Prescribing errors with High Risk Medicines (HRMs) in Hospitals

A thesis submitted to The University of Manchester for the degree of
Doctor of Philosophy
In the Faculty of Biology, Medicine and Health

2018

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<th>Description</th>
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<tbody>
<tr>
<td>ADEs</td>
<td>Adverse Drug Events</td>
</tr>
<tr>
<td>A&amp;E</td>
<td>Accident &amp; Emergency</td>
</tr>
<tr>
<td>AHRQ</td>
<td>Agency for Healthcare Research and Quality</td>
</tr>
<tr>
<td>ASHP</td>
<td>American Society of Health-System Pharmacists</td>
</tr>
<tr>
<td>BMA</td>
<td>British Medical Association</td>
</tr>
<tr>
<td>BNF</td>
<td>British National Formulary</td>
</tr>
<tr>
<td>CAQDAS</td>
<td>Computerised-Assisted Qualitative Data Analysis Software packages</td>
</tr>
<tr>
<td>CE</td>
<td>Communication Errors</td>
</tr>
<tr>
<td>COREQ</td>
<td>Consolidated Criteria for Reporting Qualitative Research</td>
</tr>
<tr>
<td>CPOE</td>
<td>Computerized Physician Order Entry</td>
</tr>
<tr>
<td>CRD</td>
<td>Centre for Reviews and Dissemination</td>
</tr>
<tr>
<td>EAU</td>
<td>Emergency Assessment Unit</td>
</tr>
<tr>
<td>ECCs</td>
<td>Error-Causing-Conditions</td>
</tr>
<tr>
<td>EMBASE</td>
<td>Excerpta Medica Database</td>
</tr>
<tr>
<td>EPR</td>
<td>Electronic Patient Record</td>
</tr>
<tr>
<td>EU</td>
<td>European Union</td>
</tr>
<tr>
<td>FY1</td>
<td>Foundation Year 1</td>
</tr>
<tr>
<td>FY2</td>
<td>Foundation Year 2</td>
</tr>
<tr>
<td>GMC</td>
<td>General Medical Council</td>
</tr>
<tr>
<td>GP</td>
<td>General Practitioner</td>
</tr>
<tr>
<td>H</td>
<td>Hospital (regarding quotes from interviews/focus groups)</td>
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<tr>
<td>HEE</td>
<td>Health Education England</td>
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<tr>
<td>Abbreviation</td>
<td>Full Form</td>
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<td>--------------</td>
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<tr>
<td>HRMs</td>
<td>High Risk Medicines</td>
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<tr>
<td>ICU</td>
<td>Intensive Care Unit</td>
</tr>
<tr>
<td>IM</td>
<td>Intramuscular</td>
</tr>
<tr>
<td>IOM</td>
<td>Institute Of Medicine</td>
</tr>
<tr>
<td>IPA</td>
<td>International Pharmaceutical Abstracts</td>
</tr>
<tr>
<td>ISMP</td>
<td>Institute for Safe Medication Practices</td>
</tr>
<tr>
<td>IV</td>
<td>Intravenous</td>
</tr>
<tr>
<td>KBMs</td>
<td>Knowledge-Based Mistakes</td>
</tr>
<tr>
<td>LMWH</td>
<td>Low Molecular Weight Heparin</td>
</tr>
<tr>
<td>MEDLINE</td>
<td>Medical Literature Analysis and Retrieval System Online</td>
</tr>
<tr>
<td>NCC MERP</td>
<td>National Coordinating Council for Medication Error Reporting and Prevention</td>
</tr>
<tr>
<td>NHS</td>
<td>National Health Service</td>
</tr>
<tr>
<td>NICE</td>
<td>National Institute for Health and Care Excellence</td>
</tr>
<tr>
<td>NIH</td>
<td>National Institute of Health</td>
</tr>
<tr>
<td>Non-HRM</td>
<td>Non High Risk Medicines</td>
</tr>
<tr>
<td>NPSA</td>
<td>National Patient Safety Agency</td>
</tr>
<tr>
<td>NRLS</td>
<td>National Reporting and Learning System</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>Non- Steroidal Anti-Inflammatory Drugs</td>
</tr>
<tr>
<td>P</td>
<td>Participant (regarding quotes from interviews/focus groups)</td>
</tr>
<tr>
<td>PCA</td>
<td>Patient-Controlled Analgesia</td>
</tr>
<tr>
<td>PEs</td>
<td>Prescribing Errors</td>
</tr>
<tr>
<td>PICO</td>
<td>Population, Issue, Comparison, Outcome</td>
</tr>
<tr>
<td>PICO-TS</td>
<td>Population, Issue, Comparison, Outcome, Time, Study type</td>
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</table>
PIS  Participant Information Sheet
PPIs  Proton Pump Inhibitors
PRHO  Pre-Registration House Officer
QDS  Four times a day
Qualidata  Qualitative Data Archival Resources Centre
RBMs  Rule-Based Mistakes
RPS  Royal Pharmaceutical Society
SAS doctors  Staff grade, Associate specialist, Specialty doctors
SHO  Senior House Officer
TDS  Three times a day
TTO  To Take Out (discharge medication)
UK  United Kingdom
UREC  University Research Ethics Committee
US  United States
USA  United States of America
USP  United States Pharmacopeia
Definitions

**Adverse Drug Events** are injuries resulting from medical interventions related to a drug, (1) occur commonly in the medical field while the patient is under the care of healthcare providers. (2)

**Medication errors** are 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. (3)

**Prescribing errors** occur when, as a result of a prescribing decision or prescription writing process, there is an unintentional significant 1. reduction in the probability of treatment being timely and effective or 2. increase in the risk of harm when compared with generally accepted practice”. (4)

**High Risk Medicines** are defined by the NHS as the medicines that are most likely to cause significant harm to the patient, even when used as intended. (5) The ISMP defined them as the drugs that bear a heightened risk of causing significant patient harm when they are used in error. (6)

**On-call** are the working hours covering the period after 5 pm until the next day at 9 am on weekdays and all the time at the weekends (Saturday and Sunday)
Abstract

The University of Manchester

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Doctor of Philosophy

Prescribing errors with High Risk Medicines in Hospitals

July 2018

Background: Prescribing errors are the most frequent type of error in the medication use process. High risk medicines (HRMs) are a sub-class of medications that if used erroneously have potentially devastating consequences which defined by Institute for Safe Medication Practices (ISMP) as the drugs that bear a heightened risk of causing significant patient harm when they are used in error. Therefore, prescribing errors with HRMs are of concern to healthcare professionals that are responsible for ensuring mitigating patient safety. This thesis examines to what extent prescribing errors with HRMs in hospital occur, the causes of prescribing errors with HRMs and the differences to non-HRMs and the prescribing errors with HRMs during the on-call period.

Method: The research adopted a mixed methods approach to explore prescribing errors with HRMs in hospitals and three studies were undertaken. The first study was a systematic review of the literature to explore the prevalence and incidence of prescribing errors with HRMs in hospitals. The second study was a secondary analysis of 59 existing interviews with foundation year doctors to explore the causes of prescribing errors with HRMs and compare them to those for non-HRMs reported in the same interviews. The third study was a qualitative study of the challenges of prescribing HRMs safely during the on-call period. This final study involved six focus groups with foundation year doctors (total participants number was 42).

Results: Overall, findings demonstrated that there is paucity of studies that explored the prevalence of prescribing errors with HRMs and this literature showed inconsistency in definitions of prescribing errors, HRMs lists, severity scales and study methods (Study One). This resulted in a very wide range of prevalence of prescribing errors with HRMs. In terms of causes of prescribing errors with HRMs (Study Two), prescribing HRMs was considered a complex task for participants, especially those requiring dosage calculations, errors in the legal prescription requirements for controlled medications occurred with HRMs only and the on-call period was a particularly challenging period to prescribe safely especially with HRMs. In Study Three, the reasons found for this include the nature of the on-call period as a fast paced environment, the methods of communication such as the bleep system, lack of accessibility to patient information and lack of plan from the primary team.
**Conclusions:** HRMs form part of general medications, meaning they share similar traits, but the potentially devastating consequences of HRMs and the complicated task posed by prescribing them makes errors in their prescription profound. Therefore, HRMs need closer attention and more concern from healthcare professionals, researchers and policymakers. Such attention could result in a significant reduction in adverse outcomes and improved patient safety.
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Dedication

I dedicate this thesis to my father, Ali, my mother, Dalal and my brothers and sisters; as well as, my small family my wife and my children Ali, Dalal, Fahad, Ola and Mohrah. I couldn’t have done any of this work without their love, prayers and support throughout this journey.
Acknowledgment

My thanks to my country Saudi Arabia, Ministry of Defence, Medical Services Department, which has fully funded this PhD studentship.

My thanks extend to my supervisory team, Dr Penny Lewis and Dr Mary Tully - I could not have asked for a better supervisory team. Thank you for sharing your incredible knowledge and experience, for your guidance, the endless support and encouragement throughout this PhD journey.
The Author

Mahdi Alanazi was awarded BSc. in General Pharmaceutical Science in 2003 from King Saud University, College of Pharmacy, Riyadh, Saudi Arabia. After completing this degree, he worked as a pharmacist in King Khalid Military Hospital, Hafer Al-Baten, Saudi Arabia for five years, which involved working in the outpatient pharmacy and department of logistics and material management. In 2008, he enrolled in the programme of Master of Science in Pharmacy (Clinical Pharmacy), the College of Pharmacy at King Saud University and was awarded the degree in 2011. After that, he worked as a clinical pharmacist with the internal medicine teams in Prince Sultan Military Medical City, Riyadh, Saudi Arabia. From 2014 to date, Mr Alanazi is undertaking his PhD in pharmacy practice, Division of Pharmacy and Optometry, University of Manchester. During this period, in 2016, he has published his first study "A systematic review of the prevalence and incidence of prescribing errors with high-risk medicines in hospitals.” In the Journal of Clinical Pharmacy and Therapeutics. In 2017, he had presented the second study at the RPS winter summit. Study Two has been submitted to PLOS ONE journal and study Three will be submitted for publication in the coming months.
1. Chapter One

1.1 Introduction

Prescribing errors are the most frequent type of error in the medication use process. (2, 7) The percentage of prescribing errors ranges from 29% to 56% of medication errors in adults, (2, 7) and these figures have been found to be higher in children, ranging from 68% to 75%. (8, 9) Such errors can double a patient’s length of hospital stay and cost of care, as well as increasing their mortality rate. (10-12) With all types of medication, hospital prescribing errors are common, occurring with 7% of medication orders, 2% of patient days and 50% of hospital admissions. (13)

Within the general medication classes there are critical types of medications termed High Risk Medicines (HRMs) that are more likely to cause harm to a patient when they are used inappropriately compared to non-HRMs. (6, 14) Examples of such HRMs include anticoagulants, insulin and opioids. HRMs have more potential to cause harm. Thus, if they are prescribed erroneously, they can have a more significantly negative impact which can be associated with higher costs and increased mortality. (6, 14)
Medication errors are preventable and prescribing errors are one type of medication error and so are also preventable. (1) Even with this group of medications HRMs that have the potential to cause devastating harm when used erroneously, the prescribing errors are preventable. (1) The paucity within the current literature regarding prescribing errors with HRMs, such as occurrence and causes, poses a significant problem. Studying these areas could lead to a clearer picture about prescribing errors with HRMs that might reveal a different picture to what we know already about medications in general. This could lead to the development of specific strategies and techniques to reduce their incorrect use, and hence reduce patient harm. Therefore, this thesis aims to explore prescribing errors with HRMs in terms of their occurrence and causes, comparing the findings with non-HRMs.

1.2 Contributors

The main researcher Mr Alanazi took the major role in the production of all papers included in this thesis. He conceptualised and designed all of the studies, collected the data, carried out the analyses, drafted and revised manuscripts of the papers, and wrote the thesis.

The first study of this thesis (Chapter Four), has already been published in the Journal of Clinical Pharmacy and Therapeutics in 2016. The second study (Chapter Five) has been presented at the Royal Pharmaceutical Society (RPS) Winter Summit,
in 2017, and the abstract was published in the International Journal of Pharmacy Practice. A manuscript of the study is ready for submission to PLOS One. The manuscript of the third study (Chapter Six) of this thesis is ready for submission in one of the journals, which has yet to be decided upon. The co-contributors, the supervisors of these studies, their qualifications and their contributions are presented below:

Mary P. Tully, PhD, FFRPS, FRPharmS

Dr Tully is the main supervisor for Mr Alanazi. She conceptualised all of these studies with Mr Alanazi, and critically reviewed all manuscripts.

Penny J. Lewis, PhD, MRPharmS

Dr Lewis is the second supervisor for Mr Alanazi. She conceptualised all of these studies with Mr Alanazi, and critically reviewed all manuscripts.

1.3 Thesis structure

This section includes the rationale for submitting the thesis in a journal-based format and the outline of the thesis structure.
1.3.1 Rationale for submitting in journal format

The University of Manchester encourages students at the early stages of their PhD programme to choose either standard thesis format or journal-based format. The University particularly encourages students to use the journal-based format as it is a better way to disseminate knowledge more widely, and prepares students for publication early in their career. Navigation of the publication process is a skill that most researchers require, and it is one that requires training and guidance from experts, such as the supervisory team. Undertaking this process of publication as part of a PhD will prepare the student to be a future researcher who can independently produce publications. The primary researcher and the supervisory team agreed upon the journal-based format for this thesis for the aforementioned reasons. Furthermore, the type of research undertaken is a factor to consider when selecting the thesis format. In this research one problem was investigated, prescribing errors with HRMs, from different perspectives as a systematic review was undertaken, with primary and secondary qualitative research. The aims of these studies are different, lending themselves to a journal-based format in which each study can stand alone, while still forming part of the overall PhD programme of work.

1.3.2 Outline of the thesis
This thesis aimed to explore prescribing errors with HRMs in the hospital setting. The exploration process was a sequential process that answered one main question then moved to address the next question. These answers were depicted in chapters within this thesis, with each chapter focusing on one element of the main theme of the thesis. The following is the outline of the thesis structure.

The second chapter is a review of the current literature surrounding prescribing errors with HRMs. The aim was to understand the area and obtain background information within this field. The general areas that were covered in the literature review are adverse drug events, medication errors, prescribing errors, foundation year doctors and the on-call period.

The third chapter of the thesis is the programme of work and methods chapter. The first part of the chapter covers the aims and objectives of the thesis, followed by the programme of work structure. The following main points in this chapter are the overview of the rationales for conducting each study, followed by a brief overview of the methods used and the data analysis undertaken. The end of the chapter summarises the ethical and governance approvals of the conducted studies.

The fourth chapter is the first study of this thesis, Study One, which is a systematic review of the prevalence and incidence of prescribing errors with HRMs in the hospital setting. The first page of this chapter, and the following chapters, indicates if
the study has been published, is waiting for journal response, or is in publication format but has not yet been submitted.

The **fifth chapter** is Study Two of the thesis. This study explored the causes of prescribing errors by foundation doctors with HRMs and compared them with non-HRMs.

The **sixth chapter** is Study Three that explored the challenges to prescribing HRMs safely during the on-call period by foundation doctors.

The **seventh chapter** discusses the findings from the overall thesis. It summarises the key findings and implications of the studies to the current body of literature. Strengths and limitations of the research were covered, as well as the directions for future research. The end of this chapter is an overall conclusion of the thesis.
2. Chapter Two: Literature review

This chapter provides a background and an overview of the topic of “Prescribing Errors in High Risk Medicines”. Specifically, this chapter will cover the literature relating to adverse drug events and medication errors, including prescribing errors. Following this, foundation year prescribers in particular will be considered as they are the group with the highest rate of prescribing errors when compared to other prescribers. The causes of prescribing errors and high risk medicines (HRMs) will be examined in detail, and finally the on-call period will be assessed.

2.1 Adverse drug events

Adverse Drug Events (ADEs), injuries resulting from medical intervention related to a drug, (1) occur commonly in the medical field while the patient is under the care of healthcare providers. (2) The landmark Harvard Medical Practice Study I was the first study to direct the attention of researchers to ADEs worldwide. It investigated 30,121 records in 51 acute care settings, randomly selected in New York State in 1984, and showed that 3.7% of inpatients had suffered an ADE. (15) Adverse drug events can be unavoidable, such as in the case of drug allergy in response to a newly prescribed medication; (16) however, a significant proportion of ADEs are preventable, while serious ADEs are more likely to be preventable. (2) Figure 1 (adapted from Gandhi et al. (17)) describes the relationship between medication
errors and ADEs, where the intersection between them is the preventable ADEs. (17) The second Harvard Medical Practice Study showed that medications accounted for the greatest proportion (19%) of all adverse events. (18) In the 1990s, the prevalence of preventable ADEs in the US was estimated to be between 380,000 to 880,000 events annually. (2, 19, 20) However, the Institute of Medicine (IOM) believed these numbers were an underestimate due to limitations in the studies’ methods of estimation. The IOM estimated the actual numbers could be as high as 1.5 million preventable ADEs annually in the US. (21) Moreover, the IOM estimated that between 44,000 and up to 98,000 of deaths which occur annually in the US are caused by preventable ADEs, a figure that was extrapolated from the Harvard studies mentioned previously. (22) These estimated numbers exceed the number of the deaths that were related to the eighth leading cause of death in the National Vital Statistics Reports of causes of total annual deaths in the US; (23) moreover, these figures overtake the numbers of deaths in that year that were caused by car accidents, breast cancer and AIDS. However, medication errors are more common than ADEs, as only a proportion of medication errors actually lead to an adverse event. The following section 2.2 will cover medication errors in greater depth.
2.2 Medication errors

2.2.1 Introduction

Medications are a key element of conventional Western medical practice and the most frequent treatment used for patients, across a wide range of conditions. One survey in the USA showed that approximately 80% of the adult population uses at least one type of medication. Despite their substantial benefits, the medication use process can lead to errors. Such errors are one of the obstacles that healthcare providers face when attempting to keep patients safe, particularly in inpatient settings where all the steps of the medication use process are occurring. However, medication errors are preventable according to the definition given by the National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP).
(3) This organisation also lists a number of strategies and techniques to prevent and minimise such errors.

2.2.2 History

Studies about medication errors have been published since the early 1960s, (26-28) with research really beginning to focus on patient safety and medication errors from the middle of 1980s; (29) however, it was in 1991 when the landmark Harvard Medical Practice Studies were first published. (15, 18) Results of the Harvard studies encouraged researchers from different countries worldwide such as Australia (30) and the UK (31) to explore medication errors. (32) Since the early 90s, medication errors have received considerable attention from healthcare institutions and providers, along with governments, due to recognition of their ability to cause substantial mortality, morbidity, and additional healthcare costs. (12, 19)

Dedicated organisations have been established to prevent medication errors and improve medication safety by increasing healthcare providers’ awareness of errors, and by providing recommendations and solutions for the prevention of such errors. (3, 6) Examples of such organisations include the Institute for Safe Medication Practices (ISMP) which was established in 1975, and the NCC MERP organisation created in 1995 by the United States Pharmacopeia (USP). (3)
The boost in attention and awareness about medication errors from healthcare providers, stakeholders, media and public started in 2000 with the release of the report “To Err is Human” based on the results from the Harvard studies. (22) Based on this report the US Department of Health and Human Services established the Agency for Healthcare Research and Quality (AHRQ). (33) In the same year, the Department of Health in the UK released the report “An Organisation with a Memory”, (34) which led to the establishment of the National Patient Safety Agency (NPSA) in 2001 as part of the National Health Service (NHS). By June 2012, the key functions and expertise for patient safety transferred from the NPSA to the NHS Commissioning Board Special Health Authority. (35) Nowadays, this patient safety function also includes the National Reporting and Learning System (NRLS), which is a central database of patient safety incident reports, which has formed a part of NHS Improvement since April 2016. (36, 37)

2.2.3 Definitions of medication errors

Defining medication errors helps in understanding them better, which can then lead to the design of interventions to prevent or minimise errors. (38) Therefore, this review will examine the different definitions of medication errors to allow for better understanding and clarity. There are many definitions for medication errors in the literature, some of which were developed by medication safety organisations, whilst others were developed by independent authors. The following definitions in this chapter were selected for further description due to their widespread use in the
literature, in comparison with other definitions. A systematic literature review of medication error definitions, published in 2010, found inconsistencies of wording and content of the definitions used in literature. (39)

The most frequently used definition of a medication error was that created by NCC MERP which is “a medication error is any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of 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”. (3)

Several national organizations have defined medication errors, such as the ISMP in the USA and the NPSA in the UK. ISMP uses two definitions for medication errors: the first is the definition of NCC MERP which we have just stated, and the second is “any error occurring in the medication use process”, which was taken from a study by Bates et al. (2) In the UK, the NPSA uses the following definition “medication errors are incidents in which there has been an error in the process of prescribing, dispensing, preparing, administering, monitoring, or providing medicine advice, regardless of whether any harm occurred”. (40)
In terms of individual authors, Bates et al. had developed three definitions for medication errors that were published from 1995 to 1999. As previously mentioned one of them has been used by ISMP, (41) another definition is “error in the process of ordering, dispensing or administering medication, regardless of whether an injury occurred or whether the potential for injury was present”, (42) and the third is “errors occurring at any stage in the process of ordering or delivering a medication”. (41) Occasionally, the authors are influenced by their practice background or their research area; therefore, they use a definition of a particular kind of medication error to define the broader term of medication errors. An example of this was the definition by Dean et al. for medication error that was published in 1995, which states “a dose administered (or omitted) that deviated from the most recently written medication order for that patient”. (43) This definition concentrated on administration errors which are only part of the broader term of medication errors.

Inconsistencies in the definitions in the literature means there is no set standard for what is meant by the term medication errors. Standards provide consistency in reporting medication errors which would allow researchers or practitioners to compare different studies, systems, or hospitals and produce reliable results when describing the prevalence of these errors. (4, 39)

2.2.4 Financial impact
The financial burden of medication errors is a cause for concern for governments, and healthcare stakeholders, because of the negative impact on the economy, and waste of resources. The Department of Health in the UK employed a specialised economic company to explore the costs of unsafe care in the NHS. The report, published in October 2014 showed that cost due to preventable errors in the NHS were over £1 billion, possibly as high as £2.5 billion annually, with the greatest costs related to medication errors. (44) In 2000 the USA’s estimations of medication error costs ranged from $17 billion up to $29 billion annually. (22, 45, 46) A more recent report was published in June 2013 which showed that medication errors cost $20 billion per year. (47) Some of the extrapolations were based on the direct cost of medication errors like admissions, (45, 46) whilst some of them calculated direct and indirect costs, such as additional care necessitated by the errors, loss of income and household productivity, and impact of disability. (22)

### 2.2.5 Inpatient settings

Certain areas within the healthcare system are more at risk of medication errors, in particular the inpatient setting, which are more vulnerable than out-patient settings in terms of adverse drug events and money spent on medication errors. (12, 47) Medication errors in these settings can lead to doubling the patient mortality rate and an increase in the cost of patient care by increasing a patient’s length of stay. (19) Additionally, one report assessing avoidable cost in healthcare settings found around
90% of the money spent on medication errors in the USA was due to preventable errors in inpatient settings. (47)

### 2.2.6 Common types of medication error

The medication use process is a complicated one with multiple steps. Therefore, medication errors are often divided into four types based upon those steps, which are: prescribing errors, transcribing errors, dispensing errors, and administration errors. (3) The literature shows that most medication errors occur during prescribing, followed by administration, then transcribing and least commonly during dispensing. (2, 7) Two milestone studies addressed the percentage frequencies of error in each process of medication use; they are Bates et al. and Leape et al. (2, 7) the results showed that errors during physician prescribing were most common (39% to 56%). (2, 7) Furthermore, in children, prescribing errors are the most frequent amongst other medication use process errors, with reported frequencies ranging from 68% to 75% of all medication errors. (8, 9) Section 2.3 discusses prescribing errors, the most common type of medication error, in greater detail.

### 2.3 Prescribing errors
2.3.1 Prevalence and incidence

Epidemiological studies that investigate prevalence and incidence rates of an issue, especially in healthcare settings, are important to determine the extent of the issue. When these studies are combined in a robust design, such as a systematic review study, it helps researchers, or those who may have concerns, such as governments, organizations, and stakeholders, to make decisions to tackle, solve, or minimize problems. Prescribing errors have been studied epidemiologically, using prevalence and incidence studies, and their rate disseminated in the literature since the late 1980s. (48, 49) In 1987, a study by Folli et al., (49) conducted in a children’s hospital, was the oldest study included in the Lewis et al. (13) systematic review. The study recorded the frequency of prescribing errors prospectively in two large hospitals and reported that 0.5% of medication orders have prescribing errors, and the incidence was 15.8 per 1000 patient days. (49) The systematic review that was conducted by Lewis et al. in 2009, systematically reviewed epidemiological studies of the prevalence and incidence of prescribing errors in inpatient settings. (13) The results, which are more reliable than those of previous studies as the systematic review is on the top of literature in terms of the strength of the evidence. This because of the big number of the included studies that produce the average of the prevalence and incidence of the included studies, the median of the included studies showed that prescribing errors were more common when compared with earlier individual studies. (48, 49) The results of this study for each denominator were found to be as follows; medication orders (7%), patient days (2%), and hospital admissions (50%). (13)
2.3.2 Definitions of prescribing errors

There are many definitions for prescribing errors in the literature established by different authors and organisations. (13, 50) This variety of definitions is one of the reasons for the wide variations in results of prescribing error studies. (51) The aforementioned systematic review, by Lewis et al., included 65 studies published from 1985 to the end of 2007, reporting on the prevalence or incidence of prescribing errors. (13) The results of this study showed great variation in the definitions that were used in the literature; 42% of the studies used the authors’ definition or definitions used in previous studies, whilst 17% used the Dean et al. (4) definition and around 18% used the medication error definition or ADE definitions that were developed by either the American Society of Health-System Pharmacists (ASHP) or NCC MERP, with the reminder of studies (23%) not using any clear definition. (13)

The most common and precisely established definition for prescribing errors, in Lewis et al. study, was developed by Dean et al. in 2000, using a two stage Delphi questionnaire technique (52, 53) which was presented to 34 UK healthcare practitioners including doctors, pharmacists and nurses. (4) The definition is “a clinically meaningful prescribing error occurs when, as a result of a prescribing decision or prescription writing process, there is an unintentional significant (1)
reduction in the probability of treatment being timely and effective or (2) increase in the risk of harm when compared with generally accepted practice”.

2.3.3 Stages of patient’s hospital stay and prescribing errors

During hospital inpatient care, prescribing errors can occur in any of the four main stages of a patient’s stay; namely hospital admission, during stay, rewriting of a prescription chart, and during discharge. A study published by Tully and Buchan in 2009, in an 880 bed teaching hospital, reviewed 33,012 new medication orders for 5,199 patients, and found 3,455 errors (10.5%) in 2,040 patients (39.2%). Errors were 41% more likely to be identified at the patient admission stage than at other times, accounting for independent confounders; specifically the seniority of the pharmacist, the checking workload, the day of the week, and the type of ward. A more recent study in 2015 conducted in 20 hospitals in the UK showed that prescribing errors at admission were the most common. These results show the need for a solution or an intervention during the admission stage. One important intervention is medication reconciliation at admission, which minimises prescribing errors and is now a mandatory requirement within the NHS.
2.3.4 Types of prescribing errors

There are many types of prescribing errors. A good model of classification for error types was established by Dean et al., (57) which was applied in other studies of prescribing errors. (55, 58) The classification divide errors into five major types; need for drug therapy, selection of a specific drug, selection of dosage regimen, administration of drug, and provide drug product. Table 2-1 depicts these major types of error and the subtypes under each one.(54, 57) The most commonly reported types in studies, based on work by Lewis et al. in a systematic review are dosage errors (55% of adult studies and 71% of child studies reported dosage errors), followed by errors of omission (15% of studies reported errors of omission), and incomplete prescriptions (12%). The rest were composed of illegibility, errors in dosage interval, incorrect formulation, drug-drug interactions, and transcription errors. (13) The highest percentage (71%) of reported prescribing errors are dosage errors for children- this is likely due to the wide range of weights and ages needed to calculate the medication dosage; resulting in imprecise calculations. (13)
Table 2-1: Types and subtypes of prescribing errors (54, 57)

1. Need for drug

<table>
<thead>
<tr>
<th>Type of Error</th>
<th>Subtype</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unintentional omission on admission</td>
<td>Omission from chart at rewrite</td>
</tr>
<tr>
<td>Unintentional omission from discharge prescription</td>
<td>Premature discontinuation</td>
</tr>
<tr>
<td>Continuation for longer than necessary</td>
<td>Not prescribed when indicated</td>
</tr>
<tr>
<td>No indication</td>
<td>Duplication of treatment</td>
</tr>
</tbody>
</table>

2. Selection of specific drug

<table>
<thead>
<tr>
<th>Type of Error</th>
<th>Subtype</th>
</tr>
</thead>
<tbody>
<tr>
<td>Significant allergy</td>
<td>Clinical contra-indication</td>
</tr>
<tr>
<td>Continuing in event of adverse drug reaction</td>
<td>Contra-indicated due to drug interaction</td>
</tr>
<tr>
<td>Not drug intended</td>
<td></td>
</tr>
</tbody>
</table>

3. Selection of dosage regimen

<table>
<thead>
<tr>
<th>Type of Error</th>
<th>Subtype</th>
</tr>
</thead>
<tbody>
<tr>
<td>Failure to specify maximum dose</td>
<td>Failure to take into account drug interaction</td>
</tr>
<tr>
<td>Dose/rate mismatch for infusion</td>
<td>Daily dose incorrectly split into subdoses</td>
</tr>
<tr>
<td>Overdose</td>
<td>Underdose</td>
</tr>
</tbody>
</table>

4. Administration of drug

<table>
<thead>
<tr>
<th>Type of Error</th>
<th>Subtype</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wrong route</td>
<td>Wrong formulation</td>
</tr>
<tr>
<td>Administration times incorrect or not specified</td>
<td>IV instructions incorrect or not specified</td>
</tr>
<tr>
<td>Start date incorrect/missing</td>
<td></td>
</tr>
</tbody>
</table>

5. Provide drug product

<table>
<thead>
<tr>
<th>Type of Error</th>
<th>Subtype</th>
</tr>
</thead>
<tbody>
<tr>
<td>Product or formulation not specified</td>
<td>Strength or dose not specified</td>
</tr>
<tr>
<td>Route unspecified</td>
<td>Medication order not signed</td>
</tr>
<tr>
<td>Controlled drugs legislation requirements not fulfilled</td>
<td></td>
</tr>
</tbody>
</table>
2.3.5 Drug type

The most frequent classes of medication in which prescribing errors occur are antimicrobials, cardiovascular medications, central nervous system medications, respiratory medications, endocrine medications, fluid and electrolyte and parenteral nutrition medications, and other medications like analgesics and gastrointestinal medications. (13, 55) Within these medication classes, there are types of medications that are more likely to cause harm to a patient when they are used inappropriately, these are termed high risk medicines and will be discussed in detail in Section 2.6.

2.4 Foundation year doctors

It is common across the world for medical doctors to work in a hierarchical structure, based on their training and experience. The studies in this PhD thesis were conducted in the UK; therefore, this section focuses on the British medical training structure. In the UK there are three overarching levels of ranks in medicine starting with medical students, followed by junior doctors and finally with senior doctors. These levels of hierarchy are described by the British Medical Association (BMA), which is the trade union and professional body for doctors in the UK. (59) Figure 2 depicts the grades and required training for medical doctors in the UK adapted from the BMA.(60) Junior doctors include foundation doctors and speciality training doctors; senior doctors include consultants, GPs and staff grade, associate specialist and
specialty doctors (SAS doctors). The latter are typically four years post-qualification with at least two years in a given specialty and spend the majority of their time working in the NHS.

Figure 2: Grades and training for medical doctors in the UK (60)

The General Medical Council (GMC) is the body that controls and certifies medical students and doctors within the UK. (61) The GMC sets standards for training and performance of medical practitioners to assure patient safety. These standards are set out in the documents ‘Tomorrows Doctors’ in 2009 (62) and ‘The Trainee Doctor’ in 2011. (63) More recently in 2016, the GMC introduced new standards for
‘Promoting Excellence: Standards for Medical Education and Training’. (64) There are ten standards under five themes; which are learning environment and culture, educational governance and leadership, supporting learners, supporting educators, and developing and implementing curricula and assessments. (64) The core of these ten standards is patient safety; therefore, applying these standards is a requirement to organisations and doctors in training such as medical students and doctors yet to be certified by the GMC. (64)

Of these grades, it is foundation doctors (foundation year 1 (FY1) and foundation year 2 (FY2)) that do the majority (70%) of prescribing. (55) In general, foundation doctors make more prescribing errors than senior doctors. (65, 66) One study reported error rates based on written medication orders in relation to doctors’ grades as following; FY1 (8.6%), FY2 (10.2%) and consultants (4.8%). (55) These figures demonstrate the importance of focusing efforts on understanding the causes of errors made by foundation doctors so that interventions can be designed to have maximum impact on improving prescribing, and thus patient safety.

Foundation year doctors, as shown in figure 2, are of two levels, which equate to a postgraduate training level. The first is that of FY1 doctors, who have provisional registration with the GMC. The second is FY2 doctors, who are fully registered with the GMC. However, both levels should work under a more experienced supervisor. (67) These titles have been in use from August 2005 and replaced the previous titles of pre-registration house officer (PRHO), equivalent to FY1, and senior house
officer (SHO), the first year of which was equivalent to FY2. (68) The term ‘junior doctor’ is often used interchangeably in reference to foundation year doctors; (69) however, the term junior doctor is applied to any doctor in training. (64) Therefore, we will explicitly use the term ‘foundation doctors’ throughout this thesis for clarity.

As FY1 doctors have just completed undergraduate medical school and moved to hospitals, to become FY1 doctors, the transition process from university student to FY1 doctor involves huge changes such as increased responsibility, workload, and the formation of new relationships with other healthcare professionals and with patients. (70) These changes can be challenging to adapt to, especially in socially and technically complicated environments, such as that of the hospital environment. (71) It has been suggested that FY1 doctors who have just transferred from studentship environment to the practice environment should be better prepared to adapt with this new environment. (72, 73) As the GMC indicates, they should work under the supervision of more experienced doctors. (67) Senior doctors have to support FY1 doctors especially at the beginning of their placements to ensure a smooth transition to the hospital environment. (74, 75) Inadequate support can be seen as ineffective teamwork, which could be a result of poor communication between healthcare professionals, where both poor teamwork and poor communication can lead to patient harm. (76) The transition between FY1 to FY2 has not been studied; however, the beginning of any placement regardless of the doctor’s level, whether they were FY1 or speciality training doctors, was attributed to increasing patient mortality rates. (77, 78)
2.5 Causes of prescribing errors

There are two approaches to understanding human error which underpins prescribing errors. These are the person centred approach and the system approach. (79) The first has been the most traditional in medicine; this approach assigns the causes of errors to the forgetfulness, carelessness and negligence of individuals. (79) However, the second approach accepts the unavoidable fallibility of humans and therefore centres efforts on changing the systems in which people work and operate. (79) There are many models based on the systems approach that have been used to classify the causes of prescribing errors such as the Yorkshire contributory factors framework, (80) the London protocol (81, 82) and Reason’s model of accident causation. (83) The latter is most commonly used to study the causes of error in the literature. (84) Figure 3 depicts Reason’s model for accident causation, also commonly known as the Swiss cheese model. (79) The three elements of Reason’s model of accident causation are active failure, error-causing conditions and latent conditions. (83) There are defence barriers in the organisation to prevent the error; however, weaknesses or holes can arise within these defence barriers. Like the Swiss cheese, when these holes line up through all these barriers, the active failures and latent conditions can cause errors to occur. (79) Therefore, errors are rarely due to a singular cause; usually there are many factors contributing to one error. (85, 86) The following paragraphs describe the elements of Reason’s model of accident causation and how this model links with prescribing errors.
The first elements of Reason’s model of accident causation are active failures. Such active failures are directly related to those on the front line, such as doctors and nurses, who have direct contact with patients. (85) Active failures can be intentional failures (considered planning failures) such as mistakes and routine violations, or unintentional failures (considered storage and execution failures). (83) Table 2-2 summarises the definitions of the active failures involved in prescribing errors. (83) Prescribing errors related to prescribing decision failure are termed knowledge-based mistakes (KBM) and rule-based mistakes (RBM). Prescribing errors relating to a failure in execution of a task can be either slips (intending to do one thing, but doing another), or memory lapses (forgetting to do something). Both mistakes and execution failures can lead to prescription-writing process failures; however, mistakes are complex and difficult to understand in comparison to execution failures. Moreover, mistakes are likely to rise from a higher level of cognitive process, unlike execution failures. Because of their nature, they are difficult to notice and even when
they are noticed they can be debatable; therefore, in comparison to execution failures, they may go unnoticed for longer. (83) In 2014, a study interviewed 30 FY1 from a variety of medical schools and hospitals within the UK. (87) The study explored the causes of prescribing errors, based on Reason’s model, and described the causes in the active failure phase extensively, particularly mistakes. Active failures were execution failures (slips and lapses) and planning failures (KBMs and RBMs). The study found that KBMs were caused by poor knowledge of practical aspects of prescribing, while the RBMs were caused by inappropriate application of the knowledge.

Table 2-2: Definitions of the different types of active failures (causes) involved in prescribing errors (83)

<table>
<thead>
<tr>
<th>Cause of the error</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Planning Failure</td>
<td>Correct execution of inappropriate or incorrect plan</td>
</tr>
<tr>
<td>a. Knowledge-Based Mistake</td>
<td>Mistakes that occur at the knowledge based performance level. Occur when faced with a novel task and have to consciously construct a plan of action. Occur when an inappropriate plan or incorrect plan is correctly executed.</td>
</tr>
<tr>
<td>b. Ruled-Based Mistake</td>
<td>Mistakes that occur at the rule-based performance level when drawing on a set of stored mental if-then rules. Occur when an inappropriate plan or incorrect plan is correctly executed.</td>
</tr>
<tr>
<td>2. Execution Failure</td>
<td>Failure in the execution of a good plan</td>
</tr>
<tr>
<td>a. Slips</td>
<td>An error that is caused by a failure in performing an intended action and that is replaced by another action</td>
</tr>
<tr>
<td>b. Lapses</td>
<td>An error that is caused by omission of a particular task</td>
</tr>
<tr>
<td>3. Violation</td>
<td>An error that is caused by a conscious decision to ignore the accepted rules or procedures of the organization</td>
</tr>
</tbody>
</table>
Another type of active failures are violations, which are “a deliberate deviation from those practices deemed necessary by organisation to maintain the safe operation of a potentially hazardous system”. (83) The difference between violations and other types of error is the intention, as violations are deliberate actions. It is believed that violations and errors involve different cognitive mechanisms inside the brain, and studies have shown that violations decline with age whilst other types of errors do not. (83, 88) This could partially explain the violations with foundation year doctors as the majority of them are young. Even though violations are deliberate actions, the subset of actions that are intended to damage the system are regarded as sabotage, which is outside of the scope of what we want to describe.

‘Good’ intentional violations, that do not intend system damage, can be divided into three types of violations: routine, exceptional and situational. (83, 85, 89) Routine violations, also called habitual violations, are the short cuts between two points used on a regular basis, which are influenced by the human nature to do the least effort for the task at hand. They can cause benign consequences that result in lack of punishment against said individuals by organisations. Routine violations are common in environments such as hospitals. (83, 85, 89) For example, prescribers may sign an IV fluid form during the on-call period without properly assessing the patient as they are busy, knowing that IV fluids in general are benign for patients. Exceptional violations occur when unusual circumstances call for an unusual response that is outside accepted practice. These violations may be inevitable and very risky; however, they are uncommon. (83, 89) Situational violations are the only applicable way to do the task when the existing rule is inapplicable in the current
situation. (85, 89) Like exceptional violations, situational violations are inevitable and involve a high degree of risk; moreover, both of these violations, when resulting in an accident will lead disciplinary action. (89) Both exceptional and situational violations are uncommon and rare to occur; therefore in medical literature there are no reports as to when they occur.

Errors and violations rarely occur in isolation; usually there are factors in the environment which promote the commission of errors and violations. There are many terms describing them such as error-causing conditions, error-provoking conditions, error-producing conditions, local climate conditions, and local conditions. In relation to errors in medicine and medication safety, particularly prescribing errors, common error-causing conditions are considered to be the individual prescriber, the working environment, the prescribing task, the patient and the healthcare team. (83)

Another factor linked to the emergence of prescribing errors is latent conditions, “whose adverse consequences may lie dormant within a system for a long time, only becoming evident when they combine with other factors to breach the system’s defences”. (83, 85) Unlike active failures, latent conditions arise from organisational level decisions. In high technology systems, such as hospitals, they may pose a greater threat to safety compared to active failures. (83) An example is the introduction of an electronic prescribing system within hospitals, a latent condition that can affect patient safety because the prescriber can prescribe patients medication
at any computer terminal around the hospital without directly assessing or communicating with them. A reactive risk management approach does not attend to latent conditions and thus there is a necessity for proactive risk management to detect the weaknesses in the system before errors occur. (79)

A systematic review by Tully et al. explored the causes of and factors associated with prescribing errors amongst hospital inpatients. (86) The review used Reason’s model of accident causation to categorise and organise the causes of prescribing errors from the literature to reach an informative conclusion about the causes of prescribing errors. (86) The review found 17 articles about the causes of prescribing errors that described 16 studies. The studies described active failures such as KBMs, (90-94) RBMs, (95) slips and lapses, (90, 92-95) and violations. (90, 92, 93, 95, 96) Error-causing conditions described were the individual prescriber (e.g. physical health and knowledge), (90, 94, 95) working environment (e.g. staffing and accessibility for drug information), (90, 94, 95, 97, 98) the healthcare team (e.g. poor communication and the relation with seniors), (93-96) prescribing task (e.g. non-routine tasks or protocols) (90, 94, 95) and the patient (e.g. difficulty with communication, complex disease). (94, 95) Latent conditions varied and were inconsistent in how they were described but included factors such as reluctance to question greater authority, (96) organisational system (97) and the low importance attached to prescribing. (94, 95) Three more recent studies published in 2013 and 2014, investigated the causes of prescribing errors, especially by foundation doctors, based on Reason’s model of error causation. (87, 99, 100) Two of these publications, the ones published in 2013, were part of one major study called PROTECT
(‘PRescribing Outcomes for Trainee doctors Engaged in Clinical Training’) that focused on investigating the prevalence and causes of prescribing errors specifically among foundation doctors in Scotland. (99, 100) Moreover, a systematic review study published in 2016 examined the causes of prescribing errors by foundation doctors, showed that approximately two third of included studies used Reason’s model of error causation. (101) A more recent use for the Reason’s model of error causation was in 2018 by a Saudi Arabian’s study, which aimed to explore physicians’ perceived causes of prescribing errors in Saudi hospitals. (102) The results of the study focused on exploring the error-causing conditions, which is the known five elements and an extra element that the study mane it as “Technology”, and latent conditions, which was mainly related to clinical pharmacists, training and management. (102) The study concluded the causes of prescribing errors in Saudi Arabian’s hospitals were multifactorial, this conclusion is consistent with the findings in developed countries such as the UK.(102)

These previous studies have all been based upon the investigation of prescribing errors made with all types of medication without any distinction made between those errors made with non-HRMs and those made with HRMs. There may be many similarities, but there could also be important differences between these classes. Section 2.6 describes HRMs in detail to give an overview of this group of medications.
2.6 High risk medicines (HRMs)

High Risk Medicines (HRMs) are defined by many organisations and authors, such as the ISMP (6) and NPSA. (5) The aforementioned organisations have focused on HRMs because of their ability to cause devastating harm when they are used inappropriately, compared to regular medicines. The ISMP uses the term “high alert medications” while the NPSA uses “high risk medicines”; however, they have the same meaning. In this research the term “high risk medicines” (HRMs) is used as this research was conducted in the UK, thus the UK derived term is used throughout.

In terms of definitions, both the NPSA and ISMP have their own definitions; these definitions have the same concept of giving awareness to healthcare professionals, while the terms used are different. The NHS, which uses the term high risk medicines, defines them as “medicines that are most likely to cause significant harm to the patient, even when used as intended”. (5) The ISMP organisation, which uses the term high alert medication, defines them as “drugs that bear a heightened risk of causing significant patient harm when they are used in error”. (6)

The first list of high alert medications was published by the ISMP in 1989 by Davis et al. The list had six medications; lidocaine, vincristine, sodium chloride (hypertonic concentrations), insulin, potassium chloride, and morphine. (103) The ISMP started to publish periodic lists of HRMs in both acute care settings and
ambulatory care settings. The lists are based on submission of error reports to the ISMP National Medication Errors Reporting Program, literature that has reported harmful errors, and which identified the medications mostly involved in harmful errors, and additionally has input from practitioners and safety experts. (6) The most recent HRM list in acute care settings was published in 2014 by the ISMP, (6) and contains 22 classes of medications (as seen in Table 2-3) and 12 specific medications (as seen in Table 2-4).
Table 2-3: ISMP list of High Alert Medications in acute care settings (Drug Classes) (6)

<table>
<thead>
<tr>
<th>Drug Classes</th>
<th>Example(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>adrenergic agonist IV</td>
<td>epinephrine, phenylephrine, norepinephrine</td>
</tr>
<tr>
<td>adrenergic antagonists IV</td>
<td>propranolol, metoprolol, labetalol</td>
</tr>
<tr>
<td>anaesthetic agents general, inhaled and IV</td>
<td>propofol, ketamine</td>
</tr>
<tr>
<td>antiarrhythmic agents IV</td>
<td>lidocaine, amiodarone</td>
</tr>
<tr>
<td></td>
<td>adrenergic antagonists IV</td>
</tr>
<tr>
<td></td>
<td>anaesthetic agents general, inhaled and IV</td>
</tr>
<tr>
<td></td>
<td>antiarrhythmic agents IV</td>
</tr>
<tr>
<td>antithrombotic agents</td>
<td>warfarin, LMWH, IV unfractionated heparin</td>
</tr>
<tr>
<td>anticoagulants *</td>
<td>factor Xa inhibitors</td>
</tr>
<tr>
<td>direct thrombin inhibitors</td>
<td>argatroban, bivalirudin, dabigatran etexilate</td>
</tr>
<tr>
<td>thrombolytics</td>
<td>alteplase, reteplase, tenecteplase</td>
</tr>
<tr>
<td>glycoprotein IIb/IIIa inhibitors</td>
<td>eptifibatide</td>
</tr>
<tr>
<td>cardioplegic solutions</td>
<td></td>
</tr>
<tr>
<td>chemotherapeutic agents parenteral and oral*</td>
<td></td>
</tr>
<tr>
<td>hypertonic dextrose, 20% or greater</td>
<td></td>
</tr>
<tr>
<td>dialysis solutions peritoneal and haemodialysis</td>
<td></td>
</tr>
<tr>
<td>epidural or intrathecal medications</td>
<td></td>
</tr>
<tr>
<td>hypoglycaemic, oral</td>
<td></td>
</tr>
<tr>
<td>inotropic medications IV</td>
<td>digoxin, milrinone</td>
</tr>
<tr>
<td>insulin subcutaneous and IV*</td>
<td></td>
</tr>
<tr>
<td>liposomal forms of drugs and conventional counterparts</td>
<td>liposomal amphotericin B, amphotericin B desoxycholate</td>
</tr>
<tr>
<td>moderate sedation agents IV *</td>
<td>dexametomidine, midazolam</td>
</tr>
<tr>
<td>moderate sedation agents oral for children</td>
<td>chlortal hydrate</td>
</tr>
<tr>
<td>narcotics and opioids IV, transdermal and oral*</td>
<td></td>
</tr>
<tr>
<td>neuromuscular blocking agents</td>
<td>succinylcholine, rocuronium, vecuronium</td>
</tr>
<tr>
<td>parenteral nutrition preparations*</td>
<td></td>
</tr>
<tr>
<td>radiocontrast agents IV</td>
<td></td>
</tr>
<tr>
<td>sterile water for injection, inhalation, and irrigation</td>
<td></td>
</tr>
<tr>
<td>sodium chloride hypertonic concentration</td>
<td></td>
</tr>
</tbody>
</table>

IV= Intravenous, LMWH= Low Molecular Weight Heparin
* HRMs included in NPSA list
Table 2-4: ISMP list of High Alert Medications in acute care settings (Specific Medications) (6)

<table>
<thead>
<tr>
<th>Specific Medications</th>
</tr>
</thead>
<tbody>
<tr>
<td>epinephrine subcutaneous</td>
</tr>
<tr>
<td>insulin U-500 *</td>
</tr>
<tr>
<td>methotrexate oral (non-oncologic use)</td>
</tr>
<tr>
<td>oxytocin IV</td>
</tr>
<tr>
<td>potassium chloride for injection concentrate</td>
</tr>
<tr>
<td>promethazine IV</td>
</tr>
<tr>
<td>epoprostenol IV</td>
</tr>
<tr>
<td>magnesium sulfate injection</td>
</tr>
<tr>
<td>opium tincture</td>
</tr>
<tr>
<td>nitroprusside sodium for injection</td>
</tr>
<tr>
<td>potassium phosphates injection</td>
</tr>
<tr>
<td>vasopressin IV or intraosseous</td>
</tr>
</tbody>
</table>

* HRMs included in NPSA list

The NPSA has its own list of HRMs containing eight classes, and is based upon 60,000 medication incidents reported to the National Reporting and Learning System (NRLS) between January 2005 and June 2006. (5) The eight classes within the NPSA list for HRMs are; anticoagulants, injectable sedatives, opiates, insulin, antibiotics (allergy related), chemotherapy, antipsychotics, and infusion fluids. The ISMP list includes all of the NPSA classes and more, apart from antibiotics (allergy related) which are only in the NPSA list. (5)

There are differences in the HRM lists within the same organisation and across medication safety organisations. The reasons behind this are numerous and include, for example, the differences in the practice settings, such as the types of medications and dosage forms commonly used. ISMP has two lists of HRMs, one for acute settings and one for the ambulatory care setting. The latter is focused on some medications that are not included in the acute care settings list; however, these medications could be prescribed in acute settings, but the safeguards and precautions are more needed in ambulatory settings. These medications are such as antiretroviral
agents, immunosuppressant agents, and pregnancy category X agents (e.g. bosentan and isotretinoin) which cause teratogenic effect in foetuses. (104)

Another reason for discrepancies between the lists is the difference between the regulations of different countries, and the differences in their healthcare systems. For instance, the NPSA list, which is a UK based organisation, has some differences with fewer classes of HRM when compared to the ISMP list, which originated in the USA. The healthcare system in the UK is mainly operated by one organisation, the NHS, which provides some consistency in the pattern of prescribed medication, which leads to narrowing of the classes of HRMs compared to the ISMP list. On the other hand, ISMP classes represent the US healthcare system, which is different to the UK but also varies considerably within the USA. These variations in regulations, policies and drug classes lead to a broader list of medications used within the USA. Due to these differences, the ISMP list contains more classes of medications, and some medications that are not used in the UK such as opium tincture. Both the NPSA and ISMP lists of medications will be used as HRMs in this PhD research, without any differentiation between them as we are interested to explore HRMs systematically and globally without focusing on single country or region.

2.7 On call
Working hours in hospitals are very long, and legislation such as the European Working Time Directive (105) in the EU try to help healthcare workers to reduce these hours. This has been enacted within the UK in the Working Time Regulations. (106) The healthcare professions have a very long journey to reach reasonable weekly working hours, comprised of a maximum 48 hours working week. (107) These reasonable working hours seek to help healthcare professionals, especially prescribers, to perform in a manner that results in improved patient safety. (106) The GMC have applied the working time regulations of a maximum of 48 hours weekly from August 2009 for junior doctors, whereas the rules have applied to seniors (consultants and SAS) for one decade longer. (108) However, in 2011 about two thirds of junior doctors reported exceeding the weekly working hours. (109) In a 2017 survey conducted by the GMC on doctors in training revealed that about 80% of them experienced at least a weekly occurrence of their working hours exceeding the working time regulations, and 30% experienced working extra hours on a daily basis. (110) Long working hours for doctors are linked to an increase in preventable medication errors; in contrast, reducing the working hours results in improved wellbeing of the prescribers and reduces the rate of errors occurring. (111-113)

In the UK, working hours for foundation doctors are usually divided into daytime working hours which are Monday to Friday from 9 am to 5 pm, and on-call working hours, which cover the period after 5 pm until the next day at 9 am on weekdays and all the time at the weekends (Saturday and Sunday). The on-call period has fewer staff covering the same number of inpatients, which could result in patient safety being diminished. There are studies that show that mortality rates increase during the
on-call period of admissions, weekends and nights. (114-116) This is also contested, as there is some evidence that more severely ill patients, urgent and emergency conditions, are admitted during the on-call period which is why the mortality is higher. (116) Therefore, there is a proposal in the UK to change working hours of NHS trusts to include all seven days rather than five days to ensure anyone who is admitted at any day during the week will have the same standards in terms of assessment, diagnosis, treatment and review. (117) This process has been trialled in some NHS trusts around the UK with an enthusiastic response from some healthcare professionals. (117)

However, there are challenges to the application of this process, as the expected cost of funding the NHS to deliver this service increases from 1.5% to 2% of the total budget, which is equivalent to an increase from 5% to 6% of the cost of a hospital admission at the NHS. (118) The NHS is already facing a shortage of money as some estimations showed £22 billion fund deficit. (119) Moreover, some doubts were expressed for the plan as it could increase the workload and affect patient safety. (120, 121) The experiment will take its time to give a better understanding of its benefits and limitations. That may result in revolutionary solutions for the gap in practice, especially for patient safety during the on-call period.
3. Chapter Three: Overview of programme of work and methods

This chapter is an overview of the programme of work including the study’s aims, objectives and structure, as well as the methods for each of the three studies and the ethical approval process which was undertaken.

3.1 Overview of programme of work

3.1.1 Aims and Objectives

Prevalence, incidence and causes of prescribing errors in general medications (regardless of whether HRMs or non-HRMs) have been addressed by a large number of published papers. However, there is a paucity of literature that distinguishes between HRMs and non-HRMs in terms of epidemiological studies, and studies of their causes. Thus, this research focuses on their differences. After conducting the second study (found in Chapter Five) about the causes of prescribing errors with HRMs and non-HRMs, it was found that the on-call period presents various challenges for foundation doctors, particularly when prescribing HRMs. Therefore, an additional aim was developed to investigate this specific area.
The aims of this PhD programme of work are to:

1. Investigate the published prevalence and incidence of prescribing errors with HRMs in hospitals.
2. Identify the causes of errors with HRMs compared to non-HRMs prescribed by foundation doctors in hospitals.
3. Explore the challenges that are encountered by foundation doctors when prescribing HRMs safely during the on-call period.

The objectives of this PhD thesis are to:

1. Explore the literature about adverse drug events, medication errors, prescribing errors, foundation doctors, causes of prescribing errors, HRMs and the on-call period.
2. Conduct a systematic review that investigates the prevalence and incidence of prescribing errors with HRMs in hospitals and compares them with the rate for non-HRMs.
3. Conduct a secondary analysis of existing qualitative data to identify and compare the causes of foundation doctors’ prescribing errors with HRMs and non-HRMs.
4. Conduct focus groups to explore the challenges that are encountered by foundation doctors when prescribing HRMs (specifically anticoagulants, insulin, and opioids) safely during the on-call period.
5. Explore similarities and differences in the challenges faced when prescribing HRMs and non-HRMs either when on-call, or during daytime working hours.

6. Generate recommendations for future research and interventions.

3.1.2 Programme of work structure

The work started with the first study (found in Chapter Four), which was a systematic review that explored the epidemiological parameters, prevalence and incidence, of prescribing errors with HRMs in hospitals. The study tried to follow the Cochrane guidelines for conducting systematic reviews as it was possible, and key databases in the medical field were searched.

The next logical step in the programme is to understand the causes of prescribing errors with HRMs. This was explored by the second study (in Chapter Five), in which a secondary analysis of existing qualitative data from 59 interviews with foundation doctors was conducted. Focusing upon foundation doctors is important as they prescribe the majority of hospital prescriptions, 70% of hospital prescriptions, and they have twice the prescribing error rate of consultants. (55) A framework analysis approach was applied, with use of NVivo®10 software. A detailed comparison between prescribing errors with HRMs and non-HRMs was conducted in order to identify the similarities and differences in causes, error-causing-conditions and latent conditions, which were the elements of Reason’s model of error
causation. (83) Furthermore, types of errors related to prescribing errors with HRMs and non-HRMs were compared.

This second study highlighted the on-call period as a particularly challenging period for foundation doctors when prescribing, especially with HRMs. Therefore, the third study (in Chapter Six) aimed to explore the challenges that are encountered by FY1 and FY2 doctors when prescribing specific HRMs safely during the on-call period. The specific HRMs that were discussed were anticoagulants, insulin, and opioids, as these are commonly prescribed HRMs that frequently cause severe patient harm or death. (14, 122) In addition, the study aimed to explore similarities and differences in the challenges faced when prescribing HRMs and non-HRMs either during on-call or during daytime working hours. To achieve this aim there was a need for a qualitative approach, and so focus groups were chosen as a data collection tool. Six focus groups with foundation doctors were conducted, three with FY1 doctors and another three with FY2 doctors, in three different hospital trusts in the North West of England. The study was granted the required ethical approvals.

This thesis ends with a discussion of the overall findings of the programme of research. The findings were pulled together to show some differences and similarities between HRMs and non-HRMs. Then focused on HRMs such as the lack of research about prescribing errors with HRMs; lack of standardisation and inconsistency with HRMs such as definitions prescribing errors, lists of HRMs, scales for measuring the severity of prescribing errors and the practice; and prescribing for children. The strengths and limitations of this thesis are then
discussed followed by some implications for practice and future research. This chapter ends with the overall conclusion for the thesis.

3.2 Study One: methods

For Study One, we chose to conduct a systematic review, over the alternative of a narrative literature review. This decision was made as systematic reviews are generally regarded as the gold standard of evidence within medical literature. (123, 124) Systematic reviews combine the current literature related to a pre-defined research question into one paper. It is started by setting a defined research question based on the component of the acronym ‘PICO’ (population, issue, comparison, outcome), sometimes ‘time’ and ‘study method’ can be added as further elements of the research question; therefore, it is abbreviated PICO- TS. These elements of the research question should be stated in a transparent way in the systematic review methods. This means that the study can be easily repeated, and allows for reproduction of the study data at a later date, which is difficult with narrative literature reviews. Therefore, we chose to explore the literature systematically to find epidemiological studies of prescribing errors with HRMs.

Epidemiological measures can give an overview of the occurrence of an issue in order to better understand this issue. The epidemiological measures that are used to calculate the occurrence of a disease state or a condition in a particular population
are prevalence and incidence. Prevalence has been defined by Rothman et al. (2008) as “a measure of status rather than of newly occurring disease, measuring the proportion of people who have the disease at a specific time”. (125) In the context of prescribing errors, the prevalence was a measure of existing, rather than of newly occurring errors, measuring the proportion of people who have a prescribing error at a specific time. Prevalence can be expressed by digit number, percentage when it is divided by 100, or ratio formula. Incidence has also been defined by Rothman et al., (2008), as “the occurrence of new cases of disease per unit of person-time”. (125) With prescribing errors, incidence was the occurrence of new errors per unit of person-time. This rate can be expressed in percentage, or in the rate ratio formula which expresses a very small rate in a simpler way than a percentage.

We aimed to explore the gap in current knowledge regarding the occurrence of prescribing errors with HRMs through use of this robust study design; a systematic review (seen in Chapter Four). A research question was developed, based on the PICO- TS style of research question, “What is the prevalence and incidence of prescribing errors in high risk medicines in hospital inpatients?”.

The next step of conducting a systematic review was searching the relevant data. Therefore, a search strategy was built based upon the breakdown of the research question, and it was divided into four categories or keywords groups, which could be used in the search box of a search engine. Categories of key words were prescribing errors, HRMs, inpatients, and incidence or prevalence. All key words and the words
with the same meaning including alternative spellings and plural forms were searched and are given appendix 4.A (at the end of Chapter Four).

Keywords were searched through OvidSP which includes the key pharmacy and medical databases: Ovid MEDLINE® and Ovid MEDLINE® In Process & Other Non-Indexed Citations and Ovid MEDLINE® Daily Update, Embase (updated daily), Evidence Based Medicine Reviews, Cochrane Database of Systematic Reviews and International Pharmaceutical Abstracts.

These databases were searched from the year 1985 onwards. We had chosen this year because of the importance of patient safety and medication errors, with the research in these fields significantly starting in this year. This was based on chart published by Lilford et al.’s study. (29) The initial search was until the 2nd of December 2014 and an updated search was performed on 14th May 2015.

The third stage of conducting the systematic review was the study selection process. This stage was composed of three different phases, which were title screening, abstract reviewing and entire article assessment. This selection process was based on the inclusion and exclusion criteria (see Chapter Four section 4.2.2 for detailed inclusion and exclusion criteria for Study One), with the results being discussed in a review meeting. During each meeting a consensus decision was taken for each phase of the selection process and for the included studies in the review. To extract
relevant data from the included articles, a form was developed based on the PICO-TS style of research question, the Cochrane checklist for Systematic Reviews of Interventions, (126) and the third edition of the Centre for Reviews and Dissemination (CRD) guidance for undertaking systematic reviews. (127) The extraction form was revised many times until it reached its final form (see Appendix 1 at the end of the thesis). The purpose of the form was to extract the relevant data in a systematic manner.

The initial search of databases resulted in a limited number of papers that were eligible for inclusion in the systematic review. Therefore, the decision was made to broaden the search by using three categories of keywords instead of four categories of keywords and add these results to the initial search results. The HRMs keywords category was eliminated, while the prescribing error keywords, hospital inpatient keywords, and the incidence and prevalence keywords were kept in the new search. The idea behind this decision was to find more studies that could have HRMs in the text, or could contain HRMs without classifying medications as HRMs and non-HRMs explicitly in the terms that can be searched.

Two methods were used to retrieve the additional studies from 1985 to 14th May 2015. The first method used studies included in Lewis et al.’s systematic review, which explored the prevalence and incidence of prescribing error for the period of 1985 to October 2007. (13) This study reviewed thoroughly the prevalence and incidence of prescribing errors without distinguishing between HRMs and non-
HRMs. Thus, the included studies were examined if they had also included data on the prevalence and incidence of HRM prescribing errors.

The second method covered the period from 2007 until 14th May 2015 to update the findings from Lewis et al.’s systematic review. The search strategy was similar to the initial search, in terms of searched databases (as previously mentioned) and three keyword categories out of four were used, as mentioned in Appendix 4.A (found at the end of Chapter Four).

Study selection went through various phases, starting with removing the duplicates of studies using EndNote X7. The next phase was evaluating the title of the remaining studies with manual searching for duplicates. Studies that passed this stage then went through abstract review. The abstracts that seemed eligible for inclusion were transferred to the last stage, which was full article review.

During full article review, each study was discussed in a review meeting. A consensus decision was made as to whether a study should be included, excluded or whether further information from the corresponding author was required. Those studies for which agreement was reached by all authors for inclusion in the review went through the data extraction process.
3.3 Study Two: rationale, method and data analysis

3.3.1 Study Two: rationale for using secondary analysis of existing data

After establishing the occurrence of prescribing errors with HRMs, there was a need to understand the causes behind these errors and distinguish any variation in comparison for non-HRMs, in order to draw a clearer picture about prescribing with HRMs. Qualitative research is the most appropriate approach to explore the phenomena in its entirety, and interviews are one way of collecting qualitative data. (128) To explore the causes of prescribing errors, semi-structured and structured interviews have been found to be the most effective methods. (84) There were 59 existing semi-structured interviews that explored foundation doctors’ prescribing errors with HRMs and non-HRMs, which were conducted by the supervisory team in three previous studies. One option in our study, to research this phenomenon of prescribing errors with HRMs, was to utilise these available interviews, or begin again by conducting new interviews to explore the causes of prescribing errors with HRMs. These studies already had the consent of participants to do further analysis for them. The advantages of conducting secondary analysis of existing qualitative data led to selection of this approach for study two.

The secondary analysis of existing qualitative or quantitative data has been used since the 1960s. (129) Qualitative data is the product of qualitative methodology.
such as focus groups and interviews. In the UK the Qualitative Data Archival Resources Centre (Qualidata) has been established, to encourage the research community to use qualitative secondary data. (129) Furthermore, organisations concerned with improving patient health such as the National Institute for Health and Care Excellence (NICE) have conducted studies using this technique. (130)

Secondary analysis of existing data has been defined as “the use of existing data, collected for the purposes of a prior study, in order to pursue a research interest which is distinct from that of the original work; this may be a new research question or an alternative perspective on the original question”. (131, 132) However, there is confusion in the literature with regards to the terms used to describe this approach, such terms are primary data analysis, secondary data, and secondary data analysis. (133) This confusion is a result of the nature of the data that was used in the analysis, specifically whether this was primary data or secondary data. (133) The National Institute of Health (NIH) in the USA eliminated this confusion by stating that primary data analysis is “limited to the analysis of data by members of the research team that collected the data, which are conducted to answer the original hypotheses proposed in the study”. (124, 133) Therefore, the term secondary analysis of existing data is the most accurate for describing this kind of analysis.

The secondary analysis of existing qualitative data, such as interview data, has many advantages over primary data analysis. Table 3-1 depicts a comparison of studies using secondary analysis of existing data with studies using primary data analysis.
The most important advantage is the availability of data. Logically, if you have a research question and the data that you need to answer this question is already available, there is no need to collect new data. In our study, the existing data were about the causes of prescribing errors with all classes of medications, and the participants had been asked to discuss previous errors that they had made, along with the type of medication associated with the error. As HRMs are just one subset of medications, and we knew these medicines would be discussed in the existing data, it would be possible to recognise and differentiate them from the non-HRMs making secondary analysis of this existing data a feasible approach for our research. Using the analysis of existing data overcame the complications of obtaining data from primary sources. Conducting a primary research study involves several steps such as protocol development and participant recruitment, which is difficult and time consuming. Another advantage is that there is a large amount of data that has been rigorously prepared and collected. This large volume of high quality qualitative data provided a cost efficient way to address the research aim, avoiding the need for further data collection and data transcribing. Furthermore, retrieving these secondary data are easy as they were under the control of the two supervisors and saved in file documents, such as PDFs and Word documents, which could be sent by email easily. On the other hand, the primary data collection process involves risk of causing harm for participants, such as stress. In general, all ethical applications for conducting interviews require distress forms, as stress is a potential risk during the interview. In our area of research the violations of prescribing rules, or legal consequences of prescribing errors, could provoke stress in the participants. Secondary analysis of existing data avoids this and prevents new participants from being exposed to these risks.
However, the actual risk of stress was very low from the supervisory team’s experience.

Table 3-1: A comparison of studies using secondary analysis of existing data with studies using primary data (adapted from Doolan et al.). (133)

<table>
<thead>
<tr>
<th>Secondary analysis of existing data study</th>
<th>Primary study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perform literature review</td>
<td>Perform literature review</td>
</tr>
<tr>
<td>Find gaps in the research, and research opportunities</td>
<td>Find gaps in the research, and research opportunities</td>
</tr>
<tr>
<td>Identify and obtain permission from the original primary investigator to analyse a data set</td>
<td>Pose research questions that could be answered given prudent sample measures, and, if applicable, follow-up</td>
</tr>
<tr>
<td>Refine research questions</td>
<td>Write a research proposal including how subjects will be recruited, what data will be collected, and what safeguards will be in place to protect subjects’ safety</td>
</tr>
<tr>
<td>Evaluate the appropriateness of the original sample, design and measures</td>
<td>Obtain approval from the organisation’s ethical committee</td>
</tr>
<tr>
<td>Establish appropriate safeguards to protect data and consider legal and ethical implications of the analysis</td>
<td>Recruit consenting subjects</td>
</tr>
<tr>
<td>Obtain approval from the organization's ethical committee</td>
<td>Obtain predetermined measures from subjects</td>
</tr>
<tr>
<td>Perform secondary analysis of the data</td>
<td>Perform the analysis of the data</td>
</tr>
<tr>
<td>Disseminate the findings</td>
<td>Disseminate the findings</td>
</tr>
</tbody>
</table>

In our data, there is another advantage for our research as the participants had the opportunity to talk truthfully about the prescribing errors without the influence of the term HRMs. Such an *a priori* classification could lead participants to express their experiences and views of the prescribing error differently, which could lead to biased descriptions of the causes. Another source of bias is a previous relationship between
the interviewer and the interviewees; (137) however, this bias was also reduced as there was no previous relationship between the interviewers and the participants in the data being reanalysed.

All types of research have their drawbacks and secondary analysis of existing data is no exception from this. Disadvantages of secondary analysis of existing data include: inability to achieve the objectives of the study, shallow and less detailed descriptions as the research question is different from the original one, consent of participants to use their data for secondary analysis, and the unfamiliarity of the new researcher with the study details that could lead to misinterpretation of the data. (131, 133, 134) However, our study eliminated some of these disadvantages, such as the consent having already been given to re-analyse the data; with the supervisory team being crucial parts of the previous studies, meaning they knew all of the existing details, aiding this study further. In general, the advantages of using secondary analysis of existing data overcame the disadvantages, which was the case with our study as well.

### 3.3.2 Study Two: methods

The second study of this thesis (in Chapter Five) is a qualitative study using interviews. The interviews that were used already existed as they had been conducted as part of previous studies; as previously mentioned, the term that describes this kind of analysis is “secondary analysis of existing data”. (133) In our
study, the data were obtained from 59 interviews conducted by the research team in three previous studies, (87, 138, 139) which had been previously audio recorded by the researchers, then transcribed by a professional transcribing company. Methods for collecting the primary interviews in the previous studies are displayed in more detail in Table 3-2.

Table 3-2: Methods of data collection for primary interviews

<table>
<thead>
<tr>
<th>Study</th>
<th>Date of data collection</th>
<th>Use of critical incident technique</th>
<th>Description of data collected (based on the content of topic guide)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study One (87)</td>
<td>2008</td>
<td>Yes</td>
<td>The topic guide was divided into three main sections</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>The first part provided background about the participant such as place of medical education, speciality and time in post.</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>The second part was an in-depth exploration of prescribing errors participants had made previously</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Details such as the nature of the error, situation of the error and participants reasons for making the error. The third part was about the experiences and attitudes towards basic medical education.</td>
</tr>
<tr>
<td>Study Two (139)</td>
<td>2014</td>
<td>Yes</td>
<td>The topic guide of this study was similar to Study One with the exception of the third part of the schedule which instead explored the differences between FY1 and FY2.</td>
</tr>
<tr>
<td>Study Three (138)</td>
<td>2013</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>------------------</td>
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</table>

The interviews explored the whole system of antimicrobial prescribing and the influence of both the intervention (structured feedback) and normal feedback practice, how both influenced prescribers’ behaviour.

Questions and prompts covered prescribing practices and participants’ knowledge, skills, their beliefs on how they could change their practice.

The intervention group topic guide also explored perspectives on the intervention process and outcomes, and any positive or negative views of their experiences and how the feedback affected their daily work practices.

The interviews of these studies were initially conducted to investigate the causes of prescribing errors in all medications types, without distinguishing any class of medications. As previously mentioned HRMs are part of general medications, and it was known that these interviews contained descriptions of errors with HRMs as well as non-HRMs.

### 3.3.3 Study Two: data analysis
The thematic framework analysis approach was chosen, which is commonly used in health research, to manage, organise and analyse the interview data. This approach has many advantages in qualitative data analysis. Our secondary analysis of existing data included 59 interviews that ranged from 14 to 80 minutes. Furthermore, the interviews covered many issues in addition to prescribing errors, such as background of participants’ education and possible interventions for the errors. The framework approach reduces and summarises the original data, making this an easier way to handle the data and achieve the research aim. One of the other advantages, of the framework analysis approach is identifying commonalities and differences in the data, as in our study we wanted to explore these between HRMs and non-HRMs. The steps of applying framework analysis are clear to follow and can result in well-structured results.

NVivo software (version 10) was used to support the handling and analysis of this large number of interviews and data. This computer software is useful for helping in organising, speeding up and analysing qualitative data and storing and the data in an easily retrievable manner.

The steps of framework analysis were applied. The first step was familiarisation with the data by reading the interviews thoroughly. This was followed by inductive coding of the interviews, which gave a better understanding of the data and allowed the researchers to draw themes from the raw data under each medication type, HRMs and non-HRMs. The third step was deductive coding of codes under a model of
categorising the causes of errors, based on Reason’s model of accident causation. (83) This model is the most common model used to categorise the causes of prescribing errors. (84) Furthermore, Reason’s model of accident causation is a comprehensive model that not only focuses on the causes; it focuses on the error-causing conditions and latent conditions. (83) The coding process was iterative; the principal investigator (MA) did the initial coding then this was discussed on multiple occasions with the other members of the research team (PL and MT) until a consensus was reached.

Based on Reason’s model of accident causation, prescribing error causes were categorised into causes, error-causing conditions, and latent conditions. (83) The causes of prescribing errors were classified as KBMs, RBMs, slips, lapses and violations; an additional category of communication errors was added based on our previous work. (87) The error-causing conditions, for both HRM and non-HRMs, were classified under the following categories: individual prescriber; healthcare team; prescribing task; the patient; and working environment.

Errors were classified into five major types based on the Dean et al. classification, (57) which was adapted from Cousins et al., (144) based on prescribing process components. This classification has been applied in many studies of prescribing errors. (55, 57, 58) The five major types of errors were; need for drug therapy, selection of a specific drug, selection of dosage regimen, administration of drug, and provided drug product. Each major type of error had its own subtypes of errors; for
example, need for drug therapy had subtypes such as omission errors, premature discontinuation, drug not prescribed but indicated, continuation for longer than needed, no indication, and duplication.

A table was established to make a comprehensive and detailed comparison between HRMs and non-HRMs to distinguish any differences. The table was drawn to compare all the aforementioned elements, such as causes of errors, error-causing conditions, latent conditions and types of errors. The content of the table was iteratively reviewed by all researchers until the final version was reached.

As this is a qualitative research study there is a need for quotes from participants’ interviews to support the overarching themes. The selected quotes were chosen based on their clear depiction of the highlighted theme. The quotes were referenced using the participant’s number and written in italic and bold font (i.e. P#). Where extraneous material has been removed from the quote, this has been indicated using an ellipsis (...). In order to submit this paper to PLOS ONE journal, the Consolidated Criteria for Reporting Qualitative Research (COREQ) checklist for interviews and focus groups was completed (See the Appendix 5.A at the end of Chapter Five).

3.4 Study Three: rationale, method and data analysis
3.4.1 Study Three: rationale for using focus groups

Third study aimed to explore the challenges that are encountered by FY1 and FY2 doctors when prescribing specific HRMs safely during the on-call period, especially with HRMs. This aim was based on the findings of the second study. Therefore, the third study (found in Chapter Six) needed a robust methodology to deeply explore the situation and circumstances surrounding these challenges. Qualitative methods are the most appropriate approach to explore a situation or a condition from the inside. (9) There are two qualitative methods, interviews and focus groups, frequently used in qualitative research about prescribing errors. (128)

Interviewing as a method of collecting qualitative data is an established approach, which has many advantages. (142) Flexibility for both interviewer and participants is one of the advantages, as the interviewers are flexible to choose the wording and order of the questions based on the participants' response, and the participants can provide their views and experiences in the way that they prefer. Data generated from interviews are deep and rich, where the interviewers use follow-up and probing questions to obtain a deep and full understanding of the participant's viewpoints. (142, 145) Therefore, we started to prepare conducting approximately 15 interviews with foundation doctors to explore the challenges during the on-call. In one of the supervisory meetings the issue of sensitivity of divulging sensitive topics arose such as discussing prescribing violations. Violations of prescribing rules, especially routine violations, were described in the second study with non-HRMs only.
Therefore, this is was one of the areas that we were interested in exploring in this study. Participants do not prefer interviews to discuss sensitive issues and more anonymous techniques such as anonymous surveys may be preferred. (145) However, surveys were excluded from the beginning as they generate shallow data, and we sought to explore, in depth, the challenges of prescribing HRMs on-call. As routine violations are a common occurrence in the work place, such as healthcare practice, (83, 85, 89) we believed doctors might reveal them in natural conversation with colleagues or other healthcare professionals who are familiar with the healthcare practice setting. Furthermore, when one participant is speaks freely about violations that may encourage other participants to divulge their experiences also. The naturalistic environment of the focus group has a normative influence on participants as they discuss their experiences leading others to reveal and discuss sensitive issues such as prescribing violations. (146) These advantages of focus groups outweighed the advantages of the interviews, especially to explore the challenges with routine violations. Consequently, we changed the data collection technique from interviews to focus groups.

Furthermore, focus groups generate new ideas that are formed by exposing participants to other participants’ viewpoints, whereas interviews rely on individual experiences, with only participant self-reflection on the discussed issues. (147) This makes the participant’s response sharpened and refined with a deeper level of thinking, (146) which had added benefit for this approach to be useful in our study. Focus groups like any other method have advantages; as well as disadvantages; Table 3-3 depicts some of the advantages and disadvantages of focus groups. (147)
Table 3-3: Summary of the advantages and disadvantages of focus-group methodology (146)

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Attitudes and opinions are socially formed; focus groups provide a social environment in which to articulate them</td>
<td>• More expensive and time consuming than quantitative evaluating procedures</td>
</tr>
<tr>
<td>• Gives us a deeper understanding of the phenomenon</td>
<td>• Harder to get everyone in the same place at the same time</td>
</tr>
<tr>
<td>• Gives us new insights</td>
<td>• Problem of obtaining a biased sample</td>
</tr>
<tr>
<td>• Complements and further explains statistical information obtained from other evaluative processes</td>
<td>• Reliability of thematic analysis</td>
</tr>
<tr>
<td></td>
<td>• Reliability of perceptions (not always accurate)</td>
</tr>
<tr>
<td></td>
<td>• Difficulties preventing a particularly vocal or dominant participant from coercing others to agree with his/her views</td>
</tr>
<tr>
<td></td>
<td>• Data obtained are very context-specific and therefore not generalizable to other institutions or contexts</td>
</tr>
</tbody>
</table>

3.4.2 Study Three: methods

A focus group topic guide was devised by the principal researcher (MA) and revised by the research team (PL and MT). It aimed to help run all of the focus groups in a systematic manner; starting with welcoming the participants, an introduction, ensuring the anonymity, ground rules and the questions of the focus group. Ten questions were generated to explore the challenges of prescribing HRMs from different perspectives particularly during the on-call period; (see Appendix 6.A at the
end of Chapter Six). Other documents that were required to conduct the focus groups and ethical approval requirements included: Participant Information Sheet (PIS) (see Appendix 2 at the end of the thesis), email invitation (see Appendix 3 at the end of the thesis), thank you email (see Appendix 4 at the end of the thesis), consent form (see Appendix 5 at the end of the thesis), pre-focus group questionnaire (see Appendix 6 at the end of the thesis) and focus group protocol.

The third study (found in Chapter Six) was built on the findings of the second study (Chapter Five). Therefore, it recruited from the same population, which was foundation year doctors, both FY1 and FY2 doctors, who were completing the Foundation Programme. The decision was made to conduct separate focus groups for each foundation level to ensure homogeneity, and to ensure that FY1 doctors were not inhibited by the presence of more senior doctors. Furthermore, the study wanted to explore whether there were differences in challenges between FY1 doctors and FY2 doctors, and separation of the groups was seen to facilitate this approach. The desired number for each foundation level was three focus groups, based on the supervisory team experience, where the minimum target was two focus groups for each level. The plan was to conduct the focus groups in different hospitals, as the challenges that are faced by doctors in different hospital organisations could differ. As the target number for each foundation level was three focus groups, three different hospitals were required. Sites of the focus groups were three hospitals in North West England, which were two large teaching hospitals and one general acute hospital. Two focus groups were to be conducted in each hospital (one for FY1 and another for FY2 doctors); each focus group would include between 4 to 9
participants. Focus group facilitators included other researchers or PhD students (Aseel Abuzour and Daniel Greenwood) and one of the supervisors (PL). The facilitators were chosen to help run the focus groups because they were fluent English speakers, unlike the principal investigator (MA), who attended all the focus groups to assist and make notes.

There was no previous relationship between the researchers and the participants, which reduces the bias to this study. Participants were contacted through their foundation year training tutors at the hospital trust that they were working in. The tutors then emailed all FY1 and FY2 doctors working at their hospital an invitation email that contained the PIS, pre-focus group questionnaire and the consent form. Those FY doctors who were interested could email their details to their training tutor or the principal researcher directly. The selection process for interested participants was based upon who responded first, which meant that the first nine participants would be selected, unless someone withdrew, in which case the next on the list would act as a replacement.

At the start of each focus group the facilitator gave the participants a brief introduction about the study and emphasised the anonymity of participants and the confidentiality of the data generated from the focus group. After audio-recording started there were ten questions on the focus group discussion guide (see Appendix 6.A at the end of Chapter Six) which were used to explore and answer the research question. The questions compared the prescribing of HRMs during the on-call period
to daytime working hours in terms of challenges to prescribing safely, support, communication and short-cuts. Furthermore, the complexity of the prescribing task and short-cuts of HRMs to the non-HRMs were compared.

The audio-recorded sound files were transcribed verbatim by a University approved professional transcribing company; consequently, transcribed texts were reviewed by MA to check for accuracy, particularly of medical terms.

**3.4.3 Study Three: data analysis**

Thematic framework analysis approach was again chosen to be used for the third study. The same reasons are applicable for this study as well as the second study; furthermore, the principal investigator became more experienced with the approach that allowed for faster analysis. This was conducted with the assistance of NVivo software (version 11). (148) It is known combining thematic framework analysis with computerised-assisted qualitative data analysis software packages (CAQDAS) such as NVivo help to manage, organise, summarise and retrieve desired data from the original data in an easier and more structured manner. (142) The analysis of the qualitative data obtained from the focus groups underwent many steps. Initially, a coding framework was developed based upon participants’ words and phrases. The framework analysis approach has been described as being more suitable with deductive approaches; (141, 149, 150) however, it is suitable for both inductive and
deductive approaches. (141) During data analysis, deductive codes based on Reason’s model of accident causation were applied, the challenges were categorised into challenge-causing conditions and latent conditions. (83) The challenge-causing conditions could be related to the following categories from this model: individual prescriber, the patient, the prescribing task, working environment, and healthcare team. In addition, challenges could be related to a communication failure or a violation, as classified by our previous work. (87)

The coding process was an iterative process as the principal investigator (MA) reviewed the codes with the research team (PL and MT) many times until it reached the final stage. A comprehensive comparison between the themes under each different category (i.e. challenge-causing conditions, communication failures and violations) was conducted to identify any similarities and differences in the data.

Results of the analysis were supported and clarified by participant’s quotes, which were selected based on their representation of the theme or the idea. The quotes were referenced to the participant’s number, Foundation Year one or two and the hospital number; with the italic and bold font (i.e. $P#$, $FY#$, $H#$); and with any extraneous material that was removed from the quote being indicated by use of an ellipsis (...).
3.5 Ethical approval

3.5.1 Study One

Ethics approval was not required as the study purpose was to review the literature.

3.5.2 Study Two

Ethics approval was not required as all the included studies had been granted ethical approval and consent had been obtained at that time from participants for future analysis of their interview data.

3.5.3 Study Three

The study was granted ethical approval by the University Research Ethics Committee (UREC) (see Appendix 7 at the end of the thesis) and governance approval was given by Health Education England (HEE) (see Appendix 8 at the end of the thesis). We needed to add more hospitals and incentives for participants to improve recruitment to the study. Therefore, we applied for amended approvals from the same organisations and we were granted the approvals for these amendments (see Appendix 9 and Appendix 10 at the end of the thesis)
4. Chapter Four: Study One

<table>
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<th>A systematic review of the prevalence and incidence of prescribing errors with high-risk medicines in hospitals</th>
</tr>
</thead>
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<tr>
<td>Type</td>
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</tr>
<tr>
<td>Authors</td>
<td>M. A. Alanazi, M. P. Tully and P. J. Lewis</td>
</tr>
<tr>
<td>Status</td>
<td>Published</td>
</tr>
<tr>
<td>Journal</td>
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</tr>
<tr>
<td>Date of publication</td>
<td>June 2016</td>
</tr>
<tr>
<td>Volume</td>
<td>41</td>
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<tr>
<td>Issue</td>
<td>3</td>
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**Note.** As this paper has been published, the formatting and layout are consistent with the published paper. Appendices and references from the paper are placed at the end of the chapter rather than at the end of the thesis.
A Systematic Review of the Prevalence and Incidence of Prescribing Errors in High Risk Medicines in Hospitals

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Summary

What is known: Prescribing errors are the most common type of error in the medication use process. However, there is paucity in the literature regarding the prevalence or incidence of prescribing errors in High Risk Medicines (HRMs). HRMs bear a heightened risk of causing significant patient harm when they are used in error.

Objective: The aim of this research was to systematically investigate the literature regarding the prevalence and incidence of prescribing errors in HRMs in inpatient settings.

Methods: A search strategy was developed based on four categories of keywords: prescribing errors, HRMs, hospital inpatients, and prevalence or incidence. All keywords were searched for in Medline, Embase, Cochrane, and the International Pharmaceutical Abstracts (IPA). The search was limited to English quantitative studies that reported incidence or prevalence of prescribing errors of medical prescribers, whether they were seniors or juniors, since 1985.

Results: Of the 3507 records identified nine studies met the review criteria. The most frequent denominator in the included studies was medication orders, in eight studies, ranged from 0.24 to 89.6 errors per 100 orders of HRMs. Two studies reported 107 and 218 errors per 100 admissions prescribed HRMs, and one study reported 27.2 errors per 100 prescriptions with a HRM. The incidence of prescribing errors could not be calculated.

What is new and Conclusion: The prevalence of prescribing errors in HRMs in the inpatient setting has a very wide range that reflects the different data collection methods used within the included studies. Future studies in prescribing errors should use standardised approaches to enable comparison.
4.1 What is known and Objective

Medications are a crucial part in the process of seeking health, when they are used wisely. However, medication errors, which are preventable by the definition of the National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) organization, (1) are one of the obstacles that face healthcare providers when keeping patients safe, particularly inpatients. Inpatient settings are vulnerable areas for medication errors, (2) which can increase the cost of patient care by increasing the length of stay in hospital, increasing pharmacy and laboratory costs, and doubling the patient mortality rate. (3)

Prescribing errors are the most frequent subtype of medication errors occurring in 7% of medication orders, 50% of hospital admissions and 2% of patients. (4) The percentage of prescribing errors ranges from 29% to 56% of medication errors in adults, (5, 6) and these figures have been found to be higher in children with a range of 68% to 75%. (7, 8)

Within the general medication classes there are critical types of medications termed high risk medicines (HRMs) that are more likely to cause harm to a patient when they are used inappropriately compared to non-HRMs. HRMs have more potential to cause harm, thus, if they are prescribed erroneously they can lead to a greater negative impact which can be associated with higher costs and increased mortality. The HRMs grabbed the attention of well-known medication safety organizations and authors concerned about patient safety, because of the devastating harm caused to
patients; hence, they addressed and specified HRMs to make it obvious to healthcare practitioners. Consequently, definitions and lists for HRMs were established by such organizations like the US Institute for Safe Medication Practices (ISMP) (9) and the UK National Health Service (NHS) (10) through the National Patient Safety Agency (NPSA). The ISMP use the term high alert medications while the NHS prefers to high risk medicines, but they are based on the same concept.

The ISMP established a list of HRMs, in acute care settings, which contains 22 classes of medications and 12 specific medications, based on its medication error reporting program. (9) The NPSA has its own list that contains eight classes, based on 60,000 medication incidents reported to the National Reporting and Learning System (NRLS). (10) The eight classes within the NPSA list for HRMs are: anticoagulants, injectable sedatives, opiates, insulin, antibiotics (allergy related), chemotherapy, antipsychotics, and infusion fluids. The ISMP list is broader than the NPSA list, apart from antibiotics (allergy related), including antithrombotics rather than anticoagulants and antiarrhythmics, adrenergic agonists and antagonists, hypoglycaemic agents, and liposomal forms of drugs. (9)

It could be assumed that prescribing errors with HRMs have a lower rate of occurrence compared to non-HRMs. There are two reasons to support this assumption. Firstly, the focus and efforts provided by the aforementioned well-known medication safety organisations may increase prescribers’ awareness of the risks associated with HRMs. Secondly, is the catastrophic patient safety outcomes when HRMs are prescribed erroneously. Such devastating consequences might lead prescribers to apply caution when prescribing HRMs to patients. To investigate this
assumption there is a need to conduct an epidemiological study to investigate the rate of prescribing errors with HRMs.

The epidemiological parameters, prevalence and incidence, of prescribing errors in general medications have been studied extensively and systematically. Nevertheless, these important epidemiological parameters have never been studied systematically explicitly in HRMs. Due to the potential harm that errors with HRMs could generate, it is important to know to what extent they occur when compared to non-HRMs. Such findings might reveal a different picture to what we know already about non-HRMs. Therefore, this study aims to systematically review the literature in order to report on the prevalence and incidence of prescribing errors in high risk medicines in hospital inpatients.

4.2 Methods

4.2.1 Search strategy

The detailed search strategies’ keywords are available in the online appendix A1. In brief, the following categories of terms, and their synonyms, were initially used: prescribing error, HRMs, inpatients, and incidence or prevalence.

Keywords were searched through OvidSP: MEDLINE®, Embase, Evidence Based Medicine Reviews: Cochrane Database of Systematic Reviews, and International
Pharmaceutical Abstracts. Databases were searched from 1985 till May 2015, apart from the Cochrane Database of Systematic Reviews which was established in 2005.

The search strategy was then broadened by eliminating the search term “high risk medicines”, in order to find studies that included HRMs in the text or contained HRMs without classifying medications using the terms HRMs and non-HRMs explicitly. In addition, studies included in Lewis et al.’s (4) systematic review were examined, which reviewed the prevalence and incidence of prescribing errors without distinguishing between HRMs and non-HRMs.

4.2.2 Inclusion & exclusion criteria

4.2.2.1 Inclusion criteria:

Due to the difficulty in translation from other languages to English, only papers written in English were included. Research on patient safety and medication errors significantly started in 1985, (11) so studies published between then and May 2015 were included in the review.

Studies of prescribing for all ages were included in the literature review i.e. children and adults. Only studies investigating prescribing by doctors, whether they were senior or junior using handwritten prescriptions were included. The patient setting
was restricted to hospital inpatients only, as this is different to the outpatient settings in terms of medication and error types.

All quantitative studies that reported incidence or prevalence of prescribing errors in HRMs were included. The included studies should have data that reported on the number of HRMs prescriptions written with and without error. Rates of prevalence could be described in terms of a medication order that contained one HRM with one or more than one error, medication prescription that contained more than one medication order, of which at least one of them was a HRM that have an error or errors, or a hospital admission where the admitted patient had at least one HRMs with one or more than one error. Hospital admission could be combined with time unit to become an incidence denominator. The review was not limited to the medications that included in the ISMP list or in the report of the NPSA for HRMs. Studies that utilised a different list of HRMs medication were eligible for inclusion.

4.2.2.2 Exclusion criteria:

Non-medical prescribers such as an independent pharmacist or nurse prescribers were excluded. Those prescribers may have different types of errors as they usually prescribe a limited number of medications and this type of practice is not recognised globally. In addition, studies conducted in primary care or outpatients were omitted from the review. Studies reporting on prescribing errors made using Computerized Physician Order Entry (CPOE) were excluded because it is associated with different
types of errors than with handwritten prescriptions. Furthermore, handwritten prescriptions still dominate as the main method of prescribing worldwide.

Abstracts of conferences or meetings, qualitative studies, or quantitative studies without prevalence or incidence were excluded. Abstracts of conferences or meetings were excluded because of lack of detailed explanations of methods and results that are important to decide whether the study is suitable for inclusion or not. If a study only reported the proportion of HRM errors, in relation to the total number of non-high-risk medicines plus HRMs combined without recording the total number of HRM prescriptions written, then these were excluded as they would not allow the prevalence or incidence of HRM errors to be determined.

4.2.3 Study selection and data extraction

The selection and extraction process was performed independently by two members of the team. Any disagreements were resolved through consensus. A standardized data extraction form was used, based on the Cochrane checklist for Systematic Reviews of Interventions (12) and the third edition of the Centre for Reviews and Dissemination (CRD) guidance for undertaking systematic reviews. (13)

4.3 Results
Nine studies met the inclusion criteria. Figure 1 depicts a flow diagram of this process.

Fig. 1: Flow diagram of the screening process
4.3.1 Study characteristics

The oldest study (14) was published in 2008, while the others were published up to 2014. (15-22) More than half of the studies (5/9) were published in 2011. (15, 16, 20-22) Studies were predominantly conducted in the USA, with around 45% (4/9) of the studies from there. (15, 17, 20, 22) Three were from Europe including the UK, (16) Germany (19) and Spain. (14) One study (21) was from Brazil and one (18) from Australia. Table 4-1 summarises the data from the included studies. Each study had been conducted in a single teaching hospital, (14-22) which provided both adult and children services.
Table 4-1: Systematic review of prevalence and incidence of prescribing error in high-risk medicines: summary of included studies.

<table>
<thead>
<tr>
<th>Author / (year)</th>
<th>Country</th>
<th>Study site</th>
<th>Setting</th>
<th>Period</th>
<th>Adults/ Children</th>
<th>Type of study</th>
<th>Method of error detection</th>
<th>Total order/admissions/patients/prescriptions</th>
<th>No. of PEs</th>
<th>Incidence or prevalence of HRMs error</th>
</tr>
</thead>
<tbody>
<tr>
<td>Collins, C. M. and Elsaid, K. A. (15) (2011)</td>
<td>USA</td>
<td>Tertiary academic hospital</td>
<td>2 years</td>
<td>No provided</td>
<td>R</td>
<td>Pharmacist intervention database</td>
<td>412 orders</td>
<td>39</td>
<td>9.47 error/100 orders</td>
<td></td>
</tr>
<tr>
<td>Davies, E. et al. (16) (2011)</td>
<td>UK</td>
<td>Multi-specialty teaching hospital</td>
<td>1 day</td>
<td>A</td>
<td>R</td>
<td>Prescription review</td>
<td>330 prescriptions</td>
<td>90</td>
<td>27.2 errors/100 prescriptions</td>
<td></td>
</tr>
<tr>
<td>Lee, B. H. et al. (17) (2009)</td>
<td>USA</td>
<td>Urban teaching hospital</td>
<td>Medical and Surgical services</td>
<td>6 months</td>
<td>C</td>
<td>Prescription review &amp; discharge form review</td>
<td>314 orders</td>
<td>257</td>
<td>82 error/100 orders</td>
<td></td>
</tr>
<tr>
<td>Manias, E. et al. (18) (2014)</td>
<td>Australia</td>
<td>Tertiary care teaching hospital</td>
<td>CC, IC, EC, OC, PC</td>
<td>1 year</td>
<td>A</td>
<td>Medical record review</td>
<td>3492 orders</td>
<td>1176</td>
<td>33.7 errors/100 orders</td>
<td></td>
</tr>
<tr>
<td>Markert, A. et al. (19) (2009)</td>
<td>Germany</td>
<td>University medical hospital</td>
<td>Haematology and Oncology Department</td>
<td>2 years</td>
<td>A</td>
<td>Prescription review</td>
<td>5250 orders</td>
<td>472</td>
<td>8.99 error/100 orders</td>
<td></td>
</tr>
<tr>
<td>Author / (year)</td>
<td>Country</td>
<td>Study site</td>
<td>Setting</td>
<td>Period</td>
<td>Adults/ Children/ Elderly</td>
<td>Type of study</td>
<td>Method of error detection</td>
<td>Total order/ admissions/ patients/ prescriptions</td>
<td>No. of PEs</td>
<td>Incidence or prevalence of HRMs error</td>
</tr>
<tr>
<td>----------------</td>
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</tr>
<tr>
<td>Milani, R. V. et al. (20) (2011)</td>
<td>USA</td>
<td>Multi-specialities academic hospital</td>
<td>2 years</td>
<td>A</td>
<td>R</td>
<td>Prescription review &amp; medical record review</td>
<td>47 orders</td>
<td>8</td>
<td>17 error/ 100 order</td>
<td></td>
</tr>
<tr>
<td>Pallas C. R. et al. (14) (2008)</td>
<td>Spain</td>
<td>Urban teaching hospital</td>
<td>Neonatal unit</td>
<td>8 months</td>
<td>C</td>
<td>P</td>
<td>Prescription review</td>
<td>327 orders</td>
<td>172</td>
<td>52.60 error/ 100 order</td>
</tr>
<tr>
<td>Silva M. D. et al. (21) (2011)</td>
<td>Brazil</td>
<td>University hospital</td>
<td>Paediatric unit (60beds) medical and surgical</td>
<td>30 days</td>
<td>C</td>
<td>P</td>
<td>Prescription review</td>
<td>705 orders</td>
<td>632</td>
<td>89.6 errors/ 100 orders</td>
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<tr>
<td>Smith H. S. and Lesar T. S. (22) (2011)</td>
<td>USA</td>
<td>Tertiary care teaching hospital</td>
<td>5 years</td>
<td>All</td>
<td>P</td>
<td>Pharmacist detected errors &amp; prescription review</td>
<td>500,191 orders</td>
<td>1205</td>
<td>2.41 errors/ 1000 orders</td>
<td></td>
</tr>
</tbody>
</table>

HRMs= High Risk Medicines, PE= Prescribing Error, A= Adult, C= Children, E= Elderly, P= Prospective, R= Retrospective, pt. = patient, CC= Cardiac Care, IC= Intensive Care, EC= Emergency Care, OC= Oncology Care, PC= Perioperative Care
Fifty five percent (4/9) of the studies were in adult patients who were cared for in a variety of settings (surgery, medical, oncology, intensive unit and cardiology). (16, 18-20) A third (3/9) of the studies were conducted solely in paediatric departments across both medical and surgical wards. (14, 17, 21) However, two studies (22%) did not specify the patient group and were based on pharmacist intercepted errors databases. (15, 22) The first study was in a hospital entirely for patients prescribed oral chemotherapeutic agents, (15) while the second study concentrated on analgesics. (22)

More than half of the studies, 55% (5/9), (14, 17, 19, 21, 22) had been carried out prospectively and 45% (4/9) retrospectively. (15, 16, 18, 20) Data collection period ranged from one day to five years. The most frequent period was two years in three studies. (15, 19, 20)

Multidisciplinary teams and doctors were the data collectors in 33% (3/9) of studies respectively. (15, 17, 19), (14, 16, 20) Pharmacists were data collectors in two studies, (21, 22) while in one study the data collectors were research assistants who were not healthcare professionals. (18) Most studies (7/9) used the prescription review method. (14, 16, 17, 19-22) The medical record review method was used in two studies, (18, 20) as was a pharmacist intercepted errors database. (15, 22) Three studies used more than one method, combinations included prescription review with either medical record review, pharmacist intercepted errors, or discharge form review. (17, 20, 22)
Seven studies, 80%, did not validate the reported errors. (14, 15, 17, 19-22) One study did partial validation of the reported errors, when one author independently randomly checked reported data. (18) Another study validated all reported errors through a panel of senior doctors. (16)

4.3.2 Definitions

The definition of prescribing errors used varied between the studies. One study created its definition by combining Dean’s definition (23) and Rosa et al.’s (24) classifications of prescribing errors with HRMs. (21) Another study used a combination of the ISMP list of error prone abbreviations (25) and its hospital formulary guidelines for good prescribing as a definition. (17) Three studies combined Dean’s definition with other definitions. (14, 15, 21) The NCC MERP definition was used once. (18) In three studies the authors conceived their own definitions. (16, 19, 22) One study did not use any definition for prescribing errors as it measured the prevalence of a single type of prescribing error i.e. prescribing a contraindicated class of HRMs. (20)

In terms of the HRMs list or definition used, two studies (22%) (18, 21) used the ISMP list as a reference for HRMs and one study (16) used the NPSA recommendations for HRMs. The rest of the studies did not refer to any pre-defined list of HRMs. (14, 15, 17, 19, 20, 22)
4.3.3 Prevalence and incidence of prescribing errors in HRMs

The prevalence of prescribing errors in HRMs was the only epidemiological measure that was found in the included studies, or could be calculated from the available data. There were three denominators used: medication orders, patient admissions, and prescriptions. Medication orders as a denominator was the most frequent, used in 90% (8/9) of the studies. (14, 15, 17-22) The prevalence of errors in HRMs ranged from 0.24 to 89.6 errors per 100 orders of HRMs. (14, 15, 17-22) In two studies, errors were 107 errors or 218 errors per 100 admissions prescribed one or more HRMs. (17, 18) One study expressed prescribing error prevalence using the denominator of prescription which was 27.2 errors per 100 prescriptions containing one or more HRMs. (16) The three highest prevalence rates (89.6%, 82%, and 52.6%) in the medication order denominator were found in paediatric patients. (14, 17, 21) Pharmacist intercepted errors databases were associated with the lowest and third lowest values of the prevalence. (15, 22)

4.3.4 HRMs involved in prescribing error

Of the two studies that used the ISMP list of HRMs, (18, 21) one found opioids were the most frequent class associated with prescribing error, followed by sedatives, (21) while the other study did not present data for individual classes or types of HRMs. (18) Opioids as a class of HRMs were found in more than the half of studies (5/9). (14, 16, 17, 21, 22) Two of the studies were solely about opioids, (16, 17) while in
the rest of the studies opioids were part of a group of medications, whether these groups were only HRMs or non-HRMs. (14, 21, 22) One of the studies that discussed opioids chose them based on a NPSA recommendation as HRMs. (16) Chemotherapeutic agents were the only class investigated in two studies, (15, 19) and one study only investigated antithrombotic agents. (20) The majority of the included studies, 66% (6/9), did not describe the medication explicitly as HRMs they merely used the drug class name or specific drug name. (14, 15, 18-20, 22) Only three studies referred explicitly to the studied medication classes as being HRMs. (16, 17, 21)

4.3.5 Types of prescribing errors detected

Two studies did not give details as to the types of prescribing errors. (19, 22) One of those studies did not distinguish the types of errors in HRMs from non-HRMs, (19) while the another did not describe the details at all. (22) Contraindicated drugs were the only type of prescribing errors that were studied in another study. (20) Dosage problems or wrong dosage was the most frequent type of prescribing errors detected in the studies with the highest percentage in 33% (3/9) of the studies, (16, 18, 21) and the second highest in one study. (15) Prescription errors such as unclear prescription and incomplete information were found in high percentages in 33% (3/9) of the studies. (14, 16, 17) Missing weight or incorrect weight, which is necessary for paediatric patients especially with HRMs, was the most frequent type of error in children in one study. (17) Table 4-2 summarises the prevalence of error types in descending pattern from the most frequent to the least frequent.
Table 4-2: Prevalence of detected types of prescribing errors

<table>
<thead>
<tr>
<th>Type of errors</th>
<th>Range of prevalence</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dosage problems or wrong dosage</td>
<td>31% to 91%</td>
<td>(14-16, 18, 21)</td>
</tr>
<tr>
<td>Prescription errors</td>
<td>31% to 59%</td>
<td>(14, 16, 17)</td>
</tr>
<tr>
<td>Missing weight or incorrect weight</td>
<td>77%</td>
<td>(17)</td>
</tr>
<tr>
<td>Prescribing policy not followed</td>
<td>38%</td>
<td>(15)</td>
</tr>
<tr>
<td>Medications omissions</td>
<td>8%</td>
<td>(15)</td>
</tr>
<tr>
<td>No or wrong prescription date</td>
<td>6%</td>
<td>(17)</td>
</tr>
<tr>
<td>Drug-drug interaction, Medications given to a known allergic patient, Medication duplication</td>
<td>1% to 2%</td>
<td>(18)</td>
</tr>
</tbody>
</table>

4.3.6 Severity of detected prescribing errors

Three studies (33%) did not report the severity or potential severity of the prescribing errors. (14, 15, 21) One study reported 87 actual severe adverse events regarding prescribing errors, but only one of them was in inpatients, were patients transferred to the ICU, this adverse event was the most frequent among the others with 44.8% (39/87) of the severe adverse events. (19)

Five studies (55%) clearly addressed the severity, whether it was actual or potential, of the prescribing errors. (16-18, 20, 22) However, each study used a different scale. Scales were established by the author, or adapted from the literature. One study adapted actual severity parameter, TIMI classification (26) of bleeding, used to classify the severity of bleeding whether it was major or minor that caused by prescribing error of antithrombotic agents. (20) Three studies (33%) adapted other authors’ scales for potential severity. (16, 17, 22) The scales were adapted from:
Overhage and Lukes scale’s, (27) Leape et al.’s scale, (6) and Taylor et al.’s scale (28) that was itself adapted and modified from another author (29) scale. One study (18) used the NCC MERP scale (30) that evaluates the actual patient harm due to medication errors. In all scales used, the lowest percentages of adverse events were in the most harmful category.

4.4 Discussion

This systematic review is the first to examine literature about the prevalence and incidence of prescribing errors with HRMs in inpatient settings. The prevalence of prescribing errors with HRMs expressed in rates of medication orders, medication prescriptions, and hospital admissions were 0.24 to 89.6 errors per 100 orders, 27%, and 107-218 errors per 100 admissions respectively. The review did not find any available data to calculate the incidence.

The reported rates of errors in medication orders for HRMs had a very wide range that could be influenced by both the method used for error detection and the patient population. Pharmacy databases that described errors detected in the dispensary area gave small number of errors compared to other methods. (14, 15, 17, 18, 20-22) The small number of errors detected in the dispensary area would have omitted errors that had been intercepted by the medical team on the ward, or may be because pharmacists have limited access to the patients’ medical records that could prevent them from identifying all errors. Children were more likely than adult patients to have prescribing errors with HRMs. This was concluded based on the finding that
the three highest values for prevalence of prescribing errors in HRMs were in studies investigating prescribing for children. These results back up the perception that children have more prescribing errors percentages than adults. (7, 8)

The method of error detection and study type has a substantial influence on the number of errors detected. Our results show the highest prescribing error rates were revealed using prospective prescription review. This method is thought to be the most comprehensive and accurate method to detect prescribing errors. (31) On the other hand, as mentioned above, pharmacist intercepted errors in the dispensary area detected the least number of prescribing errors. For example, the lowest prescribing error prevalence was 0.24%, which expressed the pharmacist intercepted errors. (22)

Dosage errors were the most frequent type of error reported. This result is consistent with other studies such as Lewis et al.’s, (4) Ghaleb et al.’s, (32) and Winterstein et al.’s. (33) In terms of definitions, prescribing error definitions were inconsistent in the included studies, and the majority were created by the authors or a combination of different authors definitions’. Moreover, HRM lists were undefined in more than the half of the studies. The heterogeneity in the definitions used was driven by authors’ preferences, local definitions and the practice speciality. An example of that is one such study (15) combined Dean et al.’s definition of prescribing errors with Ghaleb et al.’s definition of errors in, and another (21) combined Dean et al.’s definition with a local definition in Brazil, from Rosa et al. (24) There were no justified reasons given for these combinations or created definitions.
This review demonstrated the important role of healthcare professionals in the process of conducting patient safety studies as the majority (90%) of data collectors in the included studies were healthcare professionals such as doctors, pharmacists, and nurses. All studies were conducted in teaching hospitals, where usually staff are more research active and where there are often a high proportion of doctors in training.

The severity of the detected HRM prescribing errors was evaluated in more than half of the studies. However, each study used a different scale to measure severity. This inconsistency made it difficult to draw any conclusions about the severity of errors in HRMs. However, regardless of the scale used, the lowest percentage of adverse events was in the most harmful category.

Nearly a quarter of the studies that went through the full article review stage as part of the screening process were excluded because they did not have the right denominator to calculate the prevalence or incidence of prescribing errors with HRMs. Some of these excluded studies (5, 35) were well-known in the medication error field but were excluded from the review due to a lack of a denominator for HRMs, thus, the oldest study included was published in 2008. Many studies reported the proportion of prescribing errors rather than prevalence or incidence, where the denominator was the whole number of the medications prescribed without distinguishing between HRMs and non-HRMs.

In general, causes of prescribing errors could be categorized as prescribing mistakes, i.e. knowledge based mistakes and rule based mistakes, or slips and lapses. (36)
Based on Reason’s model (37) the causes of prescribing errors have been studied with any medications type. The results of the study showed around 60% of prescribing errors discussed by doctors were considered prescribing mistakes and around 40% of prescribing errors were slips and lapses. (36) However, the causes of prescribing errors in HRMs specifically are unknown. Therefore, future research can focus on the causes of prescribing errors with HRMs and compare them to general medications. There is a variety of ways that can be used to explore the causes of prescribing errors such as observational techniques and interviews. (38, 39) Thus, a better understanding will be obtained to draw a clear picture about the future solutions that could be implemented.

Limitations

Several limitations to this systematic review study need to be acknowledged. The small number of included studies and the small sample size of some studies make it difficult to generalize the results. The current review has only examined studies that were written in English and that may lead to excluding valuable studies published in different languages. Despite the process was thorough as a wide range of databases were searched, there were no data found about the incidence, and two of the prevalence denominators, hospital admission and prescriptions, were in limited studies that could make them unrepresentative when compared with other studies.
4.5 What is new and Conclusions

The prevalence of errors in HRMs per medication order have a very wide range that reflect the inconsistency of the definition of prescribing errors, HRMs lists, error detection techniques and the methods used to conduct studies, thus, a consistency in these parameters needs to be set in the future research. Opioids were the most frequently reported HRM associated with error and dosage errors were the most frequent type of prescribing error in HRMs. Errors with HRMs were found more frequently in children than adult patients. There was heterogeneity in different parameters such as prescribing error definitions, the HRMs list used, and error severity scales.

Conflict of interest: Nothing to declare

Source of funding: This systematic review is part of a PhD thesis that is funded by the Saudi Arabian government.
4.6 References


4.7 Online appendix 4.A

Search strategy keywords details

Prescribing error keywords


AND

High-Risk Medicines Keywords

(“high-risk medicine” [all] OR “high-risk medicines” [all] OR “high-risk medication” [all] OR “high-risk medications” [all] OR “high-alert medicine” [all] OR “high-alert medicines” [all] OR “high-alert medication” [all] OR “high-alert medications” [all] OR “high-risk drug” [all] OR “high-risk drugs” [all] OR “high-alert drug” [all] OR “high-alert drugs”[all])

AND

Hospital inpatients Keywords


AND

Prevalence & Incidence Keywords

(“Incidence” [all] OR “Rate” [all] OR “rates” [all] OR “prevalence” [all] OR “epidemiology” [all])

AND (“1985” [PDAT])

AND (In the limits drop list the English Language was chosen)
5. Chapter Five: Study Two

<table>
<thead>
<tr>
<th>Title</th>
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</tr>
</thead>
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<tr>
<td>Type</td>
<td>Original article</td>
</tr>
<tr>
<td>Authors</td>
<td>M. A. Alanazi, M. P. Tully and P. J. Lewis</td>
</tr>
<tr>
<td>Status</td>
<td>Submitted</td>
</tr>
<tr>
<td>Journal</td>
<td>PLOS ONE</td>
</tr>
<tr>
<td>Date of submission</td>
<td>2018</td>
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</table>

Note. Part of this study was published as a conference abstract, RPS winter summit 2017 and published in the International Journal of Pharmacy Practice. The published abstract is placed as an appendix at the end of the thesis (see Appendix 11) rather than at the beginning of this chapter. This is because this chapter is an updated version of the conference abstract. In addition, as this chapter has been written in a journal format to be submitted for publication, an abstract that represents the work in the paper has been included. Formatting and layout for this chapter are consistent with the requirements for the journal. In addition, references from the paper are placed at the end of the chapter rather than at the end of the thesis.
Prescribing errors by junior doctors- a comparison of errors with High Risk Medicines and non-High Risk Medicines

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† These authors contributed equally to this work.
Abstract

Prescribing errors in hospital are common. However, errors with high-risk-medicines (HRMs) have a greater propensity to cause harm compared to non-HRMs. We do not know if there are differences between the causes of errors with HRMs and non-HRMs but such knowledge might be useful in developing interventions to reduce errors and avoidable harm. Therefore, this study aims to compare and contrast causes of junior doctors’ prescribing errors with HRMs to non-HRMs to establish any differences.

Methods: A secondary analysis of fifty-nine interviews with foundation year doctors, obtained from three studies, was conducted. Using the framework analysis approach, through NVivo®10 software, a detailed comparison was conducted between the causes, error-causing-conditions (ECCs), latent conditions, and types of errors related to prescribing errors with HRMs and non-HRMs.

Results: There were two differences in causes and types of errors between HRMs and non-HRMs. Violations were described with non-HRMs only and errors in the legal prescription requirements for controlled medications occurred with HRMs only. There were two differences in ECCs of HRMs and non-HRMs. The first related to the complexity of prescribing HRMs, especially dosage calculations. The second regarded differences in the circumstances of communication failures: with HRMs ineffective communication arose with exchanges with individuals outside the medical team while with non-HRMs these failures occurred with exchanges within the immediate medical team. Two differences were identified with the latent conditions: with non-HRMs there was a reluctance to seek seniors help and with HRMs latent conditions related to the organisational system such as the inclusion of trade names in hospital formularies. Moreover, prescribing during the on-call period was particularly challenging especially with HRMs.

Discussion: The analysis suggests that prescribers’ confidence with non-HRMs and a reduced sense of risk can lead to violations or reluctance to seek help. With HRMs the differences were indicative of the nature of these medications as HRMs tend to involve complex calculations and additional legal requirements for prescriptions.
5.1 Introduction

Prescribing errors are the most frequent type of error in the medication use process. [1,2] Such errors can double patients’ length of hospital stay and cost of care, as well as increasing their mortality rate. [3-5] With all types of medication, hospital prescribing errors are common occurring with 7% of medication orders, 2% of patient days and 50% of hospital admissions. [6] Seventy percent of hospital prescriptions are prescribed by Foundation Year 1 (FY1) and Foundation Year 2 (FY2) junior doctors. Nonetheless they have twice the prescribing error rate compared to consultants. [7] Not all prescribing errors necessarily have the same consequences; about 41% are considered to be minor. [7] High Risk Medicines (HRMs) have a greater ability to cause devastating harm when they are used in error compared to regular medicines. This category of medicines has been singled out by the Institute for Safe Medication Practices (ISMP) [8] in the USA and the National Patient Safety Agency (NPSA) [9] in the UK as worthy of special consideration. Particularly worrying is that the prevalence of prescribing errors with HRMs is wide ranging and has been reported to reach as high as 89.6 errors per 100 orders of HRMs. [10] According to the definition of the National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) organization, medication errors, including prescribing errors, are considered to be preventable. [11] Therefore, a better understanding of the causes of HRMs prescribing errors made by junior doctors could lead to the development of strategies and techniques to reduce their incorrect use and hence reduce patient harm.
There have been many models used to categorise and classify the causes of prescribing errors. One of the most common is Reason’s model of accident causation [12], which classifies the causes of prescribing errors into knowledge based mistakes [13-19], rule based mistakes [20], slips and lapses [13,16-18,20], and violations [13,16,17,20,21]. The model also incorporates error-causing conditions (ECCs) and latent conditions, with multiple ECCs and latent conditions being possible for a single prescribing error. This model of multifactorial influences was reflected in the findings of a systematic review about the causes of prescribing errors in hospitals [22].

ECCs related to the causes of prescribing errors have been described in previous studies and include the individual prescriber (e.g. physical health and knowledge) [13,18,20], working environment (e.g. staffing and accessibility for drug information) [13-15,18-20,23,24], the healthcare team (e.g. poor communication and the relation with seniors) [15,17,18,20,21], prescribing task (e.g. non-routine tasks or protocols) [13,18,20] and the patient (e.g. difficulty with communication, complex disease) [18,20]. Latent conditions described were varied and inconsistent but included factors such as reluctance to question greater authority [21], organizational system [23] and the low importance attached to prescribing [15,18,20].

These previous studies have all been based upon the investigation of prescribing errors made with all types of medication, without any distinction made between those errors made with non-HRMs and those made with HRMs. There may be many similarities, but there could also be important differences between these classes of medicines that may help in the development of interventions to reduce prescribing
errors with HRMs. Considering the severe consequences of errors with these medicines, this could be an important focus for reducing actual harm from preventable adverse drug events.

However, to date the causes of prescribing errors with HRMs made by junior doctors has not been studied. Therefore, this study will focus on this area of potential high risk and fill the gap in this area of research.

**Aim:** This study aims to compare and contrast the causes of junior doctors’ prescribing errors with HRMs with that of non-HRMs in order to establish any differences.

### 5.2 Methods

#### 5.2.1 Design

This study used secondary analysis of existing data, [25] where the data were obtained from fifty-nine interviews conducted by the research team in three previous studies, [26-28] which were already audio recorded by the researchers then transcribed by professional transcribing company. The secondary analysis of existing qualitative data, like interview data, has many advantages; for example, it provides a large amount of data that has been rigorously collected. This large volume of high
quality qualitative data provides a cost efficient way to address the research aim, avoiding the need for further data collection and data transcribing.

The three previous studies on prescribing errors are summarised in Table 5-1. The recruitment process of these studies were started with approaching the participants by email, face-to-face or through the training tutors by providing an information sheet that described the purpose of the study prior to giving consent for interviews. The majority of participants, in Set 1 and Set 2, who agreed to participate, were purposely selected to represent a wide range of university graduates from across the UK and working in different types of hospitals; moreover, all interviews were conducted at the workplace of the participants to make it easy for them; therefore, no participant had refused or dropped out. All the studies had been granted ethical approval and consent had been obtained from participants for future analysis of their interview data.

Table 5-1: Summary of the three studies

<table>
<thead>
<tr>
<th>Set of interviews</th>
<th>Number of Participants</th>
<th>Interviewees*</th>
<th>Study information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Set 1</td>
<td>30 FY1 doctors</td>
<td>Interviews obtained from Lewis et al study [26] which discussed causes of prescribing errors in all medication types</td>
<td></td>
</tr>
<tr>
<td>Set 2</td>
<td>19 FY2 doctors</td>
<td>Interviews obtained from a study conducted about prescribing errors in all medication types in FY2 doctors [27]</td>
<td></td>
</tr>
<tr>
<td>Set 3</td>
<td>10 FY1 doctors</td>
<td>Interviews obtained from McLellan et al study [28] about antimicrobial prescribing errors</td>
<td></td>
</tr>
</tbody>
</table>

* FY1 = Foundation Year 1, FY2 = Foundation Year 2.
The interviews from these studies were initially conducted to investigate the causes of prescribing errors in all medications types without distinguishing between HRMs and non-HRMs. As the interviewees were not asked about prescribing errors in relation to medications classification as HRMs or non-HRMs, participants had the opportunity to talk truthfully about the prescribing error without the influence of the term HRMs. Such a priori classification could lead participants to express their experiences and views of the prescribing error differently, which could lead to biased descriptions for the causes. Moreover, bias was reduced as there was no previous relationship between the interviewers and the participants.

5.2.2 Data analysis

Framework Analysis was used to analyse the data, [29] a common approach for health research. [30,31] NVivo software (version 10) was used to support this analysis. [32] This computer software can be useful for analysing unstructured data, and helping in organizing and analysing qualitative data such as interviews. [29] The analysis began with Set 1 with familiarization with the data by reading thoroughly. This was followed by inductive coding of the interviews, which gave better understanding of the data and allowed the researchers to draw themes from the raw data under each medication type, HRMs and non-HRMs. The third step was deductive coding of codes under a model of categorising causes of errors, based on Reason’s model of accident causation. The coding process was iterative; the principal investigator (MA) did the initial coding then this was discussed on multiple
occasions with the other members of the research team (PL and MT) until a consensus was reached. For Set 2 and Set 3 the same iterative process was conducted and the coding added to the codes of Set 1.

Reason’s model of accident causation, which is the most common model used to categorise the causes of prescribing error; [33] was used to categorise the causes, error-causing conditions, and the latent conditions resulting in prescribing errors. [12] The causes of prescribing error were classified as knowledge and rule based mistakes, slips, lapses and violations; an additional category of communication errors was added based on our previous work. [26] Definitions are given in Table 5-2; however, some prescribing errors could be classified under more than one cause of prescribing error. In addition, the ECCs, for both HRM and non-HRMs, were classified under following categories: individual prescriber; healthcare team; prescribing task; the patient; and working environment.
Table 5-2: Definitions of the active failure (causes) of prescribing error (adapted [7,12])

<table>
<thead>
<tr>
<th>Cause of the error</th>
<th>definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>2. Planning Failure</td>
<td>Correct execution of inappropriate or incorrect plan</td>
</tr>
<tr>
<td>c. Knowledge-Based Mistake</td>
<td>Mistakes that occur at the knowledge based performance level. Occur when faced with a novel task and have to consciously construct a plan of action. Occur when an inappropriate plan or incorrect plan is correctly executed.</td>
</tr>
<tr>
<td>d. Ruled-Based Mistake</td>
<td>Mistakes that occur at the rule-based performance level when drawing on a set of stored mental if-then rules. Occur when an inappropriate plan or incorrect plan is correctly executed.</td>
</tr>
<tr>
<td>4. Execution Failure</td>
<td>Failure in the execution of a good plan</td>
</tr>
<tr>
<td>c. Slips</td>
<td>An error that is caused by a failure in performing an intended action and that is replaced by another action</td>
</tr>
<tr>
<td>d. Lapses</td>
<td>An error that is caused by omission of a particular task</td>
</tr>
<tr>
<td>5. Violation</td>
<td>An error that is caused by a conscious decision to ignore the accepted rules or procedures of the organization</td>
</tr>
<tr>
<td>6. Communication Errors</td>
<td>An error that is caused by a lack of or an error in communication between the prescriber with the healthcare team, with other healthcare professionals, or with patients.</td>
</tr>
</tbody>
</table>

Errors were classified in five major types as adapted from a study by Dean et al [34] and applied in other studies of prescribing errors. [35,36] The five major types of errors were ‘need for drug therapy’, ‘selection of a specific drug’, ‘selection of dosage regimen’, ‘administration of drug’, and ‘provide drug product’. Each major type of errors had its own subtypes of errors; for example, ‘need for drug therapy’ had subtypes such as omission errors, premature discontinuation, drug not prescribed but indicated, continuation for longer than needed, a drug prescribed with no indication, and duplication.
A comprehensive and detailed comparison was conducted between HRMs and non-HRMs to distinguish any differences. To perform this robust comparison, a table was drawn to compare all the aforementioned elements such as causes of errors, ECCs, latent conditions and types of errors. The table of differences was iteratively developed by all researchers until it reached the final version.

Based on the final comparison, categories of differences were classified under the causes of errors, types of errors, ECCs and the latent conditions. The chosen themes were the obvious differences that were associated to the specific drug class, HRMs or non-HRMs, with reasonable justification from the interviewees’ description or related to the nature of the drug class. The selected quotes were chosen based on their clear depiction of the highlighted theme. The quotes were referenced using the participant’s number and written in italic and bold font (i.e. P#). Where extraneous material has been removed from the quote, this has been indicated using an ellipsis (…).

5.3 Results

Forty-seven out of the fifty-nine interviews were included in the analysis. The remaining 12 interviews were excluded because they did not mention any prescribing errors (n= 7), did not provide the name or type of medication in which the error occurred (n= 1), or because the prescribing error occurred outside hospital settings such as in general practice settings (n= 4). The 47 interviews contained
descriptions of 108 prescribing errors; 39 errors with HRMs, for example, Low Molecular Weight Heparins (LMWH), insulin, narcotics and opioids, and antibiotic related allergy; and 69 with non-HRMs, for example, Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), paracetamol, statins, and Proton Pump Inhibitors (PPIs).

5.3.1 Causes and types of errors

The causes of prescribing errors with HRMs included 10 knowledge based mistakes, 14 rule based mistakes, 10 lapses, 5 slips, and 5 communication errors (total no. = 44). The non-HRMs contained 17 knowledge based mistakes, 26 rule based mistakes, 9 lapses, 14 slips, 2 communication errors, and 6 violations (total no. = 74).

There were five major differences between the description of HRM errors and non-HRM errors (Table 5-3). From these five differences, two overarching themes emerged, one was in the causes of prescribing errors and the other was in the types of error. The first theme related to violations, which were an obvious difference between HRMs and non-HRMs as they were described by interviewees with non-HRMs only. The second theme related to the particular type of error ‘provide drug product’, which was described by interviewees with HRMs only.
<table>
<thead>
<tr>
<th>Causes of error</th>
<th>HRMs (n=39)</th>
<th>Non-HRMs (n=69)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Violations</td>
<td>Not described(^{(1)})</td>
<td>Described (n=6)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Types of errors</th>
<th>Provide drug product</th>
<th>Administration of drug</th>
<th>Selection of specific drug</th>
<th>Need for drug therapy</th>
<th>Selection of dosage regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>KBM, RBM, Lapses</td>
<td>KBM only</td>
<td>KBM, RBM, CE, Lapses, Slips</td>
<td>RBM, CE, Lapses</td>
<td>Similar</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Subtype:</td>
<td>Subtype:</td>
<td>Subtype:</td>
<td>Except for violations as presented with non-HRMs only</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Wrong dosage form</td>
<td>• Significant allergy</td>
<td>• Drug not prescribed</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Subtypes:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Drug not prescribed</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Drug duplication</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Drug not needed</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Subtypes:</td>
<td>• Contraindication</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Unintentional drug prescription</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Subtypes:</td>
<td>• Wrong dosage form</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Wrong dose timing</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Wrong route</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Wrong administration technique</td>
<td></td>
</tr>
</tbody>
</table>

HRMs= High Risk Medicines, Non-HRMs= Non High Risk Medicines, KBM= Knowledge-Based Mistakes, RBMs= Rule-Based Mistakes, CE= Communication Errors,

\(^{(1)}\) = Underlined text to indicate where there is difference.

Violations as a cause of error were one of the major differences between interviewees’ descriptions of HRMs and non-HRMs prescribing errors. Violations were described with non-HRMs only in four of the five types of errors (Table 3). The
types of error included; ‘need for drug therapy’ which related to the premature discontinuation of medication; drug not prescribed but indicated and changing an accurate prescription to cover another healthcare professional’s mistake; the ‘selection of dosage regimen’ which occurred when the prescriber did not check the dose frequency of a medication; the ‘administration of drug’ which related to omission of the medication stop date; and the ‘selection of dosage regimen’ which occurred when the prescriber wrote a wrong dose frequency without checking if the frequency was correct or not with the intention of obtaining the medication faster from the pharmacy.

One such error occurred where a prescriber did not write the antibiotic duration as he lacked the knowledge, the seniors’ support, and the resources to find the duration: “Sometimes if I don’t know and I can’t get hold of anyone and I can’t get the BNF [British National Formulary] I don’t even write it [duration]. I don’t write for how many days, cos I know pharmacy will ring back. I’ve done that before.” (P5). Therefore, the prescriber violated the rules by intentionally sending the prescription to the pharmacy without duration. These were often routine violations, which occurred because of influences such as the prescriber being in hurry or having a high workload. One interviewee stated: “I forget to sign quite a lot. If I’m in a hurry and there’s so many drug scripts I’ll just forget, forget to put a start date or forget to put a finish date…”(P3).

It is possible that prescribers choose to make these routine violations with non-HRMs because they know that these medications are less harmful to the patient when they are prescribed wrongly. In contrast, HRMs, by their definition, can have
deleterious effects when prescribed erroneously. An example of this was described by an interviewee who knowingly prescribed nystatin incorrectly without checking the appropriate frequency, as he wanted to complete the task quickly. The prescriber believed it to be a ‘safe error’ as he felt that there would be little harm to the patient:

“...it was, prescribing nystatin for a patient with oral candidiasis and I wasn’t sure of the dosing regimen, how many times a day to give it, and I put it down as, TDS [three times a day]... my thoughts were that the difference between TDS and QDS [four times a day] it's not a huge difference, it's not going to make, that much difference if I change it, if I checked BNF... so just to get it sent away I put it as sort of TDS... didn't particularly have any feelings at that point cos I thought it was a, a safe, a safe error shall we say, it was, there was no, no harm could have done from... ”(P23).

Moreover, knowing that there was the existence of a safety net, such as senior colleagues or pharmacists (who would check the juniors’ prescriptions and correct them), together with the low risk of harm when prescribing non-HRMs, could lead to the belief that routine violations are acceptable behaviour. The junior prescribers relied on the safety net to fill gaps in their prescriptions or pick up on errors which would then be flagged along with the appropriate prescription instructions:

“...they’re both long-term treatments rather than ones that are going to instantly help somebody, but it's just making sure I remember to do it. The good thing is that we do have, people to review those, and to sort of pick up on if they have or they haven’t been prescribed it…” (P12).
Another major difference between HRMs and non-HRMs was the frequency of the type of error “provide drug product”, which, in relation to HRMs, were mainly the legal requirements of controlled drug prescriptions. In the UK, controlled medications are HRMs and require additional details when prescribing, especially for discharge prescriptions, compared to prescriptions for other medications. The causes that led to this error type were lapses as the prescriber forgot to write the numbers also in words (a legal requirement in the UK for controlled medications), rule based mistakes where the prescriber did not apply the rules of controlled drug prescriptions because they did not realise the prescribed drug required it or Knowledge based mistakes, where the prescriber lacked knowledge about how to complete the controlled drug prescription. An interviewee stated that:

“Q: And had you prescribed morphine before?

A: I'd prescribed it on a normal prescription chart, but not as, a take-home.

Q: And are they prescribed differently?

A: Yeah…

Q: And why do you think you made the error?

A: I'd just never been taught how to do it and, and then we since, just shortly after that, in fact, we had a teaching session…” (P18).

All the errors with HRMs that were classified under ‘provide drug product’ occurred with discharge medication prescriptions for controlled drugs. This transition period of time, when a patient is discharged from hospital, can be vulnerable to prescribing errors as prescribers often have a high workload requiring them to multi-task under time pressure. One interviewee described the situation when he made this error during the discharge period time:
“… I think a lot of it is because you are so busy and half the time you’re doing two, three things at once. Like, I can say, there’s been many occasions like I’d be on the phone trying to sort something out and writing a TTO [discharge medication] at the same time, and you really shouldn’t do that.” (P13).

5.3.2 Error Causing Conditions

There were similarities and differences in the ECCs of HRMs and non-HRMs errors (Table 5-4). Two key themes were drawn from these differences between HRMs and non-HRMs. The first theme related to the complexity of the task of prescribing HRMs and the second was related to the nature of communication failures.

Table 5-4: Differences in Error Causing Conditions (ECCs) between HRMs and non-HRMs

<table>
<thead>
<tr>
<th>ECC</th>
<th>HRMs</th>
<th>Non-HRMs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individual prescriber</td>
<td>Acting in an automatic way$^{(1)}$</td>
<td>Lack of senior support</td>
</tr>
<tr>
<td></td>
<td>• Slips</td>
<td>• RBMs, Slips</td>
</tr>
<tr>
<td>Healthcare team</td>
<td>Communication failure outside medical team</td>
<td>Communication failure inside medical team</td>
</tr>
<tr>
<td></td>
<td>• Communication errors</td>
<td>• Communication errors</td>
</tr>
<tr>
<td>Prescribing task</td>
<td>Complicated task</td>
<td>Similar</td>
</tr>
<tr>
<td></td>
<td>• KBM, RBM</td>
<td></td>
</tr>
<tr>
<td>The patient</td>
<td>Similar</td>
<td></td>
</tr>
<tr>
<td>Working environment</td>
<td>Similar</td>
<td></td>
</tr>
</tbody>
</table>

ECCs= Error Causing Conditions, HRMs= High Risk Medicines, Non-HRMs= Non High Risk Medicines, KBM= Knowledge-Based Mistakes, RBM= Rule-Based Mistakes. $^{(1)}$ = Underlined text to indicate where there is difference.
When comparing HRMs to non-HRMs, the nature of the prescribing task was different in two ways – the occurrence of knowledge based and rule based mistakes. These differences represented some traits of prescribing HRMs in general, as some can be complicated to prescribe or can be infrequently prescribed. Participant 24, as an example, described the rule based mistake of prescribing dalteparin for a patient with a deteriorated renal function and the complexity of the task for him, and said: “…it was the whole ideal body weight thing and working out eGFR cos essentially, eGFR I was fine, GFR was deranged and just still don’t really don’t know how to work out GFR, it’s so complicated.” (P24).

The complicated tasks described were particularly associated with calculations and prescribers’ difficulty in completing these calculations. Such calculations require intensive training and the provision of calculation instructions over the phone would not help much in understanding of these tasks. Interviewees described a lack of calculation training or instruction resulting in mistakes, one interviewee stated:

“Q: Okay. And who had asked you to prescribe those?
A: The GU [genitourinary] Consultant, over the phone.
Q: Okay. And did you ask anybody about this?
A: Well I asked him. And he was, like because, oh Microbiology also told me, because he [the patient] was quite poorly. So I had them both ringing me over the phone… But it was really complicated… The whole process that I wrote out for them was fine. But it was just the actual dose, because of the dilution, or the fact on how many grams per whatever.” (P16).

Another participant described their vague recollection of calculation training in relation to anticoagulant dosing: “…I didn’t know how much to give her and I
think it’s just as part of our training we need to know about well I possibly did have a tutorial once on ideal body weight but it probably needs to be highlighted in our training.” (P24).

In addition to the causes categorised using Reason’s model, communication errors occurred with both HRMs and non-HRMs. However, there was a difference between them. Communication failures with non-HRMs arose within the same medical team, i.e. between a junior and a senior prescriber within the same team. Seniors were described as not providing enough details or proper instructions for the juniors. For example, one interviewee prescribed the wrong infusion rate of omeprazole after basing his decision on incorrect instructions from a senior doctor: “…I was just confused because nobody actually told me how to do it, so I was just verbally taught it, informally taught and I just prescribed it but it was detected by the pharmacist basically.” (P25). Moreover, the junior doctor did not check the information that had been given by their senior:

“Q: And had you looked it up or?
A: No, basically the registrar just said yeah, this is how it is.” (P25).

Both senior and junior doctors did not give their full attention to the prescribing task, which could be related to the relatively good safety profile of non-HRMs.

In contrast, none of the communication failures with HRMs occurred as part of this “team prescribing”. The problems were with individuals outside of the medical team such as communication failures between the prescriber and the patient, the GP, or another healthcare professional. This could be related to the high awareness within the medical team to the importance of these HRMs and the consequences of
committing a mistake; therefore, communications regarding them were clear and obvious.

There were other, less notable differences such as an individual prescriber acting in automatic way with non-HRMs, as one interviewee stated when he prescribed a laxative (Senna®) instead of potassium supplement (Sando K®): “I think I might have gone back to being automatic.” (P39), but this kind of difference could occur with HRMs as well; therefore, not every difference was included as a theme. Moreover, there were some ECCs, which were described in both HRMs and non-HRMs by the interviewees many times in most causes of errors, they were challenging for the prescribing task (i.e. on-call period and TTO). However, on-call period was more often described with HRMs than non-HRMs, one participant described the on-call period as ‘crazy’ as he states:

“Q: About this particular example, was it especially busy or was it just like a normal on-call?
A: There’s no such thing as especially busy on call they’re all the same…
Q: Is it?
A: Yeah they’re all busy, they’re all crazy.”(P27)

5.3.3 Latent conditions

Differences in latent conditions were found with mistakes and violations with HRM and non-HRMs (Table 5-5). However, as well as in the causes of errors, types of errors and ECC not all the differences could be transferred to themes. Therefore, two
themes were identified: reluctance to ask seniors was a latent condition described only with the knowledge and rule based mistakes occurring with non-HRMs and ‘organisation documents leading to error’ which was found only in knowledge based mistakes with HRMs.

Table 5-5: Differences in latent conditions between HRMs and non-HRMs

<table>
<thead>
<tr>
<th>Latent condition</th>
<th>Causes of error</th>
<th>HRMs</th>
<th>Non-HRMs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Organisation documents lead to error</td>
<td>KBM</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Previous decision made by seniors</td>
<td>RBM</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prescriber reluctant to ask seniors</td>
<td>KBM, RBM</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poor staff organisation</td>
<td>KBM</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shortage of resources</td>
<td>Violation</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

HRMs= High Risk Medicines, Non-HRMs= Non High Risk Medicines, KBM= Knowledge-Based Mistakes, RBMs= Rule-Based Mistakes

A reluctance to ask seniors or to look up drug information in front of other healthcare professionals was a latent condition that was only described with knowledge based mistakes in non-HRMs. Junior doctors felt they would be perceived as incompetent, stupid, or that they would annoy seniors if they asked or looked up information about such drugs. An example of this was given by an interviewee when he prescribed the wrong dose of ibuprofen, as said:

“…someone had asked me to prescribe it and I didn’t want to look like I had to look it up.

Q: Okay.
A: Cos, you know, I didn't want to look stupid, so I, I just, I was like, I was thinking, “Yeah, I'm pretty sure it's not a round number, like 500 or 1000, I think it's about 300/400,” so I just put 300” (P18).

The medication type that was being prescribed played a role in prescriber reluctance to ask seniors for advice or help. Those medications that were perceived as being simple, and were therefore usually non-HRMs were associated with this reluctance:

“‘…Oh I'm a Doctor now, I know stuff,’ and with the pressure of, sort of, more, you know, people who are maybe, sort of, a little bit more senior than you thinking ‘what’s wrong with him… you don’t wanna [want to] always be seen to be in, you know, ‘what's the dose of paracetamol?’…” (P2).

Moreover, both types of mistakes with non-HRMs were similar, with both having the reluctance of the junior doctors to ask seniors as a latent condition. Participant 23 described this when he prescribed the wrong dose of antibiotic:

“Q: So you say that you, now you're experienced you would ask, did you not ask in, when you first started?

A: I think it's sort of a bit of scare, scariness, I was, I'd probably go and just check in the BNF at that stage.” (P23).

Organisational documents led to knowledge based mistakes with HRMs only. Using trade names is considered to be an inappropriate prescribing habit, rather than an error. However, when trade names were used within organisational documents such as formularies, it can lead to errors as prescribers may not be prompted to remember the active ingredient or indeed know it in the first place. This occurred with an
interviewee who prescribed a penicillin-based antibiotic combination for a patient who was allergic to penicillin, the hospital formulary guidelines used the trade name (Timentin®) and that misguided the prescriber:

“… I think it's because on, on this particular document that we have as, as a reference it uses, it uses a trade name as, rather than a generic name… they [trade names] can be confusing and conflicting and not really tell you what it is if you're in a rush.” (P2).

5.4 Discussion

This is the first study to investigate thoroughly the causes of prescribing errors with HRMs; moreover, it has compared the causes of HRMs to non-HRMs. Although it was a secondary analysis, the large number of interviews (59) included the descriptions of many junior doctors’ prescribing errors with both HRMs and non-HRMs resulting in data saturation. Indeed, the analysis of Set 3 did not reveal any new findings and merely confirmed the findings of the previous sets. Therefore, there was robust intra-comparison between HRMs and non-HRMs achieving the aims and objectives of this study. Moreover, many confounding factors, which are usually linked to using different data sources such as language, country, and prescribers’ experience, were avoided as all interviews were conducted in English within the UK with a similar level of experienced doctors, i.e. in their foundation years.
For a robust analysis of the available data and identification of overarching themes, the study used a hybrid, inductive and deductive, approach for the thematic analysis. [37] Inductive coding, data driven coding, gave better understanding of the data and allowed us to code and draw themes from the raw data under each medication type, HRMs and non-HRMs. The obtained codes and themes were applied on the Reason’s model of accident causation [12], deductive coding or theory driven codes. This style of iterative coding process between inductive and deductive coding is common in practice; [25] therefore, it was used in this study.

Using secondary analysis of existing data [25] has many advantages such as providing a large amount of data that has been rigorously collected based on a large scale. Secondary analysis of existing data avoids further data collection, which is the most costly, time and effort consuming phase of the research study. [38,39] Moreover, advantages include making the most of the available data by investigating new variables or concepts which were not investigated or asked initially [25,38,39]; HRMs were not the focus of the primary research yet this group of medication could compromise patient safety more than general medications. However, this study has its limitations derived from the data source, as some interviews (n=12) and prescribing errors were excluded because they could not fully answer or they did not fit our research question.

Violations were not linked to HRMs and were only reported in prescribing errors with non-HRMs. This finding could be explained by the heightened risk of harmful consequences with HRMs in comparison to non-HRMs which may lead prescribers to avoid violations with HRMs. Although violations are intentional deviations from
safe practice or the written rules of the working place, the violations described in this study with non-HRMs were intended to ensure patient benefit and to overcome workplace complexity. This finding is similar to previous findings that most violations are well-intended. [40] As well, our results confirmed that time pressures, leading to prescribers being in a hurry, high workload and lack of resources could lead to violations. [41]

Missing information from prescriptions, i.e. incomplete prescriptions, is a quite common type of prescribing error, [7] but they were not described with non-HRMs in this study. It is possible that, because HRMs have a potentially serious impact on patient safety, errors with these drugs were remembered by the prescribers for longer compared to non-HRMs. Therefore, when prescribers were interviewed they could recall them more readily than errors with non-HRMs. Furthermore, prescriptions for controlled drugs have strict legal prescription writing requirements and dispensing will be delayed until they are correct. In summary, controlled drug prescriptions seemed more susceptible to prescribing errors in comparison to other medications, particularly due to missing information. Therefore, techniques for targeting this type of prescription could improve patient care and save the time of the healthcare team.

Communication errors, such as poor written or verbal communication, have been reported previously, regardless of medication class or medication classification, without considering HRMs specifically. [15,18,20,21] Sometimes communication errors could be described outside the medical team only, i.e. with other services or departments, as observed by Kopp et al. [17] In our study, communication errors with HRMs were associated with communication failures with other teams and non-
HRMs were associated with communication failures inside the medical team. It could be hypothesised that this could be related to the nature of non-HRMs as being less harmful or viewed as less important, which result in neglect from both juniors and seniors to communicate effectively. On the other hand, concerns about HRMs may have led the medical team to communicate freely without any barriers.

Barriers to good communication that were found included a reluctance by junior doctors to ask seniors (or other healthcare professionals), which could lead to unsafe prescribing and even violations of prescribing rules. Reluctance to ask advice from others and its impact on the safety of prescribing process has been described before. [20,21,42] However, the finding that this is particularly associated with mistakes with non-HRMs is new. Poor prescribing with non-HRMs was potentially perceived as more acceptable than with HRMs, making junior doctors less likely to contact their seniors and deal with prescribing decisions themselves.

Seeking senior advice was a concern to the junior doctors which could negatively affect patient safety; in contrast, some senior doctors in other studies have described feeling discomfort if the juniors did not seek help. [42] Therefore, junior doctors should be encouraged to seek help from seniors regardless of the medication class and senior doctors should be encouraged to make themselves available, especially with non-HRMs. Moreover, health institutes should encourage an open culture of communication between staff regardless of the steep hierarchy to attain openness and a positive safety culture.
Medication safety initiatives should target HRMs with certain types of interventions such as targeting controlled-medication prescriptions especially at the discharge period, targeting HRMs dose calculations, and targeting organizational documents (i.e. hospital formularies) that could lead to prescribing errors. Interventions should be delivered at the beginning of junior doctors’ placements and interventions should be interactive such as workshops and feedback on previous prescribing tasks to emphasise the understanding of the materials. Moreover, approaches could include appropriate information provision and support such as providing junior doctors with practical, easy to understand and easy to access guidelines and key people to contact such as drug information specialists.

Future research could focus on a specific period of the prescribing process such as at discharge or during the on-call period, as these were described as particularly difficult times to prescribe safely placing a huge burden on the prescriber. Some HRMs, such as controlled drugs, insulin and anticoagulants were described as more challenging to prescribe safely. Therefore, focusing our efforts on understanding the nature of prescribing errors during the on-call period with HRMs would be beneficial to developing solutions to ensure that prescribers, especially junior prescribers (who most commonly work out of hours), can prescribe safely and that patient harm is prevented. Moreover, targeting error reduction strategies at HRMs in particular is more beneficial, especially for hospitals with limited resources, as they are less in number and high in harm in comparison to non-HRMs.
5.5 Conclusion

The differences between HRMs and non-HRMs reflect the nature of the prescribed medication class and the attitude of the prescribers toward the prescribed medication. Prescribers’ confidence with non-HRMs and the reduced sense of risk could lead to breaking the rules or reluctance to seek help. HRM related errors were illustrative of the complexity of the prescribing task with HRMs or additional rules regarding HRM prescriptions (e.g. controlled medication). Furthermore, medication class had an influence on communication as non-HRMs were associated with different types of communication failures than HRMs. In conclusion, these findings highlighted some of the areas that could be targeted by interventions in future to reduce prescribing errors and increase patient safety, with both HRMs and non-HRMs.

5.6 Acknowledgment

We would like to thank Elizabeth Seston and Lucy McLellan for conducting some of the interviews. Moreover, we would like to thank the Saudi Arabian Government as this study is part of a PhD thesis that is fully sponsored by them.
5.7 References

8. ISMP (2014) ISMP list of high-alert medications in acute care settings.
## 5.8 Appendix 5.A

**Prescribing errors by junior doctors - a comparison of errors with High Risk Medicines and non-High Risk Medicines**

Supplementary file: COREQ checklist for interviews and focus groups

<table>
<thead>
<tr>
<th>COREQ category</th>
<th>Guide questions/description</th>
<th>Response</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Domain 1: Research team and reflexivity</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Personal Characteristics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Interviewer/facilitator</td>
<td>Which author/s conducted the interview or focus group?</td>
<td>Dr Penny Lewis (PL)</td>
<td>Methods &amp; Acknowledgment</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dr Mary Tully (MT)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dr Elizabeth Seston (ES)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dr Lucy McLellan (LM)</td>
<td></td>
</tr>
<tr>
<td>2. Credentials</td>
<td>What were the researcher's credentials? E.g. PhD, MD</td>
<td>PhD</td>
<td></td>
</tr>
<tr>
<td>3. Occupation</td>
<td>What was their occupation at the time of the study?</td>
<td>PL was a lecturer in Manchester Pharmacy School, University of Manchester.</td>
<td>Not Applicable</td>
</tr>
<tr>
<td></td>
<td></td>
<td>MT was a reader in Manchester Pharmacy School, University of Manchester.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>ES was research fellow in Manchester Pharmacy School, University of Manchester.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>LM was a master student in Manchester Pharmacy School, University of Manchester.</td>
<td></td>
</tr>
<tr>
<td>4. Gender</td>
<td>Was the researcher male or female?</td>
<td>The main researcher Mahdi Alanazi (MA) is male and the main interviewers were female. This has not been reported in the study as the issues are not believed to be gender specific.</td>
<td>Not Applicable</td>
</tr>
<tr>
<td>5. Experience and training</td>
<td>What experience or training did the researcher have?</td>
<td>As a PhD student, MA has attended qualitative research training provided by the University of Manchester. Furthermore, the other members of the research team PL and MT are experienced researchers in qualitative research, who have undertaken and supervised many qualitative studies, and contributed to all parts of this study. All authors input into analysis and writing of the manuscript, and PL and MT reviewed successive drafts of the paper. Authors’ contributions were provided at the submission stage.</td>
<td>Submission information and authors’ contributions</td>
</tr>
</tbody>
</table>
### Relationship with participants

<table>
<thead>
<tr>
<th>6. Relationship established</th>
<th>Was a relationship established prior to study commencement?</th>
<th>There was no previous relationship between the interviewers and the participants</th>
<th>Methods</th>
</tr>
</thead>
<tbody>
<tr>
<td>7. Participant knowledge of the interviewer</td>
<td>What did the participants know about the researcher? e.g. personal goals, reasons for doing the research</td>
<td>All participants had received an information sheet describing the purpose of the study prior to giving consent for interview.</td>
<td>Methods</td>
</tr>
<tr>
<td>8. Interviewer characteristics</td>
<td>What characteristics were reported about the interviewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic</td>
<td>The facilitators Dr Lewis and Dr Tully are interested in patient safety and prescribing errors especially with junior doctors. They are both pharmacists and have published widely in this field. Dr Seston is an experienced health services research fellow.</td>
<td>Not Applicable</td>
</tr>
</tbody>
</table>

### Domain 2: study design

Theoretical framework

| 9. Methodological orientation and theory | What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis | Framework analysis was conducted and the codes and themes were built based on hybrid technique to underpin the analysis, as the coding and themes started with inductive based on the available data then the obtained codes and themes applied on Reason’s model as deductive coding. | Methods |

Participant selection

<table>
<thead>
<tr>
<th>10. Sampling</th>
<th>How were participants selected? e.g. purposive, convenience, consecutive, snowball</th>
<th>Participants selected purposively in two sets of interviews, while the third accepted all respondents.</th>
<th>Methods</th>
</tr>
</thead>
<tbody>
<tr>
<td>11. Method of approach</td>
<td>How were participants approached? e.g. face-to-face, telephone, mail, email</td>
<td>Face-to-face, emails and through their training tutor in the hospitals.</td>
<td>Methods</td>
</tr>
<tr>
<td>12. Sample size</td>
<td>How many participants were in the study?</td>
<td>59 participants from 3 different studies.</td>
<td>Methods</td>
</tr>
<tr>
<td>13. Non-participation</td>
<td>How many people refused to participate or dropped out? Reasons?</td>
<td>There were no participants refused or dropped out of the three studies.</td>
<td>Methods</td>
</tr>
<tr>
<td>Setting</td>
<td>Data collection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14. Setting of data collection</td>
<td>Where was the data collected? e.g. home, clinic, workplace</td>
<td>Interviews were conducted in workplaces.</td>
<td>Methods</td>
</tr>
<tr>
<td>15. Presence of non-participants</td>
<td>Was anyone else present besides the participants and researchers?</td>
<td>There was no one else present</td>
<td>Not Applicable</td>
</tr>
<tr>
<td>16. Description of sample</td>
<td>What are the important characteristics of the sample? e.g. demographic data, date</td>
<td>The important characteristic of the sample are related to their level of experience, as all participants were junior doctors either Foundation Year 1 and Foundation Year 2 doctors, who are responsible for writing of 70% of hospital prescription and they have the double rate of prescribing errors of consultants.</td>
<td>Introduction and methods</td>
</tr>
</tbody>
</table>

Data collection

<p>| 17. Interview guide | Were questions, prompts, guides provided by the authors? Was it pilot tested? | No, however the original papers had them. | Not Applicable |
| 18. Repeat interviews | Were repeat interviews carried out? If yes, how many? | No, there were no repeated interviews | Not Applicable |
| 19. Audio/visual recording | Did the research use audio or visual recording to collect the data? | The original interviews were audio recorded | Methods |
| 20. Field notes | Were field notes made during and/or after the interview or focus group? | They were made during the interviews; however, they were not added or used in the analysis. | Not Applicable |
| 21. Duration | What was the duration of the interviews or focus group? | Set 1: 20 min to 80 min  Set 2: 25 min to 65 min  Set 3: 14 min to 35 min | Not Applicable |</p>
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<td>22. Data saturation</td>
<td>Was data saturation discussed?</td>
<td>The large number of described prescribing errors by large interviews number leaded for saturation of data in term of types of errors, causes of errors, error causing conditions and latent conditions.</td>
<td>Discussion</td>
<td>22</td>
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<td>23. Transcripts returned</td>
<td>Were transcripts returned to participants for comment and/or correction?</td>
<td>No, however the facilitator reviewed and corrected the transcripts that were transcribed by specialized transcribing company</td>
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**Domain 3: analysis and findings**

Data analysis

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<td>24. Number of data coders</td>
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<td>Methods</td>
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<td>25. Description of the coding tree</td>
<td>Did authors provide a description of the coding tree?</td>
<td>Coding described in detail in the method section</td>
<td>Methods</td>
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<td>26. Derivation of themes</td>
<td>Were themes identified in advance or derived from the data?</td>
<td>It was a hybrid, where it started with inductive coding then deductive coding by applying the obtained codes on Reason’s model.</td>
<td>Methods</td>
<td></td>
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<td>27. Software</td>
<td>What software, if applicable, was used to manage the data?</td>
<td>NVivo 10</td>
<td>Methods</td>
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<td>28. Participant checking</td>
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Reporting

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<td>29. Quotations presented</td>
<td>Were participant quotations presented to illustrate the themes / findings? Was each quotation identified? e.g. participant number</td>
<td>Yes, they have been identified by participant number</td>
<td>Results</td>
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<th>30. Data and findings consistent</th>
<th>Was there consistency between the data presented and the findings?</th>
<th>Yes, data has been provided as evidence for the findings, and interpretations drawn from the data are described in the results and discussion.</th>
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<td>31. Clarity of major themes</td>
<td>Were major themes clearly presented in the findings?</td>
<td>The manuscript does not label the themes as major and minor. However, all themes were described clearly.</td>
<td>Results</td>
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<td>32. Clarity of minor themes</td>
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6. Chapter Six: Study Three

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<th>Exploring the challenges faced by foundation doctors when prescribing high risk medicines safely during the on-call period</th>
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<tr>
<td>Type</td>
<td>Original article</td>
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<tr>
<td>Authors</td>
<td>M. A. Alanazi, P. J. Lewis and M. P. Tully</td>
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<tr>
<td>Status</td>
<td>In publication format but has not yet been submitted</td>
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Note. Formatting and layout for this chapter are consistent with the requirements for journal publication. In addition, references from the paper are placed at the end of the chapter rather than at the end of the thesis.
Exploring the challenges faced by foundation doctors when prescribing high risk medicines safely during the on-call period

6.1 Introduction

Prescribing errors are the most frequent type of error in the medication use process. (1, 2) The on-call period (i.e. after working hours or during weekends) has been found to be a particularly difficult time for prescribing safely. (3) This period has been associated with higher patient mortality rates, (4-6) although there is controversy surrounding the exact figures. (6) However, there is agreement that patients admitted during the weekends have more severe medical conditions, which could increase the probability of mortality. (7) Foundation year 1 (FY1) and foundation year 2 (FY2) doctors are responsible for prescribing about 70% of hospital prescriptions, with this percentage potentially increasing during the on-call period. (8) Foundation doctors are known to make a higher ratio of prescribing errors than senior doctors; (9, 10) the error rate of medication orders in relation to doctor grades are as follows: FY1 (8.6%), FY2 (10.2%) and consultants (4.8%). (8)
High Risk Medicines (HRMs) are classified this way because they have a higher risk of causing significant patient harm when used in error. (11, 12) Examples of HRMs include anticoagulants such as warfarin and heparin, insulin, and opioids. HRMs are commonly prescribed and thus frequently cause severe patient harm or death. (13, 14) Prescribing error rates with HRMs can be as high as 89.6 errors per 100 orders of HRMs, and for each admission in which HRMs are prescribed, there may be 1 or 2 prescribing errors. (15) There have been challenges described by foundation doctors when they prescribe HRMs, such as prescribing tasks that are complicated or non-routine for the prescriber, or where communication between the prescribers and the patient and the multidisciplinary team is problematic. (3) It is possible that these challenges could be more of an issue during the on-call period, (16) or potential new challenges related to this period, but there has been no evidence to support this. Therefore, studies which focus on the prescribing of HRMs whilst on call will narrow the gap in knowledge that may in turn lead to interventions or solutions that would have a positive impact upon patient safety.

The aim of this focus group study was to explore the challenges that are encountered by FY1 and FY2 doctors when prescribing specific HRMs safely during the on-call period. The specific HRMs that were discussed are anticoagulants, insulin, and opioids, which are commonly prescribed HRMs that frequently cause severe patient harm or death. (13, 14) In addition, this study aimed to explore similarities and differences in the challenges that arise when prescribing HRMs and non-HRMs either during on-call or during daytime working hours.
6.2 Methods

6.2.1 Design

Focus groups were used as the data collection tool; this qualitative method was chosen as conversations are dynamic and the interactive naturalistic setting can lead participants to reveal more opinions than they might in a one-to-one interview. (17) This naturalistic environment has a normative influence on participants as they discuss their experiences leading others to reveal and discuss sensitive issues such as prescribing violations. (17) The participants in the focus groups were both FY1 and FY2 doctors. These are doctors who are completing the Foundation Programme, which is a two-year training programme in the UK for doctors who have just graduated from medical school. The sites of the focus groups were two large teaching hospitals, and one general acute hospital in North West England. Two focus groups were planned for each hospital (one for each grade of doctor), each including between 4 and 9 participants. Focus group facilitators included other researchers or PhD students (Aseel Abuzour and Daniel Greenwood) and one of the supervisors (PL). The principal investigator (MA) attended all the focus groups to assist and make notes. The focus groups were conducted from May until July 2017. Foundation doctors were contacted through their training tutors at the hospital trust that they were working in. Those foundation doctors who were interested in participating then emailed their details to their training tutor, or the principal researcher.
At the start of each focus group, the facilitator gave the participants a brief introduction about the study, and emphasised the anonymity of participants and the confidentiality of the data generated. Participants were asked to compare their experiences of prescribing HRMs during the on-call period to daytime working hours, in terms of challenges to prescribing them safely; the support that participants got from healthcare professionals around them such as senior doctors and pharmacists; their communications with patients, peers and senior doctors; and short-cuts taken when prescribing. They also discussed and compared the complexity of prescribing tasks with HRMs and non-HRM (Appendix 6.A depicts the focus group topic guide). The discussions were audio-recorded with consent and transcribed verbatim by a University approved professional transcribing company; the transcribed text was reviewed by MA to check for accuracy.

6.2.2 Data analysis

A thematic framework analysis, (18) commonly used in health research, (19, 20) was conducted with the assistance of NVivo software (version 11). (21) Initially, a coding framework was developed based on participants’ words and phrases. Prescribing challenges were categorised into challenge-causing conditions (the conditions that promote the commission of an error) and latent conditions (whose adverse consequences may lie dormant within a system for a long time, only becoming evident when they combine with other factors to breach the system’s defences). (22) These were deductive codes based on Reason’s model of accident causation. (22, 23) The challenge-causing conditions could be related to the
following categories from this model: individual prescriber, the patient, the prescribing task, working environment, and healthcare team. In addition, challenges could be related to a communication failure or a violation, as classified in our previous work. (16) The coding was an iterative process, as the principal investigator (MA) reviewed the codes and coding with the research team (PL and MT) multiple times until the analysis was agreed to be complete. A comprehensive comparison between the findings for FY1 and FY2 doctors for all themes was then conducted to identify any similarities or differences in the data.

Results of the analysis were supported using participant’s quotes, selected to illustrate the theme or idea. The quotes are referenced by the participant’s number, whether FY1 or FY2 and the hospital number (i.e. P#, FY#, H#). Where any extraneous material has been removed from the quote is indicated using an ellipsis (…). Ethical and governance approvals were given by the University Research Ethics Committee and Health Education England.

6.3 Results

Six focus groups were conducted in three different hospitals; three with FY1 and three with FY2 doctors. They ranged from 19 to 43 minutes in duration and four to nine participants were in each group. The data from the focus groups provided many repeated codes, resulting in robust themes. All main types of challenge-causing conditions of Reason’s causation model, and various latent conditions underpinning the challenges, and a number of violations during the on-call period were described.
6.3.1 Challenge-causing conditions

6.3.1.1 Healthcare team

Challenges during the on-call period often related to communication problems with the healthcare team such as seniors and colleagues, pharmacists and nurses. FY1 doctors described more challenges related to communication problems, especially verbal communication, compared to FY2 doctors. In contrast, the challenges relating to support from the wider healthcare team were predominantly described by FY2 doctors. There were no differences in FY1 and FY2 descriptions of the other elements in this theme, such as the difference between daytime and on-call working hours, or the impact of nurses.

Communications

FY1 doctors found verbal communication with seniors challenging when prescribing HRMs, ranging from poor to no communication during the on-call period. An example of perceived poor communication was seniors not responding to a bleep from a FY1 straight away during on-call hours. However, the initial help received gradually reduced as doctors gained more experience and seniors communicated less
with foundation doctors at the end of the FY1 year, as compared to the beginning, as one participant described:

“When we first started back in August, if you were phoning up someone more senior they did listen to you a lot more than at this point when we've been in the job for a year.” (P5, FY1, H3).

Doctors struggled with communication with the pharmacist when on-call, as the pharmacist was not on-site and would answer calls from home. They also described poor communication with nurses when being requested to prescribe medicines during the on-call period. Nurses would only provide the prescriber with limited information about the patient, which was a challenge when trying to prescribe safely as one prescriber said:

“I think at nights what tends to happen is a lot of prescribing jobs will come from ward nurses and what they’ll do is they’ll hand you a task, they won’t hand you any background” (P3, FY1, H1).

Written communication between healthcare teams included both paper and electronic forms. Unlike verbal communication, all foundation doctors described similar challenges during the on-call period regarding documentation of patient information and medication by other healthcare teams. Challenges were related to poor quality or total lack of documentation. For example, in the patient’s medication plan; height, weight and dose of medication were often absent. These challenges particularly affected HRMs during the on-call; such as insulins and anticoagulants, more than non-HRMs. An example of a lack of plan for warfarin prescribing during the on-call was described in one focus group discussion:
“... If they’ve [day teams] got patients that are being dosed on warfarin they should at least make sure that there is a clear plan... if they don’t leave that plan then you have no idea what’s going on with the patient...

I: Is this quite a common problem?

P1: Yeah.

P2: Yeah.” (P1, P2 and P3, FY2, H2).

Support

Only FY2 doctors described challenges relating to lack of specialised teams during the on-call period. Services such as diabetic nurses, the pain team, the mental health team and the Parkinson’s disease team were usually available during daytime hours only; therefore, the FY2 prescribers lacked their support during the on-call period. Furthermore, reliance upon such specialised teams during usual working hours was felt to reduce skills in prescribing certain medications, so that when doctors were to prescribe without support they lacked the required knowledge and skills, as one participant described:

“... I think insulin is particularly a problem ... I think as doctors we’re actually quite under-skilled in it because diabetes nurses have become such a big thing... I think even medical consultants would get a diabetes nurse to sort out their insulin regimes.” (P3, FY2, H1).

Both FY1 and FY2 doctors described similar challenges regarding their support from seniors and pharmacists during the on-call period. Challenges described varied from
poor support (i.e. less people around to ask for help) to a total lack of support from more senior doctors and pharmacists during the on-call period. This absence of support particularly affected the prescribing of HRMs, as one prescriber described this situation:

“One of the biggest challenges I find is with the high risk medications when I’m on-call there’s less people around to ask for help, so you’re usually by yourself on-call, you don’t have an SHO [Senior House Officer] or a registrar around on the wards to maybe ask or double check with, you don’t have a ward pharmacist who’s also on the ward at the same time. It is just you… So that’s the big challenge I face I think when I’m prescribing those high risk medications outside of the normal working day.” (P6, FY1, H2).

As with the FY1 doctors, the FY2 doctors also noticed the support from the seniors becoming less as they gained more experience compared to the beginning as one participant said:

“I think the expectation is you get taught once and then you’re meant to pick it up. So if you have many months down the line asking about something that’s quite simple I think they would get a little bit irate about it, but I think at the beginning when you’re first starting it’s not an issue at all.” (P3, FY2, H2).

The speciality of senior doctors was a factor that influenced foundation doctors when they sought support about complex medications during the on-call period. There was a difference between senior support from medical and surgical specialities, as the foundation doctors thought that it would be more beneficial to their knowledge and the care of the patient to ask queries of medical seniors than surgical seniors, as
participants of one focus group revealed: “P4: Depends whether it’s surgery or medicine really
P2: Yeah, this is true
P4: … in general you don’t think about asking the surgical registrar about complex medications.” (P2 and P4, FY1, H2).

Another challenge-causing condition for foundation doctors was related to seniors’ instructions, which were sometimes different to guidelines and protocols. For example, FY2 doctors described their experience when they were FY1 doctors, when the seniors instructed them to prescribe different doses to those mentioned in the insulin guidelines: “…when I was on-call on F1, and you’re scared of insulin. We did have guidelines for it, but then your SHO is saying ‘oh, just give them rapid PRN, so many units’, and you’re like well, that’s not the guideline, but someone’s telling you to do that and it’s not best practice, but then you have people insisting that that’s what you do, and it’s a bit difficult.” (P1, FY2, H2).

Another participant explained how this might occur, whilst still recognising the difficulties for FY1 doctors:

“Yeah, because you don’t necessarily have that experience to know what is the best thing to do. Do I follow the hospital guidelines or my senior that has done this a million times…” (P2, FY2, H2).

Impact of nurses
Nurses were perceived to have a negative impact on foundation doctors especially when prescribing, and increased the burden on them during the on-call period. Foundation doctors used language such as ‘hassle’, ‘badgering’, ‘resistance’ and ‘pushing’ to express how the nurses were asking them to prescribe medications such as insulin, opioids and IV fluids. However, the foundation doctors thought these requests were unjustified for many reasons. They disagreed with the nurses on the threshold for treating hyperglycaemia and the perception that they requested opioids to quieten agitated patients and IV fluids to get rid of handover complications or responsibility:

“I think there’s very poor understanding amongst nursing staff about IV fluids and other medications like zopiclone, they’ll often want just to make the problem go away because they’ve got a patient who’s not sleeping in the bay or something or they want benzos [benzodiazepines] for elderly patients at night who are agitated but not a threat to themselves or anyone else.” (P2, FY1, H1).

Doctors described how nurses would “point-blank refuse” to carry out their instructions to administer opioids in IV dosage form that required monitoring. The refusal could necessitate administration by the prescriber themselves, which was an unfamiliar task. However, the foundation doctors felt they lacked the support of seniors overnight to defend their decisions against nurse refusal, as one participant highlighted:

“There's nobody to back me up. Literally a body, I just need another human to say yes… particularly if they're higher than F1, whereas at night time that's just not possible.” (P4, FY1, H3).
**Daytime hours**

The foundation doctors described daytime working hours as better than the on-call period in terms of communications within the healthcare team. The language used here included ‘good communication’, ‘good feedback’, and ‘clear plan from healthcare teams’. In addition they had greater familiarity with the healthcare team, making the communication easier than the on-call period. One participant described the communication during daytime working hours:

“So you can communicate more. You can get more quick feedback and you can assess the patient and see whether, actually, was what I’ve done the right thing.” (P6, FY1, H3).

In terms of support, foundation doctors described having more support from the wider multidisciplinary healthcare team during daytime working hours, compared to the on-call period. Such support was from colleagues, seniors, pharmacists and specialised teams, such as specialist diabetes nurses. One participant described the support during day working hours as such:

“… there’s always a ward pharmacist that seems to be around during working hours… always very knowledgeable, and there’s usually an SHO or registrar around you can also ask.” (P6, FY1, H2).

### 6.3.1.2 Working environment

Working environment challenges during the on-call affected both FY1 and FY2 doctors in the same way. Both groups described challenges regarding the working
environment and used words such as ‘busy’, ‘fast paced’, ‘time pressure’ and ‘high workload’. High workload was often due to the high number of patients and wards that the foundation doctor was covering during the on-call; with one participant describing how a nurse was “completely shocked” that he was responsible for all of the patients on ten separate wards.

Lack of resources in the working environment resulted in particular challenges to prescribers when prescribing HRMs. Although these challenges occurred during daytime working hours, the need for fast action made the lack of support and other resources much more noticeable during the on-call period. An example described was a lack of cardiac monitors that could result in having to transfer patients to other wards so that potassium could be administered to correct hypokalaemia. Some missing resources were relatively inexpensive such as weighing scales and height measures, which were important to calculate patients’ doses for anticoagulant medications. One focus group described how they experienced greater difficulty when trying to weigh and measure patients than when trying to obtain a brain CT scan:

“P4: One thing I’ve found quite frustrating, just generally in F1, F2, is how hard it is to get a weight or a height on a patient, to find, if it’s ideal body weight or so. Like in A&E you can get head CT easily enough and that’s not an exaggeration. It’s not a [weighing] scale. You’ll be walking around for two hours…

P5: There’s no height measure in A&E at all. Can’t measure a height” (P4 and P5, FY2, H1).
Teaching, training and feedback are a crucial part of the foundation programme as doctors are undertaking on-the-job training. However, lack of teaching or training on prescribing HRMs such as anticoagulants and insulins was described. This lack of training led to challenges in prescribing these medications safely, particularly during on-call. One participant described it as such:

“We haven’t really had any proper prescribing training here, we had an exam just as we started to see how crap we were, apparently we all made heinous mistakes in that but haven’t had any feedback on it. And for example we’ve never had I don’t think any structured teaching on the heparin infusion, it’s always been, oh, it’s one o’clock in the morning and this is the first time I’m seeing this chart” (P7, FY1, H1).

Moreover, prescribers described how the lack of feedback on their prescribing during the on-call meant that they did not learn from their experiences, or from any errors that occurred, as one participant said:

“… you don't really get feedback on what you've done when you're on-call. You can make a ton of mistakes that aren't on your ward and you will never know that half you will never get any feedback of actually, you could've done this, this and this better.” (P6, FY1, H3).

In one hospital, it was a challenge to prescribe some HRMs safely during the on-call as the electronic system did not have the full information about medication dose or did not have the previous medications of the patient, especially at the point of admission. Another challenge caused by the local hospital system was omission of medication during patient transfer from ward to ward, as one focus group revealed:
“I’ve noticed insulin being missed, like doses, when someone goes from, say, A&E to EAU [Emergency Assessment Unit], or EAU to the ward at an awkward time” (P1, FY2, H2).

There was a reduction in both the safety net and safety checks during the on-call period. There were usually fewer nurses compared with daytime working hours, which caused challenges for prescribers when prescribing HRMs safely. Some medications (e.g. IV opioids) required monitoring by nurses, as one participant said:

“It would be unsafe to give it [IV morphine] because they can't provide the staffing to monitor it. It's very unfair not to give someone the painkillers that they need just because you don't have, well. They're like ‘give IM instead’. So it's like, I'm just going to stab someone every hour just because you can't monitor the IV drugs.” (P3, FY1, H3).

Moreover, the quality and quantity of support from the on-call pharmacists was lower than the daytime, as the on-call pharmacist was only contacted by phone and prescribers found this less beneficial in comparison to face to face communication with the ward pharmacist.

In contrast, during daytime working hours the safety net was more efficient as errors were usually caught faster than during the on-call, as there were higher numbers of nurses, and the presence of the dedicated ward pharmacist.

“In the day time, if there is a slight error, it's usually picked up very quickly by, for example, the pharmacist that's on the ward. When you're working nights, evenings, weekends ... so if you're tired or you've incorrectly given the dose, sometimes it doesn't necessarily get picked up by nursing staff as well. There
aren’t the safety checks that you would necessarily have in the normal nine to five working day.” (P3, FY2, H2).

6.3.1.3 Prescribing task

Prescribing task challenges were described similarly by both FY1 and FY2 doctors during the on-call period, with both HRMs and non-HRMs. A high workload was commonly described during the on-call, as doctors had to prescribe a high number of prescriptions of both HRMs and non-HRMs. Some participants thought this high workload was more risky with HRMs as one participant commented:

“It gives you less time to think about what you’re prescribing at the end of the day, which, if you’re dealing with high risk things, is risky.” (P6, FY1, H2). Some prescribing task challenges were described predominantly with HRMs during the on-call period, which the doctors thought should be done by the primary team during the daytime. Certain HRMs such as opioids, insulins, and anticoagulants required plans that cover the on-call period as well as weekdays. One prescriber described a request to step down a patient from opioids:

“...people get asked weird things like can we step them down off a PCA [Patient-controlled analgesia] at like 11 PM, and you think why don't the day team look at doing that?” (P5, FY2, H1).

Another challenge for prescribing HRMs during the on-call was doctors’ unfamiliarity with the prescribed HRM. This unfamiliarity could arise as FY1 and
FY2 doctors work across many different specialities when working on-call, and they could encounter medications that they have little or no experience of prescribing.

Both FY1 and FY2 doctors described the task of prescribing HRMs as complicated, as there was a need to sift through a lot of information and documentation, and that the task was ‘time consuming’, ‘terrifying’, and ‘scary’. In contrast, the participants felt more comfortable with non-HRMs as they were “aware that the risks are lower.” (P4, FY2, H3).

6.3.1.4 Individual prescriber

Lack of experience and lack of knowledge were described by both FY1 and FY2 doctors. This was expected, as at this level, they are still very much learning the knowledge and skills of new specialities that they have never experienced before. This challenge-causing condition can affect the prescribing of HRMs and non-HRMs, during both daytime hours and on-call hours. Other similarities identified were that both described being tired or in a hurry during the on-call period, which could affect prescribing of both HRMs and non-HRMs.

Fear of prescribing HRMs during the on-call period was a challenge-causing condition that could lead prescribers to be overly cautious, resulting in the prescribing of sub-therapeutic doses for patients. One participant described how a hypothetical patient could suffer agony because of doctors being cautious:
“... high risk medications, whether it's like a benzodiazepine or morphine, we'll be much more reluctant to prescribe... we might be prescribing less than we should... and the patients can be in pain longer than usual” (P5, FY2, H3).

6.3.1.5 The patient

The patient as a challenge-causing condition was similar with both FY1 and FY2 doctors during the on-call and during the daytime working hours. Complex patients included children needing HRMs (with doses requiring calculations), cancer patients and patients with an exacerbation of chronic pain. Another challenge experienced when prescribing during the on-call was doctors’ unfamiliarity with the patient. One participant described the situation:

“... on-call, you don't know the patient that you're dealing with particularly well. So if you're called to the wards you've got to prescribe X, Y, Z, so strong painkiller or warfarin. You don't know the patients. So you might not be that familiar with their past medical history, which makes prescribing potentially dangerous medication a challenge.” (P2, FY2, H3).

In contrast, during the daytime working hours the same participant described how the prescriber was familiar with the patient which “just makes it easier”.

Poor communication with the patient during the on-call period was another challenge, particularly when prescribing HRMs such as insulin and opioids. Communication problems could be related to the patient’s condition, such as confusion or delirium;
as these patients were unclear of their medications or their doses, especially of insulin and opioids.

“… a patient comes in on insulins and you check all the paperwork you can find and it all says as directed. And the patient's there in front of you, delirious.” (P6, FY1, H3).

Busyness during the on-call also affected the quality of communication which varied from poor to “non-existent”. Furthermore, electronic prescribing systems exacerbated this gap in communication, as one prescriber described:

“It’s probably better in other hospitals as well because we do have EPR [Electronic Patient Record] so we can sit in one place and prescribe for all over the hospital. Whereas I think if they had a Kardex at the end of the bed you probably would talk to them a little bit more and find out a bit more.” (P2, FY1, H2).

In contrast, during the daytime working hours’ communication was better, as prescribers had more time to engage with the patients.

### 6.3.2 Latent conditions

Both FY1 and FY2 doctors described latent conditions relating to technology, guidelines and protocols, resources, and the organisational system. However, FY1 doctors described additional latent conditions related to the lack of trust orientation and the bleep system. Drawbacks of technology affected HRMs more than non-HRMs; these were related to the trust intranet and electronic prescribing. Foundation
doctors in hospitals that did not have electronic prescribing described the process of searching the hospital intranet system to find guidelines and protocols as difficult:

“Protocols can be hard to find sometimes, you do a search on the staff net page, they don’t always come up, you have to be very specific. It’s not like Google, where it picks up lots of different words in a document. If it’s not in the title, it won’t find it” (P6, FY1, H1).

However, the electronic prescribing system had its own drawbacks as the foundation doctors described latent conditions during the on-call that affected HRMs such as insulin and warfarin. These included systems that lacked detailed medication information, such as indication and dose, and electronic systems which led to reduced prescriber-patient communication and reduced patient evaluation. Unfamiliarity with the electronic system was an issue that could lead to doctors prescribing erroneously:

“But at the same time, I find that a bit risky sometimes, the warfarin, because if people are not familiar with the system they can get confused and they’re prescribing a long course of a high dose” (P4, FY2, H2).

Inconsistency of documents such as drug charts, guidelines and protocols led to confusion for prescribers even within the same organisation. One focus group revealed the inconsistency of the insulin sliding scales within the same trust:

“P7: There’s like three different sliding scales continuously in the Trust as well
P1: … every ward seems to have their own developed approach to sliding scales.”
(P1 and P7, FY1, H1).
Limited resources and the resultant staffing structures were latent conditions for challenges to prescribe safely during the on-call period. Foundation doctors described this staff shortage as a challenge in terms of the numbers of patients they were expected to cover, and the organisation of the rota schedule. Limited numbers of computers that incorporated access to the GP records caused problems for some doctors. These computers were distributed in a haphazard way and without any sign indicating their access to GP records, making it difficult for doctors to spot them. As described previously, there were a limited number of cardiac monitors on certain wards which could result in patient transfers. Moreover, a lack of electronic prescribing was described as a latent condition, as well as the weak mobile signals of the pharmacist on-call during the on-call period.

Both FY1 and FY2 doctors raised the issue of lacking access to patients’ summary care records (an electronic record of important patient information created from GP medical records), or the complicated process of gaining access. In one hospital, they needed the support of the on-call pharmacist to send them information using a cumbersome process: “So I think the way to do it [asking for support] is you’d call the on-call pharmacist who then would get it and then fax it over to you, which at three in the morning you don’t have time to do that.” (P3, FY2, H1).

The bleep system was described by foundation doctors as a poor way of communicating with other healthcare teams, as one prescriber described:

“In terms of communication bleeps are awful. Because you have to both perfectly be in the right place at the right time. Because if someone bleeps you and you're busy when you get the bleep, they'll be sat on the other end of the phone for five
minutes. And then they'll go and they'll be like well, I can't sit around waiting all day for them to get back to me. And then you ring that phone and they're not there.” (P6, FY1, H3).

Moreover, the bleep interrupted the prescribing task and stressed the prescriber although the effect on non-HRMs was perceived to be greater than HRMs.

6.3.3 Short cuts

Both FY1 and FY2 doctors described short cuts they used during the on-call period, for both HRMs and non-HRMs. Such as copying previous prescribers’ medication decisions (insulin, warfarin and IV fluids), prescribing based on nurses’ description of patients’ pain levels without patient assessment, and signing drug charts without checking them. There were violation-causing conditions such as high workload and limited time during the on-call period. Perceived low risk medicines, such as IV fluids, were a violation-causing condition as one participant stated:

“… on the whole it’s safe [IV fluids]. If they're a young patient, you’re not going to do harm with a bag of saline.” (P3, FY2, H1).

Moreover, the complicated task of prescribing HRMs, such as calculation of heparin infusion rate, is a violation-causing condition if a drug chart is signed without first being checked. FY1 doctors had nurses’ influence as an extra violation-causing condition, in comparison to FY2 doctors, as one participant said:

“… nurses just flock to you and you’ve got drug charts being waved in your face and they’re like, just prescribe this or just prescribe that… just sign it off.” (P4, FY1, H1).
On the other hand, FY2 doctors stated they made short cuts during the on-call by prescribing only part of patients’ medications, which they needed during the night, and omitting the rest of the medications so they can be prescribed by the day teams. The reason behind this was that patients had not brought their medications or they were unfamiliar with their medications.

### 6.4 Discussion

This study identified the challenges that were encountered by FY1 and FY2 doctors when prescribing specific HRMs safely during the on-call period. It has found that foundation doctors experience challenges in communication, support, and relationships, and describe a lack of standardisation, feedback and prescribing plans, coupled with unfamiliarity with patients and the tasks at hand. Wider organisational factors also generated challenges for foundation doctors, such as problems with the bleep system and the authorisation and accessibility of patient information during the on-call period.

To our knowledge, this is the first study that has concentrated on exploring this topic. It is strengthened by its comparison between FY1 and FY2 doctors and the investigation of challenges stemming from different hospital systems, including electronic prescribing. Nevertheless, this study focused on a narrow group of healthcare professionals, foundation doctors, rather than other prescribers such as senior doctors or non-medical prescribers (for example nurses and pharmacists), who may have different opinions to those revealed in this study. Moreover, due to time
pressures experienced by our participant population, focus groups were limited in duration. This affected the depth of detail that could be covered and the amount of data collected. However, the number of the focus groups mitigated this, ensuring that all areas were covered by several focus group discussions.

FY1 doctors raised the communication problems with other healthcare professionals as a challenge-causing condition; such communication problems have been previously linked to patient harm. (24) There are many reasons that could help explain this phenomenon such as the fact that FY1 doctors have just started in a new socially complicated environment, the hospital, where they encounter and interact with healthcare professionals with different hierarchies and specialities. (25) Such relation with other healthcare professionals during the transition from student to working as an FY1, and then an FY2 doctor, involves significant changes. This can cause challenges for them when adapting to the new environment. (26) Medical students should receive adequate interprofessional education during their time in medical school, in terms of their expected communication with other healthcare professionals before they work in the clinical field as FY1 doctors. (27, 28) Otherwise, this complexity could lead to communication failures during their clinical practice. (29) FY2 doctors are one year more experienced than FY1 doctors and, in our study that resulted in more confidence and less pressure when communicating with other healthcare professionals.

Support for foundation doctors has been recommended by previous reports, especially at the beginning of their placements. (30, 31) In our study, FY1 doctors had sufficient support from the seniors, whereas FY2 doctors experienced lack of
support that caused challenges for them during the on-call period. FY2 doctors still undertake new placements in which they will need support, and other research in this field has shown how their existing knowledge was not all transferable from one placement area to another. (32) Therefore, FY2 doctors also needed senior support as well as the FY1 doctors. Support in surgical specialties for foundation doctors, in general, has been reported to be less than that in medicine. (33) Despite the greater need for support for medical problems in surgical settings, (30) this study found that foundation doctors were reluctant to seek support from the senior doctors in surgical specialities, especially for medical problems that related to HRMs.

Another crucial profession that was not available to give support during the on-call period was the pharmacist. In our study, doctors struggled to communicate and get support from pharmacists during this period because they were “on-call” and based at home, the usual system within the UK. (34) A recent study exploring the impact of an on-site on-call pharmacist revealed that it resulted in better relationships between pharmacists and healthcare professionals such as foundation doctors. (35)

Tensions in the junior doctor-nurse relationship has been reported previously and the pressure exerted by nurses can make foundation doctors uncomfortable when prescribing. (33) Our study found nurse pressure on foundation doctors to be perceived as problematic, particularly during the on-call period. However, such pressure is possibly based on different understanding of the clinical situation between the two professions. Foundation doctors are reported to feel uncomfortable with nurses’ superiority in knowledge and experience. (26) On the other hand, other studies have found that nurses feel that foundation doctors can be arrogant,
compromising their relationship. (36) Misunderstanding between nurses and foundation doctors during the on-call period could negatively affect patient safety. Therefore, a better understanding of each other’s situation between the different healthcare professionals could have a positive impact on patient safety, (36) in addition to the interprofessional education mentioned previously. (27, 28)

The doctors in this study found the inconsistency of medical documents created challenges to prescribing safely, as has been described previously. (37) Nationwide standardisation of documents could have a positive impact on the prescribing process by reducing confusion, and potentially reducing prescribing errors, (38) especially with HRMs such as insulin. Standardisation is already the case for GP prescriptions in each of the home countries and NHS Wales has a standard inpatient medical chart. (39) Standardised inpatient drug charts resulted in a one-third reduction in prescribing errors in Australia. (40) However, others suggest that standardisation is not as important as addressing other causes, such as poorly designed inpatient drug charts, (41) although this view is not universal. (42) Poor design of in-patient drug charts may increase the rate of prescribing errors, (43) and redesign, based on prescribers’ viewpoints, could reduce some of the common errors. (44) However, standardisation across a hospital is not possible and would not be applicable, for example, with oncology, mental health and paediatric care. (45) These settings need a more flexible drug chart design to fit with their specialist patient needs.

The foundation programme provides on-the-job training to help foundation doctors apply the theoretical science learned in medical school, and gain the practical knowledge to apply it. (46) It would be impossible for medical schools to cover
everything that a foundation doctor might encounter in practice; moreover, the information that is learned could be forgotten with time. Therefore, foundation doctors may need to refresh their knowledge and skills at the beginning of their rotations, especially for more frequent and challenging tasks such as prescribing HRMs. Another approach to maximise the benefit of the foundation programme, and prescribing skills in general, is enforcement of the hospitals to provide feedback to prescribers about their prescribing tasks, (47, 48) especially for the on-call prescribing tasks. Insufficient feedback on the prescribing of foundation doctors has been described before in the literature as a contributory factor to prescribing errors. (32, 49, 50) In our results, foundation doctors described these challenges and highlighted the need to encompass teaching and feedback within the program.

Day-time healthcare teams, who are primarily responsible for patient care, are usually the creators of prescribing tasks and possess a familiarity with the patients’ conditions and background. The importance of creating plans for prescribing in advance, covering both the weekdays and the weekends, to manage complex disease, states such diabetes or coagulation issues, was highlighted by foundation doctors. As many long-term diseases require the HRMs within the management plan and the foundation doctors were found to avoid interfering with the plan of the primary team during the on-call. (33) Therefore, setting a clear plan, especially with HRMs, by the day team could be beneficial for the prescriber during the on-call period and patient safety.

Prescribing in general is a complex task for all prescribers. (10, 51) Foundation doctors are particularly ill-prepared in medical school as previously described. (52-
54) However, some medical schools may be better than others in preparing students; although the GMC aims to have equally prepared students from all schools for the foundation year programme. (55) Many doctors in our study found prescribing HRMs ‘scary’ and this fear resulted in over-cautiousness and sub-optimal therapeutic doses. Medical schools already implement ‘shadowing’ during the final year to prepare their students for the practice field – this approach has been described by foundation doctors as the best technique for clinical practice. (55, 56) This could be a time to address HRM prescribing, so that students find it less worrisome or time consuming when they start in practice themselves. Although there are legal barriers, as students are not legally allowed to prescribe, medical students could write a prescription that a more senior doctor could sign. (57) However, learning to prescribe is a complex task, therefore a single intervention such as this may only result in a partial improvement. (57)

The on-call period, by its nature and our participants’ descriptions, is fast paced and time-pressured, which exacerbates the burden on prescribers and creates particular challenges to prescribing safely. In addition, day teams may not finish their tasks, as they may forget or rely upon the availability of the on-call doctors. Organisational systems could lead to incomplete tasks during working hours; for example, some laboratory test results take a long time and may result in the need to administer medications during the out of hours’ period. Therefore, day teams should help by communicating clearly what has not been finished during that shift, especially in the case of HRMs, reducing the burden on foundation doctors during the on-call period and potentially increasing patient safety.
During the on-call period, prescribers are often exposed to many different specialities, and therefore different types of patients that they may be unfamiliar with. This caused challenges, especially with HRMs, exacerbated by the fact that the on-call period mainly requires caring for patients whose conditions are both acute and deteriorating. This has impact upon the doctors’ ability to communicate with the patient. A critical condition was described previously by foundation doctors as a barrier for good doctor-patient communication. (32, 58) One study examined the causes of prescribing errors with foundation doctors, and the patient was found to be a contributory factor for prescribing errors in terms of being seen during the on-call period, and the difficulty or inability of communication with these patients. (59) This resulted in challenges to our participants, as well as those foundation doctors, to prescribe safely during the on-call period.

Foundation doctors described challenges that require higher level organisational decisions to solve them. The bleep system was described as a challenge for foundation doctors in terms of causing interruptions. These findings are consistent with previous studies that showed how the bleep interrupts doctors, with approximately half of bleeps received by foundation doctors being unnecessary, which has a negative impact upon patient care. (32, 60, 61) Other studies showed that the majority of bleeps were not urgent and could wait, rather than causing interruption. (62, 63) Many alternative ways of communication have been introduced to tackle the drawbacks of the bleep system such as smart phones, which have better ways of communicating such as voice calls and texts. (64, 65) Smart phone applications can be an alternative form of the bleep system, with there being a number of companies that provide applications. (64) Our participants had proposed
alternative ways of communicating, based on their colleagues’ experience in different hospitals, such as using walkie-talkies, message bleep systems and mobile phones.

Problems with the ease of searching and the lack of availability of information in hospital systems were described by our study participants. Easily accessible and available patient information through hospital systems has been suggested to reduce prescribing errors by foundation doctors. (32) Therefore, future interventions that improve the mode of communication and accessibility of patients’ records and guidelines could strengthen foundation doctors’ ability to prescribe all medications safely, especially during the on-call period.

Violations were described in both HRMs and non-HRMs, where participants were seeking the patient benefit regardless the risk of medication. These routine violations are common in the workplace and their consequences are usually benign. (22, 23, 66) As described in our study, time pressure is particularly problematic during the on-call period; leading to the emergence of short cuts during the on-call. This behaviour whereby doctors under pressure take short cuts in their prescribing has been reported previously. (67)

There were many areas that could be targeted by researchers or organisations to improve patient safety and improve prescribing skills, particularly during the on-call period. There is sparse epidemiological data for the on-call period, such as prevalence and incidence, especially of prescribing errors with HRMs. Interventions could be applied to reduce these challenges, starting in medical school (preparing),
hospital (feedback) and at a national level (standardisation). However, there is no single intervention that could solve all of the related problems, due to the multifactorial nature of these prescribing challenges.

6.5 Conclusion

There are many challenges which have been described in this study that have already been mentioned and discussed before in the literature, such as communication, support and relationships, lack of standardisation, feedback and unfamiliarity with patients and the prescribing tasks at hand. However, the on-call period, especially with HRMs, make these challenges more pronounced for foundation doctors because of the nature of this period and the consequences of mistakes with HRMs. We noticed the support decreased for those with greater experience (FY2), however this study demonstrated their ongoing need for support in regards to prescribing. The lack of a plan from the primary team, or “day team”, affected the safety of the patient and increased the burden and challenges for foundation doctors. Organisations should improve the on-call environment by prioritising alternative methods of communication, rather than the traditional bleep system, and improve foundation doctors’ accessibility to patient information during the on-call period.
6.6 References


11. NHS. Reducing Harm from High Risk Medicines. Institute for innovation and improvement NHS, 2008 Access date: 26/02/2015.


6.7 Appendix 6.A: Focus Group Discussion Guide

Welcome and thank you for volunteering to take part in this focus group. You have been asked to participate as your point of view on this topic is very important. I realize you are busy and I appreciate your time.

**Introduction:** This focus group discussion is designed to explore the challenges to safely prescribing specific High Risk Medicines (HRMs) such as opiates, anticoagulant, and insulin during the on-call period. The on-call period is the working hours after regular working day hours, overnight, and during the weekends. The focus group discussion will take no more than one and half hours.

**Anonymity:** Despite being recorded, I would like to assure you that the discussion will be kept confidential. The audio files will be kept safely in a locked facility until they are transcribed word for word, then after the data have been analysed and published the audio files will be destroyed. The transcribed notes of the focus group will contain no information that would allow named people to be linked to specific statements. You should try to answer and comment as accurately and truthfully as possible. However, you should not say anything that cannot be used in the research project, including revealing any previously unreported serious errors. I and the other focus group participants would appreciate it if you would refrain from discussing the comments of other group members outside the focus group. If there are any questions or discussions that you do not wish to answer or participate in, you do not have to do so; however please try to answer and be as involved as possible.

**Ground rules**
- The most important rule is that only one person speaks at a time. There may be a temptation to jump in when someone is talking but please wait until they have finished.
- There is no right or wrong answer.
- You do not have to speak in any particular order.
- When you do have something to say, please do so. There are many of you in the group and it is important that I obtain the views of each of you.
- You do not have to agree with the views of other people in the group.
- Does anyone have any questions? (answers).
- OK, let’s begin.

**Is it ok to turn the tape on?**

**Warm up**
First, I’d like everyone to introduce themselves briefly. Can you tell us your name and the current specialty that you are working in now?

**Introductory question**
I am just going to give you a couple of minutes to think about your experiences or experiences of colleagues regarding prescribing errors or near misses with HRMs during the on-call periods and what were the challenges to prescribe them safely without errors. Is anyone happy to share his or her experience?
Guiding questions

1. What are the challenges to prescribing HRMs safely during the on-call period?

2. What do you think about prescribing HRMs during regular working hours is it same or different?

3. What about the complexity of HRM prescriptions during the on-call period?

4. How does this compare with the complexity of prescribing non-HRMs during the on-call period?

5. Are there any challenges to obtaining support when you prescribe HRMs during the on-call? To what extent do you ask people, and who do you ask?

6. What do you think about the support you receive during regular working hours is it same?

7. How would you describe your communication with patients, colleagues, and senior doctors when you prescribe HRMs during the on-call period?

8. What are the differences in communication during regular working hours?

9. Do you ever need to take short cuts or speed up the process when prescribing any medicines during the on-call period? Are there differences between HRMs and non-HRMs?

10. What about regular working hours is the situation same or different?

Concluding question

Of all the things we’ve discussed today, what do you think are the most important challenges to prescribing HRMs safely during the on-call?

Conclusion

- Thank you for participating. This has been a very successful discussion
- Your opinions will be a valuable asset to the study
- We hope you have found the discussion interesting
- I would like to remind you that any comments featuring in this report will be made anonymous
7. Chapter Seven: Discussion

This chapter summarises the key findings of this programme of research and outlines the contribution and practical implications of the studies conducted in this thesis. Furthermore, the chapter presents and discusses recommendations for future research.

The overall aim of this programme of research was to explore prescribing errors with HRMs and compare the findings with prescribing errors of non-HRMs. Studying these areas could lead to a clearer picture about prescribing errors of HRMs, which may in turn reveal a different picture to what we currently know about general medications. This aim was achieved through conducting a series of three studies. The studies began with an investigation of the prevalence and incidence rates of prescribing errors of HRMs in hospitals, by systematically reviewing the current literature. The causes of prescribing errors with HRMs and non-HRMs were investigated in the second study. This second study sparked the third study which sought to explore the on-call period and challenges related to prescribing HRMs, and to compare these with non-HRMs and daytime working hours. These three studies have provided an evidence base for researchers about prescribing errors with HRMs. This could lead to the development of strategies and techniques to reduce incorrect use of HRMs, and hence reduce patient harm; moreover, this could be a foundation for future studies focussed on patient safety. The following section summarises the research findings and how these findings contributed to addressing the aim of the thesis.
7.1 Summary of findings for each study

7.1.1 Study One: A systematic review of the prevalence and incidence of prescribing errors with high-risk medicines in hospitals

The prevalence of prescribing errors in HRMs ranged from 0.24 to 89.6 errors per 100 orders of HRMs; with 107 to 218 errors per 100 admissions prescribed one or more HRMs; and 27.2 errors per 100 prescriptions containing one or more HRMs. Prevalence was the only epidemiological parameter that was found and calculated from the literature. The three highest prevalence rates (ranging from 52.6% to 89.6%) in the medication order denominator were found in paediatric patients. Missing weight or incorrect weight, which is necessary for paediatric patients, especially with HRMs, was the most frequent type of prescribing error in children, according to one study. Opioids as a subclass of HRMs were found to be associated with a high proportion of prescribing error in more than the half of studies. Types of prescribing errors related to opioids were dosage problems or wrong dosage, prescription errors and missing patient weight for children prescription.

The majority of the studies included in the systematic review, about 70%, did not describe the medications explicitly as HRMs they merely used the drug class name or specific drug name, which then could be classified during the review process as HRMs. Dosage problems or wrong dosage was the most frequent type of prescribing errors detected in the studies with the highest percentage in 33% of the included
7.1.2 Study Two: Prescribing errors by junior doctors- a comparison of errors with High Risk Medicines and non-High Risk Medicines

Prescribing HRMs was a complex task for participants, especially with respect to dosage calculations. Errors in the legal prescription requirements for controlled medications occurred with HRMs only, especially at patient discharge. Violations were described with non-HRMs only. There were differences in the circumstances of communication failures between HRMs and non-HRMs. With HRMs ineffective communication arose with exchanges with individuals outside the medical team, while with non-HRMs these failures occurred with exchanges within the immediate medical team. The reluctance to seek seniors’ support was a latent condition that was described with non-HRMs. The organisational system such as the inclusion of trade names in hospital formularies was a latent condition described with HRMs. The on-call period was a particularly challenging time during which to prescribe safely, especially HRMs.

7.1.3 Study Three: Exploring the challenges faced by foundation doctors when prescribing high risk medicines safely during the on-call period
This study has confirmed many of the challenges that have been previously discussed in the literature, with prescribing errors with all types of medications. Challenges were related to communication, support and relationships, lack of standardisation, feedback and unfamiliarity with patients and the type of prescribing tasks. These challenges are more pronounced for foundation doctors, especially with HRMs during the on-call period, because of both the nature of that period and the consequences of mistakes with HRMs upon patient safety. The FY2 doctors described how their support decreases with the perceived increase in experience; however, this study also demonstrated their continuing need for support in regard to prescribing. Lack of ongoing plans from the primary team, “day team”, affected the safety of the patient and increased the burden and challenges for foundation doctors during the on-call period. Organisations should improve the on-call environment by prioritising alternative methods of communication, rather than the traditional bleep system, and improve foundation doctors’ accessibility to patient information during the on-call period.

7.2 What this thesis tells us about prescribing errors with HRMs

This thesis has demonstrated some differences between HRMs and non-HRMs in different aspects. Study One, showed the limited quantity of research conducted about prescribing errors with HRMs compared to non-HRMs. In comparison to Lewis et al’s study of prescribing errors with general medications, which included 65 studies in total, study one included only nine studies. (13, 151) This was despite
study one being carried out seven years after the publication of Lewis et al’s systematic review in 2009. The task of prescribing HRMs was a complex task for the prescribers compared to non-HRMs, especially in relation to the dosage calculations. Another difference was related to the errors in the legal prescription requirements for controlled medications, which occurred with HRMs only. Prescribers perceived non-HRMs as ‘low-risk’ medicines in terms of patient safety, and this linked with a reluctance of junior prescribers to seek seniors’ support with non-HRMs and violations. Violations occurred also with HRMs as well as non-HRMs; the violation causing condition with HRMs was related to the complicated task of prescribing HRMs that led prescribers to take short cuts.

HRMs are part of general medications; therefore, there were many similar findings to those found in the literature on prescribing errors with all medications. One of these findings is that dosage errors were the most frequent type of error reported within prescribing errors with HRMs. This finding was consistent with previous literature about prescribing errors with all medications classes. (13, 152, 153) The prospective prescription review is the most comprehensive and accurate method to detect prescribing errors. (154) Study Two showed many similarities between HRMs and non-HRMs in terms of the causes of errors and ECCs. Such similarities were described in the ECCs, i.e. the patient and working environment, and the majority of the elements of the rest of ECCs i.e. the individual prescriber, healthcare team and the prescribing task. More similarities were described in Study Three, such as the challenges that were related to communication, support and relationships, lack of standardisation, feedback and unfamiliarity with patients and the prescribing tasks at hand. These issues were previously identified within the literature on prescribing any
medication class, such as challenges related to communication, (87, 94-96, 100) support and relationships, (74, 87) lack of standardisation, (50) lack of feedback (86, 155, 156) and unfamiliarity with patients (91, 156, 157) and the nature of the prescribing tasks being done. (91, 155, 156)

This thesis demonstrated the lack of research currently available about prescribing errors with HRMs. Study One included only nine studies that included a prevalence rate of prescribing errors with HRMs, and an incidence rate could not be found or calculated from the literature. Although Study One searched the literature systematically since 1985 and the key organisation ISMP has recognised HRMs since the early 1990s, the earliest studies included in the review were published in 2008. The initial search was modified to include studies that had not explicitly used the term HRMs, in an attempt to increase the pool of available studies. Causes of prescribing errors with HRMs have not previously been investigated prior to Study Two. All of these findings demonstrated the gap in knowledge surrounding prescribing errors with HRMs, which did not reflect the importance of vigilance for errors with this class of medication based on their potential consequences. Although HRMs are a small sub-group of all medications (22 classes based on the ISMP list), they are well-known for their potentially devastating effect when they are used erroneously. (6) It has been calculated that approximately 40% of fatal and serious adverse events related to medication errors are caused by only eight HRMs. (158) Targeting this sub-group of medications in order to reduce errors could reduce a decent proportion of their error consequences on patient safety, such as reducing hospitalisations and mortality. (158) The small number of HRMs may be one of the reasons that researchers do not find it attractive for further study. However, this
programme of work found their small number to be of benefit in terms of the feasibility of in-depth focus. Hospitals with limited resources could find it feasible to focus on reducing prescribing errors with this small number of medications, HRMs, which could provide greater potential benefit. Even well organised and capable institutions could focus on HRMs. A current example of this approach is the medication safety thermometer that has a component focusing on identifying harm from HRMs i.e. anticoagulants, opiates, sedatives, insulins and medication allergy. (159-161) Such identification of harm related to HRMs over a period of time can be used to measure the improvements in using HRMs in these institutions and give them the opportunity to compare their results to the national average numbers.(161)

7.2.1 Lack of standardisation

The findings of this thesis demonstrated that prescribing errors with HRMs involved inconsistencies and lack of standardisations in different areas within and surrounding the topic prescribing errors with HRMs. There is lack of standardisation in definitions within the studies that investigated prescribing errors with HRMs. Study One found the majority of prescribing error definitions were created by the authors, or a combination of different authors’ definitions. Another element of inconsistency was the HRM lists, which were undefined in more than half of the studies. The actual, or potential, severity of prescribing errors with HRMs was measured by different scales. Moreover, the methodology used to conduct such studies exploring prescribing errors with HRMs lacked standardisation, such as the methods that used to detect the error such as prospective or retrospective studies and the self-incidence
reporting errors. The implications of this lack of standardisation are that any comparison between literature sources is hindered making it difficult to draw a clear conclusion. This lack of standardisation is also problematic in practice, as prescriptions of controlled medications at point of discharge and the outpatient setting was different to inpatient controlled medication prescriptions, as the former required additional details when prescribing. This difference in the prescription requirements was a source of error as the prescribers were unfamiliar with the extra legal requirements for a controlled prescription. Study Three showed there was lack of standardisation of drug charts and hospital forms. This makes the prescribing task, especially with HRMs, more challenging for prescribers which could have potential negative consequences on patient safety. Another form of inconsistency was revealed in Study Three, which was related to seniors’ instructions that were sometimes different to guidelines and protocols. However, these aforementioned situations where there is a lack of standardisation, and related inconsistencies, have been described before with all types of medications. However, the dearth of information within the literature about HRMs and the consequences of prescribing errors with HRMs make the standardisation a crucial requirement for HRMs.

7.2.2 Prescribing for Children

Prescribing tasks with children are more challenging than for adults for various reasons. For example, the way that young children handle drugs is different to adults as their bodies are still developing, and so doses are based on weight and sometimes height which can dramatically change in a short period of time. (162) Another reason
that makes the prescribing task for children challenging is the lack of clinical data for many medications in children. (162-164) Children have triple the rates of potential ADEs compared to adults in general medication. (165) In Study One, the prescribing errors with HRMs in children occurred with a higher frequency than other patient populations. Study Two found prescribing tasks that involved calculations to be particularly complex, which constituted an error-causing condition for prescribing errors. Those calculations usually linked with prescribing for children. Study Three found that children were described as complex patients, especially those needing HRMs requiring a dose calculation. Children usually need adjusted doses based on their weight, (165) which is a requirement for patient prescriptions; one of this thesis’ findings, from Study One, was that prescribers were commonly omitting the patients’ weight. These two elements, dose calculation and the unavailability of patient weight on the prescription, could be account for the higher prevalence of prescribing errors with HRMs in children compared to adults, as adults require weight-based drug calculations less frequently than children. The findings of this thesis of a high prevalence of prescribing errors with children are consistent with the previous literature. (8, 9) Therefore, interventions and a deeper exploration of prescribing behaviours with this patient population, especially with HRMs, could potentially tackle a sizeable proportion of errors, and lead to better safety for this vulnerable patient population.

7.2.3 Strengths and limitations
Interviews and focus groups are common qualitative data collection methods, (128) which have been used in studies that explore prescribing errors. (87, 95, 99, 138) There is no substitute for asking the people who committed an error about what happened at the time. This approach allowed participants to raise errors that may have not been identified by anyone else, which makes these techniques of more value than observational studies where other people try to spot the error and make assumptions as to why it happened. (87) However, these qualitative collection methods still have some drawbacks, such as hindsight bias which can affect the participants’ recall of events, (166) and that the normal memory recalls previous errors in a reconstructive way that is adapted with current knowledge or beliefs rather than reproducing the exact event as it occurred. (167) The impact of these drawbacks could make the obtained data inaccurate or exaggerated to the benefit of the participants. However, the interviews that were used in this research had used the critical incident technique, (168) which stimulated the participants to describe all events surrounding the error and base their responses on actual experiences.

Focus groups proved to be a useful technique for exploring sensitive issues such as violations. Violations of prescribing rules are sensitive issues to reveal and discuss, the sensitivity would increase synergistically when these violations are combined with the critical group of medications such as HRMs. Study Two investigated 59 interviews which had a total of 108 prescribing errors. This large number of interviews included six violations; however, none of the violations described was with HRMs. On the other hand, the Third Study, which was comprised of focus groups, revealed violations with both HRMs and non-HRMs. Although the focus group topic guide had a question about violations with HRMs, the interviews used in
Study Two gave the opportunity for interviewees to reveal any prescribing errors they wanted to discuss; including violations (particularly routine violations) may be occurring in practice. The naturalistic environment could play a role in revealing sensitive violations along with the peers’ normative effect such that when participants described something freely this encouraged others to reveal similar experiences. (146)

The three studies conducted in this PhD thesis each have their limitations that should be made explicit to readers. Study One, the systematic review of the literature, lacked a quality assessment of the included studies. Although there were only a small number of included studies (nine), the application of a quality assessment tool could have allowed for classification of the studies based on their quality. This may have given a categorisation of the prevalence of prescribing errors with HRMs based on the quality of the included studies.

There were limitations in conducting a secondary analysis of existing data, which was used in Study Two. General limitations include the risk of being unable to achieve the objectives of the new study because of shallow and less detailed descriptions as the research question is different from the original one, lack of consent of participants to use their data for secondary analysis, and the unfamiliarity of a new researcher with the study details that could lead to some misinterpretation of the data. (131, 133, 134) However, our study eliminated some of these disadvantages, such as the consent having already been given to re-analyse the data and the supervisory team were also researchers in these previous studies, meaning
they possessed excellent knowledge of the details of the study and could ensure that misinterpretation was avoided.

As the principal researcher and the supervisory team were pharmacists (as well as the facilitators who helped in conducting the focus groups in Study Three), this could have influenced the participants and the accounts that they offered during the focus groups. One example of this could be that participants chose to be only positive in their opinions of pharmacists or the pharmacy department. In addition, the speciality of the research team could have some bias during the data analysis as they could be influenced by their background and experience. However, during the focus groups the facilitators were flexible and probed for different opinions. Participants in fact did describe both positive and negative experiences and perceptions of pharmacy and pharmacists especially during the on-call period. In terms of the data analysis, the themes and quotes presented were chosen to represent the ideas and the participants’ opinions regardless of the speciality that was related to the idea.

In Study Three, there were delays in gaining ethical and management approval. This meant that it was nearing the end of the academic year when the study commenced and there was a limited window in which to organise and carry out the focus groups as they were to be held before or after regular teaching slots. There were also difficulties when arranging and organising the focus groups across three different hospital trusts and two different groups of doctors in each trust. As a result of these time pressures there was no opportunity to review and revise the focus group topic guide as the study progressed. However, the topic guide of the focus groups was reviewed many times by the principal researcher and the supervisory team, who were
experts in this field and this technique and they have conducted much research in this area. Furthermore, once the data had been analysed from the focus groups there were no further questions that were thought to be needed in order to answer the study’s research question.

7.3 Implications for practice

The prescribing task of HRMs is different to non-HRMs as it is a more complicated task, which was highlighted in Study Two and Three. That led to the revelation that doctors in our study found prescribing HRMs ‘scary’ and that this fear resulted in over-cautiousness and hence sub-optimal therapeutic doses. Therefore, interventions targeting this task could make it easier to prescribe optimally as well as reduce the error associated with it. Participants in Study Two had suggested that interventions should be delivered at the beginning of junior doctors’ placements and that interventions should be interactive, such as workshops and feedback on previous prescribing tasks to emphasise the understanding of the materials. Study Three showed there was a lack of feedback on prescribing tasks for all medications, which meant foundation doctors did not learn from their mistakes. The lack of feedback and interactive teaching could be related to busyness and limited time of seniors to provide such support. Therefore, focusing on providing feedback or interactive teaching on HRMs prescribing tasks only, as they are limited in number compared to general medications, could be feasible in the fast-paced hospital environment. Feedback has been described in Study Three as a needed tool to improve the skill of
prescribing for foundation doctors during the on-call period. This finding is consistent with previous literature that reported how junior doctors welcomed feedback. (155) Literature has shown there is insufficient feedback on the prescribing of foundation doctors, which was a contributory factor to prescribing errors, (91, 155, 156) and enforcement of the hospitals to provide feedback to prescribers about their prescribing tasks could reduce prescribing errors. (169-171)

7.4 Future research

The current literature displays a paucity of information with regards to prescribing errors during the on-call period; with no information on HRM errors during the on-call period prior to the results of this study. The prevalence of prescribing errors during the on-call period is needed to establish a baseline for this obstacle, and could explore HRMs errors only, or examine errors more broadly to include all types of medications. However, the devastating consequences of prescribing mistakes with HRMs make them a potentially a high impact group for study. Another area that could be investigated is the prescribing of HRMs during the discharge period in terms of an epidemiological study or qualitative study, such as observational techniques, focus groups, and interviews to gain a deeper understanding of the causes. Based on the results of this project, we would recommend that foundation doctors continue to form the prescriber group of interest for future studies, as they are the group most commonly performing such prescribing tasks. Interventions targeting the prescribing task of HRMs, especially the ones related to calculations, could be applied and then examined for their benefit. One suggested method of
intervention is to implement a feedback protocol for foundation doctors, assessing their competency in various prescribing tasks, especially during the on-call period when prescribing HRMs. Whilst we acknowledge that no single intervention strategy is likely to form a complete solution, due to the multifactorial causes of this issue, we feel that the intervention suggested is readily applicable and would result in a measurable reduction in error rates.

7.5 Conclusions

This thesis has explored, in detail, prescribing errors with HRMs in hospitals, establishing a novel evidence base in this area. HRMs form part of general medications, meaning they share similar traits, but the potentially devastating consequences of HRMs and the complicated task posed by prescribing them makes errors in their prescription profound. Therefore, HRMs need closer attention and more concern from healthcare professionals, researchers and policymakers. Such attention could result in a significant reduction in adverse outcomes and improved patient safety.
References

24. NICE guideline. Medicines optimisation: the safe and effective use of medicines to enable the best possible outcomes. 2015.
36. NHS Improvement. Who we are 2016 [Available from: https://improvement.nhs.uk/about-us/who-we-are/].
56. NHS. NICE NPSA medicines reconciliation adults hospital 2007 [Available from: http://www.nrls.npsa.nhs.uk/resources/?entryid45=59878&q=0%C2%ACreconciliation%C2%AC.
88. Storie VJ. Male and female car drivers: differences observed in accidents. 1977.
107. Moreton A. The acrimonious road to the 48 hour week. BMJ. 2014;349:g6426.
117. NHS. Seven day services in the NHS 2017 [Available from: https://improvement.nhs.uk/resources/seven-day-services/.
118. NHS. NHS Services, Seven Days a Week Forum Costing seven day services. 2013.
160. Rostami P, Ashcroft DM, Tully MP. A formative evaluation of the implementation of a medication safety data collection tool in English healthcare


## Appendices

**Appendix 1: Study One data extraction form**

<table>
<thead>
<tr>
<th>Name of Extractor</th>
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<tbody>
<tr>
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<table>
<thead>
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</tr>
</thead>
</table>

### 1. Source

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<table>
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<th>Journal/ Source</th>
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<tr>
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<th>Definition of Prescribing Error by the article:</th>
<th>HRMs list:</th>
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<tr>
<td>Dean</td>
<td>ISMP</td>
</tr>
<tr>
<td>NCC MREP</td>
<td>NPSA</td>
</tr>
<tr>
<td>ISMP</td>
<td>None</td>
</tr>
<tr>
<td>OTHER (define):</td>
<td>OTHER (specify):</td>
</tr>
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### 2. Population

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<th>Age of Patients (mean ±SD)</th>
<th>Paediatric</th>
<th>Adult</th>
<th>Elderly</th>
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</thead>
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<td>Age category</td>
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<td>Adult</td>
<td>Elderly</td>
</tr>
<tr>
<td>Gender of patients</td>
<td>Male %</td>
<td>Female %</td>
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</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Physician</th>
<th>Junior</th>
<th>Senior</th>
<th>Both</th>
</tr>
</thead>
</table>

| Prescribing Technique | Handwritten | Electronic | Both |

#### Study Sites & Numbers

<table>
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<th>Number(s)</th>
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</tr>
<tr>
<td>Tertiary Hospital</td>
<td></td>
</tr>
<tr>
<td>Specialized Hospital</td>
<td></td>
</tr>
<tr>
<td>Community Hospital</td>
<td></td>
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<tr>
<td>Teaching Hospital</td>
<td></td>
</tr>
<tr>
<td>Other (specify)</td>
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**Total Number**

#### Study Setting & Numbers

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<th>Number(s)</th>
<th>Study Setting</th>
<th>Number(s)</th>
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</tr>
<tr>
<td>Surgery ward</td>
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<td>ICU</td>
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</tr>
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</table>

**Total Number**
3. Issue

<table>
<thead>
<tr>
<th>Prescribing errors No</th>
<th>Total Number of prescriptions</th>
<th>Total Number of patients</th>
<th>Total Number of Admissions</th>
<th>Time (period)</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>High risk medicines</th>
<th>Number of errors</th>
<th>Total Number of orders</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antithrombotic</strong> (Anticoagulants e.g. warfarin and heparins, Factor Xa Inhibitors e.g. fondaparinux and rivaroxaban, Direct thrombin inhibitors e.g. dabigatran, Thrombolytic e.g alteplase, Glycoprotein IIb/IIIa inhibitors e.g. eptifibatide)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Chemotherapeutic agents</strong>, parenteral and oral (e.g. methotrexate for non-oncologic usage)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Hypoglycaemic agents</strong> (Insulin all its forms or Oral)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Sedatives</strong> (I.V. or Oral) (e.g. Midazolam, Lorazepam)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Antipsychotics</strong> (e.g. aripiprazole, clozapine)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Opiates/Narcotics</strong> (e.g. morphine, fentanyl)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Infusion Fluid</strong> (dialysis, hypotonic or hypertonic solutions)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td></td>
</tr>
<tr>
<td><strong>Adrenergic agonists</strong> (e.g. epinephrine) or <strong>antagonists</strong> (I.V.) (e.g. propranolol)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Antiarrhythmic, I.V.</strong> (e.g. lidocaine, amiodarone)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Epidural or intrathecal medications</strong></td>
<td></td>
<td></td>
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<tr>
<td><strong>Inotropic medications</strong> (e.g. digoxin, milrinone)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Nephrotoxic agents</strong> (liposomal forms of drug or radiocontrast agents)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

4. **Timing**

| Duration of data collection |  |
## 5. Study Design

<table>
<thead>
<tr>
<th>RCT</th>
<th>Cross sectional study</th>
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</thead>
<tbody>
<tr>
<td>Prospective</td>
<td>Retrospective</td>
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<table>
<thead>
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<th>Data Collector (s)</th>
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</table>

<table>
<thead>
<tr>
<th>Validation of error</th>
<th>No</th>
<th>Yes (specify)</th>
</tr>
</thead>
</table>

- **Method of error detection:**
  - Medical Record Review
  - Prescription Review
  - Other(s) Specify:

<table>
<thead>
<tr>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
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</table>
### 6. Outcome

<table>
<thead>
<tr>
<th>Incidence of Prescribing error in High Risk Medicines</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Prevalence of Prescribing error in High Risk Medicines</td>
<td></td>
</tr>
<tr>
<td>ADE Rate of Prescribing error in High Risk Medicines</td>
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</tr>
<tr>
<td>Death Rate of Prescribing error in High Risk Medicines</td>
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<tr>
<td>Incidence of Prescribing error for non-High Risk Medicines (if mentioned)</td>
<td></td>
</tr>
<tr>
<td>Prevalence of Prescribing error for non-High Risk Medicines (if mentioned)</td>
<td></td>
</tr>
</tbody>
</table>
Appendix 2: Study Three: Participant Information Sheet (PIS)

Challenges to prescribing specific high risk medicines safely during the on-call period

Participant Information Sheet

You are being invited to take part in a research study that is a part of a PhD student thesis, which aims to investigate prescribing errors with high risk medicines. Before you decide whether or not to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. The information provided below will hopefully give you a good understanding of what the research is about and how you might be able to help. However, if you have any other questions or clarifications, please do not hesitate to contact me on the telephone number or email address given below. Please take time to decide whether or not you wish to take part. Thank you for taking the time to read this.

Who will conduct the research?

The research team includes Mahdi Alanazi, PhD student, University of Manchester; Mr Daniel Greenwood, PhD student, University of Manchester; Dr Aseel Aabozour, Research Associate in Pharmacy Practice, University of Manchester; Dr Penny Lewis, Clinical lecturer in Pharmacy, University of Manchester and Dr Mary Tully, Reader in Pharmacy Practice, University of Manchester.

What is the purpose of the research?

In our previous work exploring the causes of junior doctors’ prescribing errors it was found that the on-call period (i.e. after working hours or during weekends) was a particularly difficult time for prescribing safely. Foundation year 1 (FY1) or foundation year 2 (FY2) doctors are responsible for prescribing about 70% of hospital prescriptions and during the on-call period this percentage could be higher.

There is a specific group of medications called high risk medicines (HRMs) that are classified as HRMs because they have a higher risk of causing significant patient harm when used in error. Examples of HRMs are anticoagulants such as warfarin or heparin, insulin, and opioids. HRMs account for a large proportion of prescribed medications during the on-call period, especially those listed above. A table attached to this form has been included to give you more knowledge about HRMs; however, during the focus group we will discuss only the common ones that are anticoagulants, insulin, and opioids.

There are some challenges that have been described by FY1 and FY2 doctors when they prescribe HRMs. For example, the prescribing task might have been complicated or it might have been a non-routine prescribing task for the prescriber. Communication between the prescriber and the patient and multidisciplinary team can be problematic. These challenges could potentially be more of an issue during the on-call period.

The aim of this focus group study is to explore the challenges that are encountered FY1 and FY2 doctors when prescribing specific high risk medicines safely during the on-call period. The specific HRMs that will be discussed are anticoagulants, insulin, and opioids. Moreover, we are interested in exploring if the challenges are the same when prescribing HRMs during the regular working hours or prescribing medications that are not high risk either during on-call or the regular working hours.

Why have I been chosen?

You have been chosen as you are a FY1 or FY2 doctor, who has experienced the on-call period during your job. From your experience and your colleagues we want to understand the challenges that you are faced during the on-call when prescribing through focus groups. Each focus group will contain up to 8 participants of the same foundation year level.

What would I be asked to do if I took part?

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If you decide to take part in this study you may be asked to participate in a focus group. **Focus groups will be arranged to take place at the hospital and refreshments will be provided.** The focus group will be a conversation about challenges that FY1 and FY2 doctors face when they want to prescribe specific HRMs (anticoagulant, insulin, opioids) safely during the on-call period. Challenges could be the prescriber him/herself lacking the knowledge, factors in the working environment such as lack of resources, communication problems, or that the prescribing task is complicated. The focus group is not intended to grade the quality of your prescribing or your colleagues, but to give you an opportunity to talk through some of the challenges you feel influence safe prescribing during the on-call period. The focus group will be audio-recorded with your permission. There are no anticipated risks to taking part in this study.

**What happens to the data collected?**

The focus group recording will be transcribed and each person will be given a code number so that the data are anonymous. Then a qualitative analysis of the data will be performed. Verbatim quotes will be extracted anonymously to support the data analysis.

**How is confidentiality maintained?**

All information obtained from the focus groups and any other contact with you will be kept strictly confidential. To ensure this, data will be anonymised and securely stored. We may use quotes from the focus groups in reports or publications, but these will not be attributed to anyone by name. Anonymised transcripts of the focus groups will be stored indefinitely and used in future studies about medication and prescribing safety, such as for comparison of causes of prescribing errors over time.

In the unlikely event of uncovering a previously **unreported serious error** that directly resulted in patient harm, the researcher might be professionally obliged to report the incident through normal risk management procedures in the Trust (if this happens, you would be informed of this during the focus group).

Details of your participation will not be divulged to any person outside our research team, including other doctors. However, the other participants in the focus group will be aware of who else attended. The study will respect patient confidentiality and you will be asked not to mention patients or colleagues by name. If any details of patients are mentioned they will be promptly removed from the transcripts of the focus group data.

**What happens if I do not want to take part or if I change my mind?**

It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are still free to withdraw or cease to contribute any further up to the end of the focus group, without giving a reason and without detriment to yourself. However, it will not be possible for you to withdraw your data from the study if you leave after you have contributed to the focus group discussion, as the nature of the discussion means that later parts of the conversation may build on what you have said.

**Will I benefit from participating in the research?**

You will receive a £25 gift voucher to thank you for your participation in the focus group. It is hoped that participants will benefit from the process of reflection involved in the study and its relevance to lifelong learning (participation could be included within your portfolio). We will also provide you with a certificate of participation.

**What is the duration of the research?**

This whole process should take approximately 60-90 minutes.

14/06/2017, 3
Where will the research be conducted?

Focus groups will be arranged to take place at the hospital you work in.

Will the outcomes of the research be published?

The findings of this study will be published in a PhD thesis, as well as professional conferences posters or abstracts and in a peer reviewed paper. Those doctors who are interested in receiving feedback will be sent a summary of the results.

Who has reviewed the research project?

All research carried out by the University is looked at by an independent group of people, called a Research Ethics Committee, to protect your safety, rights, well-being and dignity. This study has been reviewed and given a favourable opinion by Manchester University Ethics Committee.

What if something goes wrong or if I want to make a minor complaint?

If something goes wrong or if you have a minor complaint then you need to contact the researcher in the first instance. You can contact the researcher on the following contacts:

Mahdi Alanazi, PhD student, School of Pharmacy and Optometry, University of Manchester.
Tel: 0161 306 0629
Email: mahdi.alanazi@postgrad.manchester.ac.uk

If you are not satisfied with the response you have gained from the researcher you can contact the research supervisor on the following contacts:

Dr Mary Tully, Reader in Pharmacy Practice, University of Manchester.
Tel: 0161 275 4242
Email: Mary.P.Tully@manchester.ac.uk

Formal Complaints

If you wish to make a formal complaint or if you are not satisfied with the response you have gained from the researchers in the first instance then please contact the Research Governance and Integrity Manager, Research Office. Christie Building, University of Manchester, Oxford Road, Manchester, M13 9PL, by emailing: research.complaints@manchester.ac.uk, or by telephoning 0161 275 2674 or 275 2046.

What Do I Do Now?

If you have any queries about the study or if you are interested in taking part then please contact the researcher.

Mahdi Alanazi, PhD student, School of Pharmacy and Optometry, University of Manchester.
Tel: 0161 306 0629
Email: mahdi.alanazi@postgrad.manchester.ac.uk

This Project Has Been Approved by the University of Manchester’s Research Ethics Committee [UREC reference number: 2017-0902-3341].

14/06/2017
### ISMP list of High Alert Medications in acute care settings (Drug Classes)

<table>
<thead>
<tr>
<th>Drug Classes</th>
<th>Example(s)</th>
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<tbody>
<tr>
<td>adrenergic agonist IV</td>
<td>epinephrine, phenylephrine, norepinephrine</td>
</tr>
<tr>
<td>adrenergic antagonists IV</td>
<td>propranolol, metoprolol, labetalol</td>
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<tr>
<td>anaesthetic agents general, inhaled and IV</td>
<td>propofol, ketamine</td>
</tr>
<tr>
<td>antiarrhythmic agents IV</td>
<td>lidocaine, amiodarone</td>
</tr>
<tr>
<td>anticoagulants</td>
<td>warfarin, LMWH, IV unfractionated heparin</td>
</tr>
<tr>
<td>factor Xa inhibitors</td>
<td>fondaparinux, apixaban, rivaroxaban</td>
</tr>
<tr>
<td>direct thrombin inhibitors</td>
<td>argatroban, bivalirudin, dabigatran etoxilate</td>
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<tr>
<td>thrombolytics</td>
<td>alteplase, reteplase, tenecteplase</td>
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<td>glycoprotein IIb/IIIa inhibitors</td>
<td>eptifibatide</td>
</tr>
<tr>
<td>cardioplastic solutions</td>
<td></td>
</tr>
<tr>
<td>chemotherapeutic agents parenteral and oral</td>
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<td>hypertonic dextrose, 20% or greater</td>
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<td>dialysis solutions peritoneal and haemodialysis</td>
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<td>epidural or intrathecal medications</td>
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<td>hypoglycaemic, oral</td>
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<td>inotropic medications IV</td>
<td>digoxin, milrinone</td>
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<td>insulin subcutaneous and IV</td>
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<td>moderate sedation agents IV</td>
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<td>moderate sedation agents oral for children</td>
<td>chloral hydrate</td>
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<td>narcotics and opioids IV, transfemoral and oral</td>
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<td>neuromuscular blocking agents</td>
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<td>sterile water for injection, inhalation, and irrigation</td>
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<tr>
<td>sodium chloride hypertonic concentration</td>
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</tbody>
</table>

IV= Intravenous, LMWH= Low Molecular Weight Heparin

14/05/2017, 3
Appendix 3: Study Three email invitation

Dear FY doctor,

**Studying the challenges to prescribing specific high risk medicines safely during the on-call period**

I’m emailing to ask if you would be willing to participate in a research study to explore the challenges that face FY1 or FY2 doctors to prescribe specific high risk medicines (HRMs) safely during the on-call period, which is the period out of working hours i.e. after 5 pm and before 8 am, and during weekends. Specific HRMs we are interested in are: anticoagulants such as warfarin and heparins; insulin; opioids i.e. morphine and codeine. This study is part of a PhD thesis that aims to understand the causes of prescribing errors made in HRMs.

Briefly, the study will involve participation in a single focus group, lasting approximately one to one and half hours. This will take place at the hospital either in a break or directly after one of your regular teaching sessions. The study involves reflection on the challenges that you encounter when on-call when prescribing HRMs. It is hoped that participants will find this advantageous, especially due to the importance of lifelong learning and reflective practice (you might like to include your participation in your portfolio- if so a certificate of your participation can be provided). The focus group is not intended to judge your prescribing in anyway but to give you an opportunity to talk through your experience about the challenges that you or your colleagues face when you are working on-call. It is hoped that the findings will enable us begin to address the challenges in this area and prevent errors in HRM in the future.

Currently there is focus group on (..../..../2017) will run at **(00:00 pm)** in the same venue as your teaching. Refreshments will be provided. Further details about the project are given in the attached leaflet, which I would encourage you to read before making up your mind.

If, after reading the participant information leaflet, you have any other questions or clarifications, please do not hesitate to contact me. If you are interested then please email mahdi.alanazi@postgrad.manchester.ac.uk or phone (0161 306 0629) stating your name, specialty, medical school attended and telephone/bleep number. All information that you provide will remain strictly confidential.

Thank you for your time

Mahdi Alanazi
Appendix 4: Study Three thank you email

Thank you email

Tel: 0161 306 0629
Email: Mahdi.alanazi@postgrad.manchester.ac.uk

[Name of doctor]
[Address of hospital]
[Date]

Dear [Name of doctor],

**Challenges to prescribing specific high risk medicines safely during the on-call period**

We would like to thank you for taking the time to fill in the questionnaire that was sent to you regarding the above study. Only a small sample of doctors was selected for the focus group according to who respond first. You were not selected to participate; therefore, you will not need to take part in the focus group. However, if participant was to withdraw for any reason we may contact you to take part.

If you are still interested in this study and would like to receive a brief copy of the findings you can contact me at the above email address.

Thank you

Mahdi Alanazi
Appendix 5: Study Three consent form

Challenges to prescribing specific high risk medicines safely during the on-call period

CONSENT FORM

If you are happy to participate please complete and sign the consent form below.

Please initial box

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>I confirm that I have read the attached information sheet on the above project and have had the opportunity to consider the information and ask questions and had these answered satisfactorily.</td>
</tr>
<tr>
<td>2.</td>
<td>I understand that my participation in the study is voluntary and that I am free to withdraw at any time before the end of the focus group without giving a reason and without detriment to myself.</td>
</tr>
<tr>
<td>3.</td>
<td>I understand that my data will remain confidential. To ensure this, data will be anonymised and securely stored.</td>
</tr>
<tr>
<td>4.</td>
<td>I understand that the focus group will be audio-recorded.</td>
</tr>
<tr>
<td>5.</td>
<td>I agree to the use of anonymous quotes in reports and papers about the study.</td>
</tr>
<tr>
<td>6.</td>
<td>I agree to my data being retained indefinitely for further research related to medication safety and prescribing safety or used as anonymous data as part of a secondary data analysis process.</td>
</tr>
</tbody>
</table>

I agree to take part in the above project

<table>
<thead>
<tr>
<th>Name of participant</th>
<th>Date</th>
<th>Signature</th>
</tr>
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<tbody>
<tr>
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<table>
<thead>
<tr>
<th>Name of researcher</th>
<th>Date</th>
<th>Signature</th>
</tr>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>

This Project Has Been Approved by the University of Manchester’s Research Ethics Committee [UREC reference number: 2017-0902-2583]

14/04/2017
Appendix 6: Study Three pre-focus group questionnaire

Expression of interest form for focus groups

Challenges to prescribing specific high risk medicines safely during the on-call period

Please contact me to discuss my potential participation in this study:

Name

Gender

Post

Department

Hospital

Contact tel. number

Email

Bleep

Or please email details to: mahdi.alanazi@postgrad.manchester.ac.uk
Appendix 7: Study Three UREC approval

Ref: 2017-001-0273
30/04/2017

Dear Mr Mohira Al-ani, Dr Penny Lewis and Dr Mary Tally

Study Title: Challenges to presenting specific IHRMs safely during on-call period

University Research Ethics Committee 5

I write to thank you for submitting the final version of your documents for your project to the Committee on 16/04/2017 13:08. I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form and supporting documentation as submitted and approved by the Committee.

Please see below for a table of the title, version numbers and dates of all the final approved documents for your project:

<table>
<thead>
<tr>
<th>Document Type</th>
<th>File Name</th>
<th>Date</th>
<th>Version</th>
</tr>
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<tbody>
<tr>
<td>Advertisement</td>
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<td>24/04/2017</td>
<td>1</td>
</tr>
<tr>
<td>Questionnaire</td>
<td>Per focus group questionnaire</td>
<td>08/02/2017</td>
<td>1</td>
</tr>
<tr>
<td>Advertisement</td>
<td>Thank you email</td>
<td>08/02/2017</td>
<td>1</td>
</tr>
<tr>
<td>Additional docs</td>
<td>Correspondence with IRR</td>
<td>17/02/2017</td>
<td>1</td>
</tr>
<tr>
<td>Topic Guide</td>
<td>Focus group topic guide (1)</td>
<td>14/04/2017</td>
<td>2</td>
</tr>
<tr>
<td>Participant Information Sheet</td>
<td>Participant Information Sheet P1 (1)</td>
<td>14/04/2017</td>
<td>2</td>
</tr>
<tr>
<td>Consent Form</td>
<td>Consent form (1)</td>
<td>14/04/2017</td>
<td>2</td>
</tr>
<tr>
<td>Distress Protocol Debrief Sheet</td>
<td>Focus group topic guide (2)</td>
<td>14/04/2017</td>
<td>2</td>
</tr>
<tr>
<td>Additional docs</td>
<td>Letter from the committee</td>
<td>14/04/2017</td>
<td>1</td>
</tr>
<tr>
<td>Additional docs</td>
<td>Response to the UREC comments (1)</td>
<td>14/04/2017</td>
<td>1</td>
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</table>

This approval is effective for a period of five years however please note that it is only valid for the specifications of the research project as outlined in the approved documentation set. If the project continues beyond the 5 year period or if you wish to propose any changes to the methodology or any other specifics within the project, an application to seek an amendment must be submitted for review. Failure to do so could invalidate the insurance and constitute research misconduct.

You are reminded that, in accordance with University policy, any data carrying personal identifiers must be encrypted when not held on a secure university computer or kept securely as hard copy in an location which is accessible only to those involved with the research.

Reporting Requirements:
You are required to report to us the following:
1. Amendments
2. Breaches and adverse events
3. Notification of progress/ end of the study

Feedback:
It is our aim to provide a timely and efficient service that ensures transparent, professional and proportionate ethical review of research with consistent outcomes, which is supported by clear, accessible guidance and training for applicants and committees. Please now complete a feedback sheet using the link below:

https://survey.manchester.ac.uk/powell/index.php/779/7581kng-eu

We wish you every success with the research.

Yours sincerely,

[Signature]
Appendix 8: Study Three HEE approval

Dear Mahdi,

RE: Challenges to prescribing specific high risk medicines safely during the on-call period

I write to confirm that your application for HEE Research Governance Approval to conduct the above study has been granted.

Approval is subject to your securing favourable ethical review from HRA and / or the academic institution sponsoring the research if applicable.

You may now proceed with the study as defined in the research protocol. Any amendment to the protocol must be submitted to this office for prior approval.

Once your project is complete please ensure that you submit a copy of your final report / publication to this office to the email or postal address above.

With best wishes.

Yours sincerely

Dr Steven J Agius
Senior Research Fellow

On behalf of Health Education England Research Governance Committee
Appendix 9: Study Three UREC amendments approval

Dear Mr Mahdi Alanazi,

Thank you for submitting your amendment request on 20/06/2017 15:44 for project: 2017-0002-3341; entitled: Challenges to prescribing specific HRMs safely during on-call period which has now been approved. Your documentation has been suitably updated to reflect the proposed changes, please ensure you use this documentation. Please note that if you have submitted revised supporting documents to accompany your amendment request, the approved versions of these are listed in a table below.

<table>
<thead>
<tr>
<th>Document Type</th>
<th>File Name</th>
<th>Date</th>
<th>Version</th>
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<tbody>
<tr>
<td>Additional docs</td>
<td>Participant Information Sheet PIS (3)</td>
<td>14/06/2017</td>
<td>3</td>
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<tr>
<td>Additional docs</td>
<td>Email invitation(3)</td>
<td>20/06/2017</td>
<td>3</td>
</tr>
</tbody>
</table>

We wish you every success with the research.

Best wishes,
Ms Patricia Gorham
Secretary to University Research Ethics Committee 5
Appendix 10: Study Three HEE amendments approval

18/06/2018

Dear Mahdi,

I have passed your email and updated documents to our reviewers who are both happy with these amendments. I will make a note on our records regarding the changes.

Many thanks,
Kirstie

Kirstie Simpson-Millear
Programme Support Manager
Education Development

Health Education England working across the North West
3rd Floor | 3 Piccadilly Place | Manchester | M1 3BN

T: 0161 625 7651
E: kirstie.simpson@hee.nhs.uk
Website: www.nw.hee.nhs.uk

From: Mahdi Alanazi [mailto:mahdi.alanazi@postgrad.manchester.ac.uk]
Sent: 30 June 2017 15:59
To: Kirstie Simpson
Cc: Mary Tully; Penny Lewis; ph.mahdi@yahoo.com
Subject: Amendments of approved project

Dear Kirstie,

I have spoken to you through the phone.

I have made amendments on my project, which I had approval from the HEE previously. The attached documents are the documents related to the amendments that are:
- Amendments application for the UREC.
- The approval of the amendments by the UREC.
- The previous approval of the HEE.
- The approved amended FIS.
- The approved amended email invitation for the participants.

In the amendments, we add two more hospitals, one focus group facilitator and £25 vouchers for each participant (all the details stated in the application of the amendments for the UREC).

Many thanks for your cooperation.

Sincerely,

Mahdi Alanazi

Mahdi Alanazi BPharm. Misc.
PhD Student
School of Pharmacy & Pharmaceutical Sciences
University of Manchester
Stopford Building
Oxford Rd
Manchester M13 9PT

Tel: +44161 306 0629

https://outlook.manchester.ac.uk/owa/
Appendix 11: Study Two conference abstract

Prescribing errors by junior doctors- a comparison of errors with High Risk Medicines and non-High Risk Medicines

Details and affiliations of the presenting and co-authors:

Mr Mahdi A Alanazi, University of Manchester, Manchester, UK
Dr Penny J Lewis, University of Manchester, Manchester, UK
Dr Mary P Tully, University of Manchester, Manchester, UK

Submissions are considered under:

Patient Safety

Introduction

Prescribing errors in hospital are common, occurring in 7% of medication orders and half of all admissions. (1) With high-risk medicines (HRMs), the prevalence of errors may be higher. (2) HRMs have a greater propensity to cause harm; therefore, it is important to understand any differences between the causes of prescribing errors with HRMs and non-HRMs. Such knowledge would be important in the development of preventative interventions.

Focal points

- It is not known whether the causes of prescribing errors in High-Risk Medicines (HRMs) and non-HRMs are similar or different.
- A secondary analysis of 59 interviews identified six themes that demonstrated clear differences between the causes of errors in HRMs and non-HRMs.
- Themes related to HRMs are: ‘provide drug product’ as a type of error, the complexity of the prescribing task and latent conditions in the organisation system; whereas, themes related to non-HRMs are violations of prescribing rules and reluctance to ask seniors.
• Communication failures with HRMs arose with exchanges with individuals outside the medical team while with non-HRM these failures occurred with exchanges within the immediate medical team.

Aim

To compare and contrast the causes of junior doctors’ prescribing errors with HRMs to non-HRMs to establish any differences.

Methods

A secondary analysis of fifty-nine interviews conducted in three previous studies about prescribing errors was conducted. Using the approach of Framework Analysis, a detailed comparison between the causes, error-causing-conditions (ECCs), latent conditions, and types of errors related prescribing errors with HRMs (based on Institute for Safe Medication Practices lists) and non-HRMs was carried out.

Ethics Statement

All studies had ethics committee approval; participants gave consent for future data analysis.

Results

There were two differences in the causes and types of errors between HRMs and non-HRMs. Violations were described with non-HRMs only and error type ‘provide drug product’ (errors that legally or practically prevent a prescription being dispensed) occurred with HRMs only. The latter, related to errors in the legal prescription requirements for controlled medications. There were two differences in ECCs of HRMs and non-HRMs. The first related to the complexity of prescribing HRMs, especially dosage calculations. The second regarded differences in the circumstances of communication failures: ineffective communication arose with exchanges with individuals outside the medical team while with non-HRMs these failures occurred with exchanges within the immediate medical team. Two differences were identified with the latent conditions: with non-HRMs there was a reluctance to ask seniors for help and with HRMs there were latent conditions within the organisation system such as the inclusion of trade names in hospital formularies. Moreover, prescribing during the on-call period was particularly challenging, especially with HRMs, such as insulin or controlled drugs.

Discussion
Although the interviews had not been conducted about errors with HRMs specifically, the analysis suggests that prescribers’ confidence with non-HRMs and potentially a reduced sense of risk could lead to violations or reluctance to seek help. With HRMs the differences were indicative of the nature of these medications as HRMs tend to involve complex calculations and sometimes additional prescription requirements. Future work could explore the causes of high-risk-medication errors made out of hours.

References
