duration of errors).
### Table 3.19  Error frequency results presented by Scarsi et al\textsuperscript{73}

<table>
<thead>
<tr>
<th></th>
<th>Undetected</th>
<th>Detected</th>
<th>% Detected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aggregate</td>
<td>116</td>
<td>24</td>
<td>17.1%</td>
</tr>
<tr>
<td>Intervention group: aggregate</td>
<td>29</td>
<td>17</td>
<td>37.0%</td>
</tr>
<tr>
<td>Prescription errors</td>
<td>14</td>
<td>16</td>
<td>53.3%</td>
</tr>
<tr>
<td>Administration errors</td>
<td>12</td>
<td>1</td>
<td>7.7%</td>
</tr>
<tr>
<td>Control group: aggregate</td>
<td>87</td>
<td>7</td>
<td>7.4%</td>
</tr>
<tr>
<td>Prescription errors</td>
<td>42</td>
<td>6</td>
<td>12.5%</td>
</tr>
<tr>
<td>Administration errors</td>
<td>24</td>
<td>1</td>
<td>4.0%</td>
</tr>
</tbody>
</table>

#### 3.3.6 Detection rates summary

The five studies informing error detection rates directly present a wide range of detection rates, though this may primarily be due to differences in the definition of undetected errors and methods of data collection. Kaushal et al\textsuperscript{27} and Bates et al\textsuperscript{26} present the detection rates for potential ADEs (errors that had the potential to cause harm if undetected) of 68\% and 57\%, respectively. Wilson et al report that around 68\% of errors were detected\textsuperscript{45}, though only 2\% of errors resulted in additional actions undertaken as a consequence of the error. One might infer that these 2\% are equivalent to the non-intercepted potential ADEs and preventable ADEs reported by Bates and Kaushal, though the proportion of detected errors that had the potential for harm is not presented. The studies reported by Kaushal et al, and by Wilson et al, were undertaken in paediatric wards.

Dale et al\textsuperscript{72} present a lower detection rate of 18\% for all prescription errors on the control (baseline) ward. Scarsi et al\textsuperscript{73} present similarly low detection rates in their control group, where 92.5\% of all errors remained undetected.

The medication errors model includes four separate error detection rates, describing the likelihood of detecting prescription errors at either the dispensing stage, or the administration stage, detecting dispensing errors at the administration stage, and detecting errors that occur during the administration stage prior to the actual administration of the medication. No direct estimates of these parameters were
identified, though Scarsi et al\textsuperscript{73} presented detection rates by stage at which an error originated – detection rates for prescription and administration errors are 12.5\% and 4\%, respectively.

As the medication errors model describes the pathway of all errors (not just those with the potential to cause harm), it is likely that the relevant detection rates are lower than the reported detection rates for potential ADEs\textsuperscript{25,27}, which are a subset of all medication errors. The estimated detection rates are based, therefore, on the aggregate rates reported by Wilson\textsuperscript{45}, Dale\textsuperscript{72} and Scarsi\textsuperscript{73}, with adjustments for the higher detection rate for prescription errors reported by Scarsi et al. The rates are presented in Table 3.20.

The baseline rate for prescription errors detected at dispensing is 30\%, which is higher than the mean rates reported by Dale\textsuperscript{72} and Scarsi\textsuperscript{73} as it is assumed that most detected prescription errors are detected at dispensing. The upper bound is 50\%, which reflects the rate reported by Wilson\textsuperscript{45}, adjusted downwards due to the reliance on incident reports that is assumed to bias the reported rates upwards. The lower bound of 5\% is assumed to be slightly lower than the lowest aggregate rate (Scarsi\textsuperscript{73}, 7.4\%).

The other detection rates are estimated to be the same as each other as there is no basis for assuming different rates. The baseline detection rate for prescribing errors, dispensing errors, and administration errors prior to administration is 10\%, which is based on the detection rate for administration errors reported by Scarsi et al\textsuperscript{73}, adjusted upwards to reflect the higher aggregate detection rate presented by Dale\textsuperscript{72}. The upper bound of 20\% is based on the aggregate rate reported by Dale. The lower bound is assumed to be close to zero (1\%), i.e. lower than the reported 4\% reported by Scarsi et al.

Table 3.20 Detection rate input parameter values

<table>
<thead>
<tr>
<th>Detection point</th>
<th>Baseline</th>
<th>Lower bound</th>
<th>Upper bound</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prescription errors at dispensing</td>
<td>30%</td>
<td>5%</td>
<td>50%</td>
</tr>
<tr>
<td>Prescription errors at administration</td>
<td>10%</td>
<td>1%</td>
<td>20%</td>
</tr>
<tr>
<td>Dispensing errors at administration</td>
<td>10%</td>
<td>1%</td>
<td>20%</td>
</tr>
<tr>
<td>Administration errors prior to administration</td>
<td>10%</td>
<td>1%</td>
<td>20%</td>
</tr>
</tbody>
</table>
3.4  **Error severity levels**

The severity of the impact of undetected errors on patients’ health is a key parameter determining the potential cost-effectiveness of medication error interventions. The medication errors model aims to describe the incidence of all errors; the pathway from incidence to reaching the patient; the proportion of errors that affect the status of the patient; and the differing levels of severity of the impact of errors that cause harm.

As noted in the previous sections, studies have used different thresholds for the potential severity of medication errors when collecting error data or reporting the number of errors that reached patients undetected. Some studies report all errors, whilst others report only those errors that have the potential to cause harm\(^{25}\), or have the potential to cause harm and have a non-negligible probability of remaining undetected\(^{40}\). In the current analysis, errors that reach the patient may be in one of three categories: errors that do not have the potential to cause harm (non-potential ADEs); errors that have the potential to cause harm, but do not cause harm (potential ADEs); and errors that cause harm (preventable ADEs).

The data reported by Wilson et al\(^{45}\), described in the section 3.3.3, provides some evidence around the proportion of undetected errors without the potential for harm, i.e. 9 of 143 (6.3%) of undetected errors were classified as requiring increased monitoring or worse.

Kaushal et al\(^{27}\) and Bates et al\(^{25}\) present data describing the numbers of non-intercepted potential ADEs and the number of preventable ADEs, from which the proportion of undetected errors with the potential for harm that actually cause harm can be estimated. These data are presented in Table 3.16. In aggregate, Kaushal et al report that 9.6% of non-intercepted ADEs with the potential to cause harm actually caused harm, the corresponding figure reported by Bates et al is 38.5%. For the two error types for which non-intercepted errors were observed the proportion of harmful non-intercepted errors were 25% (1 out of 4 errors) and 50% (1 out of 2 errors) for wrong dose and wrong frequency errors, respectively.

The relevant results of five studies reporting the severity of preventable ADEs are presented in Table 3.21. The error frequency model requires estimates of severity only for preventable ADEs that reach the patient, so the most relevant sources are the two
studies reported by Bates and colleagues. The weighted average proportions from these two studies are 20% fatal/life threatening; 41% serious; 39% significant.

### Table 3.21  Reported medication error and ADE severity

<table>
<thead>
<tr>
<th>Author</th>
<th>Setting</th>
<th>Event definition</th>
<th>Fatal/life threatening</th>
<th>Serious</th>
<th>Significant</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>No.</td>
<td>%</td>
<td>No.</td>
</tr>
<tr>
<td>Bates</td>
<td>General inpatient</td>
<td>Preventable ADEs</td>
<td>14</td>
<td>20%</td>
<td>30</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1</td>
<td>20%</td>
<td>1</td>
</tr>
<tr>
<td>Bates</td>
<td>General inpatient</td>
<td>Preventable ADEs</td>
<td>0</td>
<td>0%</td>
<td>4</td>
</tr>
<tr>
<td>Kaushal</td>
<td>Paediatrics</td>
<td>Preventable ADEs</td>
<td>26</td>
<td>9%</td>
<td>145</td>
</tr>
<tr>
<td>Gurwitz</td>
<td>Nursing home</td>
<td>Preventable ADEs</td>
<td>0</td>
<td>0%</td>
<td>3</td>
</tr>
<tr>
<td>Weingart</td>
<td>General medical</td>
<td>Preventable ADEs</td>
<td>16</td>
<td>24%</td>
<td>28</td>
</tr>
<tr>
<td>Bates</td>
<td>General inpatient</td>
<td>Intercepted potential ADEs</td>
<td>13</td>
<td>12%</td>
<td>43</td>
</tr>
<tr>
<td>Kaushal</td>
<td>Paediatrics</td>
<td>Intercepted potential ADEs</td>
<td>4</td>
<td>19%</td>
<td>5</td>
</tr>
<tr>
<td>Bates</td>
<td>General inpatient</td>
<td>Non-intercepted potential ADEs</td>
<td>2</td>
<td>4%</td>
<td>24</td>
</tr>
<tr>
<td>Kaushal</td>
<td>Paediatrics</td>
<td>Non-intercepted potential ADEs</td>
<td>16</td>
<td>9%</td>
<td>149</td>
</tr>
<tr>
<td>Gandhi</td>
<td>Outpatient</td>
<td>Preventable or ameliorable ADEs</td>
<td>11</td>
<td>6%</td>
<td></td>
</tr>
</tbody>
</table>

3.4.1  Summary of error severity levels

The medication error rates described in section 3.2 are estimate rates of all errors, not just those with a potential to cause harm. The error severity parameters in the medication errors model must, therefore, describe the proportion of all undetected errors that cause harm.

Table 3.22 presents the estimated input parameter values for the consequences of undetected medication errors. No attempt is made to differentiate between the consequences of alternative types of errors due to the lack of relevant evidence, though the model does facilitate such an approach. The baseline estimate for the proportion of errors that cause no harm is 95%, which is primarily based on the percentage reported...
by Wilson et al. the upper bound is assumed to be close to 100% (99%), whilst the lower bound is set at 80% to provide a reasonable range.

The proportions of errors that do cause harm that are in each of the three severity categories are based on the distribution of levels of severity reported by Bates and colleagues\textsuperscript{25,41}, applied to the aggregate proportion of harm-causing errors.

Table 3.22  Error consequence rates

<table>
<thead>
<tr>
<th>Undetected error consequence</th>
<th>Baseline</th>
<th>Lower bound</th>
<th>Upper bound</th>
</tr>
</thead>
<tbody>
<tr>
<td>No harm</td>
<td>95%</td>
<td>80%</td>
<td>99%</td>
</tr>
<tr>
<td>Significant harm</td>
<td>2%</td>
<td>1%</td>
<td>8%</td>
</tr>
<tr>
<td>Serious harm</td>
<td>2%</td>
<td>1%</td>
<td>8%</td>
</tr>
<tr>
<td>Severe/life threatening/fatal harm</td>
<td>1%</td>
<td>0%</td>
<td>4%</td>
</tr>
</tbody>
</table>

3.5  Model calibration

An integral part of the use of models to inform policy is the process of calibration or validation. Validation assesses the accuracy of a model by comparing the outputs of the fully populated model to observed data. Calibration involves fitting a model to observed data describing outputs of the model in order to estimate unobserved input parameter values.

The extent to which the error frequency model predicts similar output values to those observed (e.g. observed ADE rates) will be a function of the combined set of input parameter values, for example, low medication error rates may result in accurate predictions when combined with low detection rates, but not when combined with high detection rates. The initial analysis of the model requires the identification of sets (combinations) of input parameter values that predict similar output values to those observed. This is calibration.

Sections 3.2 to 3.4 described the derivation of ranges of values for each of the model’s input parameters, which are used to specify uniform distributions around each input parameter, i.e. every parameter value between the lower and upper bounds is equally likely to be sampled. Section 3.5.1 describes the observed output parameters and how they were analysed to estimate lower and upper bounds for the observed values.
Section 3.5.2 describes the methods used to calibrate the model. The results of the calibration process are presented in Chapter 6, prior to the main results of the medication errors model.

3.5.1 Observed model output parameters

Data describing ADE rates were identified for aggregate ADE rates, ADE rates by error type, and ADE rates by medication stage. The following sections describe the observed data for these model outputs, followed by a summary section that presents the output parameter sets used to calibrate the model.

3.5.1.1 ADE rates by error type

Bates et al\textsuperscript{25} and Kaushal et al report ADE rates by error type, which are presented in Table 3.16. Bates et al investigated ADEs in two general medical and one medical intensive care unit (ICU) in a US hospital in 1993. Rates are presented for preventable ADEs, non-intercepted potential ADEs, and intercepted potential ADEs that were identified across a total of 10,070 medication errors orders. The interception rate for non-potential ADEs is not presented.

Five preventable ADEs were identified. Three preventable ADEs were classified as ‘other errors’, including instances in which follow-up therapy was inadequate; a drug-drug interaction; and a transcription error. Otherwise, preventable ADE rates of 0.1 per 1,000 orders were observed for wrong dose and wrong frequency ADEs. Potential ADEs were more common, with each of the four defined error types having at least one potential ADE.

Kaushal et al\textsuperscript{27} report combined ‘non-intercepted & intercepted potential ADEs’ rates for the four error types. The aggregate number of preventable and potential ADEs is 120, whilst the four error categories represent 89 of these events (74%).

3.5.1.2 Medication errors and ADEs by medication stage

Four studies report the proportion of ADEs that originate at different stages of the medication process. The four main stages defined by these studies include ordering, transcription, dispensing, and administration, of which the most relevant stages from a UK NHS perspective are the ordering, dispensing, and administration stages. Table 3.23 presents the adjusted proportions of errors originating from these three stages.
These data show that fewest ADEs originate at the dispensing stage, but that there is variation between studies over the proportion of ADEs that originate at the ordering and administration stages. The proportion of events originating as ordering errors ranges from 0.41 for preventable and potential (intercepted & non-intercepted) ADEs in ICU to 0.91 for potential ADEs in paediatrics.

Based on these data, Table 3.23 also specifies ranges for the proportion of ADEs that originate at each of the three stages that will be used as part of the calibration process.

### Table 3.23 Stage of origination of medication errors and ADEs

<table>
<thead>
<tr>
<th>Study</th>
<th>Setting</th>
<th>Definition</th>
<th>No.</th>
<th>Prescription</th>
<th>Dispensing</th>
<th>Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bates</td>
<td>General</td>
<td>ADEs</td>
<td>27</td>
<td>0.60</td>
<td>0.04</td>
<td>0.36</td>
</tr>
<tr>
<td>Kaushal</td>
<td>Paediatrics</td>
<td>Errors</td>
<td>616</td>
<td>0.84</td>
<td>0.01</td>
<td>0.14</td>
</tr>
<tr>
<td></td>
<td>Paediatrics</td>
<td>Potential ADEs</td>
<td>120</td>
<td>0.91</td>
<td>0.04</td>
<td>0.05</td>
</tr>
<tr>
<td>Cullen</td>
<td>Non-ICU</td>
<td>Preventable &amp; potential ADEs*</td>
<td>106</td>
<td>0.46</td>
<td>0.14</td>
<td>0.40</td>
</tr>
<tr>
<td></td>
<td>ICU</td>
<td></td>
<td>158</td>
<td>0.41</td>
<td>0.11</td>
<td>0.48</td>
</tr>
</tbody>
</table>

* intercepted & non-intercepted ADEs

### 3.5.1.3 Aggregate ADE rates

Six studies were identified that reported aggregate rates across error types and medication stages for variously defined ADEs, including preventable ADEs, non-intercepted potential ADEs, intercepted potential ADEs, and all potential ADEs. All of the studies were undertaken in the US, one study was specific to paediatrics. Only two studies report ADE rates with prescription orders as the denominator, with the majority reporting errors per 1,000 patient days. The rates per 1,000 patient days presented by the other four studies are converted to rates per 1,000 patient days using the average of the ratio of days to orders presented by three papers, with ranges presented that are based on the range of the ratios. The adjusted data are presented in Table 3.24.

The adjusted rate for Bond appears to be an outlier, and whilst the adjusted rates are generally higher than the reported rates per 1,000 orders it appears that the preventable ADE rate is unlikely to be above 3 per 1,000 orders. The highest combined intercepted and non-intercepted potential ADE rate is 6.1 per 1,000 orders.
Table 3.24 Aggregate ADE estimates

<table>
<thead>
<tr>
<th>Author</th>
<th>Data period</th>
<th>Inpatient setting</th>
<th>NISME definition</th>
<th>No. Errors</th>
<th>Error rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bates68</td>
<td>Pub 1993</td>
<td>General</td>
<td>Preventable ADEs</td>
<td>12</td>
<td>1.3 (0.7-1.8)*</td>
</tr>
<tr>
<td>Bates68</td>
<td>Pub 1993</td>
<td>exc. Obstetrics</td>
<td>Preventable ADEs</td>
<td>12</td>
<td>1.7 (0.9-2.2)*</td>
</tr>
<tr>
<td>Bates41</td>
<td>1993</td>
<td>General</td>
<td>Preventable ADEs</td>
<td>70</td>
<td>1 (0.5-1.4)*</td>
</tr>
<tr>
<td>Bates25</td>
<td>1993</td>
<td>General</td>
<td>Preventable ADEs</td>
<td>5</td>
<td>0.5</td>
</tr>
<tr>
<td>Bond75</td>
<td>1992</td>
<td>General</td>
<td>Preventable ADEs</td>
<td>13</td>
<td>(6.8-17.6)†</td>
</tr>
<tr>
<td>Cullen69</td>
<td>1993</td>
<td>Medical ICU</td>
<td>Preventable ADEs</td>
<td>15</td>
<td>2 (1.1-2.7)*</td>
</tr>
<tr>
<td>Cullen69</td>
<td>1993</td>
<td>Surgical ICU</td>
<td>Preventable ADEs</td>
<td>14</td>
<td>1.5 (0.8-2)*</td>
</tr>
<tr>
<td>Cullen69</td>
<td>1993</td>
<td>Medical</td>
<td>Preventable ADEs</td>
<td>41</td>
<td>0.8 (0.4-1.1)*</td>
</tr>
<tr>
<td>Kaushal27</td>
<td>1999</td>
<td>Paediatrics</td>
<td>Preventable ADEs</td>
<td>5</td>
<td>0.05</td>
</tr>
<tr>
<td>Cullen69</td>
<td>1993</td>
<td>Medical ICU</td>
<td>Potential ADEs</td>
<td>46</td>
<td>6.1 (3.2-8.3)*</td>
</tr>
<tr>
<td>Cullen69</td>
<td>1993</td>
<td>Surgical ICU</td>
<td>Potential ADEs</td>
<td>31</td>
<td>3.2 (1.7-4.4)*</td>
</tr>
<tr>
<td>Cullen69</td>
<td>1993</td>
<td>Medical</td>
<td>Potential ADEs</td>
<td>117</td>
<td>2.4 (1.3-3.3)*</td>
</tr>
<tr>
<td>Bates41</td>
<td>1993</td>
<td>General</td>
<td>Non-intercepted potential ADEs</td>
<td>111</td>
<td>1.7 (0.9-2.3)*</td>
</tr>
<tr>
<td>Bates25</td>
<td>1993</td>
<td>General</td>
<td>Non-intercepted potential ADEs</td>
<td>8</td>
<td>0.8</td>
</tr>
<tr>
<td>Kaushal27</td>
<td>1999</td>
<td>Paediatrics</td>
<td>Non-intercepted potential ADEs</td>
<td>47</td>
<td>0.44</td>
</tr>
<tr>
<td>Kaushal27</td>
<td>1999</td>
<td>Paediatrics</td>
<td>Intercepted potential ADEs</td>
<td>68</td>
<td>0.63</td>
</tr>
</tbody>
</table>

All studies were undertaken in the US

* converted from rates per 1,000 patients days
† converted from rates per occupied bed year

3.5.1.4 ADE rates summary

ADE rates were identified in aggregate, by error type and by medication stage at which the initial error leading to the ADE occurred. For the purposes of calibration, the model requires a set of values for each of the relevant output parameters, against which the outputs of the model can be compared. The output parameters defined for the calibration
process are the preventable ADE rates associated with each of the 12 medication errors defined at the three medication stages. The estimated ADE rates for each of these errors are based on the three categories of output parameters identified, for example, the rate of preventable ADEs that originate as wrong dose prescription errors is estimated as a function of the proportion of ADEs that originate at the prescription stage and the proportion of ADEs that are defined as being due to wrong dose medication errors. Adjustments are made to reflect the fact that preventable ADE rates are not presented for some types of medication errors and that the 12 error types do not capture the full range of errors that lead to preventable ADEs.

The range of aggregate preventable ADE rates is estimated to be between 1 and 4 per 1,000 orders. Lower and upper bounds describing the proportion of preventable ADEs originating at different stages are defined, which are described in Table 3.25. Four output parameter scenarios are estimated using the combinations of lower and upper values for the aggregate preventable ADE rates and the stage proportion parameters, for example, one estimate of the rate of preventable ADEs that originate as prescription errors is:

Prescription error preventable ADEs per 1,000 orders = 1 preventable ADE per 1,000 orders x 0.5 (50% of preventable ADEs originate as prescription errors) = 0.5.

The estimated preventable ADE rates within each stage are then multiplied by the proportional distribution of preventable ADEs between the error types at each medication stage, for which two scenarios are defined, as described in Table 3.26.

<table>
<thead>
<tr>
<th>Medication stage</th>
<th>Lower bound</th>
<th>Upper bound</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prescription stage</td>
<td>0.5</td>
<td>0.85</td>
</tr>
<tr>
<td>Dispensing stage</td>
<td>0.04</td>
<td>0.14</td>
</tr>
<tr>
<td>Administration stage</td>
<td>0.11</td>
<td>0.4</td>
</tr>
</tbody>
</table>
Table 3.26 Proportional distribution of preventable ADEs by error type with each medication stage

<table>
<thead>
<tr>
<th>Prescription errors</th>
<th>Lower bound</th>
<th>Upper bound</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wrong drug</td>
<td>0.05</td>
<td>0.2</td>
</tr>
<tr>
<td>Wrong dose</td>
<td>0.35</td>
<td>0.45</td>
</tr>
<tr>
<td>Wrong route</td>
<td>0.35</td>
<td>0.45</td>
</tr>
<tr>
<td>Wrong frequency</td>
<td>0.05</td>
<td>0.1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Dispensing errors</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Wrong drug</td>
<td>0.25</td>
<td>0.35</td>
</tr>
<tr>
<td>Wrong strength</td>
<td>0.25</td>
<td>0.35</td>
</tr>
<tr>
<td>Wrong quantity</td>
<td>0.15</td>
<td>0.25</td>
</tr>
<tr>
<td>Wrong label</td>
<td>0.1</td>
<td>0.2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Administration errors</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Wrong drug</td>
<td>0.1</td>
<td>0.2</td>
</tr>
<tr>
<td>Wrong dose</td>
<td>0.2</td>
<td>0.4</td>
</tr>
<tr>
<td>Missed dose</td>
<td>0.2</td>
<td>0.4</td>
</tr>
<tr>
<td>Wrong rate</td>
<td>0.2</td>
<td>0.4</td>
</tr>
</tbody>
</table>

The lower and upper values for each of the stage of origination parameters, the ADEs by error type at each stage parameters, and the aggregate preventable ADE rate parameters were combined, and the resulting estimates analysed to estimate a lower and an upper bound for the proportion of preventable ADEs originating as one of each the 12 error types, which are presented in Table 3.27. The severity of the observed output parameters is not described and so it is not possible to calibrate the input parameters describing the severity of preventable ADEs.
Table 3.27 Preventable ADEs per 1,000 prescription orders: output scenarios for preventable ADE rates by originating error type

<table>
<thead>
<tr>
<th>Error Type</th>
<th>Lower Bound</th>
<th>Upper Bound</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prescription errors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wrong drug</td>
<td>0.025</td>
<td>0.68</td>
</tr>
<tr>
<td>Wrong dose</td>
<td>0.175</td>
<td>1.53</td>
</tr>
<tr>
<td>Wrong route</td>
<td>0.175</td>
<td>1.53</td>
</tr>
<tr>
<td>Wrong frequency</td>
<td>0.025</td>
<td>0.34</td>
</tr>
<tr>
<td>Dispensing errors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wrong drug</td>
<td>0.01</td>
<td>0.196</td>
</tr>
<tr>
<td>Wrong strength</td>
<td>0.01</td>
<td>0.196</td>
</tr>
<tr>
<td>Wrong quantity</td>
<td>0.006</td>
<td>0.14</td>
</tr>
<tr>
<td>Wrong label</td>
<td>0.004</td>
<td>0.112</td>
</tr>
<tr>
<td>Administration errors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wrong drug</td>
<td>0.011</td>
<td>0.320</td>
</tr>
<tr>
<td>Wrong dose</td>
<td>0.022</td>
<td>0.640</td>
</tr>
<tr>
<td>Wrong route</td>
<td>0.022</td>
<td>0.640</td>
</tr>
<tr>
<td>Wrong frequency</td>
<td>0.022</td>
<td>0.640</td>
</tr>
</tbody>
</table>

3.5.2 Calibration methods

The process of calibration for the medication errors model involves sampling a large number of sets of input parameter values (25,000), collecting the associated output parameter values, and comparing each set of outputs to the observed range of output values for the 12 preventable ADE rates presented in Table 3.27. The number of sampled input parameter sets was chosen on the basis of providing a reasonable sample, without overloading the software used to analyse the model [Microsoft Excel 2002].
The comparison between the predicted and observed outputs is based on the aggregate absolute distance between the predicted output parameters and the observed range of output parameter values across the 12 output parameters. The distance for each predicted output parameter value is estimated as:

- if a predicted output parameter is within the observed range for that parameter the distance is zero
- if the predicted value is below the observed range, the distance is estimated as the ‘lower bound value minus the predicted value’
- if the predicted value is above the observed range, the distance is estimated as the ‘the predicted value minus the upper bound value’

The following steps involve:

- summing the distances for each of the 12 output parameters to estimate the aggregate absolute distance
- defining the reciprocal of the aggregate distance (1 divided by the distance) as the weight for each input parameter set that reflects how closely each set predicts the observed output parameter values.

The effectiveness of the relevant medication error interventions can then be estimated against these weighted input parameter sets to produce a range of effectiveness estimates. In most evaluations, a single input parameter set may be defined as the baseline set that most accurately predicts the model’s outputs, though this is not considered appropriate for the medication errors model due to the extreme uncertainty around both the input and output parameters. Moreover, the calibration process is undertaken for a range of observed values for the output parameter set to reflect this uncertainty.

Weights could also be applied to the output parameters to reflect the relative (subjective) importance of the different output parameters, though this was not considered necessary as all the output parameters described the same event, i.e. a preventable ADE.

3.6 **Discussion**

This chapter has described the full process for populating the clinical input parameters in the medication errors model, the structure of which was described in Chapter 2. Data identified by the systematic review of the literature was analysed to define plausible
ranges for each of the model's input parameters, which found significant uncertainty around the input parameters. There was also determined to be a high level of correlation between the input parameters, for example, detection rates and error severity rates are likely to be related to medication error rates. Therefore, the estimation of point estimates for each input parameter was not considered.

Instead, a process of calibration was undertaken. This process involved the analysis of observed values for relevant outputs from the model, which were defined as the preventable ADE rates associated with each of the 12 medication errors described in the model. Data from the literature were analysed to estimate a range of values for these parameters. Outputs from the model were collected from 25,000 separate sets of input parameter values that were compared to the observed range of output values, which were used to define weights for each of the 25,000 input parameters sets that reflected the closeness of the predicted output values to the observed range of output parameter values.

The calibration process was unable to inform the parameters describing the severity of preventable ADEs as no relevant data sources were identified. The defined ranges for the severity parameters (Section 3.4) are used directly for the analysis of the model as presented in Chapter 6.

Calibration is a subjective process and many different variants could have been undertaken, for example, alternative output scenarios could have been specified, or a different inclusion threshold could have been used. There are no definitive methods of calibration, though the explicit presentation of the assumptions underlying the process allows the informed user to develop an informed opinion on the merits of the approach.

The model's cost input parameters are described in Chapter 4. Chapter 6 describes the full analysis of the model, which identifies thresholds for the effectiveness of alternative medication error interventions, beyond which the interventions may be considered to be cost-effective. This analysis involves applying the relative risk of errors occurring, or errors being detected, that are associated with the interventions at relevant points within the model, for example, a bar coding intervention may reduce the risk of errors occurring at the administration stage. The model does not allow for the differential impact of interventions on medication errors that have the potential to cause harm if undetected and those errors that would never result in an ADE. This issue could be addressed by using the same model structure to describe the flow of errors that have the potential to
cause harm (potential ADEs), which requires the adjustment of the input parameters to reflect differences in the incidence and detection of potential ADEs. However, at this stage of development of the evidence base it was felt that there was insufficient evidence to model differential intervention effects on alternative error types and the single model structure described in this chapter was analysed.
Chapter 4  Measurement and valuation of resource use and health care effects

4.1  Introduction

This chapter describes the data sources and analyses undertaken to estimate the relevant costs included in the prospective hazard and improvement analysis of medication errors. The cost estimates are used to populate the medication errors model described in Chapter 3, which will then analyse the potential cost-effectiveness of alternative medication error interventions.

In addition to the costs of implementing medication error interventions, it is important to account for other potential cost impacts on the health service. Kini & Savage\textsuperscript{76} report that Computerised Physician Order Entry (CPOE) systems are cost-saving in two respects. Firstly, resources are saved due to the reduced number of ADEs that require treatment. Secondly, evidence from early adopters suggests that there are also cost savings related to reductions in ancillary test usage (mostly laboratory) and reductions in length of stay via guideline embedding and variance analysis. The value of any health benefits to patients resulting from fewer adverse drug events (ADEs) should also be estimated, either in monetary terms or using a generic valuation tool, such as the quality adjusted lifeyear (QALY).

Thus, four broad impact categories are defined: intervention implementation costs; cost savings due to reduced treatment costs for ADEs; cost savings due to reduced resource use unrelated to ADEs (efficiency savings); monetary valuations of the health benefits due to the prevention of ADEs. The following sections describe the definition and estimation of input parameters describing these four impact categories for the purpose of populating the error frequency model.

4.2  Intervention implementation costs

The following sections describe the methods and estimated implementation costs for a range of medication error interventions.

4.2.1  Computerised Physician Order Entry (CPOE)

Kini & Savage\textsuperscript{76} report initial costs of installation of CPOE in a 400 bed general hospital is estimated at somewhere between $4 million and $7 million. This includes software as well as implementation and training. Ongoing support costs are estimated by the industry to be between 18\% and 21\% of the software cost. Kini & Savage highlight that if
costs relating to clinical data repository and pharmacy systems are included, which are described as fundamental aspects of the infrastructure, the ongoing support costs could double.

Heisler et al\textsuperscript{22} present high and low estimates for the cost of implementation, and annual maintenance costs, for a CPOE system that are based on published figures reported by Bates et al\textsuperscript{23} and by University of Colorado Health Sciences Center\textsuperscript{77}, respectively. The reported costs are presented by hospital size. The relevant comparator to the figures presented by Kini & Savage\textsuperscript{76} are for a hospital with 300-499 beds, for which the implementation costs are estimated to be between $0.5 and $1.43 million, whilst annual maintenance costs are between $0.2 and £0.29 million.

Birkmeyer et al\textsuperscript{78} estimate that first-year costs could vary from $500,000 to $4.1 million for a 200-bed hospital depending on the nature of the hospital's existing clinical information systems. Subsequent annual maintenance costs were estimated to range from $174,000 to $470,000.

Ohsfeldt et al\textsuperscript{79} used a simulation model to estimate the costs of implementing CPOE in Iowa hospitals and to evaluate the financial implications of statewide CPOE implementation. The model differentiates between hospital sizes and whether hospitals have an existing clinical information system (CIS). Using the reported co-efficient from the estimated quadratic interpolation model, the implementation costs for a 400-bed hospital range from $4.25 to $5.88 million for a hospital without an existing CIS, and a low estimate of $1.96 to $6.17 million for a hospital with an existing CIS. The ongoing system costs do not vary greatly according to whether the hospital has an existing CIS, varying between $0.4 and $1.3 million per year.

The counterintuitive result of higher cost estimates for the ‘existing’ CIS hospitals in the “high cost” scenario was thought to occur because in some cases the existing information system cannot be "remodelled" - it must be "demolished" before a functional CPOE system can be established, which results in higher initial costs. The ongoing cost estimates are slightly lower primarily due to lower incremental personnel and training costs.

4.2.1.1 CPOE cost summary

The identified costs for CPOE systems show great variation, which may be related to the complexity of the described systems though it is not possible to investigate this
hypothesis from the data presented. The full ranges of presented costs are specified as cost parameters in the error frequency model, as described in Table 4.1, assuming an approximate hospital size of 400 beds. Reported costs in US dollars are converted to UK sterling using the 2004 purchasing power parity (PPP) of 0.618 sterling to 1 dollar\textsuperscript{80}.

Table 4.1 Cost parameters for CPOE systems

<table>
<thead>
<tr>
<th>Cost parameter</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Implementation and 1st year costs</td>
<td>£0.35 - £4.9 million</td>
</tr>
<tr>
<td>Ongoing annual maintenance costs</td>
<td>£0.12 - £1 million</td>
</tr>
</tbody>
</table>

4.2.2 Pharmacists participating on ward rounds

One of the few interventions for which some effectiveness data were identified is the participation of pharmacists on ward rounds. A typical description of such an intervention is: ‘A senior pharmacist made rounds with the residents, nurses and attending staff each morning, was present in the ward for consultation and assistance to the nursing staff during the rest of the morning and was available on call as necessary during the rest of the day’. The main cost of such an intervention is assumed to be the additional time requirements for the pharmacists.

To estimate the additional cost, a baseline of pharmacist time per ward was defined through consultation with the expert pharmacists on the research team. The baseline is that pharmacists cover a minimum of 2 wards of about thirty patients over a morning to provide a basic level of pharmaceutical care, in the afternoons they have departmental commitments. The additional cost of providing a pharmacist on each ward for a full morning each day in a 400-bed hospital comprises an additional seven pharmacists, based on extra pharmacist required for half of an estimated 14 wards (14 wards x 30 beds = 420 beds). The annual cost of a Grade D pharmacist on the mid-point of the salary scale is estimated as £44,292, including salary, salary oncosts, equivalent annual cost of qualifications, post-graduate training, and capital and non-capital overheads\textsuperscript{81}. The estimated cost is £0.31 million per year.

The upper and lower boundaries for the costs of providing additional ward pharmacists presented in Table 4.2 are based on revised estimates of the baseline scenario, assuming pharmacists visit an average of 1.5 and 2.5 wards per morning.
Table 4.2  Cost parameters for additional pharmacists on ward rounds

<table>
<thead>
<tr>
<th>Cost parameter</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annual costs</td>
<td>£0.21 - £0.37 million</td>
</tr>
</tbody>
</table>

4.2.3  Bar coding systems

News items on the Internet provided the data sources for implementation and ongoing costs of bar coding systems. The following paragraphs describe the reported costs, though few details are provided around the methods used to estimate costs.

Jane Englebright, vice-president of quality at HCA Inc. in Nashville, stated in 2004 that the lack of standard bar codes required hospitals to repackage and add bar codes to drugs at a cost to a 150-bed hospital of $162,000 per year. The one-time implementation cost to equip such a hospital with bar-code technology and systems was stated to be $250,000.

Jeff Schou, director of worldwide health care markets at Symbol Technologies Inc. in Holtsville, N.Y., estimated that the cost of installing wireless LAN technology to provide connectivity for nurses dispensing drugs bedside at hospitals that lack such systems is between $50,000 and $500,000, depending on the size of the facility close.

A report on Integrated Healthcare Systems, whose bar-coding technology is currently deployed in 55 hospitals and nursing homes throughout the US described set-up costs of between $300,000 and $600,000.

Denean Rivera, president of Bridge Medical Inc., which makes software for the bar code systems, stated that a full system costs between $200,000 and $1 million, depending on the size of the hospital.

4.2.3.1  Bar coding cost summary

The cost estimates identified for bar coding technology are more difficult to assimilate as most of the sources do not state the size of the hospital for which the cost estimates are presented. It is also not clear whether some of the cost estimates include the cost of adding bar codes to drugs, though it is assumed that these costs are excluded due to the intervention by the FDA that drug companies are mandated to attach bar codes to drugs.
On the basis of the ranges presented, and the cost of $0.25 million quoted by Englebright for a 150-bed hospital, it is unlikely that the cost of implementing such a system for a 400-bed hospital is less than $0.5 million. An upper estimate of $1 million is specified on the basis of the highest estimate quoted. The costs in UK sterling are presented in Table 4.3.

Table 4.3 Cost parameters for bar coding systems

<table>
<thead>
<tr>
<th>Cost parameter</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bar coding system</td>
<td>£0.35 - £0.7 million</td>
</tr>
</tbody>
</table>

4.3 Costs of ADEs

As with the identified costs of implementing medication error interventions, all of the identified data describing additional treatment costs for patients experiencing an adverse drug event are US-based. The identified sources are reviewed below.

Bates et al23 undertook a case control costing study that defined two sets of cases as patients with an ADE, and patients with a preventable ADE. Controls were selected as patient on the same unit as the case with the most similar pre-event length of stay (LoS). Charges for LoS on ICU, intermediate and routine care units, as well as pharmacy, laboratory and surgery charges were converted to costs using ratios of costs to charges.

Comparing all patients who had ADEs with controls, length of stay was 2.2 days longer for patients (P=.04), total charges were $6341 higher for patients (P=.04), and total costs were $3244 higher for patients (P=.04). Differences were even greater for patients with preventable ADEs compared with controls: length of stay was 4.6 days longer for patients (P=.03), total charges were $11 524 higher for patients (P=.06), and total costs were $5857 higher for patients (P=.07). The costs associated with preventable ADEs were almost twice as high as the costs for the full set of ADEs.

Classen et al85 report a case control study to estimate the excess length of stay, extra costs, and mortality attributable to ADEs in hospitalised patients where controls were matched to cases on primary discharge diagnosis related group (DRG), age, sex, acuity, and year of admission; varying numbers of controls were matched to each case. Matching was successful for 71% of the cases, leading to 1580 cases and 20 197 controls. The unmatched case patients had higher mortality, acuity score, more severe
ADEs, and more drug exposures, but the causal drugs and types of ADEs did not differ from the cases. Cost outcomes were determined from a transaction-based microcosting system.

In the analysis of the matched cases, a linear regression model for total cost of hospitalisation that controlled for severity of illness, several DRGs, sex, and age, estimated that the mean additional cost of an ADE was $2262.

Nordgren et al. also used a matched case-control design to evaluate excess length of stay and costs associated with all types of errors, including falls and surgical mishaps. The mean LoS for 300 cases was 10.8 days, and the mean LoS for the 300 matched controls was 6.8 days (mean difference was 4.0 days (p < 0.001), 59% longer stays than the controls). The mean total variable cost for the 300 cases was $8,687, and the mean total variable cost for the 300 matched controls was $6,276. The mean difference was $2,411 (p = .016), which is consistent with the cost estimates reported by Bates et al.23

Schneider et al. estimated the costs of different types of medication errors, including errors requiring extra laboratory tests or treatment without an increased LoS ($95 to $227); errors prolonging length of stay ($2,596); and errors resulting in near-death experience ($2,640).

Douglas & Larrabee present a range of cost estimates as part of a presentation on the use of bar coding, for which information on the source of the estimates were not identified. The Joint Commission on Accreditation of Healthcare Organisations (JCAHO) reported cost estimates of $2,000 for an ADE (excluding malpractice), whilst the Leapfrog Group (comprising more than 170 companies and organizations that buy health care in the US) reported that 1 medication error costs $10 and that 1 ADE costs $2,000. The CA HealthCare Foundation is reported to have defined the cost of a preventable ADE as $5,000.

4.3.1 ADE treatment cost summary

The range of identified mean cost estimates for all ADEs is quite narrow, varying from $2,000 to around $3,300. However, the medication errors analysis is concerned with preventable ADEs, for which only Bates et al. present separate cost estimates that show the estimated mean cost of preventable ADEs to be double the cost of the full set of ADEs. Separate costs are estimated for preventable ADEs that are assumed to result in no addition inpatient stay (significant ADEs) and those that are assumed to require an
additional period of inpatient care (serious/severe/life threatening ADEs), which are presented in Table 4.4.

The range of cost estimates for a significant preventable ADE that did not result in an increased LoS is taken directly from Schneider et al\(^{87}\). The point estimate cost of a serious or worse preventable ADE is that presented by Bates et al\(^{23}\) ($5,857), which when converted to UK sterling using the relevant PPP for the year of publication\(^{80}\), followed by uprating the cost from the year of publication to 2004 values,\(^{89}\) is £3,894. A range of £1,000 to £5,000 is specified based on the reported cost estimates.

A range of costs for the correction of identified medication errors is also specified, based on the estimated cost presented by the Leapfrog group, though the range does include a zero cost estimate.

Table 4.4  Cost parameters for preventable ADEs

<table>
<thead>
<tr>
<th>Cost parameter</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detected medication errors</td>
<td>£0 - £6</td>
</tr>
<tr>
<td>Significant (non-increased LoS) preventable ADEs</td>
<td>£65 - £150</td>
</tr>
<tr>
<td>Serious or worse (increased LoS) preventable ADEs</td>
<td>£1,000 - £5,000</td>
</tr>
</tbody>
</table>

4.4  Efficiency savings

Efficiency savings describe cost savings that are unrelated to the occurrence of medication errors. Oren et al\(^{90}\) reviewed the effect of computerised physician order entry (CPOE), automated dispensing machines (ADMs), bar coding and computerised medication administration records (CMARs) on medication errors and ADEs. Efficiency savings were reported only for CPOE systems. A before-and-after study found that CPOE reduced costs for antibiotic agents by an average of $81 per course. Another before- and-after study found that costs for levofloxacin decreased from $231,416 to $87,972 for intravenous preparations and from $50,042 to $33,003 for oral preparations. A controlled study found that CPOE decreased vancomycin use with projected savings of $22,500 to $90,000 per year. Another study found that when physicians overrode the CPOE system, the mean costs increased from $102 to $427. One controlled time and motion study found that CPOE reduced hospital costs by 13.1%.
Walker & Jackson\textsuperscript{91} present quarterly spending on antibacterials to be around £3 million across 16 reporting hospitals in the UK over 1997 and 1998. This corresponds to an annual cost of around £0.75 million per hospital. A range of efficiency savings due to the implementation of CPOE are based on a reduction of between 10\% and 20\% of the total costs of antibacterial therapies.

Meyer et al\textsuperscript{92} measured the impact of bar-code technology on the costs of drug dispensing (i.e. within the pharmacy rather than at the administration stage), incorporating the costs of applying bar-codes to unit dose packages; time to fill patient cassettes; time to verify patient cassettes; time to process patient charges and credits; accuracy of cassette verification; and time to correct dispensing errors. The results showed a total time saving per dose of 1.52 seconds with a workload shift from professional to technical personnel and improved accuracy of the cart-fill process.

It is assumed that the savings noted by Meyer et al may also occur with the set-up of a bar coding administration system. On the basis of the 1.52 second saving per order, and the estimated 6 million seconds that a pharmacist works each year, approximately 4 million orders would require processing in order to free up the opportunity costs of a pharmacist involved in order checking. As the estimated number of prescription orders filled in a 400-bed hospital is 162,000, a bar coding system would have to be in place for 24 years to achieve such efficiency savings. It is unlikely that such a hospital would observe any real savings, and so no efficiency benefits are estimated for a bar coding system. The assumed range of efficiency savings for CPOE is presented in Table 4.5.

### Table 4.5 Efficiency savings estimates

<table>
<thead>
<tr>
<th>Category</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPOE annual efficiency savings</td>
<td>£75,000 - £150,000</td>
</tr>
</tbody>
</table>

4.5 Health benefit impacts

The monetary value of preventing the impact of ADEs on the health of affected patients may be described using a variety of methods. Firstly, data are available from the NHS Litigation Authority (NHSLA) describing the litigation payments to patients who have experienced adverse health consequences as a result of health service error. Secondly, the monetary value of alternative types of ADEs may be ascertained directly using
survey techniques that assess the amount a person is willing to pay (WTP) to prevent an event. Thirdly, the health effects of ADEs may be described in terms of a generic measure of health, such as QALYs (that describe the morbidity and mortality effects of health conditions), which can then be converted to monetary values using implied values for units of the measure. In the case of QALYs, the National Institute for Clinical Excellence is thought to use a value of between £20,000 and £30,000 per QALY gained\(^9^3\), though this value may be uprated to reflect public preferences for the prevention of health impacts caused by errors in the health service\(^8^4\).

As inputs to the error frequency model, it is necessary to estimate monetary values for the three severity categories of preventable ADEs that are described in the model. These categories are defined as:

**Significant**: resulted in temporary harm to the patient and required intervention

**Serious**: resulted in temporary harm to the patient and required initial or prolonged hospitalisation

**Severe, life threatening, or fatal**: resulted in permanent patient harm, required intervention to sustain life, or contributed to a patient’s death.

The general nature of the described severity categories meant that no relevant data sources describing monetary values based on willingness to pay were identified. Likewise, direct estimates of the QALY effects of such severity categories were not forthcoming. Section 4.5.1 describes a set of simplistic assumptions that inform rough estimates of the QALY effect. The use of data describing payments made by the NHSLA following medication errors are presented in section 4.5.2.

### 4.5.1 QALY effects of medication errors

No relevant data estimating the utility effect of the broadly defined severity categories were identified. Very approximate estimates of the QALY impact may be made by assuming a utility decrement for each category and an accompanying duration of effect. The utility decrement describes the reduction in the quality of life of a patient as a result of an ADE, a utility decrement of 0.1 indicates a 10% reduction in utility relative to perfect health. If patients’ health is assumed to be less than perfect in the absence of an ADE, the utility decrement of 0.1 describes a greater relative decline, for example, if pre-ADE utility is 0.5 a utility decrement of 0.1 represents a 20% decline in utility.
The monetary values of the QALY effects are estimated by multiplying the estimated QALY loss by the value of a QALY implied by NICE (£20 - £30,000). Table 4.6 presents some assumptions defined by the research team.

Table 4.6 describes the assumptions behind the range of monetary values for each of the three forms of ADE. The ranges specified for significant, and serious ADEs are based on discussions within the research team. The range for severe, life threatening, or fatal ADEs are also defined by the research team, though they are also informed by study of preventable deaths occurring due to medical errors (including errors occurring across the broader spectrum of medical care, e.g. including timely diagnosis) that also assessed the likelihood of death in the absence of the error, and the patients' underlying short-term prognosis.¹¹³ Hayward and Hofer found that when reviewers rated a death as at least possibly preventable, the estimated probability that these patients would have left hospital alive was 20% (95% CI, 12%-27%). For deaths identified as definitely or probably preventable, the mean estimate of the likelihood that these patients would have left the hospital alive given optimal care was 43% (95% CI, 35%-51%). These cases inform our estimates of the lower bound monetary value for severe ADEs.

Table 4.6 Assumed QALY-based monetary valuations of the preventable ADE severity categories

<table>
<thead>
<tr>
<th>Significant: resulted in temporary harm to the patient and required intervention</th>
<th>Utility decrement</th>
<th>0.1</th>
<th>0.2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effect duration</td>
<td>3 days</td>
<td>14 days</td>
<td></td>
</tr>
<tr>
<td>QALY value</td>
<td>£20,000</td>
<td>£30,000</td>
<td></td>
</tr>
<tr>
<td>Monetary value</td>
<td>£16</td>
<td>£230</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Serious: resulted in temporary harm to the patient and required initial or prolonged hospitalisation</th>
<th>Utility decrement</th>
<th>0.2</th>
<th>0.4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effect duration</td>
<td>14 days</td>
<td>56 days</td>
<td></td>
</tr>
<tr>
<td>QALY value</td>
<td>£20,000</td>
<td>£30,000</td>
<td></td>
</tr>
<tr>
<td>Monetary value</td>
<td>£153</td>
<td>£1,841</td>
<td></td>
</tr>
</tbody>
</table>
Severe, life threatening, or fatal: resulted in permanent patient harm, required intervention to sustain life, or contributed to a patient's death.

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>0.3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Utility decrement</td>
<td>1</td>
<td>0.3</td>
</tr>
<tr>
<td>Effect duration</td>
<td>1 year</td>
<td>20 years</td>
</tr>
<tr>
<td>QALY value</td>
<td>£20,000</td>
<td>£30,000</td>
</tr>
<tr>
<td>Monetary value</td>
<td>£20,000</td>
<td>£180,000</td>
</tr>
</tbody>
</table>

4.5.2 NHS litigation costs of medication errors

A dataset describing financial claims made against the NHS for health effects experienced as a result of alleged medication errors was obtained from the NHSLA. The dataset contains 655 cases in which a medication error was alleged to have resulted in injury to a patient. To inform the valuation of the health effects of medication errors, only those cases that were closed (i.e. had been settled) were included. After excluding all closed cases in which the claim value was £0, which were assumed to indicate that the case was not proven, the number of cases reduced to 251.

A short description of the error and the resulting injury is given for each case, which were qualitatively reviewed to identify ranges for the litigation costs for each of the three severity categories. The payouts ranged from £17 to over £0.5 million, though there seems to be little consistency, for example, the prescription of a wrong dose of phenobarbitone resulted in a payment of £140, whilst a negligent injection of phenytoin that resulted in scarring to a patient’s hand was awarded £194,000. These inconsistencies may be due to the limited description provided for some of the cases.

The lowest payment made for a fatality was £387 in 1996, in which a diagnosis of bacterial endocarditis was made, high dose antibiotics did not improve the condition, the patient was transferred for mitral valve replacement and subsequently died. The highest payment for a fatality was £317,009 in 1998, which was due to medication errors from dealing with gall stones/bile duct problems.

Given the inconsistencies in the database and difficulties in linking injuries to the defined categories of injury, the payments were arranged in order and the payments at a range
of percentiles were record, which are presented in Table 4.7. Ranges for each of the three ADE severity categories are specified in Table 4.8, based on the reported percentiles.

Table 4.7  Claim payments at different percentiles of the NHSLA claims database for closed medication errors payments, excluding £0 settlements

<table>
<thead>
<tr>
<th>Percentile</th>
<th>Claim</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.01</td>
<td>£145</td>
</tr>
<tr>
<td>0.05</td>
<td>£326</td>
</tr>
<tr>
<td>0.1</td>
<td>£750</td>
</tr>
<tr>
<td>0.2</td>
<td>£1,951</td>
</tr>
<tr>
<td>0.3</td>
<td>£2,812</td>
</tr>
<tr>
<td>0.4</td>
<td>£4,300</td>
</tr>
<tr>
<td>0.5</td>
<td>£6,625</td>
</tr>
<tr>
<td>0.6</td>
<td>£13,242</td>
</tr>
<tr>
<td>0.7</td>
<td>£21,000</td>
</tr>
<tr>
<td>0.8</td>
<td>£40,169</td>
</tr>
<tr>
<td>0.9</td>
<td>£89,269</td>
</tr>
<tr>
<td>0.95</td>
<td>£146,647</td>
</tr>
<tr>
<td>0.99</td>
<td>£373,088</td>
</tr>
</tbody>
</table>

Table 4.8  Percentile-based ranges for the value of alternative severities of preventable ADEs

<table>
<thead>
<tr>
<th>ADE severity</th>
<th>Value range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Significant</td>
<td>£145 - £1,951</td>
</tr>
<tr>
<td>Serious</td>
<td>£2,812 - £13,242</td>
</tr>
<tr>
<td>Severe/life threatening/fatal</td>
<td>£21,000 - £373,088</td>
</tr>
</tbody>
</table>
4.5.3  *Summary of health benefit impacts*

The range of monetary values estimated for the three ADE severity categories vary considerably according to the estimation methods used. For the first two categories, the NHSLA-based estimates are substantially higher than the estimates based on assumed QALY effects, whilst the QALY effect approach estimates higher values for the most severe category. Both methods have merit. The QALY approach provides an explicit representation of the assumptions made, which can be accepted (or rejected) by users. The NHSLA estimates are based on real data describing judgements that have been made over the value of medication error induced events. As such, the broadest range possible is specified for each severity category based on both approaches, which is presented in Table 4.9.

Table 4.9  Combined ranges of the monetary value of preventable ADE health effects

<table>
<thead>
<tr>
<th>ADE severity</th>
<th>Value range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Significant</td>
<td>£16 - £1,951</td>
</tr>
<tr>
<td>Serious</td>
<td>£153 - £13,242</td>
</tr>
<tr>
<td>Severe/life threatening/fatal</td>
<td>£20,000 - £200,000</td>
</tr>
</tbody>
</table>
Chapter 5  Expert elicitation: parameter estimation

5.1  Introduction

In this chapter we report on a two-day expert elicitation workshop. The objective of the workshop was to investigate the feasibility of using expert elicitation in a medication error context, and to potentially inform values for specific input parameters in the medication errors model that were not directly informed by the literature and to interpret data of particular uncertainty.

Specifically, the workshop assessed two broad categories of medication error parameters. On day 1, the group were asked to estimate medication error frequency and error detection rate parameters at different points in the medication pathway. On the second day, the focus was on the estimation of the effectiveness of alternative medication error interventions, with respect to how they impacted on the error frequency rates, or detection rates, at different points in the medication pathway.

At the time of the expert elicitation workshop, the decision to restrict the scope of the project to the medication process in secondary care had not been taken and so the workshop covered medication errors across both primary and secondary care. Given the subsequent concentration on secondary care, only the elicitations relating to secondary care are reported in this chapter. The additional elicitations covering medication errors occurring during the medication process in primary care are reported in Appendix 1.

The parameters presented to the experts were defined with respect to the medication pathway for patients diagnosed with depression who require inpatient care. The research team decided to elicit values for specific events (e.g. It is assumed that the correct prescription of phenelzine is made available to the administering health professionals on the ward. The uncertain parameter is the proportion of occasions in which the wrong drug is intended to be administered to the patient.), as the estimation of general events such as wrong dose dispensing errors was considered too abstract, and therefore too difficult for experts to assign informed values.

The members of the expert group are acknowledged in Appendix 1, but the positions and disciplines represented included hospital physicians, general practitioners, nurses, hospital and community pharmacists, a pharmacy specialist, and human factors specialists. Two members of the group attended from the US, and provided an alternative perspective on the issues addressed.
5.2 **Motivation**

At the beginning of the workshop, the group were provided with brief background presentations describing the general objectives and process of the prospective hazard and improvement analysis (PHIA), and the developed medication pathways for patients with depression (as described in Chapter 2). Relevant definitions and boundaries for the workshop were defined during these stages. A medication error was defined as ‘an unintended deviation from best practice’, and patient adherence was left out of the scope, i.e. it was assumed that if a patient does not detect a medication error, that they will take the medication.

5.3 **Training**

The experts were given a short presentation to explain the elicitation process. The use of subjective probability distributions for describing uncertainty was discussed, and the distinction between the subjective and frequentist interpretations of probability was highlighted. It was emphasised that the object of the exercise was to quantify how uncertain the experts were about the unknown model parameter values rather than simply to obtain estimates for the parameters. Well-known psychological biases in expert judgment such as overconfidence and anchoring effects were also explained. Finally, a practice elicitation exercise was used in which the experts were asked to consider their uncertainty about the proportion of cannabis smokers in the UK population. This was to ensure that experts fully understood the procedure for eliciting a probability distribution.

5.4 **Eliciting a distribution**

For each uncertain parameter, the experts were asked to consider the following:

Their most likely value for the parameter (interpreted to be the mode of the expert’s distribution).

Their 5th percentile, i.e. a value l such that the experts believed there was only a 5% chance that the parameter would be less than l.

Their 95th percentile, i.e. a value u such that the experts believed there was only a 5% chance that the parameter would exceed u.

A probability distribution was then fitted to these three values. Since an entire probability distribution was selected on the basis of only three probability judgments, additional features of the fitted distribution were then fed back to the experts, to see if the fitted
distribution was an acceptable representation of their beliefs. Information to conform the implied probability distributions for the parameters of interest were presented to the experts elicited in various forms, which are described below:

1) 0.1st percentile. This suggests that the experts believed there is only a 1 in 1000 chance that the true proportion is less than (approximately) 0.47. The group were told that they should feel very confident that the true proportion is higher than this value. If not, then there is either a deficiency with the fitted distribution, or they should think again if the 5th percentile should be as high as 0.6.

2) 99.9th percentile. This suggests that the experts believe that there is only a 1 in 1000 chance that the true proportion is greater than (approximately) 0.92. Similar considerations apply as in the 0.1st percentile.

3) Equivalent sample. The stated uncertainty is comparable with observing (approximately) 24 out of 33 errors successfully detected.

4) 50% interval. This suggests the experts are only 50% certain that the true proportion lies in the interval [0.69, 0.79], i.e., it’s just as likely to lie inside this interval as outside the interval. If it is felt considerably more likely to lie inside [0.69, 0.79], then this may be due to deficiencies in the fitted distribution, or the experts may feel that the original judgments for the 5th and 95th percentiles were too conservative.

5.5 Results: error frequency and detection rate parameters

The first set of results is presented for the values elicited around the occurrence and detection of medication errors in the absence of specific interventions aimed at reducing the impact of medication errors. The experts did not feel able to make probability judgments for all the parameters of interest. We first present the two secondary care based parameters for which the experts were able to define probability distributions, and then discuss the difficulties encountered with the remainder.

5.5.1 Elicited parameters

1) Parameter description:

It is assumed that the correct prescription of phenelzine is made available to the administering health professionals on the ward. The uncertain parameter is the proportion of occasions in which the wrong drug is intended to be administered to the patient.
Table 5.1  Elicitation results: potential wrong drug administration error

<table>
<thead>
<tr>
<th>Elicited Judgements</th>
<th>Feedback</th>
</tr>
</thead>
<tbody>
<tr>
<td>Most likely</td>
<td>5th percentile</td>
</tr>
<tr>
<td>0.003</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Figure 5.1  Elicited probability distribution describing uncertainty about the proportion of occasions in which the wrong drug is intended to be administered

2) Parameter description:

The wrong drug is intended to be administered. The uncertain parameter is the proportion of occasions in which the error is detected by the patient or their family.

Table 5.2  Elicitation results: wrong drug administration error detected by patient or family prior to administration

<table>
<thead>
<tr>
<th>Elicited Judgements</th>
<th>Feedback</th>
</tr>
</thead>
<tbody>
<tr>
<td>Most likely</td>
<td>5th percentile</td>
</tr>
<tr>
<td>0.05</td>
<td>0.01</td>
</tr>
</tbody>
</table>
Figure 5.2  Elicited probability distribution describing uncertainty about the proportion of potential wrong drug administration errors detected by patient or family

5.5.2  Unsuccessful elicitations

The experts did not feel comfortable making probability judgments for all the parameters. Typically, the parameters in question were frequencies of events that were considered to occur very rarely. An example of such a parameter was:

“Given an intended decision is to prescribe phenelzine (or medication from same class of drugs), What is the probability that an alternative class of drug is prescribed?”

The experts were able to consider an upper limit for this parameter, but did not feel they could suggest an appropriate 5th percentile. This difficulty is to be expected for rare events. In judging any of the uncertain proportions in question, the experts may consider how many instances of the event they are able to recall personally, and so if the event only occurs very rarely, they will have few instances available to them to consider. Hence the experts may feel confident in asserting that the true proportion is less than some specified value, but may have difficulty in considering lower limits for their range.

5.6  Results: medication error intervention effectiveness

The second part of the elicitation workshop was assigned to the discussion of the effectiveness of three specific medication errors interventions, Computerised Physician Order Entry (CPOE) systems, bar coding for inpatient medication administration, and the employment of practice pharmacists in primary care and ward pharmacists in secondary care. Each intervention was considered separately and each session began with a
discussion around the specification of the interventions, which are described in the following sections.

5.6.1 *Computerised Physician Order Entry*

This section began with a generalised discussion about CPOE systems, which raised a number of issues about the detail and implementation of such systems, and hospital medication processes, that may affect their effectiveness in reducing medication errors. One member of the group had introduced a computerised system at his pharmacy but the system was currently suspended.

The issues raised included:

- consideration of the prescriber (nurses, residents, medical students)

- the use of a standardised medical dictionary

- alerting systems, for example, 3-tiers of alerts were suggested: 1) hard alerts; 2) asks for coded reason to go forward; 3) for information

- worries that excessive alerts lead to some alerts being turned off that may have very harmful end results to a patient.

- differential requirements for primary and secondary care systems, and whether primary care system integrates with the secondary care system.

- the level of decision support included, such as the attachment of guidelines.

To inform the elicitation process it was agreed that the assessed CPOE system was ‘well-designed for the needs of the system’ and that 24-hour IT support, updates, and checks for allergies and drug interactions were included.

5.6.2 *Bar coding interventions*

Bar coding involves the provision of a bar-coded wristband to patients, and a matching bar code to medications intended for each patient, which are both scanned by a nurse with a wireless mobile computer before administering a medication to check that dispensed medications are administered to the correct patient. Initial discussion centred on potential advantages of radio frequency identification (RFID) as a technologically superior alternative to bar coding. RFID tags are microchips that act as transponders (transmitters/responders). When a transponder receives a certain radio query, it responds by transmitting its unique ID code.
5.6.3  *Ward pharmacists in secondary care*

The employment of additional pharmacists to assist at the prescription stage of the medication pathway, including the provision of additional information to patients was considered a relevant intervention in both the primary and secondary care settings. Discussions around the definition of such interventions included the distinction between implicit and tacit knowledge, and the importance of relationships between people in different roles, i.e. pharmacists, nurses, doctors.

5.6.4  *Medication error interventions elicitation*

The experts did not feel able to make probability judgments about the effectiveness of any intervention, and so quantitative elicitation was not possible. One difficulty was that regarding interventions, the experts were being asked to speculate on how a change to current practice might impact on patient safety, and so by definition there was little or no directly relevant on which to base any judgments on. The experts stated at which points in the pathway they thought the interventions would and would not impact, and these judgements were used to inform notional distributions that were chosen to represent the possible effectiveness of the interventions in the main analysis (as described in Chapter 6).

5.7  *Discussion*

The workshop illustrated clearly that elicitation is a difficult and time-consuming process. The experts were cooperative and willing to make probability judgments in some cases, but did not feel able to provide reliable assessments in all cases. Most difficulty was experienced when considering the frequency of rare events, in particular, trying to differentiate between error frequency probabilities for which low probabilities were predicted for most such events. The group initially provided estimates of ‘around 1 in a 1,000’ for events that they considered rare, though on reflection they realised that given the throughput of prescription orders in the NHS even such seemingly small proportions would result in large absolute numbers of errors. The lack of differentiation between numbers that were now considered large was thought to be problematic.

During a discussion between the health professionals about the likelihood of error, which was generally considered to be small, one of the human factors experts intervened to describe evidence from other industries that demonstrated much higher probabilities of error for similar tasks, for example, checking procedures. This intervention was accepted...
by the health professionals, though it might have served to further reduce the confidence they had in estimating the presented parameters.

However, when data are unavailable to infer an appropriate probability distribution for an uncertain parameter, expert elicitation remains the only option for dealing with this parameter uncertainty. Some general observations and recommendations are as follows:

1) It is important to recognise that experts will find elicitation difficult regardless of their subject matter expertise.

2) The experts should be given advance notice of the parameters that they are being asked to consider, with the opportunity to identify any additional information that would facilitate the elicitation prior to the elicitation.

3) Motivation and training are essential. In most cases, experts will be not be familiar with the concept of providing probability distributions to represent their own uncertainty. It is also important that the experts understand the need for eliciting their beliefs, and are aware of how the resulting distributions will be used.

4) It should be recognised that elicitation is an inherently imprecise process, and that it is important to investigate the robustness of any conclusions from the decision-modelling analysis to the choice of elicited distributions.
Chapter 6   Prospective hazard and improvement analysis results

6.1   Introduction

The main focus of this chapter is the presentation of the results of the medication errors model around the potential effectiveness, and cost-effectiveness of three interventions aimed at reducing medication errors: computerised physician order entry (CPOE); pharmacists on ward rounds; and bar coding systems at administration. The clinical input parameters describing error incidence, detection, and severity rates for the model are presented in Chapter 3, and the cost input parameters are described in Chapter 4. The final set of input parameters describing the potential effectiveness of the specified interventions are presented in the following sections of this chapter. The subsequent sections describe the baseline estimates of the predicted number of ADEs and their associated costs, followed by the predicted impact of the alternative interventions in reducing errors and costs.

6.2   Intervention effectiveness in reducing medication errors

The model incorporates the effectiveness of three interventions – computerised physician order entry (CPOE); pharmacists participating on ward rounds; and bar coding systems at administration – by describing their impact on the occurrence of errors, and on the detection of errors. A relative risk (RR) range is specified for each intervention for each of the 12 error types at the stage in the medication pathway at which the error is committed (error point) that indicates the possible effectiveness of each intervention in reducing errors at error points. RRs are also specified for each error type at the subsequent stages of the medication pathway at which the errors could be detected (detection point) representing the possible changes in detection rates at detection points. The estimated ranges are loosely based on the findings from the expert elicitation workshop that is reported in Chapter 5. Table 6.1 presents the defined impact of the three interventions at each stage in the medication process, and the following sections describe the basis for the defined ranges.

6.2.1   CPOE effectiveness parameters

CPOE may have a significant impact on knowledge-based errors, such as through the automatic display of known allergies and contra-indications (due to ongoing medication) that are enabled by the computerised linkage of patient records and the prescribing system, but also through the accompanying provision of a decision support system
(DSS) that has the potential to inform prescribers of the most up-to-date prescribing information for a patient's condition. However, the defined scope for the current analysis (as defined in section 1.3) excludes knowledge-based errors so the predicted cost-effectiveness of CPOE is likely to be underestimated.

The evaluated CPOE system is defined as ‘well-designed for the needs of the system’ and is assumed to be electronically linked to the pharmacy. This definition does not imply that a CPOE system can only have positive effects in reducing the number of medication errors that reach the patient. Anomalies are likely to remain in most systems that will cause unforeseen errors, as demonstrated by Koppel et al\textsuperscript{95} who identified new errors occurring as a result of house staff relying on CPOE systems for dosage information and delays in ordering induced by the system.

Within the defined scope, the main effect of CPOE is assumed to be on the rate at which medication errors are prevented at the prescription stage. Some may define the action of CPOE as detecting prescription errors, though the effect is the same. CPOE is assumed to reduce wrong dose, route, and frequency prescription errors by between 28% and 95%, which is based on the predicted decrease in preventable ADEs as reported by a U.S. Department of Health and Human Services report\textsuperscript{96}. CPOE is assumed to have a lesser effect on the prescription of an unintended drug (wrong drug prescription errors), due to the potential for selecting a similar sounding drug name.

CPOE is assumed to have some impact on the incidence of dispensing errors due to the replacement of handwritten prescription orders that reduces the risk of misinterpretation. A small reduction in the risk of administration errors is also assumed as nurses may be more likely to be aware of the prescribed medication if it was entered on a computerised system.

Detection rates may increase, particularly at the dispensing stage, due to the improved legibility of the order form.

6.2.2 Pharmacists on ward rounds effectiveness parameters

The increased availability of senior pharmacists on wards may impact on multiple points in the medication pathway, including the accuracy of prescriptions (preventing prescription errors), identifying prescription errors due to increased awareness of patients’ condition, monitoring and educating nurses who administer medications. Broad
ranges for each of these potential areas of impact are specified, though only positive effects are assumed (i.e. reduced errors and increased detection).

The impact on dispensing and administration errors is assumed to be lower as the ward pharmacist may make fewer direct interventions at these stages of the medication pathway (pharmacists are assumed to be on the ward only in the morning, and they will not handle all prescriptions coming from their ward). The increased RRs for detection of errors indicates that pharmacists may increase the detection of dispensing errors via improved clarity of prescription orders going to the pharmacy that means orders are less likely to be misinterpreted within the pharmacy process. The limited likelihood of improved error detection at the administration stage with increased numbers of ward pharmacists (RR 1 – 1.2) are based on assumptions around the possible educational role that pharmacists may play in improving the detection rate of nurses.

6.2.3 Bar coding effectiveness parameters

Bar coding is primarily intended to prevent errors occurring at the administration stage of the medication pathway, by identifying whether the correct medication has been selected for each patient. A minimum RR of 0.3 (i.e. a 70% reduction) is assumed, though the possibility of no impact is also included (a RR of 1) as potential ‘get rounds’ have been identified that may limit the effectiveness of a bar coding intervention, for example, nurses gathering the identification bands for all patients and cross matching medications and patients at the administration trolley rather than at the bedside. Bar coding also requires the attachment of bar codes to medications, which may also improve the accuracy of the dispensing process. The differential minimum RRs applied to the different types of dispensing errors reflects the mechanism by which bar coding is assumed to act, for example, the identification of the correct drug at the correct strength is likely to be improved most as these characteristics involve a single scan, whilst wrong quantity errors are less likely to be prevented because they may involve more manual checking. Wrong label errors are assumed to be unaffected by bar coding.

Bar coding may actually make the detection of prescription and dispensing errors at the administration stage less likely, as nurses may be more likely to assume a medication is correct because it has been identified as the correct medication by the bar coding system, i.e. a bar coding system increases confidence in parts of the system that are unaffected by the intervention. A minimum RR of 0.9 reflects a relatively small decrease in detection rates at the administration stage.
Table 6.1  Relative risk ranges for error incidence and detection

<table>
<thead>
<tr>
<th></th>
<th>CPOE</th>
<th>Pharmacists</th>
<th>Bar coding</th>
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<tr>
<td></td>
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<td>Upper RR</td>
<td>Lower RR</td>
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<tr>
<td>Prescription error probabilities</td>
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</tr>
<tr>
<td>Wrong drug</td>
<td>0.5</td>
<td>1</td>
<td>0.5</td>
</tr>
<tr>
<td>Wrong dose</td>
<td>0.05</td>
<td>0.72</td>
<td>0.5</td>
</tr>
<tr>
<td>Wrong route</td>
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<td>0.72</td>
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</tr>
<tr>
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<td>0.72</td>
<td>0.5</td>
</tr>
<tr>
<td>Dispensing error probabilities</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Wrong drug</td>
<td>0.7</td>
<td>1</td>
<td>0.65</td>
</tr>
<tr>
<td>Wrong strength</td>
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<td>0.65</td>
</tr>
<tr>
<td>Wrong quantity</td>
<td>0.7</td>
<td>1</td>
<td>0.65</td>
</tr>
<tr>
<td>Wrong label</td>
<td>0.7</td>
<td>1</td>
<td>0.65</td>
</tr>
<tr>
<td>Administration error probabilities</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Wrong drug</td>
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<td>1</td>
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<td>Wrong dose</td>
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<td>0.65</td>
</tr>
<tr>
<td>Wrong route</td>
<td>0.9</td>
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<td>0.65</td>
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<tr>
<td>Wrong frequency</td>
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<td>0.65</td>
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<td>Prescription error detection at dispensing probabilities</td>
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<td></td>
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<tr>
<td>Wrong drug</td>
<td>1</td>
<td>1.2</td>
<td>1.2</td>
</tr>
<tr>
<td>Wrong dose</td>
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<td>1.2</td>
<td>1.2</td>
</tr>
<tr>
<td>Wrong route</td>
<td>1</td>
<td>1.2</td>
<td>1.2</td>
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<tr>
<td>Wrong frequency</td>
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<td>1.2</td>
<td>1.2</td>
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<tr>
<td>Prescription error detection at administration probabilities</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Wrong drug</td>
<td>1</td>
<td>1.2</td>
<td>1</td>
</tr>
<tr>
<td>Wrong dose</td>
<td>1</td>
<td>1.2</td>
<td>1</td>
</tr>
<tr>
<td>Wrong route</td>
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<tr>
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<td>Dispensing error detection at administration probabilities</td>
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<tr>
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<tr>
<td>Wrong drug</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Wrong dose</td>
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</tr>
<tr>
<td>Wrong route</td>
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<tr>
<td>Wrong frequency</td>
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</tr>
</tbody>
</table>
6.3 **Model calibration results**

The process of calibration is described in section 3.5, which involves the comparison of the numbers of preventable ADEs (by error type and medication stage) predicted by a large number of sets of input parameters (25,000) with observed ranges for each output parameter. A measure of accuracy was defined for each input parameter set that was based on the mean difference between the predicted and observed range of values across the 12 output parameters (preventable ADEs by error type and stage of origination).

The first stage of the calibration process involved the assessment of the mean differences between the predicted and observed ranges for each of the 12 output parameters, across the 25,000 sampled input parameter sets. Based on the originally defined ranges for each of the input parameters, it was apparent that the differences between the predicted outputs and the observed outputs were greatest for the categories of preventable ADEs that originated at the administration stage of the medication pathway. The model predicted significantly higher rates of preventable ADEs that originated at the administration stage, such that the administration stage accounted for over 90% of all preventable ADEs. Table 3.23 in Chapter 3 reports observed distributions of preventable and potential ADEs among the different stages in the medication pathway. Bates et al\(^{68}\) present the only data for preventable ADEs, which shows that 36% originated at the administration stage. Other studies report distributions of potential ADEs\(^{27}\), and potential and preventable ADEs\(^{69}\); a maximum percentage of 48% of such events originating at the administration stage is reported.

The ranges specified for the input parameters involved in the estimation of preventable ADEs originating at the administration stage were re-assessed. The parameters include the rate of medication errors; the detection rate prior to administration; and the proportion of undetected errors that cause harm. The medication error rates were based on observed data and it was thought that these parameters should not be changed, as the other two categories of input parameters were not informed by observed data. As there was no empirical basis for either parameter category, it was decided to increase values for both sets of parameters. The original and revised parameter values are presented in Table 6.2. It was also decided to treat the ratio of OAEs to prescription orders as an uncertain variable, and a range of 7 to 10 OAEs per prescription order was specified.
The other category in which the predicted number of preventable ADEs was noticeably higher than the observed range was for wrong frequency prescription error preventable ADEs. Again, the error rates were not adapted as these estimates were based on observed data. Rather, the detection rates and ‘no harm’ proportions were amended to better fit the observed output data, as described in Tables 6.2 and 6.3.

Table 6.2  Original and revised values for error detection input parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Original values</th>
<th>Revised values</th>
</tr>
</thead>
<tbody>
<tr>
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<td></td>
<td></td>
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<td>Wrong drug</td>
<td>5-50%</td>
<td>10-30%</td>
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<tr>
<td>Wrong dose</td>
<td>5-50%</td>
<td>30-50%</td>
</tr>
<tr>
<td>Wrong route</td>
<td>5-50%</td>
<td>10-30%</td>
</tr>
<tr>
<td>Wrong frequency</td>
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<td>30-50%</td>
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<tr>
<td>Prescription error detection at administration probabilities</td>
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</tr>
<tr>
<td>Wrong drug</td>
<td>1-20%</td>
<td>10-30%</td>
</tr>
<tr>
<td>Wrong dose</td>
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<td>10-30%</td>
</tr>
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<td>Wrong drug</td>
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</tr>
</tbody>
</table>

Table 6.3  Original and revised values for ‘probability of NO harm’ input parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Original values</th>
<th>Revised values</th>
</tr>
</thead>
<tbody>
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<tr>
<td>Prescription wrong dose</td>
<td>80-99%</td>
<td>70-90%</td>
</tr>
<tr>
<td>Prescription wrong route</td>
<td>80-99%</td>
<td>50-70%</td>
</tr>
<tr>
<td>Prescription wrong frequency</td>
<td>80-99%</td>
<td>90-99%</td>
</tr>
<tr>
<td>Dispensing wrong drug</td>
<td>80-99%</td>
<td>96-99%</td>
</tr>
<tr>
<td>Dispensing wrong strength</td>
<td>80-99%</td>
<td>96-99%</td>
</tr>
<tr>
<td>Dispensing wrong quantity</td>
<td>80-99%</td>
<td>96-99%</td>
</tr>
<tr>
<td>Dispensing wrong label</td>
<td>80-99%</td>
<td>96-99%</td>
</tr>
<tr>
<td>Administration wrong drug</td>
<td>80-99%</td>
<td>98-99.9%</td>
</tr>
<tr>
<td>Administration wrong dose</td>
<td>80-99%</td>
<td>99-99.9%</td>
</tr>
<tr>
<td>Administration missed dose</td>
<td>80-99%</td>
<td>99.5-99.9%</td>
</tr>
<tr>
<td>Administration wrong rate</td>
<td>80-99%</td>
<td>99.5-99.9%</td>
</tr>
</tbody>
</table>
The model was re-calibrated using the revised input parameter ranges. The predicted outputs were much closer to the observed ranges, though the rate of wrong frequency administration ADEs remained high. It was decided, therefore, to revise the upper bound for the wrong frequency administration medication errors downwards from 4.8 per 1,000 orders (41.3 per 1,000 OAEs) to 4 per 1,000 orders (34.4 per 1,000 OAEs).

The final analysis produced a more even distribution of mean differences between the predicted and observed parameter values for the 12 output parameters, as presented in Table 6.4. The outputs from the model are presented as the weighted mean predictions for each of the 12 preventable ADE parameters. Weights are attached to each of the 25,000 input parameter sets representing the accuracy of the predicted outcomes relative to the defined ranges for each of the 12 output parameters, as described in section 3.5.

The calibration results show that the weighted mean predictions are within the specified range for 10 of the 12 output parameters. The only predictions lying outside the range is the rate of preventable ADEs that originate as wrong drug and wrong label dispensing errors. The relative difference is highest for the wrong label errors, though the absolute difference is only 0.018 per 1000 orders. The absolute difference for the wrong drug dispensing errors category is 0.004 per 1000 orders.
Table 6.4  Calibration results, observed and predicted preventable ADE rates per 1,000 orders

<table>
<thead>
<tr>
<th>Preventable ADEs</th>
<th>Observed range</th>
<th>Weighted predictions*</th>
<th>% Distance from range†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Minimum</td>
<td>Maximum</td>
<td></td>
</tr>
<tr>
<td>Prescription errors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wrong dose</td>
<td>0.025</td>
<td>0.68</td>
<td>0.33</td>
</tr>
<tr>
<td>Wrong drug</td>
<td>0.175</td>
<td>1.53</td>
<td>1.51</td>
</tr>
<tr>
<td>Wrong route</td>
<td>0.175</td>
<td>1.53</td>
<td>0.29</td>
</tr>
<tr>
<td>Wrong frequency</td>
<td>0.025</td>
<td>0.34</td>
<td>0.09</td>
</tr>
<tr>
<td>Dispensing errors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wrong drug</td>
<td>0.01</td>
<td>0.196</td>
<td>0.20</td>
</tr>
<tr>
<td>Wrong strength</td>
<td>0.01</td>
<td>0.196</td>
<td>0.09</td>
</tr>
<tr>
<td>Wrong quantity</td>
<td>0.006</td>
<td>0.14</td>
<td>0.04</td>
</tr>
<tr>
<td>Wrong label</td>
<td>0.004</td>
<td>0.112</td>
<td>0.13</td>
</tr>
<tr>
<td>Administration errors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wrong dose</td>
<td>0.011</td>
<td>0.32</td>
<td>0.09</td>
</tr>
<tr>
<td>Wrong drug</td>
<td>0.022</td>
<td>0.64</td>
<td>0.07</td>
</tr>
<tr>
<td>Wrong route</td>
<td>0.022</td>
<td>0.64</td>
<td>0.18</td>
</tr>
<tr>
<td>Wrong frequency</td>
<td>0.022</td>
<td>0.64</td>
<td>0.15</td>
</tr>
</tbody>
</table>

* the weighted predictions are the sum of the outputs for each iteration multiplied by the estimated weight for each iteration.
† the % distances from the range are the absolute differences between the weighted predictions and the upper or lower bound (whichever is nearest) as a percentage of the nearest bound.
6.4  Model analysis

Using the weighted sets of input parameters describing the incidence, detection, and whether an undetected error causes some level of harm, the analysis of the model involves the following steps:

1. A set of input parameters describing the incidence, detection, and whether an undetected error causes some level of harm is sampled according to their respective weights.

2. For each sampled set of input parameters, a set of error severity parameters and cost parameters are sampled from their respective distributions (as described in Chapter 3 and 4).

3. The baseline estimate of medication errors, preventable ADEs, and associated costs is estimated.

4. A set of RRs is sampled for each intervention in turn, and the revised number of medication errors, preventable ADEs, and costs is estimated for each sampled set of RRs.

5. The cost savings and monetary valuation of the health benefits due to the reduced medication error rate is estimated for each sampled set of input parameters for each intervention by subtracting the medication error costs for the intervention from the baseline medication error costs.

6. Steps 1 to 5 are repeated for 20,000 iterations, and probability distributions of the cost savings for each intervention are estimated by combining the results of 20,000 sampled sets of input parameters.

7. The net benefits of each intervention are estimated by subtracting the cost of the intervention from the cost savings. The net benefits are presented as probability distributions for different scenarios of the cost of the interventions.
6.5  Model results

The results of the medication errors model are presented in three sections. The first section describes the expected numbers of preventable ADEs with the three described interventions in place (individually, the combined implementation of the specified interventions is not considered) as well as in the base case scenario in which no additional medication error interventions are implemented. The second section describes the costs associated with the predicted medication errors and preventable ADEs. The third section describes the net benefits of the three interventions relative to no intervention, which incorporates the costs of implementing the interventions.

All of the above results are estimated in the context of a 400-bed hospital with approximately 162,000 prescription orders per year.

The results are presented using box and whisker plots, which are particularly useful for comparing the distribution of data across several groups. The box contains the middle 50% of the data (the interquartile range) and the horizontal line in the middle of the box represents the median value. The whiskers extend to the largest and smallest values excluding the outlying values. The outlying values are those values more than 1.5 box lengths from the upper or lower edges, and are represented as the dots outside the whiskers.[114]

6.5.1  Preventable ADEs

Figure 6.1 describes the expected numbers of preventable ADEs occurring in four scenarios relating to the presence or absence of the described interventions aimed at reducing medication errors. In the absence of the three described interventions, the model predicts that the median number of preventable ADEs occurring in a 400-bed hospital per year is around 450, whilst the interquartile range spans from just under 400 to around 500 per year. There are some outliers, but the expected range is between approximately 200 and 700 preventable ADEs per year.

The predicted impacts of CPOE and the increased use of ward pharmacists are similar, with the median numbers of preventable ADEs declining to around 300 in both cases, and the interquartile range approximately 250 and 350. The full range excluding outliers is predicted to be between 100 and 500 events per year. Bar coding is predicted to have a smaller effect on reducing preventable ADEs with the median event rate per year
being just under 400, with the interquartile range spanning 325 to 450. A larger range is also specified, from around 250 to 650.

Figure 6.1  Box plots for numbers of preventable ADEs occurring with and without alternative interventions aimed at reducing medication errors

![Box plots for numbers of preventable ADEs](image)

Plot numbers: 1 No intervention; 2 CPOE; 3 Ward pharmacist; 4 Bar coding. The results are estimated for a 400-bed hospital with approximately 162,000 prescription orders per year.

6.5.2 Cost effects of preventable ADEs

Three cost figures are presented, describing the direct health service cost effects, the monetary value of the health effects, and the combined aggregate costs due to preventable ADEs with and without alternative interventions aimed at reducing medication errors. Figure 6.2 presents the predicted levels of health service treatment costs due to preventable ADEs. In the base case scenario in which none of the three described interventions are implemented, the model predicts health service costs of around £1 to £1.5 million per year for a 400-bed hospital with approximately 162,000 prescription orders per year. There are some outliers at the top end of the range, but the expected annual cost is not likely to above £2.5 million.
Again, the predicted results for the impact of CPOE and additional ward pharmacists are similar, with the median costs decreasing to around £0.75 million with a narrow interquartile range. Excluding outliers, the upper end of the range is under £1.5 million in both cases. Bar coding is predicted to have a lesser impact, with a median cost of around £0.9 million and an interquartile range of £0.75 to £1.1 million. The upper end of the predicted costs of treating preventable ADEs is unlikely to rise above £2 million.

Figure 6.2  Box plots for health service treatment costs due to preventable ADEs with and without alternative interventions aimed at reducing medication errors

The y-axis scale is £millions, plot numbers: 1 No intervention; 2 CPOE; 3 Ward pharmacist; 4 Bar coding. The results are estimated for a 400-bed hospital with approximately 162,000 prescription orders per year.

Figure 6.3 describes the estimated monetary valuations of lost health due to preventable ADEs. It is immediately obvious that the predicted scale of these costs is of an order of magnitude higher than the estimated health service costs. In the base case scenario, the predicted median monetary value is £20 million, with an interquartile range of around £12 million to £26 million. The tail of the distribution of the predicted monetary values extends out to beyond £80 million, though the realistic range has an upper limit of £50 million per year.
The predicted median value of the health lost due to preventable ADEs reduces quite significantly to around £14 million with the implementation of either CPOE or additional ward pharmacists. The interquartile for both interventions has an upper bound below £20 million. Bar coding is less effective in reducing the value of lost health with median value around £17 million, with the interquartile range extending to around £22 million.

Figure 6.3  Box plots for monetary valuations of lost health due to preventable ADEs with and without alternative interventions aimed at reducing medication errors

Figure 6.4 presents the aggregate costs associated with preventable ADEs in the four scenarios. Given the size of the monetary values of the lost health attributable to preventable ADEs relative to the health service costs, the box plots are similar to the plots described in Figure 6.3.
Figure 6.4 Box plots for aggregate costs of preventable ADEs with and without alternative interventions aimed at reducing medication errors

The y-axis scale is £millions, plot numbers: 1 No intervention; 2 CPOE; 3 Ward pharmacist; 4 Bar coding. The results are estimated for a 400-bed hospital with approximately 162,000 prescription orders per year.

6.5.3 Net benefits of the medication error interventions

The net benefits of the three interventions are estimated by subtracting the costs of implementing and maintaining each intervention from the estimated reduction in the costs incurred due to preventable ADEs following the implementation of each intervention. The net benefits are estimated over a five year time horizon (discounted at 3.5% per annum) in order to incorporate costs and benefits beyond the first year of implementation, with two sets of results predicted for each intervention employing lower and upper estimates of the respective implementation and maintenance costs.

Figure 6.5 describes the six sets of net benefit estimates for the three interventions including only the health service cost savings, i.e. excluding reductions in the monetary valuations of the health effects of preventable ADEs. In scenarios 1, 2, and 3, which incorporate the lower cost estimates for the interventions, the plots show that CPOE has
the highest expected net benefits, followed by additional ward pharmacists, with bar coding predicted to provide the lowest return. All three interventions have a similar lower bound at which the interventions are predicted to produce small negative net benefits, i.e. cost savings lower than the costs of implementation and maintenance. Excluding outliers, the upper bound for the CPOE and additional ward pharmacists interventions is between £4 and £5 million, whilst the upper bound for bar coding is closer to £3 million.

If the upper estimates of implementation and maintenance costs are included, the results change significantly. CPOE becomes the least efficient intervention with almost no probability of producing positive net benefits. The results for the additional ward pharmacists and bar coding interventions are now similar with both expected to produce some positive net benefits based on the median value, with the lower bound of the interquartile range remaining positive. The lower bound of the range shows both have a small probability of producing negative net benefits.

Figure 6.5  Box plots for net benefits of interventions aimed at reducing medication errors (excluding monetary valuations of the health effects of preventable ADEs)

![Box plots for net benefits of interventions](image)

The y-axis scale is £millions, plot numbers: 1 CPOE (min intervention cost); 2 Ward pharmacist (min intervention cost); 3 Bar coding (min intervention cost); 4 CPOE (max intervention cost); 5 Ward pharmacist (max intervention cost); 6 Bar coding (max intervention cost). The results are estimated for a 400-bed hospital with approximately 162,000 prescription orders per year.
Figure 6.6 describes the net benefits of the three interventions including health service costs savings as well as reduced monetary valuations of the health effects of preventable ADEs. The net benefits are dominated by the estimated monetary valuations of the health effects of preventable ADEs, with the use of either the lower or upper estimates of the costs of implementation and maintenance having only a marginal effect on the estimated net benefits. These results show that both CPOE and additional ward pharmacists result in median predictions of net benefits of almost £30 million over a 5 year time horizon, with an upper interquartile range value approaching £50 million. The tail of the distribution of net benefits for CPOE is longer, with some predictions in the region of £200 million. The net benefits of a bar coding intervention are predicted to be lower, though still substantial with a median value of around £4 to £7 million depending on the cost of implementing the intervention.

Figure 6.6  Box plots for net benefits of interventions aimed at reducing medication errors (including monetary valuations of the health effects of preventable ADEs)

The y-axis scale is £millions, plot numbers: 1 CPOE (min intervention cost); 2 Ward pharmacist (min intervention cost); 3 Bar coding (min intervention cost); 4 CPOE (max intervention cost); 5 Ward pharmacist (max intervention cost); 6 Bar coding (max intervention cost). The results are estimated for a 400-bed hospital with approximately 162,000 prescription orders per year.
6.6 Discussion

The results of the analysis of the medication errors model presented in this chapter describe the range of preventable ADEs predicted to occur annually in a 400-bed hospital in the UK with around 160,000 prescriptions orders. The baseline analysis of a hospital with no specific medication error intervention in place predicted that the number of preventable ADEs occurring annually is likely to be in the range of 200 to 700. The associated cost of preventable ADEs is between £1 and £1.5 million if direct health care costs alone are considered, rising to an upper limit of around £50 million if the monetary valuations of the lost health associated with ADEs are included.

The impacts of three potential interventions are predicted using the medication errors model, which shows that a CPOE system or the employment of additional ward pharmacists are predicted to have the greatest impact on the number of preventable ADEs, reducing the upper bound to 500 events per year in the defined hospital setting. Bar coding at administration is predicted to have a lower effect with the upper bound remaining at over 600.

Incorporating the costs of the interventions and the cost savings due to the avoidance of preventable ADEs, the estimated net benefits for the three interventions show that CPOE has the highest potential level of net benefits when direct health care costs are considered over a 5-year time horizon if the low intervention cost is assumed. However, if the higher intervention costs are assumed, CPOE is predicted to incur negative net benefits, whilst ward pharmacists and bar coding retain significant probabilities of producing positive net benefits.

If the monetary valuations of the health impact of ADEs are included, the magnitude of the net benefits increases massively, for example, the predicted median net benefits of CPOE over a 5-year time horizon and the low intervention cost estimate increases to almost £30 million. Using the lower bound for intervention costs, CPOE has slightly higher predicted net benefits than ward pharmacists, but this relationship is reversed if the higher estimates of the intervention costs are included. Bar coding is estimated to have lower, but still substantial net benefits. The probability of negative net benefits is negligible for all interventions.
Chapter 7  Discussion

7.1  Introduction

This chapter considers the previous six chapters of this report and discusses the choice of methods for the prospective hazard and improvement analysis (PHIA) of medication errors, and the implications for the interpretation of the results of the modelled analysis. There are four main sections to this chapter, comprising discussions around the general approach to the prospective hazard and improvement analysis; the population of the baseline medication errors model; the estimation of the effectiveness of medication error interventions; and the interpretation of medication errors model results.

7.2  The prospective hazard and improvement analysis methodology

The objective of the PHIA is to identify cost-effective interventions aimed at reducing medication errors. Chapter 2 describes the framework for the PHIA of medication errors, which is centred on the use of a decision model that describes the pathway of medication errors from the point of origination to the point of impact (i.e. an erroneous medication being administered to a patient).

The prospective hazard analysis (PHA) element of a PHIA involves the identification of error points along a pathway. The basic application of a PHA may be restricted simply to the identification of error points, without the assignment of probabilities of occurrence. Similarly, the improvement analysis element of a PHIA may involve only the identification of potential solutions to the identified error points, without a quantitative estimate of the potential impact of proposed solutions. Such an approach may be adequate in situations where the cost of implementing solutions is negligible and any potentially negative effects of an intervention have been carefully considered and identified as being unimportant.

If possible solutions are considered to have potentially important negative effects, it is important that the likelihood and impact of negative effects (with and without the solution in place) are estimated to provide an explicit basis for the decision to implement a solution. In the case of interventions aimed at reducing the impact of medication errors, even if the potential for negative effects is considered negligible, the interventions generally have substantial implementation and maintenance costs, which mean that the scale of their potential benefits should be estimated in order to establish their value for money, or cost-effectiveness.
Probabilistic risk assessment (PRA), as described by Marx & Slonim\textsuperscript{97}, adds a quantitative dimension to the application of PHA that assigns probabilities to describe the likelihood of events occurring that lead to the occurrence of an error. PRA involves the development of a model structure that describes the pathways to error, and the elicitation of probabilities to populate the defined model structure, in collaboration with a group of informed participants (‘experts’). PRA is a formalised process for the application of a decision analysis in the case where no empirical data are available to populate a model. The approach used in the medication errors PHIA develops the approach specified by Marx & Slonim\textsuperscript{97}, which described the elicitation of single estimates of the proportion of times an error occurs without consideration of the uncertainty around the point estimate. The current analysis specifically considers uncertainty by describing probability distributions around each of the input parameters. Though the planned approach to elicit probability distributions for the input parameters in the medication errors model was unsuccessful, the applied calibration approach provided a means of describing the uncertainty in the analysis.

The first stage of the process involved the development of a model structure by a group of informed health professionals who identified error points along specific patient journeys – patients presenting in a primary care setting with moderate, or severe, depression. At each defined error point, a range of errors, causes, and potential solutions were identified. At this stage, the preliminary results of a systematic review of the medication errors literature had identified that there was insufficient empirical data to populate the defined model.

A wider group of experts were assembled in order to provide quantitative estimates of the error probabilities at each error point, the likelihood of error detection, and the impact of alternative interventions on the incidence of undetected errors. As described in Chapter 5, the participants at the expert elicitation workshop were unable to provide quantitative estimates of many of the parameters required to populate the originally specified model. As a result of the findings from the workshop, an alternative modelling approach using a much simpler model structure was developed. The simpler model described a more aggregated set of error points and error detection points, though it was still not possible to populate the model directly using data derived from the literature. The model was populated, therefore, using a process of calibration by which weights were
attached to a wide range of possible input parameters, which were then sampled to describe probability distributions of the relevant outputs.

The resulting analysis provides an indication of the cost-effectiveness of the alternative medication error interventions, though as discussed in more detail in section 7.5, there remains significant uncertainty and the conclusions drawn from the analysis may also have been derived from a non-quantitative assessment of the hazards and potential solutions.

7.3 Population of the baseline medication errors model

The medication errors model, as presented in Figure 2.1 (Chapter 2), describes the broad pathway of medications between the point at which a prescription is ordered and the point at which the medication is administered to a patient. The baseline model describes the incidence and impact of medication errors in the absence of any specific interventions aimed at reducing medication errors. As discussed in the previous section, it was not possible to populate the model using the intended approach of eliciting probabilities from experts, and there were insufficient empirical data to populate the full model. However, data describing some of the outputs from the model were available. The approach taken, therefore, was to estimate ranges for all input parameters (based on empirical observations where possible), to specify ranges for the observed output parameters, and then to sample a large number of sets of input parameter values and assign weights to each set that reflect the accuracy with which they predicted the observed range of output parameter values.

The main issues concern the relevance of the empirical data used to inform both the input and output parameters, and the choice of ranges for parameters for which no data were observed. A hierarchy was defined by which priority was given to UK-based studies when defining parameter ranges, though few UK studies reporting relevant outcomes were identified. Most UK studies reported error rates based on incidence reports, which are known to severely underestimate error rates.  

As discussed in chapter 3, the vast majority of the empirical data describing medication errors and preventable ADEs is US-based. The relevance of US estimates to the UK is unknown, though specific differences in the systems of health care delivery can be described, and hence inform the interpretation of the US from a UK perspective. Key differences include the requirement that transcribed prescriptions for medicine must be
clinically checked by a hospital pharmacist in the US before supplies can be made, and that there is little or no assessable ward stock, whilst the available ward stock model is used in the UK. In the US, medicine supplies are made in the form of individual unit doses supplied in individual drawers for named patients for 24 hours, as opposed to the UK where patient packs and bottles are supplied for 14 – 28 days use, or where the preparation of doses of injectable medicines by ward staff in clinical areas.

These differences are likely to reduce the opportunities for dispensing errors in the UK relative to the US, whilst possibly increasing the likelihood of administration errors. The medication errors model allowed for a proportion of medications to bypass the dispensing stage, which reduced the modelled opportunities for dispensing errors. It is not clear whether the error rates (per dose dispensed) would increase or decrease as a result of pharmacy dispensing a reduced range of items, though UK data were included in the analysis of dispensing errors.51,54

Administration error rates were also partly informed by a UK study,60 though the key data informing the end results were the output data used to calibrate the model and these data were exclusively US-based. It was difficult to adjust these data to a UK context as the overall direction of the many differences between the UK, in terms of increasing or decreasing the aggregate rate of preventable ADEs, is unclear.

No direct comparisons of error rates in the UK and the US were identified, though Taxis et al60 report an observation study that directly compared administration errors in two German hospitals and a UK hospital. Significant differences were observed between all three settings, with the UK ward pharmacy setting having the highest number of medication errors. One explanation for the differences between the UK and German sites was that one researcher observed at all three sites, whilst the other researcher who observed only at the UK site had a higher error detection rate (9.5% vs 6.5%).

In specifying ranges for the input parameters, one approach would have been to specify a range of 0 to 1 for all of the input parameters as the calibration process assigns weights to all input parameter sets that reflects the likelihood that each set matches the defined output parameters. However, this approach ignores the possibility that some inconceivable combinations of input parameter values may result in reasonable predictions of the outputs, for example, the combination of unfeasibly high probabilities of error detection and that undetected errors cause harm may result in an accurate estimate of preventable errors (a case of two or more wrongs making a right).
necessary, therefore, to specify ranges for each input parameter that were broadly feasible.

The input parameters describing the level of severity of preventable ADEs are of particular concern as these have a significant impact on the estimated net benefits of the interventions and were based solely on a couple of related US studies\(^\text{25,41}\). Until the validity of incident reporting is assured (i.e. that incident reporting identifies a complete and unbiased set of ADEs), the accurate estimation of the severity of preventable ADEs will be reliant on empirical studies that use more reliable identification techniques, such as observation or case note review. Few such studies have been undertaken, particularly in the UK. Incident reporting may be validated by comparative studies of alternative ADE detection methods that show no difference between incident reporting and other detection methods.

The specification of output parameter ranges is a key element of the model estimation process as these ranges determine the weights applied to the input parameter sets, which are then used to estimate the cost-effectiveness of the interventions. An explicit process for the specification of ranges for each of the 12 preventable ADEs based on observed US-based data is described in Chapter 3, which allows individuals to make subjective judgements their relevance, but there is no objective indication of how applicable these ranges are to the UK. As noted above, incident reports are currently an unreliable source of the frequency of ADEs, which means that specific studies measuring the frequency of ADEs in the UK are required to provide more relevant estimates from a UK perspective.

Other key drivers of the analysis are the distributions of the levels of severity of preventable ADEs, and the cost values attached to these events, in particular, the monetary valuations of the health effects of ADEs, which were not covered by the calibration process. The parameter estimates for these variables are based on limited empirical data, for example, the proportion of life threatening or fatal preventable ADEs is based on two US studies from the same institution that reported 15 such events. Likewise, the estimated monetary valuations of the health effects of preventable ADEs are based on explicit, but subjective, estimates of their QALY effects and a summary analysis of the NHS Litigation Authority database of medication error cases. Additional research on both of these parameter categories would increase the certainty of the
presented analysis, though this research would ideally be undertaken in the context of evaluations of interventions aimed at reducing the impact of medication errors.

The valuation of the health effects of ADEs in the context of primary research is difficult as the ideal would involve administering quality of life surveys to all patients on intervention or control wards, which will require large resources and be subject to significant missing data. An alternative is to develop vignettes describing a range of effects of preventable ADEs, and to obtain monetary valuations of these effects using available methods, such as the relativities approach\textsuperscript{99}.

7.4 Medication error interventions effectiveness

The systematic review of interventions aimed at reducing medication errors set limited exclusion criteria, the main such criterion being the absence of a control group, yet the review identified only thirteen relevant studies. The results of the 13 studies are presented and discussed in Appendix 2 that describes the systematic literature review. The medication errors model was used to undertake preliminary analyses of only three of the identified interventions: computerised physician order entry (CPOE); ward pharmacists; and bar coding systems. Other identified interventions, such as medication nurses, improvement of ward light and sound, and academic detailing were not evaluated as the identified evaluations of these interventions implied no effect on the frequency of medication errors. Without an assumed improvement in the impact of medication errors, the modelled analysis of these interventions would simply show that these interventions were dominated by a do-nothing alternative, as there would be implementation costs but no cost savings or health benefits. Though no evidence describing the effectiveness of bar coding was identified, this intervention was evaluated in order to provide an indication of the potential net benefits assuming it demonstrated some level of effectiveness.

The majority of the reviewed studies specified the number of medication errors occurring as the primary outcome measure. Decision models evaluating a health care technology for a specific disease usually extrapolate intermediate endpoints to the full lifetime of patients, for example, a cancer trial may describe the relative frequency of cancer recurrence in different treatment groups, which is then extrapolated beyond the trial period based on the predicted effects of recurrence. Such extrapolations are based on the assumption that a recurrence (or recurrences of particular types, if multiple recurrence sites are modelled) in the control and treatment groups have the same
prognostic impact, i.e. the subsequent pathways are the same irrespective of the initial treatment group.

Table 7.1 presents the estimated relative risks for the prevention of four different error types observed by Bates et al\(^{26}\) in an evaluation of CPOE. The results show that the relative risk (RR) for the different error types varies from 0.06 for wrong rate errors to 0.72 for wrong dose errors.

Table 7.1 Non-missed dose medication errors per 1,000 patient days\(^{26}\)

<table>
<thead>
<tr>
<th></th>
<th>Wrong drug</th>
<th>Wrong dose</th>
<th>Wrong route</th>
<th>Wrong rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>4.1</td>
<td>47.5</td>
<td>14.7</td>
<td>25.2</td>
</tr>
<tr>
<td>CPOE period 1</td>
<td>1.1</td>
<td>34.3</td>
<td>1.9</td>
<td>1.5</td>
</tr>
<tr>
<td>Relative risk</td>
<td>0.27</td>
<td>0.72</td>
<td>0.13</td>
<td>0.06</td>
</tr>
</tbody>
</table>

CPOE – computerised physician order entry

One option in the medication errors model would have been to apply these RRs to the baseline incidence rates for these error types, and estimate the reduced frequency of preventable ADEs assuming the same proportional impact of the remaining errors as in the base case. However, an assumption of similar extrapolated effects of medication errors, even if sub-divided into error type and stage of origination in the medication pathway, would be a weak assumption. This is because there is such a wide range of potential medication errors with different potential health impacts, as well as different likelihoods of detection. The assumption of equal effects of medication errors occurring in the presence and absence of an intervention would require that an intervention prevents an entirely random sample of medication errors. This is unlikely because interventions generally prevent alternative types of errors differentially. The above study by Bates et al\(^{26}\) provides an extreme example, in which the RR for all medication errors between CPOE in the first implementation period was 0.37 (145.2 versus 53.6 errors per 1,000 patient days), whilst the RR for preventable ADEs was 1.97 (2.9 versus 5.7 per 1,000 patient days).

Other issues around the estimation of the effectiveness of medication error interventions include the fact that almost all the intervention studies were conducted in the US, and as described in the section 7.3, it is unclear how relevant such studies are to the UK NHS. A particular example is bar coding where the benefits of bar coding unit dose medicines
where the medicine has already been clinically checked by a pharmacist in the USA may be less than the benefits of bar coding 28 day supplies of medicines from ward stock where no pharmacist check has been undertaken in the UK.

Moreover, the precise specification of alternative interventions is likely to alter their effectiveness. The potential for the differential effectiveness of alternative specifications is most obvious for information technology-based interventions such as CPOE, where factors such as rates of clinician acceptance and ease of use will impact on effectiveness. Such differences are observed in the identified studies of CPOE, even within the same studies, for example, Bates et al\textsuperscript{26} measured the effectiveness of alternative specifications of a CPOE system over three time periods. As noted above, the RR for preventable ADEs for the first period relative to the baseline period was 1.97, though the RR reduced to 0.38 in periods 2 and 3. Other studies found significant reductions in ADEs, e.g. King et al\textsuperscript{29} report a RR of 0.6 (95% CI 0.48 – 0.74).

Other authors are more cautionary, noting the disparity in the success of information technology as a means of improving patient safety, as Wears and Berg comment in a recent editorial\textsuperscript{100}:

“To begin to move forward, it is necessary to dispense with the commonly held notion that these problems are simply bits of bad programming or poor implementation that can easily be excised or avoided the next time around. The reality is that many of the difficulties do not result from bad parts of the systems but are inherent in the perspectives and theories of medical work (and the role of IT in this work) that are prevalent among health informaticians and those who make decisions on acquisition and implementation.” (pg1261)

A recent, primarily qualitative study of an implemented CPOE system identified a range of medication error risk associated with a widely used CPOE\textsuperscript{95}. The conclusion from this study was that as CPOE systems are implemented, clinicians and hospitals must try to minimise errors that these systems cause in addition to errors that they prevent. Such studies will assist the design of new generation CPOE systems that will hopefully increase their effectiveness. Similar issues may be hypothesised for other potential interventions, for example, the ground rules specified for the interaction between pharmacists and clinicians whilst jointly attending ward rounds, or the ease of access to the bar codes placed on medications, may well influence the effectiveness of these two interventions.
Given the scope for improvement in all of the specified interventions, combined with the problems with available data describing their current effectiveness, the modelled analysis of the effectiveness of the three defined interventions was based on the specification of wide RR ranges for each intervention at each point in the medication pathway at which an intervention was hypothesised to have a potential impact on the baseline error frequency and/or error detection probabilities. The RRs described in Chapter 6, Table 6.1, reflect a subjective interpretation of the assembled evidence that was assisted by the expert elicitation process described in Chapter 5. The elicitation identified stages in the medication pathway at which the evaluated interventions were thought to have a potential effect.

The specified RRs for each of the three interventions were based on the assumption that the interventions were well designed, or appropriately implemented. This assumption does not exclude unintended negative effects of the interventions, though it implies generally favourable estimates of effectiveness.

7.5 **Interpretation of medication errors model results**

The previous sections have highlighted some of the caveats surrounding the development and population of the medication errors model. This section discusses the analysis of the model, and the interpretation of the results from the model in the light of these caveats.

As noted in Chapter 1, the original intention of the PHIA was to evaluate the cost-effectiveness of a range of medication error interventions across the full patient journey (from primary care, through secondary care, to institutions beyond the hospital). It was recognised that the estimation of cost-effectiveness requires the consideration of the full effects of an intervention, i.e. the estimation of the effect of an intervention on all affected patients at all affected stages of the medication pathway, though it was also noted that the impact of most interventions is restricted to broad stages of the patient journey, and that the evaluation of interventions implemented in secondary care would be adequately represented by a model restricted to medication pathways within secondary care.

Though the model is restricted to secondary care medication pathways, the model structure is relatively simple, describing only four error types at each of three points along the medication pathway at which medication errors can occur. More complex structures would provide additional flexibility with which the impact of the interventions
could be described, for example, describing more specific error types and detection points. A more complex structure was not used due to the scarcity of empirical data and difficulties observed in the expert elicitation process, which meant that additional complexity would primarily be represented by assumptions developed by the research team. Areas of additional complexity include the disaggregation of the patient population into sub-groups represented, for example, by surgical, medical and intensive care wards. However, the main purpose of defining a more complex model would be to provide a more accurate representation of the impact of the interventions, for example, if a CPOE system is known to be more effective in preventing errors of a particular type in a specific patient sub-group that have a more severe impact on health outcomes. As no specific data were identified that illustrate such effects, there appears to be little to be gained from increasing the complexity of the medication errors model. The current model incorporates a significant number of assumptions already, and given the available data sources a more complex model would not provide any additional insights into the cost-effectiveness of the evaluated interventions.

The aggregate numbers of preventable ADEs predicted in the base case (without intervention) are largely predetermined by the output parameters used to calibrate the model, which are explicitly described in Chapter 3. The directly estimated ADE severity rates, and ADE cost parameters have a strong influence on the baseline estimates of the costs of preventable ADEs. The data sources and assumptions incorporated in the estimation of the above parameters are explicitly presented for consideration by the interested reader.

The estimation of the error frequency rates, and the calibration of the error detection rates and rates at which undetected errors cause harm are required to facilitate the modelled analysis of the effectiveness of the specified interventions (CPOE; ward round pharmacists; and bar coding at administration). Again, the ADE severity and ADE cost estimates influence the estimated net benefits, but so do the estimated intervention costs and the RRs applied at different points in the medication pathway.

The model is analysed probabilistically, and the distributions of the main outputs are presented as box plots. The results presented in Chapter 6 purposefully avoid the presentation of mean values (point estimates) for any of the outcomes due to the extreme level of uncertainty around many of the model's input parameters. The range of outcome values is described for all outcome variables as this range provides an
indication of the magnitude of the outcomes. More importantly, the presented results give an indication of the relative cost-effectiveness of the different interventions.

The benefits of the alternative interventions are not additive, i.e. implementing two or three of the evaluated interventions would not reduce the preventable ADEs by the sum of the individual reductions. It is likely that there is greater overlap between the effects of CPOE and the additional use of pharmacists on ward rounds in comparison to bar coded medicine administration that will primarily reduce the wrong medicines and doses being administered to patients. Given the existing uncertainty around the model’s results, we did not seek to increase the uncertainty further by attempting to estimate the additive effects of the interventions.

The presented results of the medication errors model are based on a synthesis of data from a range of sources, primarily US-based, which introduces implicit assumptions about the characteristics of the health care system to which the model applies, for example, the structure, cultures, process and implementation of other technologies within the health care pathway. If, despite these caveats, the results indicating positive net benefits for one or more of the interventions are accepted, this does not necessarily mean that those interventions should be implemented. Firstly, the net benefits are estimated independently for each of the three medication error interventions, which means that the results are only applicable in the absence of other implemented medication error interventions.

Moreover, there is a limited health care budget and larger benefits may be delivered from applying the limited resources to other areas of patient safety, or indeed other areas of the health service.

7.6 Conclusions

The reported research study developed and populated a medication errors model that described generic pathways of all medications through the secondary care phase of the patient journey. The impact of a range of interventions aimed at reducing the impact of medication errors was estimated by describing the points in the pathway at which the interventions are expected to impact on medication errors and defining notional estimates of the magnitude of the assumed impact.

The simplicity of the medication errors model, for example, the assumption of proportionality between the prevention of a limited set of different medication errors and
the occurrence of preventable ADEs, is difficult to justify from the perspective of informing resource allocation decisions. Additional research on elements of the baseline medication errors model, such as prospective studies that investigate the relationship between medication errors and ADEs from a UK perspective, may improve the accuracy of the results. However, it should be considered that there are almost infinite types of medication errors, each of which will have different probabilities of detection prior to administration, of causing harm, and of causing different levels of severity of harm. This makes the model-based extrapolation of medication error frequencies to preventable ADEs very difficult as ideally a separate error state would be created for every medication error, to which individual estimates of the likelihood of detection, harm, and severity of harm would be attached.

It may be the case, therefore, that interventions aimed at reducing the impact of medication errors cannot be definitively evaluated through the synthesis of data from disparate sources within the framework of a decision modelling approach, as is commonly undertaken for the evaluation of other health care technologies. However, the objective of the PHIA was not to inform resource allocation decisions, but rather research allocation decisions. The broad-brush analysis presented in this report may inform research allocation decisions by identifying those interventions with the largest potential for reducing the impact of medication errors and providing net benefits to the health service. The analysis suggests that CPOE systems and the provision of additional ward pharmacists have a greater potential for net benefits than bar coding systems. The variation in the reported effectiveness of the few identified studies of medication error interventions, particularly in studies of CPOE, illustrates the need for extreme attention to detail in the development of interventions, but also in their evaluation and may justify the evaluation of more than one specification of included interventions.

If further research confirms the cost-effectiveness of additional ward pharmacists, the capacity of the NHS to employ more pharmacists, i.e. how can the supply of pharmacists be increased, will be a key factor in the implementation of this intervention. Solutions to the supply issue should be considered at the same time as the evaluation of the intervention as some solutions may affect the design of evaluation studies. Critical incidence studies may be undertaken to define the attributes of pharmacists that contribute most to the reduction of medication errors, which may identify interventions
such as new training programmes for other health professionals and new processes of health care delivery.

The PHIA also identified key drivers of cost-effectiveness that should be specifically addressed in the design of primary evaluations of medication error interventions, in particular, data should be collected on the severity of ADEs occurring in the different intervention groups and additional research should be undertaken on the value attached to the prevention of such effects.
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Appendix 1  Expert elicitation workshop

1.  Participants
The following attendees donated two days of their time and their expert knowledge to inform this study by attending an expert elicitation workshop in Sheffield:

Dr Jon Karnon (Chair), Health Economics and Decision Science, ScHARR, University of Sheffield

Mr Jeremy Oakley, Probability & Statistics, University of Sheffield

Mr Paul Tappenden, Health Economics and Decision Science, ScHARR, University of Sheffield

Mr Peter Pratt, Sheffield Care Trust

Dr Ben-Tzion Karsh, University of Wisconsin, Madison

Ms Aileen McIntosh, Section of Public Health, ScHARR, University of Sheffield

Dr Peter Bath, Department of Information Studies, University of Sheffield

Mr Jerry Williams, Health & Safety Laboratory, Sheffield

Mr David Pruce, Royal Pharmaceutical Society of Great Britain

Dr Moyez Jiwa, Institute of General Practice & Primary Care, University of Sheffield

Ms Nicky Thomas, Sheffield Teaching Hospitals NHS Trust

Dr Paul Harvey, Devonshire Green Medical Centre

Ms Maxine Johnson, Section of Public Health, ScHARR, University of Sheffield

Professor Allen Hutchinson, Section of Public Health, ScHARR, University of Sheffield

Dr Tejal Gandhi, Brigham & Women’s Hospital/Harvard Medical School

Ms Joanne Dean, Section of Public Health, ScHARR, University of Sheffield

Ms Karen Beck (Minutes), Section of Public Health, ScHARR, University of Sheffield
2. Additional elicitations of medication error parameters in primary care

1) Parameter description:

The patient presents initially at a general practitioner and the intended decision is to prescribe fluoxetine (or medication from same class of drugs). The wrong dose is prescribed, and assuming a legible and complete prescription form, the uncertain parameter is the proportion of occasions in which the error is detected by the pharmacist, or during the dispensing process.

Table 5.1  Elicitation results: wrong dose detected by community pharmacist

<table>
<thead>
<tr>
<th>Elicited Judgements</th>
<th>Feedback</th>
</tr>
</thead>
<tbody>
<tr>
<td>Most likely 5th percentile</td>
<td>0.1st percentile</td>
</tr>
<tr>
<td>0.75 0.60 0.85 0.47 0.92</td>
<td>Equivalent sample 24/33 [0.69,0.79]</td>
</tr>
<tr>
<td>95th percentile</td>
<td>99.9th percentile</td>
</tr>
<tr>
<td>50% interval</td>
<td></td>
</tr>
</tbody>
</table>

Notes on feedback:

1) 0.1st percentile. This suggests that the experts believed there is only a 1 in 1000 chance that the true proportion is less than (approximately) 0.47. The group were told that they should feel very confident that the true proportion is higher than this value. If not, then there is either a deficiency with the fitted distribution, or they should think again if the 5th percentile should be as high as 0.6.

2) 99.9th percentile. This suggests that the experts believe that there is only a 1 in 1000 chance that the true proportion is greater than (approximately) 0.92. Similar considerations apply as in the 0.1st percentile.

3) Equivalent sample. The stated uncertainty is comparable with observing (approximately) 24 out of 33 errors successfully detected.

4) 50% interval. This suggests the experts are only 50% certain that the true proportion lies in the interval [0.69,0.79], i.e., it’s just as likely to lie inside this interval as outside the interval. If it is felt considerably more likely to lie inside [0.69,0.79], then this may be due to deficiencies in the fitted distribution, or the experts may feel that the original judgments for the 5th and 95th percentiles were too conservative.
Figure 5.1  Elicited probability distribution describing uncertainty about the proportion of occasions in which a pharmacist will detect a wrong dose prescription error

2) Parameter description:

Given that the wrong dose is prescribed, and assuming a legible and complete prescription form, the uncertain parameter is the proportion of occasions in which the error is detected by the patient or their family after receiving the medication.

Table 5.2  Elicitation results: wrong dose detected by patient or family

<table>
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</thead>
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<td>5th percentile</td>
</tr>
<tr>
<td>0.01</td>
<td>0.002</td>
</tr>
</tbody>
</table>
3) Parameter description:

It is assumed that the GP decides to prescribe an SSRI at the correct dosage. Given that the wrong medication is interpreted from the prescription, the uncertain parameter is the proportion of occasions in which the error is detected during the dispensing process.

Table 5.3 Elicitation results: wrong drug selected in pharmacy, but detected prior to end of dispensing process

<table>
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<td>5th percentile</td>
</tr>
<tr>
<td>0.6</td>
<td>0.2</td>
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</tbody>
</table>
Figure 5.3  Elicited probability distribution describing uncertainty about the proportion of occasions in which a wrong drug selected in pharmacy will be detected prior to end of dispensing process.

4) Parameter description:

Given that the wrong medication is interpreted from the prescription, the uncertain parameter is the proportion of occasions in which the error is detected by the patient or their family after receiving the medication.

Table 5.4  Elicitation results: wrong drug detected by patient or family

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</tr>
</thead>
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<td>5th percentile</td>
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</tr>
<tr>
<td>95th percentile</td>
<td>0.33</td>
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<tr>
<td>0.1st percentile</td>
<td>0.13</td>
</tr>
<tr>
<td>99.9th percentile</td>
<td>0.40</td>
</tr>
<tr>
<td>Equivalent sample</td>
<td>25/98</td>
</tr>
<tr>
<td>50% interval</td>
<td>[0.22,0.28]</td>
</tr>
</tbody>
</table>
Figure 5.4  Elicited probability distribution describing uncertainty about the proportion of occasions in which the patient or family will detect a wrong drug dispensing error

5) Parameter description:

The correct prescription is transcribed at the pharmacy. It is assumed that the pharmacist correctly interprets a GPs decision to prescribe an SSRI at the correct dosage. The uncertain parameter is the proportion of occasions in which an incorrect medication is dispensed to the patient.

Table 5.5  Elicitation results: wrong drug dispensing error after correct interpretation of prescription

<table>
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</tr>
</thead>
<tbody>
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<td>5th percentile</td>
</tr>
<tr>
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<td>0.001</td>
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<tr>
<td>0.004</td>
<td>0.0004</td>
</tr>
<tr>
<td>0.006</td>
<td>6/2750</td>
</tr>
<tr>
<td>0.0016, 0.0029</td>
<td></td>
</tr>
</tbody>
</table>
Figure 5.5  Elicited probability distribution describing uncertainty about the proportion of occasions in which incorrect medication is dispensed to the patient.
Appendix 2  A sub-study: a systematic review of the medication errors literature
Aileen McIntosh, Peter Bath, Joanne Dean, Jon Karnon, Allen Hutchinson

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1. Introduction

This systematic review was undertaken to provide information from research literature to inform the development of a prospective hazard and improvement analysis, including the modelling contained within that. It was anticipated that information about medication error rates, including their place of occurrence on a medication pathway, would be found in research findings. Similarly it was thought that research findings would provide information about the effectiveness of different interventions on different types of error occurring in different settings and at different points on the medication pathway.

The aims of the systematic review were firstly to identify medication error rates and secondly to assess the evidence on the effectiveness of different interventions on medication error rates. This review presents what we found.

2. Methods

It was originally envisaged that an update of the 2001 Agency for Health Care Quality and Research (AHRQ) report would provide the literature review necessary to undertake the project. However it became apparent that a more extensive, systematic literature review should be undertaken to ensure as much relevant and rigorous literature as possible would be identified to provide a good basis for the modelling and other aspects of the study. Therefore, a systematic review was undertaken of the literature about medication errors, in terms of error rates and interventions that may impact upon error rates.

Definitions of error rates can obviously vary. The definition used in the main study:

A medication error is any preventable event that causes a deviation in the medication received by an inpatient from the prescription intended by the prescriber, excluding patient non-compliance

is broad and therefore studies with differing definitions could be encompassed by the review.

Aims and objectives

The aims of the systematic review were firstly to identify medication error rates and secondly to assess the evidence on effectiveness of different interventions on medication error rates. The following review questions were formulated to address
these aims.

Error rates
What medication error rates are reported for different settings?
What error rates are reported for different types of medication error?
What error rates are reported for different points on the medication pathway?

Interventions
What interventions have an effect on medication error rates in different settings?
What interventions have an effect on different types of medication errors?
What interventions have an effect on medication error rates at different points on the medication pathway?

Searches
Searches were undertaken on the following databases:
Cochrane Database of Systematic Reviews (CDSR)
Cochrane Central Register of Controlled Trials (CENTRAL)
Embase
Medline
Cinahl

NHS Database of Abstracts of Reviews of Effects (DARE)
NHS Health Technology Assessment (HTA) database
Science Citation Index (SCI)
Social Sciences Citation Index (SSCI)

Turning Research into Practice (TRIP) database

using an optimally sensitive search strategy of subject headings and text words. The search strategies used are listed in Appendix A. No date restrictions were applied. Hand searching was not undertaken. This produced approximately 4883 hits. Attempts were also made to identify ‘grey’ literature by searching appropriate databases (e.g. Health Management Information Consortium, Index to Theses, Dissertation Abstracts),
current research registers (e.g. National Research Register, Current Controlled Trials) and the Internet.

Members of the project team independently assessed the title and abstracts of the retrieved articles. Each abstract/title was reviewed by at least two team members (for the Cinahl database this was done by AM, JK, PB, JD, for the others by JK, PB, AH). Decisions about the ordering of papers was made according to the following pre-determined criteria:

- the estimation of the frequency of medication errors and adverse drug events along the patient journey
- the effectiveness of alternative interventions

Studies that appeared to present data on any of the above in primary, secondary or tertiary care were included. No restrictions were placed on the study type (e.g. all forms of evaluation were included at this stage) or location of a study, although only English language studies were ordered.

From these abstracts approximately 450 papers were ordered, of which 55 error rate papers (1 review and 54 studies) and 19 intervention papers (1 review and 18 studies) were included.

Assessment of papers retrieved was undertaken independently by four team members (AM, JK, PB, JD). Papers were selected for inclusion on the basis of explicit relevancy and study type criteria. All papers were assessed for inclusion at least twice and by at least two team members independently, and any disagreements were resolved by discussion. Abstraction of data of selected papers was undertaken by four team members (AM, PB, JK, JD).

General approach

Different types of medication error were of interest in the review. These include; wrong drug, wrong dose, wrong route, wrong preparation (formulation), wrong time/frequency, omission, unauthorised dose, wrong rate. Different stages in the medication pathway were categorised as prescription stage, dispensing stage and administration stage. The different levels of severity associated with a medication error was also of interest. Classifications of level of severity varied but tended to range (of those that reached the patient) from fatal through significant clinical impact on patient through limited impact on
patient to no impact on patient. Information about severity levels extracted where available.

There were several general selection criteria that are worth mentioning. We decided to focus on the medication pathway from the writing of the prescription. We therefore excluded papers that were concerned with reasons why the prescription writer may choose, for example, prescribing, i.e., selecting, the wrong drug or dose. We considered these knowledge based errors and outwith the scope of the project. Only papers where a medication error had led to adverse drug reactions were included. If the adverse drug reaction was unforeseen and did not involve any medication errors then these were also excluded. We also excluded papers that considered only adverse drug reactions.

Error rate studies

We did not limit the error rate studies by country, type of setting/facility, type of health care professionals or patients involved, length of study, number of participants.

Error rate information

The selection criteria for error rate studies were concerned primarily with sufficient information being provided to allow error rates to be calculated, i.e., both a numerator and denominator were required. Ideally, the number of errors and opportunities for error in a given time period were the preferred numerator and denominator respectively. However, if numbers for a given time period (including for example patient days) were given we included the paper. Therefore any paper that only gave a number of errors observed over any given time period, without information about opportunities for error (e.g. number of prescriptions/error) were excluded. If a paper only gave an error rate, and if it was not possible to identify how the rate was calculated from information given, then it was excluded.

Study type

Observational (disguised) studies are often considered the gold standard in this field. Our inclusion criteria included these studies as well as the following study types: undisguised observation, randomised controlled trials, controlled trials, cohort studies (prospective and retrospective), case controlled studies, case studies, surveys, record reviews, audits. We also included any meta-analyses or systematic reviews that contained studies of the type we were including. We excluded papers that were qualitative studies (except observation studies mentioned above) such as Delphi studies,
general literature reviews and expert subjective reviews, policy evaluations, editorials, letters, posters, non-peer reviewed conference proceedings and other subjective comment pieces.

Study quality was considered using checklists derived from NHS CRD Report 4 and other sources.

There were numerous error rate studies identified initially. However, once selection criteria were applied, the numbers reduced significantly. Overall, the quality of the papers was quite variable, this may in part explain the vastly different error rates presented, even in relatively similar settings.

Intervention studies

We did not limit the intervention studies by country, type of setting/facility, type of health care professionals or patients involved, length of study or follow up period, number of participants.

Intervention information

We included studies that assessed interventions that addressed medication errors in different settings, different types of medication error or medication error at different points in the medication pathway. We did not include studies that looked at interventions aimed at changing knowledge prior to the actual writing of the prescription.

Study type

The selection criteria for intervention studies were concerned primarily with study designs that allowed confidence in being able to show the impact of the intervention was due to the intervention, i.e., the presence of controls. Our inclusion criteria included the following study types: randomised controlled trials, controlled trials, cohort studies (prospective and retrospective), case controlled studies, case studies. We also included any meta-analyses or systematic reviews that contained studies of the type we were including. We excluded papers that were qualitative studies, case studies, surveys, record reviews, audits, policy evaluations, general literature reviews and expert subjective reviews, editorials, letters, posters, non-peer reviewed conference proceedings and other subjective comment pieces. Simple before and after studies in one setting with no comparative group were excluded.

Study quality was considered using checklists derived from NHS CRD Report 4 and
other sources.

The systematic review and modelling

The papers (and the information contained within them) had different values/legitimacy/utility in the systematic literature review and the modelling aspects of the study. Papers that were excluded from the literature review (because of failing to meet relevancy or quality criteria) were, in some cases, included in the modelling review, as they contained information that could legitimately be used in model building. Examples include studies used to estimate error detection rate parameters in the model (as reported 3.3), which did not present relevant data to form error rates or intervention effectiveness.

Synthesising the data

One of the main difficulties in this review was the very disparate nature of the evidence. The definitions of error types and stages in medication pathways were not consistent, in most cases they were not directly comparable. This may contribute to the considerable ranges found in studies. We decided to arrange data in groupings that would allow as much comparison as possible. Our starting point was studies that were undertaken in similar settings, similar study methods and then type of medication error.
3. Error rate studies

Definitions of errors and the means to calculate them often varied in papers. Details of these definitions and methods are given in the extraction tables (Appendix B) where details were given in the papers.

The differences in health care systems also raised some difficulties in synthesising the data, for example a transcription stage (where the prescriber’s order is put onto the hospital system by the prescriber or by someone else such as a pharmacist or ward clerk) exists in the United States but not in the United Kingdom.

Previous reviews

The study by Wong et al (2004) aimed to determine the nature and incidence of dosing errors in paediatric papers. To this end, a systematic review of the literature was undertaken and a total of 16 papers met the inclusion criteria and were included in the review. The authors noted that the studies were heterogeneous, in terms of data collection methods and error definitions used. Therefore it was not appropriate to undertake a meta-analysis. The study found that dosing errors were the most common types of error among the 16 included studies, but that the rates of dosing errors varied greatly. For studies using spontaneous reporting data collection methods, the dosing error rate ranged from 0.03 errors per 100 admissions (in a UK neonatal ICU and maternity ward) to 2.43 errors per 100 admissions in an Indian paediatric general ward. For studies using chart review to identify dosing errors, the dosing error rate ranged from 0.37 per 100 medication orders in a US university hospital and 2.6 per 100 medication orders in an Australian paediatric ICU. This variation may be due to hospital setting (general wards versus ICU) and also the data collection methods and error definitions used by the studies.

UK secondary care

Observation studies

Four papers were included that were observation studies undertaken in secondary care settings in the United Kingdom. All of these four papers were concerned with errors at the preparation and administration phase(s).

Taxis & Barber (2003) report an ethnographic prospective study in a UK university teaching hospital and a UK non-teaching general hospital, to determine the incidence
and significance of errors in preparing and administering intravenous drugs. A disguised observation method was used to identify errors on 10 wards with low, medium and high use of intravenous drugs over 6-10 days on each ward in 1999. One doctor, one nurse, and two pharmacists scored the potential clinical importance of each drug error on a 0-10 VAS (referenced as validated). One or more errors occurred in the preparation and administration of 212 out of 430 intravenous drug doses – rate 49%, 95% CI 45%-54%. A total of 249 errors were identified. Fifty (14%) errors were observed in the preparation of 345 multiple step preparation drugs, and 172 (73%) errors were observed in the administration of bolus drug injections. In terms of severity, 83 (19%) were judged to be potentially minor, 126 (29%) to be potentially moderate, and 3 (1%) to be potentially severe.

Taxis et al (1999) estimated medication preparation and administration error rates over 1 week in 1997 in two adult wards in each of: a UK hospital using the ward pharmacy system; a German hospital using the traditional system similar to the UK; and a German hospital using the unit dose system. A researcher (one of two in the UK, one in Germany) attended every drug administration round for the weekdays of one week and observed the preparation of, and administration of, regularly scheduled solid oral doses of medication. Details of each dose were recorded and compared to the original prescription (concurrently in the UK, retrospectively in Germany). There were significant differences between all three settings, with the UK ward pharmacy setting having the highest number of medication errors, though the UK-only researcher may have a higher detection rate (UK detection rates: 9.5% vs. 6.5% for the researcher attending all sites). The aggregate error rate in the UK setting was 8% (6.2% - 9.8%), with error of omission being the most common (>5% of all opportunities for error (OEs)), wrong dose and wrong dosage form were both >1% of all OEs, with wrong drug being over 0.5% of OEs. Errors of omission were due to non-availability of non-stock drugs, missing doses on drug chart and not finding drugs in the drug trolley (commonly due to combination of prescribed generic name with brand name on drug packaging). Administration errors were present in over 5% of OEs and ordering errors in over 2% of OEs. An error severity scale was used that accounted for the legal classification of and the therapeutic index of the drug concerned, the number of errors resulting from each failure in the system, whether the error resulted in the drug being used outside its product license and the likelihood of any serious adverse effect. Severity scores were similar across the three sites, with over 70% scoring less than 25 (/100), less than 5% score over 50.
The objective of the study by Dean & Barber (2000) was to explore the effects of introducing a patients’ own drugs system on the incidence and severity of medication administration errors. The study site was two wards (one surgical, one medical) in an 850 bed teaching hospital in the UK. Five data collection periods took place. A medication error was defined as any dose of medication administered, or omitted, that deviated from the written medical order. Medication errors included, omission, unordered drug, extra dose, wrong drug, wrong route, wrong dose, wrong form, or deteriorated drug. Errors were also classified according to the stage of the drug distribution system in which they were considered to occur. One or two observers observed each drug round and recorded details of all doses, administered, all doses ordered and all discrepancies between them. Overall, 6067 opportunities for error (during 176 drug administration rounds) and 257 medication administration errors were observed. The overall medication administration error rate for the traditional system was 4.3%, for the patients’ own drugs system it was 4.2% (not statistically significant).

The observation study (direct, disguised observation) by Bruce et al (2001) set out to determine the error rate during the preparation and administration of parenteral medicines by nursing staff on an acute admissions ward, and to propose strategies to reduce error rates. The study took place in a UK hospital. A medication error was defined as a dose of medication that deviated from the physician’s order as written on the patient’s chart. Types of error included: wrong dose, unauthorised drug, omission error, wrong route, wrong dose, deteriorated drug, wrong time error, wrong base solution, wrong preparation, wrong rate of administration, incompatibility, incomplete labelling. Errors that occurred during the preparation and administration of parenteral medications over a four-week period (Monday – Friday, 8am-4.30pm) were observed and recorded. One hundred and seven opportunities for error were presented during the study period and 27 errors were observed (error rate, 25.2%). By excluding wrong time errors (the most frequently occurring type), the error rate was reduced to 10.3%.

Record review studies

Dale et al (2003) undertook a study to assess the incidence of prescribing errors, record clinical pharmacists’ recommendations made in response to errors identified, evaluate whether clinical pharmacist intervention influences the implementation of these recommendations, and predict the consequence of the recommendations on patient outcomes. Although the study did not meet criteria for inclusion as an intervention study,
it was considered robust enough to provide information about error levels. The intervention study was carried out on patients admitted over a 12-week period to two 30-bed acute general medical wards (average length of stay 5 days) in North Tyneside General Hospital, a 500-bed district general hospital serving a mixed urban/semi-rural population of 200,000 in the North East of England. Patients on one ward with an existing clinical pharmacy service (the only such ward in the hospital) were designated the intervention group, while patients on one ward with no previous clinical pharmacist involvement were the control group (Dale et al, 2003). For the intervention group, errors and recommendations were communicated by the appropriate medical team by face-to-face wherever possible. For the control group, theoretical recommendations were made for the prescribing errors identified but no action was taken by the pharmacist to communicate or implement them. Two assessors independently predicted the consequences of the pharmacist's recommendations on the patient outcome. The number of errors detected was similar in the intervention (mean number per patient = 3.06; range = 0-18; median = 2) and control (mean number per patient = 3.22; range = 0-14; median = 2.5) groups. Overall, 72 of the 346 (21%) recommendations were not implemented despite communication to the appropriate medical team. Sixty-nine theoretical recommendations devised for control patient group (18%) were implemented by the medical team with no pharmacist intervention. For the intervention group patients, 274 recommendations (79%) were implemented, either following communication to the appropriate medical team or directly by the pharmacist.

Ross et al (2000) is a retrospective review of medication errors documented in standard reporting forms completed prospectively over a five-year period. The study took place in a large UK paediatric hospital and was to ascertain the incidence and type of medication error and whether any error prevention programmes had influenced the level of error. They found that medication errors occurred in 0.15% of admissions (which equated to one error per 1976 bed days). The highest rate was in neonatal intensive care (0.98%), most errors took place in medical wards. Errors involving an intravenous route were most common (56%).

The prospective cohort study by Wilson et al (1998) looked at the impact of a continuous quality improvement approach involving an incident reporting scheme. The study took place in a Welsh university hospital, a 15-bed paediatric cardiac ward and a four bed paediatric intensive care units. The error frequency was of concern here rather than the
‘intervention’. Errors reported using the incident reporting system are discussed. A medication error was defined as a mistake made at any stage in the provision of a pharmaceutical product to a patient. There were 441 reported medication errors in the study period (2 years), during which time 682 patients were admitted for 5315 inpatient days. Prescription errors accounted for 68% of errors reported and administration errors were 25% of reported errors, the remainder (7%) were supply errors.

Dean et al (2002) undertook a prospective study to record prescribing errors in hospital inpatients. The study took place in a 550-bed teaching hospital in the UK. The hospital operated a typical ward pharmacy service. The study looked at prescribing errors and the significance of the errors, which was assessed by a clinical pharmacist and a clinical pharmacologist. 36,200 medication orders were written during the study period and a prescribing error was identified in 1.5% (95% CI 1.4 – 1.6) of cases. Potentially serious errors occurred in 0.4% of cases. Most errors were related to dose. This study also looked at the stage of the patient’s care at which the error occurred, with most errors occurring during the inpatient stay rather than on admission or discharge. The authors noted that whilst the majority of all errors (61%) occurred at the medication order writing stage, the most serious errors actually occurred in the prescribing decision. As noted above, knowledge based errors were considered to be outside of the remit of this study. Also, no data were provided as to the type of prescribing errors that occurred, for example, wrong drug or wrong dose.

Other study types

Yentis & Randall (2003) undertook a postal survey of all lead consultants for obstetric anaesthesia in all UK maternity units. They were asked about any drug errors in their units during the past year, also about any policies or protocols for checking anaesthetic drugs and preventing drug errors. There was a response rate of 75% (240 sent, 179 returned). It was reported that thirty nine per cent of units experienced at least one drug error during the year preceding the questionnaire (23% reported one error, 9% reported two, 2% reported three errors, 1% reported four, 2% reported more than four errors and 2% did not specify the number of errors). Units also reported the most recent type of error. Fifty seven per cent of the most recent errors were wrong drug, 14% were wrong route, 14% were wrong dose, 12% were other and 3% were not specified. It should be remembered that these were reports by consultants about units they worked in and are not based on any other data.
A study was undertaken in the UK to determine the nature and severity of prescribing errors in a psychiatric hospital (Stubbs et al 2004). Pharmacists, in the course of their work, recorded details of prescriptions they thought had prescribing errors. These were then checked and verified by two other pharmacists and a consultant psychiatrist. The study team found that 211 prescribing errors were present in 188 prescribed items and that prescription writing errors were the most common error type, accounting for 76.3% of all errors. Within the prescription-writing errors category, the most common type of prescription writing error was writing an incomplete prescription (83/211; 39.3% of all errors), followed by failure to sign a prescription (31/211; 14.7%). Severity of errors was categorised on a four-point scale. The majority of errors were graded as probably clinically insignificant (64.5%) and no errors were deemed potentially life threatening. However, 11.4% of errors were thought to be clinically significant with the potential to cause patient harm.

UK secondary care: summary

The information from the four observation studies undertaken in secondary care settings in the UK was disparate and demonstrated variation in the error types studied, how errors were defined and the stages in the medication pathways studied, making comparisons difficult and of limited value. The four studies identified a range of total error rates (8-49%), and in the error rates for ordering (2%, one study) preparation (14%, one study) and administration (4-40%, three studies). The four studies presented little information about the rates of different types of medication errors, although two studies suggested that errors of omission were the most common type of error. Information on the severity of medication errors was also limited, with one study reporting 19% to be minor and 1% to be potentially severe, and one study reporting over 70% to have a severity score of less than 25 and, less than 5% having a score of over 50.

The information on medication error rates from the four record review studies undertaken in secondary care settings in the UK contained very little comparable information, due to the differences in the way the studies were conducted, in the stages studied, in the types of medication of errors examined and in the denominators used to calculate frequencies. The overall medication error rates varied from 0.15% of admissions, to 83.0 per 1,000 patient days. The frequency of prescribing errors varied from 3.22 errors per patient, to 1.5% of medication orders, to 12.4% of prescriptions, to 68% of errors reported. Two of the studies reported on the severity of errors, one study
reporting 1.5% as potentially serious and 0.4% as potentially serious in the other.

Two other studies gave information about the types of error made but did not provide sufficient information to allow error rates to be calculated.

Therefore, the information available on error rates in UK secondary care settings is very limited with very few studies published in the literature. The error rates that have been reported contained very little comparable information, due to the differences in the way the studies were conducted, in the stages studied, in the types of medication of errors examined and in the denominators used to calculate frequencies.

UK primary / community care

Two included papers looked at a UK primary care / community setting. A feasibility study for recording of dispensing errors and near misses was undertaken in the UK by Chua et al (2002). The study was designed so that each time a near miss or dispensing error occurred, a self report data collection from was completed. Four community pharmacies in one area took part. During the study period a total of 51,357 items were dispensed during the two phases of the study. From this, 39 dispensing errors and 247 near misses were detected. The results show that near misses occur six times more often than dispensing errors. The most common type of dispensing error or near miss was the incorrect strength of medication.

Thirty five community pharmacies in the UK took part in a four-week long prospective study by Ashcroft et al (2005), during which time details of all incidents (including stage, error detected, stage of error and error type) were recorded by pharmacists. A total of 125,395 items were dispensed (total number of prescriptions not given). Three hundred and thirty incidents were identified, from 310 prescriptions. Of those, two hundred and eighty incidents were classified as a near miss (22.33/10000), 50 were classified as dispensing errors (3.99/10000).

UK primary care: summary

Only two studies looked at primary/community care in the UK, both looking at community pharmacies. Both studies found that near-misses were much more common than errors (as would be expected), both reporting about six times the number of near misses to errors. Both studies also reported low rates for errors (3.99/10000 and 7.59/10000).
Observation studies

Three studies were identified that used observational methods to identify medication errors in US secondary care. These studies gave error rates by type rather than by stage in the medication pathway.

Barker et al (2002) conducted a prospective cohort study in 36 hospitals located in Georgia and Colorado. Errors were defined as a discrepancy between the dose ordered and the dose received. Nurses and pharmacists observed the preparation and administration of doses, which were observed using the Barker and McConnell direct observation method. Errors were analysed by facility type (accredited, non-accredited and skilled nursing facilities). Errors were given in terms of type of error (wrong dose, wrong form, wrong technique, etc.) rather than stage in the medication pathway. A total of 605 errors from 3216 doses were observed (18.8%). Wrong time errors (8% of total doses, 43% of errors) and errors of omission (6% of total doses, 30% of errors) were the most common error types. Clinical significance was judged by a panel of experts (7% of errors were rated as potentially harmful).

A study by Borel et al (1995) looked at the effects of an automated nursing unit based dispensing device on medication errors using a disguised observer technique. The study took place in Dallas, Texas in three wards from a 600-bed teaching hospital. The wards were specialist units and medical surgical wards. For the purposes of this review we are interested in the error frequency data generated before the intervention was implemented. During the pre-intervention phase, there were 873 observations and 148 medication errors giving an error rate of 16.9%. Most of the errors were wrong time errors (61.5%), and errors of omission (24.3%).

An abstract by Poon et al (2004) describes an observation study that looked at the two-stage medication dispensing process (pharmacy technician picked medications from pharmacy supplies according to the order and this was checked by a registered pharmacist), in the hospital pharmacy of a large tertiary academic medical centre in the USA. They observed 19,338 medication doses that were dispensed over a two-month period. Overall, 2.9% (n=557) of the doses picked by a technician contained an error and the pharmacists intercepted 69% (n=393) of those. This, they argued, corresponds to an overall dispensing error rate of 9.2 errors per 1,000 medication doses dispensed.
Record review studies

Thirteen papers were identified as having used record review methods to investigate error rates. Several papers presented data from the same study (Lesar 1997, 2002). Most papers presented information about the type of error rather than when (in the medication pathway) they occurred.

Lesar et al (1990) investigated medication prescribing errors written by physicians in a teaching hospital in North-eastern New York in 1987. All orders detected by staff pharmacists (including the pharmacy computer, which had automated dose, duplicate therapy, allergy and drug interaction checking facilities) that required correction and change were confirmed problem orders, which were then reviewed to identify orders that were deemed likely to be carried out (in the absence of detection by pharmacy presumably) that were rated as potentially significant, serious, or fatal/severe. A total of 905 errors, and 522 significant or above errors, were identified, at rates of 3.13 and 1.8 per 1,000 orders written, respectively. Orders written in the obstetrics/gynaecology wards had the highest significant error rate (2.27 per 1,000 orders written) followed by surgery wards (1.92), medical wards (1.7), and finally paediatrics (1.26). Over 60% of significant errors were wrong dose errors, with known allergies being the only other error type over 10% (11.7%).

Lesar et al (1997) undertook a prospective review of medications orders in a 631-bed tertiary-care teaching hospital in New York, USA to quantify the type and frequency of identifiable factors associated with medication prescribing errors. The study reported that 2103 confirmed clinically significant medication prescribing errors were detected and averted, giving an overall error rate of 3.99 per 1000 orders. They also reported that 701 of these (one in every three) was evaluated for a likely related factor, and for 696 (99.6%) of these, the three reviewers agreed a specific likely-related factor to the error. Of these 696 errors, 43 (6.2%) were rated as A (potentially fatal or severe), 96 (13.8%) as B (potentially serious), and 557 (80%) as C (potentially clinically significant). The study also reported that 285 prescribing errors (40.9%; error rate = 3.51 per 1000 orders) occurred in patients cared for by surgical services, 270 (38.8%; error rate = 4.12 per 1000 orders) inpatients cared for by medical services, 63 (9.1% ; error rate = 5.89 per 1000 orders) in paediatric service patients, 43 (6.2%; error rate = 4.51 per 1000 orders) in obstetric gynaecologic patients, and 35 (5% ; error rate = 5.05 per 1000 orders) in emergency department patients (p<0.001 the differences in rates across all
Lesar (2002) reported a selected range of results from a prospective observational study (as in Lesar 1997) and using the same methods that characterised medication dosage forms prescribing errors. Data on the number of dosage form errors were collected over a five year period (1996–2000). More detailed data describing medications involved, type of error, and the nature and severity of potential adverse effects were collected over a 16-month period in 1999-2000. There was an increasing trend in the number of dosage form errors over the 5-year period, from 0.3 per 1000 orders to over 0.6 (total errors 1,115). The detailed analysis of 402 errors found that failure to specify controlled release formulation contributed to over 50% and failure to specify unique formulation with significant bioavailability differences contributed to 23%. Fifty two (13%) errors were defined as fatal/severe or serious (the remainder were classed as significant). A long-term pharmacy based error prevention program is cited as a possible cause of an increased error rate (as prescribers rely on pharmacists to detect errors) though the intervention was described as ‘staff pharmacists routinely utilised all available information resources to evaluate medication orders for appropriateness’.

These papers from Lesar reported increasing error rates over the time periods studied (also found in Little et al [2003] discussed later). The apparent increase is not accounted for. They also show different rates in different departments/specialities (also found to be higher in later studies by Lesar et al), although the order of error rates in different specialities was not consistent.

A prospective cohort study to evaluate the incident and preventability of ADEs was undertaken by Bates et al (1993) in Brigham and Women’s hospital during a 37-day period. A number of error detection methods were used, including self report and chart review. Twenty seven incidents were judged as adverse drug events (ADEs), 34 potential ADEs and 12 problem orders. Findings showed that of the four different ward types studied, the highest number of ADEs per 1000 patient days were found in coronary care units (33/1000), whilst no ADEs were observed in the Obstetrics unit. Physicians were primarily responsible for 27 of the incidents.

Bates et al (1995a) also undertook a study of medication errors using self-report by pharmacists nurse review of all patient charts and review of all medication sheets in two general medical and one medical intensive care unit (ICU) at the Brigham and Women’s Hospital, Boston Massachusetts, USA. The aim was to evaluate the frequency of
medication errors using a multidisciplinary approach, to classify these errors by type, and to determine how often medication errors are associated with adverse drug events (ADEs) and potential ADEs. The study reported 530 medication errors among 10,070 orders (= 5.3%) or among 379 admissions (= 1.4 per admission) or among 1704 patient days (= 311 per 1000 patient days). There were 25 adverse drug events among 10,070 orders (= 0.25%) or among 379 admissions (= 0.07 per admission) or among 1704 patient days (= 14.07 per 1000 patient days). Of these 25 ADEs, five were associated with medication errors and were judged preventable. Therefore five of 530 medication errors (0.9%) resulted in an ADE. Of the five preventable ADEs, one was life-threatening (20%) and four were serious (80%). Of the 20 not preventable ADEs, none were life-threatening, three were serious (15%) and 17 were significant (85%). Of the eight potential ADEs that were not intercepted, one was life-threatening (12%), five were serious (63%) and two were significant (25%). Of the 27 potential ADEs that were intercepted, three were life-threatening (11%), twelve were serious (44%) and twelve were significant (44%).

In a prospective cohort study, Bates et al (1995b) looked at assessing the incidence and preventability of adverse drug events and potential ADEs in a random sample of 11 medical and surgical units in two tertiary hospitals over a six-month period in the US. Incidents were detected by stimulated self report by nurses and pharmacists, and daily review of all charts by nurse investigators. Incidents were subsequently classified by two independent reviewers as to whether they represent ADEs or potential ADEs and severity and preventability. Over six months, 247 ADEs and 194 potential ADEs were identified. Extrapolated event rates were 6.5 ADEs and 5.5 potential ADEs per 100 non-obstetrical admissions. Of these, 1% were fatal, 12% were life threatening, 30% were serious and 57% were significant. Errors were much more likely to be intercepted if the error occurred earlier in the process, i.e., 48% at the ordering stage compared with 0% at the administration stage. Whilst the paper reported that wrong dose errors were the most common, no further information was provided relating to errors types such as wrong drug.

These papers by Bates et al give information about levels of severity of medication errors, actual and potential. Bates et al (1995b) also pointed out that there was a much higher likelihood of intercepting errors if they occurred early in the medication pathway.

Bates et al (1995c) undertook a record review of after discharge of 3137 consecutive
admissions to a medical service over a four-month period. The study aimed to evaluate screening criteria for adverse events, preventable adverse events and severe adverse events in medical patients. The primary outcome of interest was adverse events, defined as unintended injuries caused by medical management resulting in prolongation of hospitalisation or disability at the time of discharge. Chart reviews were undertaken by reviewers blinded to the eventual determination of the presence of an adverse event. The study took place in an urban tertiary care hospital in the US. Of all admissions, 341 (11%) had an adverse event identified.

Several studies looked at different units/specialities in US adult in-patient care more specifically, in part to see if there were different error rates by type of patient/unit. The studies by Cullen et al (1997) and Calabrese et al (2001) were more concerned with error rates in ICUs than most of the earlier studies discussed. Lazarus et al (2003) looked at error rates amongst trauma patients.

In a prospective cohort study, Cullen et al (1997) looked at the frequency and preventability of adverse drug events and potential adverse drug events in intensive care units (ICUs) and non-ICUs. They defined an adverse drug event as an injury resulting from medical intervention related to a drug. Potential adverse drug events are incidents with potential for injury related to a drug; in this study, this also included drug prescribing and administration errors that were intercepted before the order was administered. The study took place in 11 ICU and general care units in two hospitals, in Massachusetts, USA. Patients were eligible to be included in the study more than once, although if there was more than one incident per admission, only the first episode was evaluated. The study covered 4031 adult admissions, over a six-month period. Incidents were identified from self-report by nurses and pharmacists and a daily review of all charts by investigators. The rate of preventable ADEs per 1000 patient bed days was 19 in the ICUs (25 in medical ICU, 14 in surgical ICU) and 10 in the non-ICUs. They also reported that most individuals involved in the adverse drug events perceived that they were working under reasonably normal conditions not at the extremes of workload, stress, or a difficult environment.

Calabrese et al (2001) undertook an observation study in five surgical, medical and mixed ICUs in tertiary-care teaching facilities in the USA to study the incidence of, and to specify types of, medication error. They reported that 187 errors were detected from 5,744 observations and 851 patients during the period July to October 1999.
errors, 21 (11%) were Category B (error, but medication did not reach patient), 159 (85%) were Category C (error reaches patient, but no harm, error reaches patient, but not administered), five (3%) were Category D (error occurred, resulted in increased patient monitoring, but no harm to patient), and two (1%) were Category E (resulted in need for therapy or intervention, caused temporary harm).

Lazarus et al (2003) investigated the rate and nature of adverse drug events in trauma patients. The study examined all trauma patients admitted to a US hospital over a four-year period. The study used computerised medical records, a hospital wide surveillance programme and input from a clinical pharmacist. During the period of the study, 4,320 trauma patients were admitted and 93 (2.15%) had an adverse drug event. Five of these patients had a second ADE, giving the rate per admission of 2.3% (98 in 4,320). This compares with a rate of 1.2% (1,111 in 96,218) in non-trauma hospitalised patients during the study period (p<0.001).

The prospective cohort study by Fortescue et al (2003) looked at medication errors in paediatric in-patients. They defined adverse drug events as a medication-related patient injury and that medication errors could be the result of an error in ordering, transcribing, dispensing, administering or monitoring (they were also classified by degree of severity and whether it was a dose error, frequency, route, allergy or unknown error). The study took place in large tertiary academic medical centres, one was a paediatric hospital and one was a facility where both adults and paediatric cases were cared for, in this setting the paediatric services were independent of the adult services. The study used nine randomly-selected wards between the two hospitals. Data were collected during a six-week time frame. Two physicians independently reviewed all medication errors and adverse drug events. During the period studied, 10,778 medication orders were written for 1020 patients. Of those orders, 5.7% (616) involved an error at one or more of the stages. Most errors took place at the ordering stage (479, 77.8%). Dosing errors were the most common type (175, 28.4%). Physicians were the profession most often involved (443, 71.9%).

Guernsey et al (1983) undertook an audit study in the outpatient pharmacy of a large US teaching hospital. Eight pharmacists (six full time equivalents) were audited, for dispensing errors. A cross-sectional peer review audit was undertaken over 12 consecutive days (8am to 11pm). All auditors (4) were pharmacists with three- to eight-years dispensing experience, trained to evaluate dispensing errors using study specified
criteria. Error types were labelling errors, content errors or administrative errors. All detected errors were corrected by the auditors before the medication was delivered to the patient. All medications dispensed directly to the patients were audited manually for pharmacist error. All errors were evaluated by type of error, incidence, severity and pharmacist involved. During the audit, 9394 prescriptions were examined and 1165 (12.4%) errors were recorded, with 141 (1.5%) considered to be potentially serious. Seventy six prescriptions contained two errors and four prescriptions contained three errors.

The paper by Cullen suggest that there is a greater rate of potential ADEs in ICUs than in non-ICUs. Lazarus et al (2003) found a higher rate of ADEs in trauma patients than non-trauma patients admitted to a hospital over a reasonably long time period. Fortescue et al (2003) presented rates for paediatric patients but not rates for any different groups in the same setting, so conclusions about relative rates cannot be drawn. They did however find that most errors took place at the ordering stage in the medication pathway. Thus different units/types of patients may experience different rates of potential ADEs, but this is based on very limited evidence.

A study to determine whether associations exist between ambient sounds and accuracy of pharmacist' prescription performance in a pharmacy was studied by Flynn et al (1999/4245). Pharmacists were videotaped for 23 days as they filled prescriptions. Any deviation from the physician's written order was considered an error. A within-subjects case control study design was employed to determine whether the frequency of ambient sounds was significantly different when prescriptions with errors, compared to those without errors, were filled. A total of 5072 prescriptions were analysed and 164 errors were detected for an overall error rate of 3.23. The error rates for sets of prescriptions with one or more interruptions was 6.65%, and for the set during which there were one or more distractions 6.55%.

Other study types

Little et al (2003) analysed all errors reported voluntarily (by nurses using a medication variance form) over a five-year period in an obstetric unit in the US. The unit consisted of labour and delivery units and also the antepartum and postpartum ward. They did not include in the analysis data that was related to medication errors that did not directly affect the patient or foetus (e.g. incorrect narcotic counts). Also excluded were known side effects of drugs that led to undesired but anticipated side effects. During the study
period, 164 medication errors were reported for 73,302 patient days. Rates (per 1,000 patient days) were presented for different wards and for different types of error (e.g. omitted dose, wrong drug, wrong patient). They also reported the number of errors classified by one of three levels of severity. For the study period, the obstetric ward reported a total error rate of 2.04, the labour and delivery suite a rate of 2.68, with the combined wards rate of 2.24. They also reported that medication errors per 1,000 patient days increased slightly over the period of the study (1997, 1.7; 1998, 2.2; 1999, 2.8; 2000, 3.6; 2001, 4.2).

In a prospective cohort study, Nettleman & Bock (1996) looked at missed medication doses. The study took place over a seven-month period, in a general medical ward and an intensive care unit in a US tertiary care hospital. The study used active surveillance by the study nurse to observe missed medications as well as record review and survey (to gather views about the reasons for missed medications). There were a total of 63,031 medication doses ordered of which 906 (1.4%) were missed (39,338 ordered for ward patients with 441 missed [1.11%], and 23,693 ordered for ICU patients with 465 [1.96%] were missed). They found that the number of doses given per day were directly related to the proportion of doses that were missed (p<0.01). They also found that those patients who received nine or more doses per day missed 1.5% of all scheduled doses (an average of 0.23 doses per day) compared with 1.1% of scheduled doses for those who received fewer than nine doses per day (0.06 doses per day, p<0.01). They also reported that only 3% of missed doses occurred during a patient absence.

The study by Ness et al (1994) looked at the accuracy with which pharmacists and pharmacy technicians check medication in unit dose distribution systems. It took place in three hospitals in the US. All 3 hospitals had a 24-hour unit dose drug distribution system. The study was a quasi-experimental pre-evaluation and post-evaluation design, conducted during a six-month period. During the first three months (pharmacist verification), pharmacy technicians filled unit dose medication drawers and pharmacists checked these, during the final three months (technician verification), specially trained technicians verified the accuracy with which medication drawers were filled by other technicians. Error types were wrong medication, wrong strength, omission errors, wrong orders, wrong dose. There was 136 days of pooled data for the pharmacist verification period and 137 days of pooled data for the technician verification period.

Potential overdoses and underdoses in a random selection of 120 children with new
prescriptions were investigated by McPhillips et al (2005). Error rates in two HMOs using paper prescriptions was compared with one HMO that used an electronic prescription writer. They found dosing errors in 15% of outpatient medication prescriptions, 8% were potential overdoses and 7% were potential underdoses. They did not find that the HMO using an electronic system had lower potential medication dosing error rates.

Gandhi et al (2005) investigated medication errors, potential and preventable adverse drug events (ADEs) in a prospective cohort study using prescription and chart review and a patient survey. The study was undertaken in four adult primary care practices affiliated with an academic medical centre (2 community based, 2 hospital based) in Boston, USA. They looked at 1879 prescriptions for 1202 patients. Of those, 7.6% contained a prescribing error (n=143, 95% CI 6.4% to 8.8%). Incorrect or missing dose were the most frequent (54%, n=77). Most of the prescribing errors were deemed to have no potential for harm (55%, n=78), potential ADEs accounted for 43% of errors (n=62) and three led to preventable ADEs.

A study by Nebeker et al (2005) was undertaken at a Veterans Administration Hospital in the US to establish the type and frequency of errors that occur in a highly computerised hospital. The computerised nature of the hospital included electronic medical records and Computerised Physician Order Entry systems. Pharmacists classified ADEs from prospective daily reviews of the electronic medical records and included ADEs that necessitated a change in the treatment plan. From 2306 admissions, 483 clinically significant ADEs were identified, equating to 70 ADEs per 1000 patients or 52 ADEs per 100 admissions. Medication errors contributed to 27% of these ADEs. Nine per cent (9%) of ADEs resulted in serious harm, 22% in additional monitoring and interventions, 32% in interventions alone and 11% in monitoring alone. High ADE rates were found despite the hospital having adopted a range of computer technologies and personnel safety strategies designed to improve medication safety.

Husch et al (2005) undertook a prospective (point prevalence) study to determine the type, frequency, and severity of errors associated with IV infusion pumps in a 725-bed tertiary care academic medical centre, in Chicago, USA. Data were collected for one day from 0800 until 1700 hours on a “historically high volume day” (Thursday) in January 2003. On the assigned nursing units, using a prospective point prevalence approach, each research team compared the infusing medication, dose and infusion rate on the
pump with the prescribed medication, dose and rate in the medical ward. All epidural, patient controlled analgesia (PCA) and general use IV infusion pumps in use on inpatient care units were included in the study. 486 patients were included in the study. An IV pump was used for 286 of these patients (58.8%) during data collection period. 426 medications were observed infusing through these pumps. Of the 426 medications, 285 (66.9%) had one or more errors associated with their administration. There were 389 errors overall, of which 373 (96%) were errors that were unlikely to cause harm despite reaching the patient, eight (2%) were errors that would have required increased monitoring to preclude harm, five (1%) were errors likely to cause temporary harm and three (1%) were errors that would have caused temporary harm and prolonged hospitalisation.

US secondary care: summary

The three observation studies found that wrong time errors were most common and omission errors the next most common type. Two studies gave errors rates that were quite similar (16.9% and 18.8%, Borel et al 1995 and Barker et al 2002 respectively) whilst a third study found a much lower rate (2.9%, Poon et al [2004]).

Thirteen studies using record review were included in the review. These studies varied in their methods (including the staff involved in detection and evaluation of errors), and their settings. Overall error rates ranged from 0.03% to 12.4% (Lesar 2002, Guernsey et al 1983).

Seven studies using other methods also reported very different error rates. However as the settings, methods, and actual error definitions varied so much, it is inappropriate to bring these together in a simplistic way and report ranges.

Overall, the studies from US secondary care settings were of such diversity, in terms of setting, error definitions that drawing conclusions about the actual rate and type of error is difficult. Most of the papers discussed different types of error (wrong dose, wrong route etc) and did not provide information about the stage in the medication pathway that it took place, the study that did (Bates 1995b) suggested the earlier in the pathway the easier to catch, which is what might be expected as there remain more opportunities for capture the earlier in the process. The studies seem to suggest that error rates have been increasing over time, although it is not possible to determine if this is a real increase or is due to an increase in reporting, detection or both. The different papers
illustrate that different specialities and units have different rates, as do different professionals (although there are fewer papers about this). The most common error appears to be those of omission or wrong time errors. The papers also report variation in severity, but most had some impact on the patient and their care.

US primary / community care

There is a dearth of studies that have examined medication error in primary care, as with other aspects of patient safety. We have included only three studies, one observational study and two studies that used survey methods and chart review.

Observation study

Rupp et al (1992) reported an observational study of new prescription errors (repeat prescriptions were excluded) based in 89 community pharmacists in five states of the USA over an eight-month period in 1990. A Pharmacist Intervention Report (PIR) was filled in by senior pharmacy students for each problem that required pharmacists to interrupt their routine dispensing activities to resolve. Six hundred and twenty three (623) pharmacist interventions were observed, with an estimated aggregate rate of 18.86 per 1,000 new prescriptions. Forty five (45) high volume pharmacies (>11.3 prescriptions per hour) had a median rate of 11.7, whilst the low volume pharmacies had a median rate of 24 (p<0.05), indicating that high volume pharmacies did not check prescriptions as carefully. Over 45% (45.6%) of errors were errors of omission, of which incomplete or unavailable form/strength accounted for 40%. More than a third (36.4%) of errors were errors of commission, of which 57% were incorrect dose/regimen. Drug interactions accounted for 7.6%, which were evenly split between drug-drug interactions and allergies. In 11.1% of cases, the problematic prescription order was eventually dispensed as originally specified by the prescriber (it is not possible to link these uncorrected ‘errors’ to the error categories). In 176 cases (28.3%), two of three expert evaluators agreed that the problematic new prescription order could have caused harm to the patient if the pharmacist had not intervened.

Other study types

Gandhi et al (2003) conducted a prospective cohort study, a survey of patients and a chart review to study ADEs in ambulatory care in the US. The survey included four adult primary care practices (2 hospital based and 2 community based) in Boston and involved a total of 1202 outpatients who had recently received a prescription (same
study as reported in Gandhi et al 2005). Six hundred and sixty one (661) patients responded to the survey at two weeks (response rate 55%). Chart reviews were compared for 653 of the 661 patients. Of these, 162 had experienced an adverse drug event, with a total of 181 events. Twenty four of the events were classified as serious. Fifty one events were classified as serious, whilst 20 were classified as preventable. Of the 181 adverse drug events, 166 (92%) were identified by surveying patients, 50 (28%) by reviewing charts and 35 (19%) by both means. The medication classes most frequently involved in the adverse drug events were selective reuptake inhibitors, beta blockers and ACE inhibitors. The study did not provide information as to the error type, e.g., wrong drug or wrong dose; neither did it state whether the error occurred at the prescription or at the dispensing stage.

A US high volume mail-service pharmacy practice, comprising a network of prescription processing and dispensing was looked at by Teagarden et al (2005). They undertook a descriptive analysis of a sample (random) of completed prescriptions. They found an overall dispensing rate of 0.075% (16 errors among 21,252 prescriptions, 95% CI 0.043 – 0.122). All dispensing errors were associated with the initial stages of the prescription process, including order entry. They found no errors in the product dispensing stages which was mechanised.

US primary care: summary

These three studies give very limited information about medication errors in US primary care, although it seems clear that medication errors are as much of a concern in primary care as they are in secondary care. The two studies that were primarily concerned with (community) pharmacies gave error rates of 1.9% and 0.075%. The study in ambulatory care found that about a quarter of patients who responded to a survey (n=661, = response rate 55%) had experienced an adverse drug event.

Other countries secondary care

Observation studies

The majority of studies in this category reported frequencies relating to dose and timing errors.

The paper by Van den Bemt et al (2002b) used a disguised observation technique (observation of medication administrations by nurses, without revealing the aim of this observation) to identify the frequency, and the determinants, of drug administration
errors in the intensive care unit. The study was undertaken in the ICUs (mixed medical/surgical) of two Dutch hospitals, with different distribution systems in the ICUs. An observer followed the nurses preparing and administering drugs in both hospitals on five consecutive days from 7am to 10pm. Observations were subsequently compared with written or printed medication orders, with drug information sheet and handbook, and with general nursing protocols. When wrong-time errors were included, 104 administrations with at least one error were observed (frequency = 104 of 233, 44.6%) in the two hospitals. When wrong-time errors were excluded, 77 administrations with at least one error were observed (frequency = 77 of 233, 33.0%). Twenty eight (28) errors (49.1%) in Hospital 1 were Class B2 errors (medication administered but no harm) and 29 (50.9%) were Class C (an error is made that results in an increased monitoring but no harm is done). Fifty three (53) errors (71.6%) in Hospital 2 were Class B2 errors and 21 (28.4%) were Class C.

Another study that looked at medication errors in secondary care was by Tissot et al (2003). This was a prospective observation-based study (undisguised), to assess the rate and potential clinical significance of medication administration errors. The study took place in two units (one geriatric unit [GU] and one cardiovascular thoracic surgery unit [CTSU]) of a French university hospital. During 10 consecutive days (weekends excluded), a pharmacist observed nurses and wrote down exactly what they did when preparing and administering medications. These notes were compared with original prescriptions, recommendations of the manufacturers, literature based data and unit protocols. Medication administration errors were classified by type of error (American Society of Health-System Pharmacists classification) and also by potential clinical significance (classified by multidisciplinary team). There were 523 (289 in CTSU and 234 in GU) opportunities for error concerning 56 patients (33 in CTSU, 23 in GU) during the observation period. In this period, the medication administration error rate was 14.9% (18% in CTSU and 11.1% in GU). If wrong time errors are excluded then the error rate was 11.1% (CTSU: 13.5%, GU: 8.1%). Dose errors (omission, unauthorised or wrong dose) were the most frequent (41%) errors, then wrong time errors (26%) and wrong rate errors (19%), there were few preparation errors (4%). No potential fatal errors were observed during the observation period, 10% were considered potentially life threatening, 26% potentially significant and 64% potentially minor. The authors suggest that in this study, incomplete or illegible prescription and nurse workload were two significant risk factors for medication administration errors.
A second included study in this section by Tissot et al (1999) was a prospective observation based study, to assess the rate and potential clinical significance of medication administration errors by nurses. Those being observed were aware of the purpose of the study. The study was undertaken in a three unit, 15 bed intensive care unit in a French university hospital. The observations were undertaken on 30 days during a two-month period. Two nurses were randomly selected on each day of observation (weekends and nights were excluded), they were observed by two pharmacy residents. The observers wrote down exactly what nurses did when preparing and administering medicine. These notes were compared with original prescriptions, recommendations of the manufacturers and data from the literature. Errors were classified in six categories and potential clinical significance (four categories) were also used. During the observation period (30 days), 2009 nurses’ interventions were recorded involving 26 patients, with an error rate of 6.6%. No potential fatal errors were observed during study period, but 21% of errors were assessed as being potentially life-threatening, and the majority of errors (42%) were potentially significant.

Again, there is a large difference between the reported error rates of the different studies, particularly between Tissot et al (1999) and the study by Van den Bemt (2002b), both of which took place in ICUs (6.6% v 44.6% if wrong time errors included, 33% if excluded). The only difference between the studies is that Van den Bemt (2002b) employed the disguised observer technique whereas Tissot et al. (1999) did not.

Prot et al (2006) undertook a prospective direct-observation study in four clinical units in a paediatric teaching hospital, in Paris, France, to identify the type, frequency, potential clinical significance, and determinants of drug administration errors using direct observation in paediatric in-patients. Twelve observers accompanied all nurses giving medications and witnessed the preparation and administration of all drugs to patients during two consecutive hours in the mornings of 271 weekdays from April 2002 to March 2003. All the collected data were reviewed by the pharmacy resident for missing information and inconsistencies. Of the 1719 opportunities for error, 467 led to at least one error (error rate = 27.2%) and of these 302 were errors other than timing errors (17.6%). There were 538 errors (error rate = 31.3%) overall, and of these, 186 were timing errors (20.5%) and 352 were administration errors other than timing errors (20.5%). One hundred and forty five (145) patients (43%) experienced at least one error, committed by 190 nurses (39%). One hundred and forty four (144) errors required
no corrective action (8.4%); 240 required minor corrective action (13.9%); 20 required additional investigations (1.1%); 63 required major treatment modification (3.6%) and none was a potentially life-threatening error.

A cross-sectional study in Aarhus University Hospital, Denmark was undertaken by Lisby et al (2005), using three methods for error detection (direct observations, unannounced control visits and chart reviews) to investigate the frequency, type, and consequences of medication errors in more stages of the medication process, including discharge summaries. In total, 2467 opportunities for error were registered of which 1067 (43%) errors were detected. The estimated median error rate per patient in the first sample was 17 (11-24) errors per patient in the medical ward and 13 (7-22) per patient in the surgical ward. Of the 433 opportunities for error in the ordering stage, 167 errors occurred (39%), and of these three (2%) were fatal, 30 (18%) were serious, 67 (40%) were significant and 66 (40%) were non-significant. Of the 558 opportunities for error in the transcription stage, 310 errors occurred (56%), and of these six (2%) were fatal, 65 (21%) were serious, 127 (41%) were significant and 111 (36%) were non-significant. Of the 419 opportunities for error in the dispensing stage in the observational study, 17 errors occurred (4%), and of these none were fatal, four (25%) were serious, nine (56%) were significant and three (19%) were non-significant. Of the 119 opportunities for error in the dispensing stage in the unannounced control study, five errors occurred (4%), and of these none were fatal, one (20%) was serious, two (40%) were significant and two (40%) were non-significant. Of the 412 opportunities for error in the administration stage, 166 errors occurred (41%), and of these two (1%) were fatal, 33 (20%) were serious, 53 (32%) were significant and 77 (46%) were non-significant.

Two methods of drug distribution, ward stock versus unit supply drug distribution were investigated by McNally et al 1997. The focus was on nursing time and the influence on medication errors. The study took place in Western Australia in a 680-bed teaching hospital on a general surgical ward and a renal ward. Pharmacist observers were responsible for detecting medication errors. In the traditional ward stock distribution model, there were 247 opportunities for error in each of the ward types. Of these, on the general surgical ward there were 155 errors and on the renal ward there were 114 errors. The majority of errors on both wards were related to timing.

Fisher et al (2006) undertook a prospective single-blinded study to compare the types of medication errors and medication error rates of two medication delivery systems: in one
area medications were stored and issued in a ward bay workstation immediately outside
the patients’ rooms; in the other area, a medication trolley was used at the patients’
bedside. The study took place in a 30-bed surgical ward in a 430-bed tertiary and
referral hospital. The five nurse educators who were the observers were paired with
registered nurses (n=20). The observers used a blank medication chart to document all
medication-related activities. The observers did not view the medication orders and
documented only the medications they witnessed being issued. At the end of the shift,
the observers compared their witnessed records with the written medication orders.
Discrepancies between what was administered and the written medication orders
constituted a medication error. During the observation period, 340 opportunities for error
were observed. Of these, two gave rise to dispensing errors (0.6%) and 20 gave rise to
administration errors (5.8%). Of the 20 administration errors, four occurred from the
medication trolley (error rate = 2.6%) and fifteen occurred from the ward bay (error rate =
9.2%) with one occurring from the Dangerous Drug cupboard. (3.8%) Significantly more
medication administration errors occurred when medications were issued from the ward
bay ($\chi^2=4.47; p=0.034$).

A further undisguised observation study of nurse activity to determine the frequency and
types of error occurring in the preparation and administration of medication was
undertaken by Schneider et al (1998). The study took place in a paediatric intensive
care unit in Switzerland. Observation of all preparation and administration of prescribed
drugs by (maximum) 2 nurses per shift was undertaken over a 10-week period. Twelve
patients were included for a total of 20 observation periods. They found a total error rate
of 26.9% (74 from 275 opportunities for error). The most common type of error was
wrong administration technique (24, 8.7% of total) and wrong time error (24, 8.7% of
total).

The reported error rate for Schneider et al (1998) is again different from the reported
error rates for the other studies discussed, with the highest error rate being found in the
only study that employed a disguised observation technique. Within the studies that
used the same observation method there was still variability between the error rates;
however, this could be due to variability between the study settings and countries, for
example, differences between paediatric ICUs and adult ICUs.

Record review studies

Two studies used record review methods. The first by Kozer et al (2002) undertook a
retrospective chart review of all patients attending the Emergency Department (ED) of the Hospital for Sick children in Toronto during 12 randomly selected days in the summer of 2000. The objectives of the study were to estimate the incidence and type of drug errors in paediatric ED and to identify factors associated with an increased risk of medication errors. There were 1549 visits to the ED during the study period, of which 1532 (98.9%) were available for review. Four hundred and three (403) charts contained potential drug errors (26.3%), of which 154 were confirmed as a medication error, so that prescribing errors were identified in 154 charts (10.1%). Two hundred and seventy one (271) physician prescription errors were identified in the 154 charts. Drug administration errors were identified in 59 charts (3.9%). Two errors were ranked as severe, 47.5% were ranked as significant and 51.7% were ranked as insignificant / minimal risk. Wrong dose errors (n=133, of which 68 were significant or severe; 49.1% of prescription errors) were the most common type of prescription error followed by wrong frequency errors (n=117, of which 52 were significant or severe; 43.2% of prescription errors).

The second included study in this category was by Proctor et al (2003), who undertook an evaluation through review of patient charts and by attendance at clinical ward rounds to determine the incidence of error in relation to adverse events on a paediatric surgical ward and in a neonatal intensive care unit in the Hospital for Sick Children, Toronto, Canada. The adverse events included “medications”, i.e., incorrect selection, dosage or timing of drugs as well as incorrect administration. In the one-month study period, 64 patients were admitted, and during this time there were 108 errors, of which four (4%) were “medications”, none of which resulted in an adverse outcome.

There were no record review studies included in this category that provided medication error frequency data relating to adult patients.

Other study types

Five studies were included in the other secondary care other methods section. The methods used included two incident report studies, two audit studies and one that looked prospectively at different systems.

The first incident report study related to the introduction of an incident reporting system in a group of psychiatric hospitals in Japan and was studied by Ito & Yamazumi (2003). Incidents were reported by clinical staff. The potential severity of the incidents was self rated by the incident reporter using pre-specified definitions. Two hundred and twenty-
one incident reports were received from 85 units within 44 hospitals. 24.9% of the incidents were intercepted before reaching the patients. Wrong drug administration was the most common error type (35.7%).

The second of the incident report papers in this category is a prospective study which took place in a neo-natal paediatric ICU in a non-university teaching hospital (Frey et al 1999). It was concerned with the occurrence of critical incidents, defined as any event which could have reduced, or did reduce, the safety margin for the patient. The study period covered 467 children and 3140 patient days. Staff completed incident reports that did or potentially could affect patient safety over a one-year period was the basis of data collection. Of critical incidents reported (n=211), 29% were drug related critical incidents. Of those, 15% were wrong prescription detected prior to administration, 48% were wrong medication order carried out, 19% correctly administered drug but wrongly prepared and wrongly administered, 16% correctly prescribed drug correctly prepared but wrongly administered and 13% were due to punctuation mistakes.

The incident report studies are from very different patient populations. The first looks at adult psychiatric patients whilst the second looks at neo-natal paediatric ICU patients. The difference in population and setting may result in differences in the reported medication error rates.

The next two studies used audit methods to study medication error frequency. The first of these, by Van den Bemt et al (2002a), undertook a study during a one-week period in February 2000 in the departments of clinical pharmacy of two general hospitals in the northern region of the Netherlands: one 600-bed teaching hospital (hospital I) and one 300-bed non-teaching hospital. The objectives of the study were to analyse costs and benefits of detecting prescribing errors by hospital pharmacy staff. All medication orders in which prescribing errors were detected during routine control by hospital pharmacy staff, were collected. Van den Bemt et al (2002a) reported 351 prescribing errors in 3540 orders (9.9%). For 18 prescribing errors (5%) a prescription error had been made, but the error was so minor that the medication order could not be misunderstood. For 189 of the prescribing errors (54%) a prescribing error had been made, but the nurse could not administer the medication without further information. For 13 prescribing errors (4%) a prescription error had been made, but administration to the patient would have had no clinical consequences. For 67 (19%) of the prescribing errors, a prescribing error had been made that could result in the need for an increased frequency
of patient monitoring. For 62 of the prescribing errors (18%), a prescribing error had been made that could result in damage to the patient. For two of the prescribing errors (0.6%) a prescribing error had been made that could result in death to the patient.

The second audit study was from New Zealand which looked at adverse events in a regional feasibility study, in 3 major public hospitals in Auckland during the calendar year 1995 (Davis et al 2001). A standardised protocol using structured implicit review was applied to 515 cases generated in an audit study involving the three hospitals and in 142 cases this indicated that an adverse error was present. Only the drug related adverse error data is relevant to this systematic review. The study reported that 12.4% of drug adverse errors occurred inside the hospital, whilst 36.5% occurred outside the hospital (mostly in ambulatory settings). Using the in-hospital data, it is possible to calculate a medication error rate of 0.76%.

A prospective cohort study was undertaken by Kirk et al (2005) to assess the rate of medication errors in predominantly ambulatory patients and the effect of computer calculated doses on medication error rates of 2 commonly prescribed drugs. The study took place in a paediatric unit in Singapore and included 4274 prescriptions. Doctors could choose either the traditional system or the enhanced computer calculated dose when calculating doses for paracetamol or promethazine. There was some difference in error rates in different hospital departments. For example, the error rate in the children’s emergency department was 15.7%, whereas for outpatients it was 21.5%. Most errors were the result of an underdose (64%; 536/833). The computer calculated dose error rate was lower than that of the traditional prescription error rate, 12.6% versus 28.2% respectively. Regression analysis showed the computer calculated dose to be an important independent variable influencing the error rate (adjusted relative risk = 0.436, 95% CI 0.336 – 0.520 p<0.001).

Other countries secondary care: summary

Seven of the eight observation studies looked at the medication administration stages, with one study looking at different stages (Lisby et al 2005). Error rates for the administration stage ranged from 5.8% (Fisher et al 2006), in an (assumed) Australian hospital looking at different types of medication administration systems to 44.6% (Van den Bemt et al 2002b) in a Dutch ICU, although the latter figure was reduced to 33% when wrong time errors were excluded. The range again reflected the different approaches and definitions, which make direct comparisons between studies difficult. It
is clear that a substantial proportion of the errors involved at the administration stage are wrong time errors (somewhere between 20-30% approximately) and that error rates excluding wrong time errors were sometimes considerably lower.

Both the record review studies were from the same hospital in Canada and both reported error rates relating to paediatric patients. Kozer et al (2002) reported that 10.1% of emergency department visits resulted in a prescribing error during the study. The study by Proctor et al (2003) reports a comparatively smaller number of medication errors (4%), however, whilst the study was undertaken in the same hospital, it was in a paediatric surgical ward and a neonatal ICU, rather than an Emergency Department.

Different rates were reported by the studies using methods other than observation or record review. This ranged from an error rate of 0.76 in an audit study to an overall medication error rate of 19.5% in the prospective study by Kirk et al (2005).

Again the different settings, methods and definitions make it difficult to undertake direct and/or meaningful comparisons.

Other countries primary / community care

The only included primary care study in this category was from Westein et al (2001) who undertook a case-control study in 23 community pharmacies in the Netherlands to identify relevant factors leading to a pharmacist intervention, but which also reported aggregate error rates. Pharmacies completed standardised detailed records of all interventions (including repeat prescriptions) during one week in 1998. From a total of 39,357 prescriptions, 337 interventions were recorded (8.56 per 1,000 prescriptions, range 1.3 to 19.4). Errors of commission were the most common (37.1%), followed by errors of omission (24.3%), deviation from earlier prescription (17.8%), and drug interactions (16.3%). In 57% of cases a change or clarification concerning dosage (the split between change and clarification is not presented), use, dosage form or amount supplied was required; 21.1% required change in type of medication; 8% required clarification of co-medication use; 3.9% required ending co-medication; 5% of prescription orders were cancelled (mainly due to patient have stock of medications); 5% patient information needed to be clarified.

There were no included papers that studied medication errors at any other stages in the medication pathway (dispensing or administration), and no studies that utilised observation methods in the primary care setting. This category is very broad and the
paper in question is from one country and is extremely unlikely to be representative of
prescription error rates other countries in the other setting category, especially
considering the variation found in all other categories.

Comment

As the summary of each category suggested there was considerable variation within
each category depending on definitions, settings and study methods. As it is very
difficult to present an overview for each category presented, it is even more problematic
to present an overview that gives any indication of medication error rates either by
location, clinical setting or method. setting. It seems clear that variation in error rates,
for whatever reason, is the only common feature.

4. Intervention studies

There were many intervention papers identified in the initial searches. However, most of
the studies were small scale, located in one facility and usually did not employ any
rigorous study design. Some studies involved interventions described as quality
improvement, or whole system approaches, which made it difficult to identify exactly
what the intervention was, and how it had been defined and measured. Therefore, only
a very small number met our inclusion criteria, which were nonetheless less stringent
than often applied to intervention studies for inclusion in systematic reviews.

Eighteen intervention papers met our inclusion criteria. A systematic review by Kaushal
et al (2003) was also identified, however all the papers included in that review were
assessed against our criteria and either included or excluded and therefore the review
paper is not discussed. Another systematic review by Oren et al (2003) was identified
and is discussed below.

Earlier reviews

Oren et al (2003) undertook a systematic review that looked at patient safety issues in
general, including medication errors which is the part of their review considered here.
They identified published studies that assessed the effects of computerised physician
order entry (CPOE), automated dispensing machines (ADMs), bar coding, computerised
medication administration systems (CMARs) on medication errors and ADEs. The
authors searched PubMed for the period 1982-March 2002 and (1966- March 2002 for
automated dispensing machines (ADMs)).
Their search for articles on CPOE resulted in 103 studies, of which 92 were excluded. Of the 11 included studies, only three examined the impact of CPOE on medication errors and ADEs. One of these studies (a retrospective time-series study) demonstrated differences between baseline and follow-up medications errors for all types of medication error. The rate of all medication errors fell by 83%. The non-missed dose medication-error rate fell 81% (p<0.0001), non-intercepted serious medication errors fell by 86% (p<0.0003). The missed dose error rate per 1000 patient days increased significantly with use of CPOE, although reasons for this were not noted, and may have been for other reasons.

Their search for articles on ADMs resulted in 30 studies, of which 23 were excluded and seven studies were included. One of these studies (a prospective before-after study) demonstrated a reduction in the number of medication errors (7/929, 10.4%) with the ADM compared with the control (148/873, 16.9%) (p<0.001). There were fewer wrong-time errors after ADM implementation, but other error types were unchanged or decreased after ADM implementation. Another study (prospective before-after) reported a reduction in medication errors during medication administration when ADMs were implemented (from 0.0075 errors per patient day to 0.0058 (p<0.05)), but an increase on the cardiovascular intensive care unit (from 0.0051 to 0.0090 (p<0.05)). The number of medication errors increased by >30% in six of the seven nursing units in the study (significance not reported). Another study (prospective, controlled) showed a mean medication error rate of 10.6% for an experimental dispensing system, compared with 15.9% with a decentralised unit dose system (p<0.05). Most errors were wrong-time errors. In another study (prospective, before-after, the rate of doses administered increased by 18% following ADM implementation (p<0.05).

Their search for articles on bar coding resulted in 46 studies, of which 39 were excluded and seven included. One study (prospective, before-after) showed a reduction in “error rate” (not defined in review) in the ambulatory care pharmacy from 1.0% to 0.2% following implementation of a bar-code stock-ordering system. Another study (prospective, controlled) reported a reduction in mean percent entry errors with a bar-code method controlled substances inventory system (0.79%) compared with the existing automated controlled substances inventory system (1.53%) (p=0.0167). Another study (prospective, cross-over, controlled) demonstrated a data-entry error rate of 1.7% for a bar-code system for documenting pharmacists’ clinical interventions,
compared with 5.8% for a manual system. Another study (prospective, controlled) showed a mean (±SD) total number of errors per record with computerised bar-code data entry was 2.63 (±0.24), compared with 4.48 (±0.30) for manual entry (p<0.0001) during resuscitation in trauma cases. The mean number of omissions per record (p=0.0001) and inaccuracies per record (p=0.0038) were less with bar-code entry.

Their search for articles on CMARs resulted in eight publications studies, of which seven were excluded and one included, but this publication could not be obtained.

Computerised Physician Order Entry Systems

Most of the selected intervention papers investigated the impact of computerised physician order entry systems (CPOE). We did not include decision support systems (DSS), or that aspect of CPOE systems, as they are intended to influence the decision making of prescribers at the point of what to prescribe rather than errors that accompany the medication process, and as such was not within the scope of this review. There were six included papers that looked at CPOE.

Bates et al (1998) compared serious medication errors (preventable ADEs and non-intercepted potential ADES) between a pre-implementation phase and a CPOE system with limited drug interaction checking facilities at Brigham and Women’s Hospital, US, between 1993 and 1995. In the implementation phase, ward units were randomised to receiving a ‘team’ intervention in addition to CPOE, comprising several small interventions developed by teams of nurses, physicians and pharmacists, such as changing the role of the pharmacist and recommended dilutions chart. Errors were identified by nurses and pharmacists reported incidents; the study investigator soliciting information; and the study investigator reviewing charts daily on weekdays. A significant reduction in serious medication errors, although the reduction in preventable errors was not significant (p=0.26). The team intervention was shown to result in more errors than the CPOE alone intervention. The CPOE intervention showed a significant reduction in the wrong dose, wrong technique, wrong drug, delays, and known allergies errors. Analysis of the severity of the errors showed that the rate of serious preventable errors actually increased whilst the rate of significant preventable errors fell by almost 50%. The only class of drug that showed an increase was sedatives, for which errors doubled with CPOE.

Bates et al (1999) used the same methods to compare the same CPOE system as
evaluated by Bates et al (1998), but in three separate periods after implementation, with a pre-implementation period (1992 – 1997). Period 2 incorporated improved allergy checking and period 3 had improved drug-drug checking and potassium ordering. The preventable ADEs rate rose in period 1, but then fell back to below the baseline rate in periods 2 and 3. Most of the period 1 errors were due to the use of multiple sedating drugs, an issue not addressed by CPOE. Both non-intercepted potential ADEs and preventable ADEs showed a significant declining trend over the four time periods. Dose errors were the most common non-missed dose error type, but if potassium errors are excluded from periods 1 and 2 (the initial CPOE did not force prescribers to specify the use of divided doses, although that is standard nursing practice, which is why these errors were intercepted), the rate of dose errors actually increased over these periods: 4.96 in period 1; 7.29 in period 2, and 19.7 in period 3. The non-missed error rate was higher in the ICU unit, but also fell more in the ICU unit than in the general wards. Forty eight (48) of the 50 errors in period 3 were deemed to be potentially avoidable through further changes to CPOE. The two main changes involved improper use of the multiple routes option, whereby errors were recorded if one of the routes was not feasible; and route restrictions for some oral medications, although these error types are most likely to be intercepted. There was no observable trend in the severity of the non-intercepted serious medication errors due to the small sample, although two of 13 (15%) of such errors were life threatening in the baseline period, whilst 100% (two) of errors were only classed as significant in period 3. Comparison with the earlier study of the same CPOE system reported a pre-implementation preventable error rate of 2.9 per 1,000 patient days, whilst this study reports a rate of 4.5, which is surprising as a similar time period was covered with the same ratio of ICU to non-ICU wards included in the study.

In a randomised controlled trial, Overhage et al (1997) hypothesised that automated guideline based reminders provided to physicians as they wrote medication orders could reduce errors of omission, such as failure to order tests or treatments. The study took place in an in-patient general medical ward of a public teaching hospital in the US. Physicians who used computer workstations to write orders were randomised to intervention and control groups, with the intervention groups receiving reminders about using the corollary order system. The computer suggested corollary orders when certain tests or treatments were selected. Physicians could accept or reject the suggestions. Physicians in the intervention group ordered the suggested corollary orders in 46.3% of instances when they received a reminder, compared to 21.9% compliance by control
physicians. The study concluded that physician workstations linked to a comprehensive 
electronic medial record can be an efficient means for decreasing errors of omissions, 
and improving adherence to medical guidelines.

Potts et al (2004) undertook a prospective cohort trial to determine the impact of CPOE 
on the frequency of medication errors at the point of physician ordering in a paediatric 
critical care unit in a 20-bed multidisciplinary PCCU at an academic institution located in 
a major metropolitan area. All medical and surgical patients who were admitted to the 
PCCU during the designated study periods were included. All medication orders were 
included in the analysis except: fluids, dialysate, total parental nutrition (TPN)/ lipids, and 
chemotherapeutic agents. Data were collected for a two-month period pre-CPOE 
implementation. There was a one-month period when no data were collected to allow 
for implementation and training. Data were collected for a two-month period in the post-
CPOE implementation. A designated clinical pharmacist reviewed all eligible orders. 
Errors were identified and classified and entered into a database. They were reviewed 
for accuracy and relevance by a second clinical pharmacist. A physician reviewer 
independently evaluated all medication orders for random 10% sample of patients in pre-
and post-COPE groups to determine the level of agreement ($\kappa = 0.96$). During the pre-
CPOE period, 6803 orders were analysed and 2662 errors and RVs were identified (39.1 
per 100 orders). After additional classification, 2.2 per 100 orders were identified as 
potential ADEs, 30.1 per 100 orders as MPEs and 6.8 per 100 as RVs. During the post-
CPOE period, 7025 orders were analysed and 110 overall errors and RVs were 
identified (1.6 per 100 orders). 1.3 per 100 orders were identified as potential ADEs, 0.2 
per 100 orders as MPEs and 0.1 per 100 as RVs. Overall, CPOE led to a 95.9% 
($p<0.001$) decrease in all types of error. There was a 99.4% reduction in MPEs 
($p<0.001$), 97.9% reduction in RVs ($p<0.001$) and a 40.9% reduction in potential ADEs 
($p<0.001$).

King et al (2003) assessed the rates of medication errors in a paediatric setting in a 
Canadian hospital over a period of six years. Medication errors were reported in a 
standardised fashion by the adverse event reporting system that was present on all 
inpatient floors, once reported, the incident was reviewed and inputted onto a 
spreadsheet database. Two physicians reviewed all incident reports during the six-year 
period. A total of 804 medication errors were identified, resulting in a medication error 
rate of 4.49 per 1000 patient days. A computerised physician order entry system was
implemented in some wards during the study period, and the before and after medication error rates were computed. Prior to the implementation of CPOE medication error rates on all wards were similar. After the implementation of CPOE, wards using this system experienced a 40% reduction in medication error rates. The study concluded that on average, 490 patient days are required to see the benefit of one less medication error using CPOE.

Mekhjian et al (2002) presented a comparison of transcription errors based on 396 medication orders from 25 patients, which were analysed for transcription errors in a surgical ward with POE+eMAR, and 888 orders from 80 patients in a surgical ward with POE+manual MAR. The study was undertaken at the Ohio State University Hospital between December 2001 and January 2001. In the POE+manual MAR area there were 11.3% transcription errors (4.6% not transcribed; 3.5% transcribed incorrectly; 1.2% transcribed without corresponding physician order; 1.9% errors occurred due to incorrect order writing by the physician). There were no transcription errors in the POE+eMAR area.

CPOE summary

Overall, these papers tend to suggest that CPOE may help reduce medication errors but this is not clear cut. The papers by Bates (1998, 1999) show that reduction in serious errors was achieved, although the reduction in preventable errors was not significant, in contrast to the findings of Potts et al. (2004), who showed highly significant reductions in a 20-bed multidisciplinary paediatric critical care unit. CPOE reduced transcription errors (Mekhjian et al, 2002) and omission errors (Overhage, 1997) and overall medication error rates (King et al, 2003). However this is a very limited number of papers in quite disparate systems, and it is not possible to say these studies show conclusively that CPOE will always bring about a reduction in medication errors. The papers did not address the possible creation of ‘new’ errors accompanying the introduction of CPOE, which is not an unreasonable supposition.

Ward stock systems

The paper by McNally et al (1997) compared two methods of drug distribution; ward stock versus unit supply drug distribution. The focus was on nursing time and the influence on medication errors. The study took place in Western Australia in a 680-bed teaching hospital on a general surgical ward (ward A) and a renal ward (ward B).
Pharmacist observers were responsible for detecting medication errors. Medication errors were reduced when using the USIP system. On the general surgical ward, the percentage of medication errors reduced from 62.8% to 39.2%, whilst on the renal ward the percentage of medication errors reduced from 46.2% to 25.0%. In both wards and in both systems, the majority of errors were related to timing.

This single study suggests that unit supply drug distribution may result in fewer medication errors, although the usual caution associated with a single small study should be employed.

Computerised dose dispensing systems

Two papers considered the impact of dose dispensing systems.

Evans et al (1999) undertook a study to evaluate a computer assisted antibiotic dose monitor was in Salt Lake City, US. The study was a descriptive epidemiological study that took place between 1993 and 1996. All patients who received one of five antibiotics during the study period were included. Pharmacists received computer generated lists of those patients that may have been given an excessive dose and the antibiotic dose monitor suggested an alternative dose. In the post-intervention period 4483 patients received at least one of the five study antibiotics and 1974 (44%) were identified as receiving an excessive dose. The study found that, during the pre-intervention period, the average length of time the patient received an excessive dose was 4.7 days, compared with 2.9 days in the post-intervention period.

Fontan et al (2003) evaluated the rates and types of drug prescription and administration errors over a 1 month period in 1999 in 49 patients in 12 rooms, including three grafted patients’ rooms, in a 510-bed paediatric and maternity hospital in France. Two dispensing schemes were compared: handwritten prescription plus ward stock distribution system versus computerised prescription plus unit dose drug dispensing system. Both systems were in use simultaneously, although the ward stock system was only used during the admission period before the patient’s name was on record, when covering prescriptions occurring outside pharmacy opening hours, when the clinician had ‘no time’ to use the software, and in case of real emergency. Hence, 87% of prescriptions were computerised. Two pharmacy students photocopied prescription and administration documents on each ward each day, which were analysed by the students and a senior pharmacist. Excluding the omission of prescriber identity as an error
reduced the prescription error rate for handwritten prescriptions to 12.9%, compared to 10.6% for the computerised system. Excluding administration time errors, the unit dose system had a 29.3% administration error rate, compared to 24.3% for the ward stock system. The main concern with this study is around the highly specific circumstances in which the alternative systems were used, as demonstrated by the difference in the patient non-compliance error rates.

These two studies are very limited in range and are not of high quality, therefore although their findings suggest limited improvement through this intervention, these findings should be considered with a fair degree of caution.

Smart pumps

A prospective randomised time series trial was undertaken in the US at Brigham and Women’s Hospital by Rothschild et al (2005) to compare the serious medication error rate of a smart pump with integrated decision support compared to a standard pump. Logged errors were rated by physicians in terms of preventability and severity. Pump data were available from 774 admissions, from which a total of 180 serious medication errors were identified. The serious medication error rates were similar in both groups, 2.03 and 2.41 per 100 pump days in the control and the intervention group respectively. The authors cite poor compliance as the reason for little difference between the two groups.

Bar coding systems

Only one study was identified that met our inclusion criteria for a bar coding intervention. Low & Belcher (2002) under a retrospective cohort study of the BCMA bar coding system (12 months after implementation) compared to no bar coding (12 months prior to implementation) in two medical-surgical units at a Midwest US government hospital during 1999 to 2001. In the pre-phase, errors (not defined) were reported by nurses. In the post-phase period, errors were recorded by the BCMA system, which captured any discrepancy in medical administration, including late dose, missing dose (pharmacy), omitted dose, wrong dose, and wrong medication. A higher error rate was estimated for the post-implementation period (0.145 versus 0.125 per 1,000 doses administered), although the use of very different error observation mechanisms in the pre- and post-implementation periods reduced the value of any direct comparison.
Order sheets

A randomised controlled study was undertaken in a tertiary care paediatric hospital by Kozer et al (2005), to determine whether the use of a structured order sheet reduced the incidence of medication errors in a paediatric emergency department. There were 2157 visits to the paediatric emergency department during the period of the study, resulting in a total of 2058 charts for review (for 95.4% of visits). On the regular form there were 411 (52.2%) orders and on the new (structured form) there were 376 (47.8%). Drug errors were identified in 16.6% (n=68) of those on the regular form and 9.8% (n=37) on the new form. There were 36 significant errors on the regular form orders and one severe error and 13 significant errors on the new form orders. Thus, a reduction in the risk for an error (using the new form) was found to be significant (OR: 0.55, 95% CI 0.34 – 0.90) and even more so for severe or significant errors (OR: 0.39, 95% CI 0.21 – 0.77).

Pharmacist participation

Two studies looking at the impact of pharmacist participation on ward rounds are discussed.

The prospective cohort study by Scarsi et al (2002) evaluated the impact of pharmacist participation on a general medical service on the occurrence and duration of medical errors. The study took place in a 600-bed academic centre in the USA. The study group comprised a clinical pharmacist actively participating (e.g. investigating allergy information, monitoring trends in laboratory test values, reviewing medication orders for appropriateness of dose and medication selection) in daily rounds on medical services. They recorded all medication errors as they were discovered (filed using MedMARX). The control group comprised another pharmacist being in rounds. There were 35 patients in each group. They found that when a pharmacist participated in medical rounds, medication errors were reduced by 51% (p<0.05). They also found that the number of patients without a medication error during their hospitalisation increased (22.9% in the control group vs. 40.0% in the intervention group, p<0.05). The duration of time that an error continued after it occurred was also significantly less in the intervention group: less that one day (mean=0.73, 95% CI 0.48-0.98) and with less than one dose of medication (median= 0) in the intervention group compared with 2.4 days (95% CI 2.3-2.9) and two doses of medication in the control group. They concluded that pharmacist participation in medical rounds reduced the frequency of medication errors
as well as their duration once identified.

Kucukarslan et al (2003) investigated the impact of pharmacists’ presence as part of the ward round team on preventable ADEs in a single blinded, non randomised controlled trial. The study compared standard care (no pharmacist on team) with a team containing a pharmacist. Interventions made by pharmacists were recorded in patient records. Patient records were selected (randomly) and a blinded process of evaluation (two senior pharmacists and one senior doctor) was undertaken to measure error rates. There were 86 patients in the study group and 79 in the control group. Pharmacists made 150 interventions during the study (147 were accepted by medical staff). In the study group there were 5.7 events per 1000 patient days and in the control group there were 26.5 events per 1000 days.

Pharmacist participation summary

Both these studies suggest that pharmacist participation on ward rounds can reduce errors. The usual cautions over a limited number of studies apply.

Dedicated nurses

The RCT by Greengold et al (2003) looked at whether the medication administration error rate could be reduced by having dedicated nurses who focused exclusively on administering drugs. These dedicated nurses received training (a brief course) on safe medication use. They were responsible only for drug delivery. This was compared with general nurses, who did not receive the medication use training, and provided comprehensive patient care, including drug delivery. Two hospitals with a total of four nursing units, medical and surgical patients, participated in the study. Data was collected over six-week blocks. Eight dedicated and eight general nurses were included in the study. For both hospitals combined, medication nurses had a 15.7% total error rate and general nurses had a 14.9% error rate (the difference was not statistically significant). There were no significant differences in total errors between medication nurses and general nurses for medical units in the first hospital, however there was a significantly lower error rate for medication nurses than for general nurses in the surgical units in that hospital. The authors concluded that changes in work design and limited educational interventions do not seem to lead to decreased medication administration error rates in diverse hospital populations with complex medication-use systems.
Academic detailing

Shaw et al (2003) undertook a cohort study that investigated the impact of academic detailing on reducing errors in writing prescriptions for addictive drugs. This study did not consider whether the drugs were appropriate choices but only looked at rule based errors (on prescriptions). The study was undertaken in two hospitals. The intervention comprised one-to-one interviews with all first and second year postgraduate practitioners, who were asked if they had difficulty writing drugs of addiction prescriptions; if so, problems were discussed and summaries and sample prescriptions were given. There was a statistically significant reduction in the error rate in these prescriptions in the intervention hospital (41% to 24%, p<0.0001). The control hospital did not show an significant change in error rate. The biggest reduction appears to have been in writing of prescriptions for liquid preparations. If liquid preparations are excluded then the change was no longer statistically significant (p=0.48). In the intervention hospital, the confidence of junior doctors writing prescriptions increased. The authors concluded that academic detailing appears to be a useful method of reducing erroneous hospital prescriptions.

Working conditions

The prospective cohort study by Walsh-Sukys et al (2001) looked at the effect of modifying light and sound levels in neonatal intensive care unit and the impact these changes had on patient safety. The study was undertaken in an existing neonatal intensive care unit (seven rooms) in a US university children’s hospital. Two of the rooms (without windows or natural light) were used in the study. One was used as a control and the other was modified in a stepwise manner. The modifications were intended to reduce noise and to change the nature of the light (reduction) in the experimental room. Safety was assessed over a six-month period after the modifications, one safety parameter measured was that of medication errors. There were no differences in medication error rates between the control or experimental room over the course of the study. The authors argued that this shows that light and sound can be reduced (which is considered beneficial to staff) without impacting upon patient safety.
Patient information

Weingart et al (2004) undertook a randomised controlled trial in the US to evaluate a patient partnership intervention designed to prevent ADEs among medical inpatients. Intervention patients received drug safety information and their medication lists, controls received drug safety information only. In total, 11 patients experienced 12 adverse drug events and 16 patients experienced 18 close calls. Rates of ADEs were compared between the two groups. There was a higher ADE rate in the intervention group than in the control group (8.4% versus 2.9%). There are limitations to this study; it was a pilot study with a small sample size. Also, the same clinicians looked after patients in each arm of the trial and both arms of the trial received some information about drug safety, which may have diluted the results.

Comment

Overall there was limited evidence about the impact of interventions on rates of medication error. The studies were generally small and not of RCT design, which could be considered gold standard for interventions. Different settings and methods of error measurement, and the availability of only single studies for several interventions means that it is difficult to draw conclusions about the impact of these interventions. From these papers, none of the interventions concerned could be considered to have an evidence base of effectiveness.
## Intervention evidence summary table

<table>
<thead>
<tr>
<th>Paper</th>
<th>Intervention</th>
<th>Setting</th>
<th>(pre) intervention</th>
<th>(post) intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>King et al (2003)</td>
<td>Computerised physician order entry versus hand written orders</td>
<td>Tertiary care paediatric hospital, Canada.</td>
<td>intervention ward: 4.48/1000 patient days</td>
<td>intervention ward: 3.13/1000 patient days</td>
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<td></td>
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<td></td>
<td>control: 4.80/1000 patient days</td>
<td>control: 5.19/1000 patient days</td>
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<tr>
<td>Bates et al (1998)</td>
<td>Computerised Physician Order Entry versus Computerised Physician Order Entry and Team Intervention</td>
<td>Brigham and Women’s Hospital, US</td>
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<td>Phase 2: 81, 3.3 per 1000 patient days</td>
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<td></td>
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<td></td>
<td>CPOE only: 29, 2.6 per 1000 patient days</td>
<td>CPOE + team: 52, 3.9 per 1000 patient days</td>
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<td></td>
<td></td>
<td></td>
<td>Period 2 overall: 81, 3.3 per 1000 patient days</td>
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<td>Bates et al (1999)</td>
<td>Computerised Physician Order Entry</td>
<td>Brigham and Women’s Hospital, US</td>
<td>Total number of ADEs</td>
<td>Period 1: 39/2619, 14.9 ADEs per 1000 patient days</td>
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<td></td>
<td>Baseline: 25/1704, 14.7 ADEs per 1000 patient days</td>
<td>Period 2: 19/1784, 10.7 ADEs per 1000 patient days</td>
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<td>Period 3: 18/1878, 9.6 ADEs per 1000 patient days</td>
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<td>Study (Year)</td>
<td>Description</td>
<td>Setting</td>
<td>Pre-CPOE Findings</td>
<td>Post-CPOE Findings</td>
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<tr>
<td>Potts et al (2004)</td>
<td>Computerised Physician Order Entry</td>
<td>20-bed multidisciplinary PCCU at an academic institution located in a major metropolitan area</td>
<td>During the pre-CPOE period, 6803 orders were analysed and 2662 errors and RVs were identified (39.1 per 100 orders). After additional classification, 2.2 per 100 orders were identified as potential ADEs, 30.1 per 100 orders as MPEs and 6.8 per 100 as RVs.</td>
<td>During the post-CPOE period, 7025 orders were analysed and 110 overall errors and RVs were identified (1.6 per 100 orders). 1.3 per 100 orders were identified as potential ADEs, 0.2 per 100 orders as MPEs and 0.1 per 100 as RVs.</td>
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<tr>
<td>Overhage et al (1997)</td>
<td>Reminders about corollary orders for computerised prescription orders</td>
<td>General Medicine ward of a teaching hospital, US</td>
<td>Control: Physicians ordered the suggested corollary orders in 21.9% of cases</td>
<td>Intervention: Physicians ordered the suggested corollary orders in 46.3% of instances</td>
</tr>
<tr>
<td>Fontan et al (2003)</td>
<td>Computerised unit dose dispensing system versus ward stock distribution system (WSDS)</td>
<td>510 bed paediatric and maternity hospital, France</td>
<td>Prescribing errors Hand written: 518/ 589 (87.9%) Administration errors (including wrong time errors) Hand written prescription + WSDS: 1077/4589 (23.5%)</td>
<td>Prescribing errors CPOE: 419/3943 (10.6%) Administration errors (including wrong time errors) CPOE: 888/3943 (22.5%)</td>
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<tr>
<td>Rothschild et al (2005)</td>
<td>Smart pump with integrated decision support compared to a standard pump</td>
<td>Brigham and Women’s Hospital, US</td>
<td>control group: 2.03 per 100 pump days</td>
<td>intervention group: 2.41 per 100 pump days</td>
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<tr>
<td>Kozer et al</td>
<td>Order sheet formats</td>
<td>Tertiary care paediatric hospital,</td>
<td>Drug errors were identified in 16.6%</td>
<td>Drug errors were identified in 9.8%</td>
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<tr>
<td>Reference</td>
<td>Setting</td>
<td>Country</td>
<td>Sample Size</td>
<td>Error Rate Comparison</td>
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<tr>
<td>McNally et al (1997)</td>
<td>Ward stock (WS) method of drug administration compared with a unit supply individual patient dispensing system (USIPD)</td>
<td>Canada</td>
<td>(n=68)</td>
<td>Total number of errors/ opportunities for error. Ward A: WS: 155/247 (62.8%) USIPD: 98/250 (39.2%), p&lt;0.0005</td>
</tr>
<tr>
<td>Weingart et al (2004)</td>
<td>Patient partnership intervention</td>
<td>Medical in-patients, US</td>
<td>ADE rate in the control group 2.9%</td>
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<tr>
<td>Low et al (2002)</td>
<td>Bar coding system versus non-bar coding</td>
<td>2 medical surgical units at a Midwest Government Hospital, US</td>
<td>Mean error rate per 1000 doses administered Pre-bar coding: 0.125 Administration errors Pre-bar coding: 37 Dispensing: Pre-bar coding: 1</td>
<td>Mean error rate per 1000 doses administered Post-bar coding: 0.145 Administration errors Post-bar coding: 40 Dispensing: Post-bar coding: 3</td>
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<tr>
<td>Study</td>
<td>Intervention Description</td>
<td>Setting</td>
<td>Control Errors</td>
<td>Intervention Errors</td>
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<td>Control: 94</td>
<td>Intervention: 46</td>
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<td>Prescribing: 48</td>
<td>Prescribing: 30</td>
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<td>Administration: 25</td>
<td>Administration: 13</td>
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<td></td>
<td>Pharmacy: 6</td>
<td>Pharmacy: 0</td>
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<td></td>
<td>Discharge: 7</td>
<td>Discharge: 0</td>
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<td>Kucukarslan et al (2003)</td>
<td>Pharmacists’ presence as part of the ward round team</td>
<td>US hospital</td>
<td>In the control group</td>
<td>In the study group</td>
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<td></td>
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<td>there were 26.5</td>
<td>there were 5.7</td>
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<td>events per 1000 days</td>
<td>events per 1000 patient days</td>
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<td>Greengold et al (2003)</td>
<td>Medication nurses to administer all drugs</td>
<td>An academic community hospital and a university teaching hospital, US</td>
<td>Total number of errors/ opportunities for error</td>
<td></td>
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<td></td>
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<td>General Nurses: 545/3661</td>
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<tr>
<td>Shaw et al (2003)</td>
<td>Use of academic detailing when prescribing drugs of addiction</td>
<td>Australia</td>
<td>Error rate: 46/112 prescriptions (41%)</td>
<td>Error rate: 128/ 533 prescriptions (28%)</td>
</tr>
<tr>
<td>Walsh-Sukys et al (2001)</td>
<td>Reduction of light and sound</td>
<td>Neonatal Intensive Care Unit, US</td>
<td>Control nursery: 4.47 medication errors per 1000 patient days</td>
<td>Modified nursery: 3.14 medication errors per 1000 patient days</td>
</tr>
</tbody>
</table>
5. Comment

The studies identified by the searches were usually of poor quality and of limited relevance to the research questions. From the papers selected, a limited number met our inclusion criteria (which were quite lax). However because of the variety of settings, methods used, definitions of medication errors and overall study approach, it is not really possible to give definitive answers about what rate of errors are found in different settings and what are the effective interventions to be used to address these errors. There was, therefore, very limited information that could be used in the prospective hazard analysis and consensus decisions by the panel of experts and assumptions were used more often than findings from the research papers identified in this review.
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Van den Bemt PMLA et al. (2002). Cost-benefit analysis of the detection of prescribing errors by hospital pharmacy staff *Drug Safety* 25: 135-143


Appendix 2a Search strategy

The search strategy used in Medline (Ovid) is provided below:
1 medication errors/
2 patient safety.tw
3 adverse drug event$.tw
4 near miss$.tw
5 adverse health event$.tw
6 ((medication$ or medical or drug$ or prescription$ or prescrib$ or dispens$ or pharmacy or pharmacies or pharmacist$) adj2 (error$ or accident$ or incident$ or mistake$ or mishap$ or failure$ or safety$)).tw
7 or/1-6

This strategy was combined with methodological search filters designed to retrieve the highest levels of evidence, i.e.

Guidelines
1 guideline.pt
2 practice guideline.pt
3 health planning guidelines/
4 or/1-3

Systematic reviews
1 meta-analysis/
2 exp review literature/
3 (meta-analy$ or meta analy$ or metaanaly$).tw
4 meta analysis.pt
5 review academic.pt
6 review literature.pt
7 (systematic$ adj3 (review$ or overview$)).tw
8 or/1-7

RCTs
1 clinical trial.pt

The strategy was also combined with the following ‘interventions’ search strategy:
1 robotic$tw
2 (automat$ adj2 dispens$).tw
3 robotics/
4 (unit dos$ adj2 (system$ or device$)).tw
5 cpoe.tw
6 comp$ physician$ order$ entr$.tw
7 cdss.tw
8 clinical decision support system$.tw
9 bar cod$.tw
10 polypharmacy.tw
11 polypharmacy/
12 *pharmacists/
13 (pharmacy or pharmacies or pharmacist$).ti
14 compu$ search$ system$.tw
15 drug protocol$.tw
16 nomogram$.tw
17 incident$ monitor$ system$.tw
Finally, the following ‘patient journeys’ search strategy was also performed:

1 patient journeys/
2 (patient$ adj2 journey$).tw
3 care path$.tw
4 (care adj2 journey$).tw
5 critical path$.tw
6 critical journey$.tw
7 clinical path.tw
8 clinical paths.tw
9 clinical pathway.tw
10 step$ care.tw
11 *critical pathways/
12 or/1-10
13 depression/
14 depress$.tw
15 or/12-13
16 exp heart failure, congestive/
17 heart failure$.tw
18 coronary disease$.tw
19 heart disease$.tw
20 coronary event$.tw
21 exp coronary disease/
22 or/16-21
23 11 and 22

No date or language restrictions were applied to the searches.

In terms of cost-effectiveness literature, searches were conducted in Medline, Embase, NHS Economic Evaluations Database (EED) and OHE Health Economic Evaluations Database (HEED). Search filters designed to retrieve economic evaluations, economic models and quality of life literature were applied to the Medline and Embase search filters. An example of the filter used in Medline (Ovid) is provided below:

1 exp “costs and cost analysis”/
2 economics/
3 exp economics, hospital/
4 exp economics, medical/
5 economics, nursing/
6 economics, pharmaceutical/
7 exp budgets/
8 exp “fees and charges”/
9 budget$.tw
10 cost$.ti
11 (cost$ adj2 (effective$ or util$ or benefit$ or minimi$)).ab
12 (economic$ or pharmacoeconomic$ or pharmaco-economic$).tw
13 (price$ or pricing$).tw
(financial or finance or finances or financed).tw
(fee or fees).tw
(value adj2 (money or monetary)).tw
value of life/
quality adjusted life year/
quality adjusted life.tw
(qaly$ or qald$ or qale$ or qtime$).tw
disability adjusted life.tw
daly$.tw
health status indicators/
(sf36 or sf 36 or short form 36 or shortform 36 or sf thirty six or sf thirty six or shortform thirtysix or shortform thirty six or short form thirty six).tw
(sf6 or sf 6 or short form 6 or shortform 6 or sf six or sf six or shortform six or short form six).tw
(sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or shorttwelve or shortform twelve or short form twelve).tw
(sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or shortform sixteen).tw
(sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or shorttwenty or shortform twenty or short form twenty).tw
(euroqol or euro qol or eq5d or eq 5d).tw
(hqol or h qol or hrqol or hr qol).tw
(hye or hyes).tw
health$ year$ equivalent$.tw
health utilit$.tw
(hui or hui1 or hui2 or hui3).tw
disutil$.tw
rosser.tw
quality of wellbeing.tw
qwb.tw
willingness to pay.tw
standard gamble$.tw
time trade off.tw
time tradeoff.tw
tto.tw
exp models, economic/
*models, theoretical/
*models, organizational/
economic model$.tw
markov chains/
markov$.tw
monte carlo method/
monte carlo.tw
exp decision theory/
(decision$ adj2 (tree$ or analy$ or model$)).tw
or/1-53

In addition, a specific search on FMEAs was conducted using the following search strategy:
fmea$.tw
(failure mode adj2 effect analy$).tw
"root cause analysis".tw
"root cause analyses".tw
or/1-4
Appendix 3  Expert elicitation of events, causes, and potential interventions at different stages of the medication pathway

Box 1: Decision on appropriate medicine

Events (what could go wrong):
Wrong patient.
Wrong drug.
Wrong dose.
Wrong formulation.
Wrong route.
Wrong duration.
Wrong quantity prescribed.

Causes
Patient provides inaccurate information.
Errors in the health care system lead to the provision of inaccurate information (e.g. errors in undertaking, interpreting, or reporting tests).
Relevant data to inform treatment decision is missing.
Irrelevant knowledge.
Out-of-date knowledge.
Short-cut decision making due to time constraints (e.g. neglecting to incorporate patient preferences in the treatment decision).
All of the above may or may not be recognised or suspected – if such data deficiencies are recognised or suspected, then it is necessary to consider alternative responses, or coping strategies, to responses that occur in cases of ignorance of the above causes.

Interventions
Electronic records.
Patient-held records.
Prompts (electronic or otherwise).
Delegation of data collection (e.g. nurse asks relevant questions).
Decision support systems.
Telephone reminders to patients (e.g. to increase compliance and reduce frequency of inaccurate patient-derived data).
Enhance patient-health professional relationship.
Box 2: Prescriber writes order/prescription

Events (what could go wrong):

- Illegible.
- Incomplete.
- Illegal
- Irregular conventions. Use of abbreviations/latin terms
- Confusing.
- Use of shorthand
- Transfer of information (ward rounds) – missing dosage

Causes

- Handwriting (do we need to distinguish between standard handwriting and rushed (as a consequence of perceived time constraints) handwriting? CAPITALS
- Out-of-date knowledge (relating to incompleteness, illegality, or irregular conventions). – incorrect knowledge. Split – inaccurate; out of date; lack of knowledge; sound-alike errors
- Oversight. Slips and lapses
- Distraction – common in secondary care
- Lost prescription
- Computer generated Rx – Typing Error
- Sound alike drug errors
- Communication – use of abbreviations and latin
- Separation of decision-making and prescription (transfer or information)
- Drug and dose combinations seem ok, but less likely to be picked up

Interventions

- Electronic ordering – ‘Physician order entry computer system’ (avoids, for example, illegibility and incompleteness, but requires consideration of over-riding and practical constraints).
- Dosage calculator (also relevant to ‘decision to treat’?)
- Prescribing standard (rule-based approach – empowerment of nurses to question doctors, issues around sanction).
- Reduction of distraction
- Time management
- Protocols with triggers
- Training viewed as least effective for safety – handwriting
- PRODIGY – primary care has guidelines in reduction of distraction, e.g. if drs consulting don’t ring up
- Reduction in number of people involved in writing a prescription
- Electronic: select wrong drop down box; typing errors; put in 1st 3 letters of a drug and then brings up a list; opportunity to get drug and dose wrong, as info feed in the system
- Codes for dangerous drugs and protocols, e.g. cannot prescribe before monitored
- ?Rule-based? – always state dose
- Both clinically trained and automated systems
- Reduction in transfer of information
### Box 3: Pharmacist reviews prescription (CLINICAL CHECK FAILURE)

**Events (what could go wrong):**
- Wrong patient not identified
- Wrong drug not identified
- Wrong route
- Wrong formulation
- Wrong dose units
- Dose calculation not checked
- Contra-indication to drug e.g. allergy
- Possible drug interactions missed.
- Incorrect dosage is not noticed.
- Incorrect medicine not noticed.
- Patient’s renal function, liver function, etc. not checked – need access to these results – H can get onto path lab database, not in primary care
- Patient’s dose not adjusted for age, concurrent illness, etc., weight
- Prescription goes missing
- Miss any of errors in boxes 1 or 2/misinterpret
- Prescription does not arrive in pharmacy

**Causes**
- Pharmacist has incorrect/incomplete patient information.
- GP Drug History Incorrect/Incomplete
- Unclear/ambiguous hand-written prescription.
- Prescription amended and unclear
- Patients medical records not up to date
- Pharmacist knowledge/experience
- Prescribing doctor is not available for checking in an emergency.
- Distractions
- Prioritisation
- Knowledge
- Work process in word or pharmacy
- Translational issues – scripts go missing, fax missing, typing errors
Box 3: Pharmacist reviews prescription (CLINICAL CHECK FAILURE)
Causes (cont.)

Prescribing/Dispensing GPs
All other work processes causes/distractions/pressures on time. Usually only one dispenser in H who gets all phone calls
Pressures = waiting times for prescriptions; priorities for different wards with sickest patients; impacts on beds; different priorities on bed alerts; ITU; admissions
Different approaches to handling prescription at different levels of pharmacy
Community pharmacies; hospital pharmacies – one stop dispensing systems
Primary problem – no pharmacist

Interventions
Pharmacist competency training/mentoring (AWU)
Medical training in prescription writing
Electronic prescribing.
Electronic patient record.
(Automated computerised checking system.)?
Prioritisation systems
Access to lab results (RRS) + clinical info
Experience of wards and types of doses employed
Experienced, well trained staff, placed in appropriate tasks
Protocols with triggers
Mentoring systems
Accompanied ward visits
continuing professional development
Pharmacist reviewer intervention for 1 + 2

Clinical check
Knowing ward from where prescription has come from/experience
Clinical vs technical check
Primary care – always have check available
Access to path lab and ethical data
Box 4: Medicine is prepared and dispensed and checked (TECHNICAL CHECK)

Events (what could go wrong):
- Wrong medicine is prepared. – mainly liquid formulations – calculation errors, wrong formula, wrong diluent
- Wrong dosage is prepared.
- Correct drug is selected but wrong strength
- Wrong medicine is dispensed. – selection error
- Incorrect label – (could be label correct and drug wrong)
  Label Errors:  drug name; drug strength; drug formulation; instructions:  dose, times and route; patient’s name; number of dose units
  Systematic checking for calculations, volumes, etc.
- Dispensed – selection of drug

Causes
- Illegible writing on prescription.
- Pharmacist picks up the wrong medicine.
- Pharmacist picks correct drug but wrong strength
- Pharmacist types wrong details into computer and produces incorrect label
- Pharmacist attached the wrong label to dispensed medicine.
- Pharmacist attaches correct label but to wrong drug
- Label with wrong patient name usually previous patient!
Box 4: Medicine is prepared and dispensed and checked (TECHNICAL CHECK) (cont.)

Interventions

Original pack dispensing
Second check by pharmacy staff
Dispensing procedures
Error monitoring
Competency training - mentoring
Computerised automated dispensing/labeling + clinical pharm review
Printed prescriptions.
Bar-coding of stored medicines.
Prioritisation systems
Skill mix
Rotate staff – multi-skilled
Flexible working patterns (hour by hour)
Ability to re-engineer workflow pattern
Multiple skilled staff
Protocols with triggers
Technical check
Dispense from prescription, rather than label
Rotate staff through duties
Automated labelling systems
Clinically trained pharmacists
Check drug; label; final item
Production line errors or good checking system
Impact of unit dosing systems – range of systems
Medidose – compliance boxes
Compliance cards/charts
Primary care = pharmacist looks at it, then dispensed
Hospital = box 4 can happen before box 3, dispensed by a dispenser then received by pharmacist
Box 5: Medicine is delivered to the ward or home, etc./medicine management/storage

Events (what could go wrong):
Medicine delivered to the wrong ward.
Wrong medicine delivered to the ward (delivering error)
Medicine delivered for the wrong patient (label = dispensing error)
Delayed delivery
Missing/lost medicines
Prescription/documentation and medicine separated
No nursing available staff to receive medicine
Inappropriate storage on ward – not in fridge, trolley instead of patient locker, wrong patient locker.
Medicines management – e.g. not in fridge
In pharmacy (prior to delivery) – delivered either by pharmacy staff or nurses

Causes
Patient has transferred wards between drug being prescribed/order sent to pharmacy and delivered.
Incorrect/illegible ward details on prescription/documentation.
Incorrect/illegible labelling of medicine / carrier.
No staff to do top-up. – of stock medicines
Item not checked in pharmacy.
Placement in wrong pigeon hole. – each ward has a key that can only open their ward’s box
Long pharmacy delivery round.
Drugs not transferred with patient between wards.
Drugs buried in patient personal property bags.
Poor communication with pharmacy when patient transferred.
Pneumatic tube failure – free run.
Box 5: Medicine is delivered to the ward or home, etc./medicine management/storage

**Causes (cont.)**

Another nurse has collected and performs other errands (e.g. coffee break!)

Delivery man not trained

Handing over to patient/patient rep – handover of info – may say something that isn’t on the label

**Primary care:** identifying correct contact person; non-label additional information; non-collection of prescription - prescription substitutions

Pharmacy delivery systems – who is doing the delivery?

**Nursing home:** from pharmacy to nursing home

Problems with dosing systems (certain drugs not able to be included)

**Interventions**

Bar-coding system for medications and prescriptions (and patient?)

Ward access to bar-coding system enabling them to track prescription and medicines.

Electronic printing of prescription labels (in Step 4).

Electronic mail for improved communication.

Check all dispensed items and stock items including top-ups.

Drug transfer bags.

Increase security/audit trail around delivery/collection – scan/nurse signature.

Increase number of pharmacy delivery rounds.

Issue pharmacy porters with bleeps.

Pharmacy delivers to wrong pt

Compliance boxes also have problems
Box 6: Nurse prepares to administer medicine

Events (what could go wrong):
- The Nurse prepares to administer the wrong drug (for example a drug that is packaged similarly)
- The Nurse does not recognise a prescribing error and prepares to administer the wrong drug
- The Nurse does not recognise dispensing error
- Patient not on ward
- Nurse unable to administer – NBM, line disconnected, absconded!
- Failure to check allergy status.
- Failure to check patient ID, about to give to a different patient.
- Selects wrong diluent/device (NG drugs drawn into IV syringe)
- Inadequate aseptic technique.
- Selects wrong formulation (e.g. not SR, IM instead of IV)
- Calculation error – wrong dose, volume, dilution.
- Doesn’t check storage

Causes
- The wrong drug has been delivered to the ward
- The wrong dose of the right drug has been issued
- There has been a dispensing error by the pharmacist
- No clinical check from pharmacy
- Lack of knowledge/training of nurse
- Correct equipment/device unavailable.
- Inappropriate environment (i.e. for preparation of IVs)
- Nurse distracted – leaves drugs unattended
- Prepared items not labelled on the ward (e.g. IVs, oral syringes)
- Out of date – left in fridge far too long; TPNs not used in right sequence from fridge
- Communication failure (doesn’t know drug has already been given)
Box 6: Nurse prepares to administer medicine

**Interventions**

- Use of checklists and protocols, SOPs
- Amend packaging of similar drugs, for example use of bright coloured stickers – **controversial**!
- Train nurses to read and re-read the label.
- Improve safety culture so nurses feel able to challenge suspected prescription/dispensing errors
- Increase presence of pharmacy staff on wards
- Increase availability of centrally prepared ready-to-use products
- Dedicated area for IV preparation on each ward
- Comprehensive competency-based training for nurses (calculations, aseptic technique, risk management)
- “Do not disturb” tabards for administering nurses
- “Drugs added to this infusion” labels.
BOX 7 – Medicine is administered to patient

Events (what could go wrong):

As in Box 1
The right drug was given by the wrong route

**SELF ADMINISTRATORS EXCLUDED** If self administration occurs, the patient may self administer incorrectly (for example, the wrong dose)
Boundary around self-administering – multitude of reasons for not complying – non-professional administrators – family carers
Technical failures e.g. with pumps or IV. – wrong device; setting up
Expired medication (not used in right sequence)
Check allergy status
Wrong patient.
Wrong drug.
Wrong dose.
Wrong formulation.
Wrong route.
Wrong duration.
Wrong quantity prescribed.
Unable to administer – refuses; line comes out; patient absconded

**Causes**
The wrong drug has been prescribed
The wrong dose has been prescribed
Dose omission
The drug is being given at the wrong time
Upstream
Failure to check patient ID or allergy status
Patient provides inaccurate information.
Errors in the health care system lead to the provision of inaccurate information (e.g. errors in undertaking, interpreting, or reporting tests).
Relevant data to inform treatment decision is missing.
Irrelevant knowledge.
Out-of-date knowledge.
Short-cut decision making due to time constraints (e.g. neglecting to incorporate patient preferences in the treatment decision).

*All of the above may or may not be recognised or suspected – if such data deficiencies are recognised or suspected, then it is necessary to consider alternative responses, or coping strategies, to responses that occur in cases of ignorance of the above causes.*
BOX 7 – Medicine is administered to patient

**Senior – Junior instructions – rule based intervention?**

Change in patient condition, e.g. can no longer swallow
Could be new error or from earlier point in chain

**Interventions**

- Increase nurse vigilance and awareness when patients self administer
- Labelling of IV lines
- Include the route of administration on all prescriptions
- Patient information/interaction – keeping more informed as a checking system. Patient can request to check drug before administered
- Patient education, e.g. IT, DoH, guidelines
- Bar codes
- Electronic records.
- Patient-held records.
- Prompts (electronic or otherwise).
- Delegation of data collection (e.g. nurse asks relevant questions).
- Decision support systems.
- Telephone reminders to patients (e.g. to increase compliance and reduce frequency of inaccurate patient-derived data).
- Enhance patient-health professional relationship.

**Patient condition change**

- Unable to administer – refuses; pulled NG tube out; no longer able to swallow; patient absconded or off ward for some reason, e.g. x-ray
- Dose omission – medication error
- Good practice inpatient care
- Communication failure
- Patient checks, e.g. IT, chemo
BOX 8: Medicines recorded on patient chart (relates primarily to inpatient and nursing home care, but could also include the updating of patient notes in primary care)

Events (what could go wrong):
Wrong information recorded (wrong drug, dose, route, formulation) (also on wrong patient’s chart)
Missing information (provision of medicine not recorded). – not recorded – MOST COMMON
Illegible, Incomplete, Irregular conventions, Confusing.
Chart/notewas not observed (e.g. patient chart not readily observable)
These events are similar to causes in the ‘decision to treat’ box (1), e.g. system-error leading to inaccurate or missing data.

Record on wrong patient’s chart
Failure to document
Lack of agreement in monitoring records
Updating patients’ charts
Contradiction of records, e.g. nursing notes and drug card

Causes
Handwriting.
Out-of-date knowledge (relating to incompleteness, illegality, or irregular conventions).
Oversight.
Inaccessible placement of patient chart.
lack of communication between shifts  (Maybe couldn’t administer in Box 7, and then not recorded or passed and picked up at night when pharmacy closed
Distraction
Failure to document and sign is biggest problem in hospital
Mismatch between training and requirements, e.g. what is recorded
**BOX 8: Medicines recorded on patient chart (relates primarily to inpatient and nursing home care, but could also include the updating of patient notes in primary care)**

**Interventions**
- Electronic charts/records
- Prescribing standard
- Appropriate placement of patient charts/records
- Biggest problem – coding system for drug omissions
- Use of a coding system to report outcomes and to indicate why medicine was not administered
- See also Box 2
BOX 9: Patient response monitored – opportunity for error identification

Events (what could go wrong):

- Adverse response missed or misinterpreted.
- Adverse response not acted upon.
- Adverse response incorrectly acted upon.
- Look for therapeutic improvement
- Unanticipated therapeutic response
- Error reaches patient but does not have an adverse response
- Protocols with triggers, e.g. x does not happen if y is not in place
  assume loops back to box 1
- Lack of therapeutic response
- Look for desired therapeutic effect as well as adverse effects? Linked to recording of information; impact on future prescribing decisions

Causes

- Necessary information to monitor patient not available.
- Necessary information to monitor patient not observed.
- No-one to whom to report adverse event available.
- Different levels of monitoring in primary care
- Distraction
- Knowledge
BOX 9: Patient response monitored – opportunity for error identification

**Interventions**

- Improved handover procedures (to highlight patients requiring particular attention).
- Adverse response support systems.
- Reminders to check patients, Prompts for what to check.
- Lack of therapeutic response
- ADR – adverse drug reaction
- ADE – unintended effect
- Protocols, e.g. clozapine – prescribing; dispensing
- Pharmacy review
- Drugs not dispatched to pharmacy before can be dispensed – codes
- Increased pharmacy involvement
- Elderly – designed tool for med assessment, if score above 8, pharmacy review (risk of falls, etc.)
- Awareness of what to monitor and how often
- Protocols, e.g. clozapine and thalidomide – regulated by company – awareness/knowledge/lapse
- Prescription/dispensing checks – drug not available unless patient has gone through checks
- Pharmacy review of response – scoring system