Medication safety following hospital discharge: understanding epidemiology, aetiology, and the impact of an improvement intervention

A thesis submitted to the University of Manchester
for the Degree of
Doctor of Philosophy
in the Faculty of Biology, Medicine and Health

2022

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Total word count: 58,623 *[excluding references and appendices]*

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List of Abbreviations

Abbreviation / Acronym	Definition
ACE inhibitors	Angiotensin-Converting Enzyme Inhibitors
ADE	Adverse Drug Event
ADR	Adverse Drug Reaction
AE	Adverse Event
AHRQ	Agency for Healthcare Research and Quality
AKI	Acute Kidney Injury
BNF	British National Formulary
CCG	Clinical Commissioning Groups
CDSR	Cochrane Database of Systematic Reviews
CENTRAL	Cochrane Central Register of Controlled Trials
CI	Confidence Interval
CINAHL	Cumulative Index to Nursing and Allied Health Literature
CONSORT	CONsolidated Standards Of Reporting Trials
CQC	Care Quality Commission
CRD	Centre of Reviews and Dissemination
CRediT	Contributor Role Taxonomy
DARE	Database of Abstracts of Reviews of Effects
DMS	Discharge Medicine Service
DRP	Drug Related Problems
DVT	Deep Vein Thrombosis
EMIS	Egton Medical Information Systems
GCC	Gulf Cooperation Council
GMLPC	Greater Manchester Local Pharmaceutical Committee
GMSS	Greater Manchester Shared Services
GPs	General Practitioners
HMIC	Health Management Information Consortium
HRA	Heath Research Authority
HSRPP	Health Services Research & Pharmacy Practice
HIM	Health Innovation Manchester
ICD-10	International Classification of Diseases 10th revision
ICU	Intensive Care Unit
IDL	Immediate Discharge Letter
ID	Identification
IHI	Institute for Healthcare Improvement
INR	International Normalized Ratio
IPA	International Pharmaceutical Abstract
IQR	Inter Quartile Range
ISRCTN	International Standard Randomised Controlled Trial Number
IT	Information Technology
LOS	Length of Stay
MAR	Medication Administration Record
MD	Medication Discrepancies
MDS	Monitored Dosage System
ME	Medication Error
MeSH	Medical Subject Headings
MUR	Medicine Use Review

Abbreviation / Acronym	Definition
MRC	Medical Research Council
NCC MERP	National Coordinating Council for Medication Error Reporting and Prevention
NHS	National Health Service
NIPPS	Neighbourhood Integrated Practice Pharmacists in Salford
NMS	New Medicine Service
NRLS	National Reporting and Learning System
NPSA	National Patient Safety Agency
OR	Odds Ratio
OTC	Over The Counter
pADEs	Preventable Adverse Drug Events
PIT	Primary Incident Type
PCPP	Primary Care Pharmacy Programme
RECORD	Reporting of studies Conducted using Observational Routinely collected health Data
RDS	Research Data Storage
PINCER	Pharmacist-led information technology intervention for medication errors
PISA	Primary Care Patient Safety
PRIMM	Prescribing and Research in Medicines Management
PRISMA-P	Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols
RCT	Randomized Controlled Trial
RPS	Royal Pharmaceutical Society
SD	Standard Deviation
SIGN	Scottish Intercollegiate Guidelines Network
SMASH	Salford Medication safety dASHboard
SQUIRE	Standards for Quality Improvement Reporting Excellence
TCAM	Transfers of Care Around Medicines
UK	United Kingdom
UMD	Unintentional Medication Discrepancy
UREC	University of Manchester Research Ethics Committee
USA	United States of America
VPN	Virtual Private Network
WHO	World Health Organisation

Abstract

Background: Improving medication safety during transition between care settings is one of three international priorities for the World Health Organization's Global Patient Safety Challenge: Medication Without Harm. An expansion in published literature has supported our understanding of the epidemiology and aetiology of medication errors (MEs) and medication related harm (adverse drug events (ADEs)) on admission and at the point of discharge from hospital, with efforts now turning to the development, evaluation, and integration of remedial interventions. However, medication safety following hospital discharge has received limited attention despite emerging evidence of significant risk to patients and overall vulnerability during this stage of their care journey. In addition, whilst remedial interventions such as Transfer of Care Around Medicines (TCAM) are now being introduced to improve medication safety following hospital discharge, further evidence of impact is required alongside a need for a greater understanding of the nature and contributory factors to generate intervention theory. The aim of this thesis is, therefore, to understand the epidemiology and aetiology of medication safety challenges post hospital discharge alongside the evaluation of a TCAM intervention in order to generate learning designed to drive an improvement action agenda.

Method: The thesis presents three studies conducted during the programme of research. The first was a systematic review of international literature to synthesise knowledge of the prevalence and nature of MEs and ADEs following hospital discharge. The search was conducted on literature published between 1990 and 2019, using 10 databases and the grey literature. A second multi-method study was then conducted to identify the nature and contributory factors of medication incidents following hospital discharge by analysing patient safety incident reports submitted to the National Reporting and Learning System (NRLS) in England and Wales over a 5-year period. This included descriptive analysis of 1,121 incidents alongside content analysis of 408 incidents' free text data with coding following the Patient-safety Incidents in Primary Care (PISA) framework. The third study was a multi-method study to evaluate the 'service utilisation' and 'service impact' of the nationally adopted TCAM service launched by one English NHS Trust in February 2019, with this local TCAM service initially focusing on patients with new or existing Monitored Dosage Systems (MDS). The TCAM service is designed to enable the prompt transfer of medication information, with referrals made by hospitals at discharge to a named community pharmacy for follow up. The 'service utilisation' study included a descriptive analysis of 3,033 anonymised patient referrals to 71 community pharmacies over one year period. The 'service impact' study assessed the impact of the TCAM service on unintentional medication discrepancies (UMD) and ADEs using a retrospective before and after study (6 months before and 6 months after implementation). Data were collected across 18 general practices by 16 trained practice pharmacists using general practice electronic record systems.

Results: The first systematic review study identified 54 studies for inclusion. The median rate of MEs, UMDs and ADEs following discharge in adult patients was found to be 53% [Inter Quartile Range IQR 33–60.5] (n=5 studies), 50% [IQR 39–76] (n = 11), and 19% [IQR 16–24] (n=7) respectively. In the second study, the majority of NRLS medication incidents following discharge involved patients aged above 65 years (56%, n=626/1,121), and the prescribing stage (42%, n=479/1,121). Almost one eighth (12.6%, n=142/1,121) of incidents were associated with patient harm. The total number of identified contributory factors were 467 from 408 incidents, with organisation factors most common (82%, n=383/467) and specifically continuity of care issues (n=377/383, especially between secondary and primary care (n=308)). In the third study, TCAM 'service utilisation' data revealed that the majority of referrals (70%, 2,126/3,033) were marked as 'completed' by the community pharmacies, with 15% of completed referrals delayed beyond 30 days. A total of 411 patient records were screened in the 'service impact' study (168 pre-implementation, 243 post-implementation), with no statistically significant difference in UMD or ADE rates between the two stages using multivariable regression analysis (UMDs adjusted Odds Ratio (OR)=0.79 [95%CI 0.44-1.44, P=0.46]; and ADEs adjusted OR=1.19 [95%CI 0.57-2.45, P=0.63]). The common medication classes implicated with MEs/UMDs and ADEs post hospital discharge identified across studies One, Two and Three were the cardiovascular, endocrine and central nervous systems.

Conclusion: This thesis has found MEs and ADEs to be a common threat to patient safety post hospital discharge. An action agenda for policy, practice and research has been generated, which includes concentrating interventions on most common medication classes and patient groups, as well as the scope and design of future studies designed to evaluate these interventions to help better guide improvement efforts.

Declaration

This piece of work has not been submitted in support of an application for another degree or qualification of this or any other university or other institute of learning.

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Dedication

To the love of my life, to my first teacher in life, to my mother, Khadeija Al-Ali,
to the memory of my beloved late father, Abdulmohsen Alqenae,
to my sister and best friend, Amna Alqenae,
this work is dedicated to you.

Acknowledgement

"In The Name of Allah, the Most Beneficent, the Most Merciful"
"All praise and thanks are only for Allah, the one who, by His blessing and favour, good works are accomplished"

I did not expect writing this section to be this emotional. This work would not have been possible without the incredible support of a network of many great people. My deep gratitude goes also to the Kuwait Civil Service Commission, for funding this PhD.

I would like to take this opportunity to thank my supervisors, Dr Richard N Keers, and Dr Douglas Steinke, for their guidance, motivation, and dedicated supervision of this PhD. I am especially grateful for their encouragement, valuable comments on my writing, and the research skills that I have gained. I would also like to thank them for the opportunity to work with many great people. I would like to also thank Dr Andrew Carson-Stevens, for the guidance on the study presented in Chapter Five, and I would like to thank Dr Mark Jeffries for the opportunity to participate in qualitative research.

I want to thank the great team behind the study presented in Chapter Six. A special thanks go to Ms Hilary Belither for her continuous assistance throughout the conduct of this study. I would like to thank Mr Peter Robertson for supporting me to have frequent primary care practice visits. Data collection for this study would not have been possible without the participation of the neighbourhood integrated practice pharmacists (NIPPS) team. I would also like to thank the senior management of the NIPPS team, namely Ms Jennifer Bartlett and Dr Jessica Roberts, for the support during data collection. I want to thank also Mr Steve Williams, and Dr Lawrence Brad for attending expert panel meetings to validate data collection forms. I am also grateful to Dr Jack Wilkinson for supervising data analysis.

I would like to thank the research governance team at the University of Manchester, including Ms Lynne MacRea, Ms Stacey Body, and Dr Scott Bannister, for their guidance and advice throughout getting ethical approvals. I am also very grateful to the Doctoral Academy team, library team, IT team and Pharmacy department administrative team at the University of Manchester for the great assistance throughout this PhD.

I would like to thank everyone in the Centre of Pharmacoepidemiology and Drug Safety, and my office mates in room 1.132, especially Fatema Ikolaba, Canase Kam, and Wael Khawagi. Many thanks to my PhD friends; Asma Alturkait, Hanan Bukhari, Hessa Alaslawi, Ireny Iskandar, and Mohra Aladwani. I would like to thank my friends Afrah Alkazemi, and Fatema Fakhra for their encouragement. A special thanks go to my office mates and dearest close friends Ghadah Alshehri and Wijdan Shroukh, who not only were friends, but were family here in Manchester; their friendship was indeed the highlight of this journey.

I would like to thank my family for their encouragement. I would like to thank my sisters Huda and Mariam for their encouragement and prayers. A special thanks to my sister Amna for her endless encouragement and support. Finally, I would like to thank my mother for her continued support, encouragement, and prayers; nothing would have been possible without her. All that I am or ever hope to be, I owe it to my mother, Khadeija Al-Ali.

Dissemination of the research

Journal articles

1. Study presented in Chapter Four was published as a peer review article in Drug Safety journal. *[Alqenae, F, Steinke, D & Keers, R 2020, 'Prevalence and Nature of Medication Errors and Medication-Related Harm Following Discharge from Hospital to Community Settings: A Systematic Review', Drug Safety. https://doi.org/10.1007/s40264-020-00918-3]*.
2. **[Work affiliated to PhD programme]** Article related to study presented in Chapter Six [Jeffries M, Keers R, Belither H, Sanders C, Gallacher K, Alqenae F, Ashcroft D. *'Understanding the implementation, impact and sustainable use of an electronic pharmacy referral service at hospital discharge: A qualitative evaluation from a sociotechnical perspective', PloS One.* https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0261153]
3. **[Drafted for submission]** Study presented in Chapter Five drafted for submission for BMJ Quality and Safety Journal. *[A multi-method evaluation of medication safety incidents following transitions from secondary to primary care in England and Wales received by the National Reporting and Learning System (NRLS)]***.**
4. **[Drafted for submission]** Study presented in Chapter Six drafted for submission for Drug Safety Journal. *[A multi-method evaluation of a Transfer of Care Around Medicines intervention designed to improve medication safety for patients with monitored dosage systems following hospital discharge].*

Abstracts

1. The study presented in Chapter Four was published as an abstract in Pharmacoepidemiology and Drug Safety. The abstract was presented as a **poster presentation** at the Prescribing and Research in Medicines Management (PRIMM) UK & Ireland Conference, on 14th December 2018, in 30th Annual Scientific Meeting "Person-centred Care in the Digital Age: Nudge Nudge, Tweet Tweet". N1 1NL, London, UK. Title: "A Systematic Review of Medication Errors and Medication Related Harm Post Hospital Discharge". *[Alqenae, F, Steinke, D & Keers, R 2019, 'Prevalence and nature of medication errors and medication related harm immediately following hospital discharge from hospital to community settings: A systematic review', Pharmacoepidemiology and Drug Safety, vol. 28, no. S1, pp. 4-5. https://onlinelibrary.wiley.com/doi/epdf/10.1002/pds.4732]*
2. The study presented in Chapter Five was published as an abstract in Pharmacoepidemiology and Drug Safety. The abstract was presented as an **oral presentation** at the PRIMM UK & Ireland virtual Conference, on 11th June 2021, in 32th Annual Scientific Meeting 'Big Data…is it the Future of Medicines Optimisation?'. *[Alqenae, F, Steinke, D & Keers, R 2021, 'Medication safety challenges following hospital discharge: An exploratory analysis of incidents reported in England and Wales over a 5-year period', Pharmacoepidemiology and Drug Safety, vol 30, no. 52, pp. 14-15. https://onlinelibrary.wiley.com/doi/epdf/10.1002/pds.5315*]

3. Study presented in Chapter Six was published as an abstract in International Journal of Pharmacy Practice. The abstract was presented as **poster presentation** at the Health Services Research & Pharmacy Practice (HSRPP) on 8-9 April 2021, virtual conference. Conference title 'Designing Healthcare: Stimulating Interdisciplinarity and Co-design for Quality Healthcare'. *[Alqenae, F, Steinke, D & Keers, R 2021, ' Evaluating the Utilisation of a Service Designed to Enhance Care with Medicines Following Acute Hospital Discharge: A Retrospective Study', International Journal of Pharmacy Practice, Vol 29, Supplement 1, i42-i43. https://academic.oup.com/ijpp/article/29/Supplement_1/i42/6188834]*

Achievement

Won first prize award for poster presentation at Prescribing and Research in Medicines Management (PRIMM) UK & Ireland Conference, on 14th December 2018, in 30th Annual Scientific Meeting.

Wider dissemination and coverage of published article

1. A blog post to disseminate the finding of the article published in Drug Safety based on the Study presented in Chapter Four was published at the Research Hive. https://manchesterresearchhive.wordpress.com/2020/06/10/risk-associated-with-medications-following-discharge-from-hospital-a-new-systemic-review/ .
2. The article was one of the five most downloaded contemporary articles on the SpringerLink platform in Drug Safety journal, between January to June 2021. In addition, the paper got Altmetric score 55, at the time of writing this thesis.
3. The article has received wide media coverage, including:
    - Patient Safety Newsletter by the Government of Catalonia, Spain (04/05/2020). http://seguretatdelspacients.gencat.cat/en/detalls/noticia/Errors-de-medicacio-durant-la-transicio-dels-pacients-despres-de-lalta-hospitalaria
    - Weekly update by the Patient Safety Network (PSNet), Agency for Healthcare Research and Quality (AHRQ), United States (22/07/2020). https://psnet.ahrq.gov/issue/prevalence-and-nature-medication-errors-and-medication-related-harm-following-discharge
    - Weekly letter ''On the Radar (Issue 475)'', by the Australian Commission on Safety and Quality in Health Care (ACSQHC), Australia (03/08/2020). https://www.safetyandquality.gov.au/publications-and-resources/resource-library/radar-issue-475
    - Society of Hospital Pharmacist of Australia (SHPA)'s Pharmacy GRIT Journal [page 73, Volume 4 Issue 4, Summer 2020-2021], Australia (24/02/2021). https://www.shpa.org.au/sites/default/files/uploaded-content/website-content/GRIT%20Summer%202020-21.pdf
    - Medication safety at hospital discharge: Improvement Guide by the Royal College of Physicians, UK (1/11/2021). https://www.rcplondon.ac.uk/projects/outputs/medication-safety-hospital-discharge-improvement-guide-and-resource

Preface

This is a PhD thesis submitted to the Division of Pharmacy and Optometry, University of Manchester. The thesis was prepared by the PhD candidate Fatema Alqenae. Fatema is a pharmacist registered to practice in Kuwait. Fatema graduated from Kuwait University with a Bachelor of Pharmacy in 2009, and undertook her Master of Sciences (MSc) in Clinical Pharmacy from the School of Pharmacy, University College London (UCL) in 2014. After the MSc, Fatema worked as a clinical pharmacist in the surgical wards at a government hospital in Kuwait. Fatema has started her PhD in the Centre of Pharmacoepidemiology and Drug safety at the University of Manchester in September 2017.

Fatema gathered research experience in medication safety in the United Kingdom during her MSc and received first prize award for poster presentation, titled an 'Audit on the clinical appropriates of prescribing oxygen: benchmarking against British Thoracic Society (BTS) guidelines', at patient safety conference at North Middlesex University Hospital Trust, London, UK. During her PhD, Fatema developed her research skills by attending several workshops, and training courses, including statistical modelling with Stata, fundamentals of epidemiology and evidence synthesis: systematic reviews, which were part of the Master of Public Health Course units at the University of Manchester. Fatema has also attended a drug utilisation research summer school in Stockholm, Sweden, in June 2019, organised by EuroDRUG, Drug Utilisation Research, Special Interest Group of International Society of Pharmacoepidemiology, and Karolinska Institute. Fatema has attended several national conferences (listed in Appendix 1), and won first prize award for poster presentation at Prescribing and Research in Medicines Management (PRIMM) UK & Ireland conference. Fatema has also participated in peer reviewing two articles, one in BMJ Open Quality in July 2020, and one in PloS One journal in June 2021.

Fatema has conducted three studies as part of her PhD using diverse methodologies. Chapter Four within this thesis is a systematic review paper Fatema has published in Drug Safety. It is co-authored by Dr Richard Keers and Dr Douglas Steinke, and Fatema's contribution was leading and performing the systematic review planning, citation screening and identification, data extraction, and data analysis. The contribution of co-authors was in study conception and design, data extraction and supporting the conduction of the review. Fatema has gained experience in the research approval and data governance processes as studies presented in Chapters Five, and Six went through ethical and/or other approvals.

Chapter One: Introduction and Overview of Thesis Structure

1.1 Introduction to the research

Medication related problems are increasingly recognised as an important patient safety priority in the transition of care from secondary to primary care. This transition of care period is a disruptive and challenging time for patients, as they are adjusting their health and personal lives after a hospital discharge. It has been estimated that one in five patients will experience adverse drug events (ADEs – medication related harm) in the first month post discharge [1,2]. In March 2017, medication safety at the transfer of care was brought to global attention with the publication of the World Health Organization's (WHOs) Global Patient Safety Challenge: Medication Without Harm, as one of three priorities for action[3]. The ultimate goal of this WHO challenge was to reduce severe avoidable medication related harm globally by 50% over five years.

It has previously been observed that different types of drug related problems (DRP) that occur at discharge might manifest into problems in the community if not properly addressed, including insufficient patient counselling on medication and monitoring plans, amongst others[4]. Outcomes for patients post discharge include medication errors (MEs)[5], medication related harm[6], and medication discrepancies[7] though the literature is fragmented. Several reviews have reported that current remedial interventions may have a limited impact on medication safety post hospital discharge[8–11], which might be due to a lack of systematic understanding of the prevalence and causes of medication safety issues post hospital discharge.

Communication gaps at the transition from secondary to primary care include incomplete and poor quality of information at discharge and are very common[12]. Thus, targeting communication post hospital discharge may be an area of prioritisation. A national intervention to improve the communication of medication information and follow up with community pharmacy, named the Discharge Medicine Service (DMS), was rolled out in the United Kingdom (UK) in February 2021[13]. However, data concerning the impact of the DMS service on medication safety is limited.

The overall aim of this PhD programme was to generate new evidence concerning the epidemiology, aetiology and impact of the DMS remedial interventions addressing medication safety at the post-hospital discharge care transition. In addition, to using these findings to create recommendations for future policy, clinical practice and research to support improvement in medication safety at this crucial stage of the patients' health care journey. The thesis follows the structure of a traditional thesis and consists of nine

chapters. Herein, **Chapter One,** the introduction chapter covers the thesis structure; **Chapter Two** is a literature review focusing on the topic of medication safety following hospital discharge. **Chapter Three** then provides rational of PhD programme, the aim and objectives of the thesis.

The approach that was adopted to fulfil the aim of this PhD was to first understand the frequency of MEs and medication related harm immediately following hospital discharge. This was achieved as reported in **Chapter Four** by systematically identifying and evaluating the available international evidence on the prevalence, nature and severity of MEs and medication related harm immediately following transition of care from hospital to community settings.

The second study reported in **Chapter Five** was planned to build on our understanding of epidemiology from the first study by then exploring the nature, severity and causes of medication safety incidents occurring following hospital discharge at a national level. This was achieved via an analysis of medication related incident reports submitted within primary care to the UK National Reporting and Learning System (NRLS) over a five-year period. The study included a quantitative description of errors as well as thematic content analysis of their contributory factors.

The third study contained in **Chapter Six** was a multi-method evaluation of the utilisation and impact of a newly implemented electronic pharmacy referral service (Transfer of Care Around Medicines (TCAM)) on medicines safety. The TCAM service was designed to improve the communication of medication information by sending discharge letters and follow up requests via an electronic platform to community pharmacies and reflected similar interventions which were being rolled out nationally at the time. This project described and compared the occurrence of unintentional medication discrepancies (UMDs) and adverse drug events (ADEs) before and after TCAM was introduced using logistic regression analysis. Alongside this, TCAM service 'utilisation data' was examined over a one year period to better understand the nature and outcomes of referrals made.

Chapter Seven provides an overview and interpretation of key findings from Chapters Four, Five and Six of the thesis, followed by key strengths and limitations of the research programme. Implications and recommendations for clinical practice and policy, as well as future research priorities, are then presented and justified. **Chapter Eight** has the references, followed by **Chapter Nine** containing appendices.

The focus of this thesis is the phase post hospital discharge. The thesis is intended to generate a generalise picture of medication safety issues post hospital discharge in all community settings, for all patients' populations using medication from any medication classes. The term elderly is used in the thesis to refer to patients aged 65 years and older. While a recent call has been drawn to adopt the term older adults[14,15], but term elderly was used to ease comparison with other studies in the field. Main tables are presented in the main thesis chapters, with tables that provide further explanation are provided in appendices where supplementary materials are provided. [Refer to section 2.3.1 for the terminology of medication safety terms]

1.2 Contributors

1.2.1 Supervisory team at the University of Manchester

- Dr Richard N Keers, Clinical Lecturer in Pharmacy, University of Manchester
- Dr Douglas Steinke, Senior Lecturer in Pharmacoepidemiology, University of Manchester

Roles included supporting Fatema Alqenae with design, conduct and interpretation of all aspects of the PhD work programme within supervisory capacity.

1.2.2 Subject matter expert at Cardiff University

- Dr Andrew Carson-Stevens, Clinical reader at Division of Population Medicine, School of Medicine, Cardiff University

Dr Carson-Stevens is the founder of the Patient Safety Research (PISA) group at Cardiff University. The PISA group developed the classification framework of patient-safety incidents in primary care that was utilised in Chapter Five. Dr Carson-Stevens roles included providing insights into conceptualisation of the data study presented in Chapter Five along with consultation on the use of the PISA classification framework.

1.2.3 Collaborators at NHS acute Trust in North West of England

- Ms Jennifer Bartlett, Dr Jessica Roberts, Ms Hilary Belither, Mr Peter Robertson, Pharmacy Department, NHS acute Trust in North West of England

Their role included providing insights into and supporting result interpretation of study data presented in Chapter Six.

Ms Bartlett and Dr Roberts are the senior management team of the neighbourhood integrated practice pharmacists service (NIPPS). The NIPPS team completed the data collection for the study presented in Chapter Six. Dr Roberts facilitated the communication between Fatema Alqenae and the NIPPS team.

Mr Robertson supported Fatema Alqenae while she had general practice visits to have an overview of the discharge medication reconciliation service that pharmacists provided in general practice. Mr Robertson also piloted data collection forms and provided feedback on data collection training materials.

1.2.4 **Statistical support**

- Dr Jack Wilkinson, Division of Population Health, Health Service Research & Primary Care, School of Health Sciences, University of Manchester

Role included supervising the data analysis that Fatema Alqenae has conducted and presented in Chapter Six.

Chapter Two: Background

2.1 Transition of care: a less well understood aspect of patient healthcare journey

2.1.1 Transitions of care: definition and characteristics

Hospitalisation is a complex process, consisting of a collaboration of different medical departments in the hospital (such as individual wards, laboratory, radiology, physiotherapy, pharmacy, critical care, and nutrition), as well as between these teams and medical and social care teams in various community settings in order to facilitate optimal treatment and effective discharge. There were 5.8 million emergency hospital admissions in England between 2016 and 2017[16], and it has been estimated that the total cost of emergency hospital admissions in England between 2016 and 2017 to be £17.0 billion[17]. During hospitalisation, the patient may be at risk of iatrogenic harm (see section 2.2.1 for definition), including infection, deep vein thrombosis, delirium, distress, and hospitalisation associated disability[18–23]. Hospitalisation has a domino effect in that it not only has an impact on the patients themselves but also impacts wider society; for example, family members may experience physical and psychological symptoms as a result[24,25].

Furthermore, due to the nature of healthcare systems, patients may enter different transition of care cycles when they enter or leave different health care settings such as between secondary and primary care, within hospital areas /departments (intra-hospital transfer), and between hospitals (inter-hospital transfer)[26]. Patient transfer, therefore, includes those admitted to hospital from primary care, patients discharged from hospital to primary care, residential/nursing homes or other specialist facilities, and patients transferred from one hospital, hospital ward, or department to another[27]. Transitions of care is defined as *"changes in the level, location, or providers of care as patients move within the healthcare system"*[28]. Patients undergo intra-hospital transfer due to diagnostic or therapeutic procedures, or the need for Intensive Care Unit (ICU) admission[29]. Best practice guidance in transitions of care focuses on the decision to transfer and communication, pre-transfer stabilisation, and adequate documentation[30]. Transitions of care are intended to be seamless and safe. Seamless care at the transition of care has been defined as *'smooth, safe and timely transition of a patient between levels of health care and across care settings'*[31,32]. However, transitions of care are known to place patients at risk for adverse outcomes, including medication errors (MEs), missed test results, adverse events (AEs), and/or hospital readmission [26,33]. For example, there is a growing body of literature that recognizes inter-hospital transfers as an area of high risk, and to be associated with a longer hospital stay, high cost, AEs and mortality[34–36]. In 2020, a systematic review was

published highlighting adverse events associated with intra-hospital transfer, including delirium, infections, increased length of stay, and mortality[37]. Transfers to and from ICU were associated with adverse events, including hemodynamic and respiratory deterioration[38]. Furthermore, room transfers within the same hospital were also associated with an increased risk of delirium for elderly hospitalised patients[39]. A recent meta-analysis of 24 studies found that adverse events occur during 26.2% (95% CI 15-39.2) of intrahospital transport[29]. So far, however, there has been little attention concerning risk post hospital discharge transition compared to different care transition points.

2.1.2 The paradox of hospital discharge: hidden epidemic of patient harm

Patients are discharged from the hospital when their acute health condition(s) causing admission does not require any further intervention or monitoring – the aim is for these patients to remain in the community for the foreseeable future and not return as an inpatient to the hospital[40]. Several factors may play an important role in determining post-discharge care needs and risks. These include patient mental/physical health status, ongoing treatment requirements, patient activity level, the nature of the patient's current home, availability of family support and ability to obtain medications[41]. Patients may be discharged to either their home, a long-term care facility, a nursing home or some other specialist community facility depending on their needs (e.g. learning disability facility, hospice, supported accommodation). The patient journey post hospital discharge may be full of challenges, including changing care needs and rehabilitation, readjustment and ongoing care requirements. Although patients may be keen to be discharged from the hospital, recent evidence highlights that patients may struggle with daily activities, including cooking and bathing, after hospital discharge, which may introduce new care needs that were not there before hospital admission[42]. Hospital discharge has an impact on society in terms of community services utilised to support patients as well as family and friends as carers who may feel that they are unprepared, which also impacts their physical/ psychological health and work productivity[25,43–47]. Medication plays an important role in post hospital discharge as it supports health restoration and/or preventions further deterioration/readmission.

Immediately following discharge, due to various factors, including those identified above, patients may be considered at a period of heightened risk. The term 'post hospital syndrome' has been used to describe this state, and is described by Dr Krumholz (2013) as" *an acquired, transient condition of generalised risk"*[48]. Hospitalised patients may not

only suffer an acute illness that disturbs their physiological system, but they may also be under stress due to information overload and worrying about their health[48]. Moreover, hospitalised patients may suffer from discomfort, pain, sleep deprivation, inadequate nutrient intake, poor bowel management, personal hygiene, and impaired stamina[48]. Thus, the period immediately following hospital discharge can be a challenging time for patients, both in terms of safety but also socially (e.g. adjusting back to life at home) and emotionally (e.g. anxiety about illness and self-care, coming to terms with life-altering changes).

However, it is apparent that not all patient care needs/risks are managed appropriately at and beyond discharge. Consequences include readmission to hospital, and emergency department visits[49]. Research evidence suggests that around 20% of patients are readmitted to the hospital within 30 days of discharge in the United States of America (USA)[50]. Factors related to hospital discharge that have a significant association with hospital readmissions include timeliness and documentation in the discharge summary, and drug related problems at hospital discharge[49]. Hospital readmissions may be due to different reasons, including premature discharge, nosocomial infections, pressure ulcers, failed handoffs, complications following procedures, therapeutic errors, adverse drug events and other medication related issues[51]. Some studies have estimated that the proportion of preventable readmission from total all cause readmission within 30 days of hospital discharge is 23% [95% CI 21.7-24.5%] in a meta-analysis (16 studies utilising different methodology)[52], and the median proportion to be 27% [range 5-79%] in a systematic review (34 studies)[53]. However, a recent single centre study from the Netherlands found it to be 13%, and 26% if incorporating patient interviews[54]. The wide range of the proportion of preventable readmissions may be due to the heterogeneity in study methods[55]. A recent single centre study from the Netherlands found that the most common causes of preventable readmissions are diagnostic (30%), followed by medication-related (27%)[54]. Moreover, Davies (2010) reported that one-fifth of patients readmitted to the hospital within one year of their index admission were due to adverse drug reactions in the UK[56], with a recent systematic review of 19 studies has shown that medication related readmission account for 20% of total hospital readmission[57]. In their analysis of factors affecting all causes of hospital readmission in the USA, Feigenbaum and colleagues (2012) identified five areas to focus quality improvement initiatives, including transitions care planning and care coordination, clinical care, logistics of follow-up care, end-of-life needs, and medication management[58].

Following hospital discharge, Tsilimingras, et al. (2015) identified that 28.7% of patients in the USA would experience one or more adverse events 3-6 weeks post discharge, with the most common adverse events reported as adverse drug events (ADEs), management errors, procedural complications, therapeutic errors, diagnostic errors, and hospital acquired infections[59]. Forster and colleagues, (2004) identified that 23% of patients discharged from general internal medicine service at a hospital in Canada were affected by adverse events post hospital discharge, with adverse drug events being the most common adverse events accounting for 72% of the total adverse events post hospital discharge, in addition to therapeutic errors, nosocomial infections, procedure-related problems, pressure ulcers, diagnostic errors and falls[2]. Moore and colleagues (2007) have also identified that 35.9% of recommended workups, including diagnostic procedures, subspeciality referrals and laboratory tests, were not followed post hospital discharge[60].

Previous studies exploring healthcare providers (physicians and nurses) and patient feedback on challenges and responsibilities after hospital discharge have identified that patients may not feel empowered at the discharge handover, and that communication issues and problems in patient follow-up may occur[61–63]. In addition, nurses providing services within home health care in the USA expressed that there are communication issues after hospital discharge, including 'challenges connecting with physicians by telephone' and 'lack access to hospital records'[64,65]. Furthermore, evidence from the UK, the Netherlands and Switzerland found that hospital and community pharmacists have reported a lack of patient involvement in the discharge process, and issues of poor discharge information / communication[66–68]. Moreover, patients have also mentioned that there is inadequate service post hospital discharge, and a lack of patient engagement in the discharge planning[69–71].

In their recent publication, Markiewicz and colleagues, conducted a Delphi consensus study with clinical and non-clinical primary care staff in the UK on the topic of threats to safety transitions post hospital discharge[72]. The five most common threats that received consensus (agreement > 90%) in round 3 were poor quality of discharge letter, discharge arrangement, unsafe medication provision, workload handover and problems in sending discharge letters.

2.1.3 Assessment of transition of care: safety and quality aspects

The safety of transfer of care could be assessed via assessing AEs and unwanted incidents, while the quality of the health care service at the transfer of care could be assessed using

satisfaction measures, delays, and hospital readmission rates[73]. Systematic reviews such as that conducted by Melle (2018) have shown that the most common outcome and process measures used in the transition of care were medication discrepancies, adverse events, health status, patient satisfaction, emergency department visits and hospital readmission[73].

Hospital readmission is widely used as a quality indicator of hospitalisation[74]. Hospital readmission can be defined as being readmitted to the hospital within one month of the index discharge date[75]. In the USA, and the UK, hospitals with high readmission rates may be given financial penalties[76]. However, evidence has shown that the flaws in the methods used in assessing hospital readmission include the distinction between planned and unplanned readmission limit its use as a quality indicator measure[76].

2.2 Patient safety and adverse events

2.2.1 Iatrogenic harm: definition and outcomes

''The medical establishment has become a major threat to health.''

Ivan Illich (Medical Nemesis: The Exploration of Health, 1976)[77]

In his powerful argument, Medical Nemesis, Ivan Illich has introduced the concept of iatrogenesis, a Greek word, where *''iatros''* meaning ''physician'', and *''genesis''* meaning ''origin''[77]. Publication of the landmark Harvard Medical Practice Study in the year 1991, captured the attention of the world in identifying the scale and nature of iatrogenic patient harm in 51 hospitals in the USA[78].

Iatrogenic harm or illness is defined by (Steel et al., 1981) as *"any illness that resulted from a diagnostic procedure, from any form of therapy, or from a harmful occurrence that was not a natural consequence of the patient's disease*"[79]. Iatrogenic harm can be a result of medication, medical devices, surgical errors and unsafe blood products, among other examples. The most common iatrogenic harms across health care services are medication-related harm (e.g. adverse drug events (ADEs) and adverse drug reaction (ADRs)), diagnostic harm (e.g. delayed diagnostic process), clinical management harm (e.g. wrong referral), the harm related to invasive medical procedures (e.g. bleeding after tracheostomy), the harm caused by inpatient acquired infections (e.g. nosocomial urinary tract infection), the harm related to surgical procedures (e.g. infection), and system related harm (e.g. technical errors)[80]. A scoping review by Masotti et al. (2010) found that adverse events have serious health and economic outcomes, with examples including functional loss or decline, temporary injury or pain, permanent injury or harm, and death[81]. Examples

of the economic consequences include the increased need for treatment or care, increased patient or caregiver time and unplanned hospitalisation[81]. In October 2014, Frontier Economics published a report, commissioned by the Department of Health entitled *"Exploring the costs of unsafe care in the NHS: A report prepared for the department of health"* where it estimated the potential cost to the NHS of preventable adverse events, including MEs was between £1 - £2.5 billion annually[82].

2.2.2 Causes and risk factors of adverse events

It has previously been observed that the most common causes of adverse events in the Netherlands (2010) are active human failures (knowledge-based behaviours, rule-based behaviours, skill-based behaviours, and violation), followed by patient related factors and organisational factors[83]. In addition, Wilson and colleagues (1999) have identified that the most common causes of adverse events to be complications or failure in the performance[84]. Furthermore, Jagsi et al. (2005) have surveyed resident physicians and identified that most adverse events occurred due to mistakes[85]. It has been noted that adverse events that occurred as a result of organisation factors have the highest proportion of preventable adverse events[83].

2.2.3 Patient safety: policy context, and influential reports.

For the last quarter-century, patient safety has become a central issue for not only healthcare providers but also economic, political and social advocates[86]. Patient safety is defined as *"avoidance, prevention, and amelioration of adverse outcomes or injuries stemming from the processes in healthcare*"[87]. The issue of patient safety received little critical attention until the publication of the *"Harvard Medical Practice Study"* in the early 1990s, which found that in a sample of 30,121 patients across 51 hospitals, adverse events occurred in 3.7% of hospitalisations in the USA[78]. An investigation of citation classics in patient safety found that the *"Harvard Medical Practice Study 1"* by Brennan et al. (1991) and *"Harvard Medical Practice Study 2"* by Leape et al. (1991) are the top two cited studies in the field of patient safety, and that related publications grew considerably following the year 2000[78,88,89]. Using Harvard Medical Practice Study's protocol to estimate the incidence rate of adverse events in hospitals in other countries, Wilson (1995) reported the rate in Australia to be 16.6%[90], Vincent (2001) found the rate to be 10.8% in the United Kingdom (UK)[91], Davis (2002) found it to be 11.2% across 13 hospitals in New Zealand[92], while Baker (2004) reported a rate of 7.5% in Canada[93]. As a result of the comparable rate of adverse

events in hospitals worldwide, the global healthcare community started to take action to tackle the issue.

Some of the above referenced studies prompted the publication of the reports '*To Err is Human'* (Institute of Medicine, 1999) and '*An Organisation with a Memory'* (National Health Service, 2000) at the turn of the millennium[94,95]. The 'To Err is Human' report estimated that between 44,000-98,000 people died in hospital as a result of preventable medical errors each year in the USA, with medication a major contributor followed by improper transfusion, surgical injuries and wrong site injury, suicides, restraint-related injuries or death, falls, burns, pressure ulcers and mistaken patient identities[94]. The 'Catalyst for Change' report mentioned not only the loss in human lives, but also the economic losses due to preventable medical errors, where it was estimated between $17-29 billion annually in hospitals nationwide[94]. *'To Err is Human'* report (Institute of Medicine, 1999) was a widespread success due to the comprehensive strategy that was explicitly mentioned to resolve the issue of medical errors[94]. One of the recommendations the report gave was to form a national centre for patient safety for Healthcare Research and Quality[96]. President Bill Clinton approved this recommendation by signing Senate Bill 580, the Healthcare Research and Quality Act of 1999[97]. The implication of this is that countries worldwide started to follow the path of the USA in dealing with patient safety concerns, and patient safety was a priority on the healthcare agenda in several countries. Table 2.1 lists examples of patient safety initiatives and organisations in the USA and the UK[98,99].

Table 2.1 - Examples of patient safety initiatives and organisation in the USA and the UK

Country	Year	Patient safety initiatives and organisation
USA	2002	The National Patient Safety Foundation (NPSF) [established in 1997] launched patient safety awareness week campaign.
	2003	The Joint Commission on Accreditation of Health Care Organisation (JCAHO) declared the National Patient Safety Goals (NPSGs).
	2004	The Institute for Healthcare Improvement (IHI) launched the 100,000 lives campaign.
	2005	The Patient Safety and Quality Improvement Act (PSQIA) was approved in the USA which called for reporting of safety incidents.
	2006	The Agency for Healthcare Research and Quality (AHRQ) in collaboration with the department of defence developed the Team Strategies and Tools to Enhance Performance and Patient Safety (TeamSTEPPS).
	2008	The AHRQ implemented the Comprehensive Unit-based Safety Program (CUSP)
	2011	Centres for Medicare and Medicaid services implemented "Partnership for Patients".
	2016	Centres for Medicare & Medicaid Services (CMS) launched Hospital Improvement Innovation Networks (HIINs).
UK	2000	The publication of the revolutionary report by the Chief Medical Officer "An organisation with a memory".[95]
	2001	The establishment of the National Patient Safety Agency (NPSA) for England and Wales (UK) by the National Health Service (NHS).
	2001	The publication of a whole issue of the high-profile journal "British Medical Journal" that was dedicated to medical errors.
	2003	The launch of the National Reporting and Learning System (NRLS).
	2004	The launch of Seven Steps to Patient Safety publication.
	2016	The establishment of NHS Improvement.
	2017	The establishment of Healthcare Safety Investigation Branch (HSIB).
	2018	The publication of the Care Quality Commission (CQC) document ''Opening the door to change – NHS safety culture and the need for transformation''[100].
	2019	Launch of NHS Patient Safety Strategy by NHS England and NHS Improvement [101].

On an international level, the World Health Organisation (WHO), the public health specialist agency established by the United Nations (UN) in 1948, launched the World Alliance for Patient Safety in 2004[102]. The World Alliance for Patient Safety then announced the First Global Patient Safety Challenge: *''Clean Care is Safe Care''* in October 2005, where Save Lives: Clean Your Hands initiative was produced[103]. The former global patient safety challenge was launched to tackle the issue of health care associated infection. In June 2008, the Second Global Patient Safety Challenge: *''Safe Surgery Saves Lives''* was launched with the development of the surgical safety checklist[104]. In March 2017, the Third Global Patient Safety Challenge: *''Medication Without Harm''* was launched, which emphasised polypharmacy, high risk situations (for example, high risk medication), and transitions of care as targets[3]. The three major topics covered by the WHO patient safety challenges were chosen due to the high prevalence of harm as a result of their inappropriate use. The WHO

also worked on other initiatives, including; the launching of the 5S project in 2006[105], the multi-professional patient safety curriculum guide that encouraged and promoted patient safety education in 2011, and the safe birth checklist in 2015. Furthermore, the WHO called for the first Global Ministerial Patient Safety Summit in 2016 in London[106]. In the second Global Ministerial Patient Safety Summit in 2017[107], in Bonn, Germany, the Third Patient Safety Challenge *''Medication Without Harm''* was launched[3].

Despite the launch of these organisations and publications in the field of patient safety over recent decades, adverse events are still common in healthcare globally[108,109]. As Schiff and Shojania (2021) identify patient safety as a *''successful social movement in healthcare''* from a qualitative point of view, but not as successful from a quantitative point of view[110]. That is the rationale behind the renewed focus on patient safety in the UK, with the launch of the Patient Safety Strategy in 2019[101], and worldwide by the launch of the WHO Global Patient Safety Action Plan 2021 – 2030[111].

2.2.4 Methods to study patient safety

Different data collection methods have been utilised to collect data related to the prevalence and causation of adverse events and MEs[112,113]. The chosen method may influence the rate and nature of events recorded, and combining methods may overcome some disadvantages of using particular methods alone[114]. Examples of some data collection methods, their definition and relative advantages and disadvantages are summarised below.

2.2.4.1 Retrospective chart review and trigger tool

Retrospective review of medical records has been widely used to collect patient safety data; it was the data collection method in the *Harvard Medical Practice Study*[78]. This method has the advantages of using already available data; however, the method is limited by the fact that medical records are sometimes incomplete, and data collection can be time-consuming[115,116]. Retrospective use of trigger tool has been used in patient safety research[117–119], which have the advantages of using few resources[120].

2.2.4.2 Patient source: patient reported events, complaints letters, malpractice claims and social media

Patient reported adverse events and complaints have recently been used to study patient safety. In his analysis, Zhu et al. (2011) found that patients can identify adverse events, and when these were reviewed by physicians, 71.2% of them were confirmed to be an actual

adverse event[121]. On reviewing patient reported hospital adverse events with medical record review, it was found that patients can identify more serious and preventable events[122]. A systematic review on the use of patient's complaints in healthcare found that the most common area of complaint was treatment followed by communication. To better utilise patient complaints, Reader and colleagues (2014) have developed a coding taxonomy[123]. A recent realist review by Van Dael et al. (2020) identifies the lack of strategic policy on complaints reporting and analysis[124].

Malpractice claims have also been used to study adverse events[125,126]. A study investigating malpractice claims in primary care in the USA found that 23% (n=5921/26,126) of claims were related to negligence, of these the most common causes were diagnosis error 34%, failure to supervise/monitor case (16%), improper performance (15%), and MEs (8%)[127]. Rothschild et al. (2002) have analysed 10 years' worth of medication related malpractice claims in the USA, state that malpractice claims could be a valuable source of severe ADEs in outpatient settings[128]. The advantage of this method includes the detection of latent errors; however they are limited by reporting bias[115]. Nevertheless, malpractice claims use in research is limited due to problems in coding and analyses of this data[115].

Data extracted from social media platforms have been used as a novel source to study medication safety issues[129]. The extraction of the data is via text mining methods[130]. This method has advantages, including large coverage, and the availability of sensitive data directly from patients[131]. However, this method of the collection includes limitations and challenges, including the large volume of the data that is hard to manage, social media bias, lack of patient's demographic details, privacy issues, and quality of the data (colloquial terms)[131,132].

2.2.4.3 Incident reports

2.2.4.3.1 Incident reporting – a brief history

Incident reporting is widely used in healthcare systems to learn from near misses and accidents. The United States Institute for Safe Medication Practice (ISMP) was the first to establish a national Medication Error Reporting Programme (MERP) in 1987[133]. Other programmes followed globally, including: the Advanced Incident Management System (AIMS) in Australia in 1998, the Canadian Medication Incident Reporting and Prevention System (CMIRPS) in 2002, and in 2003 the National Reporting and Learning System (NRLS) in the UK[133,134]. In the UK, the NRLS was launched by the National Patient Safety Agency (NPSA), who later made reporting of serious patient safety incidents a mandatory

contribution to health care organisations through the Serious Incident Reporting and Learning Framework (SIRL) in 2010[133]. From 2012, the NRLS was placed in control of National Health Service (NHS) England and NHS Improvement[135]. A new project to replace the NRLS, called Patient Safety Incident Management System (PSIMS), will formally launch the new service (Learn From Patient Safety Events (LFPSE)) in August 2022[136].

2.2.4.3.2 Incident reporting – opportunities and challenges

The NRLS is the world's largest and most comprehensive patient safety incident reporting system[137]. One of the core purposes of incident reporting systems like the NRLS is to inform safer clinical practice, and to this end, data from the NRLS has been used to produce regular reports and Patient Safety Alerts (PSAs)[138]. PSAs are issued by the Central Alerting System (CAS) and NHS in response to patterns of incident reporting considered at high risk, in order to warn others of these risks and provide guidance on preventing potential incidents[138]. One example of PSAs is Safer Lithium Therapy, in response to evidence of harm and fatalities due to (often preventable) lithium toxicity; as a result, lithium record and information packs (a 'purple book') are now issued and are used routinely in practice[139]. Data extracted from NRLS has also been used to describe the nature and patterns of reporting in several research papers covering different topics, including; medication incidents[140,141], anaesthesia patient safety incidents[142–144], insulin safety incidents[145], palliative care[146], primary care dentistry[147], diagnostic error in the emergency department[148], and paediatric immunisation patient safety incidents [149].

Incident reports can be used to support patient safety improvement by firstly highlighting unsafe practices and their causes[150–152], and secondly by initiating a broad in-depth investigation. However, there is debate regarding whether incident reporting has achieved its potential for health care improvement[150,153]. According to Argyris and Schon (1979)[154], addressing factors that lead to the occurrence of the incident will lead to *'single-loop learning'*, while addressing other organisational factors (including organisation objectives and policies) leads to *'double-loop learning'*. A recent systematic review commented that incident reporting systems could promote *'single-loop learning'*, which involves correcting errors by dealing with procedures and methods[155]. However, in their systematic review Stavropoulou and colleagues (2015)[155] reported that incident reports are not associated with double-loop learning, which supports culture change, as Drupsteen and Guldenmund (2014) [156]states *'Opportunities for double-loop learning are now often missed due to difficulties in the identification of organisational factors and managerial weaknesses that created the conditions for the event to occur'*.

Incident reporting has a role in improving safety, for example, where countries share their incident report data through their patient safety organisations to identify shared lessons[133]. Healthcare practitioners have also reported that incident reporting systems not only improve safety but also generate knowledge[157]. In addition, incident reports are considered a valuable source to monitor clinical practices[158], identify trends of incidents and their causes, support learning, and understand why unsafe care has occurred[159]. Howell and colleagues suggest that patient safety incident reports should not be used to assess hospital safety on how commonly patient safety incidents occur, but instead be used as a learning method[160]. This view is echoed in the Institute of Medicine in the *"To Err is Human"*[94] report which states that the aim of the reporting system is not data collection, but their object is to analyse data to prevent a future incident from occurring. Although incident reports yield the least number of safety incidents compared to other data collection methods (as the purpose is not to measure prevalence), it may yield more sensitive data which help to understand the nature and causes of events (to guide improvement).

Whilst incident reporting has a number of advantages as a method to study medication safety; it also experiences challenges[161]. One of these challenges is poor report quality, although other researchers argue the opposite; as Macrae (2015) stated, *''Improving the quality of incident data thus misses the purpose of reporting—triggering inquiry. The need for improved quality lies with the investigations, not with the reports themselves''*[150]. Other challenges include under reporting, and reporting bias. The under-reporting of patient safety incidents affects many countries and is caused by many barriers. A recent review of the literature concerning factors affecting patient safety incident reporting by Archer and colleagues (2017) found that fear of negative consequences (including fear of adverse consequences associated with incidents reports, fear of litigation, fear of blame, fear of judgment) were the most common barriers of incident reports[161]. This was followed by process and system of reporting (including time required to complete an incident report, the complexity of reporting process, lack of anonymity, reporting format), and incident characteristics (including the low level of harm incidents and unpreventable incidents)[161]. In addition, further barriers to report incidents includes, knowledge and skills (including lack of reporting clarity), work environment (including workload, and accessibility), organisation factors (including lack of feedback, and lack of positive reporting culture), team factors (including the impact of reporting on team relationship), and finally professional ethics[161].

2.2.4.3.3 Incident reports used in research

Incident reports are used in patient safety research to generate learning to find targets for interventions. Different methods are used to study incident reports, including quantitative methods, which are used to test associations among data using, for example, descriptive statistics (that explores the nature of events, and trends over time)[162]. Other methods are also used, for example, comparative analysis, root cause analysis and content analysis. Mixed methods approaches may include descriptive statistics and methods such as free text analysis[162]. Data retrieved from incident reports may be analysed using different approaches, including commonly used classifications (e.g. NRLS, the National Coordinating Council for Medication Error Reporting and Prevention "NCC MERP"); classification systems are the mechanisms to operationalise conceptual approaches and conceptual approaches (e.g. Reasons model of accident causation) which help to understand the origins of complex patient safety incidents[162]. Different patient safety incident classification framework has been utilised in research to code data, including the NRLS, the International Taxonomy of Medical Errors in Primary Care (LINNAEUS), the NCC MERP, and the Primary Care Patient Safety (PISA) classification framework. The PISA framework is specific for primary care.[162].

The PISA classification framework was developed by a team of researchers led by Prof Carson-Stevens by analysing national patient safety incidents from general practices in England and Wales[158]. The PISA study, funded by the NIHR, used data from the National Reporting and Learning System (NRLS), the largest study that characterises patient safety incidents in general practice worldwide[158]. The PISA framework is a classification inclusive of several coding frameworks aligned to major WHO International Classification of Patient Safety (ICPS) concepts. It has been empirically developed through a constant comparative method from clinician-led analysis of more than 80,000 patient safety incident reports. Previous studies have characterised the nature of patient safety incident data from the NRLS utilising the PISA framework to code the data including palliative care[146], primary care dentistry[147], diagnostic errors in the emergency department[148], and paediatric immunisation patient safety incidents [149].

2.2.5 Transitions of care as part of the patient safety agenda

Patient safety is well studied in hospital settings, followed by ambulatory / primary care settings[163–165]. However, recent attention has been drawn to patient safety at transitions of care due to the special characteristic of this phase. In 2016, the WHO has published a report highlighting transitions of care[166]. In addition, there have been national initiatives in

the UK to improve care transitions, including handover[167,168], and medication reconciliation[169]. Various methodologies have been utilised by researchers to investigate the prevalence, risk factors and the causes of patient safety at the transition of care, including incidents reports and malpractice claims[170,171] .

It is now well established that hospital discharge care transitions and post discharge phase are high risk areas. In addition, few studies have shown that communication of the discharge letter and the involvement of MEs to be associated with adverse events. What is less clear is the nature of these MEs post hospital discharge and their causes.

2.3 Medication safety – a patient safety priority

It has been highlighted in earlier sections 2.1 and 2.2 that medication is a key contributor to adverse events in health care, and is also a driver of transitions of care safety challenges. In addition, previous sections identified a specific focus on medication safety at transitions of care nationally in the UK and internationally.

2.3.1 Medication safety: definitions, evidence and consequences

Medication safety concerns any event during the four stages of the medication process, including prescribing, dispensing, administration and monitoring stage[172]. Medication safety includes, medication errors (MEs), adverse drug events (ADEs), and drug related problems (DRPs)[173] (Terminology in Table 2.2). Medication safety also includes medication discrepancies, which is part of MEs. Medication safety issues do not discriminate between patients residing in different health care settings. Different personnel might play a part in shaping the problem of medication safety, including prescribers via prescribing errors, nurses via administration errors, pharmacy staff via dispensing errors, and patients via medication non-adherence.

Table 2.2 – Terminology of medication safety terms

Term	Definition
Adverse drug events (ADEs)	*''An injury resulting from medical intervention related to drug"*[174]
Adverse drug reaction (ADRs)	*"A response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function"*[175]
Drug related problem (DRPs)	*''An event or circumstance involving medication therapy that actually or potentially interferes with an optimum outcome for a specific patient''*[176]
Medication errors (MEs)	*"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"*[177]
Medication discrepancies	*''Difference between medications taken by a patient using the most up to date list of prescribed medication from the GP and the medications on the hospital discharge letter''*[178]
Unintentional medication discrepancies (UMDs)	*''Unexplained differences in documented medication regimens across different cite of care.''*[179]

A systematic review and meta-analysis review by Panagioti (2019) for the General Medical Council on preventable patient harm across healthcare services found that medication related incidents were the most common causes of iatrogenic harm[80]. According to the National Patient Safety Agency (NPSA), a medication incident was the third most commonly reported type of incident during 2017 in England[180]. Eleven per cent of the incidents reported to the NPSA were medication related between April 2016 and June 2017[180]. According to Elliott, et al. (2019), it has been estimated that the annual cost of definitely preventable ADEs in England to be more than £98 million[181].

A large proportion of previous medication safety research has focused on hospital settings. Barker and colleagues (1962) published one of the earliest studies regarding medication safety in the 1960s[182]. Another early influential investigation of medication safety emerged during 1991 when Leape et al. (1991) published the findings of the second *Harvard Medical Practice Study*, reporting that drug complications were the most common type of adverse event across 51 hospitals at 19% of total adverse events[89]. Medications are a key contributor to in-hospital adverse events, as highlighted in Table 2.3.

Table 2.3 – Description of in adverse drug events (ADEs) in hospital settings

Description	Reference
ADEs as a proportion of adverse events	Drug or fluid related adverse events were the second most common type of adverse event in a national study in Canada. Here, it has been estimated as **23.6%** of the total rate of adverse events. (Baker, 2004)[93]
	A systematic review by De Vries (2008) found that **15.1%** of the total adverse event rates in hospitals are medication-related.[183]
	In a recent national study by Rafter (2017), medication related adverse events were the third most common adverse events in Irish hospitals.[184]
Preventability of ADEs	In 1995, Bates et al. published a paper in which they found that **28%** of adverse drug events in a hospital setting are preventable.[174]
ADEs causing hospital admission	Howard (2003) found that **4.3%** of hospitalisations in the UK were caused by preventable adverse drug events.[185]

Several studies have evaluated medication safety in ambulatory settings. Woods (2007) stated that 31.7% of ambulatory care adverse events in the USA are medication related, and 13.1% of ambulatory care preventable adverse events are medication related[163]. Furthermore, Gandhi (2003) found that the rate of adverse drug events was 25% in community settings in the USA[186]. In addition, a systematic review by Tache (2011) estimated that around 20.1% of patients taking medication in ambulatory settings experience adverse drug events[187]. Furthermore, Tache (2011) found that the most

common drug groups associated with adverse drug events are cardiovascular drugs, central nervous system drugs, anti-infective drugs and analgesic drugs[187]. A systematic review of 29 studies reporting the incident and nature of preventable adverse drug events (pADEs) in ambulatory care by Thomsen (2007) found that 86.5% of pADEs were caused by cardiovascular drugs, analgesics and hypoglycaemic agents together[188]. Moreover, Thomsen (2007) found that medication errors resulting in pADEs in community settings happened most commonly in the prescribing and monitoring stages[188]. Thus, previous research has well established the scale of medication related harm in secondary and primary care.

2.3.2 **Medication safety at the transition of care**

In March 2017, medication safety at the transfer of care was brought to global attention with the publication of the World Health Organization's (WHOs) Global Patient Safety Challenge: Medication Without Harm, as one of three priorities for action[3]. The ultimate goal of this WHO challenge is to reduce severe avoidable medication related harm globally by 50% in the next five years[3]. In addition, the WHO Global Patient Safety Action Plan, 2021 – 2030, published in August 2021 listed action points to direct the management of medication safety at transitions of care[111].

At transfer of care, it has been estimated that around 30-70% of patients may experience MEs or unintentional medication changes[169]. Different types of medication related problems can occur at and following the transfer of care, including medication errors, discrepancies, adverse drug events, non-adherence and inappropriate prescribing[189]. Medication discrepancies have been reported at all levels of the transition of care, whether it is transfer of care between facilities, different services within the same hospital, at admission or hospital discharge[189]. Medication discrepancies with potential for harm can easily lead to actual harm in certain circumstances[172]. Recent studies have observed that the proportion of ADE-related 30-day hospital readmissions from all potentially avoidable readmission was 13%, and 16% in the USA and the Netherlands respectively[190,191].

Elderly patients are at higher risk of DRPs, due to several factors, including age related changes to pharmacokinetic and pharmacodynamic, co-morbidities and polypharmacy[192–194]. Elderly patients are also at a higher risk of medication non-adherence[195,196], due to factors related to cognitive impairment and complex medication regimens[197]. Medication adherence can be adversely affected by care transition, with only 6.5% of discharged elderly patients in the USA reporting complete adherence to discharge medication post

discharge[198]. Evidence suggests that medication non-adherence is also common post hospital discharge, affecting between 40% and 55% of elderly patients 30 days post hospital discharge[196,199,200]. Compliance aids such as monitored dosage systems (MDS) have been suggested to improve patient adherence to medication, although their impact is unknown[201,202].

While there has been considerable research and reviews published in the area of medication related problems on admission to hospital, comparatively less attention has been given to hospital discharge[203–205]. However, the hospital discharge stage is not without medication risk, though evidence from the available literature is fragmented (see below sections). As it has been highlighted earlier that hospital discharge is a sensitive time for patients. Braund (2014) estimated that 25% of discharge prescriptions had drug related problems, and Westberg (2017) identified the highest severity of drug therapy problems following hospital discharge to be nonadherence and adverse drug reactions[206,207]. In addition, Coleman (2005) reported that the prevalence of post hospital medication discrepancies was 14%, with discrepancies caused by patient factors including nonadherence and financial barriers, as well as healthcare system factors including conflict information and incomplete discharge summaries[208].

2.3.3 Medication safety post hospital discharge: prevalence, nature, and risk factors

The published evidence indicates that a variety of drug related problems may occur following hospital discharge[209–211]. However, the extent and nature of DRPs, such as MEs and ADEs occurring at and following hospitalisation is not fully known due to fragmentation in the literature and a lack of systematic reviews into this topic. In two well-known but now potentially outdated studies from the USA, it was estimated that one in five patients experienced adverse drug events at the first month post discharge[2,6].

A review by Morath and colleagues (2017), which aimed to identify the risk factors of adverse health outcomes after hospital discharge that are potentially modifiable after pharmacist interventions, reported these to be diabetes mellitus, chronic obstructive pulmonary disease, obesity, smoking, and polypharmacy[212]. This means that identifying patients with these risk factors and directing them to receive pharmacist interventions should be encouraged to minimise the risk of harm. Elsewhere, earlier studies have explored risk factors for ADE post hospital discharge, where the number of medications, patient older age and hospital Length of Stay (LOS) was associated with higher risk[6,213–215].

In addition, age was also associated with a higher risk of patients experiencing at least one UMDs[215]. It has been found that the risk of ADE in patients discharged to home health care in the USA is higher than that in patients discharged to long-term care facilities[216].

There is little further published data on the risk factors and causes of medication safety challenges after hospital discharge. However, a number of scholars have evaluated the risk factors of medication related readmission[217–219]. A recent study in Sweden by Glans and colleagues (2021), has identified polypharmacy, medication changes during hospitalisation and comorbidities as increasing risk of medication related readmission (odds ratio (OR) 1.74 (95% CI 1.07-2.8, P=0.02), 1.63 (95% CI 1.05-1.25, P=0.002) and 1.15 (95% CI 1.03-2.5, P=0.03), respectively[220].

2.3.4 **Medication safety post hospital discharge: causes**

During the patient journey through the transitions of care cycle, when the patient first enters the cycle through hospital admission, they may experience medication changes and changes to their diagnosis and morbidities[221]. At the end of the cycle, at hospital discharge, the patient remains at risk of intentional and unintentional medication changes[222]. In order to capture and reduce the risk associated with these changes, medication reconciliation at transitions of care was implemented in 2003 to reduce medication errors when different healthcare providers are in charge of patient care[223,224].

Moreover, patients at post discharge stage are still recovering from their acute illness, where all these factors make this stage full of challenges[48]. In addition, family caregivers may feel unprepared for post hospital discharge medication management[45]. Many factors are combined that produce circumstances that may lead to problems at care transition, where poor communication may be found to be a key factor among them[12].

Medication safety issues at the care interface may often arise due to inadequate communication between healthcare providers and of information given to caregivers[69]. During hospitalisation, the patient's medication regimen may undergo several changes, where medications are stopped, replaced by a similar or an identical substance, undergo changes in terms of doses or frequency, and new medications may be started at the hospital[225]. These changes might lead to medication discrepancies between care boundaries. Patients at and beyond the point of hospital discharge are at risk of unique safety challenges due to the complex nature of the discharge process, where for example, discharge medications may frequently change[226]. Viktil et al., (2012) studied 105 patients

throughout their hospital stay and beyond, finding that drug regimens reported during hospitalisation of 90 of these patients were changed within 4-5 months of discharge by their General Practitioners (GPs) in Norway[227]. Viktil also found that on average, each study patient used 5.6 drugs on admission, had 4.4 drug changes while in hospital, used 7.6 drugs at discharge and finally had 3.4 drug changes within 4-5 months of discharge[227] . At discharge, healthcare providers may not adequately educate patients regarding medication changes, nor do they always contact patients' primary care providers effectively[228]. Himmel et al, (1996) followed up 130 patients after discharge and found that the GP received a detailed discharge letter with reasons for drug changes on discharge in only five patients from the study sample[229]. In an audit of 3444 discharged summaries in the UK, Hammad and colleagues, (2014) reported that only 49% of therapy change information was documented[230]. Moreover, patients may not always be followed up, as health care is very complex with lots of different agencies in the community[231]. These issues can increase the risk of communication failures and medication errors/harm.

The experience of understanding/managing their medicines at this time for patients can be chaotic, and patients may not always be told about the changes that were done on their medications[232]. Furthermore, patients may be unwell, with some experiencing life changing events that affect their attention and retention of information[233,234]. Then, at discharge, they may not be going back to their home, or they may need additional care. Patients have reported feeling overwhelmed at discharge by the education given to them regarding many topics including, activity level, diet, wound care, follow-up appointment and discharge medications[235,236]. This may lead to an incomplete understanding of discharge medications resulting in medication errors[237]. Their medications may also change at discharge, and the GP is not always given accurate and timely information about hospital admission[238]. Patient safety at discharge has been under-recognised as a researched topic in the medical domain research field. Healthcare providers report encountering recently discharged, confused patients that are uncertain about continuing medications prescribed before hospital admission or taking only the discharge medication regimen provided[239,240]. In Carpenter's, (2013) own words to describe this issue, "*When patients are discharged from the hospital, they may be uncertain about whether they should resume their previous medication regimen or only take the medication listed on their discharge instructions*"[241]. Unjustified medication at hospital discharge affects patient safety and comes with added financial burden[242].

2.3.5 Methods to study medication safety post hospital discharge

2.3.5.1 Retrospective chart review, and prospective study

Retrospective chart reviews and prospective data collection have been utilised to evaluate medication safety challenges post hospital discharge. Prospective data collection methods were also utilised using participant observation to describe visiting nurses medication management at patients home[243]. Bonaudo et al. (2018) evaluated UMDs post hospital discharge via comparing discharge prescription to the first prescription in primary care, and found it affected 14% of adult patients post hospital discharge in Italy[244]. Compared to prospective data collection, Schnipper et al. (2006) evaluated UMDs post hospital discharge via telephone follow-up interview and medical record review and found it affected 65% of adult patient post hospital discharge in the USA[245]. Although that these two referenced studies were in two different countries, with different healthcare systems.

Other outcomes have also shown variation in the rate based on the data collection forms. In their retrospective evaluation via screening case notes, Donovan et al. (2012) evaluated ADEs and found them to affect 19% of elderly patients post hospital discharge in the USA[246]. Compared to Parekh, et al. (2018) where they found that ADE affected 37% of elderly patients post hospital discharge in the UK using patient telephone interviews and GP records. These results do not mean that the rate is dependent on the data collection method, as these studies are different in many variables[247].

2.3.5.2 Patient source: complaints letters

A study using 1,110 patient complaints requested from NHS Digital from across England, UK found that problems occurred when patients entered and exited the healthcare system and considered them as ''blind spots''[248]. A ''blind spot'' was defined as a ''domain of individual or organisational functioning that is either unobservable or incorrectly observed''[248]. The team stated that complaints data may address one known incident report limitation, in that complaints provide a more complete picture of the events. It was noted that the problems related to hospital discharge, were mainly related to medication, side effects and premature hospital discharge. However, the paper fails to provide an in-depth analysis of the medication involved in the complaint letters[248].

2.3.5.3 Interviews

Qualitative data collection methods have been utilised with healthcare staff and patients to investigate medication related issues post hospital discharge. Examples of research that

utilised qualitative methods to collect data about medication safety post hospital discharge are summarised in Table 2.4. However, the majority of qualitative research in the area of medication safety post hospital discharge was with patients and caregivers using interviews and / or focus groups regarding their feedback of medication management post hospital discharge[70,249–253]. Studies with healthcare providers or patients designed to identify causes or contributory factors of medication safety challenges post hospital discharge appear more limited.

Table 2.4 – Qualitative studies on medication safety post hospital discharge

Topic	Method of data collection	Reference
Problems in medication management post hospital discharge	Focus group - Patients and physicians in primary and secondary care	240
Reasons of changes in drug therapy post hospital discharge	Interview - Patients and GPs	254
Communicating medication changes	Semi structure interview - Community pharmacists	239
Medication management care	Interview - Pharmacists	255
Barriers that delay resolving of medication discrepancies	Focus group - Nursing home staff	256

2.3.5.4 Incident reports - medication related incidents at transitions of care from secondary to primary care

A PSA on risks arising from the breakdown and failure to act on communication during handover at the time of discharge from secondary care was issued in 2014 by NHS England[257]. This alert reported on an analysis of 10,000 incidents reported to the NRLS between October 2012 and September 2013 about patient safety incidents related to discharge. The analysis included a review of a random 300 incidents occurring after discharge from acute and mental health settings, and showed that of 192 incidents that occurred after discharge from acute settings, medication was a key factor in 13% of them. Shortly after this PSA was published, Williams et al. (2015) investigated harms from discharge to primary care using patient safety incident reports from the NRLS (n=598)[258]. A mixed-methods analysis of all incident reports resulting in severe harm or death from 2003 to 2012, was analysed. Later, Scott et al. (2019) investigated safety incidents (n=278) related to transfer, handovers and discharges in the care of older adults, cardiology, orthopaedics and stroke over twelve months (2014-2015) in two NHS trusts in the UK[259]. In the same year Poldervaart et at. (2019) published an investigation into transitional safety incidents (n=548) from three hospitals and 56 affiliated general practices in the Netherlands from 2011 to 2015[170]. However, these studies investigated patient safety incidents more broadly with no detailed assessment of medication-related incidents. For

example, data were missing concerning the most common medications associated with the incident reports, the patients' age / health groups commonly affected, the common types of medication incident involved, and contributory factors of medication related incident post hospital discharge. In addition, in his study, Williams et al. (2015) extracted data from incident reports that led only to severe harm or death, and minor harm incidents were excluded, which could lead to limited insights into the safety challenges at this important transition[258], indeed, according to Heinrich's triangle, minor injuries and near-miss incidents help us better understand the safety issues to avoid fatality or major injury in the future[260,261]. Finally, Scott et al. (2019) involved two NHS trusts[259], with limited opportunities for national learning, and Williams et al. (2015), although being on a national level[258], reviewed incidents reported between 2003 to 2012, which is now outdated and given incident reporting was compulsory for serious or fatal incidents since 2010, there is a possibility that more recent data contains more detail/opportunity for learning.

2.3.6 Medication safety post hospital discharge: World Health Organisation policy documents

There are a number of documents published by the WHO that provided recommendations regarding reducing MEs at the transfer of care (a summary of the policy documents is found in Table 2.5). Despite the presence of these quality standard documents, there is little published research that focuses on exploring the burden of medication errors and associated harm resulting from transitions of care from hospital to community settings. A systematic review of literature in the field of the transition of care will enable us to see whether all the earlier policy documents' recommendations have influenced discharge medication safety over the years.

Table 2.5– Summary of transition of care policy documents by the WHO

Policy document	Recommendations
"Assuring medication accuracy a transition of care" (2007)[262]	• Use a standardised system to collect and document patients' medication information. • Ensure having clear policy and procedure in place regarding having patient medication list being displayed in a consistence, highly visible location. • Incorporate medication reconciliation training into the education curriculum and orientation for healthcare providers.
''Transitions of care'' - Technical series on safer primary care (2016)[166]	• Involve patient in the process of medication reconciliation
''Medication safety at transitions of care document'' - Technical report (2019)[263]	• Patient and family empowerment to participate actively in their medication management. • Target medication reconciliation to high risk patients (elderly, polypharmacy, multimorbidity) • Use process and outcome measure to monitor medication safety.

2.3.7 Interventions to improve medication safety during hospital discharge transitions: what do we know?

There have been a number of published studies and reviews reporting initiatives to improve medication safety and reduce ADEs during the transition of care, including pre discharge and post discharge services[264–266]. Pre discharge services have included medication reconciliation and the use of the multidisciplinary team, while the post discharge services include medication reconciliation post discharge, Information Technology (IT) based interventions, Medicine Use Review (MUR), and New Medicine Service (NMS)[267].

Medication reconciliation is defined as *''a method by which healthcare providers identify the most accurate and up-to-date list of medications that the patient is currently taking, and compare it to what is currently prescribed to identify discrepancies and optimise therapy''*[268]. It has been used to avoid and ameliorate medication errors during the transition of care. A systematic review of 18 studies published by Kwan et al. in 2013 found that medication reconciliation alone does not reduce clinically significant unintentional discrepancies, post discharge hospital readmission or emergency department visits[269]. In addition, a recent meta-analysis of 14 studies on the effectiveness of pharmacist-led medication reconciliation in the community after hospital discharge found evidence of resolving medication discrepancies, but the impact on patient outcomes was not consistent[270]. Similar findings were presented in two systematic reviews and meta-analyses[266,271], that the use of electronic medication reconciliation interventions at the transition of care do not have a consistent effect on reducing the number of patients with

unintentional discrepancies. The latter indicates that more evaluation of the impact of digital technology on medication discrepancies must be completed.

Most research evaluating interventions designed to improve medication management post hospital discharge targeted other outcomes than MEs/ ADEs (for example, impact of interventions to improve the communication of discharge letters on hospital readmission). A systematic review and meta-analysis of 19 Randomised Controlled Trials (RCT) by Becker et al. (2021) found that interventions to improve communication post hospital discharge significantly reduces the rate of hospital readmission[272]. Moreover, a systematic review was published by Motamedi in 2011, which aimed to examine the efficacy of computer-enabled discharge communication interventions on mortality, readmission, adverse events, timeliness, accuracy, quality/completeness and physician/patient satisfaction[273]. Motamedi included 12 unique studies and concluded that this intervention reduces medical errors/ adverse events and improves patient and physician satisfaction, but the effects on mortality and readmission were less commonly reported[273]. In contrast, a review by Mills and others (2016) found that an electronic interim discharge solution did not reduce prescribing errors compared to the traditional handwritten method (n=4)[11]. Furthermore, a systematic review of cost and cost-effectiveness of electronic discharge communications, concluded that a conclusion could not be made based on the available evidence, and further work is warranted in this area[274].

Evidence presented earlier showed that communication between hospital and community pharmacies is not optimal, which may compromise medication safety[67,239,275]. The Royal Pharmaceutical Society (RPS) has recommended that community pharmacies access patient health records[276]. However, community pharmacists showed some conservative thoughts regarding sharing electronic patient record[10,277], which highlight that implementing such interventions may be complicated and may not show benefit unless everyone's views are considered. A recent randomised controlled study (RCT) published by Gurwitz et al. (2021) reported that clinical pharmacist intervention directed for patients discharged with high-risk medication (anticoagulant, diabetes agents, opioid) in the USA did not show a reduction in the rate of ADEs post hospital discharge[278].

Moreover, no conclusion was drawn from a systematic review of 47 studies reporting hospital-initiated transitional care interventions, including predischarge interventions (e.g. medication reconciliation, dedicated transition provider, multidisciplinary discharge planning team) and post discharge interventions (e.g. medication reconciliation, follow-up

telephone call) as a patient safety strategy, due to the strength of the evidence[279]. A similar conclusion was reached in another review published in 2007 [280]. In addition, a review of post hospital discharge intervention to improve elderly patient safety recommends that future interventions must have a multicomponent approach[281]. A systematic review and meta-analysis by Daliri et al. (2021) on the impact of medication related interventions (mainly patient education and medication reconciliation) delivered in hospital and following discharge, found them to have an effect on hospital readmission but not medication related problems and medication adherence[264]. It seems that the lack of interventions impact on medication safety post hospital discharge may be attributed to the lack of theoretical understanding of contributory factors (section 2.3.3) and causes (section 2.3.4) of medication safety challenges post hospital discharge, which could inform the design of robust interventional studies[282,283]. In addition, there is a lack of process evaluation of interventions which could enable the understanding of why interventions do/don't work[284].

2.4 The context for the United Kingdom

2.4.1 The National Health Services (NHS) in the United Kingdom: brief overview

The National Health Service (NHS) founded in 1948, provides health care services in the UK, including England, Wales, Scotland, and Northern Ireland[285]. The NHS was ranked 16th among 35 European countries based on health consumer index[286], and 23rd among 195 countries around the world based on access to care and quality of care[287]. NHS funding and the number of GPs were at the top of the political agenda in the UK general election in 2019[288]. Recently in 2020, there have been two major obstacles that impacted the NHS. The first obstacle was the COVID-19 pandemic due to the high demand, staff/ devices shortage and waiting time for non-COVID-19 patients[289]. The second obstacle was Brexit[290–292], with 5.4% (n=70,000) (as of September 2021) of the NHS workforce are from the European Union, the NHS funding was affected due to the change in the economy that occurred due to Brexit, and the access to medicines and medical devices that have been affected as results of Brexit[293].

In 2015, Health Watch England published a report, *''Safely Home: what happens when people leave hospital and care settings?''* highlighting the lack of support that patients may receive after hospital discharge[294]. In addition, a report was published by the Health Inspectorate Wales in August 2018 titled *"Patient Discharge from Hospital to General Practice: Thematic Report 2017-2018"*[295]. The report highlighted that hospital discharge

accounts for 11% of patient safety incidents in Wales and England during the period April 2016 – March 2017. Moreover, the report identified that the quality of patient discharge from hospital to community settings is poor from different stakeholders' perspectives[295].

2.4.2 Medication safety post hospital discharge: policy documents

There are a number of organisations that provide recommendations regarding reducing medication errors at the transfer of care (Summary of the policy documents is found in Table 2.6). Despite these quality standard documents, there is little published research that focuses on exploring the burden of medication errors resulting from transitions of care from hospital to community settings. A systematic review of literature in the field of the transition of care will enable us to see whether all the earlier policy documents' recommendations have influenced discharge medication safety over the years.

Table 2.6– Summary of transition of care policy documents in the United Kingdom

Policy document	Scope	Recommendations
National Health Service - National Prescribing Centre (NHS-NPC) *"Medicine Reconciliation : A Guide to Implementation"* **(2008)**[27]	• National standard for information communication at care transition • Medication reconciliation process in details • Key skills for medication reconciliation	• Advice on proper implementation of medication reconciliation • Monitoring implementation – impact assessment and process measures
Royal Pharmaceutical Society (RPS) *"Keeping Patient Safe at Transfer of Care"* **(2012)**[169]	• Older patients and patients with long term conditions are at higher risk at transfer of care • Risk of miscommunication and unintentional changes at transfer of care • RPS encourage healthcare professionals to take responsibility for the transfer of medication information • RPS encourage the development of a common dataset to support the transfer of patients' medication information at transfer of care • RPS encourage patients to have active participation in patient groups to understand their medication in order to have safe transfer of care	• Advice on making the best use of technology • Advice that all community pharmacies should have NHS.net website • Advice on regular auditing • Gave recommendation on core content of records for medicines when patient transfer care providers • Core points for professionals: 1. Patient information about medication should be accurately recorded 2. Confirm that all patient information is recorded when taking over the care of new patient 3. Patient, family and providers must actively know and participate in the process of medication reconciliation 4. Information about medication should be communicated in a way that is accurate, safe and ideally electronically at transfer of acre • Core points for organisations: 1. Ensure safe system in place to transfer patient information 2. Monitor and audit transfer of patient information at transition of care 3. Encourage sharing good and poor practice to encourage a safety culture
Scottish Intercollegiate Guidelines Network (SIGN) *"The SIGN Discharge Document"* **(2012)**[296]	• Provides a standard, minimum dataset, template for discharge documents • Use of electronic means for sending discharge document • Not for patients discharged from a psychiatric care	• Advice of timely sending the discharge document; immediate (core) discharge document should be sent on the day of discharge and (extended) discharge summary should be sent within seven days of discharge. • Medication reconciliation at discharge • Sharing discharge document with patient's community pharmacist, in accordance with local protocol • Consultation or senior doctor sign-off discharge document

Policy document	Scope	Recommendations
		• Advice of accurately reporting all diagnoses, operation and procedure relevant to patient admission • Work with e-Health lead at healthcare improvement Scotland to support the implementation of the SIGN discharge document template • Awareness-raising activities • Audit tools for healthcare professionals
National Health Service (NHS) England *"Patient Safety Alert on risks arising from breakdown and failure to act on communication during handover at the time of discharge from secondary care"* **(2014)**[297]	• National Reporting and Learning System (NRLS) has received around 10,000 reports of patient safety incidents related to discharge • Herein, communication at handover accounted of around 33% of the 10,000 incidents report received • Incidents lead to harm and death	• Ask NHS organisations to: 1. Identify any work that was undertaking to ensue communication information transferred on discharge to primary care, community and social care is safe and timely. This information needs to be shared with the NHS using best practice template 2. Identify a person within the organisation to be the link with NHS England 3. Participate in a safety improvement at discharge related questionnaire 4. Share this patient safety alert with the main voluntary sector organisations that the organisation work with on discharge 5. Encourage staff to attend webinars at the Patient Safety First Website
National Institute for Health and Care Excellence (NICE) *"Medicine Optimisation: the Safe and Effective use of Medicines to Enable the Best Possible Outcomes"* **(2015)**[298]	• Safe and effective use of medication • Relevant information that should be shared at transfer of care	• Recommendation on medicines-related communication system when patients move from one care setting to another • Medication reconciliation • Medication review • Send discharge letter to patient' community pharmacy
Royal College of Physician (RCP) *''Medication safety at hospital discharge: improvement guide and resource''* **(2021)**[299]	• Quality improvement guide	• Medication reconciliation • Patient and family involvement • Medication optimisation

2.4.3 Strategies in use across National Health Service (NHS) hospitals in the United Kingdom to reduce medication safety incidents following hospital discharge.

In the UK, when patients are discharged from the hospital, their care will usually be transferred back to their primary care physician, where they are registered[300]. Herein, hospital stay information will be communicated to the primary care physician via two discharge documents; one is an immediate discharge document that is for uncomplicated cases and is sent on the day of discharge[296]. While the other discharge document is a discharge summary that ideally is sent out within a week of hospital discharge[296]. The poorly affiliated nature between healthcare providers across different settings makes the transition of care a fertile ground for medication errors.

Interventions have been evaluated and/or introduced into clinical practice in order to improve medication safety and reduce adverse events related to the transition of care[301]. These provided by the NHS in the UK include New Medicines Service (NMS), discharge counselling by the pharmacist, telephone helpline and post discharge pharmacist follow-up (e.g. phone call)[301]. However, the effect of these services on patient safety is not consistent. A recent review of Medicine Use Review (MUR) and NMR services provided by community pharmacists in the UK found that service efficacy and patient related outcomes were rarely evaluated in interventional studies[302].

In 2000, Sexton and colleagues conducted a national survey of 163 chief pharmacists in UK trusts to identify services that hospital pharmacists provided to facilitate seamless care post discharge[301]. There was a wide reported variation in services, including discharge counselling by a pharmacist, copy medication records to patients, and telephone helplines[301]. Since this survey was published in 2000, interventions to contain the issue of medication safety post hospital discharge has been attracting a lot of interest, yet based on my knowledge, no recent national survey was recently published.

Technology has more recently received a wider recognition as a tool to improve medication safety at care transfer, including E-mail and using electronic referral system interventions[303–306]. At hospital discharge, 'Transfer of Care Around Medicines' (TCAM) interventions are undergoing widespread adoption in UK hospital care, particularly after the 'Discharge Medicines Service' (DMS) (similar to TCAM service) became an essential service in the community pharmacy contractual framework in February 2021[307]. It involves using a dedicated e-referral tool (for example, within the PharmOutcomes™ platform[308]) to

send timely discharge letters and sharing discharge documents with a named community pharmacy, to improve medication safety. There is emerging evidence of the impact of such TCAM and related interventions in the UK. A qualitative evaluation by Ferguson and colleagues (2018), including 26 interviews with hospital/ community pharmacists, reported that pharmacists believed that the service implemented in one trust had the potential to reduce human errors and make communication with the general practitioner (GP) better[309]. Mills and colleagues (2017) reported that UK hospital staff (including doctors, pharmacists and nurses) perceived that a TCAM service improved patient safety and challenged staff to improve the clarity and completeness of their documented activity following implementation[310]. A similar service was implemented in Leeds[311], UK, using the Connect with Pharmacy project and in West Lancashire, UK, using the 'Refer to Pharmacy' project. Nazar and colleagues (2016) evaluated a similar service in the North East of England and indicated that referral had a positive effect on hospital readmission rate and length of hospital stay[312]. However, the main weakness of Nazar's study is the outcome of interest which was all cause readmission, rather than medication related readmission ,and the failure to reach a significant powered sample size, including 1,386 patients where only 501 had received community pharmacy follow-up and had a rate of readmission of 12.7% (n=64/501) within 90 days of hospital discharge which was lower than those who did not receive community pharmacy follow-up (35%, n=309/885).

Currently available studies which have evaluated the impact of TCAM have focused on evaluating service utilisation/experiences or all-cause readmissions[312,313]. Such approaches, however, have failed to address the effect on medication safety directly, which is one of the primary aims of the service. There has been a powerful argument about targeted surveillance, as Shojania and Thomas (2013) commented *'Detecting the modest improvements associated with most interventions will require targeted surveillance for the events targeted by effective interventions'*[108].

2.5 Conclusion

This chapter has highlighted patient safety challenges associated with different levels of transition of care, with emphasise on DRP after hospital discharge. This chapter has listed different methods that were utilised to study DRP after hospital discharge. The following chapter, Chapter Three, summarised the evidence presented in this chapter and explained the rationale of the PhD programme.

Chapter Three: PhD Thesis Aim and Objectives

3.1 Rationale of PhD programme

In recent years there has been a growing body of research on medication errors (MEs) and medication related harm (adverse drug events or ADEs) at the transition of care. Admission to hospital has been the subject of considerable original research and systematic reviews[203–205,314]. Numerous literature reviews and studies have investigated the frequency of medication safety issues at the point a patient is discharged from the hospital (e.g. comparing hospital discharge prescription with inpatient drug chart, or medication reconciliation at discharge)[222,315,316], and reported on the prevalence and nature of medication discrepancies[67,316,317], medication errors, and adverse drug events[33,210,318]. However, the epidemiology and aetiology of DRPs post hospital discharge transitions are comparatively less well understood, with fragmented data starting to emerge. One review paper published in 2010 discussed drug related problems post hospital discharge in elderly patients, but failed to provide the prevalence of medication safety challenges, including medication errors, adverse drug events and unintentional medication discrepancies[319]. In addition, our understanding of the number and types of studies that have investigated medication safety issues immediately following hospital discharge is limited as to our knowledge; there is no available review about this topic. Moreover, Kwan (2013) had systematically reviewed literature about patient safety (ADEs) during the transition of care but relied on medication reconciliation as the only method for data collection[9].

3.1.1 Lack of synthesis of collective knowledge of medication safety post hospital discharge

A comprehensive review of the literature has not previously been undertaken of all types of medication related harm and errors (including discrepancies) following the point of discharge and focusing on patients in the community in the post discharge period. Systematic reviews are known to be helpful in informing guidelines, policy and future research goals[320]. In virtue of the lack of collective knowledge, a systematic review, which is on top of the hierarchy of evidence, is needed to identify the prevalence, nature, and severity of medication error and medication related harm immediately following the transfer of care between hospitals to community settings. The outputs from a systematic review will help researchers and healthcare decision-makers direct limited resources towards the areas of most critical need in the interest of understanding and improving medication safety risks[321]. Several published systematic reviews in the field of medication safety focussed on different stages of the patient journey or speciality and provided foundation data via describing the prevalence of adverse drug events[183,187,188,322–325], and

medication errors[204,325–327]. Table 3.1 lists examples of systematic reviews that evaluated ADEs and MEs. A comprehensive review is therefore needed to determine, with more confidence, the epidemiology, nature, and severity of medication safety issues post hospital discharge to select targets for remedial intervention and determine whether further research is needed to better quantify the risks in the UK and elsewhere. A systematic review of international literature using bibliographic databases and grey literature may facilitate deeper insights of the problem worldwide when compared to using national databases (e.g. Clinical Practice Research Datalink (CPRD), The Secure Anonymised Information Linkage (SAIL Databank)). The use of such databases is limited due to data protection access restrictions for free text GP consultation data and discharge summary letters, making it difficult to identify the rate of ME and ADEs post hospital discharge.

Table 3.1 – Examples of medication safety systematic reviews

	Topic
Adverse drug events (ADEs)	Paediatrics[324]
	Mental health hospital[325]
	Intensive care[323]
	Secondary care hospital[183]
	Ambulatory care[187,188,322](in the community, not focus on the transfer of care)
Medication errors (MEs)	Paediatrics[326]
	Mental health hospital[325]
	Elderly[327]
	Hospital admission[204]

3.1.2 Lack of understanding of causes and contributory factors of medication safety post hospital discharge: leading to ineffective interventions

Sections 2.3.3 and 2.3.5 identified that previous studies have not specifically evaluated the causes and contributory factors of medication safety challenges post hospital discharge. Although Chapter One made reference to potential contributory factors such as medication changes during admission and communication problems in discharge letters, evidence presented in Chapter Two revealed that previous studies have examined the causes/factors behind more general patient safety incidents post discharge without focusing on medication, or explored potential contributory factors without directly linking them to the occurrence of ME/ADE. Our limited knowledge of the causes of such events may explain the lack of consistent impact of several interventions on reducing medication safety challenges post hospital discharge. It is therefore crucial to explore in-depth and at scale the aetiology of medication errors and harm that occurs post hospital discharge in order to develop theory-driven interventions suitable for use across the health service. An analysis of national patient safety incident report data would be suitable to address this need by capturing the nature of and contributory factors associated with medication related

incidents post hospital discharge. This method allows identification of the full range of contributory factors from national data with learning applied across multiple organisations; smaller local studies may miss important contributory factors or the full range of error types, and limit learning to only that context. However, one problem with using incident report data is the lack of a detailed description of the incident and the understanding of the contributory factors that qualitative data (using interviews, for example) can provide. Despite this problem, incident report data have been utilised to change practice nationally [139]. In addition, as interventions are being rolled out nationally (for example, the Discharge Medicines Service (DSM)) to address medication safety post hospital discharge, we need to examine causation at this level to direct these efforts.

3.1.3 Lack of constructive evaluation of a newly implemented national service in the United Kingdom aimed to improve medication safety post hospital discharge

Section 2.4.3 reported that many studies evaluating interventions targeting medication safety post hospital discharge, including the TCAM intervention, focus on the impact of the outcome ''all cause readmission'' which may lack sensitivity to medication events. As Shojania and Thomas (2013) argued about the importance of adopting targeted surveillance *'Showing the benefits of an effective hand-hygiene campaign, requires focused surveillance of healthcare associated infections. Periodic application of a general trigger tool will not have the power to detect to changes in infections. And the overall adverse event rate will go down only if this hospital has also implemented effective strategies targeting multiple other event types'*[108]. Thus, a targeted assessment of the impact of TCAM intervention on carefully selected measures that reflect the intended outcome of the service (including unintentional medication discrepancies) is needed alongside concurrent service utilisation work to explore service uptake and experience, and to optimise future implementation and sustainable utilisation. Service utilisation studies are important because impact is dependent on the extent of a service embedding in the social fabric of the organisation. Studying service utilisation can be completed using staff interviews to explore experiences and perceptions, and using electronic records to capture intervention delivery at scale. Publications that concentrate on evaluating pharmacy service utilisation more frequently examine records of interventions made and stakeholder perspectives[328]. Studying service utilisation will provide context to interpret service impact study results. In addition, results from a service utilisation study will identify targets to improve the service, for example, if greater service embedding was following certain events. As Peter Drucker,

modern business management inventor, states: *''If you can not measure it, you can not improve it''*[329]. Furthermore, according to the Medical Research Council (MRC) guidance for evaluating complex interventions, it is recommended to evaluate both intervention process and outcomes[330]. Thus, evaluating the utilisation and impact of the TCAM service is particularly important given the rollout of the DMS in England, and the increased focus on medication safety at the transfer of care worldwide[3].

3.2 Aim of PhD programme

The overall aim of this PhD programme was to generate new evidence concerning the epidemiology, and aetiology of ME/ADE at the post-hospital discharge care transition alongside the impact of the TCAM remedial interventions in addressing these outcomes, and to use these findings to create recommendations for future policy, clinical practice and research to support improvement in medication safety at this crucial stage of the patients' health care journey. The PhD programme has the following objectives:

3.3 Objectives of PhD programme

1. Comprehensively identify and appraise international published evidence to determine the frequency and nature of medication errors and medication related harm following hospital discharge using a systematic review, (Chapter Four)
2. Explore in-depth at a national level the nature and contributory factors influencing medication errors and related harm occurring following the transition of care from secondary to primary care using incident report data, (Chapter Five)
3. Evaluate the utilisation (using PharmOutcomes activity data) and impact on medication errors and drug related harm of a TCAM service for patients discharged from acute hospital to primary care in order to inform national roll-out and optimal ongoing use in the NHS, and (Chapter Six)
4. Generate a policy, research and clinical practice action agenda to drive improvement in medication safety at this crucial care transition point. (Chapter Seven)

Chapter Four: Prevalence and Nature of Medication Errors and Medication Related Harm Immediately Following Discharge from Hospital to Community Settings: a Systematic Review

4.1 Introduction

Chapter Two has established the importance of studying transition of care as a patient safety improvement topic. Transitions of care can be defined as *"changes in the level, location, or providers of care as patients move within the healthcare system"*[28]. They have been associated with an increased risk of iatrogenic harm, including medication errors (MEs), and missed test results [33]. As healthcare providers may be poorly affiliated across care boundaries, miscommunication during handoff makes transition of care a fertile ground for MEs and preventable harm[331]. In March 2017, the burden of risk associated with medication safety at transfer of care was brought to the global attention with the publication of the World Health Organization's (WHOs) Third Global Patient Safety Challenge: Medication Without Harm, where transitions featured as one of three priorities for action[3].

Medication safety challenges at the point of hospital admission have been well documented [203,205], but these issues may also occur shortly after hospital discharge and have been comparatively less well studied. The time period immediately following hospital discharge can be a challenging time for patients, both in terms of safety but also socially and emotionally, when patients may be anxious and suffer from functional impairment[332]. This, in turn, may have a negative impact on medication adherence, and may increase the risk of adverse drug events (ADEs) [228,250]. Medication regimens are often known to undergo significant changes during hospitalisation, where medications may be stopped, replaced, undergo changes in doses or frequency, and new medications may be initiated[225]. Communication gaps may compound risk and include delayed/lack of discharge letters, insufficient monitoring plans[4,331], and incomplete or poor-quality discharge summaries[12,297]. Recent evidence indicates that adverse drug reaction (ADR)-related hospital readmissions occur with a median rate of 20% of patients [interquartile range (IQR) 7-23] (n=4), and ADE related hospital readmissions with a rate of 13% (n=1)[333]. Unjustified medication at hospital discharge may not only affect patient safety but may also be associated with a high financial burden[242].

There is an emerging body of literature that reports on the prevalence and nature of MEs and ADEs[334], as well as medication discrepancies[67,316,317] at the point of hospital discharge (i.e. before patients return home). The collective understanding from available studies investigating the burden of MEs and ADEs in the period following hospital discharge to the community is limited, due in part to fragmentation of the literature and there being no up-

to-date published systematic reviews in this topic across all patient groups. One previous systematic review (included 20 studies) of drug related problems occurring post hospital discharge in elderly populations was published almost 10 years ago [319], and another from 2018 focused on medication related harm also in elderly populations [335]. Given the level of interest in this stage of the patient journey amongst health leaders[169] and as new studies emerge in the field[211,247], there is a need to identify and collectively appraise global evidence on the burden and nature of MEs/ADEs post hospital discharge across populations. This is to determine whether further epidemiological work is required, and to best inform the development of remedial interventions and advance the WHO patient safety agenda.

4.2 Aim and objectives

This systematic review aimed to comprehensively identify and appraise international published evidence to determine the frequency and nature of medication errors and medication related harm following hospital discharge

The objectives of this study are as follows:

1- Develop a systematic review protocol according to international standards (PRISMA) in order to describe inclusion criteria clearly and follow transparent search and data extraction processes.
2- Determine the rate of MEs and ADEs during the immediate post hospital discharge period to community settings.
3- Determine the nature of MEs and ADEs in terms of type and severity, and to identify which type of medication error/harm are most common and which are associated with most actual/potential harm following transfer of care from hospital to community settings.
4- Assess the quality of retrieved papers that would be included in the systematic review.
5- Produce recommendations for further study based of the results on the systematic review.

4.3 Methods

This systematic review follows the criteria specified in "Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA)", 2015 statement[336]. A PRISMA checklist is included in Appendix 2.

4.3.1 Search Strategy

Ten electronic databases were searched: MEDLINE, EMBASE, International Pharmaceutical Abstracts (IPA), Health Management Information Consortium (HMIC), PsycINFO, Cochrane Database of Systematic Reviews (CDSR), Cochrane Central Register of Controlled Trials (CENTRAL), Database of Abstracts of Reviews of Effects (DARE), Cumulative Index to Nursing and Allied Health Literature (CINAHL) and Web of Science[337,338]. A grey literature search was completed using Open Grey via the website http://www.opengrey.eu which is based on the "System for Information on Grey Literature in Europe" (SIGLE) database. The grey literature includes unpublished research (e.g. dissertations or theses), published non-research literature (e.g. government reports or newsletters), studies in progress and recently published studies pending to be referenced in databases[339].

The search was limited to between January 1990 to March 2019. The search strategy was developed using terms related to three categories, including:

- **Epidemiology:** incidence, prevalence, frequency, rate, number, epidemiology, epidemiological studies, descriptive statistics.
- **Process:** patient transfer, patient discharge, hospital discharge, (discharge adj3 hospital), care transition, transitional care, (transition adj2 care), (follow adj2 discharge), continuity of patient care, (post adj2 discharge), seamless care, care interface, hospital readmission.
- **Outcome:** Drug related side effect and adverse drug reaction, medical error, medication error, adverse drug event, adverse drug reaction, medication related problem, drug related problem, drug related adverse event, drug safety, medication safety, drug error, prescription error, prescribing error, administration error, dispensing error, transcription error, therapeutic error, treatment error, discrepancy, near miss, omission, adverse drug incident, adverse drug outcome, adverse drug effect, adverse medication event, adverse medication reaction, adverse medication incident, adverse medication outcome, pharma* intervention*,

adverse medication effect, (safety or harm) AND (medicine or medicating or treatment or therapy or drug or prescription).

All search terms in each category were combined using the Boolean operator (OR), followed by combining all the three categories using the Boolean operator (AND). The search included the following keywords and their synonyms: ('rate' OR 'prevalen*') AND ('hospital discharge*' OR 'care transition*') AND ('medication error*' OR 'adverse drug event*'). Search terms underwent minor modification to suit different databases. An example of a search strategy is included in Appendix 3.

A variety of outcome related terms were used in order to capture a range of academic published papers. This reflects the findings of previous systematic reviews of medication errors and ADEs, which describe a variety of definitions used to describe these outcomes[340–342].

Golder et al, (2013), assessed individual search terms describing adverse effects in MEDLINE and EMBASE, and found that certain Medical Subject Headings (MESH) terms and EMTREE terms had very low sensitivity in detecting adverse drug event or adverse drug reaction related studies, and the terms were; toxicity, contraindication, adverse drug reactions reporting system, ADRs, drug monitoring, adverse adj2 (outcome or reaction), undesirable effect[343]. This was the rationale for not using these terms in this search strategy.

4.3.2 **Definitions**

Studies that reported events broadly meeting the adapted outcome definitions (see Table 4.1) were included. Unintentional medication discrepancies (UMDs) were considered MEs but were reported separately. Studies reporting prescribing errors and medication administration errors were considered MEs. Studies evaluating drug related problems were included if they explicitly reported distinct ME or drug related harm data and rates were able to be subsequently extracted. Studies evaluating medication adherence were not included as the focus was on iatrogenic complications. The patient populations were considered to be/include the elderly if studies predominantly included patients with chronological age ≥60 years, or if studies said/implied they were studying elderly patients[344,345].

A common methodology investigating transitions of care involves utilizing medication reconciliation to assess medication discrepancies. Some researchers use discrepancies instead of ME at transition of care, where discrepancies indicate a lack of agreement between different medication regimens[215,244]. Thus, for the review, an explicit criteria for studies were set to detect medication discrepancies, where only unintentional medication discrepancies (UMD) were considered a medication error as most of the literature in the field of medication reconciliation are highly diverse in terms of method and outcome measures[346]. Thus, the outcome of interest was studies that report UMD with a least one clinical independent assessor, other than the person who completed the medication reconciliation (or clearly identified by the person completing the medicines reconciliation by contacting the prescriber), to distinguish between intentional and unintentional discrepancies[215,244]. The rationale for these criteria is that the review aimed to not overestimate the rate of ME if included a study that did not incorporate a panel or any healthcare provider to differentiate intentional from nonintentional discrepancies.

Table 4.1 - Definitions

Term	Definition
Adverse Drug Reactions (ADRs)	*"A response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function."* **(World Health Organisation (WHO) Technical Report No 498 (1972))**[175]
Adverse Drug Events (ADEs)	*"An Injury resulting from medical intervention related to drug"* **(Bates et al., 1995)**[174]
Preventable Adverse Drug Events (pADEs)	*"Harm caused by the use of a drug as a result of an error".* **National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP, 2015)** [347]
Medication Errors (MEs)	*''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''* **(NCC MERP, 2015)** [177]
Unintentional Medication Discrepancies (UMD)	*''Difference between medications taken by a patient prior to admission and medications ordered in the hospital''* **(Pippins et al, 2008)**[178]**.** Pippins (2008) stated that discrepancies are either intentional (not an error, either documented or not) or unintentional (medication error). For this study unintentional medication discrepancies were included only, using an adapted definition by **Mueller et al (2012)**[179] *"unexplained differences in documented medication regimens across different cite of care".*

4.3.3 **Inclusion Criteria**

Quantitative studies that reported a rate of MEs, UMDs, and/or medication related harm, including ADRs and/or ADEs identified during the time period following hospital discharge to community settings (or provided enough data to calculate a rate manually) were sought. Studies were included if data were collected after discharge to community settings, including the patients' own home, care/nursing homes, rehabilitation / intermediate care facilities and other long-term care facilities. Interventional studies were only included if they provided baseline data on outcome rates. Grey literature and all original peer-reviewed research except review and editorial articles were included. The reference lists of relevant reviews/editorials were screened for additional studies. Conference abstracts were included only if they provided suitable data regarding ME/UMD or drug related harm rates (or enough data to calculate these). No restrictions were applied to the age or groups of patient populations included. No language restriction was applied.

4.3.4 **Exclusion Criteria**

Studies that reported an estimated denominator or those that did not use empirically collected data (data gathered by experimentation or observation) were excluded. Studies restricted to measuring non-adherence, or potentially inappropriate prescribing were excluded. Studies which measured outcomes of interest arising from interviews and questionnaires, or used data from incident reporting systems alone were also ineligible due to reporting and hindsight bias[348]. Studies that reported outcome rates for a specialised ward(s)/ward group(s)/hospital(s)(e.g. oncology, cardiac), a single disease, single drug class, single drug or pre-defined drug class were excluded, as the review intended to produce generalisable findings. Studies that reported outcome rate data limited to events arising from new or altered medication regimes during hospitalisation or at discharge were excluded. Finally, studies were excluded if they predominantly focused on patients discharged home from the emergency department or those with regular, planned admissions.

4.3.5 **Screening process**

The study screening process was completed by the lead researcher based on the inclusion and exclusion criteria. Initially, duplicate titles were removed, followed by the title screening stage and then an abstract screening stage[349]. This was followed by full text screening along with the identification of additional studies from the reference lists of included studies and relevant review articles. Titles, abstracts and full texts that were

considered unclear for inclusion were discussed with the review team, and consensus was reached.

Papers published in non-English language had their English abstract screened for inclusion. The abstract mentioning discharge and medication had their full paper translated into English by Google translate® for inclusion. Google translate®, was found to be around 90% accurate in a recent study by Jackson et al. [350]. If the study was deemed potentially relevant and considered for full text review, a medically trained native speaker would be sought to translate the paper[351]. However, no non-English language papers were found relevant for full text review.

4.3.6 Data Extraction

Data extraction for each included study was carried out independently by two reviewers using a standardised tool in Appendix 4. The data extraction tool contents were imported into Microsoft Excel®, 2010 (Microsoft, Redmond, Washington, US) for analysis, where each row represented one publication. The reviewers then met to discuss the results and resolve any discrepancies.

Published study authors were contacted for missing or unclear information. Authors of conference abstracts were contacted to determine if a full text publication was available. Each author was contacted a maximum of three times, over eight weeks; if no answer was provided then the paper was excluded[352]. Detailed information provided in this section is in accordance with the recommendation provided, by (Mullan et al, 2009), on reporting of author contact process in order to reduce reporting bias[353]. For all screened papers and the cohort of included papers, the author response rate following contact attempts was 55% (76/139) and 61.5% (24/39), respectively.

4.3.7 Quality Assessment

Prior to inclusion, exclusion criteria were applied to ensure included studies presented empirically collected data with a suitable denominator [354]. The second stage of quality assessment was completed by the lead researcher using an adapted, validated quality appraisal framework for medication safety studies established by Allan and Barker (1990) [355]. The framework used to assess the quality of included studies was originally made to assess medication error studies; however, we have adapted the tool to assess the quality of ME and ADE studies. This framework has been successfully applied in other systematic

reviews of MEs and ADEs[325,326,356,357]. The framework appraises study internal validity by assessing the quality of outcome reporting.

4.3.8 Data Synthesis

Outcome event rates including ME, UMD, ADE and ADR rates were calculated as either the denominator value affected by at least one event (numerator) per total denominator value (e.g. patients affected by at least one ME over the total number of included patients), or as the total number of events per total denominator value (e.g. total number of MEs per total number of patients). Denominator values were either discharged patients, doses administered, individually prescribed medications or whole prescriptions. Only studies that provided the outcome rate using the denominator value affected by at least one event (numerator) were used in median (IQR) calculations to avoid inflating outcome rates if more than one event could be counted per denominator value.

The degree of heterogeneity of the included studies meant that a meta-analysis of the data was not possible. Instead, median outcome rates for different medication safety outcome denominators and studies focusing on particular age groups were calculated along with interquartile ranges (IQRs). Comparisons were drawn between studies, and basic descriptive statistics provided for the country/year of origin, method of data collection, definitions of outcome events, the severity of outcome events, and medication types/classes involved. Medication classes implicated with events were considered 'common' if they were at least reported in four studies as being within the top three most common medications involved in safety events.

4.4 Results

4.4.1 Overview of included studies

The total number of citations identified was 22,082. After removing duplicates, this number fell to 16,571. The PRISMA flow diagram (Figure 4.1) illustrates the citation review stages. All included studies are summarised in one table in Appendix 5, followed by tables in Appendix 6 - Appendix 9 which summarise these studies based on medication safety measures (ME, ADE, ADR, UMD).

In total, 54 studies were included in the systematic review, including 20,895 hospital discharges across 26 countries. The included studies consisted of 41 published papers[5,6,215,244,245,247,358–363,59,364–373,206,374–383,207,384,209–211,213,214], and 13 conferences

abstracts[246,385,394–396,386–393]. One of the included conference abstracts[386] was combined with one letter to the editor[397]. All included studies were published in English.

The majority of included studies were conducted in the United States of America (USA) (17/54, 31.5%)[6,59,371,382,390,391,394,395,398,207,209,210,213,215,246,366,368], followed by the United Kingdom (UK) (7/54, 13%)[247,363,364,369,385,389,392]. Forty-three (79.6%) studies were published from the year 2010 onwards[5,59,246,247,358,359,365–370,206,371,374–378,380–383,207,384–393,209,394–396,210,211,214,215,244]. Of the 54 studies, 28 (51.8%) included adult patients, 18 (33.3%) focused specifically on elderly patients. Three studies (5.5%) were exclusively carried out with paediatric patients[5,361,389]. Most studies (85.2%, 46/54) were prospective in design[5,6,358–366,368,59,369,370,373–380,206,381–384,387–392,211,393–396,213–215,245,247].

Seventy six percent of studies (41/54) included patients that were discharged to home[5,6,247,358,359,361,363–368,59,369,371,372,374,375,377–380,382,206,383–387,389–393,207,398,209,210,214,215,246], with three (5.5%) including patients discharged to nursing homes[370,376,392]. The most frequent data collection method was screening case summaries (e.g. discharge medical record and discharge summary) (43/54, 79.6%), followed by telephone follow-up interviews with the patient (25/54, 46.2%). Data collectors were mostly pharmacists (27/54, 50%). Almost a quarter of included studies (13/54, 24%) utilised a follow up period post discharge of one month, with the next most common time period being one week (7/54, 12.9%). The shortest follow up period was two days, and the longest was 180 days. Table 4.2 summarises key study characteristics.

Table 4.2 – Characteristics of included studies

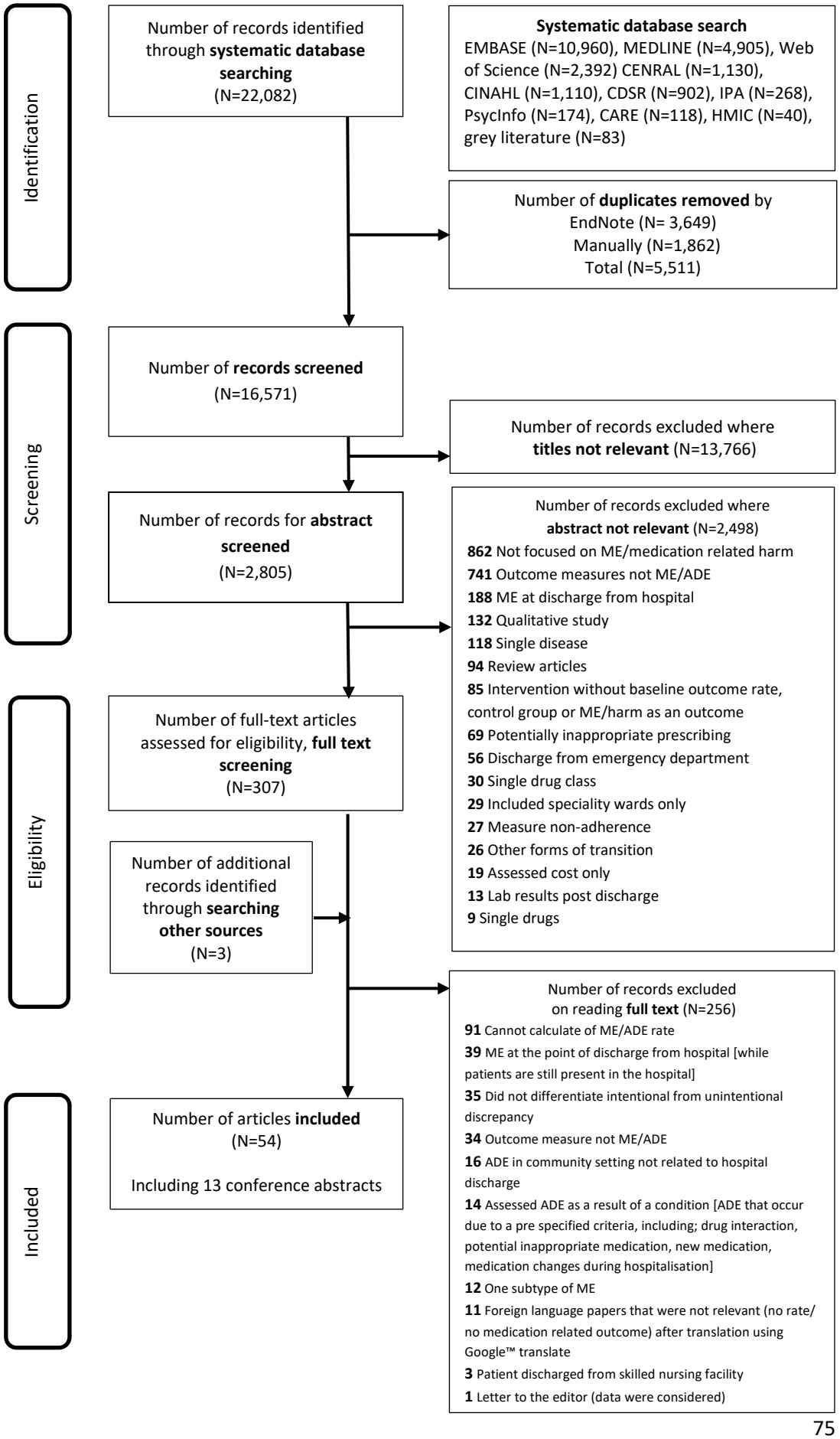
Characteristics	Number of Studies (n=54)	%	References
Country			
USA	17	31.5	6,59,371,382,390,391,394,395,398,207,209,210,213,215,246,366,368
UK	7	13	247,363,364,369,385,389,392
Norway	4	7.4	361,370,375,384
Canada	3	5.5	367,373,387
Netherlands	2	3.7	358,386
Australia	2	3.7	362,383
France	2	3.7	372,393
Sweden	2	3.7	360,376
Switzerland	2	3.7	211,365
India	2	3.7	5,378
Italy	1	1.8	244
New Zealand	1	1.8	206
Belgium	1	1.8	388
Croatia	1	1.8	374
Ireland	1	1.8	380
Egypt	1	1.8	377
Europe[a]	1	1.8	379
Jordan	1	1.8	381
Oman	1	1.8	359
Sri Lanka	1	1.8	396
Saudi Arabia	1	1.8	214
Publication year			
1990-1999	3	5.5	213,363,364
2000-2009	8	14.8	6,360–362,372,373,379,398
2010-2019	43	79.6	5,59,246,247,358,359,365–370,206,371,374–378,380–383,207,384–393,209,394–396,210,211,214,215,244
Patient Demographics			
Adults	28	51.8	6,59,364–366,368–370,377,379–381,207,382–385,392,393,396,398,209,210,214,215,244,359,363
Elderly[b]	18	33.3	211,213,374–376,378,386,388,390,395,246,247,358,360,362,367,371,373
Paediatric	3	5.5	5,361,389
All age groups	1	1.8	372
Not specified	4	7.4	206,387,391,394
Study Design			
Prospective	46	85.2	5,6,358–366,368,59,369,370,372–379,206,380–384,386–390,211,391–396,213–215,245,247
Retrospective	8	14.8	207,209,210,244,246,367,371,385

Characteristics	Number of Studies (n=54)	%	References
Study Setting*			
Home	41	75.9	5,6,247,358,359,361,363–368,59,369,371,372,374,375,377–380,382,206,383–387,389–393,207,398,209,210,214,215,246
Home care[c]	5	9.2	211,213,247,370,376
Nursing home	3	5.5	370,376,392
Other[d]	5	9.2	244,360,362,373,394
Not specified	3	5.5	388,395,396
Study Focus**			
ME	12	21.8	5,206,394,395,211,375,379,380,385,390,391,393
UMD	14	25.9	215,244,388,389,392,398,360,363,364,368–370,376,386
ADR	17	30.9	207,210,378,379,381–384,396,247,358,365–367,372–374
ADE	17	30.9	6,59,361,362,371,377,387,391,398,209,210,213–215,246,247,359
Data Collection Method***			
Screen case note	43	79.6	5,6,244,246,247,358–364,59,365,366,368–371,373–376,206,377–380,382–385,388,389,207,392,394,398,209–211,214,215
Telephone follow-up	25	46.2	6,59,373,375,377–382,388,389,207,391,393,395,398,213–215,247,359,366,369
Home visit	12	22.2	358,363,389,390,364,367,373,374,379,384,386,387
Other[e]	16	29.6	5,209,382,383,385,387,390,395,210,211,358,361,368,372,374,379
Not specified	1	1.8	396
Profession of data Collector****			
Pharmacist	27	50	206,207,367,370,371,373,376,379,381–384,209,385,387,391–395,210,214,246,247,360,361,366
Physician	6	11.1	6,215,244,372,374,386
Nurse	5	9.2	59,211,215,244,390
Research assistant	7	12.9	213,358,359,369,375,377,398
Pharmacy student	1	1.8	365
Not specified	10	18.5	5,362–364,368,378,380,388,389,396
Follow-up period*****			
1-15 days	20	37	206,210,376,379,380,382,386–388,391,393,395,211,214,361,363,364,367,368,370
16- 30 days	19	35.1	6,207,372–374,377,381,389,390,398,209,213,215,358–360,366,369
31-180 days	11	20.3	59,246,396,247,362,371,378,383–385,392
Not specified	4	7.4	5,244,365,394

[a]One study included data from six countries in Europe including; Austria, Germany, Denmark, Spain, The Netherlands, and Portugal.
[b]Among the 18 studies, nine studies included patients aged ≥65 years[213,246,335,360,367,371,374–376], one study included patients aged ≥64 years[211], 3 studies included patients aged ≥60 years[358,373,378], five studies did not mention a cut off age[362,386,388,390,395]. Among the five studies that did not mentioned the cut off age, two studies mentioned the mean age and referred to patients as older adults[362,386], one study included patients discharged from a geriatric ward[388], one study included veteran geriatric patients[390], and one study included Medicare Advantage patients[395].
**Studies could have patient discharged to more than one location*
***Study focus could be more than one outcome*
[c] providing care at patient home
[d]long term care facility, local care settings, local care home programme, outpatient rehabilitation facility, community healthcare
****Studies could have more than one data collection method*
[e] Follow-up visit at hospital/clinic, medication reconciliation post discharge, GP database, reporting of incident, questionnaire, interview at community pharmacy, medication reconciliation (via secure messaging at home), reporting of incident
*****Studies data collectors could be from more than one profession*
******Follow up period for the outcome of interest*

Abbreviation: *ADE (adverse drug event), ADR (adverse drug reaction), ME (medication error), n (number), UMD (unintentional medication discrepancy)*

Figure 4.1- PRISMA flow diagram



4.4.2 **Quality assessment of included studies**

A summary of the quality assessment of included studies is provided in Table 4.3. The quality assessment score was low (score = 1-4) in 14.8% of studies (8/54), moderate (score = 5-8) in 72.2% (39/54) and high (score = 9-12) in 12.9% (7/54). The aim and objectives were clearly described in all but one paper[390] and the outcome definition was clearly mentioned in 27 papers[5,6,358–361,363,364,367,369–371,206,372,374,378,380,382,384,386,207,209,210,214,215,244,247]**.** In studies which measured drug related problems (DRPs) but also reported data on MEs/ADEs, reported definitions of DRPs were accepted. The definition of a DRP was provided in six studies[207,209,358,367,382,384] out of the cohort of 27 studies that mentioned outcome definition**s.** Error categories were mentioned in 14 studies[5,206,384,385,391,395,211,215,247,370,371,375,379,380] but were only defined in five[5,206,370,380,385]. The outcome denominator was clearly defined in all papers and the data collection method was described clearly in all but one study[396]**.** The study setting was clearly described in all but seven studies[359,381,388,392,395,396]**.** Validity measures, to assess if independent personnel or an expert panel evaluated the event other than the data collector were applied in 29 studies [6,59,247,358–362,364,368,369,371,207,372,374–377,380,383,389,398,209,211,213–215,244,246] to confirm the occurrence of medication safety outcomes**.** Reliability measures to evaluate if a formal test/evaluation (e.g. Kappa test or consensus) was completed to assess inter-rater reliability were applied in 12 studies [6,59,376,398,207,215,247,359,360,364,371,375]**.** Nearly two thirds of the included papers reported their limitations with 16 papers (including 11 conference abstracts[246,358,391–396,361,363,377,378,387–390]) not reporting this information**.** Only nine studies[5,247,359,360,369,370,373,384,392] calculated sample size**,** with five studies[5,360,370,383,392] describing any assumptions made**.**

Table 4.3 - Quality assessment

Study ID	Aim / objective	ME/ADE definition	Error categories specified	Error categories defined	Denominator clearly defined	Data collection method described clearly	Study setting clearly described	Validity measure applied to confirm the occurrence of error	Reliability measure applied	Listed of study limitation	Calculation of sample size described	Mentioned of any assumption made	Total score of criteria achieved (out of 12)
Ahmad, 2014 [358]	√	√ DRP			√	√	√	√					6
Al-Ghamdi, 2012 [214]	√	√			√	√	√	√		√			7
Al-Hashar, 2018 [359]	√	√			√	√		√	√*	√	√		8
Alldred, 2010 [385]	√		√	√	√	√	√			√			7
Armor, 2016 [210]	√	√			√	√	√			√			6
Bergkvist, 2009 [360]	√	√			√	√	√	√	√*	√	√	√	10
Bonaudo, 2018[244]	√	√ UMD			√	√	√	√		√			7
Braund, 2014[206]	√	√	√	√	√	√	√			√			8
Buajordet, 2002[361]	√	√			√	√	√	√					6
Cameron, 2010[387]	√				√	√	√						4
Claeys, 2013[388]	√				√	√							3
Crotty, 2004[362]	√				√	√	√	√		√			6
Donovan, 2012[246]	√				√	√	√	√					5
Duggan, 1996[363]	√	√			√	√	√						5
Duggan, 1998[364]	√	√			√	√	√	√	√	√			8
Eichenberger, 2010[365]	√				√	√	√			√			5
Falangan, 2010[367]	√	√ DRP			√	√	√			√			6
Fanizza, 2018[366]	√				√	√	√			√			5
Forster, 2005[6]	√	√			√	√	√	√	√	√			8
Gray, 1999[213]	√				√	√	√	√		√			6
Hawes, 2018[209]	√	√ DRP			√	√	√	√		√			7
Heyworth, 2014[368]	√				√	√	√	√		√			6
Hockly, 2018[369]	√	√			√	√	√	√		√	√		8
Holdhus, 2019[370]	√	√ UMD	√ UMD	√ UMD	√	√	√			√	√	√	10
Huynh, 2013[389]	√				√	√	√	√					5
Kannan, 2013[371]	√	√	√		√	√	√	√	√	√			9
Leland, 2012[390]					√	√	√						3
Letrilliart, 2001[372]	√	√			√	√	√	√		√			7
MacAulay, 2008[373]	√				√	√	√			√	√		6

Study ID	Aim / objective	ME/ADE definition	Error categories specified	Error categories defined	Denominator clearly defined	Data collection method described clearly	Study setting clearly described	Validity measure applied to confirm the occurrence of error	Reliability measure applied	Listed of study limitation	Calculation of sample size described	Mentioned of any assumption made	Total score of criteria achieved (out of 12)
Marusic, 2014[374]	√	√			√	√	√	√		√			7
Mesteig, 2010[375]	√		√		√	√	√	√	√*	√			8
Meyer-Massetti, 2018[211]	√		√		√	√	√	√		√			7
Midlov, 2012[376]	√				√	√	√	√	√*	√			7
Ibrahim, 2012[377]	√				√	√	√	√					5
Mohammad, 2011[391]	√		√		√	√	√						5
Nagaraju, 2015[378]	√	√			√	√	√						5
Osorio, 2014[215]	√	√ UMD	√ UMD		√	√	√	√	√*	√			9
Parekh, 2018[247]	√	√	√		√	√	√	√	√*	√	√		10
Patel, 2011[392]	√				√	√					√	√	5
Paulino, 2004[379]	√		√		√	√	√			√			6
Pourrat, 2017[393]	√				√	√	√						4
Riordan, 2016[380]	√	√	√	√	√	√	√	√		√			9
Salameh, 2019[381]	√				√	√				√			4
Schnipper, 2006[398]	√				√	√	√	√	√	√			7
Sittambalam, 2015[394]	√				√	√	√						4
Solanki, 2017[5]	√	√	√	√	√	√	√			√	√	√	10
Tantipinichwong, 2017[395]	√		√		√	√							4
Tetuan, 2018[382]	√	√ DRP			√	√	√			√			6
Tong, 2015[383]	√				√	√	√	√		√		√	7
Tsilimingras, 2015[59]	√				√	√	√	√	√	√			7
Westberg, 2017[207]	√	√ DRP			√	√	√	√	√*	√			7
Wijekoon, 2017[396]	√				√								2
Willoch, 2012[384]	√	√ DRP	√		√	√	√			√	√		8
Wilting, 2012[386]**	√	√			√	√	√			√			6

**Consensus meeting*

*** Information mentioned in the letter to the editor[397] were used in the quality assessment*

Abbreviation: *ADE (adverse drug event), DRP (drug related problem), ID (identifier), ME (medication error), n (number), UMD (unintentional medication discrepancy*

4.4.3 Medication Error Studies

In total, 12 studies[206,211,375,379,380,385,390,391,393,395] reported data concerning the frequency of MEs**.** Six studies used established definitions of MEs[5,206,211,379,380,385], with one study developing their own definition[395], and five not reporting any definition[375,390,391,394]. Five studies[379,380,385,391,395] reported data specifically concerning prescribing errors, of which two[380,385] used the prescribing error definition proposed by Dean et al., (2000)[399].

All studies explicitly used the number of discharged patients as their denominator**.** Seven studies which used patients affected by at least one medication error as their numerator are summarised below [5,211,380,385,390,393,394]. Across five studies from three settings which reported ME rates per discharged patient [211,385,390,393,394] a median of 53% (IQR 33-60.5%) of adult and elderly patients' experienced MEs post discharge. Two prospective studies[390,393] out of these five reported ME rates for patients discharged to home as 47-53% of discharged patients. A range of 19-53% of elderly discharged patients (n=2) experienced at least one ME post discharge[211,390].

One study[380] reported that one or more prescribing errors affected 43% of discharged patients**.** Another study[385] reported that 3.5% of discharge medications were affected by at least one monitoring error post discharge. One study[5] reported ME and medication administration error rates for infants as 66.3% and 54.0% of discharged patients respectively.

4.4.4 Unintentional Medication Discrepancy Studies

In total, 14 studies reported data concerning the frequency of unintentional medication discrepancies (UMD)[215,244,388,389,392,398,360,363,364,368–370,376,386]**.** Three studies[244,360,388] used an established UMD definition, seven[215,363,364,369,370,389,398] developed their own, and four[368,376,386,392] did not report any definition.

The majority of included studies explicitly used the number of discharged patients affected by at least one event as their numerator, except two studies which used the number of discharge medications affected by one or more UMDs[363,364]**.** These latter studies[363,364] reported that 11-52.7% of individual prescribed medications had at least one UMD post discharge. One study[389] reported that at least one UMD affected 12% of discharged paediatric patients. Across eleven studies[215,244,398,360,368–370,376,386,388,392] a median rate of 50% (IQR 39-76) of adult and elderly patients experienced at least one UMD post discharge

(range 14-93.5%). Four studies[215,369,388,398] that used telephone follow-up among data collection methods, and five studies using case note screening[244,360,370,376,392] reported the rate of UMD to be 65-93.5%, and 14-76% respectively per adult and elderly patient discharged. A range of 36.5-93.5% of discharged elderly patients (n=5) experienced UMD post discharge[360,370,376,386,388].

4.4.5 Adverse Drug Events

Seventeen studies[6,59,361,362,371,377,387,391,398,209,210,213–215,246,247,359] reported ADE rates post hospital discharge, 17 studies[207,210,378,379,381–384,396,247,358,365–367,372–374] reported non preventable ADE rates (ADRs) post discharge, one study[247] reported both.

4.4.5.1 Non Preventable ADEs (Adverse Drug Reactions)

Three studies[372,374,378] used the ADR definition proposed by the WHO in 1972, nine studies[207,210,358,365,367,373,379,382,384] used a broader DRP definition which included ADRs, and three[366,383,396] did not state a definition.

All studies explicitly used the number of discharged patients as their denominator. Across five studies[247,358,374,381,396] which used patients affected by events as their numerator a median of 27% (IQR 18-40.5) of adult and elderly patients experienced one or more ADRs post hospital discharge. Two studies[247,381] that used telephone follow-up as the most common data collection method reported the rate of ADRs post discharge to be 20.4-27% of discharged patients. A range of 27-51% of elderly discharged patients (n=3) experienced ADRs post discharge[247,358,374].

4.4.5.2 Adverse Drug Events

Four studies[359,361,371,398] used the ADE definition proposed by Bates et al., 1995 [174]. Seven studies[59,213,246,362,377,387,391] did not formally define ADEs. All studies explicitly used the number of discharged patients as their denominator. One study[361] reported the rate of post discharge ADEs as 9% of paediatric patient hospital discharges. One study[210] reported the mean number of ADEs per discharged patient as 3. Across seven studies[6,213,214,246,247,371,398] which used patients affected by at least one event as their numerator, the median ADE rate was found to be 19% (IQR 16-24%) of adult and elderly patients experiencing one or more ADEs post discharge. Two studies[359,398] reported that between 11-16% of discharged patients experienced one or more preventable ADEs.

Five studies[6,213,214,247,398] that used telephone follow-up interviews among data collection methods reported 11-37% (median 20.3%, IQR 13.5-30.5) of adult and elderly patients discharged experienced one or more ADEs. Two studies[246,371] that used case note screening among data collection methods reported that 18.7-18.9% of discharged patient were affected by ADEs post hospital discharge. Two studies[6,59] adapted Bates definition of ADEs and used the same data collection method reported that 11-16% of adult and elderly patients had at least one ADE after hospital discharge. The highest reported ADE rate was 37% of patients using a telephone interview method in one study[247] in the UK. A range of 18.7-37% of elderly discharged patients (n=4) experienced ADEs post discharge[213,246,247,371].

Table 4.4 summarises outcome rates of the included studies per patient population.

Table 4.4 - Outcome rate summary

Patient group	Error and discrepancy		Harm	
	ME (n=12)	**UMD (n=14)**	**ADR (n=17)**	**ADE (n=17)**
Paediatrics	• 66.3% of discharged patients (n=1)[5] • 54.2% of discharged patients (administration error) (n=1)[5]	• 12% of discharged patients (n=1)[389]	• NA	• 9% of discharged patients (n=1)[361]
Adults and elderly	• 19-63% of discharged patients, median rate 53 % [IQR 33-60.5] (n=5) [211,385,390,393,394] • 43% of discharged patients (prescribing error) (n=1) [380] • 3.5% of medications in discharge prescription (monitoring error) (n=1)[385]	• Range 11-52.7% of medications in discharge prescription (n=2)[363,364] • Range 14-93.5% of discharged patients, median rate 50% [IQR 39-76] (n=11) [215,244,398,360,368–370,376,386,388,392]	• Range 15.7-51% of discharged patients (median 27%, IQR 18-40.5) (n=5)[247,358,374,381,396]	• Range 11-37% of discharged patients, median rate 19 % [IQR 16-24] (n=7)[6,213,214,246,247,371,398]
Adults [excluding elderly]	• 43% of discharged adult patients (prescribing error) (n=1)[380] • 3.5% of medications in discharge prescription (monitoring error) (n=1)[385]	• Range 11-52.7% of medications in discharge prescription (n=2)[363,364] • Range 14-82% of discharged patient median rate 57.5% [IQR 35-76.7] (n=6) [215,244,368,369,392,398]	• Range 15.7-20.4% of discharged patient (n=2) [381,396]	• Range 11-24% of discharged patients (n=3) [6,214,398]
Elderly	• 19-53% of discharged patients (n=2) [211,390]	• Range 36.5-93.5% of discharged patients (n=5) [360,370,376,386,388]	• Range 27-51% of discharged patients (n=3) [247,358,374]	• Range 18.7-37% of discharged patients (n=4) [213,246,247,371]
All age groups	• NA	• NA	• 0.4 % of discharged patient (n=1)[372]	• NA

Abbreviation: *ADE (adverse drug event), ADR (adverse drug reaction), IQR (interquartile range), ME (medication error), n (number), NA (Not Available), UMD (unintentional medication discrepancy)*

4.4.6 **Severity of Events**

Eighteen[6,59,371,372,374,376,380,386,389,396,209,213–215,246,247,359,369] (18/54, 33.3%) studies reported severity data of identified outcome measures, including one ME study[380], three ADR studies[372,374,396], nine ADE studies[6,59,209,213,214,246,247,359,371] and five UMD studies[215,369,376,386,389]. Seven studies [6,59,359,371,372,374,380] reported severity assessment based on existing rating scales published in the literature. Of these, three studies[6,59,371] used the severity rating proposed by Bates et al., 1995[174], with various other scales being used by remaining studies.

Comparability of the severity of events was limited due to heterogeneity across studies in presenting severity of event data (e.g. number of patients affected by one or more serious incidents, or number of serious incidents), severity rating scale, and the small number of included studies particularly when divided across patient populations. One study reported that 86% of adult patients affected by MEs were considered to be moderate harm events[380]. Among patients affected by ADRs, three studies reported that serious ADRs affected 6.9%, 47%, and 60% of elderly, adult and all age groups patients respectively[372,374,396]. Among patients affected by ADEs post hospital discharge, serious ADEs were reported to affect 13.3% of adult, and 81% of elderly patients in two studies[6,247]. Four studies reported that the median rate of serious ADEs was found to be 29% (IQR 21-38.5%) of adult and elderly patients experiencing one or more ADEs post discharge[214,246,359,371]. Among patients affected by UMDs, three studies reported that between 25-34% of elderly patients[376,386], and 63.3% of paediatric patients were affected by moderate harm events[389]. Two studies reported that 33-38% of UMDs identified post hospital discharge were associated with high potential of harm in adult patients[215,369]. Appendix 10 includes a summary of severity data of the included studies.

4.4.7 **Medication Involved in UMDs/ADEs**

Fourteen studies[6,59,372,374,379,396,207,209,210,213,215,247,367,371] reported data regarding individual medications or drug classes associated with UMDs (n=1) and ADEs (n=14). Studies evaluating MEs did not report data regarding medications involved. The most common drug classes that were reported to lead to post discharge ADEs across fourteen studies[6,59,372,374,379,396,207,209,210,213,215,247,367,371] were antibiotics, antidiabetics, analgesics, and cardiovascular drugs (common subclasses were anti-hypertensive and anticoagulant medications)**.** Only one study[374] reported a statistical method to formally associate prescription of warfarin with ADEs. Appendix 11, summarises medications and medication

classes that were reported to be involved in UMDs/ADEs, classified according to the British National Formulary system[400].

4.4.8 Studies identified from updated search

The search was updated to cover the period between 1st January 2019 and 24th November 2021. The updated search summarised yielded 8,048 studies, identified from the included databases: EMBASE (N=4,720), MEDLINE (N=1,758), CENRAL (N=686), CINAHL (N=541), CDSR (N=215), IPA (N=61), PsycInfo (N=50), Web of Science (N=17), CARE (N=0), HMIC (N=0). One study was identified as eligible from the updated search strategy, and one study was identified via hand search that was published on 29th November 2021.

One randomized controlled study from Croatia evaluated the impact of integrated medication reconciliation; including medication reconciliation on admission, at discharge, at community health care, at community pharmacy in addition to patient education and optimizing pharmacotherapy during admission[401]. The intervention was found to reduce UMDs from 34.5% (n=59/171), to 14.8% (n=27/182) in elderly patients post hospital discharge.

The second novel study [402], used a primary care database in Spain to identify MEs after hospital discharge detected in primary healthcare. The study analysed data of 6,115 patients records after hospital discharge from internal medicine, cardiology, digestive, and respiratory wards. Medication errors were found to affect 37% (n=2,278/6,115) of patients after hospital discharge. However, the study failed to provide further details about patient characteristics beyond age and gender, hospital discharge information or most common medication classes implicated to MEs.

4.5 Discussion

This is the first systematic review of published international evidence concerning the epidemiology of MEs and ADEs post hospital discharge across population groups. The study identified that medication poses a frequent and enduring risk to patient safety following discharge from hospital, which reinforces care transfer being a WHO Global Patient Safety Challenge priority for action.

The current study identifies that MEs and ADEs affect a median of one in two, and one in five adult and elderly patients after hospital discharge, respectively. Higher rates of

medication related error and harm were observed in the elderly. This systematic review found that medication classes most implicated in harm post hospital discharge were cardiovascular, analgesic, antibiotic, and antidiabetic medications. Similar findings have been reported by other literature[188,403,404] investigating medication related harm in ambulatory settings and medication related causes for hospital admission.

The study observed that research has been accelerating in the field of medication safety post hospital discharge since the year 2010. The study found that with the exception of included studies reporting data from the USA, UK and Norway, nations that have multiple studies included in this review rarely contained data across all outcome measures, which limits global assessment of risk. This systematic review identifies that the burden of MEs and ADEs following hospital discharge is comparatively under-researched in paediatric and nursing/care home settings. Direct comparison between papers was limited due to heterogeneity in studies in the field, as observed by other researchers[325,405].

Systematic reviews of epidemiological studies have previously shown a substantial influence on public health policy[406,407], playing a role in translational research via knowledge validation and dissemination[408]. The findings of this review provide a foundation from which future remedial interventions may be planned through the identification of targets relating to outcome rate, medication classes and patient groups. Identification of such targets supports pre-evaluation procedures of intervention design[409,410] . In addition, these findings can be used for benchmarking the rate of error and harm for future epidemiological and intervention work (although those rates were variable due to heterogeneity in methods and definitions). Furthermore, the review could be used to inform the development and update a medication related harm prediction tools via identifying the most common medication classes implicated in harm[411].

It is anticipated from the identified rates of ME/ADEs in this study that the cost of "no action taken" is high in terms of patients' subsequent use of the healthcare services post hospital discharge. A number of reviews have been published that evaluated interventions (including medication reconciliation, community pharmacy involvement and electronic communication interventions) to reduce MEs and ADEs post discharge [9–11,265,270,273,412]. However, none have reported consistent reductions in these outcomes. Understanding the epidemiology and nature of medication safety challenges post hospital discharge paves the way for research to examine in-depth their nature and causes, where study in this area could better support the development of interventions [155,157]. Studies have been limited to

incident report analysis[258,297] (although that their focus being not medication, and from one institution), and staff surveys, which report that communication deficits have been implicated in harm post hospital discharge[67] (although that their focus being not medication). This research should be used by academics, policymakers and health care staff alongside the findings of this review and explorations of the causes of MEs/ADEs post-discharge at a scale from national data to reduce medication safety risks from a more holistic perspective.

4.6 Conclusion

This is the first known comprehensive systematic review of the burden and nature of MEs and ADEs harm following hospital discharge across general populations, and informs global efforts directed toward understanding and addressing medication related morbidity associated with care transitions. Medication errors and adverse drug events have been found to be common following hospital discharge, but detailed comparison between studies was limited due to differences in the design of included studies. Despite this, a number of important targets were identified for future study that could guide the development of successful remedial interventions and move forward the global safety agenda.

Chapter Five: Analysis of Medication Safety Incidents Following Transition from Secondary to Primary Care in England and Wales Received by the National Reporting and Learning System (NRLS): Multi-Method Study

5.1 Introduction

Transition of care from hospital to community settings has been identified as an area of high medication safety risk and is currently the focus of international improvement efforts[3]. There is, therefore, a need to empirically study and understand the prevalence and origins of MEs/ADEs, and impact of existing interventions targeting this stage of the care journey in order to inform future practice and research. On the first step of this path, Chapter Four has presented a comprehensive search of the existing literature exploring MEs, UMDs and medication related harm (including ADEs and ADRs) following hospital discharge, which has confirmed their role as a frequent and serious threat to patient safety. Important potential targets for remedial intervention were also identified in the previous chapter, including commonly observed medication classes (including medication for the cardiovascular, endocrine and central nervous system) and the elderly with robust UK data highlighting the frequency of ADEs post hospital discharge.

As the epidemiology of these events in the UK context is now better understood, attention can turn towards exploring at scale their nature and aetiology in order to drive theory-based intervention development[95]. Indeed, Chapters Two and Three highlighted our limited understanding of the causes of medication safety challenges post hospital discharge, with current evidence focusing on wider safety issues with little sensitivity towards medication in areas such as incident severity and contributory factors [170,257–259]. Previously, the nature and origins of patient safety incidents following hospital discharge have been explored at a national level using incident report review[258], a technique which yields sensitive data to understand causes of events and guide improvement[150]. This approach is, therefore, a suitable means by which to evaluate the aetiology of these incidents following hospital discharge. Chapter Two, section 2.3.5.4, has highlighted that available evidence using analysis of patient safety incidents post hospital discharge were either not focused on medication safety incidents, or were not on a national level.

This present study was designed to address these limitations by presenting an up-to-date and in-depth insight into the nature and contributory factors of MEs and ADEs occurring following hospital discharge at a national level in the UK, in order to inform more representative improvement strategies[413,414].

5.2 Aim and objectives

The aim of this study was to explore in-depth at a national level the nature and contributory factors influencing MEs and ADEs occurring following the transition of care from secondary to primary care reported to the National Reporting and Learning System (NRLS) across England and Wales.

The objectives of this study are as follows:

1. Describe in-depth the nature of medication safety incidents following transition of care from hospital to home, including the class of medications involved, potential/actual severity of incidents, type of safety incident, and patient age group involved with the incidents.
2. Explore the inter-relationship between incident characteristics and trends over time, e.g. severity linked to types of medication involved.
3. Identify and understand the contributory factors underpinning these medication related incidents, including any common interactions between factors on the incident pathway.
4. Make recommendations for improvement and future research based on the findings.

5.3 Methods

The overall structure of this study follows the criteria specified in The Reporting of studies Conducted using Observational Routinely collected health Data (RECORD) Statement[415]. The study design was a retrospective multi-methods study, where a quantitative descriptive analysis of all incidents was completed, followed by free text based content analysis of incident contributory factors.

5.3.1 Data source

The research team obtained anonymised medication-related patient safety incident reports pertaining to the transition from secondary to primary care from NHS England and NHS Improvement, in the form of a Microsoft Excel® database. Formal ethical approval for this study was not sought from the University of Manchester research ethics committee due to the anonymised nature of the data based on Health Research Authority (HRA) guidance; instead, a Data Sharing Agreement was established (5033) with the National Patient Safety Team at NHS England and NHS Improvement.

The acquisition of the data was in two stages; first, a random sample of 500 primary care related patient safety incidents from the year 2017 was received in the initial exploratory stage, followed by the full dataset. The initial exploratory stage involved manual independent screening of the incidents by three members of the research team and helped to identify incident types of interest for the main data extraction. Based on the prevalence of medication related incidents post hospital discharge in this sample (2%, n=9/500), a five-year period was selected to capture sufficient data.

The data analytics team at NHS Improvement then performed the main extraction of data from the NRLS dataset for incident category *"medication"* and the care setting of occurrence is equal to *"general practice".* It was not possible to limit incident reports by time since hospital discharge, so the research team made an assessment of eligibility based on free text data. To compile the dataset, NRLS analytics completed a free text search based on the term 'discharge', including misspelling and variations in the free text column fields (including a description of what happened, reoccurrence, apparent cause).

5.3.2 Eligibility criteria

The data consisted of medication related patient safety incidents pertaining to the transition from secondary care to any settings in primary care, reported to the NRLS in England and Wales between 1st January 2015 and 31st December 2019. For the study population selection, all free full-text data were reviewed against eligibility criteria that included whether the incident was related to medication and post hospital discharge stage. Discharges from the accident and emergency (A&E) department were included, because in some cases, it was apparent that the patient had a hospital admission after being admitted via A&E. Exclusion criteria included patients discharged from outpatient clinics, hospice care, rehabilitation settings or care/nursing homes.

5.3.3 Variables and definition

The term 'patient safety incident' was defined in this study as *"Any unintended or unexpected incident that could have or did lead to harm for one or more patients receiving NHS-funded healthcare"*[416]*.* Throughout this chapter, the terms 'medication related patient safety incident' and 'incident' are used interchangeably to mean medication related patient safety incidents that occurred after hospital discharge. For the contributory factors analysis, the term 'contributory factor(s)' was defined as "*any agent thought to have played a part in the origin or development of an incident, or to increase the risk of an incident*"[417].

The term 'monitoring errors' was defined as *''either explicit i.e. the hospital indicated monitoring should be undertaken, or implicit i.e. monitoring would be expected in routine practice based on published guidelines''*[385].

The NRLS dataset consisted of 24 original variables, including descriptive structural data, and free text data. The variables that were provided as free text data included a description of what happened, actions preventing reoccurrence, and apparent cause(s). Incident severity data could have been reported as either potential or actual severity by the incident reporter. A complete list of variables with variable descriptions and a table of codes are provided in Appendix 12, and Appendix 13.

5.3.4 Data cleaning and data coding

Initially, the lead researcher (FA) generated incident codes and a coding system, and completed data cleaning. Incidents not meeting the eligibility criteria were separated in a list which was independently reviewed by two researchers (DS and RNK). The research team, including members ACS and RNK experienced in analysing patient safety incident reports, then had frequent concordance meetings to discuss the data and agree on the final list of excluded incidents.

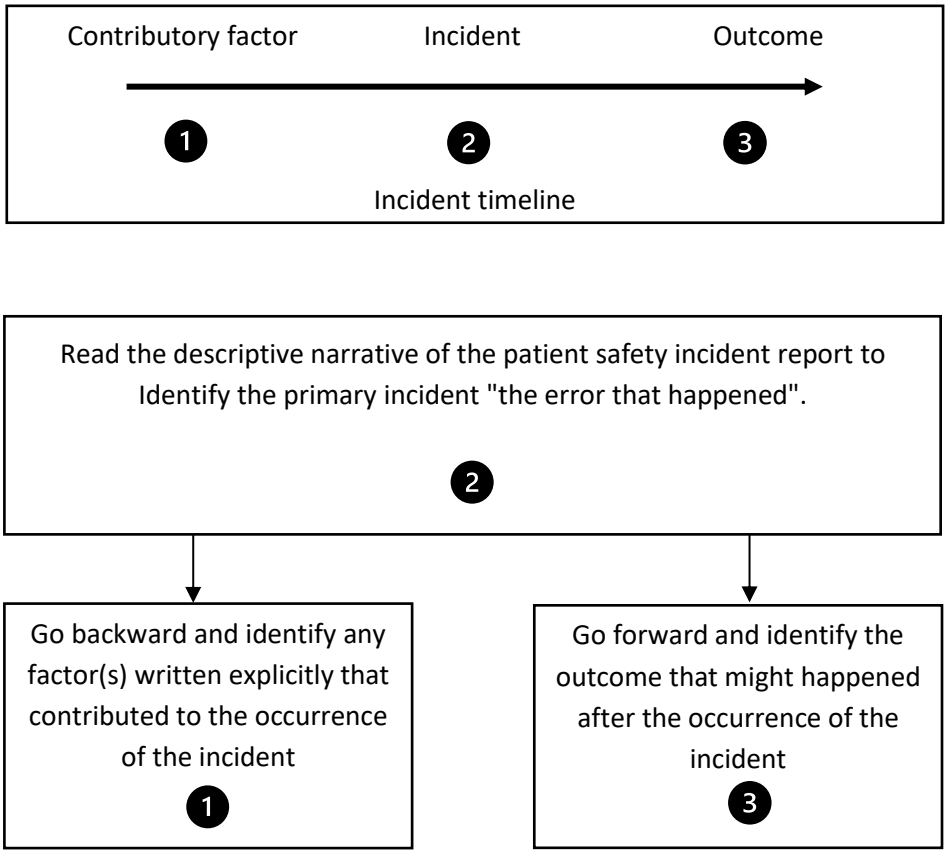
After compiling the included medication related-patient safety incident list, this was followed by data coding. Data coding was completed in Microsoft Excel®, 2010 (Microsoft, Redmond, WA, USA). Coding of medication was based on medication classification in British National Formulary (BNF) chapters (access via https://www.medicinescomplete.com in April 2020)[418]. The medication in the three most commonly observed BNF chapters were further coded based on individual medication groups (see Appendix 14 for completed medication coding list).

Data were further coded without modification of fields based on existing categories from the NRLS. The exception was the severity of harm, which was re-coded where there was explicit evidence to warrant the need to amend the severity using the classification of patient-safety incidents in primary care[419]. This was undertaken to support the capture of actual (rather than potential/uncertain) harm events, an approach carried out by other researchers studying the severity of harm of NRLS data[420]. The re-coded severity of harm was used in the results section instead of the severity of harm provided by the incident reporter. The 'origin' of each incident was also newly coded by the lead author (FA) based on the free text description of the incidents to be either within secondary or primary care.

Any incidents related to patient adherence were assumed to originate from secondary care unless otherwise stated.

Free text analysis was completed for all incidents to identify the contributory factor(s), outcomes and harm severity. The coding of the descriptive free text data was based on the Patient Safety Research Group (PISA) coding classification. The lead researcher (FA) screened the descriptive free text data and systematically applied codes from coding frameworks to deconstruct incident report narratives, an approach used by other researchers in the field[413,414]. The first step included identification of the primary incident type (PIT), followed by following the events in the incidents chronologically; backwards to identify the contributory factor(s) and forward to identify the outcome(s). The PISA classification includes 4 main contributory factor codes (including patient factors, staff factors, equipment, and organisation factors) and 178 sub-codes for the contributory factors, along with 5 main outcome codes with 153 sub-codes. The free text narrative was coded using a two step process, using main theme codes and sub-theme codes, which served as a quality check of the free text data. The coding was explicitly based on the data in the incident narrative, where no assumption was made regarding the incident's context or patient clinical condition. Figure 5.1 summarise the steps of coding of the free text data with examples. A summary of the screening and coding steps is provided in Figure 5.2.

Figure 5.1 - Coding patient safety incident reports using PISA classification.



Examples:

Case 1*: "Patient discharged from hospital and practice clinical pharmacist reconciled discharge medication on letter with medication on practice clinical computer system. Added fentanyl patches and lansoprazole that were prescribed in hospital but failed to add hyoscine tablets that were also added. Also failed to remove codeine and lontec from clinical computer repeat medication list that would have been available to request in addition to fentanyl patches . ."*

Incident: Underlined text

Contributory factor: not known, code as missing data [Code 999]

Outcome: No outcome described

Case 2: *''Patient discharged on XX from XX with no discharge information to GP or sent with patient and only enough medication to cover until XX. I was asked to take an urgent phone call from the patient's partner on XX at 6pm asking me to prescribe further medication. I subsequently phone XX at 6.15 pm but my phone call was not answered . .''*

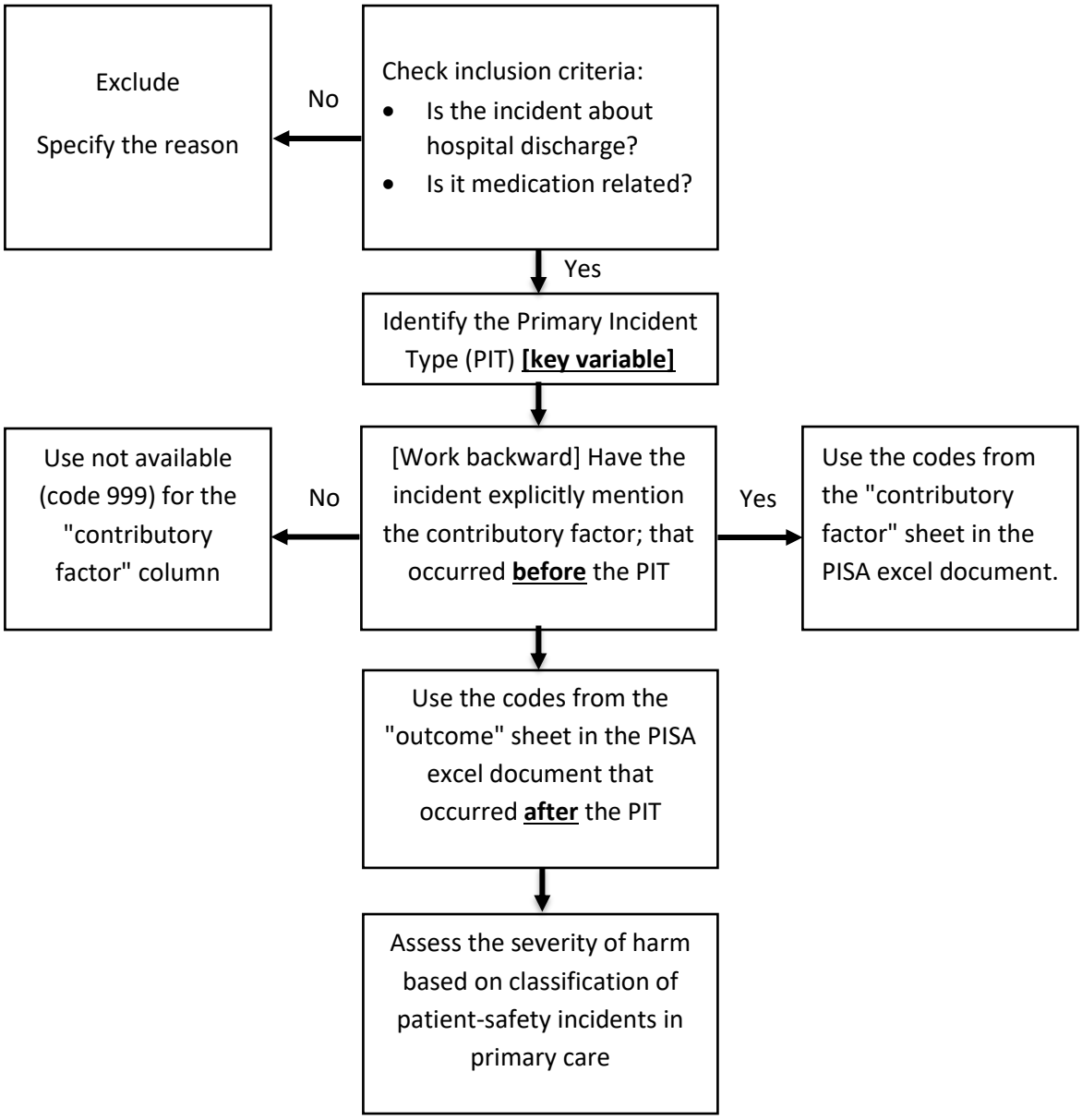
Incident: Underlined text

Contributory factor: Continuity of care between secondary and primary care

Outcome: Organisational inconvenience:

- Phone calls/ follow-up
- Treating patient without sufficient information

Figure 5.2- Flowchart for screening and coding the free text sections of the incident.



5.3.5 Data validation

Twenty per cent of the data (n=237/1,121 incidents) was independently coded by two researchers (RNK and DS) to confirm the accuracy of coding and validate the coding framework. Each researcher reviewed around 130 incidents, which is equivalent to 10% of the total included sample. This coding included the contributory factors and outcome using the PISA classification, and the severity of harm. The team then had frequent concordance meetings with ACS; an international expert in analysis of patient safety incident reports and the lead author of the PISA coding framework. The concordance meetings were to discuss the results of the independent coding validation process and to agree on the strategy for identification of the primary incident type (PIT), and final coding approach. Where required, incidents were re-coded by FA following these consensus meetings.

5.3.6 Data analysis

Data analysis was completed in Stata® version 14.0 software (StataCorp, College Station, TX USA). Once data was coded, quantitative data analysis involved an exploratory analysis of all medication related incidents to find emerging patterns and trends. This involved analysis of the categorical variables 'structured data' field and simple textual 'unstructured data' field responses pertaining to incidents (e.g. type of medication error, medication involved) across the entire data set. Descriptive analysis of all reported incidents was applied to describe the nature (and patterns over time) of medication safety incidents, including the stage of medication process at which medication safety incidents occurred (i.e. prescribing, administration and monitoring), age group of patients involved with the incidents, class/name of the medication, and potential/actual severity of medication safety incident). Cross tabulation was completed to compare variables to determine any patterns (e.g. incident types across different harm severities). If more than one medication was associated with an incident, then each medication was counted in the analysis. Thus, the total number of medications involved was more than the number of incidents.

It was sought to omit completing descriptive statistical analysis to evaluate the difference between groups. That is because this analysis will report observations of what was reported rather than the true extent of what is happening in the NHS. The included sample may not be representative due to unclear denominators, and other challenges, including under reporting,

poor reporting culture, and reporting bias. Given that the aim of this study which was to explore in-depth the nature and aetiology of medication safety incidents post hospital discharge, statistically analysis is not required as the study is seeking to reveal a form of 'reality' about medication safety incidents post hospital discharge. Therefore, the focus was on building a picture of the medication safety risks to patients post hospital discharge, rather than a quality assurance study of what did or did not get reported.

A detailed analysis of free text incident descriptions was performed in order to examine the contributory factors for incidents. The free text analysis involved content analysis, where the lead researcher screened the free texts to identify data that aligned to PISA coding categories as described earlier. This data was then grouped into emerging categories, an approach used by other researchers in the field[413,414].

5.3.7 Data quality assessment

Data quality assessment was completed by determining the number of words used in the incident free text description, in accordance with previous research[421,422].

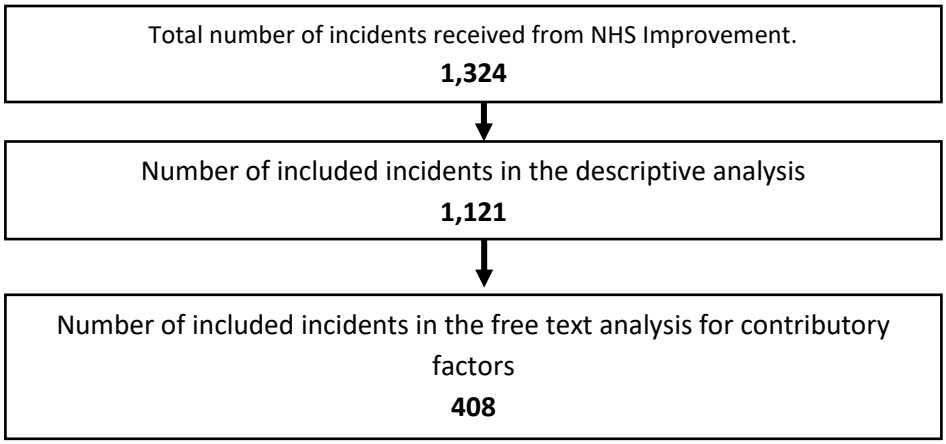
5.4 Results

5.4.1 Overview of dataset

Of 1,324 medication-related incident reports, 203 were subsequently excluded due to being not related to medication, or hospital discharge (see Figure 5.3). The reasons for exclusion were incident being not hospital discharge related (n=131), discharge from clinic (n=33), repeated incidents (n=28), discharge from rehabilitation settings (n=4), discharge from prison (n=3), discharge from hospice care (n=3) and discharge from a care/nursing home (n=1). The final data set included 1,121 medication related incidents reported to take place following hospital discharge.

The month and year of submission of the incidents, medication process and error category were structural variables. Patient age was inconsistently provided as a structured variable and was present in 79% (n=888/1,121) of reports. The level of harm variable was a structured and unstructured variable that was identified from free text. Factor and outcome variables were not captured via structured variables.

***Figure 5.3 – Dataset* identification**



5.4.2 Descriptive data

5.4.2.1 Summary statistics

The majority of reported incidents involved patients aged above 65 years (56%, n=626/1,121), followed by patients aged 18-65 years old (19%, n=218/1,121). However, these percentages may be an underestimate as patient age was specified in only 79% (n=888/1,121) of reports. The percentage of incidents involving patients aged above 65 would be 70% (n=626/888) excluding those incidents with an unspecified age category.

Medication incidents occurred most frequently in the prescribing (42%, n=479/1,121) followed by the administration stage (22.5%, n=253/1,121), and then the monitoring stage (12%, n=140/n=1,121). The most reported medication error categories were wrong or unclear dose or strength (19%, n=212/1,121), followed by omitted medicine (13%, n=148/1,121) and then wrong drug/medicine (10%, n=118/1,121).

The majority of the incidents (61.5%, n=689/1,121) originated from secondary care (and included, for example, issues related to sending discharge letters) and 38.5% (n=432/1,121) of incidents originated from primary care (including for example issues related to actioning referrals, or failed monitoring).

Using the re-coded severity of actual harm, it was found that almost one eighth (12.6%, n=142/1,121) of incidents were associated with patient harm (low harm (5.1%, n=58/1,121), moderate harm (6.1%, n=69/1,121), severe harm (0.7%, n=8/1,121), and death (0.6%,

n=7/1,121)). In addition, 77.6% of the incidents did not contain sufficient information to code harm outcome**.** Table 5.1 presents summary statistics for the categorical variables.

A total of 11 reports contained multiple incidents that were submitted in one form, of these incidents 6 resulted in no harm, 4 resulted in minor harm and one resulted in moderate harm. An example of a compound incident is provided in**Appendix** 15.

Table 5.1– Summary statistics of categorical variables from N=1,121 incident reports

Patient age range	n (%)	Error category	n (%)
<18 years	44 (4%)	Wrong / unclear dose or strength	212 (19%)
18 – 65 years	218 (19%)	Omitted medicine / ingredient	148 (13%)
>65 years	626 (56%)	Wrong drug / medicine	118 (10%)
Missing data	233 (21%)	Wrong quantity	68 (6%)
Level of harm*	**n (%)**	Wrong frequency	60 (5%)
No harm	108 (9.6%)	Contra-indication to the use of the medicine in relation to drugs or conditions	58 (5%)
Low harm	58 (5.1%)	Mismatching between patient and medicine	45 (4%)
Moderate harm	69 (6.1%)	Wrong formulation	21 (1.8%)
Severe harm	8 (0.7%)	Wrong / omitted verbal patient directions	18 (1.6%)
Death	7 (0.6%)	Wrong method of preparation / supply	16 (1.4%)
Unclear	871 (77.6%)	Adverse drug reaction (when used as intended)"	10 (0.9%)
Medication process	**n (%)**	Wrong / omitted / passed expiry date	8 (0.7%)
Prescribing	479 (42%)	Patient allergic to treatment	6 (0.5%)
Administration / supply of a medicine from a clinical area	253 (22.5%)	Wrong / transposed / omitted medicine label	5 (0.4%)
Monitoring / follow-up of medicine use	140 (12.5%)	Wrong storage	2 (0.1%)
Preparation of medicines in all locations / dispensing in a pharmacy	64 (5.7%)	Wrong route	2 (0.1%)
Advice	42 (3.7%)	Wrong / omitted patient information leaflet	1 (0.1%)
Supply or use of over-the-counter (OTC)	3 (0.2%)	Other	303 (27%)
Other	140 (12.5%)	Unknown	20 (1.8%)
Incident origin	**n (%)**		
Secondary care	689 (61.5%)		
Primary care	432 (38.5%)		

**Re-coded severity of harm*

5.4.2.2 Medication process and error categories

Table 5.2 presents a contingency table which compares the medication process associated with incidents in different patient age groups. Incidents involving patients aged less than 18 years were associated with the highest proportion of incidents occurring at the administration stage compared to other age groups (34%, n=15/44), whereas incidents involving patients aged

between 18 and 65 were associated with the highest proportion occurring at the prescribing stage (49%, n=107/218). Incidents involving patients aged more than 65 years old were associated with the highest proportion of incidents occurring at the monitoring stage (14%, n=89/626).

Table 5.2 compares the top five medication error categories associated with incidents in different patient age groups. Incidents involving patients aged less than 18 years old were associated with the highest proportion of incidents occurring due to wrong / unclear dose or strength (29%, n=13/44) and wrong quantity (16%, n=7/44), while incidents included patients aged more than 65 years old had the highest proportion of incidents occurring due medication omission (15%, n=93/626) (See Appendix 16 for full list).

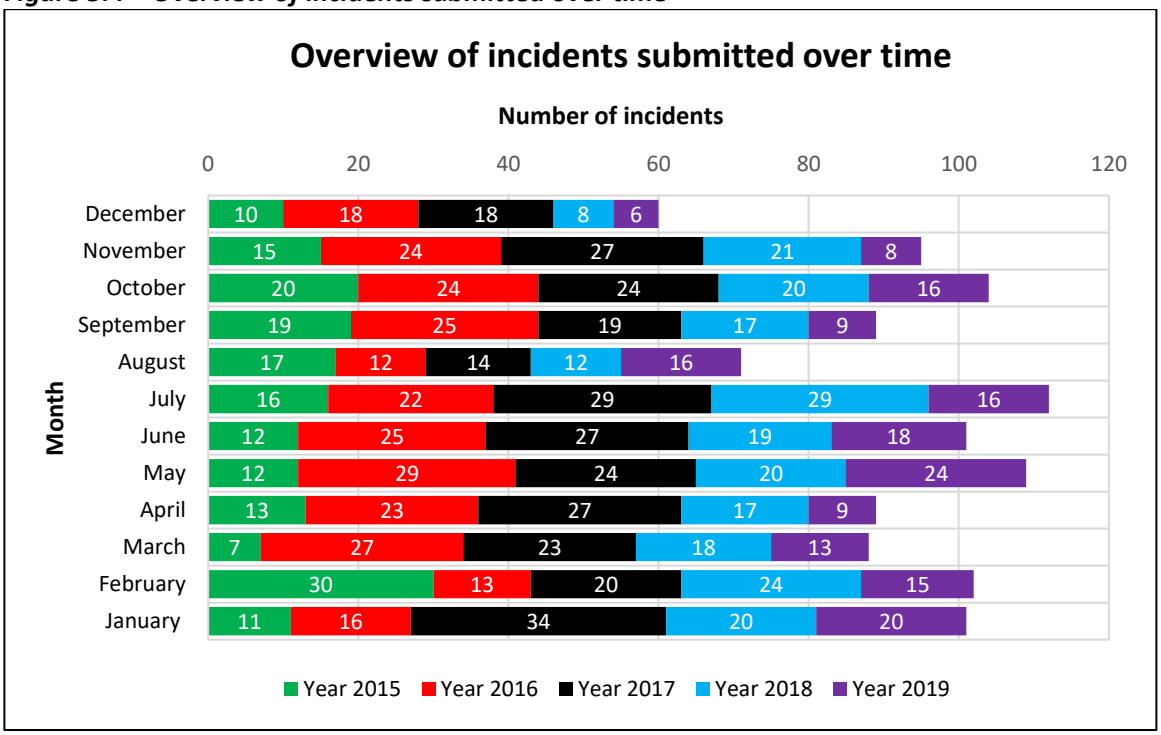
Table 5.2 – Medication process stages/error categories stratified by patient age groups

	Age groups				
	<18 years	**18 – 65 years**	**>65 years**	**Missing data**	**Total**
Medication process					
Prescribing	17 (38%)	107 (49%)	244 (39%)	111 (47.6%)	**479**
Administration / supply of a medicine from a clinical area	15 (34%)	41 (19%)	158 (25%)	39 (16.7%)	**253**
Monitoring / follow-up of medicine use	2 (4%)	20 (9%)	89 (14%)	29 (12.4%)	**140**
Preparation of medicines in all locations / dispensing in a pharmacy	2 (4%)	16 (7%)	32 (5%)	14 (6%)	**64**
Advice	2 (4%)	9 (4%)	23 (4%)	8 (3.4%)	**42**
Supply or use of over-the-counter (OTC) medicine	1 (2%)	1 (0.4%)	0 (0%)	1 (0.4%)	**3**
Other	5 (11%)	24 (11%)	80 (13%)	31 (13.3%)	**140**
Medication error category					
Wrong / unclear dose or strength	13 (29%)	49 (22%)	108 (17%)	42 (18%)	**212**
Omitted medicine / ingredient	3 (7%)	28 (13%)	93 (15%)	24 (10%)	**148**
Wrong drug / medicine	3 (7%)	28 (13%)	67 (10.7%)	20 (8%)	**118**
Wrong quantity	7 (16%)	12 (5%)	32 (5%)	17 (7%)	**68**
Wrong frequency	1 (2%)	12 (5%)	35 (5.5%)	12 (5%)	**60**
Other	17 (38.6%)	89 (40.8%)	291 (46.4%)	118 (50.6%)	**515**
Total	**44 (100%)**	**218 (100%)**	**626 (100%)**	**233 (100%)**	**1,121**

5.4.2.3 Data trends over time

Figure 5.4 compares the breakdown of medication safety incidents according by month and year of submission. Over the five year period of study the number of submitted patient safety incidents were the lowest during March, April, August, and December. These are the months that host UK national holidays, including Christmas, Summer, and Easter holidays. The highest number of medication safety incidents were submitted in the year 2017. (See Appendix 17)

Figure 5.4 – Overview of incidents submitted over time



5.4.2.4 Incident origin

Table *5.3* compares the number of patient safety incidents by medication process stage associated with the origin of the incident report.

Table 5.3– Medication process stage based on the origin of incident report

Medication Process	Origin of incidents		
	Primary care	Secondary care	Total
Prescribing	221 (46.1%)	258 (53.8%)	**479 (100%)**
Administration / supply of a medicine from a clinical area	66 (26%)	187 (73.9%)	**253 (100%)**
Monitoring / follow-up of medicine use	64 (45.7%)	76 (54.2%)	**140 (100%)**
Preparation of medicines in all locations / dispensing in a pharmacy	26 (40.6%)	38 (59.3%)	**64 (100%)**
Advice	8 (19%)	34 (80.9%)	**42 (100%)**
Supply or use of over-the-counter (OTC)	2 (66.6%)	1 (33.3%)	**3 (100%)**
Other	45 (32.1%)	95 (67.8%)	**140 (100%)**
Total	432 (38.5%)	689 (61.4%)	**1,121 (100%)**

Examples of incidents originating in primary care were seen to involve repeat prescriptions (n=9) and prescriptions with Monitored Dosage Systems (MDS) (e.g. blister pack) (n=46). Regarding incidents related to repeated prescription in the dataset (n=11) it was noticed that the majority of these incidents originated in primary care (81.8%, n=9/11), where repeat prescriptions were issued before receiving the discharge letter or before reviewing the discharge letter. For example, one patient safety incident report mentioned *"medication issued from GP surgery at request of chemist whilst in hospital – surgery had no info to say patient in hospital or discharged".* Regarding the involvement of MDS with patient safety incidents post hospital discharge in the dataset(n=88). It was noted that in the majority of these incidents originated in primary care (52.2%, n=46/88). Some incidents involved the supply of 4 weeks of medication in MDS before receiving the discharge letter that was subsequently mixed with new MDS reflecting the latest discharge prescription, leading to patient safety incidents.

Regarding examples of incidents which were considered to originate in secondary care, three recurrent categories were noticed including dispensing pediatric liquid medication, communication with anticoagulation clinic, and district nurse. It was noted that all prescription incidents involving pediatric patients occurred when syrup or suspension quantity was not enough prompting further supplies (n=12) were originated from secondary care. One incident stated, *"Patient discharged with med. Letter states 10 days given. Patient only received 5 and*

was told to get the rest from GP". It was also noted that the majority of incidents related to referrals to the anticoagulation clinic after hospital discharge originated in secondary care (59%, n=13/22). The theme in some incidents mentioned that local anticoagulation services were not being made aware of the patient's warfarin status (start/ stop warfarin) post discharge; other incidents stated that the absence of arrangement for International Normalized Ratio (INR) testing and follow-up with the anticoagulation clinic. One incident stated, *"Patient discharged after DVT on warfarin but no referral to anticoagulation clinic done, only given 3 days warfarin and clexane and told to go to GP for INR testing and onward management".* In addition, a high proportion of incidents associated with district nurses originated in secondary care (68%, n=30/44). The themes were around nurses not being aware that the patient was discharged, and no administration sheet / prescription was being sent to the nurse. One incident report mentioned "*District nurses stated that they were not aware of the discharge and that they should give the patient this daily injection".*

5.4.2.5 Medication

The total number of medications involved in the incidents was 1,504, with some incidents involving more than one medication. In addition, 53 incident reports had no information about the name of medication(s) involved. Table 5.4 reports the three most common medication classes associated with medication incidents which were the cardiovascular system (48.8%, n=734/1,504), central nervous system (18%, n=273/1,504), and endocrine system (12%, n=183/1,504). Table 5.5 then provides the most common specific medications within these common medication classes associated with incidents – antiplatelets (n=126) followed by factor Xa inhibitors (n=124), opioids (n=79), insulin (n=76), beta-adrenoceptor blockers (n=76), heparins (n=71), vitamin K antagonists (n=67), and diuretics (n=66) (see Appendix 18 for a full list). The most common medication classes associated with incidents in the monitoring stages were antithrombotic medications namely warfarin (n=34), antiplatelets (n=21), and factor Xa inhibitors (n=19). Warfarin was associated with a higher proportion of incidents related to monitoring stage (51%, n=34/67). Incidents involving heparin (46% n=32/70) followed by insulin (33%, n=25/76) were associated with a higher proportion related to the administration stage than other stages (see Appendix 19). The most frequently observed medication classes associated with incidents in patients aged less than 18 years old, 18-65 years old, and more than 65 years old were anti-infective medications (36%, n=17/47), cardiovascular medications

(40.2%, n=126/313), and cardiovascular medications (53.9%, 458/849), respectively. (for full list see Appendix 20).

Table 5.4 – Medication associated with medication incidents based on BNF chapter

BNF Chapter	Frequency (%)
Cardiovascular system	734 (48.8%)
Nervous system	273 (18.15%)
Endocrine system	183 (12.16%)
Gastro-intestinal system	81 (5.38%)
Anti-infective	61 (4.05%)
Respiratory system	51 (3.39%)
Nutrition and metabolic disorders	45 (2.99%)
Blood and blood-forming organs	19 (1.26%)
Genito-urinary system	15 (0.99%)
Malignant disease	15 (0.99%)
Eye	9 (0.59%)
Musculoskeletal system	7 (0.46%)
Immune system	3 (0.19%)
Skin	3 (0.19%)
Poisoning	2 (0.13%)
Medical emergencies	1 (0.06%)
Nose	1 (0.06%)
Vaccine	1 (0.06%)
Total	1,504 (100%)
Missing data field or unknown	53

Table 5.5 – Most frequently observed medications from the three most common BNF chapters associated with incidents

BNF Chapter	Medication class	Total
Cardiovascular (n=734)	Antithrombotic drugs, antiplatelet drugs	126
	Antithrombotic drugs, factor Xa inhibitors	124
	Beta-adrenoceptor blockers	76
	Antithrombotic drugs, heparins	71
	Antithrombotic drugs, vitamin K antagonists	67
	Diuretics	66
Endocrine (n=183)	Insulin	76
	Blood glucose lowering drugs	40
	Corticosteroids	23
	Thyroid disorders	19
	Bisphosphonates	14
	Female sex hormone responsive conditions	7
Central Nervous System (n=273)	Analgesics, opioids	79
	Antiepileptics	54
	Antipsychotics	40
	Antidepressants	35
	Hypnotics, sedatives, and anxiolytics	21
	Parkinson's disease, dopaminergic drugs	14

There was a recurrent example regarding the quantity of liquid antibiotic medication dispensed to pediatric patients (n=12). One incident stated, *"This child was discharged from hospital; according to discharge he should be on antibiotics for 2 weeks but was given only one bottle and was advised to ask GP for another".* Another recurrent example was short medication regimens that were continued for the long term (n=15), with the most common medication being antiplatelet (n=8), and anticoagulant (n=3). One incident stated *''Patient attended for medication review May 2016 – noted been on clopidogrel since ACS in December 2010. Discharge letter recorded to continue clopidogrel for 9 months only. Discussed with patient and medication stopped following review medical records''*. Referral to an anticoagulation clinic after hospital discharge (n=22) was a recurrent theme in the data. The most common incident type was in the monitoring stage (59%, n=13/22). It is important to highlight that 41% (n=9/22) of these incidents resulting in harm, with two incidents resulted in death.

The involvement of community nursing staff (n=22) and district nurse (n=44) were also a recurrent example in the data. Insulin administration was the most common medication implicated with incidents associated with community nurse (n=11/22), and district nurse (n=16/44), one incident stated *''The patient was discharged from ward to home on the 4th of June. The hospital did not arrange the community nurse to administer daily insulin but listed this as action for the GP on the discharge summary. There was no telephone communication to inform of this. The discharge summary was not received and processed until the 8th of June and the patient was without insulin until the 9th of June'', another incident stated "District nurses stated that they were not aware of the discharge and that they should give the patient this daily injection".*

5.4.3 Outcome data 'harm severity'

Table 5.6 represents the observed differences between the harm severity originally provided in the incident report data and the severity of 'actual' harm following re-coding. A total of 77.6% of the data was re-coded as 'unclear' in determining actual harm severity. Appendix 21 provides examples of the discrepancies in incident severity of harm coded by the NRLS and those coded by the research team. These examples include those down-graded, up-graded, and unclear incidents.

Table 5.6 – Comparison of severity of harm provided by NRLS and the recoded ones

Harm severity provided in original dataset	Actual harm severity as coded by the study research team						Total
	Insufficient details	No harm	Low	Moderate	Severe	Death	
No harm	643	93	18	9	3	0	**766**
Low	164	11	31	8	1	0	**215**
Moderate	59	2	9	48	2	0	**120**
Severe	5	1	0	4	2	2	**14**
Death	0	1	0	0	0	5	**6**
Total (%)	**871 (77.6%)**	**108 (9.6%)**	**58 (5.1%)**	**69 (6.1%)**	**8 (0.7%)**	**7 (0.6%)**	**1,121 (100%)**

To assess the effect of different variables on harm severity, contingency tables were used. Table 5.7 compares the re-coded harm severity stratified by patient age and origin of incidents. A higher proportion of incidents originating from secondary care were associated with harm that those originated from primary care. In addition, a higher proportion of 'any harm' incidents involved patients aged more than 65 years old compared to other age groups.

Table 5.7 – Severity of harm stratified by patient age and origin of incident

	Harm severity [Re-coded]							Total
	Insufficient details	No harm	Any harm	Low	Moderate	Severe	Death	
Origin of incidents								
Primary care	325	54	53 (12%)	16	33	2	2	**432**
Secondary care	546	54	89 (13%)	42	36	6	5	**689**
Age range								
<18	35	5	4 (9%)	2	1	1	0	44
18-65	175	17	26 (12%)	12	11	2	1	218
>65	469	63	94 (15%)	35	49	4	6	626
Missing information	192	23	18 (8%)	9	8	1	0	233
Total	**871**	**108**	**142 (13%)**	**58**	**69**	**8**	**7**	**1,121**

**See Appendix 22 for a copy of this table using severity of harm provided by the NRLS*

Table 5.8 shows the distribution of re-coded actual harm incident severity according to medication use process stage, and medication error categories. The table shows the monitoring (17%) and administration (15%) stages were associated with a higher proportion of harmful incidents compared to the other stages. The table also highlights that for medication error types reported at least 60 times, medication omission was associated the greatest proportion of 'harmful' incidents (19%, n=28/148) followed by 'wrong drug/medicine' (16%, n=19/118).

Table 5.8 – Severity of harm stratified by medication process/error categories

	Insufficient details	No harm	Any harm	Harm severity [Re-coded] Low	Moderate	Severe	Death	Total
Medication Process								
Prescribing	364	58	57 (12%)	28	24	2	3	**479 (100%)**
Administration / supply of a medicine from clinical area	198	16	39 (15%)	14	21	3	1	**253 (100%)**
Monitoring / follow-up of medicine use	106	10	24 (17%)	7	14	1	2	**140 (100%)**
Preparation of medicines / dispensing	48	9	7 (11%)	4	3	0	0	**64 (100%)**
Advice	33	4	5 (12%)	2	2	1	0	**42 (100%)**
Supply or use of over-the-counter (OTC)	3	0	0 (0%)	0	0	0	0	**3 (100%)**
Other	119	11	10 (7%)	3	5	1	1	**140 (100%)**
Medication error category								
Wrong / unclear dose or strength	164	25	23 (11%)	12	9	2	0	**212 (100%)**
Omitted medicine / ingredient	112	8	28 (19%)	8	15	1	4	**148 (100%)**
Wrong drug / medicine	83	16	19 (16%)	8	10	0	1	**118 (100%)**
Wrong quantity	53	8	7 (10%)	0	6	0	1	**68 (100%)**
Wrong frequency	49	7	4 (7%)	2	2	0	0	**60 (100%)**
Contra-indication to the use of the medicine in	45	3	10 (2%)	3	6	1	0	**58 (100%)**
Mismatching between patient and medicine	31	6	8 (18%)	4	3	1	0	**45 (100%)**
Wrong formulation	19	1	1 (5%)	1	0	0	0	**21 (100%)**
Unknown	14	3	3 (15%)	1	1	0	1	**20 (100%)**
Wrong / omitted verbal patient directions	15	0	3 (17%)	1	2	0	0	**18 (100%)**
Wrong method of preparation / supply	12	3	1 (6%)	0	1	0	0	**16 (100%)**
Adverse drug reaction (when used as intended)	7	0	3 (30%)	2	1	0	0	**10 (100%)**
Wrong / omitted / passed expiry date	6	0	2 (25%)	1	1	0	0	**8 (100%)**
Patient allergic to treatment	4	1	1 (17%)	0	1	0	0	**6 (100%)**
Wrong / transposed / omitted medicine label	4	0	1 (20%)	0	1	0	0	**5 (100%)**
Wrong route	0	0	2 (100%)	1	0	1	0	**2 (100%)**
Wrong storage	1	1	0 (0%)	0	0	0	0	**2 (100%)**
Wrong / omitted patient information leaflet	1	0	0 (0%)	0	0	0	0	**1 (100%)**
Other	251	26	26 (8%)	14	10	2	0	**303 (100%)**
Total	**871**	**108**	**142 (13%)**	**58**	**69**	**8**	**7**	**1,121 (100%)**

**See Appendix 23 for a copy of this table using severity of harm provided by the NRLS*

Table 5.9 reveals that the most common medication group associated with a higher proportion of 'any harm' incidents among the top three most frequent implicated medication classes were medications for the central nervous system (15.3%, n=42/273). The medication classes that were associated with patient death were cardiovascular medication (n=5), nervous system medication (n=1), and medication for the endocrine system (n=1).

Table 5.9 – Severity of harm for different medication classes

BNF Chapter	Harm severity [Re-coded]			Total*
	Insufficient details	No harm	Any harm	
Cardiovascular system	572 (77.9%)	65 (8.8%)	97 (13.2%)	**734**
Nervous system	200 (73.2%)	31 (11.3%)	42 (15.3%)	**273**
Endocrine system	138 (75.4%)	23 (12.5%)	22 (12%)	**183**

**some incidents included more than one medication*

5.4.4 **Incident outcomes**

The outcome of all included medication safety incident reports is presented in Table 5.10. This includes a total of 1,660 with some incidents containing several reported outcomes. From the cohort of identified outcomes, 34% (n=564/1,660) were organisation inconvenience, 27% (n=455/1,660) were an inconvenience to the patient, and 13% (n=216/1,660) were patient clinical harm. The most common outcomes related to organisation inconvenience were phone calls / follow-up (73%, n=412/564), and the most common outcome related to patient inconvenience was missed dose(s) of medication (23%, n=107/455). Table 5.10 presents the breakdown of the top four most common outcomes in each main category (See Appendix 24 for full list). The 'no outcome' theme included 29 reports which described incidents identified by relatives and harm prevented, with one incident example reporting: *''New medication was added from a discharge summary to the wrong patient and script issued. This was picked up by the patient's husband when he went to collect the script from the chemist''*

Table 5.10 – Frequency of most common medication related incident outcomes

Outcome	Outcome sub-category	Total	Total
Organisational inconvenience	Phone calls/follow-up	412	**564 (33.9%)**
	Treating patient without sufficient information	110	
	Destruction of medication	19	
	Increased documentation	10	
Inconvenience to patient (non-clinical)	Missed dose(s) of medication*	107	**455 (27.4%)**
	Unnecessary treatment**	90	
	Repeated visits to/from health care providers	76	
	Hospital admission	55	
Patient clinical harm (Pathophysiological / disease-related pain)	Changes in physiological parameters	41	**216 (13%)**
	Discomfort/pain	22	
	Missed dose***	22	
	General deterioration/progression of condition	21	
Staff outcomes	Psychological harm	1	**1 (0.06%)**
No outcome (or error identified, and harm prevented)	No outcome described	247	**424 (25.5%)**
	Unclear outcome/insufficient information to ascertain outcome	105	
	Patient identified error and harm prevented	27	
	Relatives identified error and harm prevented	29	
	Carer (not a healthcare worker) identified error and harm prevented	9	
	Patient identified error and further harm prevented	1	
	Relatives identified error and harm further prevented	6	
Total		**1,660**	**1,660 (100%)**

**The first missed dose outcome refers to when the outcome caused inconvenience to the patient without reported patient harm.*

******* If the patient had a medication with a wrong frequency (more than what is intended), or if had been given a medication that was used before but is no longer needed.*

****The second missed dose outcome refers to when the patient had a clinical harm as a results*

5.4.5 **Contributory factors**

A total of 36% of the reported incidents (n=408/1,121) contained at least one contributory factor explicitly mentioned in the incident free text narrative. Among the incidents with known contributory factors (n=408) the majority of incidents (87%, n=357/408) had one contributory factor, 10.7% (n=44) of the incidents had two factors, 1.4% (n=6) of incidents had three factors, and 0.2% (n=1) incidents had four reported contributory factors. The total number of identified contributory factors were therefore 467 from 408 incidents. Only 7% (n=86) of the incidents explicitly mentioned the contributory factor data in the appropriate column of the NRLS data file, with the majority of data originating in the free text data in the 'Description of what happened' and 'Actions preventing reoccurrence' fields.

Table 5.11 presents summary statistics for the contributory factors identified from the free text descriptions. The most common contributory factors reported were organisation factors (82%, n=383/467) followed by staff factors (16%, n=75/467). Almost all organisation factors (98% (n=377/383)) were related to continuity of care (the delivery of a seamless service through integration, co-ordination, and the sharing of information between different providers), followed by working conditions (1%, n=5/383), and protocols/policies/standards/guidelines inadequate, inefficient absent or not available (n=1/383). The most common continuity of care related organisation factor was continuity of care between secondary and primary care (n=308) and included issues in the discharge letters such as hard to read discharge letter, contradicting information in discharge letter, delay in sending discharge letter, and no discharge letter communication was sent. This was followed by continuity of care issues between wider healthcare and pharmacy services (n=35).

A total of 47% (n=35/75) of staff related contributory factors were cognitive issues, followed by task related issues (44%, n=33/75). Other staff related factors included failure to follow protocol (n=14), and wrong professional carries out task (n=14). Table 5.12- Incident's extract of the most common contributory factors in each category provides examples of incident report extracts describing these factors.

The most common types of factors involved in the 51 incidents with multiple contributory factors were organisation factors (65%, n=72/110), followed by staff factors (30%, n=33/110). A summary of contributory factors in incidents with multiple contributory factors is available in

Appendix 25. The most common combination of factors in incidents with multiple contributory factors were continuity of care issues between secondary and primary care, and between healthcare and pharmacy (20%, n=10/51) (See for Appendix 26 incident example).

For the incidents caused by organisation factors 13.5% of them resulted in 'any harm' (n=52/383), and from the incidents caused by staff factors 16% of them resulted in harm (n=12/75). Appendix 27 shows the re-coded harm severity of incidents caused by different contributory factors.

Appendix 28 compares the breakdown of contributory factors according to the medication process. Organisation factors were the major factor affecting monitoring stage (36%, n=56/153), administration stage (32.8%, n=87/265), and prescribing stage incidents (28%, n=142/505).

The involvement of Monitored Dosage Systems (MDS) (blister packs) with patient safety incidents post hospital discharge emerged from the data (n=88). The most common contributory factors being involved in these incidents were organisational factors, including continuity of care between secondary and primary care (27%, n=24/88), followed by continuity of care between healthcare and pharmacy (21.5%, n=19/88). Incidents stated that MDS were involved in incidents in a variety of ways, including confusion and errors due to sending a faxed discharge letter to community pharmacy but not to the GP, discharging patients with medication in an MDS but also with loose tablets, listing all medication in the stop section of the prescription and asking for a MDS at the same time, and supplying the patient with 4 weeks of medication in MDS (before receiving discharge letter) that was then mixed with a new MDS containing different medications. One incident stated *''Pt discharged home from hospital with blister pack – he was given Madopar 62.5mg capsules while in patient [but then] discharged on madopar tablets in the blister pack but also madopar capsules in a bottle''*. The analysis showed that 37.5% (n=33/88) of these incidents occurred in the prescribing stage, and 19% of these incidents occurred in the administration stage. Furthermore, the analysis of these incidents involving MDS showed that 63% resulted in at least minor harm. The most common medication associated with these incidents was antiplatelet medication (n=29). Appendix 29 lists common examples from the dataset, and Appendix 30 summarises incidents related to MDS.

Table 5.11 – Frequency of incidents' contributory factors

Contributory factors category	Contributory factors (subcategories)	Total	Total
Organisation	**Continuity of care – the delivery of a seamless service through integration, coordination and the sharing of information between different providers**		
	Between Secondary and Primary Care	308	
	Between healthcare and pharmacy	35	
	Unknown to staff have not been made aware of a patient by colleagues	13	
	Within Primary Care e.g. when a patient is seen by multiple GPs within the same practice and there is therefore a resulting failure to a pattern or increasing severity of patient symptoms	13	
	Out of Hours Service	1	
	Registering with a GP	2	
	Locum/ agency staff	5	
	Working conditions		
	Staff behavior	2	
	Busy/overloaded by work	3	
	Protocols/Policies/Standards/Guidelines inadequate, inefficient absent or not available		
	Poor design of prescription	1	383
Staff factor	**Cognitive: includes abilities such as perception, learning, memory, language, concept formation, problem solving, and thinking.**		
	Mistake	7	
	Misread/Did not read	9	
	Distraction/Inattention/Oversight/Forgot	6	
	Similar patient names	4	
	Similar medication names / appearances confused	2	
	Haste/Poor time management	1	
	Hand writing	5	
	Did not consider all clinical possibilities	1	
	Task-a piece of work to be done or undertaken.		
	Failure to follow protocol – failure to adhere to procedures or regulation.	14	
	New protocol	3	
	Inadequate skill set/knowledge	2	
	Wrong professional carries out task. Eg) Admin clerk filling out prescriptions.	14	
	Junior staff	3	
	Verbal reporting used	3	
	Physical and mental wellbeing		
	Fatigue – extreme tiredness resulting from mental or physical exertion or illness	1	75
Patient factor	**Behaviour: the way in which patients/family act or conduct themselves**		
	Non-compliance: patient does not follow advice or instructions	2	
	Fraudulent behaviour	1	
	Knowledge: patient or parent of child has poor understanding	1	
	Language: patient unable to communicate in English	1	5
Equipment	**Use of fax machine**	3	
	Poor equipment designs: the design of equipment is impractical, faulty or in some way inadequate	1	4
Total			467

Table 5.12- Incident's extract of the most common contributory factors in each category

Contributory factors (subcategories)
Organisation **Continuity of care - the delivery of a seamless service through integration, coordination and the sharing of information between secondary and primary care [n=308]**
''Patient discharged on 24/X from XX with no discharge information to GP or sent with patient and only enough medication to cover until 26/XX. I was asked to take an urgent phone call from the patient's partner on 25/XX at 6pm asking me to prescribe further medication. I subsequently phone XX at 6.15 pm but my phone call was not answered.''
Organisation **Continuity of care - the delivery of a seamless service through integration, coordination and the sharing of information between healthcare and pharmacy [n=35]**
''Discharge summary went into F2 inbox. Medicine reconciliation performed but doctor failed to check it went to pharmacy. Patient had memory issues and lived alone. Mr XX emailed me on a bank holiday Monday; concerned that the medicines on discharge had not been supplied to his father. He had taken the 7 days given by the hospital but had no new supplies. The patient's heart failure had worsened as a result which constitutes a major alert. We have added a new stage to the reconciliation process to include pharmacist alerted in a new template''
Staff factor **Failure to follow protocol - failure to adhere to procedures or regulation [n=14]**
''An FP10 was issues by a psychiatrist on discharge with 9 items on. The chemist refused to issue as did not comply to national guidance of a max of 4 items per scrips.''
Staff factor **Wrong professional carries out task. eg) Admin clerk filling out prescriptions [n=14]**
''Member of reception staff added incorrect discharge letter to patients notes. Doctor prescribed medication mentioned on letter to incorrect patient. Incorrect patient noticed new medication on repeat slip and contacted the surgery to bring to our attention.''
Patient factor **Behaviour: Non-compliance: patient does not follow advice or instructions [n=2]**
''Patient admitted on 24/XX with confusion, general malaise, during medicines reconciliation noted patient discharged 19/XX with dosette box containing paracetamol and meptazinol. Discharge letter received by GP on SystmOne. On 23/XX patient requested co-codamol from GP for knee pain, GP prescribed co-codamol 30/500 . On 24/XX, home visit doctor noted patient drowsy, stopped co-codamol and supplied codeine 15mg tds prn and paracetamol. Noted: pt has poor compliance with medicines. Codeine and meptazinol stopped on admission due to confusion.''
Equipment **Use of fax machine [n=3]**
''Pt discharged from 6/XX following episode of meds related orthostatic hypotension. Meds changed significantly on discharge. Went through eDNF and GP records pre (failed) visit today. Some changes had been made but was still on previous dose bumetende and ISMO and prescription had been done on 7/XX for regime that was inconsistant with Ednf. Hospital pharmacy had annotated ednf as faxed to community pharmacy but appeared not to be received by pharmacy. Hospital pharmacy have reviewed process and communicated to team ie to annotate discharge once faxed.''

5.4.6 Data quality assessment

The quality of the incident report narratives was assessed by counting the number of words used in describing the incidents. Table 5.13 provides summary statistics on this data. The median number of words in the free text data describing the incidents was 88, with the mean number of words used to mention a *"description of what happened", "actions preventing reoccurrence",* and *"apparent causes"* was 99.6, 13.1, and 6.8 respectively.

Table 5.13 – Number of words in the incident description

Variable (n=1,121)	Median	Inter quartile range	Mean	Standard deviation	Minimum	Maximum
Total words	**88**	**51-154**	**119.69**	**104.25**	**5**	**791**
• Number of words in incident description	77	44 – 128	99.69	82.02	5	676
• Number of words in action taken	0	0 – 0	13.15	46.37	0	648
• Number of words in contributory factor	0	0 – 0	6.84	22.46	0	209

5.5 Discussion

This is the first comprehensive multi-method analysis of reported medication related patient safety incidents following hospital discharge at a national level and provides an in-depth understanding of their nature and underpinning contributory factors. The results of this study highlight that the period following hospital discharge is a high-risk phase of care associated with medication errors, harm and inconvenience to patients and health providers, reflecting current international and national safety priorities. The findings identify important targets for further exploration in order to develop remedial interventions including the elderly population, monitoring stage, and cardiovascular, endocrine and central nervous system medication. These findings build on those of Chapter Four, which identified the elderly and cardiovascular, endocrine, and central nervous system medication as a target for remedial interventions. These most common identified medication classes further support results by previous papers [188,404,423]. The findings highlight the contributory factors to these incidents, emphasising that their origins arise across both primary and secondary care and therefore identifying interface working as an important safety improvement goal [3,101].

This study adds important understanding regarding the underlying origins of medication errors and harm arising post-hospital discharge. Organisational issues were the most commonly

reported contributory factors and frequently involved lack of co-ordination of care between secondary and primary care, and between healthcare and pharmacy services. The data showed a lack of coordination in sending discharge related documentation with community pharmacies. These results further support the observation that community pharmacies may be left out of the loop at care transition[239]. These results support previous literature indicating the valuable role of community pharmacies in hospital discharge care transitions [424,425]. In addition, these findings support the implementation of electronic interventions to improve timely communication of discharge letters between health care providers[307].

In addition, among the most common staff related contributory factors, ''wrong professional carries out task, for example, admin clerk filling out prescriptions" featured (n=14), which highlights administrative tasks as a cause of medication safety incidents post hospital discharge. This is in agreement with previous research indicating that administrative procedures are a leading cause of adverse events in primary care settings[426,427]. These and wider findings in this Chapter support focusing on skill mix as an improvement target, such as by integrating clinical pharmacists in general practices[303]. Yet, the results presented in this chapter highlighted that in a number of incidents, the cause was multifactorial, which highlight the need for a complex intervention to tackle all possible contributory factors.

An important finding to emerge from this analysis is the consequences of medication incidents post-discharge, in terms of organisational and patient inconvenience. Providers and patients often needed to work across care boundaries to resolve medication issues, taking time and resource away from self-care and other interventions. Medication errors have already shown to have a significant economic burden attached to them[181], and this study adds to this narrative. For example, this study found that monitoring errors commonly led to extended courses of medication[428], sometimes lasting years, when they were intended for a specific short course. As one incident stated: *''Patient attended for medication review 20th May 2016 - noted been on clopidogrel since acute coronary syndrome (ACS) in December 2010. Discharge letter recorded to continue clopidogrel for 9 months only. Discussed with patient and medication stopped following review medical records''.* However, the financial implication of these incidents was not factored in this analysis, and few previous studies have investigated this cost[247].

In addition, this study observed that the medication process implicated with a higher proportion of patient harm was the monitoring stage. This might be due to the context surrounding this stage of the care journey, where an error in conducting medication monitoring might be unnoticed without adequate follow up and result in patient harm.

Another significant finding to emerge from this study is the involvement of MDS prescribing and supply errors in medication safety incidents. These results align with those observed in a recent report of patient harm due to MDS through analysing incident reports submitted to the NRLS in 2018, which found that prescribing errors were the most common error associated with MDS[429]. In addition, the analysis found that 63% of these incidents resulted in harm. These findings suggest that future research is needed to improve medication safety for patients supplied and using MDS post hospital discharge.

A limitation of this study lies in the number of words used to describe each incident as a representation of incident quality. What is missing in the description of some incidents includes characteristics of hospital admission and discharge that might have influenced the outcome. Although one might argue that number of words is not an indication of incident report quality and that quality of description is a better reflection than the quantity of words[420], some incidents reports with death outcomes were written using a brief description, for example, one incident stated *''Patient with atrial fibrillation admitted to hospital, discharged home with diagnosis of pneumonia but anticoagulation stopped (due to fall). Died following day, postmortem showed cause of death pulmonary embolism''*. Despite the quality of incidents (based on word count), the study has identified targets for future interventions which includes the elderly, MDS use, medication monitoring, anticoagulant medication communication and monitoring, and insulin use communication with the community nursing team.

However, the results from this study must be interpreted with caution. It is important to consider the limitations associated with using incident reports which are limited by under-reporting and risk of incomplete/low quality report data[161]. This study identified only 36% (n=408/1,121) incidents with sufficient free text data to analyse contributory factors. Thus, when viewed alongside known under-reporting of incidents, it is possible that additional, undetected contributory factors may have contributed to these incidents. To explore this issue further, future qualitative studies should be considered. Although limitations associated with

incident report research also include a lack of denominator data which alongside under-reporting precludes analysis of event rates, the strength of reporting lies in the ability to detect safety signals and understand their aetiology rather than measure true rates. In addition, there was a risk of data coding misclassification due to the nature of the free text data and use of the PISA classification which has multiple fields. Despite the limitation of the research method, the study has identified the major common contributory factors underpinning medication related incidents from the world's largest incident report database. In addition, the findings highlight the importance of improving reporting of incidents to facilitate learning.

5.6 Conclusion

This is the first study to perform an in-depth analysis of the nature and contributory factors underpinning medication-related incidents occurring after hospital discharge in the UK. The study found that almost one-eighth of included incidents were associated with patient harm and that the most common contributory factors were organisational (continuity of care) factors, followed by staff factors. The study highlights the importance of adequate skill mix, cross interface working and accurate and prompt communication of discharge letters post hospital discharge, which highlights and informs the role of interventions in improving communication post hospital discharge, and their impact on medication safety. Furthermore, the study highlights MEs and harm associated with MDS use post hospital discharge.

Chapter Six: A multi-method evaluation of a Transfer of Care Around Medicines intervention designed to improve medication safety for patients with monitored dosage systems following hospital discharge

6.1 Introduction

6.1.1 Medication safety following transition from secondary to primary care

In order to develop effective interventions to improve medication safety at care interfaces, it is important to base their design on known causes of medication errors (MEs) and adverse drug events (ADEs). In Chapter Five, it was established that the most common contributory factors implicated in medication safety incidents post hospital discharge were communication and continuity of care across care interfaces alongside staff factors including wrong profession carrying out tasks, with opportunities for intervention identified including cross-sector working, use of technology and identifying those with appropriate skills and expertise to understand this work. In addition, the role of Monitored Dosage Systems (MDS) in a number of these incidents was highlighted and explored, with MDS widely used to dispense medication to support adherence for mainly the elderly population. The elderly population has been found to be a high-risk patient population for MEs and ADEs affected post hospital discharge in Chapters Four and Five.

Chapter Two highlighted the limited impact of wider interventions targeting medication safety post hospital discharge, including medication reconciliation. The 'Discharge Medicine Service' (DMS) could be a promising intervention to improve medication safety post discharge as it addresses the above improvements goals by combining electronic tools, interface working and professional accountability and expertise in the pharmacy team. However, Chapter Two also, highlighted the need to better understand the impact of DMS on medication safety in addition to assessing its implementation and use in practice (including, process evaluation and utilisation data. This chapter will therefore evaluate the utilisation and impact on medication safety of a DMS service (in the local site, the intervention is called 'Transfers of Care Around Medicines' (TCAM)) for patients discharged with MDS from acute hospital to primary care in order to inform national roll-out in the NHS.

6.1.2 The discharge medicine service (DMS)

Technology has more recently received a wider recognition as a tool to improve medication safety at care transfer, including Email and using electronic referral system interventions[303–305]. For hospital discharge, Transfer of Care Around Medicines (TCAM) interventions are undergoing widespread adoption in UK hospital care, particularly after the 'Discharge

Medicines Service' (DMS) (similar to TCAM service, but throughout the thesis, the service will be called TCAM) became an essential service in the community pharmacy contractual framework in February 2021. TCAM involves using the dedicated e-referral tool within an Information Technology (IT) system (for example, PharmOutcomes™ platform[308]) to send a timely discharge medication documentation and any follow up tasks to a named community pharmacy to improve medication safety. There are a number of service models of TCAM in the UK, including the 'Connect with Pharmacy' project in Yorkshire[311] and in the 'Refer to Pharmacy' project in Lancashire[430], with evidence of the effectiveness of such services now emerging. A qualitative evaluation of 'Refer to Pharmacy' project by Ferguson and colleagues (2018) reported that pharmacists believed that the service had the potential to reduce human errors and make communication with the general practitioner (GP) better[309]. Mills and colleagues (2017) reported that UK hospital staff (including doctors, pharmacists and nurses) perceived that a TCAM service improved patient safety and challenged staff to improve the clarity and completeness of their documented activity following implementation[310]. Nazar and colleagues (2016) evaluated a TCAM service in the North East of England and indicated that referral had a positive effect on hospital readmission rate and length of hospital stay[312]. However, the main weakness of Nazar's study was the failure to gather a large enough sample to with confidence estimate the impact on re-admissions[312]. In Nazar's study, examining data from 1,386 patients, it was shown that the rate of readmission for those who received community pharmacy follow-up to be 12.7% (n=64/501) within 90 days of hospital discharge which was lower than those who did not receive community pharmacy follow-up (35%, n=309/885)[312]. Appendix 31 summarises different projects that utilised the PharmOutcomes™ platform.

As stated earlier in Chapter Two, available studies evaluated TCAM interventions focused on either service utilisation data or all-cause readmissions[312,313]. Such approaches, however, have failed to address the effect on medication safety directly; one of the primary aims of the service.

6.1.3 Transfers of care around medicines (TCAM) at NHS acute Trust in North West of England: context and Intervention

The TCAM project[431] in an NHS acute Trust in North West of England is in collaboration with Health Innovation Manchester (HIM) (the Academic Health Science Network for Greater

Manchester) and the Greater Manchester Local Pharmaceutical Committee (GMLPC). The TCAM project involves sharing discharge information from NHS acute Trust in North West of England to 71 community pharmacies in the local area, and was implemented in February 2019. The recipients of the TCAM intervention are both patients and healthcare providers, via one-on-one contact. The intervention involves sending admission and discharge notifications to primary care sites and community pharmacies and sending discharge letters to community pharmacies. Table 6.1 and Figure 6.1 describe the TCAM service at NHS acute Trust in North West of England that is delivered through the PharmOutcomes™ platform. The PharmOutcomes™ platform facilitates services provided by community pharmacies such as medication reconciliation. At the base, before February 2019, the acute Trust in North West of England had some problems with using fax to send discharge related medication information with community pharmacies, such as delayed sending or poor quality image, which had risk to medication safety.

PharmOutcomes™ TCAM service data is routinely collated in an NHS acute Trust in North West of England systems at the patient level. Pharmacy staff at NHS acute Trust in North West of England who were responsible for delivering the service had access to this data. The data were collected to monitor the service update and delivery and follow-up with community pharmacies regarding referrals.

The initial focus of the NHS acute Trust in North West of England TCAM project was to provide the TCAM service to patients with new or existing monitored dosage systems (MDS) (Multi compartment compliance aids (MCAs) or blister packs, which have different brand name including Nomad®, Dossette®, Medidos®, Venalink®)[432]. In a recent survey in England, it was estimated that a median of 20 MDS are being administerd by community pharmacies per month[433]. It has been estimated that 64 million MDS are dispensed to around 1.2 million patients by community pharmacies in England annually[429]. MDS are widely used to dispense patient medication with the aim of supporting patient adherence and simplifying the treatment[434,435]; however, despite widespread use there is a lack of evidence of MDS benefits[436,437] unless these are combined with other interventions[438]. Incidents of patient confusion regarding changing MDS brands post hospital discharge have been documented[439]. Evidence is contradictory in confirming whether MDS increases patient independence[440], or affects patient independence and autonomy negatively[437].

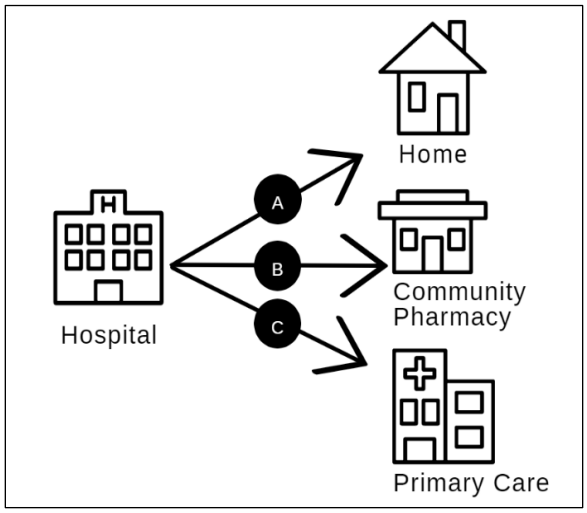
The use of MDS has been shown to be associated with a high prevalence of potentially inappropriate medications and risk of hospital re-admission in recent studies in the UK[441,442]. Moreover, a survey in 2005 in the UK found that information about patients' MDS were communicated to almost 50% of patients' community pharmacies after hospital discharge which raised medication safety concerns[443]. The reason for targeting this specific vulnerable group of patients is that MDS often are refilled with their medication supply on a weekly basis. This makes the patient a frequent user of community pharmacies. Sometimes a 4 week supply is issued at once, which may lead to errors as medication doses may be changed, and the MDS needs to be re-filled. A recent report of patient harm due to MDS used analysed incident reports submitted to the National Reporting and Learning System (NRLS), found that the number of incident reports related to MDS use increased[429]. In 2017, 972 incident reports were submitted to NRLS, including 79 low harm incidents and 17 moderate harm incidents[429]. Anecdotally, communication between the hospital and community pharmacy was also reported to be poor for this group of patients – for example, hospitals were previously required to send the discharge letter for the patient with MDS to the community pharmacy via fax, but this did not always occur and suffered from poor resolution of document images.

Table 6.1 – Comparison between usual care and TCAM intervention steps

Process	Usual care (up until Feb 2019)	TCAM intervention (Feb 2019 onwards)
Clinical pharmacist at hospital sends admission notification to community pharmacy via: • PharmOutcomes™		✓
Clinical pharmacist at hospital sends discharge notification to community pharmacy via: • PharmOutcomes™		✓
Clinical pharmacist at hospital sends discharge letter (with up-to-date medication list) to community pharmacy via: • PharmOutcomes™ • Fax	✓	✓
Clinical pharmacist at hospital sends discharge letter to general practice via DocMan system	✓	✓
Communication between healthcare providers at the primary care site and community pharmacies is via email or telephone.	✓	✓

Figure 6.1 - Description of TCAM service at NHS acute Trust in North West of England

Transfer of Care Around Medicines (TCAM) at NHS acute Trust in North West of England



The TCAM service initiative at the NHS acute Trust in North West of England is a project that targeted patient discharges from hospital to community settings (e.g. home) **[Arrow A].** The project consists of sending electronic admission and discharge notification, as well as the hospital discharge summary to the patients' named community pharmacy to enable referral via an encrypted platform (PharmOutcomes™), and an email alert instead of fax **[Arrow B].** The service also includes an auto-report sent from NHS acute Trust in North West of England to primary care pharmacists in general practices **[Arrow C].** The auto-report is an Excel® spreadsheet with patient initials, age and hospital number that notifies the practice pharmacist that the patient was discharged from NHS acute Trust in North West of England and that they have been referred within the TCAM service. The intervention focus and involves **[Arrow B]**, and does not actively involves **[Arrow A and C].**

After a referral from the hospital pharmacy, the nominated community pharmacies can accept, complete or reject the referral. If the referral is left unaccepted or rejected a follow-up call will be received from the hospital pharmacy team. Reasons for rejection might include that the patient is not/no longer a customer at this particular community pharmacy. The community pharmacy also can document medication side effects, any given care/service following discharge, and validate if a first repeat prescription is correct.

Four training events were organised for hospital and community pharmacy staff for the TCAM service, followed by a service launch during February 2019. Two training sessions were for hospital pharmacists and a further two sessions were for community pharmacy staff. Attendance at the training sessions was not mandatory. The first training session was planned by the Local Pharmaceutical committee in January 2019 and invited pharmacists via a newsletter, with the second taking place in July 2019. There was a demonstration of the TCAM system in the training session.

A 'PharmAlarm' was disseminated to community pharmacies in July 2019 to support actioning referrals. A 'PharmAlarm' is a device that, once inserted into computer universal serial bus (USB) port, flashes once a referral is received to alert the pharmacy team to review the referral.

The communication of the discharge letter to community pharmacies in this service is intended to reduce discrepancies in medication prescribing and dispensing between secondary and primary care, as both the community pharmacy and the general practice are quickly made aware of all details regarding patients' medication during and following the hospital episode. This project is also intended to improve monitoring and reporting of adverse drug reactions (via documenting in the system), improve communication between pharmacy teams across sectors, reduce medicines waste, improve the quality of information transfer and improve patient adherence.

6.2 Aim and objectives

This study aimed to evaluate the utilisation and impact of the TCAM service on medicines safety in an NHS acute Trust in North West of England. The specific objectives of this study were:

1. Assess TCAM 'service utilisation' via descriptively analysing retrospective anonymised patient referral data within the PharmOutcomes™ platform,
2. Assess TCAM 'service impact' on the prevalence and nature of unintentional medication discrepancies (UMDs) and adverse drug events (ADEs).
3. Identify any patient, medication and TCAM service factors associated with increased risk of UMDs and ADEs, and
4. Generate recommendations to improve the TCAM service as well as for future research regarding interventions to address medication safety challenges post hospital discharge.

6.3 Methods

The overall structure of this chapter follows the reporting criteria specified in *"Standards for Quality Improvement Reporting Excellence (SQUIRE 2.0)"*[444], and *"CONsolidated Standards Of Reporting Trials (CONSORT)"*[445]. The protocol of the study is registered at the International Standard Randomised Controlled Trial Number (ISRCTN) registry (registration number 17094460, https://doi.org/10.1186/ISRCTN17094460). This service evaluation study was exempt from approval by the University of Manchester Research Ethics Committee (UREC) [2019-7048-10983]. Heath Research Authority (HRA) [Integrated Research Application System (IRAS) project ID 262688], and host organisation approvals were obtained. Copies of UREC letter and HRA approval letters are provided in Appendix 32, and Appendix 33.

Study metadata includes:

- Data Management Plan
- Study Protocol
- Distress protocol
- Study Introduction Letter
- Data Collection Training material; presentation material and patient cases

- Data Collection Guide (see Appendix 34)
- Master Patient Link Code Sheet (see Appendix 35)
- Data Collection Form (see Appendix 36 – Data Collection forms)
- Expert Panel Assessment Tool (see Appendix 37)

6.3.1 **Study design**

This Chapter consists of two parallel studies; a 'service impact' and 'service utilisation' study. The design of the 'service utilisation' study was a retrospective analysis of anonymised previously collected PharmOutcomes™ data. The design of the 'service impact' study was an uncontrolled, retrospective before and after study, where two cohorts of patients from the same general practice sites were investigated before and after the TCAM intervention was introduced.

A concurrent qualitative process evaluation study of this service was also separately completed by a researcher (MJ) in the Pharmacy Department at the University of Manchester, which is part of this wider evaluation study presented in this Chapter. The discussion section of this Chapter highlights the results of the qualitative study in context of the findings presented in this Chapter, with further discussion of the findings from both studies together in Chapter Seven.

6.3.2 **Terminology**

For the different sections of the chapter, the terms 'service utilisation' (what happened in the service – PharmOutcomes™ data) and 'service impact' (what is the service impact on UMD/ ADE rates), were used. These definitions of the key medication safety measures for the 'service impact' study are in Table 2.2, Chapter Two.

The study adopted the Institute for Healthcare Improvement (IHI) definition of medication reconciliation[268], which is *''The process of obtaining an up-to-date and accurate medication list that has been compared with the most recently available information and has documented any discrepancies, changes, deletions or additions resulting in a complete list of medication accurately communicated''* in order to capture 'service impact' data. However, in order to reflect local practices (where medicines reconciliation may not always be carried out by pharmacy staff due to resource constraints, and may not label it as 'medicines reconciliation' like the pharmacy team do) the study also accepted as 'medicines reconciliation' for data

collection purposes any medical record entries sufficiently similar to this activity and conducted by a member of non-pharmacy practice staff – this judgement was made by the clinical pharmacist data collectors (see below)(some practice staff may complete medicines reconciliation type activity, but not record it in the same way as pharmacy staff or label it as medicines reconciliation). The methodology in this study assumed that medication reconciliations/identification of medication discrepancies completed by practice staff is accurate. No independent medication reconciliation was completed by the research team. Any undocumented, unexplained medication change was considered unintentional medication discrepancy[215,244,245,370,446,447], unless it was documented as confirmed with the prescriber to be otherwise – clinical pharmacist data collectors were also trained to identify UMDs.

6.3.3 Study setting

Data collection in general practices was conducted to identify the impact of the service on UMDs / ADEs using the electronic health record system – any changes in medications or other interventions brought about by the service were postulated to involve communication between community pharmacies, patients and general practices, and to then affect ongoing care which would be captured in the medical record (e.g. as medication related harm, or through medicines reconciliation entries). These general practices were in a local area in North West of England, which have a total population of 262,697 (as of 2020)[448]. These general practices were drawn from across all 5 local area general practice groups/boroughs and differed in the number of patients, the average number of medication reconciliations done weekly, the average number of patients on MDS and software used (including Vision or Egton Medical Information Systems (EMIS)). An integrated health care record across primary and secondary care is available in the local area Clinical Commissioning Groups (CCG). All general practices involved in the study had a practising pharmacist who was either general practice employed or/and neighbourhood integrated practice pharmacists (NIPPS). The NIPPS service was introduced in the local area by NHS acute Trust in North West of England to deploy pharmacists in general practices between 3 to 5 days a week, based on the size of the practice. Pharmacists were providing medicines optimisation services, including medicines reconciliation.

6.3.4 Sampling

6.3.4.1 Sampling strategy and eligibility

The 'Service utilisation' study data included service electronic referral data from NHS acute Trust in North West of England to all community pharmacies involved in the service (n=71) via the PharmOutcomes™ platform, in the local area. These community pharmacies included 32 national multiple stores, 23 independent pharmacies (those who have a maximum 2 stores), 12 regional multiple stores (with more than 2 stores in the region belonging to one particular company A), and 4 regional stores (with more than 2 stores in the region belonging to one particular company B). The sampling was from database covering all referrals over one year period (further details about data collection in sections below).

The 'service impact' study data collection was conducted in 18/43 (42%) general practices in the local area. Initially all practices in the local area Clinical Commissioning Groups (CCG) (n=43) were contacted via emails and at relevant Primary Care Network (PCN) meetings to be involved in data collection for the service impact study. However, 25 practices were excluded due to local resource constraints (n=13) and/or low numbers of eligible MDS patient referrals (n=12 practices) (median referrals 11, range 1 – 19). Characteristics of the remaining 18 general practices included in the 'service impact' study are summarised in Table 6.2. The number of patients in each practice in February 2019 were retrieved from NHS digital.

Table 6.2– Characteristics of general practices involved in 'service impact' study

Local area – Neighbourhood*	Practice anonymised code	Number of registered patients in Feb 2019**	GP IT system
A	I	5 - < 10 thousand	Emis
	J	10 - < 15 thousand	Emis
	K	10 - < 15 thousand	Emis
B	G	5 - < 10 thousand	Emis
	H	5 - < 10 thousand	Emis
C	E	5 - < 10 thousand	Emis
	F	15 - < 20 thousand	Vision
D	N	1 - < 5 thousand	Vision
	O	1 - < 5 thousand	Emis
	P	5 - < 10 thousand	Vision
	Q	5 - < 10 thousand	Vision
	R	5 - <10 thousand	Emis
E	L	5 - < 10 thousand	Vision
	M	10 - < 15 thousand	Emis
F	C	1 - < 5 thousand	Emis
	D	15 - < 20 thousand	Vision
G	A	1 - < 5 thousand	Vision
H	B	1 - < 5 thousand	Vision

References *[449] **[450]

6.3.4.2 Sample size calculation

Calculation of sample size in the 'service impact' study was completed for the two primary outcome measures UMDs and ADEs. It was estimated that ADE data was required from 638 patients for the study, including 319 patients for the baseline data and 319 patients after service implementation. Table 6.3 summarises sample size calculation based on Dawson and Trapp calculations. To collect data of 638 patients to meet sample size calculations, data for up to 50 patients were planned to be collected from each of the 18 general practices.

Table 6.3 – Sample size calculations

α = 0.05 level of significance	β = 0.2 (80%) Statistical power	
Fn(α β)	Fn= 7.9	
$n = \frac{P1\ (100 - P1) + P2\ (100 - P2)}{(P2-P1)^2} X\ \ F(\alpha\ \beta\ )$ n= sample size P = Proportion of outcome in the general population		
Baseline rate	50%	
Relative reduction	20%	
Baseline rate	**Reduction 20%**	**Sample size**
37% of patients affected by ADE[247]	29.6%	637
50% of patients affected by one or more UMDs (based on the median rate identified in Chapter Four)	40%	387

6.3.5 Data sources

Data were collected from two independent datasets: PharmOutcomes™ TCAM data for the 'service utilisation' component and general practice electronic health records for 'service impact' data (including free text consultations, laboratory data, prescribing data and medication reconciliation/ medication review activity).

6.3.6 Data collection – Patient Identification

6.3.6.1 'Service Utilisation' study

For the 'service utilisation' study, patients were identified from a PharmOutcomes™ database of referrals provided to the NHS trust TCAM service leadership. Patients needed to be discharged from NHS acute Trust in North West of England and referred via the TCAM service between March 2019 and February 2020 to be eligible for the evaluation; all referrals were included in the study over this time window excluding any duplicates. PharmOutcomes™ TCAM service 'utilisation' data was routinely collated in an NHS acute Trust in North West of England systems at the patient level, and included patient age, and gender, and TCAM referral information.

6.3.6.2 'Service Impact' study

The 'service impact' study included all patients aged 18 or older at the time of hospital discharge, who were discharged from in-patient hospital stay at NHS acute Trust in North West of England (staying at least 24 hours in the hospital) between August 2018 and August 2019 with a new or recurrent MDS. For the post-implementation phase of this study, this also

included patients who were referred via the TCAM to a named community pharmacy using the PharmOutcomes™ platform. Patients also had to be registered with one of the 18 named general practices in the local area. Patients with a planned admission (e.g. day-case surgery, or dialysis) or discharged from the emergency department were excluded. Patients who did not have a medicines reconciliation (or equivalent) entry in their general practice record, or those who died directly after hospital discharge were excluded at the data collection stage.

The pharmacy department at NHS acute Trust in North West of England identified from their electronic patient record system patients discharged with MDS to practices within the local area Clinical Commissioning Group (CCG) and sent an individual report per practice via NHS.net email to each pharmacist data collector. The research team at the University of Manchester had no access to this list to protect patient confidentiality. Eligible patient discharges between August 2018 and January 2019 for retrospective data collection were identified for the TCAM pre-implementation stage and between March 2019 and August 2019 for the post-implementation stage. For patient selection, each patient discharge was assigned by the pharmacy team a sequential number (to preserve patient confidentiality and to assure a random sample is included) which was sent to the lead researcher (FA) who then selected discharges at random for inclusion in the study using a random sample generator in Microsoft Excel®, 2010 (Microsoft, Redmond, WA, USA). These numbers were then sent to the pharmacist data collectors to generate the final sample of usable 638 patient records across 18 general practices. Additional random numbers were later generated (using the above referenced method) and sent to the practices as up to 30% discharges screened by pharmacist data collectors were not eligible for inclusion in the study (e.g. admitted for <24 hours, or elective planned admission). NHS acute Trust in North West of England, the employer of the NIPPS team, were provided with a payment to support their time screening and collecting this extra data.

6.3.7 Data collectors

6.3.7.1 'Service Utilisation' study

For this study, a senior pharmacist collaborator based at NHS acute Trust in North West of England who was responsible for the delivery of the TCAM service gathered and anonymised 'service utilisation' data from the PharmOutcomes™ platform and sent this to the research

team for analysis via NHS.net email in June 2020. The senior pharmacist collaborator routinely had access to this data as part of their role.

6.3.7.2 'Service impact' study

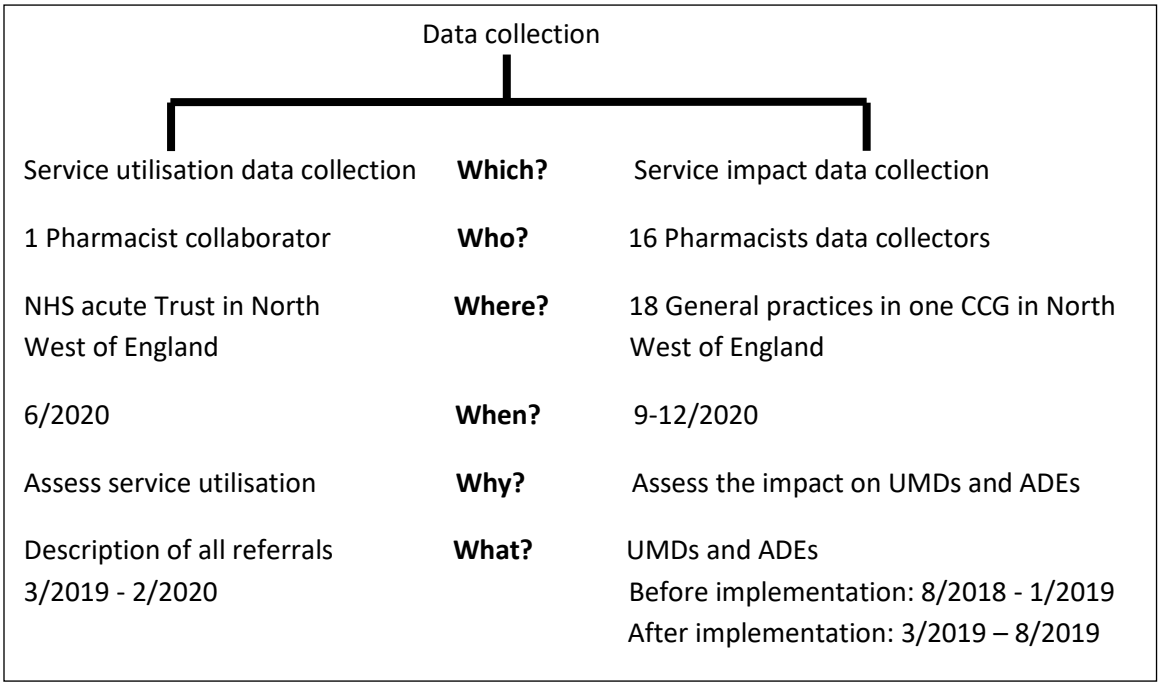
Data were collected across 18 general practices by 16 trained practice pharmacists either as a practice employed (n=1) or NIPPS pharmacists (n=15). Among NIPPS team data collectors, four pharmacists were Agenda for Change (AfC) band 8a, seven pharmacists were AfC band 7, and four pharmacists were AfC band 6. These data collectors were routinely providing medication reconciliation and optimisation activity in the practices involved, and were considered ideally placed to identify UMD and ADEs in medical records as described in earlier studies[451]. The number of pharmacists in the NIPPS Team who routinely work in the 18 included practices is 23, however 15 pharmacists from the NIPPS team (and one practice employer pharmacist) were involved in data collection due to pharmacist circumstances including sick leave, maternity leave, or registration/leaving the NIPPS team.

Each data collector received a three-hour face-to-face group training session from the research team before data collection. In addition, four visits to individual general practices were arranged to provide training by FA, along with three virtual refresher sessions. The training session covered the study aim, outcome definition, examples of UMDs and ADEs to work through, discussion of the ADE trigger tool and instructions for collecting the data. The training session also included familiarisation with the data collection tools (available in Appendix 36). Data collectors also received a data collection guide (see Appendix 34) containing all information covered in the training session including descriptions of UMDs and ADE definitions, instruction on the process of data collection, and a list of triggers that could guide them to identify ADEs. Data collectors had the opportunity to explore and clarify their understanding of the topics with the lead researcher and their peers during the training sessions. Three trigger tools were used to create a single ADE trigger tool for use in the training and Data Collection Guide, including the Outpatient Adverse Event tool[452], Skilled Nursing Facility Trigger Tool for measuring ADEs[453], and Trigger tool for measuring Adverse Drug Events[454].

Frequent update emails were also sent during the study data collection period every 1-2 weeks by the lead researcher to the pharmacist data collectors with advice about data collection and submission deadlines, sharing the frequently asked questions that were received from data

collectors, and celebrating data collection achievements. A summary of overall data collection steps across the 'service impact' and 'service utilisation' studies is provided in Figure 6.2 below.

Figure 6.2 – Steps of data collection for 'service impact' and 'service utilisation' studies



Abbreviation: ADEs (Adverse Drug Events), CCG (Clinical Commissioning Group), NHS (National Healthcare Services), UMD (Unintentional Medication Discrepancies).

6.3.8 **Data collection process**

6.3.8.1 'Service Utilisation' data

PharmOutcomes™ TCAM service utilisation data were extracted and anonymised retrospectively by NHS acute Trust in North West of England pharmacist HB between January-June 2020 before being sent securely using an anonymised password protected Excel® spreadsheet to the research team at the University of Manchester via secure NHS.net email. This staff member received reimbursement for their time completing this activity. The data represented patients with new or existing MDS discharged from NHS acute Trust in North West of England and referred via TCAM between March 2019 to February 2020. The data consisted of different variables including patient age and gender, final provisional date (the last date any activity was made on patient referral), referral status, side effects, yellow card completion, community pharmacist feedback, and community pharmacist added services. In addition, it included information if the community pharmacist acknowledged that the patient had a

cardiovascular condition, respiratory condition or diabetes, or knew how and when to take the medication and the purpose of their medication, based on prior contact. The data also included information if the community pharmacist has initiated a referral to the GP and the nature of the referral.

The 'service utilisation' data was provided in one electronic sheet in Microsoft Excel®, 2010 (Microsoft, Redmond, WA, USA). Each row in the dataset represented one referral from NHS acute Trust in North West of England to one community pharmacy. A single patient could therefore have multiple hospital admissions and thus multiple referral rows of data during study time frame. The variable and outcome list in the service utilisation data are summarised in Table 6.4.

Table 6.4 – Variable list for PharmOutcomes™ data in 'service utilisation' study

Variable name	Description	Description, type of variable	Example
Provision date	Date of sending referral	Date	22/10/2019
Final provision date	Last date any activity was made on patient referral	Date	30/10/2109
Patient age in years	Patient chronological age	Numbers, coded as categorical data	80-89
Patient gender	Patient biological gender	Categories	Female
Cardiac, diabetes, respiratory condition	Community pharmacist acknowledged that the patient has certain conditions	Categorical	Yes
Side effect identified	If community pharmacist identifies a side effect	Categorical	No
Availability of repeat prescription	If the prescription included a repeat prescription	Categorical	Yes
Repeat prescription reconciliation	If community pharmacist identifies an error at the discharge letter while conducting a medication reconciliation	Free text	
Referral status	Status of the referral at the community pharmacy	Categorical	Completed
Pharmacist feedback	Pharmacist feedback of the referrals	Categorical	Yes
GP referral necessary	If community pharmacist identified that the patient needs a GP referral	Categorical	Yes
GP referral notification status	The medium of communication with the GP	Categorical	Sent by email
Referral reconciliation	Issues identified by community pharmacy while completing medication reconciliation	Free text	
Additional action	Additional notes regarding the services provided at the community pharmacy	Free text	
Support outcomes	Additional notes regarding the discharge letter	Free text	
Added service	Services completed by community pharmacies after completing the referrals	Free text, coded as categorical data	

6.3.8.2 'Service Impact' data

Medication safety data, including UMD and ADEs were collected from general practice electronic record systems, which the data collectors had routine access to. Pharmacist data collectors collected data via remote access to the clinical records via NHS acute Trust in North West of England virtual private network (VPN) within normal working hours and/or at a time convenient to the data collectors, as per routine working arrangements in place due to the ongoing COVID-19 pandemic. Pharmacists reviewed medication reconciliation records or similar entries made within 30 days of hospital discharge to find UMD. Alongside medicines reconciliation data, consultation data, laboratory data and prescribing data within a 90 day

period post-hospital discharge was screened to identify ADEs. These two time frames were chosen because medication reconciliation usually occurred in the general practices within 7 days, and previous literature commonly assessed ADEs 90 days post discharge[455,456]. Based on pilot work at two general practices involving two pharmacists, it was estimated to take 10-15 minutes to screen and complete data collection forms for one discharged patient. Each pharmacist data collector screened records for a maximum of 6 hours; 3 hours each in the pre- and post-implementation stages, over a 3-month period between September and December 2020.

Data were extracted by pharmacists using data collection forms (See Appendix 36) that were adapted from existing studies[457,458]. Data collection forms were completed electronically in Microsoft Word and sent via NHS.net email to the Chief Investigator at The University of Manchester before being uploaded to Research Data Storage (RDS) for analysis. Data collectors first completed 'Data Collection Form 1' for each patient they screened – they were advised to use the electronic primary care heath record, hospital discharge document and TCAM alert to record data and patient details on 'Data Collection Form 1' for everyone they screened regardless of whether they were eligible for inclusion or not. Then data collectors determined whether the patient was eligible to continue data collection for ADEs using 'Data Collection Form 2'.

In 'Data Collection Form 2', data collectors screened healthcare records and laboratory results and recorded any ADEs that were identified in patient records, and provided a full description of what happened (what is the ADE(s) detected, what is/are trigger identified, and what are the factors that help describe the harm or potential reason(s) it occurred). Pharmacist data collectors were advised to use their professional judgement and experience to look for evidence that supports the presence of ADEs, and to use the ADE triggers[452–454] list in the Data Collection Guide (Appendix 34) to help identify ADEs.

It was possible that one patient might experience more than one episode of medication related harm (ADE) during the three months post hospital discharge. If data collectors found that the patient has more than one suspected ADE, they were advised to complete a copy of 'Data Collection Form 2' for each suspected harm episode that was identified. In case the suspected harm involved multiple medications, data collectors were advised to describe in detail the

medications involved and the reason(s) why the event happened. Data fields in forms Data Collection 1 and 2 are summarised in Table 6.5.

During data collection pharmacist data collectors assessed the severity of any identified medication discrepancy (identified from medication reconciliation or related activity and listed in the data collection forms) and categorized the severity based on the national coordinating council for medication error reporting and prevention (NCC MERP) criteria[459] summarised in Table 6.6. Pharmacist data collectors were also instructed to use the ADE severity assessment tool in the Data Collection Guide (Appendix 34) to rate ADE harm severity.

Before being sent to the University of Manchester for analysis, data were pseudonymised by removing patient and practice identifiers. Data collectors were instructed to follow guidance about data anonymisation during their training and in the Data Collection Guide. When starting data screening for an individual patient, data collectors assigned a unique pseudonymised identifier number for each patient and practice and kept a record of this in a 'Master Patient Link' Code Sheet (see Appendix 35), which was stored on the secure pharmacy team virtual shared drive. These unique codes were used on the main Data Collection Forms 1 and 2. This process also ensured that the practice pharmacist could identify and track their patients if required (e.g. requests for clarification from the research team).

Data collection was terminated if a patient died, was transferred to another hospital or had another hospital stay (readmitted) within three months following hospital discharge – in these cases data was collected until the point of death or the episode of hospital readmission.

Table 6.5 – Summary of data collection forms (1 and 2)

Form	Section	Description
1	A	This section was designed to record some basic information of the data collector, phase of data collection and practice site.
	B	This section was designed to record basic anonymised information regarding patient demographics.
	C	This section was designed to record basic information regarding patient eligibility criteria for the study.
	D	This section was designed to record data on medication reconciliation or equivalent medication entries activity that were identified in patient records during one-month post hospital discharge, and record information of medication discrepancies identified, including a description of medication discrepancies, the severity of discrepancies, and action taken.
2	A	This section was designed to record data regarding the nature of suspected patient ADE, the outcome associated with this ADE and any history potentially related to the reported ADE (e.g. laboratory result, potential drug-drug interaction, smoking and alcohol use and liver/kidney problems) to help confirm the presence of ADE.
	B	This section was designed to record data on any drugs involved with the ADE that were described (including name, dose, frequency, route, and when the medication has started).
	C	This section was designed to record the likelihood that a particular drug(s) is/are the cause of the observed ADE and how avoidable the harm is/was.

Table 6.6 – Categories of medication discrepancies severity

Category	Description
A	Circumstances or events that have the capacity to cause error
B	An error occurred but the error did not reach the patient (An error of omission does reach the patient)
C	An error occurred that reached the patient but did not cause patient harm
D	an error occurred that reached the patient and required monitoring to confirm that it resulted in no harm to the patient and/or required intervention to preclude harm
E	an error occurred that may have contributed to or resulted in temporary harm to the patient and required intervention
F	An error occurred that may have contributed to or resulted in temporary harm to the patient and required initial or prolonged hospitalization
G	an error occurred that may have contributed to or resulted in permanent patient harm
H	An error occurred that required intervention necessary to sustain life
I	An error occurred that may have contributed to or resulted in the patient's death

6.3.9 Data Validation

6.3.9.1 'Service Impact' study

6.3.9.1.1 Adverse Drug Events

Following data collection, expert panel meetings were carried out to review the ADE data from the 'Service Impact' study. The expert panel consisted of a GP and two pharmacist medication safety experts with experience of hospital and general practice pharmacy, who were not directly involved with data collection. The expert panel meetings were conducted virtually via Zoom. There were four expert panel meetings held between November 2020 – February 2021, each lasting three hours. The lead researcher (FA) provided the panel members via email with an overview of the study aim, objectives, and method, in addition to copies of expert panel assessment forms. During expert panel meetings panellists rated ADEs using information provided on screen by FA. Panellists were blinded to the data collector, practice site, study phase (before or after TCAM service implementation) and relevant dates. Any disagreement between panel members was resolved by discussion until consensus was reached. Monetary remuneration was provided for each panel members for their time.

For ADE validation, the expert panel met to confirm the causality, preventability and severity of identified ADEs by consensus, following similar approach by previous ADE studies[457,460]. The assessment was based on the amended Hallas criteria for causality of ADEs[185,461], Helper criteria for preventability of ADEs[462], National Patient Safety Agency criteria for severity of ADEs[463] (assessment form in Appendix 37). The expert panel members evaluated the potential ADEs against relevant local and national policies and best practice guidelines, and based their judgements on what was contained in the data collection forms only, except in a limited number of cases (n=3) where expert panel had some queries to data collectors to clarify some issues in the data collection forms.

6.3.9.1.2 Unintentional medication Discrepancies

This assessment was carried out to confirm if the collected data was a UMD or intentional medication discrepancy based on the data collector information provided in Form 2. All data collection forms (n=85) with at least one medication discrepancy were evaluated independently by the supervisors (RNK and DS) who are both pharmacists with medication

safety research experience to assess the medication discrepancies. The researchers were not blinded to the stage of data collection (pre/post service implementation). This review process was followed by consensus meetings (FA, RNK, DS) where disagreements were resolved through discussion with the lead researcher (FA). Thirty seven percent of the data collection forms were assessed to either not have a medication discrepancy at all or to have an intentional medication discrepancy (37%, n=32/85) and these were excluded from the subsequent data analysis. A total of 15% (n=13/85) of discrepancies were not clearly either intentional or unintentional, however were included in the analysis as UMD as previously described.

6.3.10 Data cleaning method

6.3.10.1 'Service Impact' study

All information in the Microsoft Word data collection forms were manually entered in one sheet in Microsoft Excel®, 2010 (Microsoft, Redmond, WA, USA). Each row in the resulting dataset represented one data collection form submitted by a data collector. Therefore, one patient could have had multiple rows if they had multiple included admissions randomly selected during the data collection time frames. In addition, some data collection forms included multiple UMD and/or ADE, where these were assigned multiple columns. Each column header represented one question in the data collection form (which could befree text or numerical). This was followed by a data entry validation whereby all data collection forms were compared against the resulting electronic dataset to identify errors including transcribing or transposition errors. The lead researcher (FA) sent query emails to the data collectors to clarify data collection forms where information was not clear or unknown abbreviations used. The variable and outcome list in service impact data are summarised in Appendix 38.

The lead researcher (FA) reviewed the quantitative data and coded them using numeric values. Medication classification was based on the British National Formulary (BNF) chapters (access via https://www.medicinescomplete.com in June 2021)[418], a copy of this coding in Appendix 39. The medication in the three most commonly reported BNF chapters were further coded based on the specific medication groups.

Number of medications was coded as numeric and categorical data. If the number of medications prescribed to the patient as recorded in the data collection forms equalled 5 or

more, this was coded as polypharmacy based on a definition commonly used by studies cited in a recent systematic review[464]. Furthermore, a number of 10 or more was coded as excessive polypharmacy [465–468].

6.3.11 Data Analysis

After receiving all data collection forms, the lead author FA completed data entry to compile study population lists in Microsoft Excel®, 2010 (Microsoft, Redmond, WA, USA). Data entry and analysis was via remote desktop access from the University of Manchester, using a secure University of Manchester virtual private network (VPN) to access the Research Data Storage (RDS) drive where the data was housed. All data analysis were carried out using Stata, version 14.0 (StataCorp LLC, Texas, USA).

6.3.11.1 'Service Utilisation' data

To address the first objective of this study, the PharmOutcomes™ referral data underwent descriptive analysis presented in tables using percentage by FA including categorical and continuous fields: nature and number of referrals (including patient gender, age, and referral details) and outcome of referral (including referral status, actions arising, and pharmacist feedback). In addition, all free text data entered by community pharmacists regarding potential side effects or concerns about patient medication used were coded as categorical data. Chi-square test was calculated to evaluate the interaction between patient characteristics including age and gender on number of services provided at community pharmacies. Statistical significance was concluded for values of $P<0.05$.

6.3.11.2 'Service Impact' data

For objective 2 of this study, which is assessing the 'service impact' on UMDs and ADEs prior to and following implementation service implementation the analysis was as follows. Firstly, a descriptive analysis to characterise the study participants before and after service implementation was completed. Patients involved were described by sociodemographic characteristics, including age (years), gender, and discharge diagnosis (International Classification of Diseases 10th revision (ICD-10)). Secondly, an unadjusted analysis comparing outcomes (UMDs and ADEs) before and after service implementation was completed, via comparing the rate, nature and severity of UMDs and ADEs. The nature of UMDs and ADEs

includes number of UMD and ADEs, and class/name of medication involved. Thirdly, an adjusted analysis for potential confounding variables was completed via logistic regression analysis. The analysis was adjusted for potential confounding variables, that were chosen based on literature review, including patient, medication, and service-related variables.

For the regression analysis, at the beginning a univariate analysis of the variable 'stage of service implementation' was completed, followed by multivariable regression analysis for the outcome rate of UMDs and ADEs. The multivariable regression analysis was planned by firstly choosing the confounders that were included in the analysis. Potential confounding variables (risk factors for ADEs and UMDs) were identified from the existing literature to be controlled/adjusted via using multivariable regression analysis[469]. Each variable in the study was reviewed against evidence to evaluate if literature supported it impacts on the dependent variable (ADEs, and UMDs), or if these variables were included in the regression analysis model by previous works of literatures exploring the rate of ADEs, or medication related readmission. Excluded variables that were not included in developing the model were practice' electronic system, ethnicity, discharge ward, discharge diagnosis, discharge destination, data collector band, practice locality, and time to send a discharge letter to practice. The final list of included confounders is summarised in Table 6.7 and Figure 6.3, and was selected based on clinical relevance. Clinically significant important confounders using a clinical method model building were used in the multivariable logistic regression model to assess the factors associated with medication discrepancies and adverse drug events[470]. The covariates, including age, gender, number of medications, and length of hospital stay, were included in the regression analysis based on previous literature[214,215]. The covariates adjusted the analysis to account for confounding and effect modification. A multivariable logistic regression analysis was completed for the outcome presence of UMDs or ADEs as these are binary (dichotomous) outcomes, where the dependent variable is the presence of the outcome of interest (UMDs or ADEs).

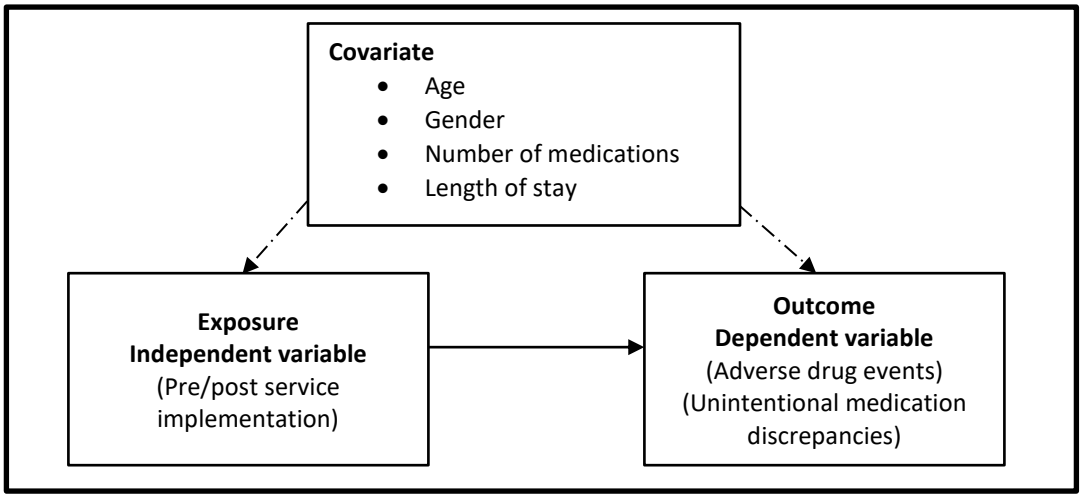
For objective 3 of this study, which is identifying risk factors (patient, medication, and service factors) associated with UMDs and ADEs the analysis was as follows. First, a descriptive analysis using full dataset was completed. This was followed by logistic regression analysis of the baseline data for UMDs and ADEs. This was conducted to identify risk factors that may impact the baseline rate of UMDs and ADEs, without the interference of the TCAM service.

Descriptive analyses were presented in tables using percentages, while logistic regression analysis was presented using the odd ratio (OR), 95% confidence interval (CI), and the number of observations. Any odds ratio below 1 (negative association) was considered a protective factor against the outcome of interest (UMDs or ADEs), while an odds ratio above 1 (positive association) was interpreted as a risk factor increasing the probability of the outcome of interest appearing (UMDs or ADEs).

Table 6.7 – References for the list of covariates identified from literature

Covariate	Impact on		
	ADE	UMD	Readmission
Age (continuous variable)	214,215	215	191,333,471,472
Gender	213		333,471
Number of medication (continuous variable)	6,213		191,471
Length of stay (LOS) (continuous variable)	209		471

Figure 6.3 – Covariate list



6.4 Results

6.4.1 ‘Service utilisation'study

6.4.1.1 Patient demographics

Between March 2019 and February 2020, there were 3,033 TCAM referrals from NHS acute Trust in North West of England to 71 community pharmacies across the local area via the PharmOutcomes platform. Most of the referrals were for patients aged 70 and above (72%, n=2,195), with 14% (n=184/3,033) of referrals being for patients aged 20-59 years old. Sixty-five per cent (n=1,713/3,033) of the referrals were for female patients. The community pharmacist identified 32(1%), 38 (1%), and 165 (5%) patients with respiratory conditions, diabetes, and cardiac conditions, respectively (based on prior knowledge of the patient, irrespective of New Medicines Service (NMS) service provision). Table 6.8 represents patient demographics.

Table 6.8 – Patient demographics in all TCAM referrals

Characteristics	Frequency	Percentage
Age		
20-49	184	6.0
50-59	258	8.5
60-69	396	13.0
70-79	722	23.8
80-89	1,091	35.9
90-100	382	12.7
Gender		
Missing data	1	0.03
Female	1,713	56.47
Male	1,319	43.48
Respiratory condition		
Missing/unknown*	907	30.0
Yes	32	1.0
No	2,094	69.0
Diabetes		
Missing/unknown*	907	30.0
Yes	38	1.2
No	2,088	68.8
Cardiac condition		
Missing/unknown*	907	30.0
Yes	165	5.4
No	1,961	64.6

**uncompleted referral*

6.4.1.2 Community pharmacy information about the patient medication use practice

Community pharmacists recorded, based on their knowledge of the patient, that 23.5% (n=713/3,033) of referred patients confirmed that they knew the purpose of their medications, that 35% (n=1,066/3,033) knew how to take/use their medication, and that 43.25% (n=1,312/3,033) knew when to take/use their medication. Furthermore, from the cohort of patients with completed referrals (n=2,126), an almost identical proportion of female and male patients showed favourable results with regard to community pharmacist feedback on their knowledge about the use of their medication. Table 6.9 and Table 6.10 below represents this information.

Table 6.9 – Community pharmacy information about patient medication use practice

Characteristics	Frequency (n=3,033)	Percentage
Patient knows the purpose of their medication		
Missing/unknown*	907	30
Yes	713	23.5
No	1,413	46.5
Patient knows how to take/use their medicines		
Missing/unknown*	907	30.0
Yes	1,066	35.1
No	1,060	35.0
Patient knows when to take/use their medication		
Missing/unknown*	907	29.9
Yes	1,312	43.2
No	814	26.8

**Uncompleted referral*

Table 6.10 – Patient characteristics in the completed TCAM referrals

Total (n=2,126)	Patients know the purpose of their medication (n=713)	Patients know how to take/use their medicines (n=1,066)	Patients know when to take/use their medication (n=1,312)
Gender			
Female (n=1,217)	418 (34%)	608 (50%)	752 (61.7%)
Male (n=909)	295 (32%)	458 (50%)	560 (61,6%)
Statistical test	Pearson chi2(1) = 0.8370, **P-value = 0.360**	Pearson chi2(1) = 0.0378, **P-value = 0.846**	Pearson chi2(1) = 0.0075, **P-value = 0.931**
Age groups			
20-49 (n=147)	56 (38%)	84 (57%)	89 (60%)
50-59 (n=187)	58 (31%)	107 (57%)	123 (66%)
60-69 (n=279)	95 (34%)	152 (54%)	176 (63%)
70-79 (n=510)	169 (33%)	242 (47%)	326 (64%)
80-89 (n=756)	251 (33%)	365 (48%)	454 (60%)
90-100 (n=247)	84 (34%)	116 (47%)	144 (58%)
Statistical test	Pearson chi2(5) = 2.0358, **P-value = 0.844**	Pearson chi2(5) = 12.252, **P-value = 0.031**	Pearson chi2(5) = 4.7651, **P-value = 0.445**

6.4.1.3 Referrals completed by community pharmacies

6.4.1.3.1 Patient age and gender, and completed referrals

Overall, the majority of referrals (70%, 2,126/3,033) were marked as 'completed' by the community pharmacies, with 30% (n=907) left uncompleted. As shown in Table 6.11, three

quarters of referrals for patients aged between 20-59 years were completed (75.5%, n=334/442), while 69% of referrals for patients aged between 60 and 100 were completed (n=1,792/2,591). Referrals for the youngest patients had a higher completion rate than the most older patient groups, where Table 6.11 summarises this as 80% (n=147/184) for patients age between 20 and 49, while patient age between 90 and 100 had 64% (n=247/382) completion rate. Table 6.11 also show that an almost equal percentage of referrals were completed for female and male patients which were 71 and 69%, respectively.

Table 6.11– Number of all and completed TCAM by patient gender and age

Characteristics*	Number of all referrals (n=3,033)	Number of completed referrals (n=2,126)	Percentage completion
Age			
20-49	184 (6%)	147 (6.9%)	80%
50-59	258 (8.5%)	187 (8.7%)	72%
60-69	396 (13%)	279 (13.1%)	70%
70-79	722 (23.8%)	510 (23.9%)	70%
80-89	1,091 (35.9%)	756 (35.5%)	70%
90-100	382 (12.5%)	247 (11.6%)	64%
Gender			
Missing data	1 (0.03%)		
Female	1,713 (56.7%)	1,217 (57.2%)	71%
Male	1,319 (43.4%)	909 (42.7%)	69%

**Statistical test was not feasible, as this data was provided separately as two lists; one of which for all referrals and another one for completed referrals. However, a statistical test was completed for a preliminary dataset (missing 88 completed referrals) in Appendix 40 - TCAM referrals by month of referral, patient gender and age.*

6.4.1.3.2 Referrals per month

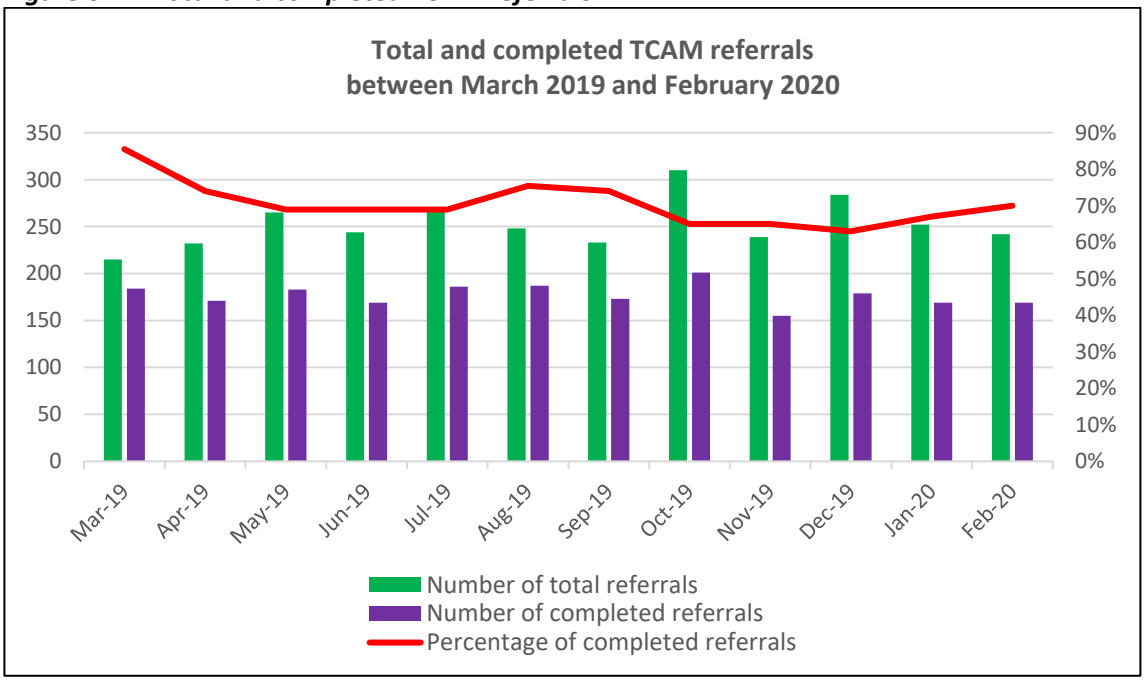
The number of referrals varied between 215 and 310 referral per month (median 246, Inter quartile range [IQR] 234 – 268). The completion rate varied between 63 and 85.5% per month (median 69, IQR 65.5 – 74). The lowest completion rate (63%) was in December 2019. Table 6.12 and Figure 6.4 represents the number of referrals in each month and the percentage of completed referrals.

Table 6.12 – Number of all and completed TCAM referrals by month of sending referrals

Month*	Number of all referrals	Number of completed referrals	Percentage of completed referrals
March 2019	215	184	85.5%
April 2019	232	171	74%
May 2019	265	183	69%
June 2019	244	169	69%
July 2019	269	186	69%
August 2019	248	187	75.4%
September 2019	233	173	74%
October 2019	310	201	65%
November 2019	239	155	65%
December 2019	284	179	63%
January 2020	252	169	67%
February 2020	242	169	70%
Total	**3,033**	**2,126**	**70%**

**Statistical test was not feasible, as this data was provided separately as two list; one of which for all referrals and another one for completed referrals. However, a statistical test was completed for a preliminary dataset (missing 88 completed referrals) in Appendix 40. There was statistically significant difference between completed and uncompleted referrals P-value = 0.001.*

Figure 6.4 – Total and completed TCAM referrals



6.4.1.3.3 Completed referrals per community pharmacy type

Table 6.13 represent number of referrals sent stratified by pharmacy type. It can be seen that the majority of the referrals were sent to large national multiple community pharmacies (38.3%, n=1,167/ 3,040), followed by independent pharmacies (37.6%, n=1,145/3,040).

However, the highest proportion of completed referrals where in local regional multiple community pharmacies which get the lowest number of referrals.

Table 6.13 – Number of referrals stratified by type of community pharmacy

Pharmacy type*	Total number of referrals	Number of completed referral	Percentage of completed referrals
Large national multiple	1,167	785	67.2%
Local regional multiple	728	569	70.9%
Independent	1,145	759	66.2%
Total	**3,040***	**2,113***	**69.5%**

**There was an issue with extracting this data by the trust, the numbers are not the same as the rest of the dataset. Statistical analysis was not feasible as this data was provided as aggregated data.*

6.4.1.3.4 Time to completing referrals

For the first 12 months of TCAM service implementation, community pharmacists acted on most referrals they received within same month of referral, with 15% of referrals completed/ or any activity saved after 30 days, over a median of 7.5 months [IQR 4.2-11.7] (as seen in Table 6.14).

Table 6.14 - Number of months to complete referrals

Referrals completed within		Frequency (2,126)	Percent (100%)	Cumulative percentage
Number of months	Number of days			
1	< 31 days	1,813	85.28	85.28
2	< 61 days	120	5.64	90.92
3	< 91 days	71	3.34	94.26
4	< 121 days	44	2.07	96.33
5	< 151 days	30	1.41	97.74
6	< 181 days	13	0.61	98.35
7	< 211 days	9	0.42	98.77
8	< 241 days	4	0.19	98.96
9	< 271 days	1	0.05	99.01
10	< 301 days	5	0.24	99.25
11	< 331 days	2	0.09	99.34
12	< 361 days	2	0.09	99.43
13	< 391 days	1	0.05	99.48
14	< 421 days	3	0.14	99.62
15	< 451 days	1	0.05	99.67
user errors		7	0.33	100.00

Table 6.15 represent number of completed referrals within months of sending referrals. Figure 6.5 represent the number of completed referrals within 30 days. The percentage of completed referrals in the same months of receiving referrals was observed to be increasing in the last three months of evaluation. Appendix 41 provides table with number of completed TCAM

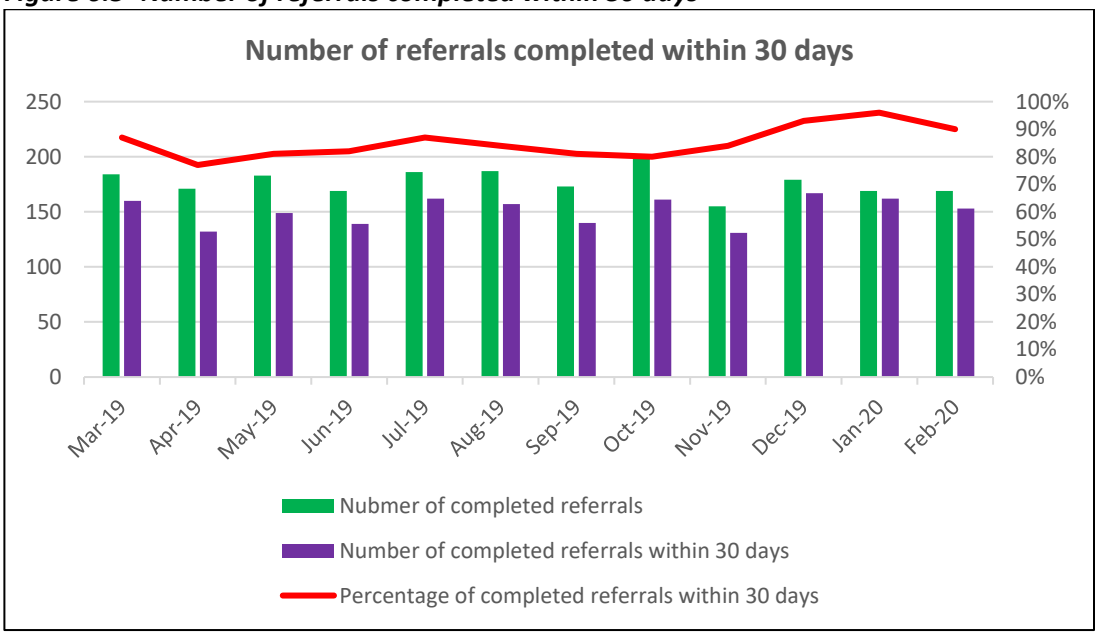
referrals by month of actioning referrals, figure with number of completed referrals in the same month of sending referrals.

Table 6.15- Number of completed referrals within months of sending referrals

Completed within X months	Month of sending referrals												
	March 2019	April 2019	May 2019	June 2019	July 2019	Aug 2019	Sep 2019	Oct 2019	Nov 2019	Dec 2019	Jan 2020	Feb 2020	Total
1	160 (87%)	132 (77%)	149 (81%)	139 (82%)	162 (87%)	157 (84%)	140 (81%)	161 (80%)	131 (84%)	167 (93%)	162 (96%)	153 (90%)	1,813 (85%)
2	7	8	14	21	13	6	11	11	10	7	6	6	120
3	3	19	10	5	2	4	4	4	10	1	0	9	71
4	9	3	1	1	0	4	1	18	3	2	1	1	44
5	0	1	4	1	0	4	15	3	0	2	0	0	30
6	0	2	0	0	0	10	0	0	1	0	0	0	13
7	0	0	2	0	1	2	1	3	0	0	0	0	9
8	0	0	1	0	2	0	1	0	0	0	0	0	4
9	0	1	0	0	0	0	0	0	0	0	0	0	1
10	0	0	0	0	5	0	0	0	0	0	0	0	5
11	2	0	0	0	0	0	0	0	0	0	0	0	2
12	1	0	0	1	0	0	0	0	0	0	0	0	2
13	0	1	0	0	0	0	0	0	0	0	0	0	1
14	0	3	0	0	0	0	0	0	0	0	0	0	3
15	1	0	0	0	0	0	0	0	0	0	0	0	1
*	1	1	2	1	1	0	0	1	0	0	0	0	7
Total	184	171	183	169	186	187	173	201	155	179	169	169	2,126

**User errors (final provision date was manually entered by mistake by community pharmacies) – excluded from the analysis here in this table*

Figure 6.5- Number of referrals completed within 30 days



6.4.1.4 Community pharmacy activities in relation to medication safety

Community pharmacies recorded having identified five patients affected by adverse drug reactions (ADRs) from the cohort of 2,126 patients with completed referrals. None of these ADRs were recorded as being submitted in a Yellow Card to the Medicines and Healthcare Products Regulatory Agency (MHRA)[473], if required. Three patients affected by an ADR had a manageable and non-harmful ADR (patient continued using the medication) and two patients had stopped taking the medicine in question and were referred to the GP.

The community pharmacist had completed the designated section for feedback in the PharmOutcomes™ platform for 11 'completed' patient's referral. However, this data generally includes further comments on the referrals, including, for example being unable to contact the patient, not receiving a detailed discharge letter, and that the patient was readmitted to hospital.

The usual repeat prescriptions requested by the practice were available in 56% (n=1,193) of patients from the cohort of 2,126 patients with completed referrals. Twenty-seven (27/1,193, 2%) of these repeat prescriptions were not reported to be correct as assessed by community pharmacies during medication reconciliation. The most common issues were medicines stopped in the hospital still on repeat (n=13), missing medications (n=5), new medications not on repeat/ added (n=3), wrong strength (n=3), wrong formulation (n=2), and other (n=1).

Community pharmacists identified 45 referrals (20 female and 25 male patients) from the cohort of 2,126 'completed' referrals (45/2,126; 2%) having issues that needed a referral to the GP. Forty of these referrals were completed via email, while five were needed to be sent manually. The most common reasons for referral to GP were due to the identification of medication changes, incorrect repeat prescriptions following discharge, to request a new prescription or weekly tray, and to inform GP that patient has stopped taking medication.

6.4.1.5 Community pharmacy services offered in response to TCAM referrals

Different services were reported as being carried out in community pharmacies once a referral was received, which then changed the referral status to 'completed'. Among the 2,126 completed referrals, the five most common services commenced were: 1004 (47.2%) completed a medication reconciliation, 1004 (47.2%) information reviewed, 841 (39.5%)

offered home delivery, 503 (23.6%) reviewed MDS arrangements, 400 (18.8%) commenced MDS. Table 6.16 below summarises the number of services completed in community pharmacies.

The other services offered include 10 documentations about patient death, 7 documentations that patients went into a care home, 4 public health interventions, 3 stop smoking services, 3 specialist medicines management service assessments, 3 documentations about medication changes and referral to GP, 2 flu vaccinations, 1 inhaler technique checks, 4 communications with patient's caregiver, and other unspecified services (n=25).

Table 6.16 – Number of completed services in community pharmacies

Services completed in community pharmacy (Number of completed referrals 2,126)	Frequency (Total 4,959)	Percent (100%)
Medicines Reconciliation completed	1004	47.2
Information reviewed	1004	47.2
Home delivery	841	39.55
Review MDS arrangements	503	23.65
Commenced MDS	400	18.8
Pharmacy managed repeat service	265	12.46
Medication administration record (MAR) chart provided	195	9.17
New Medicines Service	153	7.19
Easy open tops	134	6.30
Medicines Use Review	109	5.12
Review dose form	93	4.37
NHS Repeat dispensing initiated	89	4.18
Large print labels	75	3.52
Talking labels	32	1.50
Other	**62**	**2.91**

From the cohort of patient with completed referrals, 28.6% of patients received one service (n=609/2,126), 44.8% of patients received two services (n=953/2,126), 15% of patients received three services in community pharmacy (n=320/2,126), 5.2% of the patients received four services (n=111/2,126), 2.3% of the patients received five services (n=50/2,126), and 1% of the patients received six services (n=22/2,126). Three percent of the patients received from 7 to 14 services (n=61/2,126). Table 6.17 summarises the most common combined services commenced in community pharmacy.

Although the service targeted patients with MDS, only 23.6% of completed referrals had their MDS arrangement reviewed by community pharmacy (n=503/2,126), and 18.8% of patients

had their MDS commenced by community pharmacy (n=400/2,126). Table 6.17 below represents the most common (top 20) combined services commenced.

The results in Table 6.18 show that there was a statistically significant (P=0.01) difference in age of patients between those receiving one, or more than one service. Patients aged between 50 and 59 years old had the highest proportion of receiving more than one service.

Table 6.17 – Most common combined services commenced in community pharmacies

Combined services completed in community pharmacies	Frequency
Information reviewed, Medicines Reconciliation completed	629
Commenced MDS; Home delivery	101
Information reviewed, Medicines Reconciliation completed; Review MDS arrangements	68
Pharmacy managed repeat service; Home delivery	55
Information reviewed, Medicines Reconciliation completed; MAR chart provided	41
Information reviewed, Medicines Reconciliation completed; Home delivery	37
Review MDS arrangements; Home delivery	34
MAR chart provided; Easy open tops; Home delivery	27
Easy open tops; Home delivery	24
Review MDS arrangements; Commenced MDS	24
Large print labels; Easy open tops; Home delivery	22
Information reviewed, Medicines Reconciliation completed; Review MDS arrangements; Home delivery	21
Review MDS arrangements; Pharmacy managed repeat service; Home delivery	20
Commenced MDS; Pharmacy managed repeat service; Home delivery	20
Information reviewed, Medicines Reconciliation completed; Pharmacy managed repeat service; Home delivery	15
Information reviewed, Medicines Reconciliation completed; New Medicines Service; Medicines Use Review; MAR chart provided; Talking labels; Easy open tops; Review dose form; Review MDS arrangements; Commenced MDS; Pharmacy managed repeat service; NHS Repeat dispensing initiated; Home delivery	12
New Medicines Service; Home delivery	12
Review dose form; Review MDS arrangements	12
Information reviewed, Medicines Reconciliation completed; Commenced MDS	11
Information reviewed, Medicines Reconciliation completed; MAR chart provided; Review MDS arrangements; Home delivery	11

Abbreviation: MDS (Monitored Dosage System), MAR (Medication Administration Record).

Table 6.18 – Patient age and gender stratified by number of services provided at community pharmacy

Variable	Number of services completed in community pharmacy 1 (n=609)	>1 (n=1,517)	Total (n=2,126)	Significant test
Gender				
Female	352 (28.9%)	865 (71.0%)	1,217 (100%)	Pearson chi2(1) = 0.10, P-value = 0.743
Male	257 (28.2%)	652 (71.7%)	909 (100%)	
Age rage				
20-49	38 (25.8%)	109 (74.1%)	147 (100%)	Pearson chi2(5) = 14.14, P-value = 0.015
50-59	36 (19.2%)	151 (80.7%)	187 (100%)	
60-69	74 (26.5%)	205 (73.4%)	279 (100%)	
70-79	147 (28.8%)	363 (71.1%)	510 (100%)	
80-89	244 (32.2%)	512 (67.7%)	756 (100%)	
90-100	70 (28.3%)	177 (71.6 %)	247 (100%)	

Community pharmacist information about patients and those who received Medicine Use Review (MUR) and New Medicines Service (NMS) services is highlighted in Appendix 42 and shows that 4% (n=31/1,060) of patients who do not know how to take/use their medication received MUR service. In addition, around 3% (n=13/446) of the patients who received NMS had a respiratory condition, diabetes or cardiac condition.

Furthermore, the PharmOutcomes™ data contains a section for additional actions. Thirty-two entries were added, including 10 about medication change issues, 6 about communication with a caregiver, 5 about patients being discharged to nursing/intermediate care, 5 about referral issues, 2 about patients being readmitted back to the hospital, 2 about patient contact, and 2 about patient death.

6.4.2 'Service Impact' study

6.4.2.1 Hospital discharge information and patient demographics

6.4.2.1.1 Number of patients

The number of completed data collection forms submitted to the research team at the University of Manchester were 594, including 242 data collection forms pertaining to patients discharged in the pre-implementation stage, and 351 data collection forms to patients discharged in the post-implementation stage. Table 6.19 and Figure 6.6 summarise the

completed data collection forms. However, 183 (30.8%) data collection forms were excluded due to several reasons, the most common being the unavailability of medication reconciliation entry or related activity (n=93), followed by the patient did not stay at least 24 hours in an NHS acute Trust in North West of England (n=21) and patient discharged from the emergency department (n=17). Table 6.20 summarises the reasons and number of excluded data collection forms. Therefore, the total number of completed data collection forms included in the subsequent analysis was 411, where 41% of the data collected pertained to the TCAM service pre-implementation stage (n=168) and 59% of the data collected represented the post-implementation stage (n=243).

Table 6.19 – Number of completed data collection forms by implementation stage

	Pre-implementation stage	Post-implementation stage	Unknown stage	Total
Included forms	168 (69.4%)	243 (69.2%)		411 (69.2%)
Excluded forms	74 (30.5%)	108 (30.7%)	1	183 (30.8%)
Completed forms	**242 (100%)**	**351 (100%)**	**1**	**594 (100%)**

Figure* 6.6 *– Completed data collection forms

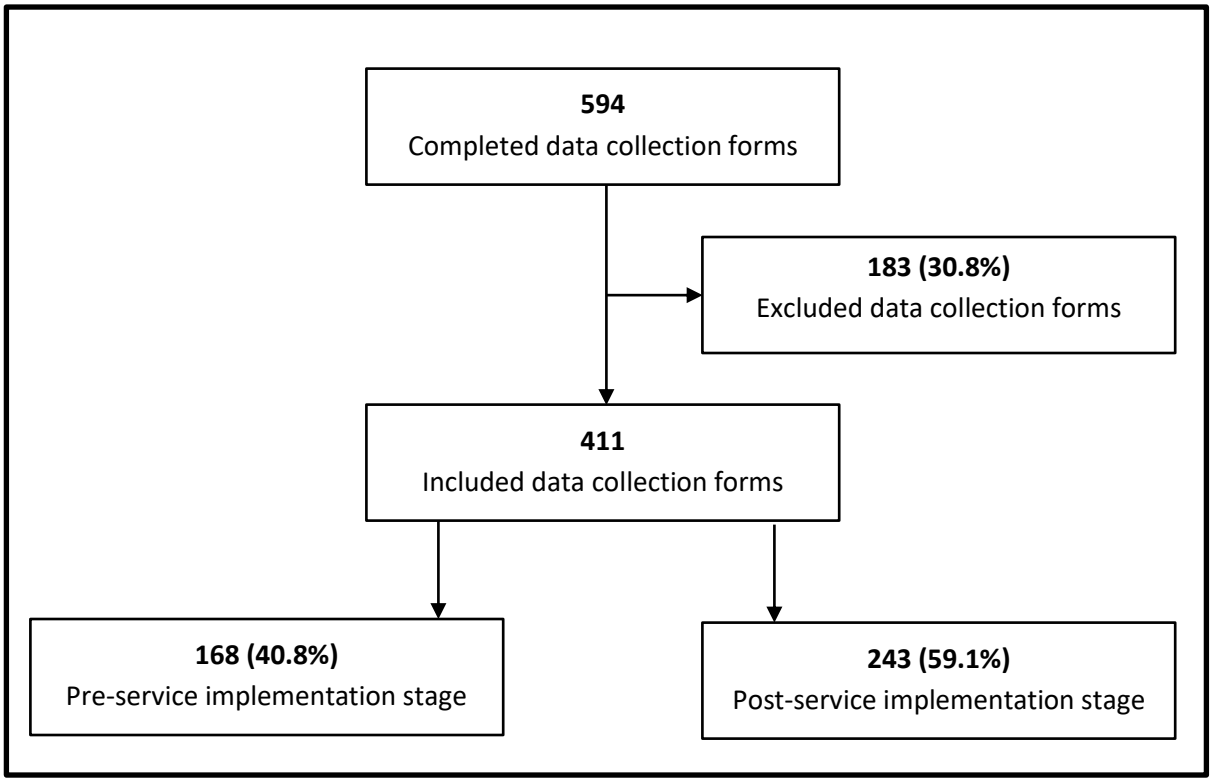


Table 6.20 – List of excluded data collection forms

Exclusion reasons	Total	Stage		
		Pre	Post	Unknown
Patient did not have a **medication reconciliation** or (equivalent activity)	93 (50.8%)	34 (45.9%)	59 (54.6%)	
Patient did not stay at least **24 hours** in an NHS acute Trust in North West of England	21 (11.4%)	9 (12.1%)	12 (11.1%)	
Patient did not discharge from an in-patient hospital stay at NHS acute Trust in North West of England (e.g. transferred to another hospital)	18 (9.8%)	8 (10.8%)	10 (9.2%)	
Patient discharged from **emergency department**	17 (9.2%)	7 (9.4%)	9 (8.3%)	1
Type of hospital admission: **planned hospital admission** (e.g. elective surgery)	11 (6.0%)	4 (5.4%)	7 (6.4%)	
Patient **died** before discharge	13 (7.1%)	8 (10.8%)	5 (4.6%)	
No discharge letter received	10 (5.4%)	4 (5.4%)	6 (5.5%)	
Total	**183 (100%)**	**74 (100%)**	**108 (100%)**	**1**

In the post-implementation stage data collectors recorded the reason(s) why a TCAM service was made. Most of the referrals were for recurrent MDS (n=204), followed by new MDS (n=30), and the need for an additional service (n=5). Four data collection forms did not state the reason of referral.

Data collection forms were completed by 16 data collectors; the range of screened data collection forms per data collector was 9 – 77, with a mean and median of 37 and 31.5, respectively [Inter Quartile Range (IQR) 23.7 – 52.2].

6.4.2.1.2 Patient demographics

Table 6.21 provides an overview of the patient's gender included in the study. The majority of included patients were female (n=241/411, 58%). Appendix 43 shows the breakdown of included patient ages by stage of TCAM service implementation – almost one-quarter of the patients were aged less than 64 years old (n=70/411), with most aged 75-94 years old (62%, n=254/411), with a mean age of 77 years. The median was 80 years old (mean 76.8, Standard Deviation (SD) 13.9, range 25 – 98, IQR 71-86) in the pre implementation stage, compared to 80 years old (mean 77, SD 13.4, range 21 – 100, IQR 70 -86) for patients in the post implementation stage. The two cohort of patients were of similar age, and gender proportion

with no statistical difference between them. Table 6.21 also provides the breakdown of the ethnicity of the included patients. Most of the included patients were white (92%, n=378/411).

Table 6.21 – Patient demographics by stage of TCAM service implementation

Patient demographics	Pre-implementation stage	Post-implementation stage	Total
Patient (mean) age	76.8	77	77
Patient gender*			
Female	97 (57.7%)	144 (59.2%)	241 (58.6)
Male	69 (41%)	98 (40.3%)	167 (40.6%)
Missing data**	2 (1.1%)	1 (0.4%)	3 (0.7%)
Patient ethnicity			
White	153 (91%)	225 (92.5%)	378 (91.9%)
Asian	2 (1.1%)	1 (0.4%)	3 (0.7%)
Black	0	1 (0.4%)	1 (0.2%)
Pakistani	0	1 (0.4%)	1 (0.2%)
Middle East	1 (0.5%)	0	1 (0.2%)
Other/unknown/unspecified	11 (6.5%)	9 (3.7%)	20 (4.8%)
Missing data	1 (0.5%)	6 (2.4%)	7 (1.7%)
Total	**168 (100%)**	**243 (100%)**	**411 (100%)**

***was unable to clarify this data*

**Pearson chi2(1) = 0.0467, P-value = 0.829 [without the missing data]*

**Pearson chi2(2) = 0.8784, P-value = 0.645*

6.4.2.1.3 General Practice sites

The range of completed data collection forms from each practice site was 13-59 [mean 33, median 26 and IQR 22.7-43.7] with an observed range of 1 to 46 data collection forms that were subsequently included in the analysis per practice site [mean 22, median 19, and IQR 13.2-35.2].

It can be seen from Table 6.22, that there was an uneven distribution of completed data collection forms between practice locality that ranged between 14 and 89, median 60. In addition, Table 6.22 also shows the breakdown of included data collection forms per practice site and whether the site used EMIS or Vision electronic systems. The two cohorts of patients included in the pre-implementation and post-implementation stages were similar in general practice site information except electronic system used.

Table 6.22 – Completed data collection forms by general practice site information

Practice information	Pre-implementation stage	Post-implementation stage	Total
Practice locality*			
A	39 (23.2%)	50 (20.5%)	89 (21.4%)
B	29 (17.2%)	44 (18.1%)	73 (17.7%)
C	29 (17.2%)	37 (15.2%)	66 (16.0%)
D	31 (18.4%)	31 (12.7%)	62 (15.0%)
E	18 (10.7%)	41 (16.8%)	59 (14.3%)
F	15 (8.9%)	16 (6.5%)	31 (7.5%)
G	4 (2.3%)	13 (5.3%)	17 (4.1%)
H	3 (1.7%)	11 (4.5%)	14 (3.4%)
Practice size (patient list size)**			
<15 thousand	65 (38.7%)	88 (36.2%)	153 (37.2%)
<10 thousand	84 (50%)	109 (44.8%)	193 (46.9%)
<5 thousand	19 (11.3%)	46 (19%)	65 (15.8%)
Practice electronic record system***			
EMIS	80 (47.6%)	152 (62.5%)	232 (56.4%)
Vision	85 (50.6%)	90 (37%)	175 (42.5%)
Missing data	3 (1.8%)	1 (0.4%)	4 (0.9%)
Total	**168 (100%)**	**243 (100%)**	**411 (100%)**

** Pearson chi2(7) = 10.4063, P-value = 0.167*
*** Pearson chi2(2) = 4.3707, P-value = 0.112*
**** Pearson chi2(2) = 10.1392, P-value = 0.006*

6.4.2.1.4 Hospital discharge information

Table 6.23 provides an overview of included patient length of hospital stay, with most patients staying 7 days or less in the hospital during admission (54.7%, n=255/411). The median length of hospital stay was 6 days (mean 12.9, SD 18.5, IQR 3 – 13.5, range 1 – 103) for patients in the pre implementation stage, and 7 days (mean 14, SD 19.7, IQR 3 – 16, range 1- 180) for patient in the post implementation stage.

Table 6.23 also presents an overview of discharging ward for included patients. Most of the included patients were discharged from medical wards (88%, n=362/411). Table 6.23 shows that the majority of included patients were discharged to home (90%, n=369/411). In addition, Appendix 44 presents an overview of included patient hospital discharge diagnosis according to the International Classification of Diseases 10th revision (ICD-10). A total of 17% of included

data collection forms did not specify patient diagnosis but specified patient signs or symptoms instead (n=73/411).

Table 6.23 – Hospital discharge information by stage of TCAM service implementation

Hospital discharge information	Pre-implementation stage	Post-implementation stage	Total
Hospital length of stay			
1-7 days	101 (60.1%)	124 (51%)	225 (54.7%)
8-30 days	51 (30.3%)	86 (35.3%)	137 (33.3%)
31-60 days	7 (4.1%)	24 (9.8%)	31 (7.5%)
>60 days	9 (5.3%)	9 (3.7%)	18 (4.3%)
Discharge ward			
Medical / Intermediate care / Elderly care	144 (85.7%)	218 (89.7%)	362 (88%)
Surgical	15 (8.9%)	12 (4.9%)	27 (6.5%)
Missing data	3 (1.7%)	9 (3.7%)	12 (2.9%)
Other / Unspecified	6 (3.5%)	4 (1.6%)	10 (2.4%)
Discharge destination			
Home	149 (88.6%)	220 (90.5%)	369 (89.7%)
Intermediate care	3 (1.7%)	9 (3.7%)	12 (2.9%)
Residential home	6 (3.5%)	4 (1.6%)	10 (2.4%)
Nursing home	1 (0.5%)	2 (0.8%)	3 (0.7%)
Hospice	1 (0.5%)	0	1 (0.2%)
Assisted living	0	1 (0.4%)	1 (0.2%)
Sheltered house	0	1 (0.4%)	1 (0.2%)
Temporary residence	1 (0.5%)	0	1 (0.2%)
Other	2 (1.1%)	2 (0.8%)	4 (0.9%)
Missing data	5 (2.9%)	4 (1.6%)	9 (2.1%)
Total	**168 (100%)**	**243 (100%)**	**411 (100%)**

Appendix 45 presents an overview of the date difference between sending discharge letters via DocMan platform from secondary to GP practice primary care. The results show that 40% of the discharge letters were sent to the general practice on the same date of discharge (n=165/411), with 34.3% (n=141/411) and 20.4% (n=84/411) of discharge letters were sent in between one to two days, and three to seven days post hospital discharge to primary care, respectively. The median number of days from sending the discharge letter from secondary care to primary care was 1 day (mean 1.7, SD 2.9, range, IQR 0-25) in the pre implementation stage, and 1 days (mean 1.8, SD 8.3, range 0 – 123, IQR 0 -2) in the post implementation stage.

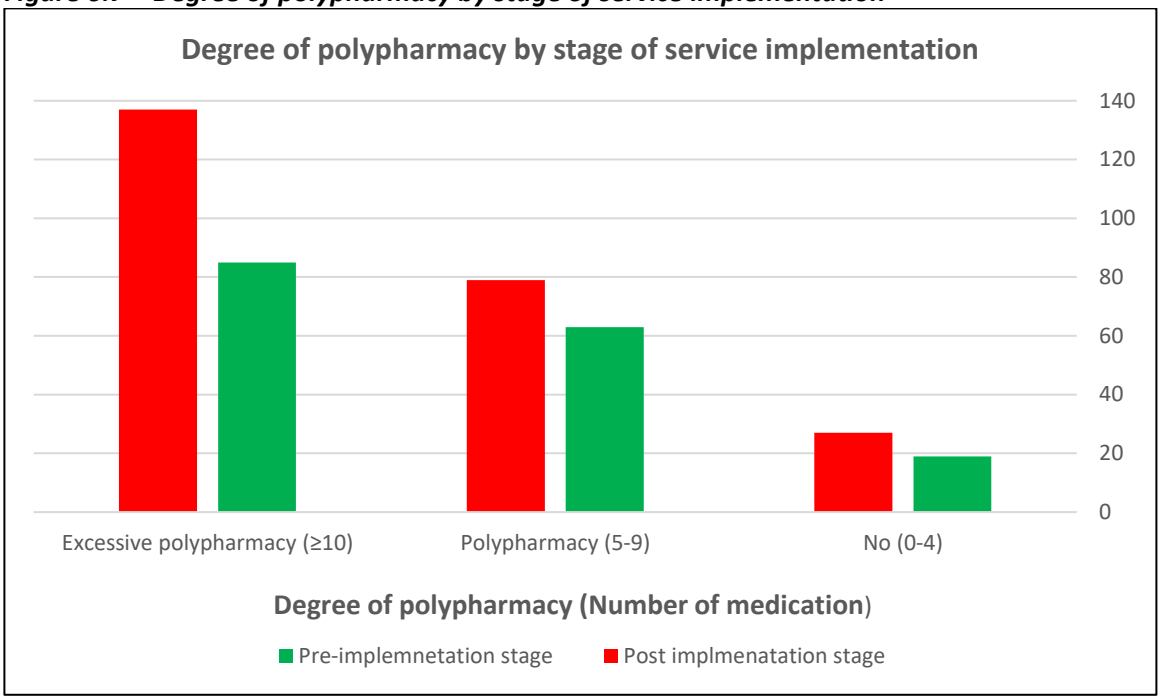
The majority (88.5% (n=364/411)) of completed data collection forms indicated that patients experienced polypharmacy (number of prescribed medications ≥5), and Table 6.24 and Figure *6.7* provides a summary of the degree of polypharmacy in the completed data collection forms.

Table 6.24 – Degree of polypharmacy by stage of TCAM service implementation

Polypharmacy (Number of medication)	Pre-implementation stage	Post-implementation stage	Total
No (0-4)	19 (11.3%)	27 (11.1%)	46 (11.2%)
Polypharmacy (5-9)	63 (37.5%)	79 (32.5%)	142 (34.5%)
Excessive polypharmacy (≥10)	85 (50.6%)	137 (56.3%)	222 (54%)
Missing data	1 (0.6%)	0	1 (0.2%)
Total	**168 (100%)**	**243 (100%)**	**411 (100%)**

Pearson chi2(3) = 2.7808, P-value = 0.427

Figure 6.7 – Degree of polypharmacy by stage of service implementation



6.4.2.1.5 Medication reconciliation in general practice

As shown in Appendix 46, it is apparent that the source of 67% of the recorded medication reconciliation was pharmacy staff, followed by other equivalent activities completed by a medical doctor / GP at the primary care site (20%, n=82/411), such as review discharge letter and entering any medication related data in patent record.

6.4.3 Descriptive results

6.4.3.1 Unintentional medication discrepancies

6.4.3.1.1 Description of unintentional medication discrepancies

The total number of data collection forms containing suspected medication discrepancies was 85/411 (20.6%). Following review of these discrepancies by the research team (see section 6.3.9.1.2), 38.9% (33/85) of the data collection forms were assessed to not have a medication discrepancy or have an intentional medication discrepancy and were excluded from further analysis. The final included forms with UMD were therefore 52. There were 36 data collection forms with one UMD, ten data collection forms with 2 UMDs, and 6 data collection forms with 3 or more UMDs. Appendix 47 provides a breakdown of data collection forms with UMD. The total number of medications associated with at UMDs were 89, from 52 data collection forms (n=52/411, 12.6%).

Table 6.25 below presents summary statistics for the UMDs per stage of service implementation. From the table it can be seen that the rate of UMDs has decreased after service implementation.

Table 6.25 – Patient affected by UMD by stage of service implementation

Unintentional medication discrepancies	Pre-implementation stage	Post-implementation stage	Total
No	145 (86%)	214 (88%)	359 (87%)
Yes	23 (14%)	29 (12%)	52 (13%)
Total	**168 (100%)**	**243 (100%)**	**411 (100%)**

Regarding patient demographics affected by UMDs, a descriptive summary is provided in Table 6.26, and Appendix 48– Demographic of patients affected by unintentional medication discrepancies. Table 6.26 shows that the proportion of male patients (13.2%, n=22/167) affected by UMDs was slightly higher than the proportion of female patients affected by UMDs (12.4%, n=30/241). Appendix 48 shows that the majority of UMDs occurred in patients aged between 75-84 years old (n=39/52, 75%), however, UMDs affected a higher proportion of younger patient aged between 45 and 64 (20.6%, n=12/58). Regarding patient ethnicity, it was found that 92% of patients affected by UMDs were of white ethnicity (n=48/52), and the ethnicity of the rest of the patients was unknown (8%, n=4/52) (see Appendix 48).

Table 6.26 shows the severity of UMDs as assessed by the data collectors using the national coordinating council for medication error reporting and prevention (NCC MERP) criteria[459]. The majority of UMDs were assessed to have the capacity to cause error (63%, n=56/89), and/or cause potential harm (92%, n=82/89) at face value as presented in Table 6.26 – Description of unintentional medication discrepancies by stage of service implementation

Table 6.26 – Description of unintentional medication discrepancies by stage of service implementation

	Pre-implementation stage (n=168)	Post-implementation stage (n=243)	Total frequency (n=411)
Patient affected by UMD	23 (13.6%)	29 (11.9%)	52 (12.7%)
Gender			
• Male	11 (15.9%)	11 (11.2%)	22 (13.2%)
• Female	12 (12.3%)	18 (12.5%)	30 (12.4%)
Age			
• > 65 years	5 (21.7%)	7 (24.1%)	12 (17%)
• ≤ 65 years	18 (78.3%)	21(72.4%)	39 (11.5%)
Total number of included patient in stage	**168 (100%)**	**243 (100%)**	**411 (100%)**
Nature of UMD			
Medication affected by UMDs	41	48	89
Medication discrepancy severity (NCC MERP criteria)			
A: Circumstances or events that have the capacity to cause error	26 (63.4%)	30 (62.5%)	56 (63%)
B: An error occurred but the error did not reach the patient	6 (14.6%)	7 (14.5%)	13 (14.6%)
C: An error occurred that reached the patient but did not cause patient harm	2 (4.8%)	9 (18.7%)	11 (12.3%)
D: An error occurred that reached the patient and required monitoring to confirm that it resulted in no harm to the patient and/or required intervention to preclude harm	6 (14.6%)	1 (2%)	7 (7.8%)
E: An error occurred that may have contributed to or resulted in temporary harm to the patient and required intervention	1 (2.4%)	0	1 (1.1%)
Missing data	0	1 (2%)	1 (1.1%)
Medication discrepancy harm			
Potential harm	37 (90.2%)	45 (94%)	82 (92.1%)
No harm	3 (7.3%)	1 (2%)	4 (4.4%)
Actual harm	1 (2.4%)	0	1 (1.1%)
Missing data	0	2 (4%)	2 (2.2%)
Total medications affected by UMD	**41 (100%)**	**48 (100%)**	**89 (100%)**

UMD (unintentional medication discrepancies)

The most common medication classes associated with UMD were medication for the cardiovascular system (n=39), central nervous system (n=15), and gastrointestinal system (n=9). Details of medication classes associated with UMD is described, and the medication groups featuring in the top three most commonly observed medication classes is provided in Table 6.27.

Table 6.27 – Medication classes based on BNF Chapters associated with unintentional medication discrepancies

Medication class based on BNF Chapters	Pre - stage	Post - stage	Number of medications associated with unintentional medication discrepancy
Cardiovascular system	20	19	39 (43.8%)
Central nervous system	6	9	15 (16.8%)
Gastrointestinal system	4	5	9 (10.1%)
Endocrine system	2	3	5 (5.6%)
Respiratory system	2	3	5 (5.6%)
Blood and blood forming organs	1	3	4 (4.4%)
Musculoskeletal system	1	2	3 (3.3%)
Skin	1	2	3 (3.3%)
Genito-urinary system	1	1	2 (2.2%)
Nutrition and metabolic disorders	1	1	2 (2.2%)
Anti-infective system	1	0	1 (1.1%)
Eye	0	1	1 (1.1%)
Total	**40**	**49**	**89**
Gastrointestinal system	**4**	**5**	**9**
Laxatives	3	4	7
Proton pump inhibitors	1	1	2
Central nervous system	**6**	**9**	**15**
Opioids	4	1	5
Antidepressants	0	4	4
Analgesics, non-opioid	1	2	3
Antiepileptics	1	0	1
Hypnotics, sedatives, and anxiolytics	0	1	1
Local anesthesia	0	1	1
Cardiovascular system	**20**	**19**	**39**
Angiotensin- converting enzyme (ACE) inhibitors	4	6	10
Diuretics	5	3	8
Statins	2	4	6
Antithrombotic	3	2	5
Calcium-channel blockers	3	1	4
Beta-adrenoceptor blockers	1	1	2
Cardiac glycosides	0	1	1
Angiotensin II receptor antagonists	1	0	1
Antiarrhythmics, class III Nitrates	0	1	1
Vasodilator, Potassium-channel openers	1	0	1

6.4.3.1.2 Associated factors

Table 6.28 provides an overview of UMDs stratified by general practice information. This table reveals that two local areas had no report of UMDs, with three having rates of 15% of screened patients or above. In addition, Table 6.28 presents the summary of UMDs identified per different practice sizes. Most UMDs occurred in practice sites with the total registered number of patients between 10, 000 and 5,000. Furthermore, Table 6.28 shows that the majority of UMDs occurred to patients discharged from medical wards (75%, n=39/52), and the highest proportion of UMDs occurred to patients discharged from surgical wards. Moreover, Table 6.28 shows that the majority of UMDs occurred to patients discharged home (86.5%, n=45/52), and the highest proportion of UMDs occurred to patients discharged to residential home (49%, n=4/10). Table 6.28 shows that most UMDs occurred in patients who had a length of hospital stay of between 1 to 7 days (46%, n=24/52). In addition, 19.2% (n=10/52) of patients who had a length of stay more than 31 days had UMDs. Appendix 48 shows the breakdown of UMDs according to diagnosis at hospital discharge. It can be shown that the most common diagnosis implicated with UMDs was the disease of the circulatory system.

Table 6.28 ***–Patients affected by unintentional medication discrepancies (UMD) by*** **practice site and** ***hospital discharge information***

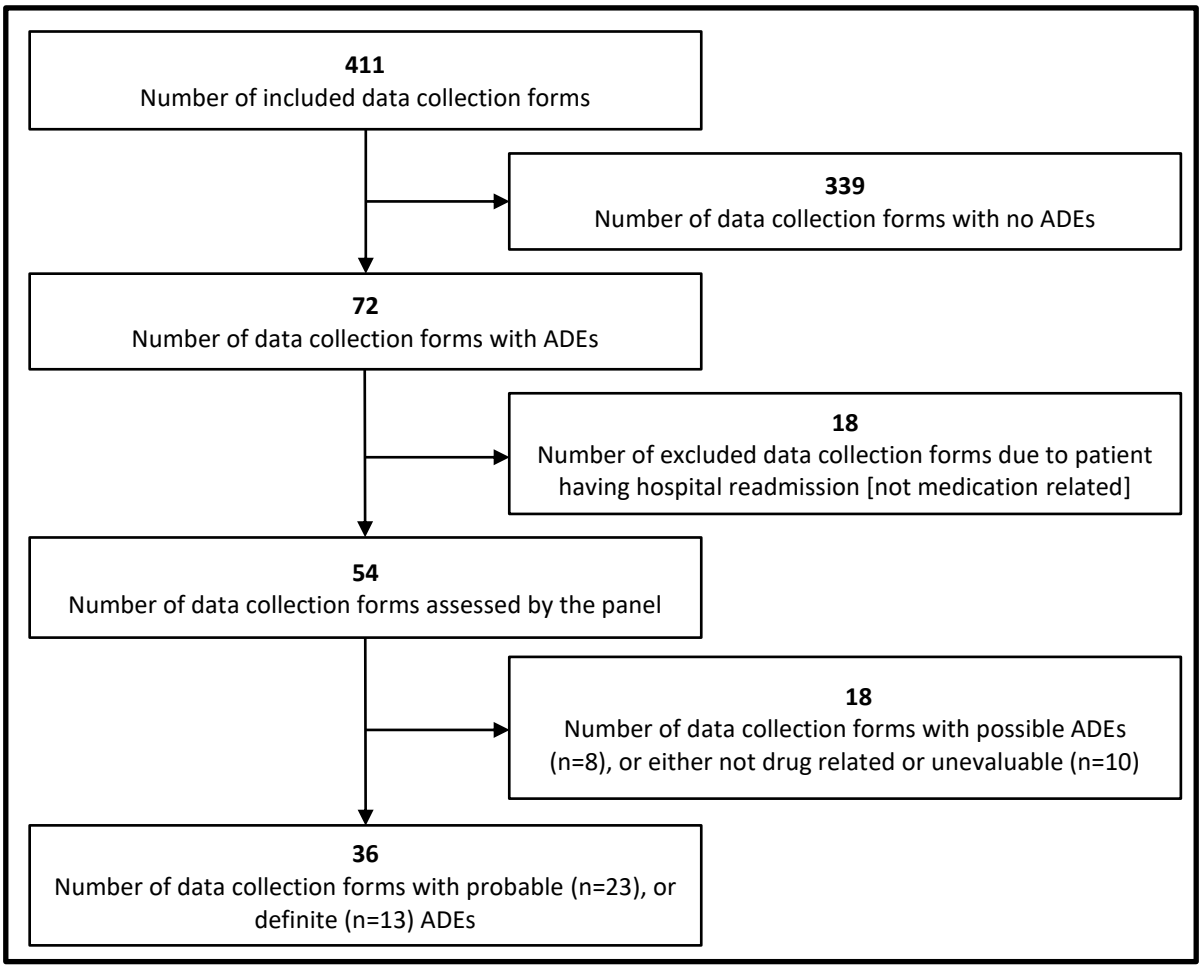
	Pre-implementation stage		Post-implementation stage		Both stages	
	UMD	**Total**	**UMD**	**Total**	**UMD**	**Total**
Practice site information						
Practice locality						
A	9 (23%)	39	7 (14%)	50	16 (18%)	89
B	3 (10.3%)	29	8 (18.1%)	44	11 (15%)	73
C	2 (6.8%)	29	5 (13.5%)	37	7 (11%)	66
D	6 (19.3%)	31	7 (22.5%)	31	13 (21%)	62
E	0	18	0	41	0	59
F	2 (13.3%)	15	1 (6.2%)	16	3 (10%)	31
G	1 (25%)	4	1 (7.6%)	13	2 (12%)	17
H	0	3	0	11	0	14
Practice size						
1 - <5 thousand	1 (5.2%)	19	4 (8.6%)	46	5 (7.7%)	65
5 - <10 thousand	13 (15.4%)	84	16 (14.6%)	109	29 (15%)	193
10- <15 thousand	9 (13.8%)	65	9 (10.2%)	88	18 (12%)	153
Practice electronic system						
EMIS	12 (15%)	80	20 (13.1%)	152	32 (13.7%)	232
Vision	9 (10.5%)	85	9 (10%)	90	18 (10.2%)	175
Missing data	2 (66.6%)	3	0	1	2 (50%)	4
Hospital discharge information						
Hospital length of stay						
1-7 days	13 (12.8%)	101	11 (8.8%)	124	24 (11.7%)	225
8-30 days	7 (13.7%)	51	11 (12.7%)	86	18 (13.1%)	137
31-60 days	2 (28.5%)	7	5 (20.8%)	24	7 (22.6%)	31
>60 days	1 (11.1%)	9	2 (22.2%)	9	3 (17.7%)	18
Discharge ward						
Medical, Elderly, Intermediate care	14 (9.8%)	142	25 (11.3%)	220	39 (10.8%)	362
Surgical	6 (35.2%)	17	3 (30%)	10	9 (33.3%)	27
Missing data	0	3	1 (11.1%)	9	1 (8.3%)	12
Unspecified/ other	3 (50%)	6	0	4	3 (30%)	10
Discharge destination						
Home	18 (12%)	149	27 (12.2%)	220	45 (12%)	369
Intermediate care	0	3	0	9	0	12
Residential home	2 (33.3%)	6	2 (50%)	4	4 (40%)	10
Nursing home	1 (100%)	1	0	2	1 (33%)	3
Assessed living	0	0	0	1	0	1
Sheltered house	0	0	0	1	0	1
Hospice	1 (100%)	1	0	0	1 (100%)	1
Temporary residence	1 (100%)	1	0	0	1 (100%)	1
Other	0	2	0	2	0	4
Missing data	0	5	0	4	0	9
Total	**23 (13.6%)**	**168**	**29 (11.9%)**	**243**	**52 (12.6%)**	**411**

6.4.3.2 Adverse drug events

6.4.3.2.1 Description of adverse drug events

The number of data collection forms with ADEs associated with at least one medication was 72. However, after reviewing data collection forms by the expert panel, 18 data collection forms were excluded due to insufficient information or the patient having a hospital readmission that was not medication related. Thus, the number of data collection forms with ADEs associated with at least one medication confirmed by the expert panel were 54. Following causality assessment, expert panel members assessed 18 ADEs to be either possible ADEs (n=8), or either not drug related or unevaluable (n=10). Thus, a total of 36 ADEs were identified for further analysis and inclusion, including 23 probable ADEs (64%), and 13 definite ADEs (36%) which are represented in Figure 6.8 below.

Figure 6.8 – Completed data collection forms with adverse drug events (ADEs)



The majority of the included ADEs occurred in the post-implementation stage (64%, n=23/36), with 36% of ADEs occurring in the pre-implementation stage (n=13/36). Table 6.29 compares the breakdown of ADEs according to the stage of service implementation. The crude, unadjusted rate of ADEs was 8% in the pre-implementation stage (n=13/168), and 9.5% in the post implementation stage (n=23/243).

Table* 6.29 *– Patients affected by adverse drug events by phase of service implementation

Adverse drug events	Pre-implementation stage	Post-implementation stage	Total
No	155 (92%)	220 (90.5%)	375 (91%)
Yes	13 (8%)	23 (9.5%)	36 (9%)
Total	**168 (100%)**	**243 (100%)**	**411 (100%)**

Following expert panel assessment, almost half of confirmed ADEs were considered preventable (55.5%, n=20/36). Most preventable ADEs occurred in the post-implementation stage (n=13/20). It was found that 6 data collection forms included more than one ADE. Most confirmed ADEs were rated by the expert panel to be of mild clinical severity (n=25/36, 70%), with the remaining 30% of ADEs of moderate severity (n=11/36). Most mild and moderate severity ADEs occurred in the post-implementation stage (60%, n=15/25 and 73%, n=8/11. Respectively). An example of the free text description of ADEs in data collection forms are presented in Table 6.30. The most common medication classes associated with ADEs were medications for the cardiovascular system, nervous system, and gastrointestinal system. Table 6.31 shows the summary statistics for ADEs data, via providing a breakdown of patients affected by ADEs according to the stage of service implementation. As shown in the table that the rate of preventable ADEs and the occurrence of moderate ADEs had an increase after service implementation from 3.5% to 4.1%, and from 1.7% to 3.2%, respectively. The table showed that the most common medication classes implicated to harm to be cardiovascular (the most subclass to be diuretics), central nervous system and gastro-intestinal medication. The most common consequences of ADEs were reduced renal function or Acute Kidney Injury (AKI) (n=5), followed by oedema, or swelling (n=5). Regarding patient demographics affected by ADEs, a descriptive summary is provided in Appendix 49 , and Appendix 50. The majority of patients affected by ADEs were female (75%, n=27/36), and aged between 75-84 years old (n=25/36, 69%). Regarding patient ethnicity, it was found that 94.5% of patient affected by ADEs were white ethnicity (n=34/36), and the ethnicity of the rest of the patient was unknown (5.5%, n=2/36).

Table 6.30 – Qualitative description of preventable confirmed adverse drug events

Description	Causality	Severity	Preventable
''Metolazone not in blister pack despite prescriptions having been issued. No further documentation on this- no description of problems with symptoms. Patient readmitted to hospital and then on to hospice from deteriorating end stage heart failure.''	Probable	Moderate	Yes
''Patient was identified to have been in acute kidney injury (AKI). A primary contributor was his dose of bumetanide and on assessment by the heart failure nurse this was reduced to 1mg once daily.''	Definite	Low	Yes

***Table 6.31 – Quantitative description of adverse drug events* (ADE)**

	Pre-stage (n=168)	Post-stage (n=243)	Total (n=411)
Patients affected by ADEs	13 (7.7%)	23 (9.4%)	36
Gender			
• Male	1 (1.4%)	8 (8.1%)	9
• Female	12 (12.3%)	15 (10.4%)	27
Age			
• > 65 years	1 (3.4%)	2 (4.8%)	3
• ≤ 65 years	12 (8.6%)	21 (10.4%)	33
Clinical severity of ADEs			
• Low	10 (5.9%)	15 (6.1%)	25
• Moderate	3 (1.7%)	8 (3.2%)	11
Preventability of ADEs			
• Preventable	6 (3.5%)	10 (4.1%)	16
• Non-preventable	7 (4.1%)	13 (5.3%)	20
Medication classes associated with ADEs			
• Anti-infective	0	1	**1**
• Blood and blood forming organs	0	1	**1**
• Skin	0	1	**1**
• Respiratory system	1	0	**1**
• Gastro-intestinal system (laxative)	2	1	**3**
• Nervous system	1	6	**7**
○ Antiepileptics	1	1	2
○ Analgesics, opioid	0	2	2
○ Analgesics, non-opioid	0	1	1
○ Antipsychotics	0	1	1
○ Antidepressants	0	1	1
• Cardiovascular system	9	13	**22**
○ Diuretics	3	8	11
○ ACE inhibitors	3	0	3
○ Antithrombotic, antiplatelet drugs	2	1	3
○ Calcium-channel blockers	0	2	2
○ Beta-adrenoceptor blockers	0	1	1
○ Angiotensin receptor antagonists	0	1	1
○ Antithrombotic, factor Xa inhibitor	1	0	1

	Pre-stage (n=168)	Post-stage (n=243)	Total (n=411)
Symptoms of ADEs			
• Reduced renal function, or acute kidney injury	2	3	5
• Oedema or swelling	2	3	5
• Diarrhoea	2	2	4
• Uncontrolled blood pressure (high or low)	2	2	4
• Drowsiness or dizziness	1	2	3
• Anaemia	1	0	1
• Belching and burping	1	0	1
• Bruising	1	0	1
• Shortness Of Breath (SOB), dry mouth	1	0	1
• Accidental overdose	0	1	1
• Deteriorate heart failure	0	1	1
• Flare up of eczema	0	1	1
• Gastritis	0	1	1
• Hyperkalaemia	0	1	1
• Infected Percutaneous Endoscopic Gastrostomy (PEG)	0	1	1
• Low Glasgow Coma Scale (GCS)	0	1	1
• Nausea	0	1	1
• Pain	0	1	1
• Panic attack	0	1	1
• Sedation	0	1	1

6.4.3.2.2 Associated factors

An overview of ADEs stratified by stage and general practice site information is provided in Table 6.32. In addition, Table 6.32 presents the summary of ADEs identified stratified by practice list size. A higher rate of ADEs occurred in patients registered with practice sites with the total registered number of patients less than 5,000 patients. Furthermore, Appendix 50 shows the breakdown of ADEs according to diagnosis at hospital discharge. It can be shown that the most common diagnosis implicated with ADEs was the disease of the circulatory system (27%, n=10/36). Table 6.32 shows that the majority of ADEs occurred to patient discharged from medical wards and discharged home, respectively. Table 6.32 shows that the majority of patients affected by ADEs had hospital stays between 1 to 7 days. However, a higher percentage of patients who had a longer hospital length of stay was affected by ADEs.

Table* 6.32 –*Patient affected by adverse drug events (ADEs) by* general practice site and *hospital discharge information

	Pre-implementation stage		Post-implementation stage		Both stages	
	ADEs	**Total**	**ADEs**	**Total**	**ADEs**	**Total**
General practice site information						
Practice locality						
A	1 (2.5%)	39	5 (10%)	50	6 (6.7%)	89
B	5 (17.2%)	29	4 (9%)	44	9 (12.3%)	73
C	2 (6.8%)	29	3 (8.1%)	37	5 (7.6%)	66
D	5 (16.1%)	31	2 (6.4%)	31	7 (11.3%)	62
E	0	18	5 (12.1%)	41	5 (8.5%)	59
F	0	15	3 (18.7%)	16	3 (9.7%)	31
G	0	4	1 (7.6%)	13	1 (5.9%)	17
H	0	3	0	11	0	14
Practice size						
<5 thousand	4 (21%)	19	6 (13%)	46	10 (15.4%)	65
<10 thousand	8 (9.2%)	84	6 (5.5%)	109	14 (7.3%)	193
<15 thousand	1 (1.5%)	65	11 (12.5%)	88	12 (7.8%)	153
Practice electronic system						
EMIS	7 (8.7%)	80	19 (12.5%)	152	26 (11.2%)	232
Vision	4 (4.7%)	85	4 (4.4%)	90	8 (4.5%)	175
Missing data	2 (66.6%)	3	0	1	2 (50%)	4
Hospital discharge information						
Hospital length of stay						
1-7 days	12 (11.8%)	101	11 (8.8%)	124	23 (10.2%)	225
8-30 days	0	51	6 (6.9%)	86	6 (3.4%)	137
31-60 days	0	7	4 (16.6%)	24	4 (13%)	31
>60 days	1 (11.1%)	9	2 (22.2%)	9	3 (16.7%)	18
Discharge ward						
Medical, Elderly, Intermediate care	13 (100%)	144	21 (9.6%)	218	34 (9.4%)	362
Surgical	0	15	1 (8.3%)	12	1 (3.7%)	27
Missing data	0	3	0	9	0	12
Unspecified/other	0	6	1 (25%)	4	1 (10%)	10
Discharge destination						
Home	13 (100%)	149	22 (10%)	220	35 (9.5%)	369
Intermediate care	0	3	1 (11.1%)	9	1 (8.3%)	12
Residential home	0	6	0	4	0	10
Nursing home	0	1	0	2	0	3
Assessed living	0	0	0	1	0	1
Sheltered house	0	0	0	1	0	1
Hospice	0	1	0	0	0	1
Temporary residence	0	1	0	0	0	1
Other	0	2	0	2	0	4
Missing data	0	5	0	4	0	9
Total	**13 (7.7%)**	**168**	**23 (9.4%)**	**243**	**36 (8.7%)**	**411**

6.4.4 Regression analysis

6.4.4.1 Unintentional medication discrepancies

Table 6.33 present the regression analysis exploring the impact of the TCAM service on UMD rates. The test of the difference between the variable of substantive interest; study periods (pre and post intervention) using regression analysis adjusting the covariates age, gender, number of medication and length of stay did not show a statistically significant difference between the two stages, with a P-value of 0.46. The corresponding unadjusted odds ratio was 0.85 (95% CI 0.47-1.53) while the adjusted odds ratio was 0.79 (95% CI 0.44-1.44). Table 6.33 below includes some wider confidence intervals because of the low number of events.

Table* 6.33 – *Unintentional medication discrepancy univariate and multivariable analysis

	Number of observations	Odds ratio	[95% CI]		P-value
Univariate logistic regression					
Stage (0 pre, 1 post)	411	0.85	0.47	1.53	0.59
Multivariable logistic regression					
Stage (0 pre, 1 post)	406	**0.79**	**0.44**	**1.44**	**0.46**
Gender (0 male, 1 female)		0.93	0.51	1.69	0.82
Age (continuous)		0.99	0.97	1.01	0.51
Number of medications		1.00	0.94	1.06	0.93
Length of stay (continuous)		1.00	0.99	1.02	0.21

6.4.4.2 Adverse drug events

Table 6.34 presents the regression analysis to determine the impact of the TCAM service on ADE rates. The regression analysis did not show a statistically significant difference between the two stages following adjustment of covariates age, gender, number of medications and length of hospital stay. The unadjusted odds ratio was 1.24 (95% CI 0.6-2.5, P-value = 0.54) while the adjusted odds ratio was 1.19 (95% CI 0.57-2.45, P-value = 0.63).

Table* 6.34 – *Adverse drug events univariate and multivariable analysis

	Number of observations	Odds ratio	[95% CI]		P-value
Univariate logistic regression					
Stage (0 pre, 1 post)	411	1.24	0.61	2.53	0.54
Multivariable logistic regression					
Stage (0 pre, 1 post)	406	**1.19**	**0.57**	**2.45**	**0.63**
Gender (0 male, 1 female)		2.16	0.98	4.78	0.05
Age (continuous)		1.01	0.98	1.05	0.20
Number of medications		1.08	1.00	1.16	0.02
Length of stay (continuous)		1.00	0.98	1.02	0.52

6.4.5 Regression analysis (baseline data only)

6.4.5.1 Unintentional medication discrepancies

The baseline rate (pre-implementation stage) of UMDs in this study is 14% (n=23/168). The results obtained from the univariate regression analysis of this baseline data are presented in Table 6.35 below. There was no observed statistically significant risk factor predicting the occurrence of UMD.

Table* 6.35 – *Baseline unintentional medication discrepancies

Variable	Number of observations	Odds ratio	95% CI	P-value
Univariate logistic regression				
Gender (0 male, 1 female)	166	0.74	0.30 – 1.80	0.51
Age (continuous)	167	0.99	0.96 – 1.03	0.98
Number of medications	167	1.00	0.91 – 1.10	0.88
Length of stay (continuous)	168	1.00	0.98 – 1.02	0.75
Multivariable logistic regression				
Gender (0 male, 1 female)	165	0.72	0.29 – 1.79	0.48
Age (continuous)		1.00	0.96 – 1.03	0.97
Number of medications		1.00	0.91 – 1.10	0.85
Length of stay (continuous)		1.00	0.98 – 1.02	0.78

6.4.5.2 Adverse drug events

The baseline rate of ADEs in this study baseline group was 7.7% (n=13/168). The results obtained from the univariate and multivariable regression analysis are presented in Table 6.36 below. There was a significant positive correlation in the univariate regression analysis between patient gender (female) and the risk of experiencing one or more ADEs (OR 9.5, P=0.03, 95% CI 1.21-75.68). Although that the CI is wide due to the small sample size and low number of patients with the outcome of interest (n=13).

Table* 6.36 – *Baseline adverse drug events

Variable	Number of observations	Odds ratio	95% CI	P-value
Univariate logistic regression				
Gender (0 male, 1 female)	166	9.59	1.21 – 75.68	0.03
Age (continuous)	167	1.05	0.99 – 1.11	0.08
Number of medications	167	1.05	0.93 – 1.18	0.36
Length of stay (continuous)	168	0.97	0.92 – 1.02	0.38
Multivariable logistic regression				
Gender (0 male, 1 female)	165	7.59	0.94 – 60.95	0.05
Age (continuous)		1.04	0.98 – 1.11	0.15
Number of medications		1.05	0.92 – 1.19	0.43
Length of stay (continuous)		0.97	0.92 – 1.02	0.35

6.5 Discussion

This is the first study to address both the utilisation and impact on medication safety of a TCAM service post hospital discharge, and adds much needed knowledge to the field which currently focuses on service implementation experiences and rates of all-cause hospitalisations. This study has found that the TCAM service in one Clinical Commissioning Groups (CCG) in North West England was not associated with a statistically significant difference in UMD and ADE rates post hospital discharge in patients using MDS. The study more directly assesses the TCAM service against its own aims, whilst also providing new insights into management of MDS post hospital discharge including rate of UMDs and ADEs post hospital discharge, and community pharmacy services provided for this cohort of patients. In addition, findings from this study shed new light on the utilisation of TCAM services, finding differences in completion rates across patient age and time groups. In the context of the ongoing introduction of DMS in England and elsewhere in accordance with safety priorities endorsed by the World Health Organisation and others, it is now important to explore these findings in more detail to help guide further roll out and optimisation of existing systems.

The 'service utilisation' study provided insight into the breadth of services embedded, with an observed increasing percentage of completed referrals being made in the same month of receiving referrals in the later months of evaluation. It may be possible that community pharmacist required education and experience in the use of TCAM over time. This highlights that user feedback could be sought on the use of PharmOutcomes™ platform to help guide improvement in real time. More research is needed using mixed method design with the qualitative component being an interview with community pharmacists to better understand the causes of referral rejections, and delay in completing referrals. If conducted properly, with the appropriate number of participants and a strong integration plan, a mixed method study could answer questions from this study and pave the way for better implementation of the TCAM service. This research has thrown up many questions in need of further investigation. Perhaps a possible future approach is implementation research to better plan an implementation strategy[474].

This study broadly supports the findings reported by Jeffries (2021) who conducted qualitative interviews with the healthcare providers and patients/ carers regarding their feedback of the

TCAM implementation in the same (Clinical Commissioning Group) CCG in the North West of England[475]. This includes the challenges in providing Medicine Use Review (MUR) or New Medicines Service (NMS) services for the cohort of included patients which explains the low number of completed MUR and NMS services in community pharmacies as shown by the 'service utilisation' data. In addition, the qualitative study highlighted how the TCAM service facilitated communication with patients and their family, where the data in PharmOutcome™ platform confirms that the receipt of referrals by community pharmacy initiated opportunities to contact patients to follow up on the discharge. The qualitative study by Jeffries (2021) highlighted that the challenges in the previous system of sending discharge letters to community pharmacies via using hand written letter or fax[475]. In addition, it outlines how the TCAM service improved communication between community pharmacies and GP/ prescribing team at the practice. Furthermore, it illustrates positive feedback regarding the use of TCAM service as an easy to use and secure system that improves efficiency.

Recorded services provided in community pharmacies to patients referred by TCAM following discharge were diverse, with only 23% (n=482/2,038) and 18% (n=380/2,038) of included patients having their MDS requests reviewed and commenced by their community pharmacy, respectively (these were in the top 5 provided services). Patients therefore also received a combination of other services. The three most common services provided were medication reconciliation and review information (47.2%), home delivery (39.5%), and review MDS arrangements (23.6%). These results differ from Nazar's 2016 evaluation which found that the three most common services provided in community pharmacies after hospital discharge TCAM referrals were Medicine Use Review (MUR) (46.6%), New Medicines Service (NMS) (38.9%), and home delivery (22.3%)[312]. The breadth of services observed in this study, including easy open tops (6%), large print labels (3.5%) and talking labels (1.5%) reflect the vulnerable nature of the included patients, those on MDS. Furthermore, it was noted that there have been 13 occasions where patients were referred for TCAM via PharmaOutcomes™ who were deceased. These findings reflect those of Wilcock and Yelling, (2019)[476], and suggests the need to update the referral system to prevent sending these referrals.

The lack of impact on the TCAM service on reducing the rate of UMDs/ADEs observed in the study presented in this chapter, could be attributed to the special characteristic of the acute NHS Trust in the North West of England and the Clinical Commissioning Groups (CCG) where

the service was implemented. In addition, the study was in one UK region and focused on patients with MDS, which could limit the findings. Further discussion about the lack of impact is presented in detail in section 7.3.3.

The current study found that the majority of patients affected by ADEs or UMDs were female and aged 75 years old and older[322]. The most common medication classes associated with ADEs and UMDs belonged to the cardiovascular, central nervous, and gastro-intestinal system, with diuretics being the most common group implicated with harm post discharge. Comparison of the findings with those presented in Chapter Four and Five confirms that these medication classes are implicated with ADEs post hospital discharge and should be the target for future interventions. In addition, the study has also found that in the pre-implementation stage (baseline data) ADE and UMD rates were 7.7% (n=13/168), and 14% (n=23/168) respectively which are lower than in previous literature and systematic review[247,369,392], albeit not focusing on those with MDS as this study did. Potential reasons for this could be that medication in MDS are frequently reviewed by healthcare providers due to the frequent nature of prescribing / dispensing them to patients.

The findings of this study reinforce the NHS integration agenda[477]. There has also been a recent movement by the NHS to adopt community pharmacy services for several purposes, including a minor ailment scheme (consultation service) to minimise the workload on primary care services. This study can be used to inform the design and ongoing implementation and use of the discharge medicine service (DMS) in England. Greater efforts are needed to ensure that DMS is appropriately implemented. For example, multiple interventions might yield better improvement in outcomes than single interventions, in the context of this work sending the referrals via PharmOutcomes™ platform to primary care sites could be of a benefit. Previous systematic reviews of interventions to improve medication use post hospital discharge (Appendix 51) provided preliminary data that a single intervention might not be as effective as multiple interventions. A recent systematic review by Killin (2021) assessed the effect of advanced discharge medication reconciliation (including an electronic format or enhanced medication reconciliation) concluded that the effect on MEs and ADEs is inconsistent due to a lack of agreement between studies[8]. Further work needs to be done to investigate the reason for intervention inconsistency results. Strong recent evidence have arisen that emphasize patient engagement[424,478–481], and that the intervention must be more patient centred.

6.6 Conclusion

This is the first study evaluating the utilisation and the impact of the TCAM service on medication safety post hospital discharge. Whilst the TCAM facilitated a number of community pharmacy services being offered to patients with MDS these did not translate to a statistically significant impact on UMD and ADE rates post hospital discharge. The TCAM service supports community pharmacies to work in partnership with general practice to provide a safe clinical care for patient after hospital discharge, by facilitating the communication and future effort should seek to explore how to improve service utilisation and impact.

Chapter Seven: Discussion

7.1 Introduction

The main aim of this PhD programme was to understand the epidemiology, and aetiology of medication errors (ME) and adverse drug event (ADE) following hospital discharge and evaluate a specific intervention to improve medication safety at this transition point with the goal of generating an action agenda for future research and clinical practice. To achieve this aim, three studies were conducted and presented in Chapters Four, Five, and Six. Chapter Four is a systematic review that explored and identified the frequency and nature of MEs, medication discrepancies and ADEs immediately following hospital discharge. Chapter Five presents a multi-methods analysis of medication related incident reports occurring in primary care following hospital discharge from the NRLS over a 5-year period designed to explore in detail their nature, and underlying contributory factors. Chapter Six evaluates the utilisation and impact of a 'transfer of care around medicines' pharmacy-led hospital discharge service on unintentional medication discrepancies (UMD) and ADEs occurring in the community in a local area in the North West of England.

This current chapter has seven subheadings: (1) an overview of key findings from each study presented in Chapters Four, Five, and Six, (2) overall interpretation of the findings of this thesis in the context of the available literature, (3) key strengths and limitations of the body of work, (5) emerging implications for clinical practice and policy arising from this research programme, (6) recommendations arising from this body of work for future research, and (7) an overall conclusion. Subheadings 5 and 6 address the four study objectives from Chapters Four, Five and Six, which focused on developing a research and clinical practice agenda to reduce MEs and ADEs in the future.

7.2 Overview of key findings

7.2.1 Chapter Four: Prevalence and nature of medication errors and medication-related harm following discharge from hospital to community settings: a systematic review

The systematic review presented in Chapter Four synthesised 54 studies, including 20,895 hospital discharges across 26 countries. The majority of studies (47/54, 87%) included in this review originated from developed nations (in particular, the USA and UK) with limited evidence from developing countries [482]. It was found that across included studies, a median of one in two adult and elderly patients were affected by at least one medication error (ME) post-hospital discharge; one in two were affected by one or more unintentional

medication discrepancy (UMD); and one in five affected by one or more ADEs. The median rate of MEs, UMDs and ADEs post-hospital discharge was 53% [IQR 33–60.5] (n = 5), 50% [IQR 39–76] (n = 11) and 19% [IQR 16–24] (n = 7), respectively. In this review, only two studies reported preventable ADEs occurring in 11-16% of discharged patients. A median of nearly one third of adult and elderly patients reported being affected by clinically serious ADEs post-hospital discharge. Medication classes most commonly reported with ADEs were antibiotics, antidiabetics, analgesics and cardiovascular drugs. It was also observed in this study that the rate of MEs and ADEs was higher in the elderly population. The highest rate of ADE in the elderly post hospital discharge was observed from a study in the UK, to be 37%[247].

Other important findings from this review included the observation that nations that had multiple studies rarely contained data across all outcome measures, and that direct comparison were limited because of the observed heterogeneity in the country of origin, patient groups studied, data collection methods and outcome definitions. In addition, the systematic review identified that the burden of MEs and ADEs following hospital discharge is comparatively under-researched in paediatric and nursing/care home settings.

7.2.2 Chapter Five: A multi-method evaluation of medication safety incidents following transition from secondary to primary care in England and Wales received by the National Reporting and Learning System (NRLS)

The study presented in Chapter Five analysed 1,121 medication safety incidents related to hospital discharge submitted from primary care to the NRLS between 2015 and 2019. The study reported that almost one eight of medication safety incidents resulted in patient harm, and that the elderly were associated with elevated incident numbers. This study also found that the most common medication incidents occurred in the prescribing stage (42%, n= 479/1,121) followed by the administration stage (22.5%, n=253/1,121), but the medication processes implicated with a high proportion of patient harm were drug monitoring (17%, n=24/140) and administration stages (15%, n=39/253). This study observed wrong or unclear dose or strength and medication omission as the most commonly reported error categories (n=212/1,121), while medication omission was associated with a high proportion of more actual harmful incidents (19%, 28/148). It was observed that the most common incidents reported involved medications for the cardiovascular, endocrine or central nervous systems, with the most common specific medications being antithrombotic medications, insulin, beta-blockers, diuretics and

opioids. Among the top common medications classes, incidents associated with medication for the central nervous system showed a higher proportion being associated with actual harm. The study found that the most common outcome from the cohort of the cohort of identified outcomes to be organisation inconvenience (34%, n=564/1,660), followed by patient inconvenience (27%, n=455/1,660), and patient clinical harm (13%, n=216/1,660). This study reports the involvement of monitored dosage system (MDS) prescribing and supply errors in medication safety incidents.

Content analysis of incident descriptions revealed that 36% (n=408/1,121) reported at least one contributory factor explicitly mentioned in the incident free text narrative, and the total number of identified contributory factors were 467 from 408 incidents. A total of 51 incidents were found to have more than one contributory factors. Organisational issues (n=383/467, 82%) were the most common contributory factors leading to the occurrence of medication related patient safety incidents post hospital discharge. These issues frequently involved a lack of co-ordinated care between secondary and primary care, and between healthcare and pharmacy. The next most common identified contributory factor was staff factors (n=75/467, 16%), which involved cognitive issues ''cognitive: includes abilities (such as perception, learning, memory and problem solving) (n=35), followed by task related issues (n=33). The identified contributory factors from this study helped in setting ideas for interventions to improve medication safety post hospital discharge, such as electronic systems to communicate discharge letters, making the best use of skill mix in general practice, and involving collaboration across care boundaries.

7.2.3 Chapter Six: A multi-method evaluation of a transfer of care around medicines intervention designed to improve medication safety for patients with monitored dosage systems following hospital discharge

The study presented in Chapter Six evaluated using multiple methods the utilisation and impact of a TCAM service on patients using monitored dosage systems across one Clinical Commissioning Group in North West England. First, a descriptive ‘service utilisation’ analysis of 3,033 TCAM patient referrals over one year revealed that 86% of patients referred were aged 60 years or older. The majority of referrals (70%, 2,126/3,033) were marked as ‘completed’ by the community pharmacies through this varied between 63 and 85.5% per month (median 69, IQR 65.5 – 74) and a median of 23.4% [IQR 16-29.9] of referrals were completed/or any activity saved in the month following the index month where referrals were sent (i.e. they took more than a month to be completed). In addition,

corresponding referral 'completion' rates were found to be lower for those aged 90+ years (64%. n=247/382) and higher for those aged <50 years (80%, n=147/184). The most common services commenced in community pharmacies to complete referrals included medication reconciliation, information reviewed, offered home delivery, review MDS arrangements, and commenced MDS. The study found that from the cohort of patients with completed referrals, 28.6% of patients received one service (n=609/2,126), with 71.3% of patients received two or more services (n=1,517/2,126).

The impact of the TCAM service on medicines safety was evaluated through the identification of UMD and ADEs by general practice-based clinical pharmacists for 411 patients using an uncontrolled pre-post design. The current study also found that the majority of patients affected by ADEs, or UMDs were female and aged 75 years old and older. The most common medication classes associated with ADEs and UMDs were cardiovascular, central nervous system and gastro-intestinal, with diuretics being the most common groups implicated with harm post discharge. The study reported that the TCAM service was not associated with a statistically significant difference between study periods using multi-variable logistic regression analysis in UMD (adjusted OR 0.79, 95% CI 0.44-1.44, P=0.46) and ADE rates (adjusted OR 1.19, 95% CI 0.57-2.45, P = 0.63). The study has also found that in the pre-implementation stage (baseline data), ADE and UMD rates were 7.7% (n=13/168) and 14% (n=23/168), respectively, which is lower than the literatures presented in Chapter Four; however, this study is focused on patients using MDS.

7.3 Overall interpretation of thesis findings in context of available literature

7.3.1 Prevalence, nature and outcome of medication safety incidents post hospital discharge

The focus of the review presented in Chapter Four was on both process measures such as MEs and UMDs and outcome measures such as ADEs [483]. Medication errors and UMD that occur irrespective of harm are an important window into the safety of healthcare systems. This helps understand what can turn errors into ADEs where risks may lie dormant and what patterns emerge that may support learning to prevent harmful events occurring in the future. Many studies included in the review presented in Chapter Four report MEs and UMD following the evaluation and comparison of medication lists in hospital case notes and discharge prescriptions to data obtained from interviewing patients in the community setting following hospital discharge. However, these studies often omit data from primary care records post-hospital discharge, which may have led to inaccurate ME/UMD rates

being reported [369]. The results presented in Chapter Five reflect those of Riordan et al. (2016) and Ashcroft et al. (2009), who also found that medication omission was the most common prescribing error at or post hospital discharge[380,484].

Chapter Six showed that the baseline rate of ADEs in the evaluation of a TCAM intervention (8%) to be lower than the median rate (19%) across 7 studies identified in the systematic review of Chapter Four. Possible explanations for this finding are discussed in more detail in section 7.3.3 below and may be linked to the setting and patient group involved. The review presented in Chapter Four has revealed that similar median rates of ADEs and/or UMD occur post hospital discharge to those reported on hospital admission[204], during inpatient stay [183] and whilst residing in ambulatory care[188]. This indicates that the transition of care from hospital to home should be considered an equal priority to other stages of the patient journey by researchers and health care policymakers. Evidence indicates that hospital discharge has been the subject of emerging attention in patient safety policy documents[166,169,296–298], where these documents are translated into action in the form of new initiatives [485].

A previous review of literature related to drug related problems in the elderly published in 2010 [319] found that ADEs post-hospital discharge affected 20% of elderly patients (n = 1 study) [213], while the review in Chapter Four updates and strengthens this evidence with a rate of 18.7–37% of discharged elderly (n = 4) [213,246,247,371]. While two previous systematic reviews of medication safety incidents post-hospital discharge in the elderly were informative [319,335], they examined the elderly in isolation, whereas the review in Chapter Four compared this patient group with other populations to help determine priorities. Chapters Five and Six also found that elderly patients were associated with the majority of incidents and harm incidents, which supports evidence from previous observations that elderly patients are more at risk from MEs, UMD and ADEs. Older patients may be a high-risk group owing to factors including pharmacodynamic / pharmacokinetic differences, co-morbidities and polypharmacy [192–194,486,487]. It also reinforces the recent WHO Medication Safety in Transitions of Care – Technical Report, which recommend targeting medication reconciliation interventions to high-risk patients [189].

Cardiovascular and central nervous system medications were the most common medication classes implicated in ME, UMD and ADEs in Chapters Four, Five, and Six, followed by the endocrine system medications (common subclass was antidiabetics) and antibiotics in Chapters Four and Five. These results further support the hypothesis raised by

others previously that these medication groups are implicated in MEs and patient harm across stages of the patient health care journey, where similar findings have been reported by others[188,403,404,488–491] investigating medication-related harm in ambulatory settings and medication-related causes for hospital admission. Comparison of the findings with a recent systematic review confirms that cardiovascular medication are the most common medication classes implicated to harm post hospital discharge[492]. In addition, recent studies outline that antibiotic overuse post hospital discharge (defined as 'potential for harm exceeds the possible benefit') to be common[493–495]. Chapter Five and Six also reported that whilst not as common as other groups, gastrointestinal medication (the most common subclass was laxatives) was an important contributor to ADE, UMD and ME – this is not a medication subclass with a common historical association, although that it is commonly used by elderly.

Chapter Four found that the most common cardiovascular medication subclass implicated with harm post hospital discharge to be antihypertensives and anticoagulants. Comparing the findings with studies in Chapters Five and Six, which found that the most common subclass to be anticoagulant and diuretics, respectively, confirm that these two medication classes are associated with harm. Furthermore, Chapter Five found that the most common medication classes implicated in harm in the monitoring stage were antithrombotic medication, which could indicate that care arrangements for patients on anticoagulant medication are not properly communicated in the fragmented healthcare system. These results are in agreement with those obtained by a Delphi consensus study in the UK identifying anticoagulant medication to have the greatest risk to patients post hospital discharge compared to other medication classes[72]. Oral anticoagulant adverse events are higher in the first 30 days , compared to one year post hospital discharge[496]. Medication classes identified from across chapters four, five and six, including antithrombotic, antihypertensives and diuretics, should be the targets for remedial intervention. These medication classes have been highlighted by others, and are the subject of national patient safety alerts in the UK[497,498] (though these alerts are not being followed by NHS trusts[499]). This aligns with WHO ''Medication Without Harm'' priority on ‘transitions of care’[3], and recent UK government overprescribing report[500].

Opioid medications were among the most common medication classes implicated with medication related patient safety incidents in Chapter Five (with most common incidents were in the prescribing stage (51%, n=40/79), followed by the administration stage (9%,

n=20/79)), and implicated with UMDs in Chapter Six. Opioids are high risk medications, that have shown to be associated with dependence[501], and severe harm and death[140,502]. Opioids are the most common medication classes associated with prescribing errors among high-risk medication[503]. The risk of unintentional overdose is associated with using long-acting opioids, where Chapter Five has shown that two out of three incidents with opioid overdose were with prescription with long-acting opioids (fentanyl)[504]. There has also been a plethora of evidence regarding prolonged opioid use, however, this observation was not found in studies presented in Chapter Four, Five or Six, possibly because of the widely used definition of ''prolonged use'' which is more than 90 days[505]. Two recent meta-analysis showed that 4.3% (95% CI 2.3 % -8.2%) (n=37) [506] of trauma or surgical patients, and 6.7% (95% CI 4.5% - 9.8%) (n=33) [507] of surgical patients discharged from hospital on opioids respectively, became a chronic opioid user after discharge. One recent systematic review found that the prevalence of patients with prolonged opioid use post hospital discharge after total joint arthroplasty to be 12% (95% CI 10-14%) (n=15) [508]. Previous opioid use has been found to be a risk factor for prolonged opioid use [507–509]. Adverse drug events associated with opioids post hospital discharge formed the central focus of a recent study by Kurteva et al. (2021) in which the author found it to affect 4% of adult patients[510]. In addition, it was found that 11% of opioids prescriptions not to be filled 30 days post hospital discharge in Canada highlighting gap in discharge letter communication[510]. In Victoria, Australia, not all hospitals had hospital level opioids discharge guidelines, with time, funding and resources being common barriers to implementing such guidelines[511]. Factors leading to opioid misuse post hospital discharge include lack of patient education about disposable and storage of opioids[512]. Elderly patient risk factors associated with opioids related ADEs post hospital discharge includes age 80 years and older, prescription long-acting opioids, and certain medical conditions including dementia, anxiety disorder, intestinal disorder and musculoskeletal system injuries[513].

The study presented in Chapter Five captures, for the first time, wider costs associated with medication related incidents post hospital discharge beyond patient harm. In 2017, the Health Division at the Organisation for Economic Co-operation and Development (OECD) published a report ''the economics of patient safety'' which included a wide range of costs beyond patient harm, including financial costs, reduced productivity of patients and carers, and reduced trust in healthcare services[514]. A recent time-motion study in the UK highlighted the impact of missing information in discharge letters and communication gaps

on GP time[515]. In his systematic review of approaches for calculating the cost of MEs, Patel et al. (2016) conclude that few studies assessed the indirect cost of MEs [516].

7.3.2 Contributory and risk factors for medication safety challenges post hospital discharge

The contributory factors for medication incidents reported post-hospital discharge identified in Chapter Five are consistent with earlier research[12,67,239,428]. Examples include the practice of sending discharge letters to community pharmacies which were inconsistent and may lack quality (e.g. missing information). The identified organisational factors broadly support the work of other studies in the area of patient safety linking medical errors with administrative system errors[426,427]. It is also encouraging to compare with a recent systematic review of 45 studies summarising causes of unplanned all cause hospital readmission which found that hospital role in organisation of care to be the most common cause highlighted in almost all included articles (n=44), followed by patient self-management related causes (for example non adherence) (n=21), patient disease (n=19), and integrated care (n=18)[517]. The results are in agreement with those in Chapter Five, where the majority of the incidents were found to be originated from secondary care (61.5%, n=689/1,121) but highlights the importance of cross-interface working as a potential solution.

In accordance with 'staff ' related contributory factors identified in Chapter Five, evidence have demonstrated the importance of adequate space, time and concentration to complete tasks[100]. The 'do not disturb strategy' has been shown to decrease prescribing errors whilst writing discharge prescriptions[518]. The identified staff factors do align to recent studies, indicating that colleagues completing work for others (e.g. signing (authorising) prescriptions) may be considered a cause of prescribing errors, and that administrative procedures are a leading cause of adverse events in primary care settings[426,428,519]. This work highlights the importance of ensuring adequate skill mix for carrying out these tasks, for example triaging discharge letters by a clinical pharmacist in primary care might be a promising intervention. As compared to nurses, pharmacists identified more medication discrepancies[520]. Another recent study investigated general practice staff perceptions of factors leading to failure in actioning discharge letters by Spencer and colleagues (2018)[521], and highlighted issues related to medication reconciliation including the accuracy of medication reconciliation, reception team completing the task, and the positive impact of general practice pharmacists.

Chapter Six found a significant positive association between patient gender (female) and the risk of ADEs (OR 9.5, 95% CI 1.21-75.68, P=0.03). Female patients were shown to be associated with more ADEs post hospital discharge in a previous study in the UK[411]. This study supports evidence from previous observations [322,522,523], that female patients and older adults are more affected by MEs, and ADEs, due to the biological gender influencing medication pharmacokinetics, and to female practice of using medications[524–526].

7.3.3 Impact of TCAM service on medication safety

Currently available studies which have evaluated the impact of TCAM have focused on evaluating either activity data alone and/ or all-cause readmissions. Such approaches, however, have failed to address the effect on medication safety directly, which is one of the primary aims of the service. Services such as DMS appear to be supported in their theoretical underpinnings by the evidence presented in Chapter Five, which highlights the potential importance of combining electronic systems with appropriate skill mix and interface working. There is a powerful argument for targeted surveillance (Shojania and Thomas, 2013) [108], and so the first study to determine the impact of TCAM on UMDs and ADEs affecting patients post hospital discharge was presented in Chapter Six, and with a focus on the vulnerable MDS patient group highlighted in Chapter Five. Service utilisation was explored using PharmOutcomes™ data to help understand from a broader perspective how service use/delivery may interlink with impact. The study presented in Chapter Six, had a concurrent evaluation following Medical Research Council (MRC) evaluating complex intervention guidance, which advice to evaluate both intervention process and impact[330]. In addition, Chapter Six provided a detailed description of the intervention following MRC guidance[330].

The service utilisation data revealed that almost one in ten TCAM referrals were not being completed within the first month of being made, which could have limited the impact of the intervention during the time period studied (though the number of all referrals and proportion of completed referrals were higher than in previous literature[312,313,476]). The service utilisation study in Chapter Six raised speculation that pharmacists are not completing medication reconciliation correctly in community pharmacies, as few highlighted any discrepancies or ADEs occurring and was recorded in PharmOutcome™ despite data from Chapter Six indicating that these occurred quite commonly, with issues related to prescriptions that necessitated a referral to the GP not seen frequently (2%, n=45/2,126). Medication reconciliation was also the most common service provided in

community pharmacies (47.2%) in this study. Medicines reconciliation has been added as a standard service in community pharmacy within the new Community Pharmacy Contractual Framework (CPCF) for 2019/20 to 2023/2024[527], and thus attention must be drawn to the appropriate conduct of the service. The service utilisation data in Chapter Six also found that patients could benefit from the integration of information between different healthcare settings, where community pharmacists can work as a safety net by reviewing the discharge letter in a timely manner should primary care staff have missed any useful information. Thus, the study reinforces strategy 3.5, in the global patient safety action plan 2021-2030 that was launched in August 2021, titled *"Toward eliminating avoidable harm in health care",* which emphasises the implementation of an integrated healthcare systems to enable the flow of information with GP pharmacist as well as community pharmacy[111].

The apparent lack of impact of the TCAM service on rates of UMD and ADEs following multivariable regression analysis may be attributed to a number of factors requiring further exploration. As the TCAM service continues to be deployed nationally, it is therefore important to gather wider evidence of impact on medication safety or medication related readmission as a priority. There may also be factors related to the study context that could have influenced this finding. The reasons for this difference are not clear, but it may be attributed with the existence to advanced medication safety services being previously deployed in the study area (Salford Medication safety dASHboard (SMASH) and Pharmacist-led information technology intervention for medication errors (PINCER)), the use of an integrated health care record across primary and secondary care and the sustained implementation of a general practice clinical pharmacy team for nearly 7 years. Other possible reasons could be that the included cohort, patients on MDS who are considered high risk, might have fewer UMDs and ADEs, due to the frequent reviewing by healthcare providers to prepare the MDS, although there is a lack of evidence to support this argument and it requires further investigation. Another factor may be related to the retrospective data collection method used in this study, where other studies utilised prospective approaches[528,529], however it may be argued that retrospective methods reflect clinical practice without the interference of the research team. Furthermore, prospective approaches of data collection were under scrutiny by leaders in patient safety, arguing that the limitation that they exhibit, including observer variation, introduces variation in ADE assessment[530,531]. In addition, the study sample size did not reach statistical power for ADEs analysis and therefore further evaluation may be required on a larger scale of included patients. There has not been an evaluation of the effectiveness of the NIPPS team on

medication safety in primary care sites in the local area in North West of England. The NIPPS Team are also active in conducting new initiatives to improve medication safety, including *"Rationalisation and safety review of DOACs in primary care"*[532]. Another explanation could be that the implementation of the service was not strong as staff training sessions were poorly attended, there was no hands-on training using a live system, there the time was not adequate to implement the service as the training was in January 2019 and the service was implemented in February 2019. To highlight the contextual factor that might affect patient safety practice implementations, Taylor (2011) conducted an expert panel discussion and highlighted in his seminal paper that existing quality/safety infrastructure to have a high priority on intervention implementation assessment, while implementation tools (staff training) received split views by the panel[533].

7.4 Key strengths and limitations of the research programme

This research programme provides an in-depth study of the epidemiology and aetiology of medication safety post hospital discharge, whilst also evaluating the impact of a novel intervention currently the focus of national attention in England. A key strength of the programme of research presented in this thesis is following a systematic, a logical process in exploring the research question by first synthesizing the nature and prevalence, followed by assessing the causes, then evaluating an intervention on the improvement pathway, where each stage informed the next[95].

Another key strength is the diverse methodology utilised across the three studies in addressing its objectives. Each method chosen was suited to explore particular PhD programme objectives, including the use of the gold standard systematic review to synthesising the rate and nature of medication safety challenges post hospital discharge in Chapter Four. In addition, studies presented in Chapter Five and Six utilised multiple methods of data collection/analysis, which enabled an in-depth exploration of the research question. Each study was completed using an established, validated reference tool/ framework including, Cochrane Systematic review methods in Chapter Four, PISA coding framework in Chapter Five, and ADEs causality, preventability, and severity criteria in Chapter Six. The quality of each study was assessed using a quality assessment framework for medication safety studies in Chapter Four, number of words used in the incident free text description in Chapter Five, and reviewing ADEs via expert panel meetings and independent review of UMDs in Chapter Six. Each study was reported using approved reporting criteria endorsed by the Equator network[534], including the PRISMA guideline in

Chapter Four, RECORD statement in Chapter Five, and SQUIRE 2.0 and CONSORT in Chapter Six. The strengths of each study are presented below.

The systematic review presented in Chapter Four was conducted using a comprehensive search strategy across the grey literature and ten electronic databases covering the modern healthcare era, with search criteria involving no restrictions on language, study country or patient demographics. This study also presented a transparent review methodology with reporting following the PRISMA approach, and an author contact section [353] to reduce reporting bias. This study also performed a quality assessment of included studies to help frame the findings in context. The analysis of incident report data in Chapter Five has several strengths include that a systematic approach to coding of the incident reports using a validated framework (PISA classification) that has been used previously by several incident report analysis papers, alongside the use of independent validation of incidents with consensus meetings within the research team. The study also examined incidents over a 5-year period in order to capture medication related patient safety incidents after hospital discharge and based the approach on the findings of a preliminary data analysis phase involving 500 incidents to support the refinement of the data extraction strategy. The evaluation of the TCAM service presented in Chapter Six has included service utilisation and service impact data over one year period (which show the fluctuation of referrals over time, and the extent and speed of service imbedding), covering a large single geographical area. Pharmacist data collectors were trained, where a data collection guide was provided, and regular emails with frequently asked questions about data collection were sent to support consistency and accuracy in data collection. Also, data validation was completed for the ADEs data by three experts blinded to the stage of data collection, and coding for all collected medication discrepancies were reviewed independently by two researchers. Regression analysis was completed to adjust the effect of confounding on the exposure and outcome.

The main limitation of the programme of research is that the patient voice was not articulated in the thesis via patient and public involvement, where for example, this could have been done using the ACTIVE framework for Chapter Four[535]. The limitations of each study are presented below. The systematic review in Chapter Four has several limitations that affected the internal validity, including no independent quality assessment, and single author screening of citations, which could have led to the omission of relevant studies (though uncertain cases were discussed amongst the research team) [536]. A meta-analysis of

outcome rate data was also not possible because of the heterogeneity of included data. Inherent limitations associated with incident report research in Chapter Five include a lack of further patient demographic information such as gender and co-morbidities, which may enhance the understanding of incident context through other fields such as incident type and incident location were completed in all reports[114,537]. A limitation of the data may also relate to the quality of the free text information that was written to describe the incidents, as this study identified only 36% (n=408/1,121) incidents with sufficient free text data to analyse contributory factors. This is in common with earlier research[413,414]. The severity of harm re-coding was reliant on what was written in the data, whereas judgements on the severity of harm made by the incident reporter may have included more information known to the reporter at the time of the incident that was not recorded in the incident report. However, these judgements may have been based on potential, rather than actual, harm particularly if they were not familiar with the case or made the error themselves.

The TCAM evaluation in Chapter Six has a number of limitations. The retrospective nature of data collection[531], as the quality of the collected data is dependent on the quality of the documented data in patient records[538]. Secondly, history bias may have been introduced through the study design, a before and after study – whilst the research team were unaware of other interventions/changes in practice which could have influenced the safety outcomes, the possible influence of temporal changes cannot be ignored that may otherwise have been minimised through the use of a control group[539]. Although that this was not feasible as the TCAM intervention was rollout across the whole clinical commissioning group (CCG). In addition, it is arguable that the utilisation of the control group would not exclude history bias, as there would still be the changes in practice that could have influenced the safety outcomes. In addition to bias that is introduced due to factors matching. However, the before and after design that was adopted in this study may have enabled consistency because the practice site characteristics may have been less likely to change. Thirdly, data was not collected about the level of expertise or education of the person who completed medication reconciliation for each included patient, and this was not factored in the analysis, as evidence showed that there is a positive correlation between education level and conducting good medication reconciliation[540]. Fourthly, the generalisability of this study was limited in terms of including patients from one geographical area (though data were collected from 18 primary care sites in 8 local areas, and regression analysis controlled this variable). Fifthly, pharmacists' data collectors were trained to collect data about UMD, but they were required to record any discrepancy they

suspected as UMD so some pharmacists collected data on intentional medication discrepancies as well as UMD. However, the team had a review process to determine if medication discrepancies were UMD or intentional medication discrepancy, and included only UMDs in the analysis. In addition, the study did not reach power for the ADE sample size analysis. With regards to service utilisation data, there were few free text descriptions of the service utilisation completed by community pharmacies. In addition, referrals occurring in February 2020 had a short follow-up period (three months as data was extracted in June 2020) compared to referrals in the early phase, which might affect completion rate. Despite that, the completion rate in February 2020 were the highest in this dataset.

7.5 Implications of the results for clinical practice and policy

7.5.1 Medication classes

The medication groups identified from Chapters Four, Five and Six may become a focus of attention by researchers and healthcare staff as potential targets for remedial action that could improve patient outcomes[541]. The review in Chapter Four can be used to inform the development and update a medication-related harm prediction tools that focus on post-discharge risk[411,542,543], by including opioid and anticoagulant drug classes. Prescribing safety indicators could be used following hospital discharge in a more targeted way, including elderly patients (65 years and older) prescribed these medication classes without planned monitoring post hospital discharge. There could be incorporated into prescribing indicator tools/interventions, for example, the pharmacist-led information technology intervention for medication errors ((PINCER) [541,544–546], which is an IT intervention that is implemented in 41% of primary care sites in England[547]. The roll-out of the PINCER intervention on a national level has taken place after the publication of the WHO Third Patient Safety Challenge ''Medication Without Harm'' in 2017. Perhaps a practical approach to use PINCER and similar interventions post hospital discharge maybe adding a designated section in the discharge letter, similar to the surgical safety checklist that could highlight factors increasing risk of medication safety challenges post hospital discharge (such as use of certain medications) that may be then prompt delivery of PINCER for these patients in primary care.

The USA's *'National Action Plan for Adverse Drug Event Prevention'* published in 2015 focused on three medication classes, namely anticoagulants, antidiabetics, and opioids,

where the main recommendations related to the transition of care focused on improved linkage of electronic health records and patient education[548]. Elsewhere these findings could also inform ongoing use of the National Health Services (NHS) New Medicines Service in community pharmacies in the UK[549], which involves counselling the patient starting new medications for chronic diseases including diabetes mellitus and hypertension and those starting new anticoagulant medications. The findings suggest that longer term analgesic medications could be considered for inclusion in the New Medicines Service. The results of this thesis perhaps suggest that a new service might be needed that uses high risk medications and patient characteristics (e.g. older age) to identify those at high risk of post discharge ME / ADE. In addition, remedial interventions like the DMS and pharmacist review should focus on these medication classes.

Regarding opioid medication, an expert consensus guideline on the perioperative use of opioids in the UK was recently published in April 2021 by the Faculty of Pain Medicine at the Royal College of Anaesthesia, in collaboration with high profile organisations in the UK[550]. The document highlighted the importance of clear communication between secondary and primary care regarding opioid dose and duration, and opioids use monitoring post hospital discharge. Opioids are also a specific goal for improvement in the Medication Safety Improvement Programme (MedSIP) in the UK[551]. In addition, a recent systematic review found that patient education is effective in reducing opioid use[552], where Chapter Five has identified an opioid related incident that led to severe harm where the patient applied a fentanyl patch on a wound, thinking that it was a wound dressing. Thus, patient education on opioid use must be highlighted at and post hospital discharge, and be used combined with other interventions. Furthermore, among the strategies performed by the opioids stewardship programme, which are common in the USA, are limiting opioid supplies at discharge[553].

Antibiotic stewardship post hospital discharge was reported as a promising area that requires attention[554], as a high proportion of patients are exposed to antibiotics after hospital discharge. However, Daniels and Weber 2021, stated in a recent systematic review of 6 studies that antimicrobial stewardship at hospital discharge as an intervention to improve antibiotic prescribing was associated with no statistically significant reduction in antibiotic duration[555]. This suggests that further research is needed in this area.

One of the emerging targets for intervention highlighted in the study presented in Chapter Six is the emphasis on reassessing patient kidney function after discharge and checking

acute kidney injury (AKI) risk with the use of diuretics, as they were the most common groups implicated to harm post hospital discharge in this study. There is also an ongoing need to re-enforce the use of indicators, for example in Salford Medication safety dASHboard (SMASH) included *'triple whammy'*; which is the concurrent use of a diuretic, non-steroidal anti-inflammatory drug (NSAID), and either angiotensin converting enzyme inhibitor (ACEI) or angiotensin II receptor blocker (ARB), for AKI and other monitoring indicators[556]. There has been a national effort to optimise medication in patients with AKI *''Think Kidney''*[557], where there has been an emphasis on diuretic and advice on patient counselling before discharge, and the availability of complete information in discharge summary regarding restart and monitoring.

7.5.2 Prescribing and prescription related implications

Polypharmacy has been found to be associated with an increased risk of hospital readmission[471]. There have been scholars who suggested that deprescribing is a suitable way to move forward to contain the problem of medication safety post hospital discharge[558]. The Department of Health and Social Care has recently published a policy document in September 2021 regarding polypharmacy and overprescribing, highlighting issues in hospital discharge letters that contribute to overprescribing[500]. Intensifying hypertensive and antidiabetic medication at hospital discharge for elderly patients has been associated with adverse effects and low clinical long-term impact[559–561].

Several measures can be implemented in secondary care include implementing measures to confirm the addition of a length of treatment to the discharge letter with clear information about the patient clinical case and diagnosis. A number of implications to general practice were also identified. An electronic system that prompts GP about the length of treatment might help in reducing prolonged unnecessary medication regimens. In addition, attention must be drawn to procedures related to issuing repeat prescriptions to avoid processing repeat prescriptions while the patient is admitted or before receiving a discharge letter[562–564]. Furthermore, the recommendation for GP or practice staff to oversee monthly ordering patterns of medication by a patient, and to prompt patient who is not requesting (subject to practice sites capacity / resources). In addition, in certain circumstances where medication is intended as a short course (less than 30-28 days) then medication might be better dispensing from the secondary care.

A significant finding to emerge from Chapters Five and Six is the involvement of MDS prescribing errors in medication safety incidents. These findings, while preliminary, suggest

that MDS use and the patients whom they are supplied to post discharge might be associated with medication errors and patient harm that require attention by healthcare providers by prioritising the inclusion of patients using MDS in any intervention targeting medication use post hospital discharge. Despite their wide use, there remains a paucity of evidence on the impact of MDS. In addition, different study methodologies need to be used to determine the prevalence of medication safety challenges post hospital discharge associated with the use of MDS, in addition to studying their benefit. As it has been argued that combined data collection methods are needed as different information is found using different data collection methods, including chart reviews, global trigger tool method, direct observation method, and computer monitoring[112–114,116,117].

7.5.3 Shared care agreement and inter professional communication

Findings from Chapter Five highlighted how the unavailability of anticoagulation shared care instructions at hospital discharge with the anticoagulation clinic can affect medication safety. It is important that shared care instructions/agreements are properly communicated before discharging the patient, and that staff are aware of the guidelines in the area of shared care agreements[565].

Chapter Five highlighted the need for better communication across care interfaces. Continued effort is needed for healthcare staff education and training on the topic of medication management at transitions of care[566–569], in addition to the adoption of interprofessional education to enhance collaborative work between pharmacists and physicians post hospital discharge. Commenting on inter professional communication of elderly patient medication across transition of care, Manis (2021) observes *' Medication safety was compromised across transitions of care due to unclear processes for disseminating discharge information and transfer of accountability to community doctors. Pharmacists often received delayed notifications of changing medication and transfer plans, despite all health professional disciplines acknowledging their significant role to manage medications at admission and discharge'*[570]. Evidence has also shown that community pharmacists feel hesitance toward interprofessional collaboration in the transition of care[571]. An interesting recent study by Manges (2019) found that teams with high shared mental models between the team manage patient hospital discharges more effectively[572]. In another point of view, Mclean (2019) argues to *'changing the language used from discharge summary to clinical handover'*[573].

7.5.4 **Patient engagement**

Chapter Five reported that in 72 incidents, the patient or relative/carer identified the error, and harm were prevented or mitigated. Comparison of this finding with those of other recent studies confirms that the active involvement of patients and carers can have a positive impact on patient safety[170,574–581]. These results further support the incorporation of patient and family engagement in patient safety strategies, including NHS patient safety strategy 2019[101], and the Global Patient Safety Action Plan 2021 – 2030 that was launched in August 2021[111]. Attention has recently been drawn to the patient's experience of hospital discharge, where patients reported pressured discharges, the complicated nature of discharge, communication issues and healthcare system fragmentation (e.g. lack of shared electronic records across care boundaries affected their medication management post-discharge) [69,228,240,253]. Indeed, recent research has included the valuable patient perspective on discharge and how they may manage their medication effectively [70,240,249,250,252,253,582]. Patient could manage their medications more effectively after discharge. Fylan and colleagues (2017) have summarised strategies adopted by patients post hospital discharge in a qualitative study with patients in the UK[250]. Firstly, patients anticipated medication discrepancies and thus adopted the habit of checking medication given at hospital discharge and comparing it with a repeat prescription. Secondary, patients played a role in facilitating the communication after hospital discharge via highlighting medication changes to the GP.

Incorporating patients' voices in research has been shown to increase understanding. It has been debated that integrating patients' complaints data provides new insights. In a recent study analysing insights from patients' complaints and staff reported incidents (incident reports being compared directly to complaints data regarding the same incident, n=446) in a large multisite hospital in London, UK found that patient complaints described higher harm severity than those described in incident data (60%, n=266/446)[583]. In addition, regarding incidents causing complaints were found to give an opposite point of view than incidents in 46% (n=204/446) of cases, and complementary point of view in 26% (n=115/446) of incidents. Interestingly, patient letters of compliment were also utilised in research and showed valuable insights of positive quality healthcare from patient point of view. It is estimated that in 2017 there were around 50 thousand formal compliment letters submitted to NHS trusts[584]. In a study analysing compliment letters from 54 English NHS trusts (limited to 26 letters per trust received between 2011-2012), it has been estimated that 12% (n=148/1,267) of them to highlight safety issues including medication

prescribing[584]. This could be a promising avenue that could drive forward learning from what goes right in the system, which is the main principle underpinning Safety 2 concept[585].

Patient engagement and empowerment could therefore be a promising avenue to address the issue of medication safety challenges post discharge[45,70,71,106,166,586]. Patient empowerment should start on an individual level via advertising on-site and on social media platforms by high profile organisation / companies as part of their corporate social responsibilities to improve patient knowledge of the issue of medication safety post hospital discharge[587–589]. Thus, the public message might be *"check your medication is up to date after hospital discharge".* In addition, patient empowerment could be on an interpersonal level via education to motivate patients to challenge healthcare providers once medication issues arise post hospital discharge. Furthermore, it could be on an organisational level via institutional policy to increase healthcare providers' awareness of the issue, where healthcare providers already showed a positive attitude regarding patient empowerment[590]. Patient empowerment is already well situated in the context of the political landscape[106,591–593].

Patient empowerment was highlighted by NHS long term plan via accessing health records by the patient with long term conditions via NHS smartphone application, where this could be adopted by NHS services like TCAM/DMS by incorporating discharge letters in NHS smartphone application and empowering patients to play role in following up referrals to community pharmacy. The revolutionary report ''The Topol Review'', led by Dr Eric Topol published in 2019, highlighted the digital future of the NHS and the use of artificial intelligence (AI) and digital medicine instead of routine administrative work[594]. The Topol Review highlighted the use of smart wearable devices to monitor patients, which is one of the methods to empower and involve patients[594]. It is anticipated that it is not long until these implications are hopefully implemented, due to the strong will to digitalise the NHS as seen by the merge of NHS digital with NHS England in November 2021, following the publication of a high profile independent report[595]. Other possible digital technology platform includes cloud and blockchain (a secure distributed database) could be utilised in sharing medication information post hospital discharge [596,597].

7.5.5 **National reporting and learning system (NRLS)**

In Chapter Five, severity of harm data was re-coded to determine the occurrence of actual patient harm, because the reported severity of harm provided by the NRLS might reflect potential severity rather in some cases and the actual severity of harm in others. During

this process, the original harm severity was commonly up-graded based on the evidence provided; the harm severity of 11.2% of incidents were downgraded (n=28/250), 17.2% of incidents were upgraded (n=43/250), 71.6% of incidents had the same harm severity as the NRLS (n=179/250), with 871 incidents having insufficient details. This finding is consistent with that of Scott et al. (2019), who found that 41% (n=114/278) of incident harm severity were regraded to a higher level of harm using the NRLS definition of harm[259]. This may reflect the level of detail provided in the reports, as in this study, the identified level of harm was not specified in 78% (n=871/1,121) of incidents which is higher than in other studies (36%, Carson-Stevens, et al. (2016)) who used similar rating criteria to this study[158,419]. This showcases the need for enhanced training and a standardised system of classifying the severity of harm at a local level within organisations to improve comparability of incident report data and enhance learning[598].

Chapter Five has identified that the quality of the incident report was not optimal. Currently, NRLS input requires reporters to describe incidents in more than four characters which is not sufficient; however, the new system (Learn From Patient Safety Events (LFPSE)) that will be formally launched nationally in August 2022, is expected to collect more useful data than the existing NRLS system[136,599]. There is a need for the new system that captures important information that can aid learning, including patient gender, and reporter profession. Furthermore, incident reports may often be submitted to the NRLS before a local investigation and/or by people who did not make the original error; this may limit the amount of more valuable information. However, despite these concerns regarding the quality of the incident reports, the study has identified a wide range of inter-connected contributory factors. Chapter Five identified several targets for improvement, due to the rich data describing contributory factors underpinning the incident free text description. Despite the useful data that can be identified from the NRLS data analysis, it is still under-utilised in research. NHS Improvement could work collectively with researchers to achieve the aim of learning from their incidents, where this cannot be done efficiently unless it introduces a designated team to deal with queries related to research outside the NHS /government sector. In September 2020, a policy document was published by the Department of Health and Social Care (DHSC), and the Department of Education (DoE) titled ''Reducing bureaucratic burden in research, innovation, and higher education'', focused on providing more funding opportunities for researchers[600]. However, the document failed to highlight the role of stakeholders, including the NHS, in facilitating applied health research. As NHS England/ Improvement are launching a new incident

reporting system nationally by mid-2022 that is designed to facilitate the reporting of incidents, now is the opportunity to put in place systems to expedite meaningful use for research and to benefit patient safety.

7.5.6 **Discharge medicine service (DMS)**

The studies presented in Chapters Four, Five and Six support the implementation of interventions to improve timely and accurate communication between health care providers, such as the NHS Discharge Medicine Service (DMS) implemented in February 2021. The DSM service was launched/ commissioned by NHS England as an essential service. The DMS involves sending electronic discharge letters to a named community pharmacy in a timely manner. To date, the availability of evidence supporting the positive impact of the service is limited to the impact on hospital readmission. The evidence from Chapter Six of this thesis adds to this discourse, presenting the first evaluation of its impact on ADE and UMD rates alongside highlighting the potential of the PharmOutcomes™ platform for service evaluation as well as other purposes, including audits[601–603]. Based on findings in Chapters Four, Five, and Six, the DMS could be utilised to target elderly patients and the most common medication groups more closely.

Greater efforts are needed to ensure that DMS is appropriately implemented. Chapter Six has shown that the practice of medication reconciliation was not consistent, where it was not completed for some patients or completed after a number of days. The community pharmacy framework 2019-2024 has also introduced a new medication reconciliation service at hospital discharge [527]. Thus, it is important for local areas to have a regular audit to oversee to the practice of medication reconciliation completed at general practices and community pharmacies. Other possible methods to improve TCAM through PharmOutcomes™, could be via extracting data automatically from community pharmacy medication records to be stored in PharmOutcomes™, where pharmacists in general practice can review what community pharmacists dispense. In addition, data could be extracted automatically once a patient is admitted and notification could be generated to community pharmacies and general practices without the need for clinical pharmacists to set up the initial steps of sending this notification while a patient is hospitalised. Patient could be given access to the system as well, where PharmOutcomes™ could be as used as an electronic medication passport.

The DMS is a commissioned service, for £35 per referral to be paid for community pharmacy[604]. The question here is not whether the service is worth the money and investment. The question that needs to be asked, however, is whether a single intervention like TCAM alone would be effective. Hospital discharge occurs in a complex system, and involve multiple players with different level of authority, which requires multiple remedial interventions that target all these abnormalities. It seems possible that this is the reason why previous interventions did not work, as they need to target all communication pathway, to minimise the risk of medication errors. Thus, it is now established that multiple interventions might yield better outcomes in the area of patient safety post hospital discharge[281]. Previous systematic reviews of interventions to improve medication use post hospital discharge provided preliminary data that a single intervention might not be as effective as multiple interventions. Thus, combining TCAM with other interventions, including staff and patient education, might result in better results. Providing patients with medication charts could be added as well, due to its promising results[605]. Furthermore, frequent cycles of Plan-Do-Study-Act (PDSA) must be completed to assess the sustainability of the intervention.

A national report by Care Quality Commission (CQC) *''Opening the door to change - NHS safety culture and the need for transformation''* published in 2018, evaluated in 18 NHS trusts the issue of never events, which are patient safety incidents that resulted in preventable serious patient harm[100]. The report has informed the National Patient Safety Strategy published in 2019[101], which focuses on staff education and training. Concentrating efforts on staff education and training might be a good pragmatic approach. However, Chapter Five has shown that few medication safety incidents after hospital discharge occurred as a result of staff knowledge. Thus, it is time to follow Medical Research Council (MRC) developing complex intervention guidance to plan effective interventions based on theoretical understanding of error causes[330]. There is no good a theoretical connection between knowledge of medication safety incidents causes and the premise of TCAM intervention. Future research must concentrate on planning interventions based on knowledge of error nature and causes. This view is supported by the improvement guide published by the Royal College of Physicians in November 2021 *''Medication safety at hospital discharge''* which highlighted the need to identify and measure the problems in local areas before planning the interventions[299]. Chapter Five has found that the most common contributory factors to be continuity of care issues between secondary and primary care. Going back to the TCAM / DMS intervention, the service could be improved

via using a standardised system (PharmOutcomes) to send discharge letters to primary care (and community nursing team) as well as community pharmacies. A recent study evaluating inter-hospitals transitions found that across NHS acute trusts in England using electronic health record systems, 78% (n=92/117) use a system from 21 system providers, 10% (n=12/1170 use multiple systems, and 11% (n=13/117) use the in-house developed system, which impacts patients transfer to nearby trusts[606]. Chapter Five has also shown that the most common staff related contributory factors (n=75) were related to cognitive (n=35/75) and knowledge (n=33/75). Thus, attention must be given to developing the pharmacist's non-technical skills, including task management, teamwork and communication, situation awareness, and decision making[607].

7.5.7 Has COVID-19 pandemic influenced the context and impacted results implications?

The COVID-19 pandemic caused dramatic changes in the healthcare landscape, including hospital discharge and care transition. A report by the British Red Cross and Healthwatch England titled *'590 people's stories of leaving hospital during COVID-19'* was published in October 2020 describing the issue of rushed discharge and highlighted the importance of adequate post discharge assessment and follow up[608,609]. A recent survey in the UK assessing the impact of the COVID-19 pandemic on community pharmacy found that there has been an increase in workload, and working hours, as well as having impact on pharmacist well-being and physical health[610]. Another national survey in the USA assessing the impact of COVID-19 pandemic on pharmacy operations, found that there has been a reduction on the staffing, salary, and medications. In addition, to the negative impact on medication reconciliation and discharge counselling[611]. The COVID-19 pandemic had a negative impact on the postgraduate pharmacy trainees training experience in the USA[612].

Among the measures that have been adopted to reduce the spread of COVID-19 infection, there has been a shift to using and sharing health data electronically, prescriptions delivery, and telehealth follow-up consultations[613–615]. NHS England has also updated the hospital discharge operating policy in July 2021[616], highlighting the *'Discharge to Assess (D2A)'* pathway that was implemented in March 2020 to speed hospital discharge and support patients after hospital discharge, who require rehab/care home or support at home[617]. The D2S pathway consists of 4 main workstreams, including pathway 0, 1, 2, and 3[617]. Thus, it is clear that COVID-19 has complicated the context of hospital discharge and potentially medication safety, highlighting the need for an integrated care system.

7.5.8 Recommendation strategy for a new model of care post hospital discharge

The discharge letter could be considered a form of clinical handover. A seminal study in the area of clinical handover is the work of Catchpole and colleagues (2007), who conducted a study to improve patient handover from surgery to intensive care in the UK[618,619]. Interestingly Catchpole and colleagues (2007), have consulted a team responsible for Formula 1 pit-stop (a quick stop during a race to service the car)[619]. A number of learning points were highlighted including, planning procedures based on predictable problems, the importance of discipline in conducting routine work, and task allocation / assigning a responsible person for each task[619]. Similarly, Chapters Four, Five and Six highlighted the importance of these points. Thus, an 'optimal' future model of care pathway post hospital discharge may concentrate on points highlighted in Table 7.1 below. Priority must be given to elderly patients and those on specific high risk medication classes, including anticoagulants, diuretics, insulin, and opioids. This strategy aligns with the goals of several recent NHS documents, including the NHS Long Team Plan, and NHS Patient Safety strategy[101,477].

Table 7.1 – New model of care pathway post hospital discharge

Stage	Safety theme*	Description
At hospital discharge	Predicting and planning	Digital technology to improve communication
	Predicting and planning	A system to identify high risk medications and referral to primary care for review
	Involvement	Patient involvement and education
Post hospital discharge	Predicting and planning	Indicators to help identify patients at risk in primary care post discharge, and monitor high risk medications
	Predicting and planning	Pharmaceutical prioritisation tool for post hospital discharge review
	Task allocation	Creating a new dedicated services or roles, following hospital discharge to improve safe and efficient capture of medication information and changes
	Discipline	Implement a 'do not disturb strategy' while dealing with discharge letter
	Review meetings	Learning from unsafe incidents

**adopted from* [619]

7.6 Recommendation for future research priorities

7.6.1 Improve standardisation and measurement in the field

Previous systematic reviews of MEs [326,340,341] and ADEs [188,325,620] also report similar limitations to Chapter Four regarding the inability to make a direct comparison between studies. For example, this study observed no pattern in included studies with regard to the

follow-up period post-discharge and the outcome rate or their definitions. There is currently no consensus regarding the specific time point to stop collecting data [621]. There is also wide variation and disagreement in time frame definitions used in research concerning hospital readmission [28,69,622]. This suggests that greater consistency and standardisation of methods (for example, standardisation of the outcome definition via the Delphi technique [623]) are required between studies investigating the transfer of care to enhance comparability of results and ultimately the development of remedial interventions. Aside from standardisation of methods, there is also a need to improve the quality of reporting in studies of care transitions as few studies reported outcome definitions and other essential information. A similar deficit in the quality of reporting of medication safety studies [357] and observational epidemiological studies have been noted previously [624], where standard tools for reporting to a higher standard were proposed. However, most studies were rated as moderate or high quality.

7.6.2 Specific process measures

Considerably more work is required to explore the causes of monitoring errors that lead to medication safety challenges post hospital discharge associated with specific medication classes to include anticoagulants, opioids, and insulin. To my knowledge, few studies have specifically evaluated monitoring errors in community settings. According to a recent systematic review of medication errors in the community setting by Assiri and colleagues (2018)[322], they included one paper that highlighted monitoring errors (using a predefined list of 17 medications)[625], and found that incomplete monitoring occurs in 73% of patients in Lebanon. In comparison, Avery, et al. (2013) found that the prevalence of monitoring errors in English general practice to be as low as 0.9% (number of medication =55/6,048) for all medication, or 7% (n=53/770) for medication that required blood test monitoring[626]. While in the context of monitoring errors at hospital discharge, one study from 2010 in the UK found that the prevalence of monitoring errors post hospital discharge was 3.5% (number of medication=18/514)[385].

7.6.3 Specific research populations; developing countries, ethnic minority and special patient groups

Further research is required exploring medication safety post hospital discharge in developing countries, as currently, Chapter Four has highlighted this to be an under-researched area. There are low levels of patient support post-hospital discharge as a result of underdeveloped primary care services reported in some developing countries [627].

Furthermore, studies do not often factor in the impact of patient socio-economic status on medication safety post hospital discharge (due to the retrospective nature of data collection)[628], where evidence has shown that quality of medication prescribing, and clinical management is affected by this variable[629,630].

The data about ethnic minorities collected in Chapter Six indicated that most patients included were white. More inclusive research in the future on the topic of medication safety post hospital discharge could specifically focus on recruiting and studying patients from ethnic minority backgrounds to be included in the study, to have clear evidence on the influence of ethnicity on medication safety. The National Institute for Health Research (NIHR) has recently published a guide on conducting inclusive research, which could be of benefit for future researchers[631].

Evidence indicates that medication safety challenges for paediatric and patients in nursing/ care home settings exist both during hospitalisation[326] and at the point of discharge from the hospital [632]. Further work to explore the burden and causes of medication safety challenges following transfer to nursing and care homes is also required as unique factors have been reported to complicate these care transitions, including the older age of patients and their elevated severity of illness/ care needs [633], as well as apparent challenges with accountability and communication among staff [64,256].

Improving medicines safety in nursing homes is currently a focus on the Medication Safety Improvement Strategy[634]. Recent studies have found that the rate of unintentional medication discrepancies and medication errors after hospital discharge to a nursing home or home care to be 76% (n=44/50)[370], and 19% (n=19/100)[211], respectively. In addition, evidence indicates that medication error-related incidents during the transition to nursing homes have higher odds of harm compared to those not occurring during this transition[635]. This finding does not imply that nursing staff are associated with incidents, as there are recent reviews that found nursing staff to have an integral role in medication management during translational care[636]. However, this finding reflects those of Vogelsmeier (2014), who also found in a qualitative study that nursing staff are working in isolation and that they are being relied on with regards to resident medication[637]. These findings suggest that more research is needed in this area, to improve communication with nursing staff in community settings.

7.6.4 **Discharge medicine service (DMS)**

Recent studies evaluating interventions to improve medication safety post hospital discharge did not show benefit or marginal benefit[638,639], including a randomised controlled study in the USA evaluating clinical pharmacists' intervention for a patient on high-risk medication medications where the results showed no statistically significant reduction in the rate of ADEs[278].

Findings from the TCAM evaluation study presented in Chapter Six suggest that more research is needed to explore in depth how the service is implemented and used in different contexts and with wider patient groups, given that the DMS is currently nationally implemented in England. Areas of further exploration include determining service impact on medication related hospital admissions using a multi-site study with adequate statistical power and working with community pharmacists to better understand the causes of referral rejections, and delays in completing referrals. A future approach is implementation science-based research to better plan an implementation and sustainability strategy for this service[474]. Another natural progression of the work presented in Chapter Six, and the few medication errors reported by the community pharmacists, would be a further study with more focus on community pharmacists' engagement with the referral system. In addition, a study to assess general practice pharmacists' perceptions of barriers to improve collaboration with secondary care is needed, which may highlight the need for an electronic platform to improve communication. In his analysis of interviews with healthcare providers in the local area in the North West of England following TCAM service implementation, Jeffries (2020) identified that relationship was built between general practices and community pharmacies[475]. Future research must investigate ways to strengthen the partnership between healthcare providers within primary care, including staff at the GP and community pharmacies.

A future study with the aim of exploring community pharmacies engagement with the DMS could be via using a mixed-method, sequential explanatory design where a quantitative study is conducted first followed by a qualitative study. The quantitative component of the mixed-method study must be both a questionnaire to community pharmacies, and an analysis of referral activity data from a random sample of community pharmacies across England. The questionnaire should identify context related characteristics that might have impacted the utilisation of the service, including community pharmacy types (high street, supermarket, multiples, independents), and number/ nature of staff in community

pharmacy who interact with the service. This would be followed by a qualitative study which must be an interview with community pharmacies staff. The areas that could be explored in the interview would be based on the quantitative data analysis' results, which must include reasons of referral rejections, reasons of completing referrals beyond two weeks, and methods adopted to prioritise referrals.

There is now a need for further study to assess in-depth user interaction and feedback with the use of the PharmOutcomes™ platform, to explore how user friendly the platform is, how referrals align to workloads and if certain functionalities in the platform need to be changed to make it easier to use, for example through an automated population of data fields. This may then help support a better understanding of referral completion timelines and rates, and improve data capture. For example, data collected by pharmacists in Chapter Six revealed that UMDs were common in the patient cohort studied, yet reporting of MEs and other medication related issues in the PharmOutcomes platform was not frequent. Wider evidence suggests that general practice and community pharmacy staff work together to resolve medication related issues post-discharge arising from the TCAM, but this is yet to be quantified. Further research could explore how the service may be rolled out and include general practice staff to enhance impact. In addition, Chapter Six speculates that the low rate of ADEs and UMDs identified in the study to be attributed to the availability of the NIPPS team, which if confirmed by future study then this evidence might be considered as a model for future pharmacy practice in general practice settings to maximise positive outcomes with medication support.

There is a need to improve reporting of medication safety issues and to complete medication reconciliation in community pharmacies. Although previous studies have failed to evaluate the accuracy of medication reconciliation in community pharmacy. The service utilisation data reported that community pharmacists offered a wide variety of services in response to the referrals; thus, future research is needed to better understand the scale and impact of these services. A possible method to examine if pharmacists are conducting a proper medication reconciliation, an argument arises from data presented in Chapter Six, could be by comparing medication reconciliation recommendation by national protocol and local standard operative procedure (work-as-imagined) to how pharmacist complete medication reconciliation via direct observation (work-as-done) using the hierarchical task analysis, where this method has been utilised in previous studies in the pharmacy field[640].

7.6.5 Research implication in Kuwait

As this PhD is funded by the Kuwait Civil Service Commission, it was important to translate the results to fit the Kuwait context. Chapter Four has identified that two papers were from the Gulf Cooperation Council (GCC) countries, namely Oman and Saudi Arabia, with the prevalence of preventable ADEs being 16% in both studies cites[214,359]. Not only there is a lack of understanding of MEs and related harm post hospital discharge in Kuwait, but also a collective knowledge about MEs in Kuwait is lacking in all health care settings. A recent systematic review of MEs in hospitals in the Middle East published in 2019 did not include any studies from Kuwait[641]. Previous published studies are limited to assessing potentially inappropriate medication[642], and drug therapy problems[643]. It is anticipated that the rate of preventable ADEs to be similar to the above referenced GCC countries due to the similar context. With regards to the pharmacist's role in Kuwait at hospital settings, there are limited services involving direct patient care[644], with new clinical pharmacy services only recently starting to emerge. Clinical pharmacy services are based on pharmacists' own initiative, due to a lack of policy[645]. In addition, there are limited medication reconciliation services provided in the hospital settings due to lack of policy that enables pharmacists to complete this role in hospital settings[646]. After considering these findings, future research could follow the same strategy as this PhD programme focusing on (1) measuring the epidemiology of MEs and ADEs post hospital discharge, (2) understanding the aetiology of these incidents, to use this as a foundation to develop interventions alongside health care context.

7.7 Overall conclusion

The body of work presented in this PhD thesis highlights that the period following hospital discharge is a high-risk phase of care associated with medication errors, discrepancies and medication related harm, along with inconvenience to both patients and health providers. Focusing on this stage of the patient care journey is recommended and reflects current national and international patient safety priorities. However, these findings identify new targets for these priorities to develop them further, including older patients, certain medication groups and learning to help design the DMS remedial intervention in order to facilitate improvement in medication safety. Finally, this thesis develops an action agenda for future practice and research focusing on measurement, learning and the effective planning and execution of interventional studies.

Chapter Eight: References

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Chapter Nine: Appendices

9.1 Appendix 1- List of conferences attended during the programme of research

1- Attended conference Health Services Research & Pharmacy Practice (HSRPP) on 12th and 13th April 2018, at Newcastle University. The conference title 'Innovative healthcare in the 21st century: providing smarter, safer, and patient-centred health services'.

2- Attended the Prescribing and Research in Medicines Management (PRIMM) UK & Ireland, Conference, on 14th December 2018, at London, UK. The 30th annual scientific meeting titled 'Person-centred Care in the Digital Age: Nudge Nudge, Tweet Tweet'. **[Poster presentation]**

3- Attended the HSJ Patient Safety Congress in Manchester, UK on 2-3 July 2019. **[Poster presentation]**

4- Attended the PRIMM UK & Ireland virtual Conference, on 11th June 2021. The 32th Annual scientific meeting titled 'Big Data…is it the Future of Medicines Optimisation?'. **[Oral presentation]**

5- Attended the HSRPP on 8-9 April 2021, virtual conference. Conference title 'Designing Healthcare: Stimulating Interdisciplinarity and Co-design for Quality Healthcare'. **[Poster presentation]**

9.2 Appendix 2 - PRISMA checklist

Section/ topic	#	Checklist item	Reported in section
Title			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	**4**
Abstract			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	**3.1** **4.12.3.3**
Introduction			
Rationale	3	Describe the rationale for the review in the context of what is already known.	**3.1** **4.1**
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	**4.2**
Methods			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	-
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	**4.3.3** **4.3.4**
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	**4.3.1**
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	**9.3**
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	**4.3.5**
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	**4.3.6**
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	**4.3.2**
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	**4.3.7**
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	**4.3.8**
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	**4.3.8**
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	-
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	-

Section/ topic	#	Checklist item	Reported on page #
Results			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	**4.4.1**
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	**4.4.1**
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	**4.4.2**
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	**9.59.5** **9.6** **9.89.7** **9.8** **9.9**
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	**4.4**
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	-
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	-
Discussion			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	**4.5** **7.2.1** **7.3.1**
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	**7.4**
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	**4.6**
Funding			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	**16**

9.3 Appendix 3 – Search strategy example

	Searches Embase (OVID) 1980 to 2019 Week 10 (14 March 2019)	Results
1	exp incidence/	408,964
2	inciden*.mp.	1,210,110
3	frequen*.mp.	2,074,579
4	exp prevalence/	655,539
5	prevalen*.mp.	1,075,507
6	rate.mp.	2,850,249
7	epidemiological studies.mp.	54,385
8	exp hospital discharge/	107,223
9	hospital discharge*.mp.	118,998
10	patient discharge*.mp.	3,692
11	patient transfer.mp.	1,325
12	care transition*.mp.	2,330
13	continuity of patient care.mp.	712
14	exp transitional care/	1,961
15	transitional care.mp.	3,229
16	(discharge adj3 hospital).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]	128,108
17	(''Drug-Related Side Effects and Adverse Reactions'').mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]	746
18	medical error*.mp.	20,235
19	exp medication error/	17,562
20	medication error*.mp.	18,849
21	adverse drug event*.mp.	5,507
22	exp therapeutic error/	1,425
23	therapeutic error*.mp.	1,621
24	discrepanc*.mp.	90,564
25	medication safety.mp.	3,196
26	omission.mp.	12,302
27	drug related problem*.mp.	2,804
28	prescribing error*.mp.	1,287
29	exp inappropriate prescribing/	4,369
30	medication related problem*.mp.	817
31	drug error*.mp.	601
32	treatment error*.mp.	567
33	exp drug safety/	345,384
34	drug safety.mp.	347,834
35	near miss.mp.	2,147
36	prescription error*.mp.	773
37	administration error*.mp.	1,102
38	dispensing error*.mp.	491
39	transcription error*.mp.	484
40	drug related adverse event*.mp.	3,287
41	((adverse drug or adverse medication) adj1 (event* or reaction* or incident* or outcome* or effect*)).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]	1,327,840
42	number.mp.	2,206,341
43	(medicine or medication or treatment or therapy or drug* or prescription*).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]	14,371,867

44	(safety or harm).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]	1044886
45	43 and 44	803,942
46	epidemiol*.mp.	1,397,787
47	seamless care.mp.	304
48	hospital readmission.mp.	50,863
49	care interface.mp.	277
50	(follow* adj2 discharge).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]	10,125
51	(transition* adj2 care).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]	8,138
52	(post adj2 discharge).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]	10,897
53	descriptive statistics.mp.	42,851
54	pharma* intervention*.mp.	24,131
55	1 or 2 or 3 or 4 or 5 or 6 or 7 or 42 or 46 or 53	8,180,035
56	8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 47 or 48 or 49 or 50 or 51 or 52	187,781
57	17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 45 or 54	2,001,817
58	55 and 56 and 57	11,070
59	limit 58 to yr="1990 -Current"	**11,007**

9.4 Appendix 4 – Data extraction form

Study ID and General Information			
Data extractor:		Date of extraction:	
Study ID:		First author:	
Year of publication:		Publication type:	
Title of source material:		Study duration:	
Language of publication:		Source of study if not published:	
Country of Origin:		Source of funding:	
Study type (e.g. RCT, observational study)		Study title:	
Study citation:			
Study objective/ research question			

Eligibility Criteria	
Duration of follow up post-discharge	
Setting (Which stage of the discharge process were examined): -the time period following discharge	
Outcome measure(s): Rate of medication errors or medication related harm	
Eligibility criteria met?	

DO NOT PROCEED IF PAPER EXCLUDED FROM REVIEW

Study Characteristics			
Study location (city & country)		Study geographic location, eg; urban, rural	
Study setting e.g.; Hospital, community		Specialities wards included or excluded	
Inclusion criteria		Exclusion criteria	
Study main focus (DRPs, ADE, ADR, ME)		Definition used (DRPs, ADR, ARE, ME)	
Participant characteristic (age, gender, ethnicity)		Method of recruitment of participants	
Data captured method (e.g. incident reports, survey)		If an error was to occur, did the observer intervene? O Yes O No If yes did the observer have any training in this process?	
Duration of follow up		Outcome measures	
Start & end date of the study		Total study duration	
Study method (eg; retrospective, prospective)		Methods of identifying ME/ADEs (severity assessment)?	
Methods of identifying ME/ADEs (causality assessment)?		Person involved in data collection?	
Professions of data collector?		Data collectors training?	
Method of confirming identified ME/ADEs (e.g. group discussion, specialist review, definition, training given, checklist)		Was the study testing an intervention?	
Additional information regarding study design			

Study Results			
Type of denominators used for ME/ADEs		Total number checked for error (e.g. total number of prescription chart checked)	
Number of ME/ADEs reported		Rate of ME/ADEs reported	
Sub-type of ME/ADEs reported		Most frequent error subtype reported	
Other Relevant Information			
Factors associated with reported ME/ADEs		Statistical method used to calculate the association of factors that lead to ME/ADEs	
Drug class associated with ME/ADEs			
Information Related to Severity of Harm Associated with Error			
Who assessed the severity		Method by which the severity was assessed	
Severity of ME/ADEs reported			
Notes			
Conflict of interest			
Related publication			
Translation?			
Contact with authors			
Study strength			
Study limitation			
Extra information captured from the author			

Please indicate by unclear or not described or inapplicable for any missing information

9.5 Appendix 5– Summary characteristics of included studies

Reference (Author, year)	Origin	Study setting Discharge from	to	Study design	Study focus [g]	follow up (within)	Data Collection, Data source	Data Collector	Denominator	Numerator	Rate
Ahmad, 2014 [358]	NLD	8 Hosp, (2 AC & 6 non-AC)	Home	O, P [e]	DRP (ADR)	4 w *	• Patient interview at CP • Home visit (If necessary) • Discharge record	Researcher	340 patients	174 patients affected by ADR	ADR 51%
Al-Ghamdi, 2012 [214]	SAU	Med ward at Tert Hosp	Home	O , P	ADE	2 w	• Telephone follow-up call • Questionnaire • Review medical record	Pharmacist	87 patients	• 21 patients (ADE 23 [b] incidents) • 14 p ADEs [b]	• ADEs 24% • p ADE 61% of ADE • p ADE 16% [a] of patient
Al-Hashar, 2018 [359]	OMN	Med wards, Tert UNI Hosp	Home *	RCT , P	pADE	30 d	• Review electronic health records • Telephone interviews (research assistance)	Research assistant (interview), Senior pharmacist (health record and interview data)	301 patients	59 pADE • 49 patient had pADE	• pADE 16%
Armor, 2016 [210]	USA	AC Hosp *	Home*	O, R	**DRP** (ADE, pADE, ADR)	1 w*	• Medication reconciliation • Hospital record • Outpatient clinic EMRs • Patient's current pharmacies	Outpatient clinic based pharmacist *	43 patients	• 1 ADR[b] • 124 ADEs/ pADEs	ADR 2.3% [a] ADEs/pADEs Mean 2.9[a]
Bergkvist, 2009 [360]	SWE	Hospital Clinic comprises of 3 wards	Community health care	I, L, P	ME (UMD [e])	3 w *	• Compare medication list in discharge summary with first medication list in community health care	Pharmacist *	• 63 patients • 549 drugs	• 23 Patients with ME • 66 drugs with ME	• ME 36.5% patient • ME 12% drug
Bonaudo, 2018 [244]	ITA	Urban Hospital (internal medicine, geriatrics, neurology and orthopaedics)	Four local care settings, long care stay, rehabilitation , supports discharged multiple facility, integrate home care	L, R	UMD	NA	• Compare discharge prescription to the first prescription in local care setting	Doctor, nurse collect	• 356 patient	• 51 patient affected by 58 UMD	• UMD 14%
Braund, 2014 [206]	NZL	2 Hosp	Home, 32 CP	P	DRP (ME)	3 d *	• Discharge prescription	CP staff	1,374 Discharge prescription	• 71 Errors of omission [b] • 72 Error of commission [b]	• ME 10.4%
Buajordet, 2002 [361]	NOR	Department of Paediatrics at UNi Hosp	Home	O, P	ADE	2 w	• Spontaneous reporting of suspected ADEs either by the physicians or by the parents • Reviewing medical records	Pharmacist	579 patient (children)	• 54 patients had ADEs • 112 ADEs [b]	ADE 9% patient

Reference (Author, year)	Origin	Study setting Discharge from	to	Study design	Study focus [g]	follow up (within)	Data Collection, Data source	Data Collector	Denominator	Numerator	Rate
Crotty, 2004 [362]	AUS	3 Metropolitan public Hosp	long term care facility	RCT, P	DRP (ADE)	8 w	• Review medication chart and case note	NA	44 patients	• 19 ADE in 44 patients	• ADE 43%
Duggan, 1996 [363]	UK	5 General Med wards in AC Hosp	Home	O, P	UMD in drug supply	1 w	• Patient given a discharge letter to GP • 2 patient interviews at home via questionnaire • Review copies of the labels on the medicines from the pharmacy; discharge letters and compare it with discharge supplies	NA	• 50 patients, 297 drugs	• UMD [b] visit one 33	• UMD visit one 11%[a]
Duggan, 1998 [364]	UK	AC Hosp	Home	I, P	UMD	2 w	• Visit patients at home • Medical notes • Compare CP supplies	NA	237 patient, **1,328 drugs**	**700 UMD [b]**	UMD 52.7 % [a]
Eichenberger, 2010 [365]	CHE	Hosp	Home	O, P	DRP (ADR)	NA	• 64 CP offer internships for pharmacy students • Collected hospital discharge and primary care prescriptions	Fifth-year pharmacy student	265 patients	1 ADR [b]	ADR 0.37% [a]
Fanizza, 2018 [366]	USA	Hosp	Home	P	DRP (ADR)	17 d	• Telephone based comprehensive medication review and patient electronic medical record	Community pharmacist	18 patients	5 ADR	ADR 27.7%[a]
Flanagan, 2010 [367]	CAN	Community Hosp	Home	O, R *	DRP (ADR)	1 w	• Home visit (medication assessment)	Pharmacist	110 patients	28 ADR [b]	ADR 25.4% [a]
Forster, 2005 [6]	USA	Tert AC Hosp	Home	C, P	ADE	24 d	• Telephone interview • Chart review • Handover notes • Discharge summaries • Clinic notes all in hospital documentation	Internist	400 patients	45 patient developed ADE	ADE 11% • 27% of events preventable • 33% of events ameliorable
Gray, 1999 [213]	USA	Hosp	home (receiving home health service)	C, P	ADE	1 m	• Patient interview (phone)	Trained clinical researcher	256 patients	52 reported ADE	20.3%
Hawes, 2018 [209]	USA	AC Hosp	Home	R, C	DRP (ADE)	30 d	• Hospital follow-up visits in primary care centre • Face to face • Review EMR and prescription	Clinical pharmacist	86 patients	7 ADE [b]	ADE 8%[a]
Heyworth, 2014 [368]	USA	Veterans Affairs medical centre	Home	O, P	UMD	72 h	• Medication reconciliation independently at home, via secure messaging via SMMRT programme • Review against discharge prescription	NA	51 patients, 34 patients returned the messaging	26 UMD in 17 patients.	UMD 50% [a]
Hockly, 2018 [369]	UK	Hosp	Home	RCT, P	UMD	3 w	• Current medication record from GP surgery • Telephone interview	Researcher, Analysis by pharmacist	• 16 patients (GP dataset) • 14 patients (Pt dataset)	• 12 patients with discrepancy (GP dataset) • 11 patients with discrepancy (pt data set)	• UMD 75% GP dataset • UMD 78.5% pt dataset • UMD 26% drugs GP dataset • UMD 23% drugs Pt dataset

Reference (Author, year)	Origin	Study setting Discharge from	to	Study design	Study focus [g]	follow up (within)	Data Collection, Data source	Data Collector	Denominator	Numerator	Rate
									• 191 drugs (GP dataset) • 133 drugs (Pt dataset)	• 50 drugs with discrepancy (GP dataset) • 31 drugs with discrepancies (Pt dataset)	
Holdhus, 2019 [370]	NOR	3 Med wards (pulmonary & neurology disorders or general Med) in UNI Hosp	Nursing home or home care	RCT	UMD	10 d	• Compare medication list at primary care to discharge list	Clinical pharmacist	55 patients	• Discrepancies were found in (N = 42) Patients	• Discrepancy 76%
Kannan, 2013 [371]	USA	large multispecialty group practice	Home	O, R	ADE	45 d	• medical record reviews (hospital discharge summaries, emergency department visits; office visit notes) • review of telephone encounters and between individual and providers and between providers.	Clinical pharmacist	1000 discharges	• 187 discharges affected by ADE. • 242 ADE • 84 p ADE	• ADE 18.7% • p ADE 8.4%
Letrilliart, 2001 [372]	FRA	Hosp	Home	O, P	ADR	30 d	• patient attended general practice • data were transmitted on a real time basis via teleinformatics from the general GP's office to the database centre	GP	7540 Patient	• 29 patients affected by ADR • 30 ADR [b]	• A rate of 0.4 post discharge ADRs per 100 admissions resulted from GP referral
MacAulay, 2008 [373]	CAN	Family Practice & Geriatrics Program or from various Med programs	local home care program	I, P	DRP (ADR)	1 m	• 3 Home visit or telephone consultation. • Chart review	Clinical pharmacist	27 patients	6 ADR [b] (During first visit)	ADR 22% [a]
Marusic, 2014 [374]	HRV	Internal Med, UNI Hosp	Home	O, P	ADR	30 d	• medical records review 24 hr before discharge • follow-up visit at hospital • Patients unable to come to the hospital were seen at home • patients were interviewed for any or worsening symptoms	Physician specialist in clinical pharmacology	209 patients 1268 prescriptions	63 patients had ADR	ADE 30.1% [a]
Mesteig, 2010 [375]	NOR	Department of Geriatrics, UNI Hosp	Home	O, P	Administration error	4 w	• The Ambulatory Team (AT) visited the patients during the first week after discharge • Afterwards weekly telephone calls to the patient • Review patient's hospital record, the hospital database and the decision from the discharge-planning meeting. • Record unwanted incidents in registration form	Ambulatory Team member	118 patients	• Wrong drug/incorrect dosage 16 [b] • No written information on drug regimen in patients' homes 8 [b]	ME 20% [a]

Reference (Author, year)	Origin	Study setting Discharge from	to	Study design	Study focus [g]	follow up (within)	Data Collection, Data source	Data Collector	Denominator	Numerator	Rate
Meyer-Massetti, 2018 [211]	CHE	3 Hosp	home care (not a nursing home)	P, O	DRP (ME)[g]	1 w	• 2 structured questionnaires • Prescription quality was assessed	Nurses	100 patients	19 patient affected by ME	ME 19%
Midlov, 2012 [376]	SWE	3 departments of internal Med	nursing home or home care	I , P [e]	(UMD [e])	14 d	• All medical records containing information on drug treatment were collected from hospital departments, the community care service and GPs.	Pharmacist	32 patients with dispensing system (period 1) 39 all patient	Patient affected 16	UMD 50% (apodos) UMD 41% (all patient)
Ibrahim, 2012 [377]	EGY	AC Hosp	Home	RCT, P	ADE/ pADE	30 d	• Patients were contacted by phone • Review case summaries	Research assistance	125 patients	• 23 ADE [b] • 18 p ADE [b]	• ADE 18% • p ADE 14%
Nagaraju, 2015 [378]	IND	Med Dep, Tert AC Hosp	home	O, P	ADR	90 d	• Patients care record forms and patients and care given verbal information over telephonic interview	NA	50 patients	3 mild ADRs[b] .	ADR 6%[a]
Osorio, 2014 [215]	USA	General Med, Tert Hosp	Home	P, O	UMD, ADE	30 d*	• Compare medication lists from hospital discharge & first ambulatory visit • Patient self-report via telephone survey • Review inpatient & outpatient electronic health record.	Research nurse and research physician *	100 patient	82 patient had at least one UMD • 291 UMD event ○ 98 high potential of harm ○ 189 low harm ○ 7 ADE ○ 6 pADE	UMD 82% ADE 7%* self-calculate pADE 6%
Parekh, 2018 [247]	UK	5 AC Hosp, Med wards	Home and care home	P, C, O	DRP (ADE, ADR)	8 w	Patient telephone interview and GP record	Pharmacist	1116 patient	Number of patients affected by: • MRH (**413)** • ADRs (301) • MEs (14) • prescribing error (11) • dispensing error (4) • administration error (4)	MRH 37% ADR 27% [c] MEs related harm 1.7% [c]
Paulino, 2004 [379]	EU: AUT, DNK, DEU, NLD, PRT, ESP	Hosp	Home	P, cross sectional *	DRP (ADR, ME)	2 w *	• Telephone interview • Home visit or a visit from the patient or proxy to the pharmacy • Or interviewed at CP • Patient questionnaire • Pharmacist documentation	community pharmacist in 112 CP in Europe	435 patients	• ADRs 105 [b] • Prescribing error 29 [b]	• ADR 24% [a] • Prescribing error 6.6% [a]

Reference (Author, year)	Origin	Study setting Discharge from	to	Study design	Study focus [g]	follow up (within)	Data Collection, Data source	Data Collector	Denominator	Numerator	Rate
Riordan, 2016 [380]	IRL	AC Hosp	Home	O , CS, P	Prescribing error	14 d	• Telephone to identify actual medication use • CP, general practitioners and hospital prescribers were contacted to corroborate actual and intended medication use.	NA	83 patients	• 36 patients	prescribing error 43%
Salameh, 2019 [381]	JOR	Tert UNI Hosp, Med Dep	Home *	RCT	Side effect **(ADR)***	1 m	• Telephone follow-up	Pharmacist	98 patient	• 20 Patients	• ADR 20.4%
Schnipper, 2006 [398]	USA	Urban, general Med service at urban UNI Hosp	Home	RCT, P	ADE , unexplained discrepancy (UMD[e])	30 d	• Telephone and medical record review	Research assistance	84 patients (73 patient included in the analysis)	• 12 patients affected by ADE • 8 patient had preventable ADE • 43 patients had UMD (out of 66 patient)	• ADE 16% • p ADE 11% • UMD 65%
Solanki, 2017 [5]	IND	NICU Tert Urban care Hospital	Home	CS , Descriptive, P [e]	ME	NA	• Follow-up at High Risk newborn Follow-up Clinic • Interviewed caregiver attending the high-risk newborn follow-up clinic for their first follow-up visit post discharge. • Review discharge summary.	NA	166 Patient 166 prescriptions 486 drugs	• 110 patient ME • 90 patient had administration error	• ME 66.3% • Administration error 54.2%
Tetuan, 2018 [382]	USA	Rural non-profit Hosp	Home	P	DRP (ADR)	2 d	• Telephone based medication reconciliation and comprehensive medication review	Community pharmacist	35 patient	• ADR 6[b]	• ADR 17%[a]
Tong, 2015 [383]	AUS	General Med unit, Tert AC Hosp	Home	Pilot study, P	DRP (ADR)	60 d	• Attend outpatient follow-up clinic • Pharmacist scheduled consultation after patient appointment with doctor • Medication reconciliation interview and medication therapy review	Pharmacist	87 patients	6 ADR [b]	ADR 6.8% [a]
Tsilimingras, 2015 [59]	USA	community Hosp	Home	C, P	ADE	3-6 w	• Telephone interviews • Health record review	Nurse	684 patients	204 ADE [b] 58 p ADE [b]	ADE 29.8% [a] p ADE 8.4% [a]
Westberg, 2017 [207]	USA	3 Hosp	Home	O, R	DRP (ADR)	30 d	• Face-to-face, telephonic, or virtual comprehensive medication management visit • Electronic medication record	Pharmacy practitioner	408 patient	141 ADR [b]	ADR 34.5% [a]
Willoch, 2012 [384]	NOR	Rehabilitation ward at a general Hospl	Home	RCT, P	DRP (ADR)	3 m	• Home visit, questionnaire interview, direct patient communication • Discharge medication list	Pharmacist	29 patients	19 ADR [b]	ADR 65.5% [a]
Conference Abstract											
Alldred, 2010 [385]	UK	Hosp	Home	O, R	ME	3 m	• Attend GP practices in two primary care trusts • Review notes and prescriptions	Clinical pharmacist	• 67 patients	• 42 patients had prescribing or monitoring error	• 63% of patients (prescribing or monitoring error)

Reference (Author, year)	Origin	Study setting Discharge from	to	Study design	Study focus [g]	follow up (within)	Data Collection, Data source	Data Collector	Denominator	Numerator	Rate
									• 514 prescriptions	• 87 prescriptions had ME (monitoring errors (18/87).	• ME 17% of medicine • Monitoring error 3.5% of medicine
Cameron, 2010 [387]	CAN	Hosp	Home	O, P	DRP (ADE)	14 d	• Visit patient home • Medication reconciliation and a pharmaceutical care assessment	Pharmacist	• 30 patients	• 22 ADE [b]	• ADE 73% [a]
Claeys, 2013 [388]	BEL	3 Hosp, (geriatric and orthopaedic wards)	NA	C, P , I control group	UMD	15 d	• Contacted by phone • Prescription review	NA	• 184 patients	• 172 patients had UMD	• UMD rate 93.5 %
Donovan, 2012 [246]	USA	Large medical group	Home	R	ADE	45 d	• Reviewed the ambulatory medical records	Clinical pharmacist	1000 patient	• 189 patients had 244 ADEs • 84 pADE [b]	• ADE 18.9% • pADE 7.4%[a]
Huynh, 2013 [389]	UK	5 NHS Hosp	Home	O, P	UMD	21 d	• Telephone call or home visit depending on patient preference. • Compare discharge letter with medication at follow-up	NA	182 patients	22 patients had UMD	12% UMD
Leland, 2012 [390]	USA	Veterans inpatient care unit at Hosp	Home	I, P	ME	28 d	• Home based transition of care program • Home visit and medication reconciliation	Nurse and Kinesiotherapist	120 patients	NA	53% of patient had ME
Mohammad, 2011 [391]	USA	Hosp	Home	I, P	DRP (ADE, ME)	72 h	• Telephone medication evaluation • Contacting patient's physician and pharmacy	Inpatient pharmacist	45 patients	• 8 prescribing errors [b] • 11 ADE [b]	• Prescribing error 17.7% [a] • ADE 24% [a]
Patel, 2011 [392]	UK	2 General Med wards, UNI Hosp	(home or nursing home) *	I, P	UMD *	6 w	• Compare patient drug chart, hospital discharge letter and GP medication list	Research pharmacist	• 74 patients • 557 medications	• 18 patients had 28 errors at discharge letter • 31 patients had 73 errors at GP records • 40 patient records had 101 errors (total)	• UMD 24% discharge letter • UMD 42% GP record • UMD total 54% [a]
Pourrat, 2017 [393]	FRA	22 Hosp	Home	Cluster randomized, P	DRPs (ME)	7 d	• Phone from patient and CP	pharmacist *	518 patients	patient with at least one error at home 242/518	ME 47%
Sittambalam, 2015 [394]	USA	NA	Out Pt rehab facility	O, P	ME	NA	• Screened patient medication reconciliation sheets by a pharmacist upon patient arrival to rehab facility.	pharmacist	55 patients	32 patients had ME	ME 58.18%
Tantipinichwong, 2017 [395]	USA	Tert AC Hosp	NA	P	DRPs (ME)	72 h	• Phone call post discharge Medication reconciliation • Inpatient pharmacy team hand off notification	clinical pharmacist	628 patients	510 DRP were caused by prescribing errors	Prescribing error 81% [a]
Wijekoon, 2017 [396]	LKA	Tert Hosp	NA	O, P	ADR	6 m	• NS (active surveillance)	NA	715 patients	112 patient had ADR	ADR 15.7%

Reference (Author, year)	Origin	Study setting Discharge from	to	Study design	Study focus[g]	follow up (within)	Data Collection, Data source	Data Collector	Denominator	Numerator	Rate
Wilting, 2012 [386]**	NLD	Geriatric ward, AC Hosp	home	I , P	UMD	1 w	• Home visit	Physician *	41 patients 576 prescriptions	16 patient UMD 21 prescriptions	UMD 39% patient UMD 3.6% prescription

Notes:

- ***Abbreviation:*** *AC (Academic), ADE (Adverse Drug Events), AE (Adverse Events), CP (Community Pharmacy), D (Discrepancy), DC (Discontinuation), DEP (Department), DRP (Drug Related Problem), EMRs (Electronic Medical Records), GP (General Practitioner), H (Hour), HMR (Home Medicines Review), HOSP (Hospital), MD (Medication Discrepancy), MED (Medical), NA (Not Available), NICU (Neonatal Intensive Care Unit), NRLS (National Reporting Learning System), Out Pt (Out Patient), Rehab (Rehabilitation), Tert (Tertiary), UMD (Unintentional Medication Discrepancy), UNI (University)*
- ***Study design:*** *C (Cohort study), CS (Cross Sectional), I (Interventional study), L (Longitudinal study), O (Observational study), P (Prospective), R (Retrospective)*
- ***Origin:*** *AUS (Australia), AUT (Austria), BEL (Belgium), CAN (Canada), CHE (Switzerland), DEU (Germany), DNK (Denmark), EGY (Egypt), ESP (Spain), EU (Europe), FRA (France), HRV (Croatia), IND (India), IRL (Ireland), ITA (Italy), JOR (Jordan), LKA (Sri Lanka), NLD (The Netherlands), NOR (Norway), NZL (New Zealand), OMN (Oman), PRT (Portugal), SAU (Saudi Arabia), SWE (Sweden).*
- ***Superscript:***

  [a] The number of patient affected by ME/ADE was not reported. The rate was calculated based on the number of ME/ADE.

  [b] Number of events

  [c] Self calculated

  [d] Self identify

  [e] Self identify from definition

  [f] Author contacted and confirmed that data of adverse events represents ADR

  [g] Study focus represent outcome measure(s) reported in the original study, and then presented those types of outcomes that we extracted that met the inclusion criteria I.e. ADE, ADR, ME, unintentional discrepancies

  ** Data source is author contact*

  ***The results were combined with a published letter to the editor*[397]

9.6 Appendix 6- Studies examining medication errors following transition of care from secondary to primary care

ME (12)	Origin	Definition	Patient group	Study design	Setting	Data collection method	Data collector	Follow up period	Denominator	Nominator	Rate
Alldred, 2010 [385]	UK	Dean, 2000 [399]	Adults	R	Home	Screen case note (medical record/ discharge prescription/ medication list) post discharge	Pharmacist	3 m	67 patients 514 prescriptions	87 prescriptions had ME Monitoring errors (18/87)	63% of patient (Prescribing or monitoring error) 17% of medicine had ME 3.5% of medicine had monitoring error
Braund, 2014 [206]	NZL	DRP, (Rupp et al, 1992) [647]	NA	P	Home	Screen case note (medical record/ discharge prescription/ medication list) post discharge	Pharmacist	3 d*	1,374 Discharge prescription	71 Errors of omission [b] 72 Error of commission [b]	ME 10.4% [a]
Leland, 2012 [390]	USA	NA	Elderly	P	Home	Home visit and medication reconciliation	Nurse	28 d	120 patients	NA	53% of patient had ME
Mesteig, 2010 [375]	NOR	NA	Elderly, mean (SD/range) 83.2 (± 6.4/66-98)	P	Home	Telephone follow-up interview	Ambulatory team member	4 w	118 patients	42 Drug administration error event [b]	Administration error 35% [a]
Meyer-Massetti, 2018 [211]	CHE	DRP (PCNE)[648]	Elderly, age ≥64	P	Home care	2 Questionnaires & assess prescription quality	Nurses	1 w	100 patients	19 patients affected by ME	ME 19%
Mohammad, 2011[391]	USA	NA	NA	P	Home	Telephone follow-up interview	Pharmacist	72 hr	45 patients	8 prescribing errors [b]	Prescribing error 17.7% [a]
Paulino, 2004 [379]	EU	DRP (Westerland, 1999) [649]	Adults, average age 59.1	P	Home	Telephone follow-up interview or home visit or visit to pharmacy, patient questionnaire, pharmacist documentation	Pharmacist	2 w*	435 patients	29 prescribing error [b]	Prescribing error 6.6% [a]
Pourrat, 2017 [393]	FRA	NA	Average age 62.1	P	Home	Telephone follow-up interview	Pharmacist*	7 d	518 patients	242 patients with at least one error	ME 47%
Riordan, 2016 [380]	IRL	Dean, 2000 [399]	Adults, median (IQR) 70 (60–77)	P	Home	Telephone follow-up interview with patient, GP, CP, and hospital prescriber	NA	10-14 d	83 patients	36 patients	Prescribing error 43%
Sittambalam, 2015 [394]	USA	NA	NA	P	Out pt rehab facility	Medication reconciliation post discharge	Pharmacist	NA	55 patients	32 patients had ME	ME 58%
Solanki, 2017 [5]	IND	NCC MERP	Infants (<3 months)	P	Home	Follow-up visit at hospital/clinic and review discharge summary	NA	NA	166 Patient 166 prescriptions 486 drugs	110 patients had ME 90 patient had administration error	ME 66.3% Administration error 54.2%
Tantipinichwong, 2017 [395]	USA	Developed own	Elderly	P	NA	Phones call medication reconciliation post discharge and Inpatient pharmacy team hand off notification	Pharmacist	72 hr	628 patients	510 DRP caused by prescribing errors[b]	Prescribing error 81% [a]

Notes:

- ***Abbreviation:*** *ADE (Adverse Drug Events), AE (Adverse Events), CP (Community Pharmacy), D (Discrepancy), DC (Discontinuation), DRP (Drug Related Problem), EMRs (Electronic Medical Records), g(gram), GP (General Practitioner), HMR (Home Medicines Review), MD (Medication Discrepancy), mg (milligram), ml(millilitre), NA (Not Available), NICU (Neonatal Intensive Care Unit), NRLS (National Reporting Learning System), O (outcome), Paeds (paediatrics), Pt (Patient), Rehab(Rehabilitation), UMD (Unintentional Medication Discrepancy), W (week).*
- ***Study design:*** *P (Prospective), R (Retrospective)*
- ***Superscript:***
  [a] The number of patient affected by ME was not reported. The rate was calculated based on the number of ME.
  [b] Number of events
  ** Data source is author contact*

9.7 Appendix 7- Studies examining unintentional medication discrepancy following transition of care from secondary to primary care

UMD (14)	Origin	Definition	Patient group	Study design	Setting	Data collection method	Data collector	Follow up period	Denominator	Nominator	Rate
Bergkvist, 2009 [360]	SWE	Leap, 1995	Elderly, age ≥65, median (SD) 84(6.7)	P	Community health care	Screen case note (medical record/ discharge prescription/ medication list) post discharge	Pharmacist *	3 w *	63 patients 549 drugs	23 Patients with event 66 drugs with event	36.5% patient 12% drug
Bonaudo, 2018 [244]	ITA	Pippins, 2008	Age 18 and older (mean age 80)	R	Four local care settings[c]	Compare discharge prescription to the first prescription in local care setting	Doctor, nurse collect data,	NA	356 patients	51 patients affected by 58 UMD	UMD 14%
Duggan, 1996 [363]	UK	Develop own	Adults	P	Home	Home visit	NA	1 w	50 patients 297 drugs	UMD 33	UMD 11% per drug
Duggan, 1998 [364]	UK	Develop own	Adults, 16-79 yrs	P	Home	Home visit and review drug discharge list	NA	2 w	237 patients **1,328 drugs**	**700 UMD**	UMD 52.7 %
Claeys, 2013 [388]	BEL	Clayes, 2012[650]	Elderly	P	NA	Telephone follow-up interview and prescription review	NA	15 d	184 patients	172 patients had UMD	UMD rate 93.5 %
Heyworth, 2014 [368]	USA	NA	Adults	P	Home	Medication reconciliation (via secure messaging at home) and review against discharge prescription	NA	72 hr	51 patients, **34** patients returned the messaging	26 UMD in **17 patients**.	UMD 50%
Hockly, 2018 [369]	UK	Develop own	Adults, mean age 66	P	Home	Telephone follow-up interview and review medication record from GP	Researcher	3w	• 16 patients, 191 drugs (GP dataset) • 14 patients, 133 drugs (Pt dataset)	• 12 patients with UMD, 50 drugs with UMD (GP dataset) • 11 patients with UMD 31 drugs with UMD (pt dataset)	• **UMD 75% pt -GP dataset** • UMD 78.5% pt- pt dataset • UMD 26% drugs GP dataset • UMD 23% drugs pt dataset
Holdhus, 2019 [370]	NOR	Develop own	Aged 18 or older, mean (range) 79 (57–102)	P	Nursing home or home care	Compared medication list at primary care to discharge list	Clinical pharmacist	10 days	55 patients	42 Patients	UMD 76%
Huynh, 2013 [389]	UK	Develop own	Paeds	P	Home	Telephone follow-up interview and reviewed discharge letter	NA	21 d	182 patients	22 patients had UMD	UMD 12%
Midlov, 2012 [376]	SWE	NA	Elderly, age ≥65, mean(rage) 84.4(65-99)	P	Nursing home, or home care	Screen case note (medical record/ discharge prescription/ medication list) post discharge	Pharmacist	14 d	39 all patient in period 1*	Patient affected 16	UMD rate 41% *
Osorio, 2014 [215]	USA	Develop own [J]	Adults, median 58 (24–48)	P	Home	Compare medication lists from hospital discharge, first ambulatory visit, and patient self-report via patient telephone survey. Review inpatient and outpatient electronic health records.	Research nurse and research physician *	30 days *	100 patients	82 patients had at least one UMD 291 UMD event	UMD 82%
Patel, 2011 [392]	UK	NA	Adults, mean age 60 (19.7)	P	Home or nursing home *	Screen case note (medical record/ discharge prescription/ medication list) post discharge	Pharmacist	6 w	74 patients 557 medications	18 patients had 28 UMD at discharge letter, **31 patients had 73 UMD at GP records**, 40 patient records had 101 UMD (total)	• UMD 24% discharge letter • **UMD 42% GP record** • UMD total 54% [a]
Schnipper, 2006 [398]	USA	Develop own	Adults, mean (SD) 57.7 (15.9)	P	Home	Telephone follow-up interview and medical record review	Research assistance	30 d	84 patients (66 pt used in analysis)	43 patients had UMD	UMD 65%
Wilting, 2012 [386]**	NLD	NA	Elderly, mean age 83	P	Home	Home visit	Physician *	1 w	41 patients 576 prescriptions	16 patient UMD 21 prescriptions	UMD 39% patient UMD 3.6% prescription

Notes:

- ***Abbreviation:*** *ADE (Adverse Drug Events), AE (Adverse Events), CP (Community Pharmacy), D (Discrepancy), DC (Discontinuation), DRP (Drug Related Problem), EMRs (Electronic Medical Records), g(gram), GP (General Practitioner), HMR (Home Medicines Review), MD (Medication Discrepancy), mg (milligram), ml(millilitre), NA (Not Available), NICU (Neonatal Intensive Care Unit), NRLS (National Reporting Learning System), O (outcome), Paeds (paediatrics), UMD (Unintentional Medication Discrepancy), W (week).*
- ***Study design:*** *P (Prospective), R (Retrospective)*
- ***Superscript:***

  [a] The number of patient affected by ME/ADE was not reported. The rate was calculated based on the number of ME/ADE.

  [b] Number of events

  [c] Local care settings, including long care stay, rehabilitation, supports discharged multiple facility, integrate home care

  [j] the term "unexplained" rather than "unintentional" medication discrepancies was used because healthcare providers were not interviewed.

  ** Data source is author contact*

  *** The results were combined with a published letter to the editor*[397]

9.8 Appendix 8- Studies examining adverse drug reaction following transition of care from secondary to primary care

ADR (17)	Origin	Definition	Patient group	Study design	Setting	Data collection method	Data collector	Follow up period	Denominator	Nominator	Rate
Ahmad, 2014 [358]	NLD	DRP (PCNE, 2006)	Elderly, age ≥60, median(range) 76 (60-95)	P	Home	interview at community pharmacy & review discharge record	Researcher	4 w *	340 patients	174 patients affected by ADR	ADR 51%
Armor, 2016 [210]	USA	DRP (Cipolle et, 2012)	Adults, Mean (SE) 59 (2)	R	Home	Medication reconciliation post discharge, screen EMR	Pharmacist	1 w *	43 patients	1 ADR [b]	ADR 2.3% [a]
Eichenberge, 2010 [365]	CHE	DRP (PCNE, 2006)	Adults	P	Home	Screen case note (medical record/ discharge prescription/ medication list) post discharge	Pharmacy student	NA	265 patients	1 ADR [b]	ADR 0.37% [a]
Fanizza, 2018 [366]	USA	NA	Aged 18 years or older, median age 65.5 IQR 57.3-73.3	P	Home	Telephone based comprehensive medication review and patient (hospital and pharmacy EMR)	Community pharmacist	17 d	18 patients	5 ADR [b]	ADR 27.7%[a]
Flanagan, 2010 [367]	CAN	DRP (strand, 1990)	Elderly,age ≥65	R *	Home	Home visit (medication assessment)	Pharmacist	1 w	110 patients	28 ADR [b]	ADR 25.4% [a]
Letrilliart, 2001 [372]	FRA	WHO, 1972	All age groups [l]	P	Home	GP database	Physician	30 d	7540 Patient	29 patients affected by ADR 30 ADR [b]	A rate of 0.4 post discharge
MacAulay, 2008 [373]	CAN	DRP (strand, 1990)	Elderly mean/SD 81/ 7.1 (range) (60-91)	P	Local care home	Home visit and chart review	Pharmacist	1 m	27 patients	6 ADR [b] (During first visit)	ADR 22% [a]
Marusic, 2014 [374]	HRV	WHO, 1972	Elderly, age ≥65, median (range) 74(65-89)	P	Home	Follow-up visit at hospital/clinic and review medical record	Physician	30 d	209 patients 1268 prescriptions	63 patients had ADR 2 ADR (preventable)[b]	ADR 30.1% p ADE 1%[a]
Nagaraju, 2015 [378]	IND	WHO, 1972	Elderly, age ≥60	P	Home	Telephone follow-up interview and review medical record	NA	90 d	50 patients	3 mild ADRs [b]	ADR 6%[a]
Parekh, 2018 [247]	UK	European Medicine Agency, 2017 [651]	Elderly, age ≥65, median (IQR), 81.9 (75.5–86.9)	P	Home and care home	Patient telephone interview and GP record	Pharmacist	8 w	1116 patient	301 patients affected by ADR	ADR 27%
Paulino, 2004 [379]	EU	DRP (Westerlund, 1999)	Adults, average age 59.1	P	Home	Telephone interview or home visit or visit to pharmacy, patient questionnaire, pharmacist documentation	Pharmacist	2 w *	435 patients	ADRs 105 [b]	ADR 24% [a]
Salameh, 2019 [381]	JOR	Side effects	Aged 18 years or older, Mean (SD) 63.9 (13.4)	P	Home *	Telephone follow-up	Pharmacist	1 m	98 patients	20 Patients experienced side effects	ADR 20.4%
Tetuan, 2018 [382]	USA	DRP (Cippolle, Strand, 1998)	Aged 18 years or older	P	Home	telephone based medication reconciliation and comprehensive medication review	Community pharmacist	2 d	Number of patient (N = 35)	6 ADR [b]	ADR 17%[a]
Tong, 2015 [383]	AUS	NA	Adult, mean (range) 73 (22-91)	P	Home	Follow-up visit at hospital/clinic and discharge plan review	Pharmacist	60 d	87 patients	6 ADR [b]	ADR 6.8% [a]
Westberg, 2017 [207]	USA	DRP (Cipolle et, 2012)	Adult, mean (SD) 67.7 (13.8)	R	Home	Telephone follow up interview and case note review	Pharmacist	30 d	408 patient	141 ADR [b]	ADR 34.5% [a]
Wijekoon, 2017 [396]	LKA	NA	Adults	P	NA	NS (Active surveillance)	NA	6 m	715 patients	112 patients affected by ADR	ADR 15.7%
Willoch, 2012 [384]	NOR	DRP (PCNE definition)	Adults, Mean (SD) [range] 76.8 (11.71) [42–94]	P	Home	Home visit	Pharmacist	3 m	29 patients	19 ADR [b]	ADR 65.5% [a]

Notes:

- ***Abbreviation:*** *ADE (Adverse Drug Events), AE (Adverse Events), CP (Community Pharmacy), D (Discrepancy), DC (Discontinuation), DRP (Drug Related Problem), EMRs (Electronic Medical Records), g(gram), GP (General Practitioner), HMR (Home Medicines Review), MD (Medication Discrepancy), mg (milligram), ml(millilitre), NA (Not Available), NICU (Neonatal Intensive Care Unit), NRLS (National Reporting Learning System), O (outcome), Paeds (paediatrics), UMD (Unintentional Medication Discrepancy), W (week).*
- ***Study design:*** *P (Prospective), R (Retrospective)*
- ***Superscript:***

  [a] The number of patient affected by ME/ADE was not reported. The rate was calculated based on the number of ME/ADE.

  [b] Number of events

  ** Data source is author contact*

  [l](Letrilliart, 2001) all age groups, median age (range): patient experiencing ADR 77 (15-96y), patient not experiencing ADR 68 (1 month-99y)

9.9 Appendix 9- Studies examining adverse drug events following transition of care from secondary to primary care

ADE (17)	Origin	Definition	Patient group	Study design	Setting	Data collection method	Data collector	Follow up period	Denominator	Nominator	Rate
Al-Ghamdi 2012 [214]	SAU	Nebeker et al, 2004	Adults, Mean(SD) 55(23)	P	Home	Telephone follow-up interview and questionnaire. review medical record	Pharmacist	2 w	87 patients	• 21 patients (ADE 23 [b] incidents) • 14 p ADEs [b]	• ADEs 24% • p ADE 61% of ADE • p ADE 16% [a] of patient
Al-Hashar, 2018 [359]	OMN	Bates, 1995	Aged, Mean(DS) 57(17)	P	Home *	Review electronic health records and telephone interviews	Research assistant	30 d	301 patients	59 pADE • 49 patient had pADE	pADE 16%
Armor, 2016[j] [210]	USA	DRP (Cipolle et al, 2012)	Adults, Mean (SE) 59 (2)	R	Home	Medication reconciliation post discharge, screen EMR	Pharmacist	1 w *	43 patients	124 ADEs/ pADEs	ADE/p ADE Mean 2.9
Buajordet, 2002 [361]	NOR	Bates, 1995	Paeds	P	Home	Reporting of incident and review medical records	Pharmacist	2 w	579 patients	• 54 patients had ADEs • 112 ADEs [b]	ADE 9% patient
Cameron, 2010 [387]	CAN	NA	NA	P	Home	Home visit. Medication reconciliation and a pharmaceutical care assessment	Pharmacist	14 d	30 patients	22 ADE [b]	ADE 73% [a]
Crotty, 2004 [362]	AUS	NA	Elderly, mean, 95% CI 83.4 [81.7-85.1	P	long term care facility	Screen case note (medical record/ discharge prescription/ medication list)	NA	8 w	44 patients	19 ADE in 44 patients	ADE 43% [a]
Donovan, 2012 [246]	USA	NA	Elderly age ≥65,	R	Home	Screen case note (medical record/ discharge prescription/ medication list)	Pharmacist	45 d	1000 patient	• 189 patients had 244 ADEs • 84 pADE [b]	• ADE 18.9% • pADE 7.4%
Forster, 2005 [6]	USA	Bates, 1995	Adults, age 57 +/- 17	P	Home	Telephone follow-up interview and chart review	Physician	24 d	400 patients	45 patient developed ADE	ADE 11% (27% of events preventable and 33% of events ameliorable)
Gray, 1999 [213]	USA	NA	Elderly, age ≥65, mean (SD) 80 (7.3)	P	Home	Telephone follow-up interview	Clinical researcher	1 m	256 patients	52 reported ADE	20.3%
Hawes, 2018 [209]	USA	DRP (PCNE, 2010)	Aged 18 years or older	R	Home	Hospital follow-up visits in primary care and review EMR and prescription	Clinical pharmacist	30 d	86 patients	ADE 7[b]	ADE 8%[a]
Kannan, 2013 [371]	USA	Bates, 1995	Elderly, age ≥65, mean (SD) 78.8(7.1)	R	Home	Screen case note (medical record/ discharge prescription/ medication list)	Pharmacist	45 d	1000 discharges	187 discharges affected by ADE. P ADE (84 event)	• ADE 18.7% • p ADE 8.4% [a]
Mohammad, 2011 [391]	USA	NA	NA	P	Home	Telephone follow-up interview	Pharmacist	72 hr	45 patients	11 ADE [b]	ADE 24% [a]
Ibrahim,2012 [377]	EGY	NA	Adults, mean (SD); 59.8 (16.8)	P	Home	Telephone follow-up interview and review case note	Research assistance	30 d	125 patients	• 23 ADE [b] • 18 p ADE [b]	• ADE 18% • p ADE 14%
Osorio, 2014 [215]	USA	Develop own	Adults, median 58 (24–48)	P	Home	Compare medication lists from hospital discharge, first ambulatory visit, & patient self-report via telephone survey. Review inpatient and outpatient electronic records.	Research nurse and research physician *	30 d*	100 patients	7 ADE [b] 6 pADE[b]	• ADE 7%* • pADE 6%
Parekh, 2018 [247]	UK	Develop own	Elderly, age ≥65, median (IQR), 81.9 (75.5–86.9)	P	Home and care home	Patient telephone interview and GP record	Pharmacist	8 w	1116 patient	413 patient had MRH	• MRH 37%
Schnipper, 2006 [398]	USA	Bates, 1995	Adults, mean (SD) 57.7 (15.9)	P	Home	Telephone follow-up interview, and medical record review	Research assistance	30 d	73 patients	• 12 patients affected by ADE 8 patient had preventable ADE	• ADE 16% • p ADE 11%
Tsilimingras, 2015 [59]	USA	NA	Adults	P	Home	Telephone follow-up interview, and health record review	Nurse	3-6 w	684 patients	204 ADE [b] 58 p ADE [b]	ADE 29.8% [a] p ADE 8.4% [a]

Notes:

- ***Abbreviation:*** *ADE (Adverse Drug Events), AE (Adverse Events), CP (Community Pharmacy), D (Discrepancy), DC (Discontinuation), DRP (Drug Related Problem), EMRs (Electronic Medical Records), g(gram), GP (General Practitioner), HMR (Home Medicines Review), MD (Medication Discrepancy), mg (milligram), ml(millilitre), NA (Not Available), NICU (Neonatal Intensive Care Unit), NRLS (National Reporting Learning System), O (outcome), Paeds (paediatrics), UMD (Unintentional Medication Discrepancy), W (week).*
- ***Study design:*** *P (Prospective), R (Retrospective)*
- ***Superscript:***

  [a] The number of patient affected by ME/ADE was not reported. The rate was calculated based on the number of ME/ADE.

  [b] Number of events

  [c] Self calculated

  [d] Self identify

  [e] Self identify from definition

  [f] Author contacted and confirmed that data of adverse events represents ADR

  [g] Study focus represent outcome measure(s) reported in the original study, and then presented those types of outcomes that we extracted that met the inclusion criteria I.e. ADE, ADR, ME, unintentional discrepancies

  [h] Data source is author contact

  **Data source is author contact*

  [j] (Armor, 2016) DRP: when patient experiences or likely to experience disease or symptom having an actual or suspected relationship with drug therapy [DRP = ADEs/ p ADEs]
- ***References:***

  1- Strand et al., 1990 [652]

  2- Claeys et al., 2012 [650]

  3- Bates et al., 1995 [174]

  4- Nebeker et al., 2004 [653]

  5- Leape., 1995 [654]

  6- National Coordinating Council for Medication Error Reporting and Prevention. [177,347]

  7- Cornish et al., 2005 [203]

  8- Dean et al., 2000 [399]

  9- Institute of Medicine, 2003 [655]

9.10 Appendix 10– Severity assessment and severity results of the included studies

Reference (Author, year)	Method of identifying ME/ADEs (validity and severity assessment)	Severity of ME/ADEs reported
Ahmad, 2014 [358]	• Two independent clinical pharmacologists	NA
Al-Ghamdi, 2012 [214]	• Two independent clinicians	**Severity n (%)** • Life threatening (0) • Serious 9 (39) • Significant 14 (61)
Al-Hashar, 2018 [244]	• ADE events were assessed based on criteria derived from Winterstein et al. (2002)[656] • Two reviewers (masked to group allocation) • Consensus meeting and a third reviewer to resolve disagreement	**Severity categories (Morimoto, et al., 2004)**[657]**:** • 0 Life threatening • 22 Serious p ADE • 36 Significant p ADE
Armor, 2016 [210]	NA	NA
Bergkvist, 2009 [360]	• Consensus by pharmacists	NA
Braund, 2014 [206]	NA	NA
Bonaudo, 2018 [244]	• Clinical pharmacist evaluated the discrepancies	NA
Buajordet, 2002 [361]	• Naranjo algorithm • Clinical pharmacologist assessed events • Discussed the events with medical clinicians	NA
Crotty, 2004 [362]	• Independent blinded pharmacist assessed medication chart	NA
Duggan, 1998 [364]	• Reviewing panel of severity (10% of sample) • Consensus panel of four medical consultant • Assessed inter-rater reliability	NA
Duggan, 1996 [363]	NA	NA
Eichenberger, 2010 [365]	NA	NA
Fanizza, 2018 [366]	NA	NA
Flanagan, 2010 [367]	NA	NA
Forster, 2005 [6]	• Two board-certified internists • Independently assessed • Assessed inter-rater reliability	Used severity rating proposed by Bates and colleagues, 1995[174], 45 patient developed ADE: • significant injuries (32 patients) • serious (6 patient) • Life threatening (7 patient) Among patients with an ADE: • 7% required laboratory test • 78% experienced new symptoms • 13% had non-permanent disability • 2% had permanent disability
Gray, 1999 [213]	• Naranjo's scale *[this was not a validity assessment on its own]* • Validated via principal investigator	Of 64 ADEs: • 23 possible • 37 probable • 4 definite

Reference (Author, year)	Method of identifying ME/ADEs (validity and severity assessment)	Severity of ME/ADEs reported
Hawes, 2018 [209]	• Using Medication Assessment and Planning (iMAP) and American Hospital Formulary Service (AHFS) therapeutic class, and medication • 2 pharmacists verified the events	• 7 Moderate ADE (from 7 total)
Heyworth, 2014 [368]	• Physician and pharmacist review	NA
Hockly, 2018 [369]	• Major discrepancy was confirmed if it has tendency to cause an adverse effect on the patient • Second pharmacist reviewed the discrepancies to reduce subjectivity	• 19 Major discrepancies in the GP data set • 4 Major discrepancies in patient data set
Holdhus, 2019 [370]	NA	NA

Kannan, 2013 [371]	• Interdisciplinary panel
	• Assessed inter-rater reliability
		Used severity rating proposed by Bates and colleagues, 1995[174]
		• ADE (overall 242)
		  • less serious 185
		  • serious 51
		  • life threatening 6
		Of the 242 ADEs identified (**35% (n=84) were preventable**):
		  • 63% (n=53) less serious
		  • 32% (n=27) serious
		  • 5% (n=4) life threatening

Letrilliart, 2001 [372]	• Reviewed by a GP and a hospital internist • Validated according to the case definition - likelihood of ADR preventability was assessed via evaluation scheme proposed by French experts in pharmacovigilance.	Seriousness criteria delivered from the FDA Medwatch criteria (30 ADRs): • 59% preventable • 60% serious (18 ADRs) were serious (life-threatening reaction: 14 ADRs) or (re hospitalisation: 10).
MacAulay, 2008 [373]	NA	NA
Marusic, 2014 [374]	• Naranjo scale • Independent Physician evaluated events	Severity assessment using WHO, 2013 guide: • 23 (31.9%) possible • 41 (56.9%) probable • 8 (11.2%) definite. • 35 (48.6) ameliorable • 2 (2.8%) preventable • 5 (6.9%) serious, hospital admission
Mesteig, 2010 [375]	• Consensus (geriatric nurse, project coordinator and medical officer)	NA
Meyer-Massetti, 2018 [211]	• Clinical Pharmacist assessed prescription quality based on questionnaire	NA
Midlov, 2012 [376]	• Evaluation was completed independently by two members • consensus between group member	• Degree of clinical risk based on errors at discharge at period 1 (39 patient) • Low: 6 patients • Moderate: 10 patients
Ibrahim, 2012 [377]	• Blinded clinical pharmacist blinded assessed ADE • Naranjo algorithm	NA
Nagaraju, 2015 [378]	NA	NA
Osorio, 2014 [215]	• A pair of physician reviewers evaluated all medication discrepancies. • Disagreements resolved by discussions, with a third adjudicator	291 UMD events: • 98 high potentials of harm • 198 low harms • 7 ADE
Parekh, 2018 [247]	• ADR causality assessment (Naranjo)	(556 MRH events per 1000 discharges), of which

Reference (Author, year)	Method of identifying ME/ADEs (validity and severity assessment)	Severity of ME/ADEs reported
	• Assessed severity of MRH using the approach of Morimoto et al: fatal, life threatening, serious and significant. • Independent committee assessed events • Confirmed events consensus	• 214 (52%) potentially preventable: o 'definitely' preventable in 44 cases o 'possibly' preventable in 170 MRH cases • 336 (81%) cases were serious: o Four participants (1.0%) experienced a fatal event associated with the MRH o Nine participants (2.2%) had a life-threatening event, o MRH was serious in a further 323 participants (78.2%)
Paulino, 2004 [379]	NA	NA
Riordan, 2016 [380]	• Four clinicians validate the events • Four independent assessors (hospital doctor, GP and two hospital pharmacists)	Severity was assessed based on method proposed by Dean and colleagues, 1999[658] 36 patients had MEs, for whom the majority (n = 31, 86 %) were at risk of moderate harm. • Potential for harm consequent to post-discharge medication error Mean score/ Scores assigned to the error (%) /Score assigned to the patient Minor 1–2 /14 (21.2) / **4** Moderate 3–7 /51 (77.3) / **31** Severe 8–10 / 1 (1.5) / **1** **Denominator 66 errors /36 patients**
Salameh, 2019 [381]	NA	NA
Schnipper, 2006 [398]	• Naranjo algorithm • 2 blinded physician adjudicators • Independently assess ADE • Assessed interrater reliability	NA
Solanki, 2017 [5]	NA	NA
Tetuan, 2018 [382]	• Cippolle, Morley and Strands' 7 classifications of DRP. [this was not a validity assessment on its own]	NA
Tong, 2015 [383]	• Review by pharmacist • Using a tool published in the Society of Hospital Pharmacists' Australia Standards of Practice for Clinical Pharmacy Services	NA
Tsilimingras, 2015 [59]	• Two independent physician-adjudicators • Naranjo algorithm • Reach consensus • Assessed inter-rated reliability	**Used severity rating proposed by Bates and colleagues, 1995**[174] • **ADE Urban** (preventable 29. ameliorable 45, non-preventable nor ameliorable 26) • **ADE Rural** (preventable 29. ameliorable 36, non-preventable nor ameliorable 39)
Westberg, 2017 [207]	• Teams of 3 investigators (consensus)	**NA**
Willoch, 2012 [384]	NA	NA
	Conference abstract	
Alldred, 2010 [385]	NA	NA
Cameron, 2010 [387]	NA	NA
Claeys, 2013 [388]	NA	NA
Donovan, 2012 [246]	• Pair of physician-reviewers • Independently classified incidents	Of 244 ADEs identified: • 34% (n=84) preventable. • 77% less severe • 21% serious • 2% were life-threatening

Reference (Author, year)	Method of identifying ME/ADEs (validity and severity assessment)	Severity of ME/ADEs reported
		54% of serious and life-threatening events were considered preventable, compared to 21% of the less severe events.
Huynh, 2013 [389]	• Six clinicians assessed the clinical severity of UMD • Using a visual analogue scale	UMD affecting 22 patients resulted in: • 63.3% of patients moderate-severe discrepancy • 45.5% of patients' minor discrepancy.
Leland, 2012 [390]	NA	NA
Mohammad, 2011 [391]	NA	NA
Patel, 2011 [392]	NA	NA
Pourrat, 2017 [393]	NA	NA
Sittambalam, 2015 [394]	NA	NA
Tantipinichwong, 2017 [395]	NA	NA
Wijekoon, 2017 [396]	NA	Of 154 ADRs: • 51.9% (80/154) potentially avoidable • 47% (73/154) of ADRs serious adverse events o 13 life threatening o 46 caused hospitalization o 14 caused disability
Wilting, 2012 [386]**	NA	34.1% Patients had potentially harmful discrepancies

- ***References:***
  1- *Morimoto et al., 2004* [657]
  2- *Agenzia Italiana del Farmaco (AIFA).* [659]
  3- *Winterstein et al., 2002.* [656]

*** The results were combined with a published letter to the editor*[397]

9.11 Appendix 11- Summary of medications involved in adverse drug events post discharge in the included studies in the systematic review

Therapeutic areas	Medication class	Medication class reported in the study	References
Endocrine system	Diabetes mellitus and hypoglycaemia	Antidiabetic	Armor, 2016; Letrilliart, 2001; Marusic, 2014; Wijekoon, 2017 [210,372,374,396]
	Corticosteroid responsive condition	Corticosteroids	Forster, 2005 [6]
		Prednisone	Gray, 1999 [213]
Cardiovascular system		Cardiovascular drugs	Forster, 2005; Gray, 1999; Hawes, 2018; Kannan, 2013; Osorio, 2014*; Paulino, 2004; Tsilimingras, 2015; Westberg, 2017 [6,59,207,209,213,215,371,379]
	Blood pressure condition	Antihypertensives	Armor, 2016; Parekh, 2018; Wijekoon, 2017 [210,247,396]
		Metoprolol	Flanagan, 2010 [367]
		Diuretics	Kannan, 2013 [371]
		Furosemide	Marusic, 2014; Gray, 1999 [213,374]
		Ramipril	Flanagan, 2010 [367]
	Thromboembolism	Anticoagulants	Letrilliart, 2001; Osorio, 2014*; Tsilimingras, 2015 [59,215,372]
		Warfarin	Wijekoon, 2017; Marusic, 2014[374,396]
Nervous system		Central nervous system agent	Gray, 1999; Hawes, 2018; Paulino, 2004 [209,213,379]
		Psychoactive drugs	Letrilliart, 2001 [372]
		Psychotropic and hypnotics	Westberg, 2017 [207]
	Mental health disorders	Psychiatric medications	Armor, 2016[210]
	Pain	Analgesics	Westberg, 2017 [207]
		Opioids	Kannan, 2013; Parekh, 2018 [247,371]
Anti-infective		Antibiotics	Forster, 2005; Gray, 1999; Parekh, 2018; Tsilimingras, 2015 [6,59,213,247]
Respiratory system		Pulmonary medication	Osorio, 2014* [215]
Gastro-intestinal system		Gastrointestinal agents	Hawes, 2018 [209]

**Medication associated with unintentional medication discrepancies*

9.12 Appendix 12- Data variables in the data that consisted of 1,324 lines in Excel

Variable name	Description, type of variable	Example
Incident ID	Number	12
Care setting of occurrence	Categorical, nominal	General practice
Date of incident occurred "DDMMMYYYY"	Date was codded as categorical variable (Month and year)	22 Jan 2016
Location (Level 1)	Categorical, nominal	Primary care setting
Location (Level 2)	Categorical, nominal	GP surgery
Location (Level 3)	Categorical, nominal	Treatment room
Location (free text)	Free text data	
Incident category	Categorical, nominal	Medication
Description of what happened	Free text data	
Actions preventing reoccurrence	Free text data	
Apparent causes	Free text data	
Age group	Categorical, nominal	76 to 85 years
Speciality (Level 1)	Categorical, nominal	Primary care / community
Speciality (Level 2)	Categorical, nominal	General practice
Speciality (free text)	Free text data	
Reported degree of harm (severity)	Categorical, ordinal	No harm
Stage of medication process	Categorical, nominal	Prescribing
Medication error category	Categorical, nominal	Wrong frequency
Approved drug name	Free text data	

9.13 Appendix 13– Data variables and corresponding codes

Variable name	Description	Coding	Codes
Incident ID number	Number		
Date of incidents "DDMMMYYYY"	Date month	• Jan	• 1
		• Feb	• 2
		• Mar	• 3
		• Apr	• 4
		• May	• 5
		• Jun	• 6
		• Jul	• 7
		• Aug	• 8
		• Sep	• 9
		• Oct	• 10
		• Nov	• 11
		• Dec	• 12
	Date year	• 2015	• 1
		• 2016	• 2
		• 2017	• 3
		• 2018	• 4
		• 2019	• 5
Age group	Categorical	• Under 28 days	• 1
		• 1 month to 1 year	• 2
		• 2 years to 4 years	• 3
		• 5 years to 11 years	• 4
		• 12 years to 17 years	• 5
		• 18 years to 25 years	• 6
		• 26 years to 35 years	• 7
		• 36 years to 45 years	• 8
		• 46 years to 55 years	• 9
		• 56 years to 65 years	• 10
		• 66 years to 75 years	• 11
		• 76 years to 85 years	• 12
		• Over 85 years	• 13
		• Missing data	• 999
Stage of medication process	Categorical	• Monitoring / follow-up of medicine use	• 1
		• Supply or use of over-the-counter (OTC) medicine	• 2
		• Advice	• 3
		• Preparation of medicines in all locations / dispensing in a pharmacy	• 4
		• Monitoring / follow-up of medicine use	• 5
		• Other	• 6
		• Administration / supply of a medicine from a clinical area	• 7
		• Prescribing	• 8
		• Missing data	• 999

Reported degree of harm (severity)	Categorical	• No harm	• 1
		• Low	• 2
		• Moderate	• 3
		• Severe	• 4
		• Death	• 5
Location (Level 1)	Categorical	• Primary care setting	• 1
		• General / acute hospital	• 2
		• Residence / home	• 3
		• Community hospital	• 4
		• Social care facility	• 5
		• Mental health unit / facility	• 6
		• Public place (specify)	• 7
		• Other	• 8
		• Unknown	• 9
		• Not applicable	• 10
		• Missing data	• 999
Location (Level 2)	Categorical	• Minor injury unit / medical assessment unit	• 1
		• Community mental health facility	• 2
		• Dental surgery	• 3
		• Optician / optometrist	• 4
		• Prison / remand centre	• 5
		• General areas	• 6
		• Intermediate care setting	• 7
		• Community pharmacy	• 8
		• Nursing home	• 9
		• Residential care home	• 10
		• Health centre / out-of-hours centre	• 11
		• Inpatient areas	• 12
		• Outpatient department	• 13
		• Private house / flat etc.	• 14
		• Other	• 15
		• GP surgery	• 16
Location (Level 3)	Categorical	• Hospital buildings (inside)	• 1
		• Ward	• 2
		• Waiting room / reception	• 3
		• Dispensary	• 4
		• Other	• 5
		• Treatment / consulting room	• 6
Location (free text)	Free text		
Description of what happened	Free text		
Actions preventing reoccurrence	Free text		
Apparent causes	Free text		
Speciality (Level 1)	Categorical	• Primary care / Community	• 1
		• Accident and Emergency (A)	• 2

		• Learning disabilities	• 3
		• Medical specialties	• 4
		• Mental health	• 5
		• Not applicable	• 6
		• Obstetrics and gynaecology	• 7
		• Other	• 8
		• Other specialties	• 9
		• Primary care / Community	• 10
		• Surgical specialties	• 11
		• Unknown	• 12
Speciality (Level 2)	Categorical	• Community nursing	• 1
		• Community teams	• 2
		• General practice - with specialism relevant to this patient (specify)	• 3
		• Health visiting / school nursing	• 4
		• Infectious diseases	• 5
		• Palliative medicine	• 6
		• Renal surgery	• 7
		• Residential care	• 8
		• Forensic mental health	• 9
		• General surgery	• 10
		• Inpatient assessment and treatment	• 11
		• Nephrology / renal	• 12
		• Obstetrics	• 13
		• Older adult mental health	• 14
		• Community medicine	• 15
		• Adult mental health	• 16
		• Care of older people	• 17
		• Cardiology	• 18
		• Intermediate care	• 19
		• General medicine	• 20
		• Pharmacy (inpatient)	• 21
		• Other	• 22
		• General practice - no specialism	• 23
Speciality (free text)	Free text		
Stage of medication process	Categorical	• Monitoring / follow-up of medicine use	• 1
		• Supply or use of over-the-counter (OTC) medicine	• 2
		• Advice	• 3
		• Preparation of medicines in all locations / dispensing in a pharmacy	• 4
		• Monitoring / follow-up of medicine use	• 5
		• Other	• 6
		• Administration / supply of a medicine from a clinical area	• 7
		• Prescribing	• 8
		• Missing data	• 999

Medication error category	Categorical	• Other	• 1
		• Wrong / omitted patient information leaflet	• 2
		• Wrong route	• 3
		• Wrong storage	• 4
		• Wrong / transposed / omitted medicine label	• 5
		• Wrong / omitted / passed expiry date	• 6
		• Patient allergic to treatment	• 7
		• Wrong method of preparation / supply	• 8
		• Adverse drug reaction (when used as intended)	• 9
		• Wrong / omitted verbal patient directions	• 10
		• Wrong formulation	• 11
		• Unknown	• 12
		• Mismatching between patient and medicine	• 13
		• Contra-indication to the use of the medicine in relation to drugs or conditions	• 14
		• Wrong frequency	• 15
		• Wrong quantity	• 16
		• Wrong drug / medicine	• 17
		• Omitted medicine / ingredient	• 18
		• Wrong / unclear dose or strength	• 19

9.14 Appendix 14– Medication categories and codes

BNF	1	2	3	4	5	6	Code
1	Anti-infective	Viral infection	Herpesvirus infections	Antivirals	Nucleoside analogues	Acyclovir	
1	Anti-infective	Viral infection	HIV infection	Antivirals	Nucleoside reverse transcriptase inhibitors	Tenofovir (viread)	
1	Anti-infective	Viral infection	HIV infection	Antivirals	Nucleoside reverse transcriptase inhibitors	Emtricitabine with tenofovir disoproxil (Truvada)	
1	Anti-infective	Viral infection	HIV infection	Antivirals	Nucleoside reverse transcriptase inhibitors	Efavirenz with emtricitabine and tenofovir disoproxil (Atripla)	
1	Anti-infective	Viral infection	Influenza	Antivirals	Neuraminidase inhibitors	Oseltamivir (Tamiflu)	
1	Anti-infective	Helminth infection	Anthelmintics			Mebendazole	
1	Anti-infective	Bacterial infection	Antibacterials, other			Nitrofurantoin	
1	Anti-infective	Bacterial infection	Antibacterials, other			Linzolide	
1	Anti-infective	Bacterial infection	Antibacterials, other			Trimethoprim	
1	Anti-infective	Bacterial infection	Antibacterials	Glycopeptide antibacterials		Vancomycin	
1	Anti-infective	Bacterial infection	Antibacterials	Glycopeptide antibacterials		Teicoplanin	
1	Anti-infective	Bacterial infection	Antibacterials	Cephalosporins	Cephalosporins, first-generation	Cefalexine	
1	Anti-infective	Bacterial infection	Antibacterials	Cephalosporins	Cephalosporins, third-generation	Rocephine (Ceftriaxone)	
1	Anti-infective	Bacterial infection	Antibacterials	Nitroimidazo		Metronidazole	
1	Anti-infective	Bacterial infection	Antibacterials	Sulphonamides		Sulfadiazine	
1	Anti-infective	Bacterial infection	Antibacterials	Tetracyclines and related drugs		Doxycycline	
1	Anti-infective	Bacterial infection	Antibacterials	Tetracyclines and related drugs		Minocycline	
1	Anti-infective	Bacterial infection	Antibacterials	Tetracyclines and related drugs		Demeclocycline	
1	Anti-infective	Bacterial infection	Antibacterials	Macrolides		Clarithromycin	
1	Anti-infective	Bacterial infection	Antibacterials	Macrolides		Azithromycin	
1	Anti-infective	Bacterial infection	Antibacterials	Macrolides		Erythromycin	
1	Anti-infective	Bacterial infection	Antibacterials	Quinolones		Ciprofloxacin	
1	Anti-infective	Bacterial infection	Antibacterials	Lincosamides		Clindamycin	
1	Anti-infective	Bacterial infection	Antibacterials	Penicilllins	Penicillins, penicillinase-resistant	Flucloxacillin	
1	Anti-infective	Bacterial infection	Antibacterials	Penicilllins	Penicillins, broad-spectrum	Amoxicillin	
1	Anti-infective	Bacterial infection	Antibacterials	Penicilllins	Penicillins, broad-spectrum with beta-lactamase inhibitor	Co-amoxiclav	

1	Anti-infective	Bacterial infection	Antibacterials	Penicilllins	Penicillins, beta-lactamase sensitive	Phenoxymethylpenicillin (Penicillin V)	
1	Anti-infective	Bacterial infection	Antibacterials	Penicilllins	Penicillins, beta-lactamase sensitive	Benzylpenicillin	
1	Anti-infective	Fungal infection	Anifungals	Triazole antifungals		Fluconazole	
1	Anti-infective	Fungal infection	Anifungals	Polyene antifungals		Nystatin	
2	Blood and blood forming organs	Anaemias	Megaloblastic anaemia	Vitamins and trace elements	Vitamin B group	**Cyanocobalamine (vitamin b12)**	
2	**Blood and blood-forming organs**	Neutropenia and stem cell mobilisation	Neutropenia	Immunostimulants	**Granulocyte-colony stimulating factors**	**Filgrastim**	
2	**Blood and blood-forming organs**	Neutropenia and stem cell mobilisation	Neutropenia	Immunostimulants	**Granulocyte-colony stimulating factors**	**Lenograstim**	
2	Blood and blood forming organs	Anaemias	Hypoplastic, haemolytic, and renal anaemias	Sickle-cell disease	Antineoplastic drugs	Hydroxycarbamide (Hydroxyurea)	
2	Blood and blood-forming organs	Anaemias	Hypoplastic, haemolytic, and renal anaemias	Epoetins		**Darbepoetin alfa (arenesp)**	
2	Blood and blood-forming organs	Anaemias	Hypoplastic, haemolytic, and renal anaemias	Epoetins		**Epoetin alfa**	
2	Blood and blood-forming organs	Anaemias	Hypoplastic, haemolytic, and renal anaemias	Epoetins		**Erythropoietin**	
2	Blood and blood forming agents	Anaemias	Iron deficiency anaemia	Minerals and trace elements	Iron, injectable	**Ferinject (ferric carboxymaltose)**	
2	Blood and blood forming agents	Anaemias	Iron deficiency anaemia	Minerals and trace elements	Iron, oral	Pregaday (Ferrous fumarate with folic acid)	
3	Cardiovascular system	Blood pressure conditions	Hypertension	Beta-adrenoceptor blockers	Beta blocking agents, non - selective	Propranolol	3001
3	Cardiovascular system	Blood pressure conditions	Hypertension	Beta-adrenoceptor blockers	Beta blocking agents, selective	Bisoprolol	3001
3	Cardiovascular system	Blood pressure conditions	Hypertension	Beta-adrenoceptor blockers	Beta blocking agents, selective	Metoprolol	3001
3	Cardiovascular system	Blood pressure conditions	Hypertension	Beta-adrenoceptor blockers	Beta blocking agents, selective	Atenolol	3001
3	Cardiovascular system	Blood pressure conditions	Hypertension	Beta-adrenoceptor blockers	Alpha- and beta-adrenoceptor blockers	Carvedilol	3001
3	Cardiovascular system	Blood pressure conditions	Hypertension	Calcium-channel blockers		Lercanidipine	3002
3	Cardiovascular system	Blood pressure conditions	Hypertension	Calcium-channel blockers		Diltiazem (adizem)	3002
3	Cardiovascular system	Blood pressure conditions	Hypertension	Calcium-channel blockers		Amlodipine (istin)	3002
3	Cardiovascular system	Blood pressure conditions	Hypertension	Calcium-channel blockers		Verapamil	3002
3	Cardiovascular system	Blood pressure conditions	Hypertension	Calcium-channel blockers		Felodipine	3002
3	Cardiovascular system	Blood pressure conditions	Hypertension	Calcium-channel blockers		Lacidipine	3002
3	Cardiovascular system	Blood pressure conditions	Hypertension	Calcium-channel blockers		Nifedipine	3002
3	Cardiovascular system			Calcium-channel blockers		Nimodipine	3002

3	Cardiovascular system	Blood pressure conditions	Hypertension	Drugs acting on the renin-angiotensin system	ACE inhibitors	Ramipril	3022
3	Cardiovascular system	Blood pressure conditions	Hypertension	Drugs acting on the renin-angiotensin system	ACE inhibitors	Enalapril	3022
3	Cardiovascular system	Blood pressure conditions	Hypertension	Drugs acting on the renin-angiotensin system	ACE inhibitors	Lisinopril	3022
3	Cardiovascular system	Blood pressure conditions	Hypertension	Drugs acting on the renin-angiotensin system	ACE inhibitors	Perindopril	3022
3	Cardiovascular system	Blood pressure conditions	Hypertension	Drugs acting on the renin-angiotensin system	ACE inhibitors	Indapamide (tanatril)	3022
3	Cardiovascular system	Blood pressure conditions	Hypertension	Drugs acting on the renin-angiotensin system	Angiotensin II receptor antagonists	Candesartan	3003
3	Cardiovascular system	Blood pressure conditions	Hypertension	Drugs acting on the renin-angiotensin system	Angiotensin II receptor antagonists	Valsartan	3003
3	Cardiovascular system	Blood pressure conditions	Hypertension	Drugs acting on the renin-angiotensin system	Angiotensin II receptor antagonists	Irbesartan	3003
3	Cardiovascular system	Blood pressure conditions	Hypertension	Drugs acting on the renin-angiotensin system	Angiotensin II receptor antagonists	Losartan	3003
3	Cardiovascular system	Blood pressure conditions	Hypertension	Alpha-adrenoceptor blockers		Doxazosin	3023
3	Cardiovascular system	Blood pressure conditions	Hypertension	Diuretics	Thiazides and related diuretics	Bendroflumethiazide	3004
3	Cardiovascular system	Blood pressure conditions	Hypertension	Diuretics	Thiazides and related diuretics	Metolazone	3004
3	Cardiovascular system	Blood pressure conditions	Hypertension	Diuretics	Postassium-sparing diuretics, other	Eplenernone	3004
3	Cardiovascular system	Blood pressure conditions	Hypertension	Diuretics	Postassium-sparing diuretics	Spironolactone	3004
3	Cardiovascular system	Blood pressure conditions	Hypertension	Diuretics	Postassium-sparing diuretics	Amiloride	3004
3	Cardiovascular system	Blood pressure conditions	Hypertension	Diuretics	Postassium-sparing diuretics	Co-amilofruse	3004
3	Cardiovascular system	Blood pressure conditions	Hypertension	Diuretics	Loop diuretics	Furosemide	3004
3	Cardiovascular system	Blood pressure conditions	Hypertension	Diuretics	Loop diuretics	Bumetanide	3004
3	Cardiovascular system	Blood pressure conditions	Hypotension and shock	Sympathomimetics	Sympathomimetics, vasoconstrictor	Midodrine	3005
3	Cardiovascular system	Hyperlipidaemia	Lipid modifying drugs	Statins		Atorvastatin	3006
3	Cardiovascular system	Hyperlipidaemia	Lipid modifying drugs	Statins		Simvastatin	3006
3	Cardiovascular system	Hyperlipidaemia	Lipid modifying drugs	Statins		Pravastatin	3006
3	Cardiovascular system	Bleeding disorders	Antihaemorrhagics	Antifibrinolytics		Tranexamic acid	3007
3	Cardiovascular system	Blood clots	Thromboembolism	Antithrombotic drugs	Factor Xa inhibitors	Apixiaban	3008
3	Cardiovascular system	Blood clots	Thromboembolism	Antithrombotic drugs	Factor Xa inhibitors	Rivaroxaban (xarelto)	3008
3	Cardiovascular system	Blood clots	Thromboembolism	Antithrombotic drugs	Factor Xa inhibitors	Edoxaban	3008
3	Cardiovascular system	Blood clots	Thromboembolism	Antithrombotic drugs	Factor Xa inhibitors	Fondaparinux	3008

3	Cardiovascular system	Blood clots	Thromboembolism	Antithrombotic drugs	Antiplatelet drugs	Aspirin / clopidogrel /prasugrel /Dipyridamole	3009
3	Cardiovascular system	Myocardial ischaemia	Acute coronary syndromes	Antithrombotic drugs	Antiplatelet drugs	Ticagrelor (brilique)	3009
3	Cardiovascular system	Blood clots	Thromboembolism	Antithrombotic drugs	Vitamin K antagonists	Warfarin	3010
3	Cardiovascular system	Blood clots	Thromboembolism	Antithrombotic drugs	Heparins	Enoxaparin	3011
3	Cardiovascular system	Blood clots	Thromboembolism	Antithrombotic drugs	Heparins	Daltaparin (fragmin)	3011
3	Cardiovascular system	Blood clots	Thromboembolism	Antithrombotic drugs	Heparins	Tinzaparin (inohep)	3011
3	Cardiovascular system	Blood clots	Thromboembolism	Antithrombotic drugs	Heparins	Heparin	3011
3	Cardiovascular system	Blood clots	Thromboembolism	Antithrombotic drugs	Thrombin inhibitors, direct	Dabigatran	3012
3	Cardiovascular system	Arrhythmias	Cardiac glycosides			Digoxin	3013
3	Cardiovascular system	Arrhythmias	Beta-adrenoceptor blockers	Beta blocking agents, non-selective		Sotalol	3001
3	Cardiovascular system	Arrhythmias	Antiarrhythmics	Antiarrhythmics, class la		Disopyramide	3014
3	Cardiovascular system	Arrhythmias	Antiarrhythmics	Antiarrhythmics, class lc		Flecainide	3014
3	Cardiovascular system	Arrhythmias	Antiarrhythmics	Antiarrhythmics, class III		Dronedarone	3014
3	Cardiovascular system	Arrhythmias	Antiarrhythmics	Antiarrhythmics, class III		Amiodarone	3014
3	Cardiovascular system	Myocardial ischaemia	Acute coronary syndromes	Nitrates		Isosorbide dinitrate	3015
3	Cardiovascular system	Myocardial ischaemia	Acute coronary syndromes	Nitrates		Isosorbide mononitrate	3015
3	Cardiovascular system	Myocardial ischaemia	Acute coronary syndromes	Nitrates		Isosorbide trinitrate	3015
3	Cardiovascular system	Myocardial ischaemia	Vasodilators	Potassium-channel openers		Nicorandil	3016
3	Cardiovascular system	Myocardial ischaemia	Piperazine derivatives			Ranolazine	3017
3	Cardiovascular system	Heart failure	Selective sinus node if inhibitors			Ivabradine	3018
3	Cardiovascular system	Blood pressure conditions	Hypertension	Pulmonary hypertension	Endothelin receptor antagonists	Ambrisentan	3019
5	Endocrine system	Antidiuretic hormone disorders	Diabetes insipidus	Pituitary and hypothalamic hormones and analogues	Vasopressin and analogues	Vasopressin	15001
5	Endocrine system	Antidiuretic hormone disorders	Syndrome of inappropriate antidiuretic hormone secretion	Diuretics	Selective vasopressin V2-receptor antagonists	Tolvaptan	15001
5	Endocrine system	Diabetes mellitus and hypoglycaemia	Diabetes mellitus	Insulin		Insulin (rapid, intermediate, long) acting [Tresiba, Humulin, novorapid, abasaglarins, novomix, kwikpen, Humalog, Levemir, flex pen,	5002
5	Endocrine system	Diabetes mellitus and hypoglycaemia	Diabetes mellitus	Blood glucose lowering drugs	Sodium glucose co-transporter 2 inhibitors	Dapagliflozin (forxiga)	5003

5	Endocrine system	Diabetes mellitus and hypoglycaemia	Diabetes mellitus	Blood glucose lowering drugs	Alpha glucosidase inhibitors	Acarbose	5003
5	Endocrine system	Diabetes mellitus and hypoglycaemia	Diabetes mellitus	Blood glucose lowering drugs	Dipeptidylpeptidase -4 inhibitors (gliptins)	Sitagliptin, Saxagliptin	5003
5	Endocrine system	Diabetes mellitus and hypoglycaemia	Diabetes mellitus	Blood glucose lowering drugs	Glucagon-like peptide-1 receptor agonists	Lixisenatide	5003
5	Endocrine system	Diabetes mellitus and hypoglycaemia	Diabetes mellitus	Blood glucose lowering drugs	Glucagon-like peptide-1 receptor agonists	Linagliptin	5003
5	Endocrine system	Diabetes mellitus and hypoglycaemia	Diabetes mellitus	Blood glucose lowering drugs	Meglitinides	Repaglinide	5003
5	Endocrine system	Diabetes mellitus and hypoglycaemia	Diabetes mellitus	Blood glucose lowering drugs	Biguanides	Metformin (Glucophage)	5003
5	Endocrine system	Diabetes mellitus and hyperglycaemia	Diabetes mellitus		Sulfonylureas	Gliclazide	5003
5	Endocrine system	Diabetes mellitus and hyperglycaemia	Diabetes mellitus		Sulfonylureas	Glipizide	5003
5	Endocrine system	Diabetes mellitus and hyperglycaemia	Diabetes mellitus		Sulfonylureas	Tolbutamide	5003
5	Endocrine system	Disorders of bone metabolism	Bisphosphonates			Alendronic acid (fosamax)	5004
5	Endocrine system	Disorders of bone metabolism	Bisphosphonates			Risedronate	5004
5	Endocrine system	Sex hormone responsive conditions	Female sex hormone responsive conditions	Oestrogens combined with progestogens		Estradiol with norethisterone (evorel)	5005
5	Endocrine system	Sex hormone responsive conditions	Female sex hormone responsive conditions	Oestrogens		Estradiol (oestrogel)	5005
5	Endocrine system	Sex hormone responsive conditions	Female sex hormone responsive conditions	Progestogens		Medroxyprogesterone acetate (provera)	5005
5	Endocrine system	Sex hormone responsive conditions	Female sex hormone responsive conditions	Anti-oestrogens	Ovulation stimulants	Clomifene	5005
5	Endocrine system	Thyroid disorders	Hyperthyroidism	Antithyroid drugs	Sulfur-containing imidazoles	Carbimazole (Tegretol)	5006
5	Endocrine system	Thyroid disorders	Hypothyroidism	Thyroid hormones		Levothyroxine	5006
5	Endocrine system	Corticosteroid responsive conditions	Corticosteroids			Prednisolone	5007
5	Endocrine system	Corticosteroid responsive conditions	Corticosteroids			Dexamethasone	5007
5	Endocrine system	Corticosteroid responsive conditions	Corticosteroids			Hydrocortisone	5007
5	Endocrine system	Corticosteroid responsive conditions	Corticosteroids			Fludrocortisone	5007
5	Endocrine system	Gonadotrophin responsive conditions	Pituitary and hypothalamic hormones and analogues	Gonadotrophin-releasing hormones		Leuprorelin (prostap)	5008

6	Eye	Glaucoma and ocular hypertension	Sympathomimetics	Alpha2-adrenoceptor agonists		Brimonidine	
6	Eye	Glaucoma and ocular hypertension	Carbonic anhydrase inhibitors			Brinzolamide	
6	Eye	Glaucoma and ocular hypertension	Carbonic anhydrase inhibitors			Acetazolamide	
6	Eye	Glaucoma and ocular hypertension	Prostaglandin analogues and prostamides			Latanoprost	
6	Eye	Glaucoma and ocular hypertension	Prostaglandin analogues and prostamides			Travoprost	
6	Eye	Glaucoma and ocular hypertension	Prostaglandin analogues and prostamides			Bimatoprost	
6	Eye	Glaucoma and ocular hypertension	Prostaglandin analogues and prostamides			Travoprost with timolol	
6	Eye	Eye infection	Bacterial eye infection	Antibacterials	Antibacterials, other	Chloramphenicol	
6	Eye	Allergic and inflammatory eye conditions	Inflammatory eye conditions	Corticosteroids	Corticosteroids combinations with anti-infectives	Dexamethasone with hypromellose, neomycin and polymyxin B sulfate (maxitrol)	
6	Eye	Allergic and inflammatory eye conditions	Inflammatory eye conditions	Corticosteroids	Corticosteroids	Prednisolone eye drops	
6	Eye	Allergic and inflammatory eye conditions	Inflammatory eye conditions	Corticosteroids	Corticosteroids	Dexamethasone (Maxidex)	
7	Gastro-intestinal system	Liver disorders and related conditions	Biliary disorders	Bile acids		Ursodeoxycholic acid	
7	Gastro-intestinal system					Triple therapy /PPI	
7	Gastro-intestinal system	Reduced exocrine secretions	Pancreatic enzymes			Pancreatin (creon)	
7	Gastro-intestinal system	Chronic bowel disorders	Inflammatory bowel disease			Sulfasalazine	
7	Gastro-intestinal system	Gastro-intestinal smooth muscle spasm	Antispasmodics			Mebeverine	
7	Gastro-intestinal	Constipation	Laxatives	Stimulant laxatives		Bisacodyl	
7	Gastro-intestinal	Constipation	Laxatives	Stimulant laxatives		Senna	
7	Gastro-intestinal	Constipation	Laxatives	Stimulant laxatives		Glycerol (glycerine suppository)	
7	Gastro-intestinal	Constipation	Laxatives	Osmotic laxatives		Lactulose	
7	Gastro-intestinal	Diarrhoea	Antidiarrhoeals	Antipropulsives		Loperamide	
7	Gastro-intestinal	Disorders of gastric acid and ulceration	Gastric and duodenal ulceration	Gastroprotective complexes and chelators		Sucralfate	

7	Gastro-intestinal	Disorders of gastric acid and ulceration	Gastric and duodenal ulceration	H2-receptor antagonists		Ranitidine	
7	Gastro-intestinal	Disorders of gastric acid and ulceration	Gastric and duodenal ulceration	Proton pump inhibitors		Omeprazole	
7	Gastro-intestinal	Disorders of gastric acid and ulceration	Gastric and duodenal ulceration	Proton pump inhibitors		Esomeprazole	
7	Gastro-intestinal	Disorders of gastric acid and ulceration	Gastric and duodenal ulceration	Proton pump inhibitors		Pantoprazole	
7	Gastro-intestinal	Disorders of gastric acid and ulceration	Gastric and duodenal ulceration	Proton pump inhibitors		Lansoprazole	
7	Gastro-intestinal	Disorders of gastric acid and ulceration	Gastric and duodenal ulceration	Proton pump inhibitors		Rabeprazole	
7	Gastro-intestinal	Gastro-intestinal smooth muscle spasm	Antispasmodics			Peppermint oil	
7	Gastro-intestinal	Gastro-intestinal smooth muscle spasm	Antimuscarinics			Hyoscine	
7	Gastro-intestinal	Gastro-intestinal smooth muscle spasm	Antimuscarinics			Propantheline	
8	Genito-urinary system	Bladder and urinary disorders	Urinary retention	Alpha-adrenoceptor blockers		**Tamsulosin**	
8	Genito-urinary system	Bladder and urinary disorders	Urinary retention	Alpha-adrenoceptor blockers		**Tamsulosin with dutasteride**	
8	Genito-urinary system	Bladder and urinary disorders	Urinary frequency, enuresis, and incontinence	Antimuscarinics	Antimuscarinics, urinary	**Oxybutynin 15**	
8	Genito-urinary system	Bladder and urinary disorders	Urinary frequency, enuresis, and incontinence	Antimuscarinics	Antimuscarinics, urinary	**Tolterodine (neditol)**	
8	Genito-urinary system	Bladder and urinary disorders	Urinary frequency, enuresis, and incontinence	Antimuscarinics	Antimuscarinics, urinary	**Solifenacin**	
8	Genito-urinary system	Bladder and urinary disorders	Urinary frequency, enuresis, and incontinence	Beta3-adrenoceptor agonists		Mirabegron	
8	Genito-urinary system	Vaginal and vulval conditions	Vaginal atrophy	Oestrogens		Estriol	
8	Genito-urinary system	Erectile and ejaculatory conditions	Erectile dysfunction	Phosphodiesterase type-5 inhibitors		Sildenafil	
9	Immune system	Immune system disorders and transplantation	Immunosuppressants	Purine synthesis inhibitors		Mycophenolate (myfortic)	
9	Immune system	Immune system disorders and transplantation	Immunosuppressants	Calcineurin inhibitors and related drugs		Ciclosporin	
10	Malignant disease					Etanercept	
10	Malignant disease					Methotrexate	

10	Malignant disease					Anticipatory meds	
10	Malignant disease	Hormone responsive malignancy	Hormone responsive breast cancer	Hormone antagonists and related agents	Aromatase inhibitors	Exemestane	
10	Malignant disease	Hormone responsive malignancy	Antineoplastic drugs	Anti-androgens		Enzalutamide	
10	Malignant disease	Hormone responsive malignancy	Pituitary and hypothalamic hormones and analogues	Somatostatin analogues		Lanreotide	
10	Malignant disease	Hormone responsive malignancy	Pituitary and hypothalamic hormones and analogues	Somatostatin analogues		Octreotide	
10	Malignant disease	Hormone responsive malignancy	Hormone responsive breast cancer	Antineoplastic drugs	Anti-oestrogens	Tamoxifen	
10	Malignant disease	Hormone responsive malignancy	Hormone responsive breast cancer	Hormone antagonists and related agents	Aromatase inhibitors	Letrozole (femera)	
12	Musculoskeletal system	Arthritis	Disease-modifying anti-rheumatic drugs			Penicillamine	
12	Musculoskeletal system	Arthritis	Disease-modifying anti-rheumatic drugs			Hydroxychloroquine	
12	Musculoskeletal system	Arthritis	Antineoplastic drugs	Monoclonal antibodies		densosumab	
12	Musculoskeletal system	Neuromuscular disorders	Myasthenia gravis and Lambert-Eaton myasthenic syndrome	Anticholinesterases	Anticholinesterases, other	Pyridostigmine bromide	
12	Musculoskeletal system	Neuromuscular disorders	Spasticity	Muscle relaxants	Muscle relaxants, centrally acting	Baclofen	
12	Musculoskeletal system	Neuromuscular disorders	Spasticity	Muscle relaxants	Muscle relaxants, centrally acting	Methocarbamol	
12	Musculoskeletal system	Neuromuscular disorders	Myotonic disorders	Myotonic disorders	Drugs for neuromuscular disorders	Mexiletine	
13	Nervous system	Mental health disorders	Bipolar disorder and mania	Antipsychotics	Lithium salt	Lithium	13001
13	Nervous system	Mental health disorders	Psychoses and schizophrenia	Antipsychotics	Antipsychotics, first generation	Levomepromazine	13001
13	Nervous system	Mental health disorders	Psychoses and schizophrenia	Antipsychotics	Antipsychotics, first generation	Prochlorperazine	13001
13	Nervous system	Mental health disorders	Psychoses and schizophrenia	Antipsychotics	Antipsychotics, first generation	Flupenthixol decanoate	13001
13	Nervous system	Mental health disorders	Psychoses and schizophrenia	Antipsychotics	Antipsychotics, first generation	Haloperidol	13001
13	Nervous system	Mental health disorders	Psychoses and schizophrenia	Antipsychotics	Antipsychotics, second generation	Quetiapine (Seroquel)	13001
13	Nervous system	Mental health disorders	Psychoses and schizophrenia	Antipsychotics	Antipsychotics, second generation	Clozapine	13001
13	Nervous system	Mental health disorders	Psychoses and schizophrenia	Antipsychotics	Antipsychotics, second generation	Aripiprazole	13001
13	Nervous system	Mental health disorders	Psychoses and schizophrenia	Antipsychotics	Antipsychotics, second generation	Risperidone	13001
13	Nervous system	Mental health disorders	Psychoses and schizophrenia	Antipsychotics	Antipsychotics, second generation	Paliperidone	13001
13	Nervous system	Mental health disorders	Psychoses and schizophrenia	Antipsychotics	Antipsychotics, second generation (depot injections)	Olanzapine (Zyprexa)	13001

13	Nervous system	Mental health disorders	Attention deficit hyperactivity disorder	CNS stimulants	Centrally acting sympathomimetics	Methylphenidate	13002
13	Nervous system	Mental health disorders	Depression	Antidepressants	Serotonin uptake inhibitors	Trazodone	13003
13	Nervous system	Mental health disorders	Depression	Antidepressants	Serotonin and noradrenaline re-uptake inhibitors	Duloxetine	13003
13	Nervous system	Mental health disorders	Depression	Antidepressants	Serotonin and noradrenaline re-uptake inhibitors	Venlafaxine	13003
13	Nervous system	Mental health disorders	Depression	Antidepressants	Tricyclic antidepressants	Clomipramine	13003
13	Nervous system	Mental health disorders	Depression	Antidepressants	Tricyclic antidepressants	Amitriptyline	13003
13	Nervous system	Mental health disorders	Depression	Antidepressants	Tricyclic antidepressants	Dosulepin	13003
13	Nervous system	Mental health disorders	Depression	Antidepressants	Selective serotonin re-uptake inhibitors	Citalopram	13003
13	Nervous system	Mental health disorders	Depression	Antidepressants	Selective serotonin re-uptake inhibitors	Escitalopram	13003
13	Nervous system	Mental health disorders	Depression	Antidepressants	Selective serotonin re-uptake inhibitors	Paroxetine	13003
13	Nervous system	Mental health disorders	Depression	Antidepressants	Selective serotonin re-uptake inhibitors	Sertaline	13003
13	Nervous system	Mental health disorders	Depression	Antidepressants	Selective serotonin re-uptake inhibitors	Fluoxetine	13003
13	Nervous system	Mental health disorders	Depression	Antidepressants	Tetracycline antidepressants	Mirtazapine	13003
13	Nervous system	Mental health disorders	Anxiety	Hypnotics, sedatives, and anxiolytics	Benzodiazepines	Diazepam	13004
13	Nervous system	Mental health disorders	Anxiety	Hypnotics, sedatives, and anxiolytics	Benzodiazepines	Lorazepam (Ativan)	13004
13	Nervous system	Mental health disorders	Anxiety	Hypnotics, sedatives, and anxiolytics	Benzodiazepines	Temazepam	13004
13	Nervous system	Mental health disorders	Anxiety	Hypnotics, sedatives, and anxiolytics	Benzodiazepines	Chlordiazepoxide	13004
13	Nervous system	Sleep disorders	Insomnia	Hypnotics, sedatives and anxiolytics	Non-benzodiazepine hypnotics and sedatives	Zopiclone	13004
13	Nervous system	Sleep disorders	Insomnia	Hypnotics, sedatives and anxiolytics	Non-benzodiazepine hypnotics and sedatives	Melatonin	13004
13	Nervous system	Dementia	Anticholinesterase	Anticholinesterase, centrally acting		Donepezil	13005
13	Nervous system	Dementia	Anticholinesterase	Anticholinesterase, centrally acting		Rivastigmine	13005
13	Nervous system	Dementia	Dopaminergic drugs	NMDA receptor antagonists		Memantine	13006
13	Nervous system	Epilepsy and other seizure disorders	Hypnotics, sedatives, and anxiolytics	Benzodiazepines		Clobazam	13004
13	Nervous system	Epilepsy and other seizure disorders	Hypnotics, sedatives, and anxiolytics	Benzodiazepines		Clonazepam	13004
13	Nervous system	Epilepsy and other seizure disorders	Status epilepticus	Hypnotics, sedative and anxiolytics	Benzodiazepines	Midazolam	13004

13	Nervous system	Epilepsy and other seizure disorders	Antiepileptics	Barbiturates		Phenobarbital	13007
13	Nervous system	Epilepsy and other seizure disorders	Antiepileptics			Pregabalin	13007
13	Nervous system	Epilepsy and other seizure disorders	Antiepileptics			Ethosuximide	13007
13	Nervous system	Epilepsy and other seizure disorders	Antiepileptics			Gabapentine	13007
13	Nervous system	Epilepsy and other seizure disorders	Antiepileptics			Carbamazepine	13007
13	Nervous system	Epilepsy and other seizure disorders	Antiepileptics			Topiramate	13007
13	Nervous system	Epilepsy and other seizure disorders	Antiepileptics			Sodium valproate (Epilim)	13007
13	Nervous system	Epilepsy and other seizure disorders	Antiepileptics			Levetiracetam (Keppra)	13007
13	Nervous system	Epilepsy and other seizure disorders	Antiepileptics			Phenytoin	13007
13	Nervous system	Epilepsy and other seizure disorders	Antiepileptics			Lamotrigine	13007
13	Nervous system	Epilepsy and other seizure disorders	Antiepileptics			Valproic acid - valproate semisodium (depakote)	13007
13	Nervous system	Movement disorders	Parkinson's disease	Dopaminergic drugs	Dopamine precursors	Stalevo (Carbidopa, Entacapone, Levodopa)	13008
13	Nervous system	Movement disorders	Parkinson's disease	Dopaminergic drugs	Dopamine receptor agonists	Ropinirole	13008
13	Nervous system	Movement disorders	Parkinson's disease	Dopaminergic drugs	Dopamine receptor agonists	Cabergoline	13008
13	Nervous system	Movement disorders	Parkinson's disease	Dopaminergic drugs	Dopamine receptor agonists	Rotigotine	13008
13	Nervous system	Movement disorders	Parkinson's disease	Dopaminergic drugs	Dopamine receptor agonists	Apomrphine	13008
13	Nervous system	Movement disorders	Parkinson's disease	Dopaminergic drugs	Dopamine precursors	Benserazide (Co-beneldopa, madopar)	13008
13	Nervous system	Movement disorders	Parkinson's disease	Dopaminergic drugs	Dopamine precursors	Co-beneldopa	13008
13	Nervous system	Movement disorders	Parkinson's disease	Dopaminergic drugs	Dopamine precursors	Co-careldopa (Duodopa, Sinemet)	13008
13	Nervous system	Movement disorders	Parkinson's disease	Antimuscarinics		Procyclidine	13014
13	Nervous system	Nausea and labyrinth disorders	Antiemetics and antinauseants	Dopamine receptor antagonists		Metoclopramide	13009
13	Nervous system	Nausea and labyrinth disorders	Antihistamines	Sedating antihistamines		Cinnarizine	13010
13	Nervous system	Nausea and labyrinth disorders	Antihistamines			**Cyclizine**	13010

13	Nervous system	Pain	Analgesics	Analgesics, non-opioid		Paracetamol (calpol)	13011
13	Nervous system	Pain	Analgesics	Non-steroidal anti-inflammatory drugs		Mefenamic acid	13011
13	Nervous system	Pain	Analgesics	Non-steroidal anti-inflammatory drugs		Ibuprofen	13011
13	Nervous system	Pain	Analgesics	Opioids		MST (morphine slow release)	13012
13	Nervous system	Pain	Analgesics	Opioids		Morphine (Zomorph) (oramorph)	13012
13	Nervous system	Pain	Analgesics	Opioids		Tramadol	13012
13	Nervous system	Pain	Analgesics	Opioids		Alfentanil	13012
13	Nervous system	Pain	Analgesics	Opioids		Dihydrocodeine (co-dydramol)	13012
13	Nervous system	Pain	Analgesics	Opioids		Buprenorphine (BuTrans transtec, butec)	13012
13	Nervous system	Pain	Analgesics	Opioids		Methadone	13012
13	Nervous system	Pain	Analgesics	Opioids		Oxycodone (shortec, longtec)	13012
13	Nervous system	Pain	Analgesics	Opioids		Fentanyl (Matrifen)	13012
13	Nervous system	Pain	Analgesics	Opioids		**Codeine**	13012
13	Nervous system	Local anaesthesia				**Lidocaine**	**13013**
14	Nose	Nasal congestion	Sympathomimetics	Sympathomimetics, vasoconstrictor		Xylometazoline	
15	Nutrition and metabolic disorders	Fluid and electrolyte imbalances	Calcium imbalance	Hypercalcemia and hypercalciuria	Calcium regulating drugs	**Ciacalcet**	
15	Nutrition and metabolic disorders	Fluid and electrolyte imbalances	Bicarbonate			**Sodium bicarbonate**	
15	Nutrition and metabolic disorders	Fluid and electrolyte imbalances				**Phosphate**	
15	Nutrition and metabolic disorders	Fluid and electrolyte imbalances				**Magnesium**	
15	Nutrition and metabolic disorders	Fluid and electrolyte imbalances				**Calcichew**	
15	Nutrition and metabolic disorders	Fluid and electrolyte imbalances				**Adcal**	
15	Nutrition and metabolic disorders	Fluid and electrolyte imbalances				**Sando-K (Pottasium)**	
15	Nutrition and metabolic disorders					Dalivit	
15	Nutrition and metabolic disorders					Fortisip	
15	Nutrition and metabolic disorders					Renavit	

15	Nutrition and metabolic disorders					Sanatogen A-Z complete	
15	Nutrition and metabolic disorders	Vitamin deficiency	Vitamins and trace elements	Vitamin D and analogues		Alfacalcidol	
15	Nutrition and metabolic disorders	Mineral and trace elements deficiencies	Zinc deficiency	Electrolytes and minerals	Zinc	Zinc sulfate	
15	Nutrition and metabolic disorders	Vitamin deficiency	Neural tube defects (prevention in pregnancy)	Vitamins and trace elements	Folates	Folic acid	
15	Nutrition and metabolic disorders	Vitamin deficiency	Vitamins and trace elements	Vitamin B group		Thiamine	
15	Nutrition and metabolic disorders	Vitamin deficiency	Vitamins and trace elements	Vitamin B group		Vitamin B complex	
15	Nutrition and metabolic disorders	Vitamin deficiency	Electrolytes and minerals			Calcium	
15	Nutrition and metabolic disorders	Vitamin deficiency	Electrolytes and minerals			Colecalciferol with calcium carbonate (Calceos)	
15	Nutrition and metabolic disorders	Vitamin deficiency	Vitamins and trace elements			Vitamin E (Alpha tocopherol)	
15	Nutrition and metabolic disorders	Vitamin deficiency	Vitamins			Menadiol (Vitamin K)	
15	Nutrition and metabolic disorders	Vitamin deficiency	Vitamins and trace elements	Vitamin D and analogues		Cholecalciferol (Fultium)	
17	Poisoning	Drug toxicity	Paracetamol toxicity	Antidotes and chelators	Antidotes and chelators, other	Acetylcysteine	
18	Respiratory system	Conditions affecting sputum viscosity	Mucolytics			Carbocisteine	
18	Respiratory system	Allergic conditions	Antihistamines	Sedating antihistamines		Hydroxyzine	
18	Respiratory system	Allergic conditions	Antihistamines	Sedating antihistamines		Promethiazine	
18	Respiratory system	Allergic conditions	Antihistamines	Non-Sedating antihistamines		Cetirizine	
18	Respiratory system	Allergic conditions	Antihistamines	Non-Sedating antihistamines		Fexofenadine	
18	Respiratory system	Airway diseases, obstructive	**Xanthines**			Aminophylline	
18	Respiratory system	Airway diseases, obstructive	**Xanthines**			Theophyllin (uniphyllin)	
18	Respiratory system	Airway diseases, obstructive	**Antimuscarinics**			Tiotropium (Spiriva)	
18	Respiratory system	Airway diseases, obstructive	**Antimuscarinics / Selective beta2-agonists (long-acting)**			Tiotropium with olodaterol	
18	Respiratory system	Airway diseases, obstructive	**Antimuscarinics / Selective beta2-agonists (long-acting)**			Umeclidinium with vilanterol (anoro ellipta)	

18	Respiratory system	Airway diseases, obstructive	**Antimuscarinics**			Aclidinium bromide (Eklira)	
18	Respiratory system	Airway diseases, obstructive	**Antimuscarinics**			Aclidinium bromide with formoterol (duaklir)	
18	Respiratory system	Airway diseases, obstructive	**Antimuscarinics**			Glycopyrronium bromide (seebri breezhaler)	
18	Respiratory system	Airway diseases, obstructive	**Antimuscarinics**			Glycopyrronium with indacaterol (ultibro)	
18	Respiratory system	Airway diseases, obstructive	**Beta2-adrenoceptor agonists, selective**	Selective beta2-agonists (short acting)		Terbutaline	
18	Respiratory system	Airway diseases, obstructive	**Beta2-adrenoceptor agonists, selective**	Selective beta2-agonists (short acting)		Salbutamol	
18	Respiratory system	Airway diseases, obstructive	**Beta2-adrenoceptor agonists, selective**	Selective beta2-agonists (long acting)		Fluticasone with salmeterol (seretide)	
18	Respiratory system	Airway diseases, obstructive	**Beta2-adrenoceptor agonists, selective**	Selective beta2-agonists (long acting)		salmeterol	
18	Respiratory system	Airway diseases, obstructive	**Leukotriene receptor antagonists**			Montelukast	
18	Respiratory system	Airway diseases, obstructive	**Corticosteroids**			Budesonide	
18	Respiratory system	Airway diseases, obstructive	**Corticosteroids**			Beclomethasone	
18	Respiratory system	Airway diseases, obstructive	**Corticosteroids**			Beclomethasone with formoterol (fostair)	
18	Respiratory system	Airway diseases, obstructive	**Corticosteroids**			Beclomethasone, formoterol, glycopyrronium (Trimbow)	
19	Skin					Aqueous cream	
20	Vaccines	Vaccination				Pneumococcal vaccine **(pneumovax)**	
20	Vaccines	Vaccination				Bacillus Calmette-Guérin vaccine (BCG Vaccine)	
20	Vaccines	Vaccination				Meningococcal group B vaccine	
20	Vaccines	Vaccination				Influenza vaccine	

9.15 **Appendix 15 - Compound incidents**

Examples:

Case 1: *''Patient was discharged from hospital on the 20 / XX / XX for the administration of lemograstine 263mcg daily for five days, starting that day. the hospital provided the patient with 7 injections and told the patient that all injections need to be given. the night DN [district nurse] gave the 1st three injections. the day DN took over on 23 / XX / XX . on the fifth day my the nurse who attended the patient told the patient and family that the injection given was the last dose. the husband refuse and say no the hospital told them it's for 7 days. the nurse spoke to the daughter who explained that she do not need the injection. the following day the daughter called and I explained to her only five is needed to be given. the nurse who went on the sixth day was not in on wed but patient was mistakenly allocated to the patient. the nurse read the authorisation wrongly and gave the injection… root cause was patient allocated when visit not required however nurse did not check authorisation which clearly states 5 days . .''*

Incident: Underlined text

Contributory factor:

- mistake in nurse allocation
- nurse misread the authorisation

Outcome: patient inconvenience - unnecessary treatment

Origin of incident report: secondary care [if the incorrect quantity was not given, the incident could not have happened]

9.16 Appendix 16– Patient age in incidents occurred at different medication process

Medication error category	Age groups				Total
	<18 years	18 - 65 years	>65 years	Missing data	
Wrong / unclear dose or strength	13 (29%)	49 (22%)	108 (17%)	42 (18%)	212
Omitted medicine / ingredient	3 (7%)	28 (13%)	93 (15%)	24 (10%)	148
Wrong drug / medicine	3 (7%)	28 (13%)	67 (11%)	20 (8%)	118
Wrong quantity	7 (16%)	12 (5%)	32 (5%)	17 (7%)	68
Wrong frequency	1 (2%)	12 (5%)	35 (6%)	12 (5%)	60
Contra-indication to the use of the medicine in relation to drugs or conditions	1	12	35	10	58
Mismatching between patient and medicine	1	10	24	10	45
Wrong formulation	2	6	10	3	21
Wrong / omitted verbal patient directions	0	4	8	6	18
Wrong method of preparation / supply	1	1	11	3	16
Adverse drug reaction (when used as intended)	0	1	7	2	10
Wrong / omitted / passed expiry date	1	2	4	1	8
Patient allergic to treatment	0	1	4	1	6
Wrong/ transposed/ omitted medicine label	1	0	4	0	5
Wrong storage	0	1	1	0	2
Wrong route	0	2	0	0	2
Wrong / omitted patient information leaflet	0	0	0	1	1
Unknown	1	2	12	5	20
Other	9	47	171	76	303
Total	44 (100%)	218 (100%)	626 (100%)	233 (100%)	1,121

9.17 Appendix 17– Overview of incidents submitted over time.

Month	Year					Total	%
	2015	2016	2017	2018	2019		
1	11	16	34	20	20	101	9
2	30	13	20	24	15	102	9
3	7	27	23	18	13	88	8
4	13	23	27	17	9	89	8
5	12	29	24	20	24	109	10
6	12	25	27	19	18	101	9
7	16	22	29	29	16	112	10
8	17	12	14	12	16	71	6
9	19	25	19	17	9	89	8
10	20	24	24	20	16	104	9
11	15	24	27	21	8	95	8
12	10	18	18	8	6	60	5
Total	182	258	286	225	170	1,121	100
%	16	23	25	20	15	100	

9.18 Appendix 18 - Medication class from the three most common chapters associated with incidents

BNF Chapter	Medication class	Total
Cardiology (n=734)	Antithrombotic drugs, antiplatelet drugs	126
	Antithrombotic drugs, factor Xa inhibitors	124
	Beta-adrenoceptor blockers	76
	Antithrombotic drugs, heparins	71
	Antithrombotic drugs, vitamin K antagonists	67
	Diuretics	66
	Calcium-channel blockers	51
	ACE inhibitors	40
	Statins	32
	Cardiac glycosides	20
	Nitrates	15
	Angiotensin II receptor antagonists	13
	Antiarrhythmics	11
	Antithrombotic drugs, thrombin inhibitors, direct	5
	Vasodilators, potassium-channel openers	5
	Antihaemorrhagics, antifibrinolytics	4
	Heart failure, selective sinus node inhibitors	2
	Alpha-adrenoceptor blockers	2
	Hypertension medication	1
	Myocardial ischaemia, piperazine derivatives	1
	Thromboembolism medication	1
	Pulmonary hypertension, endothelin receptor antagonists	1
Endocrine (n=183)	Insulin	76
	Blood glucose lowering drugs	40
	Corticosteroids	23
	Thyroid disorders	19
	Bisphosphonates	14
	Female sex hormone responsive conditions	7
	Gonadotrophin-releasing hormones	3
	Antidiuretic hormone disorders, vasopressin and analogues	1
Nervous system (n=273)	Analgesics, opioids	79
	Antiepileptics	54
	Antipsychotics	40
	Antidepressants	35
	Hypnotics, sedatives, and anxiolytics	21
	Parkinson's disease, dopaminergic drugs	14
	Analgesics, analgesics, non-opioid	11
	Dementia, anticholinesterase	6
	Antiemetics and antinauseants	4
	Dementia, dopaminergic drugs	4
	Antihistamines	2
	Local anaesthesia	2
	Parkinson's disease, antimuscarinic	1
	Total	1,190

9.19 Appendix 19– Medication classes associated with incidents at different medication process stage

BNF chapter	Medication	Monitoring	Supply	Advice	Preparation	Other	Administration	Prescribing	Total
Cardiology (n=734)	Antiplatelet	21 (17%)	0 (0%)	3 (2%)	10 (8%)	8 (6%)	19 (15%)	65 (51%)	126
	Factor Xa inhibitor	19 (15%)	0 (0%)	5 (4%)	3 (2%)	18 (14%)	26 (21%)	53 (43%)	124
	Beta blockers	8 (10%)	0 (0%)	2 (2%)	6 (8%)	5 (6%)	15 (19%)	41 (53%)	77
	Heparins	9 (13%)	1 (1%)	2 (3%)	2 (3%)	10 (14%)	32 (46%)	14 (20%)	70
	Warfarin	34 (51%)	0 (0%)	5 (7%)	0 (0%)	6 (9%)	11 (16%)	11 (16%)	67
	Diuretics	8 (12%)	0 (0%)	2 (3%)	7 (11%)	10 (15%)	8 (12%)	31 (47%)	66
	Calcium channel blockers	7	0	1	4	4	9	26	51
	ACE Inhibitors	2	0	3	2	10	11	12	40
	Statins	2	0	0	3	0	6	21	32
	Cardiac glycoside	4	0	0	1	0	2	13	20
	Nitrates	0	0	0	1	4	2	8	15
	ARBs	0	0	0	0	3	3	7	13
	Antiarrthymics	0	0	1	1	3	1	5	11
	Direct thrombin inhibitor	0	0	0	0	0	2	3	5
	K channel opener	0	0	0	1	2	0	2	5
	Antifibrinolytics	1	0	0	0	0	2	1	4
	Ivabradine	0	0	0	1	0	0	1	2
	Doxazosin	0	0	0	0	0	1	1	2
	Ambrisentan	0	0	0	0	0	0	1	1
	Piperazine derivatives	1	0	0	0	0	0	0	1
	Hypertensive med	0	0	0	0	1	0	0	1
	PE medication	0	0	0	0	1	0	0	1
Endocrine (n=183)	Insulin	8 (10%)	0 (0%)	3 (4%)	1 (1%)	13 (17%)	25 (33%)	26 (34%)	76
	Blood glucose drugs	7 (17%)	0 (0%)	2 (5%)	1 (2%)	6 (15%)	12 (30%)	12 (30%)	40
	Corticosteroids	2 (9%)	0 (0%)	2 (9%)	0 (0%)	4 (17%)	4 (17%)	11 (48%)	23
	Thyroid disorders	1	0	1	3	3	2	9	19
	Bisphosphates	1	0	0	0	1	3	9	14
	Female sex hormone	1	0	1	0	0	1	4	7
	Gonadotropin hormone	0	0	1	0	0	2	0	3
	Antidiuretic hormone	1	0	0	0	0	0	0	1
Nervous system (n=273)	Opioids	7 (9%)	0 (0%)	2 (2%)	3 (4%)	7 (9%)	20 (25%)	40 (51%)	79
	Antiepileptics	0 (0%)	0 (0%)	6 (11%)	8 (15%)	7 (13%)	6 (11%)	26 (49%)	53
	Antipsychotics	4 (10%)	0 (0%)	0 (0%)	2 (5%)	7 (17%)	7 (17%)	20 (50%)	40
	Antidepressant	1	0	2	3	1	9	19	35
	Hypnotics, sedative	0	0	1	1	2	6	11	21
	Dopaminergic drugs	0	0	0	2	1	0	11	14
	Analgesics	1	0	0	0	0	7	4	12
	Anticholinergics	1	0	0	1	0	0	4	6
	Dopaminergic drugs	0	0	0	0	0	1	3	4
	Antiemetics	0	0	0	0	2	1	1	4
	Antihistamine	0	0	0	1	0	1	0	2
	Local anaesthetics	0	0	0	0	1	0	1	2
	Procyclidine	1	0	0	0	0	0	0	1

9.20 Appendix 20 - Medication classes stratified by patient age affected by incident

BNF Chapter	Age groups				Total
	<18 years	18 - 65 years	>65 years	Missing data	
Cardiovascular	7 (14.8%)	126 (40.2%)	458 (53.9%)	143	734
Nervous system	3 (6.3%)	87 (27.7%)	127 (14.9%)	56	273
Endocrine system	3 (6.3%)	38 (12.1%)	108 (12.7%)	34	183
Gastro-intestinal	3 (6.3%)	12 (3.8%)	44 (5.1%)	22	81
Anti-infective	17 (36%)	21 (6.7%)	17 (2.0%)	6	61
Respiratory system	6 (12.7%)	12 (3.8%)	22 (2.5%)	11	51
Nutrition and metabolic disorders	4 (8.5%)	7 (2.2%)	28 (3.2%)	6	45
Blood and blood forming organs	0	3	11	5	19
Gastro-urinary system	0	2	12	1	15
Malignant disease	0	1	11	3	15
Eye	1	0	4	4	9
Musculoskeletal system	0	2	4	1	7
Immune system	0	1	2	0	3
Skin	1	1	0	1	3
Poisoning	0	0	0	2	2
Medical emergency	0	0	1	0	1
Nose	1	0	0	0	1
Vaccines	1	0	0	0	1
Total	47 (100%)	313 (100%)	849 (100%)	295 (100%)	1,504 (100%)

9.21 Appendix 21- Examples of discrepancies in harm severity between the harm severity provided by NRLS and the recoded data

Free text description of incident report	Severity of harm	
	NRLS	Re-coded
Down-graded		
''An 87 year old female patient went to the UCC service at XX Hospital. She had a week previously knocked her leg and been looking after it herself. The discharge letter clearly states that she is allergic to Penicillin but she was given a prescription for flucloxacillin 500mg. This lady is partially sighted and it was only due to her daughter seeing the prescription that she did not take any. Harm could have come to her.''	Death	No harm
''Patient was discharged from XX Hospital, Elderly Care ward. Upon checking medications given to patient upon discharge it was noted that Alendronic Acid - 70mg was issued for daily use. The patient has 70mg Alendronic Acid weekly not daily. Therefore, this medication error could have had serious complications for the patient if they had taken daily as advised on the discharge summary.''	Severe	No harm
''Drug added from discharge letter and was already on patients medication both was issued - chemist did not issue both medications to patient.''	Moderate	No harm
Up-graded		
''A patient who was a type one diabetic attended XX after a hypo and her insulin was stopped. The practice was not informed and no follow up was put in place. she was discharged. She became hyperglycaemic and acidotic She was readmitted to hospital when a GP realised what had happened. The patient died 8 days later.''	Severe	Death
''Patient was discharged from hospital after being diagnosed with Pulmonary embolism. His discharge summary stated rivaroxaban 15mg bd and also rivaroxaban 20mg. There were start and stop dates however the information was split over two pages. I feel the dosing and start, and stop should be made clearer with text against each prescription, also there was no mention of doses in the summary or plan. The nursing home gave 15mg bd plus the 20mg ON which resulted in an admission. I feel this could happen again unless made clearer. The practice had not prescribed any medication it had come from the hospital. I was informed that the nurse at the home had written up the mars sheet incorrectly.''	Low	Severe
''Patient readmitted to XX on 14/11. Medicines reconciliation completed 15/11. Noted that dose of LEVOTHYROXINE was increased to 125micrograms OD during a previous admission 17/09 to 01/11. This was highlighted on the discharge summary as a dose change. On 15/11, the GP Summary Care Record still listed the previous dose of 75 micrograms OD. This was confirmed with the community pharmacy who provide the NOMAD to the patient. Patient has been receiving a sub - optimal dose of levothyroxine post - discharge (approx 10-14 days). Readmitted with confusion and constipation.''	Low	Severe
''Temporary patient discharged from hospital to XX care for respite given amoxicillin for chest infection was allergic to but discharge letter only mentioned flucloxacillin allergy. carer informed surgery that patient was allergic to amoxicillin and comes out in rash 24 hours later. Immediate action SEA completed and discussed contacting permanent gp to gain records for allergies.''	No harm	Low harm
Unclear		
''Discharge letter with wrong medication dose [rivaroxaban].''	Severe	Unclear
''Discharge summary received from XX stated methotrexate 12.5mg every night.''	Severe	Unclear
''Pt discharged from hospital on medication [Clexane] to be taken at night. Pt had been given the nightly dose at hospital prior to discharge. On arrival to care home pt was again given a night dose. Communication error, double dose received.''	Severe	Unclear

9.22 Appendix 22 - Severity of harm stratified by patient age and origin of incident

			Harm severity [Provided in the data]				
	No harm	Any harm	Low	Moderate	Severe	Death	Total
Origin of incidents							
Primary care	310 (72%)	122 (28%)	75	41	4	2	432
Secondary care	456 (66%)	233 (34%)	140	79	10	4	689
Age range							
<18	37	7 (16%)	3	4	0	0	44
18-65	158	60 (27%)	34	23	2	1	218
>65	398	228 (46%)	137	76	10	5	626
Missing information	173	60 (26%)	41	17	2	0	233
Total	**766**	**355**	**215**	**120**	**14**	**6**	**1,121**

9.23 Appendix 23 - Severity of harm stratified by medication process/error categories

	No harm	Any harm	Harm severity				Total
			Low	Moderate	Severe	Death	
Medication Process							
Prescribing	349 (73%)	130 (27%)	91	32	6	1	479 (100%)
Administration / supply of a medicine from a clinical area	151 (60%)	102 (40%)	59	38	3	2	253 (100%)
Monitoring / follow-up of medicine use	84 (60%)	56 (40%)	25	26	3	2	140 (100%)
Preparation of medicines in all locations/ dispensing in a pharmacy	43 (67%)	21 (33%)	13	8	0	0	64 (100%)
Advice	34 (80%)	8 (20%)	3	5	0	0	42 (100%)
Supply or use of over-the-counter (OTC)	3 (100%)	0 (0%)	0	0	0	0	3 (100%)
Other	102 (73%)	38 (27%)	24	11	2	1	140 (100%)
Medication error category							
Wrong / unclear dose or strength	157 (74%)	55 (26%)	35	18	2	0	212 (100%)
Omitted medicine / ingredient	86 (58%)	62 (42%)	31	25	3	3	148 (100%)
Wrong drug / medicine	75 (63.5%)	43 (36.5%)	28	15	0	0	118 (100%)
Wrong quantity	52 (76.5%)	16 (35.5%)	7	6	2	1	68 (100%)
Wrong frequency	49 (82%)	11 (18%)	7	4	0	0	60 (100%)
Contra-indication to the use of the medicine in relation to drugs or/conditions	33 (57%)	25 (43%)	13	9	3	0	58 (100%)
Mismatching between patient and medicine	28 (62%)	17 (38%)	11	6	0	0	45 (100%)
Unknown	13 (65%)	7 (35%)	2	3	1	1	20 (100%)
Wrong formulation	16 (76%)	5 (24%)	5	0	0	0	21 (100%)
Wrong / omitted verbal patient directions	10 (56%)	8 (44%)	5	3	0	0	18 (100%)
Wrong method of preparation / supply	13 (81%)	3 (19%)	3	0	0	0	16 (100%)
Adverse drug reaction (when used as intended)	4 (40%)	6 (60%)	3	3	0	0	10 (100%)
Wrong / omitted / passed expiry date	4 (50%)	4 (50%)	2	2	0	0	8 (100%)
Patient allergic to treatment	4 (67%)	2 (33)	0	1	0	1	6 (100%)
Wrong / transposed / omitted medicine label	2 (40%)	3 (60%)	3	0	0	0	5 (100%)
Wrong route	1 (50%)	1 (50%)	1	0	0	0	2 (100%)
Wrong storage	2 (100%)	0 (0%)	0	0	0	0	2 (100%)
Wrong / omitted patient information leaflet	0 (0%)	1 (100%)	1	0	0	0	1 (100%)
Other	217 (72%)	86 (28%)	58	25	3	0	303 (100%)
Total	**766 (68%)**	**355 (32%)**	**215**	**120**	**14**	**6**	**1,121 (100%)**

9.24 Appendix 24– Frequency of incidents outcome (outcome sub-categories)

Outcome	Outcome sub-category	Total	Total	Total
Organizational inconvenience	Phone calls/follow-up	412	412	564
	Treating patient without sufficient information	110	110	
	Destruction of medication	19	19	
	Increased documentation	10	10	
	Organizational consequences	8	8	
	Legal implication	4	4	
	More equipment / supplies used	1	1	
Inconvenience to patient (non-clinical)	Missed dose(s) of medication*	107	107	455
	Unnecessary treatment**	90	90	
	Repeated visits to/from health care providers	76	76	
	Hospital admission	55	55	
	Additional monitoring required	37	37	
	Delays in management (assessment or treatment)	16	87	
	treatment changed	14		
	wrong treatment	57		
	Increased documentation	2	2	
	Repeated tests / procedure / additional treatment	1	1	
Patient clinical harm Pathophysiological/ disease-related pain	Changes in physiological parameters	41	41	216
	Discomfort/pain	22	22	
	Missed dose***	22	22	
	General deterioration/progression of condition	21	21	
	Medication overdose	13	13	
	Wrong treatment given	10	10	
	Bleeding	8	8	
	Psychological / emotional distress	1	8	
	Anger			
	Anxiety	3		
	Upset / emotional distress	2		
	Psychological difficulty e.g as indicated by evidence of longstanding anxiety, insomnia or low mood	1		
	Not requiring treatment	1		
	Death	7	7	
	Thrombosis	1	7	
	Deep Vein Thrombosis (DVT)	2		
	Pulmonary Embolism (PE)	4		
	Medication underdose	6	6	
	Confusion	5	5	
	Dizziness	4	4	
	Falls	4	4	
	Poor diabetic control	4	4	
	Drowsiness	3	3	

	Stroke	3	3	
	Acute renal failure	3	3	
	Drug toxicity	3	3	
	Difficulty breathing	3	3	
	Rash	2	2	
	Vasovagal	2	2	
	Seizure	2	2	
	Constipation	2	2	
	Anaphylaxis	1	1	
	Visual loss	1	1	
	Nausea/vomiting	1	1	
	Faint/Loss of consciousness	1	1	
	Dizziness	1	1	
	Fracture	1	1	
	Missed opportunity for curative treatment	1	1	
	Infection	1	1	
	Heart failure	1	1	
	Diarrhea	1	1	
	Psychological / emotional distress	1	1	
Staff outcomes	Psychological harm	1	1	1
No outcome	No outcome described	247	247	424
	Unclear outcome/insufficient information to ascertain outcome	105	105	
	Patient identified error and harm prevented	27	65	
	Relatives identified error and harm prevented	29		
	Carer (not a healthcare worker) identified error and harm prevented	9		
	Patient identified error and further harm prevented	1	7	
	Relatives identified error and harm further prevented	6		
Total		1,660		

**The first missed dose outcome refers to when the outcome caused inconvenience to the patient without reported patient harm.*

******* If the patient had a medication in a wrong frequency (more than what is intended), or in the patient had been given a medication that was used before but is no more needed.*

****The second missed dose outcome refers to when the patient had a clinical harm as a results*

9.25 Appendix 25- Contributory factors in the incidents with multiple contributory factors involved

Contributory factors	Total	Contributory factors (subcategories)	Total
Organisation	72	**Continuity of care - the delivery of a seamless service through integration, coordination and the sharing of information between different providers**	7
		Unknown to staff- staff have not been made aware of a patient by colleagues	
		Within Primary Care e.g. when a patient is seen by multiple GPs within the same practice and there is therefore a resulting failure to recognise a pattern or increasing severity of patient symptoms	6
		Registering with a GP	2
		Between Secondary and Primary Care	38
		Locum/ agency staff	2
		Between healthcare and pharmacy	15
		Working conditions	
		Staff behaviour	2
Staff factors	33	**Task-a piece of work to be done or undertaken.**	
		Failure to follow protocol - failure to adhere to procedures or regulation.	9
		New protocol	1
		Inadequate skill set/knowledge	2
		Wrong professional carries out task. eg) Admin clerk filling out prescriptions.	5
		Cognitive: includes abilities such as perception, learning, memory, language, concept formation, problem solving, and thinking.	
		Mistake	1
		Distraction/Inattention/Oversight/Forgot	3
		Similar patient names	2
		Misread/Did not read	4
		Hand writing	2
		Junior staff	2
		Verbal reporting used	2
Patient factors	3	**Language: patient unable to communicate in English**	1
		Behaviour	
		Fraudulent behaviour	1
		Knowledge: patient or parent of child has poor understanding	1
Equipment	2	**Use of fax machine**	2
Total	110		110

9.26 Appendix 26- Example of the most common contributory factors in incidents with multiple factors

Incident free text:

''Patient was discharged from hospital, a medication had been withheld due to AKI, to be reviewed following repeat bloods in a weeks' time. The blood test had been requested as required. However, the medication was in a NOMAD. The nominated pharmacy had not been informed, therefore the medication had been sent out in the tray. The discharge had gone to GP, on its return to reception this had not been actioned. It went into the filing to be scanned''.

Contributory factor:

- continuity of care issues organisation factors between secondary and primary care
- continuity of care issues organisation factors between pharmacy mistake in nurse allocation

9.27 Appendix 27- Frequency of contributory factors and reported degree of harm

Contributory factors	Insufficient details	No harm	Any harm	Re-coded harm severity				Total
				Low	Moderate	Severe	Death	
Organisation factor	286	45	52 (13.5%)	20	22	7	3	**383**
Staff factor	50	13	12 (16%)	4	6	0	2	**75**
Patient factor	3	0	2 (40%)	1	1	0	0	**5**
Equipment	4	0	0	0	0	0	0	**4**
Missing factor	567	58	88 (12.3%)	37	45	3	3	**713**
Total	910	116	154 (13%)	62	74	10	8	**1,180**

9.28 Appendix 28– Frequency of contributory factors for incidents and medication process

Medication process	Contributory factors					
	Patient factor	Staff factor	Equipment	Organisation factor	Missing factor	Total
Prescribing	2 (0.4%)	39 (7%)	2 (0.4%)	142 (28%)	320 (64%)	505 (100%)
Administration / supply of a medicine from a clinical area	0 (0%)	16 (6%)	0 (0%)	87 (33%)	162 (61%)	265 (100%)
Monitoring / follow-up of medicine use	2 (1%)	9 (6%)	0 (0%)	56 (37%)	86 (56%)	153 (100%)
Preparation of medicines in all locations / dispensing in a pharmacy	1 (1%)	5 (7%)	0 (0%)	18 (27%)	43 (65%)	67 (100%)
Advice	0 (0%)	3 (7%)	1 (2%)	14 (33%)	25 (58%)	43 (100%)
Supply or use of over-the-counter (OTC)	0 (0%)	0 (0%)	0 (0%)	2 (50%)	2 (50%)	4 (100%)
Other	0 (0%)	3 (2%)	1 (1%)	64 (45%)	75 (52%)	143 (100%)
Total	5 (0.4%)	75 (6.4%)	4 (0.3%)	383 (32.5%)	713 (60.4%)	1,180 (100%)

9.29 Appendix 29- Examples of frequent categories in the dataset

Main category	Sub-category	Keyword	Quotes
Monitored Dosage System (MDS) (n=88)	• List all medication in the stop section of the prescription and ask for a MDS at the same time. • Sending faxed letter to community pharmacy but not GP. • Patient was taking medication from MDS and take the same medication from care at home team. • Discharging patient with medication on MDS and as a loose tables / capsule in a bottle. • Supplying patient with 4 weeks of medication in MDS (before receiving DC letter) that is being mixed with new MDS.	• Nomad trays • Dossett box • Blister pack • MDS • Vena link • Nomad box • NOMAD • Weekly nomad system • Tray • Weekly medication box • Batch medication	• *''We received original discharge summary on the XX which still listed all patient's med in the stopped and doses changed section but to put in nomad tray and continue''* • *''Pt discharged home from hospital with blister pack - he was given Madopar 62.5mg capsules while in patient discharged on madopar tablets in the blister pack but also madopar capsules in a bottle''* • *''On discharge pt started on titrating dose of memantine , and sent home with scripts - had dosette box - memantine added at 20mg nocte for ongoing treatment - to be added to box - issued and sent out immediately - carers questioned the extra dose - so no harm''* • *''How they expected us to get the d / c summary and order her another dossett box toi continue before the 7 days ran out, I have no idea. Also, they are fully aware that they must prescribe the first 3 months' worth before transferring care to us. This is happening on a weekly basis as consultants are telling pts to see their gp for more medication, or they send ut the care transfer for monitoring WITH the initial d / c rather than 3 months later. The pharmacists on the ward need to be made aware that they cannot send home patients with dementia with only 7 days' worth of medication and expect, without calling us to warn us, that we can get the d / c summary and organise another Dossett box before the 7 days runs out.''* • *''Medication for one of our elderly monthly blister pack (DDS) patients was delivered by one of our dispensers on her way home from work and whilst dropping it off she noted the patient already had numerous packs of medication untouched at home. The dispenser brought the excess medication back for us to investigate only to find one of the weeks was a blister pack of discharge medication dispensed from another pharmacy after a hospital stay a couple of weeks prior to this. The rest of the packs at home were ones she had at home before she went into hospital, and she had started taking these again after finishing her hospital discharge pack. We, in her regular pharmacy, had no idea she had been in hospital hence why we were continuing to deliver her previously prescribed medication. And we were also completely unaware about any changes in her medication.''*
District nurse (n=44)	• Patient allocated when visit not required • Nurse not aware that patient was discharged • Nurse donot check authorisation • No administration sheet / prescription is being sent to nurse	• District nurse (DN)	• *''District Nurses stated that they were not aware of the discharge and that they should give the patient this daily injection ''.* • *''District nurses were contacted about why they had not visited, they informed GP surgery that the patient was not on their caseload, implying that they had not been informed about discharge or need for injections''*
Anticoagulation clinic (n=22)	• Local anticoagulation service not aware patient was requested to start/ stop warfarin post discharge	• INR test • Warfarin	• ''Patient discharged after DVT on warfarin but no referral to anticoagulation clinic done, only given 3 days warfarin and clexane and told to go to GP for INR testing and onward management'' • *''Patient discharged 29/11 on warfarin. D/C letter received 2/12. Not anticoagulation referral form received. No INRs / doses in patient Yellow Book. Patient attended surgery 2/12, INR subtherapeutic 1.9. Patient verbally states been on 3mg OD. Dosed based on this information''* • *''Patient was on warfarin prior to admission and under the care of the anti coag team. Patient was discharged home after being switched from warfarin to edoxaban , team only found this out after the husband rang to inform us of changes . Ice*

Main category	Sub-category	Keyword	Quotes
	• Not arranging for INR testing and follow-up with clinic • No discharge letter/ INR test		*discharge states switch made as per anti coag team, however, patient was never referred to us for education / advice on switching.''*
Community nurse (n=22)	• Unaware of discharge • Hospital not arranging with nursing staff to administer medication • Handling patient post discharge without medication slip (prescription sheet) • Discharging patient without analgesic	• Community nursing team	• *''The patient was discharged from ward to home on the 4th of June. The hospital did not arrange the community nurse to administer daily insulin but listed this as action for the GP on the discharge summary. There was no telephone communication to inform of this. The discharge summary was not received and processed until the 8th of June and the patient was without insulin until the 9th June.''* • *''humalog mix 25 40 units administered to patient from given prescription in home unaware dose had been changed when discharged from hospital to humalog mix 25 30 units. Informed matron on duty and got husband to check wife blood sugar 13.3mmols at 12.30 and advised if patient condition changes to contact a medical professional.''* • *''Staff are not to accept referral without an appropriate drug / prescription sheet - regardless of knowledge / history of the patient''* • *''Incident identified by community cardiac nurse (CCN) at client phase two cardiac rehabilitation assessment. Limited faxed referral to community cardiac nursing team from referring Hospital XX . Client asked to confirm medications on return home, contact from CCN. GP surgery contacted by CCN to confirm medications prescribed on client records and to request copy of Hospital discharge letter be faxed to cardiac nursing team urgently. CCN - continuing concern re management plan therefore on call Cardiologist (Registrar) at referring Hospital contacted. Latter medic returned telephone communication to CCN following discussion with on call Cardiologist and instructed medications omitted to be prescribed urgent.''*
Nursing home (n=21)	• Not aware of discharge • Communication of discharge letter	• Nursing home	• *''Patient's son rang district nurses to say that his mother was discharged from xx hospital on Thursday and that no one had been to administer his mother's clexane injection for the past 3 days. I explained to him that we were not aware that his mother had been discharged from hospital and hadn't received a message or transfer of care from the ward to inform us about his mother or her clexane injection.''* • *''Patient was discharged from XX on Tinzaparin for DVT. Nursing home contacted surgery on 5 /xx in the evening requesting for a prescription for Tinzaparin. However, there was no discharge advice note from hospital about the admission. Nursing home staffs had threw away the box the Tinzaparin came in . Surgery admin staff tried contacting hospital for discharge advice note or dosage of Tinzaparin to be given. We were told discharge advice note not done and patient notes have gone back to records so nobody can tell us the diagnosis or treatment''.*
Medication duration (n=15)	• Medication that was intended for short period, but were dispensed for years	• Medication continued	• *''Patient prescribed Nitrofurantoin MR 100mg BD since June 2014 in weekly box in error. Came to light on Dec 15 when pharmacy phoned to advise problems with supply. Pt had been prescribed low dose prophylactic antibiotics for recurrent UTI since May 2011 cycling between nitrofurantoin 50mg at night and trimethoprim 100mg at night. In June 2014 she was found to have a UTI at a pre - op assessment and was given a course of Nitrofurantoin 100mg MR BD for 1 wk. This medication was detailed under current medication when she was discharged and was added to her weekly nomad system. Discussed with patient and she was fine having suffered no side effects.''* • *''Patient attended for medication review May 2016 - noted been on clopidogrel since ACS in December 2010. Discharge letter recorded to continue clopidogrel for 9 months only. Discussed with patient and medication stopped following review medical records.''*

Main category	Sub-category	Keyword	Quotes
Paediatric and antibiotic (n=12)	• Liquid quantity	• Further supply	• ''Patient discharged with meds. letter states 10 days given. Patient only received 5 and was told to get the rest from *GP.''* • *''Patient told verbally to obtain further supply form the GP ideal if hospital able to supply whole course, this would avoid confusion with patient and GP.''* • *''This child was discharged from hospital; according to discharge he should be on antibiotics for 2 weeks but was given only one bottle and was advised to ask GP for another''* • *''Patient discharged from hospital with infection around elbow. On discharge letter and parents informed that he should take antibiotics for 10 days. Hospital pharmacy only gave 7 days' supply Family had to contact surgery for further 3 days' supply.''*
Repeat prescription (n=11)	• Repeat prescription issued before receiving discharge letter • Repeat prescription issued for patients while they are admitted • Inpatient left hospital to collect repeat prescription and went back to hospital	• Repeats issues • Repeat medication	• *''Patient has been in hospital from 02/xx until 28/xx. Yet prescription request from pharmacy on 11/xx , which was issued . Patient had thus been in hospital for over a week before prescription was requested. Ideally prescription should be requested only on request from the patient, rather than request being generated by a community pharmacist. Patient now discharged to a nursing home that is not supplied by this pharmacy - so a whole month supply of medicines will be wasted. Additionally, medications changed while in hospital''.* • *''Patient returned to the ward after visiting his GP in the community with a full supply of their current medication. Patient proudly told us that they had seen his GP and got a prescription which they used to obtain them from a local chemist''.* • *''Medication issued from GP surgery at request of chemist whilst in hospital - surgery had no info to say patient in hospital or discharged. medication withheld or stopped whilst in hospital - if taken could have resulted in readmission or worse*''.
Amber level 3 drug (n=6)	• Patient not informed that they must obtain it from the hospital • GP not happy to issue • Secondary care not aware of the amber list	• Amber • Level 3 drug • Restricted medication	• *''A patient was discharged from hospital without adequate instructions on where to obtain a six-month supply of the specialist drug - Tenofovir 250mg tablets. This medication is restricted to supply in the hospital. The GP was aware of the restrictions and declined to issue a script. This is not an isolated occurrence and happens on a regular basis. Hospital Clinicians and their staff must take the time to explain to patients that in cases where a specialist drug is prescribed ..it must be obtained from the hospital pharmacy. This represents a risk to prescribing errors and patient safety''* • *''Hospital doctors not aware of AMBER shared care arrangements & are writing treatment f / u plans which are incompatible with these arrangements (??or maybe just disagree with the arrangements & hope GP will take over care of patient & hope for the best re relapse risk) No information regarding what the patient was told would be happening but I suspect he was expecting GP to be providing script for olanzapine & organising blood tests & BP monitoring & adjusting treatment regime .''*
Bank holiday (n=6)	• Obtaining prescription from GP • INR test not done	• Between the bank holiday and weekends for the Christmas / New Year period • bank holiday weekend • easter holiday	• *''Patient discharged from hospital on 24/12, insulin doses had been reviewed for morning administration. Nurses have administered this amended dose from the front sheet of the referral letter until yesterday. There has been no discharged medication advice for the service. Patient was in hospital overnight on 30th to the 31st of December - there is no new referral for this date. There have been two dates where a formal permission to give slip could have been obtained from a GP. These dates are 29th December and 2nd January - between the bank holiday and weekends for the Christmas / New Year period. A formal permission to give slip is required for community drug administration at the earliest opportunity - this has been missed in this incident''*
To take a way (TTO) letter (n=6)	• Discrepancy between medication of the discharge letter and TTO • Free text in discharge letter mention medication not in TTO	• TTO	• *''Patient admitted to XX Hospital with XX probable hypoglycaemic episode; Part of medicines on admission was gliclazide 80mg each morning AND 40mg at teatime. Discharge letter received at surgery 23 / XX / XX - under medication changes gliclazide 40mg at teatime dose stopped BUT still listed on TTO medication list. Script done 23 / XX / XX by GP for XXX incorrect XX dose of gliclazide but retrieved before issue to patient. Repeat template subsequently altered. .''*

Main category	Sub-category	Keyword	Quotes
Mental health (n=4)	• Mental health team ask GP to prescribe due to time scale. • GP prescribes without specialised training • Discharge letter not clear regarding mental health medication	• Mental health team	• *''Referral was made to mental health team who normally undertake this service, including prescribing. Due to time scales, mental health team asked GP to prescribe''*

9.30 Appendix 30- Incidents related to monitored dosage system

Origin of incident	Total
Primary care	**46**
Secondary care	**42**
Patient age range	**Total**
18 to 25 years	**1**
26 to 35 years	**1**
36 to 45 years	**1**
46 to 55 years	**4**
56 to 65 years	**4**
66 to 75 years	**17**
76 to 85 years	**18**
Over 85 years	**25**
Missing data	**17**
Error category	**Total**
Wrong / unclear dose or strength	**12**
Omitted medicine / ingredient	**10**
Wrong drug / medicine	**10**
Wrong frequency	**8**
Wrong quantity	**6**
Contra-indication to the use of the medicine in relation to drugs or conditions	**4**
Adverse drug reaction (when used as intended)	**2**
Mismatching between patient and medicine	**2**
Wrong storage	**1**
Wrong method of preparation / supply	**1**
Wrong / transposed / omitted medicine label	**1**
Patient allergic to treatment	**1**
Unknown	**2**
Other	**28**
Level of harm*	**Total**
No harm	**56**
Low harm	**22**
Moderate harm	**10**
Medication process	**Total**
Prescribing	**33**
Administration / supply of a medicine from a clinical area	**17**
Preparation of medicines in all locations / dispensing in a pharmacy	**14**
Monitoring / follow-up of medicine use	**14**
Supply or use of over-the-counter (OTC)	**1**
Other	**9**

Medication	Total
Anti-infective	**1**
Blood and blood-forming organs	**1**
Cardiovascular system	
• Antithrombotic drugs, antiplatelet drugs	**29**
• Diuretic	**16**
• Beta-adrenoceptor blockers	**14**
• Antithrombotic drugs, heparin	**12**
• Calcium-channel blockers	**12**
• Antithrombotic drugs, Vitamin K antagonists	**11**
• ACE inhibitors	**10**
• Statins	**10**
• Antithrombotic drugs, factor Xa inhibitors	**7**
• Angiotensin II receptor antagonists	**3**
• Nitrate	**3**
• Antiarrhythmics	**3**
• Vasodilator - Potassium-channel openers	**3**
• Antithrombotic- Thrombin inhibitors, direct	**2**
• Heart failure, Selective sinus node if inhibitors	**1**
• Cardiac glycosides	**1**
• Antihaemorrhagics, Antifibrinolytics	**1**
Endocrine system	
• Blood glucose lowering drugs	7
• Thyroid disorders	5
• Insulin	4
• Corticosteroids	3
• Bisphosphonates	**2**
• Gastro-intestinal system	**5**
• Genito-urinary system	**2**
• Malignant disease	**1**
Nervous system	
• Antidepressants	**11**
• Antipsychotics	**10**
• Antiepileptics	**7**
• Opioids	**5**
Dementia - Dopaminergic drugs	**3**
• Parkinson - Dopaminergic drugs	**3**
• Hypnotics, sedatives, and anxiolytics	**3**
• Analgesics, non-opioid	**2**
• Parkinson - Antimuscarinc	**1**
• Antihistamines	1
• Nutrition and metabolic disorders	**4**
• Respiratory system	**1**

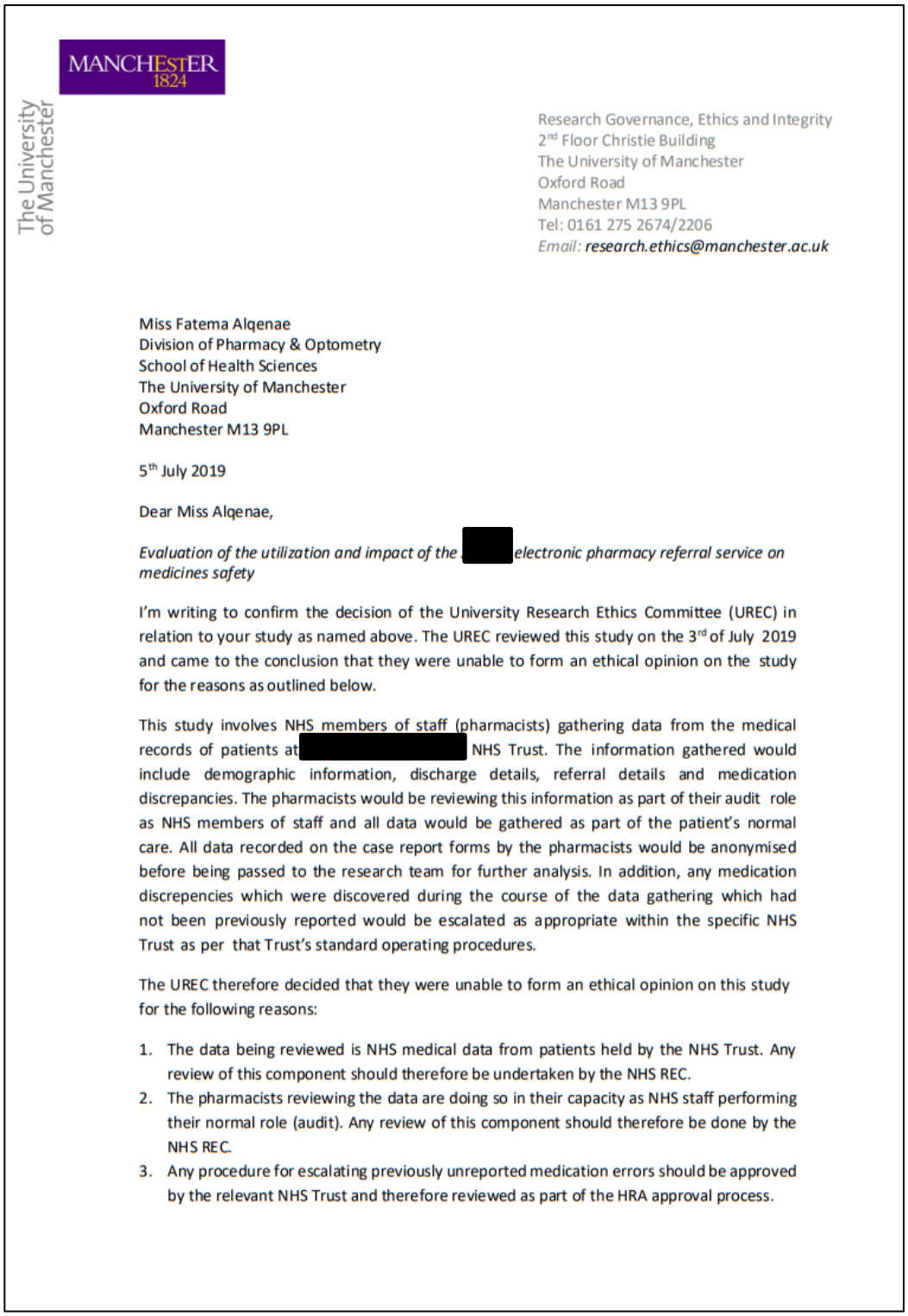
Factors	Total
Patient factors	
• Behaviour: the way in which patients/family act or conduct themselves	
○ Non-compliance: patient does not follow advice or instructions	**1**
Staff factor	
• Task-a piece of work to be done or undertaken.	
○ Failure to follow protocol - failure to adhere to procedures or regulation.	**3**
○ Wrong professionnal carries out task. eg) Admin clerk filling out prescriptions.	**1**

• Cognitive: includes abilities such as perception, learning, memory, language, concept formation, problem solving, and thinking. o Mistake	**1**
o Distraction/Inattention/Oversight/Forgot -	**1**
o Misread/Did not read	**1**
o Hand writing	**1**
Organisation • Continuity of care - the delivery of a seamless service through integration, coordination and the sharing of information between different providers o Within Primary Care Ð e.g. when a patient is seen by multiple GPs within the same practice and there is therefore a resulting failure to recognise a pattern or increasing severity of patient symptoms	**1**
o Between Secondary and Primary Care	**24**
o Locum/ agency staff	**1**
o Between healthcare and pharmacy	**19**
Outcomes	**Total**
No outcome • No outcome described	**7**
• unclear outcome/insufficient information to ascertain outcome	**7**
• patient identified error and harm prevented	**2**
• relatives identified error and harm prevented	**3**
• carer (NOT a healthcare worker) identified error and harm prevented	**2**
• relatives identified error and harm FURTHER prevented	**1**
Patient clinical harm Pathophysiological/disease-related Pain • Discomfort/pain	**2**
• Changes in physiological parameters	**1**
• Vasovagal	**1**
• Falls	**2**
• Medication overdose	**1**
• Medication underdose	**1**
• Confusion	**2**
• Bleeding	**2**
• Fracture	**1**
• Diarrhoea	**1**
• Constipation	**1**
• Psychological difficulty e.g as indicated by evidence of longstanding anxiety, insomnia or low mood	**1**
• Anger	**1**
Inconvenience to patient (non-clinical) • Delays in management (assessment or treatment)	**1**
o treatment changed	**1**
o wrong treatment	**11**
• Repeated visits to/from health care providers	**6**
• Unnecessary treatment	**12**
• Hospital admission	**2**
• additional monitoring required	**2**
• Missed dose(s) of medication	**9**
Organisational inconvenience • Increased documentation	**1**
• Phone calls/follow-up	**45**
• More equipment / supplies used	**1**
• Treating patient without sufficient information	**9**
• Destruction of medication	**4**

9.31 Appendix 31 – Examples of literatures evaluate the use of PharmOutcomes™ platform

Study ID (Author, Year)	Evaluation	Settings	Follow-up period	Results
Nazar, 2016 [312]	• Evaluate electronic patient referral system • Readmission rate	• One trust, 2 hospital sites and 207 community pharmacies • North East of England, Newcastle-upon-Tyne	• 13-month period • (1st July 2014 – 31st July 2015).	• Number of referrals 2029 • Number of rejected referrals 955 (45.3%) • Number of completed referral 619 (31%) • Reduction of readmission
Sabir, 2019 [313]	• Evaluate electronic patient referral system on readmission rate	• One trust • Leeds teaching hospital NHS trust	• 6 months before and 6 months after intervention • (January -April 2017)	• Number of all patients 977, included patient 627 • Percentage of completed referrals 84% • Emergency readmission rates following the intervention reduced by 16.16%
Wilcock, 2019 [476]	• Reasons for rejection	• Royal Cornwall hospitals NHS trust • 85 community pharmacies	• 6 months • (from January 2018)	• Number of patients 1,562 • 23% of referrals were rejected (n=363) • Common reason of rejection was unable to contact patient
Buchanan, 2016 [601]	• Link new Hepatitis C diagnosis at community pharmacy with specialist care	• The Isle of Wight (IOW) • 2 community pharmacies	• 9 months • (September 2014 – May 2015)	• 88 tests were made • All cases were refereed and seen by hepatologist. • Reduce burden of undiagnosed cases
Nazar, 2017 [660]	• Evaluate pharmacy emergency repeat medication supply service	• 12 Clinical Commissioning Group (CCGs) • 277 community pharmacies • Calls to NHS 111 for out of hours care regarding medication were referred to community pharmacies	• Dec-2014 until Aril 2015	• 635 patients called NHS 111, and 70% received emergency supply • 1286 self-presenting patient, 46% received emergency supply • Patients were happy regarding the service
Specialist pharmacy service, 2014 [603]	• Evaluate the safety of Non Steroidal Anti-inflammatory Drugs (NSAID) prescribing with gastro- protection agent	• National audit across England • 1,278 community pharmacies • 3 NHS England area teams, 2 in the North and 1 in the South		• PharmOutcomes™ system made the audit easy
Specialist pharmacy service, 2017 [602]	• Hydration messages to prevent Acute Kidney Injury (AKI)	• 176 CCGs across England • 75 community pharmacies	• 9 months in 2016	• PharmOutcomes™ system made the audit easy • 14,908 patients • 94% of patients had hydration advice

9.32 Appendix 32 – University Research Ethics Committee (UREC) letter



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Research Governance, Ethics and Integrity
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Manchester M13 9PL
Tel: 0161 275 2674/2206
Email: research.ethics@manchester.ac.uk

Miss Fatema Alqenae
Division of Pharmacy & Optometry
School of Health Sciences
The University of Manchester
Oxford Road
Manchester M13 9PL

5th July 2019

Dear Miss Alqenae,

Evaluation of the utilization and impact of the [redacted] electronic pharmacy referral service on medicines safety

I'm writing to confirm the decision of the University Research Ethics Committee (UREC) in relation to your study as named above. The UREC reviewed this study on the 3rd of July 2019 and came to the conclusion that they were unable to form an ethical opinion on the study for the reasons as outlined below.

This study involves NHS members of staff (pharmacists) gathering data from the medical records of patients at [redacted] NHS Trust. The information gathered would include demographic information, discharge details, referral details and medication discrepancies. The pharmacists would be reviewing this information as part of their audit role as NHS members of staff and all data would be gathered as part of the patient's normal care. All data recorded on the case report forms by the pharmacists would be anonymised before being passed to the research team for further analysis. In addition, any medication discrepencies which were discovered during the course of the data gathering which had not been previously reported would be escalated as appropriate within the specific NHS Trust as per that Trust's standard operating procedures.

The UREC therefore decided that they were unable to form an ethical opinion on this study for the following reasons:

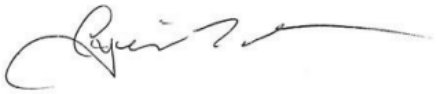
1. The data being reviewed is NHS medical data from patients held by the NHS Trust. Any review of this component should therefore be undertaken by the NHS REC.
2. The pharmacists reviewing the data are doing so in their capacity as NHS staff performing their normal role (audit). Any review of this component should therefore be done by the NHS REC.
3. Any procedure for escalating previously unreported medication errors should be approved by the relevant NHS Trust and therefore reviewed as part of the HRA approval process.

4. The research team are in receipt of fully anonymised data with explicit permission from the data controller and with consent from the data subjects. This component does not require review by the UREC as it is classed as secondary data analysis which meets all the requirements for ethical exemption issued by the University of Manchester.

As the NHS REC have ruled that this study is classed as audit and therefore exempt from NHS REC review, the study will proceed for HRA approval only.

Please accept a copy of this letter as confirmation of the decision of the UREC and should you have any further queries regarding the decision please let us know.

Yours sincerely,



Mrs Genevieve Pridham
Research Governance, Ethics and Integrity Officer (Ethics)

9.33 Appendix 33 – Health Research Authority (HRA) approval letter

Ymchwil Iechyd a Gofal Cymru
Health and Care Research Wales

NHS
Health Research Authority

Dr. Richard Keers
First Floor, Stopford Building
Division of Pharmacy and Optometry, School of Health Sciences, University of Manchester
Oxford Road, Manchester, UK
m13 9pt

Email: hra.approval@nhs.net
HCRW.approvals@wales.nhs.uk

24 October 2019

Dear Dr. Keers

HRA and Health and Care Research Wales (HCRW) Approval Letter

Study title:	**Evaluation of Medication Discrepancies and Adverse Drug Events Following Transition from Secondary to Primary Care Before and After Implementation of Electronic Transfer of Care to Pharmacy in [redacted] Greater Manchester**
IRAS project ID:	**262688**
Sponsor	**University of Manchester**

I am pleased to confirm that HRA and Health and Care Research Wales (HCRW) Approval has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications received. You should not expect to receive anything further relating to this application.

Please now work with participating NHS organisations to confirm capacity and capability, in line with the instructions provided in the "Information to support study set up" section towards the end of this letter.

How should I work with participating NHS/HSC organisations in Northern Ireland and Scotland?
HRA and HCRW Approval does not apply to NHS/HSC organisations within Northern Ireland and Scotland.

If you indicated in your IRAS form that you do have participating organisations in either of these devolved administrations, the final document set and the study wide governance report (including this letter) have been sent to the coordinating centre of each participating nation. The relevant national coordinating function/s will contact you as appropriate.

Please see IRAS Help for information on working with NHS/HSC organisations in Northern Ireland and Scotland.

How should I work with participating non-NHS organisations?
HRA and HCRW Approval does not apply to non-NHS organisations. You should work with your non-NHS organisations to obtain local agreement in accordance with their procedures.

What are my notification responsibilities during the study?

The *"After HRA Approval – guidance for sponsors and investigators"* document on the HRA website gives detailed guidance on reporting expectations for studies with HRA and HCRW Approval, including:

- Registration of Research
- Notifying amendments
- Notifying the end of the study

The HRA website also provides guidance on these topics and is updated in the light of changes in reporting expectations or procedures.

Who should I contact for further information?
Please do not hesitate to contact me for assistance with this application. My contact details are below.

Your IRAS project ID is **262688**. Please quote this on all correspondence.

Yours sincerely,

Maeve Ip Groot Bluemink
Approvals Specialist

Email: hra.approval@nhs.net

Copy to: *Ms. Lynne Macrae*

List of Documents

The final document set assessed and approved by HRA and HCRW Approval is listed below.

Document	*Version*	*Date*
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [Insurrance letter]		18 September 2019
IRAS Application Form [IRAS_Form_01102019]		01 October 2019
Letter from sponsor [Sponsor letter]		18 September 2019
Organisation Information Document [OID]	3	03 September 2019
Other [Master patient link code sheet]	3	25 May 2019
Other [Introduction letter]	6	30 September 2019
Other [Evaluation of Electronic Transfer of Care to Pharmacy]		08 October 2019
Other [Data collection form]	9	03 September 2019
Other [Risk assessment form]	1	23 June 2019
Other [Data collection guide]	6	03 September 2019
Other [Combined To Whome It May Concern]	1	02 May 2019
Other [Employers' Liability Insurrance]		01 June 2019
Other [UREC letter]		05 July 2019
Research protocol or project proposal [Protocol]	9	03 September 2019
Research protocol or project proposal	9	03 September 2019
Schedule of Events or SoECAT	1 (assessed)	24 October 2019
Summary CV for Chief Investigator (CI) [CV Dr. Keers]		12 July 2019
Summary CV for student		08 July 2019
Summary CV for supervisor (student research)		

9.34 Appendix 34 – Data Collection Guide

MANCHESTER 1824
The University of Manchester

Version 8 10.10.2020
IRAS Project ID: 262688

Evaluation of Medication Discrepancies and Adverse Drug Events Following Transition from Secondary to Primary Care Before and After Implementation of Transfers of Care Around Medicines (TCAM) in [redacted], Greater Manchester

Data Collection Guide

For any enquiries, please contact:

Fatema Alqenae (Lead researcher)

Division of Pharmacy and Optometry
School of Health Sciences
Faculty of Biology, Medicine and Health
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Background

Medication related problems are recognised as an important patient safety priority in transition of care from secondary to primary care. In March 2017, medication safety at transfer of care was brought to global attention with publication of the World Health Organization's (WHOs) Global Patient Safety Challenge: medication without harm, as one of three priorities for action. The ultimate goal of this WHO challenge is to reduce severe avoidable medication related harm globally by 50% in the next five years. Many initiatives have been started worldwide to address this problem including in Salford, UK.

This project is a retrospective before and after study to evaluate the impact of a new electronic referral system used to refer patients to community pharmacy in [redacted] after hospital discharge from [redacted] The Transfers of Care Around Medicines (TCAM) service was deployed in February 2019 in Salford with the purpose of reducing medication discrepancies, reducing medication waste and improving monitoring and reporting of adverse drug reactions. The evaluation will be based on the effect of the new service on medication discrepancies, adverse drug events (ADEs), community pharmacy activity and time to identification of discrepancies after discharge by evaluating pseudonymised patient data from primary care and the TCAM referral data platform (PharmOutcomes™). The results of the study may inform the ongoing development of electronic referral systems to maximise reductions in medication discrepancies and medication related harm post hospital discharge.

This guide is designed to provide background information on definitions and guidance for collecting data in primary care general practice in order to evaluate TCAM service in [redacted] This guide is intended for practice employed and NIPPs pharmacists at primary care practices within [redacted] who will evaluate medication discrepancies, time to medication reconilaition and ADE data. The TCAM referral data from PharmOutcomes™ system will be collected without input from general practice pharmacists (this data will include number of patients referred using PharmOutcomes™ platform and outcome of referrals).

This guide contains the following:

1. Definition of key terms
2. Data collection instructions – overall process

3. Master patient link code sheet
4. Data Collection Forms 1
5. Data Collection Form 2
6. Terminating data collection
7. Frequently Asked Questions
8. ADE trigger tools

The figures in this guide contain examples of completed fictitious entries to aid understanding the form.

1. **Definitions of key terms used in this project:**

Before conducting the review of patient records to identify medication discrepancies and adverse drug events (ADEs), the data collectors need to be familiar relevant key definitions.

- **Adverse drug event**: An injury resulting from a medical intervention related to a drug
- **Harm**: temporary or permanent impairment of physical or psychological body function or structure
- **Hospital readmission**: Readmission to hospital within one month (30 days) of the index discharge date
- **Medication discrepancies**: Difference between medications taken by a patient using the most up to date list of prescribed medication from the GP and the medications on the hospital discharge letter
- **Medicines reconciliation**: The process of obtaining an up-to-date and accurate medication list that has been compared with the most recently available information and has documented any discrepancies, changes, deletions or additions resulting in a complete list of medication accurately communicated

2. **Data collection instructions – overall process**

- The data collection period will be over three months from October 2019 to January 2020. All data collectors need to collect data of 30 patient over 6 hours. Where data collectors are advised to collect data of 15 patient over 3 hours for both, the pre-implementation and post-implementation phase.
- It is advised for all data collectors to have for each discharged patient ONE completed 'Data Collection Form 1', however there may be more than one completed 'Data Collection Form 2' for each discharged patient if they experience more than one ADE post-hospital discharge (multiple forms for each patient should be kept together). See Part 4 and Figure 3 for more details.
- Firstly, all data collectors need to identify patients before and after the TCAM service went live who were prescribed MDS and were discharged from SRFT during the data collection windows. The process of patient identification will be as follows:
  - The Pharmacy department at [redacted] will provide a report from their electronic patient record system on the number and identity of patients discharged from [redacted] with MDS to the pharmacist data collectors at each practice, both before and after the TCAM intervention was implemented. The report will be sent via secure NHS email to the practice pharmacists data collectors so that they can screen these records for data collection. The e-referral service was implemented in February 2019. Data will be collected for patients discharged during two collection periods: before service implementation (August 2018 –January2019) and after service implementation (March 2019 – August 2019).
  - The Pharmacy department at [redacted] will assign sequential number to eligible patient discharges between August 2018 and January2019 for the preimplementation phase and between March 2019 and August 2019 for the post-implementation phase. Then, Fatema, the lead researcher will randomly generate numbers using a random sample generator and these numbers will be sent to the practices to match with sequential number linked to patient record in order to generate the final sample of usable 638 patient records across 43 practices to be reviewed.

- Each data collectors will randomly select 15 discharges before and after the TCAM went live.

- Secondly, data collectors should record these patient details on the 'Master Patient Link Code Sheet' (see Part 3 and Figure 2) and assign them an pseudonymised patient number. They should also assign their practice a number using Table 1 below.
- Then, data collectors are advised to use the electronic primary care heath record, hospital discharge document and e-referral alert to record data and patient details on 'Data Collection Form 1' for everyone they screen regardless of whether they are eligible for inclusion or not. Then data collectors can determine whether the patient is eligible to continue data collection for discrepancies and ADEs.
- For data collection regarding medication discrepancies:
  - If the discharged patient is eligible, data collectors are advised to use the documented medicines reconciliation (or similar) activity to extract the discrepancy data and time from discharge to completion of this activity.
  - Data collectors are advised to use data from medication reconciliation/similar medication entries activity by pharmacist, doctor, nurse or administrative staff.
- For data collection regarding adverse drug events (ADEs):
  - Then, data collectors need to screen the whole electronic health record from the date of discharge up to a **3 month period post hospital discharge** to identify ADEs. This includes blood tests, and all documented activity including consultations, medicines reconciliation/review and other entries by practice staff. Data collectors are advised to look for evidence that supports the presence of ADEs and the use the ADE triggers at the end of this document for support. For each suspected ADEs identified, data collectors should complete one copy of 'Data Collection Form 2' – if a single patient discharge has multiple copies of 'Data Collection Form 2', please ensure these are kept together along with their 'Form 1' and returned to the research team.
- Please return the data collection forms to Fatema Alqenae, the lead researcher at the University of Manchester via recorded postal delivery. The cost of the postal delivery will be covered by the University of Manchester. Please send the payment receipt electronically via email to Fatema Alqenae with the bank details, and expenses will be reimbursed. Data collection forms can be completed electronically in Microsoft Word® if you wish, and send via NHS email to Dr. Richard Keers at Richard.keers@nhs.net .
- See Figure 1, flow diagram for stepwise process of data collection.

3. Master patient link code sheet

The 'Master Patient Link' code sheet is designed to ensure confidentiality and anonymity of patient information. In this sheet, each reviewed record should be assigned a unique number (e.g. use 001, 002,003…) that corresponds to the patient NHS number. The Practice name will also be written and then pseudonymised using the codes provided in Table 1 below. This unique code will be used on the main data collection forms 1 and 2 so that patients are not identifiable by the research team. It will also enable patient record tracking whilst also keeping NHS numbers confidential. Please store the 'Master Patient Link code sheet' forms in a locked filing cabinet at your practice and ensure only the pharmacy team can access it. (See Figure 2)

Figure 1 – Flow diagram for the data collection process

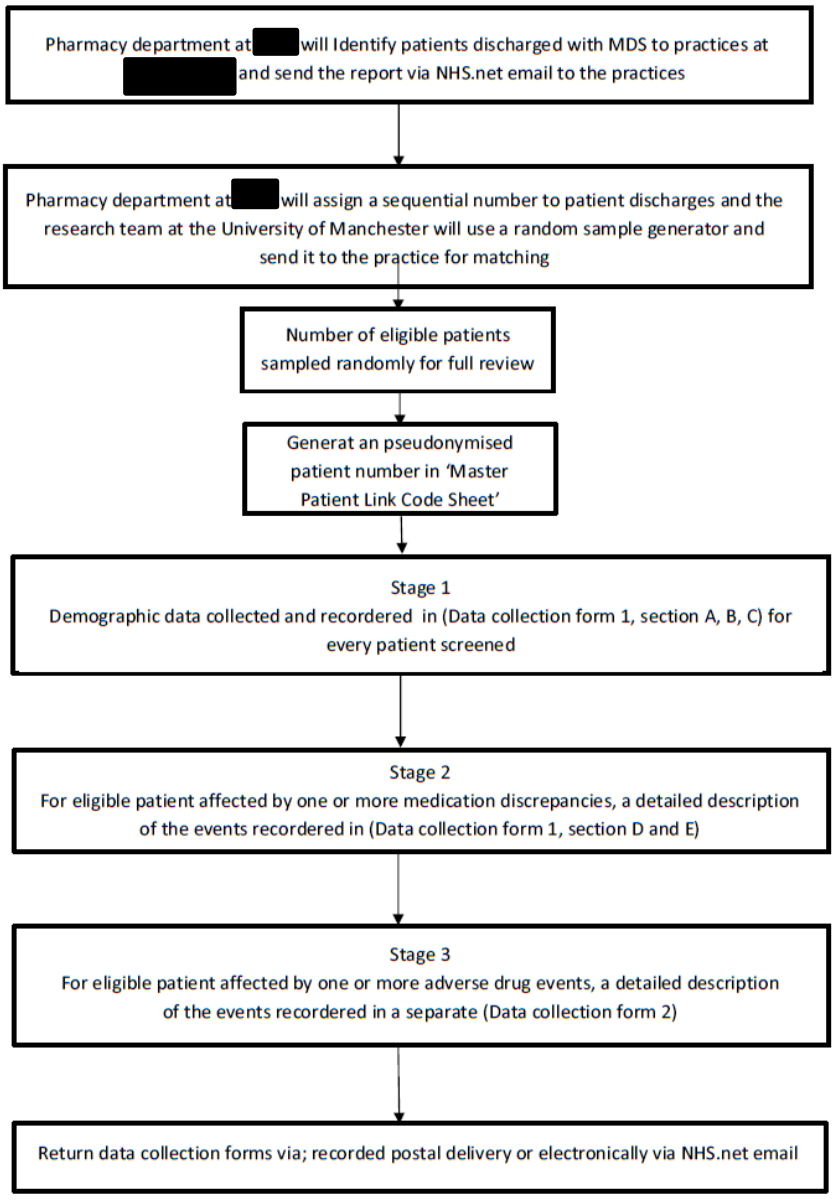

Table 1 – Names and codes of the practices

[redacted]	Code
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Figure 2– Master patient link code sheet

Master Patient Link Code Sheet

Date: 30/09/2019	
General practice name: Flower	
General practice number*: 17	
Data collector: RG	
Patient NHS number	**Patient link code***
450 557 6623	001
170 223 9923	002
950 506 7104	003

*Guidance on practice number and generating patient link code is in the data collection guide.

Please use multiple sheets if required.

Please store in Masterfile in secure place in the practice.

4. **Data collection Form 1**

- There are two data collection forms: data collection forms 1 and 2.
- 'Data collection Form 1' is designed to collect data for all sampled patients records.
    - Section A is designed for you to record some basic information of the data collector, phase of data collection and practice site.
    - Section B is designed for you to record basic anonymised information regarding patient demographics.
    - Section C is designed to record basic information regarding patient eligibility criteria for the study. Thus for any patients who are not found to be eligible for inclusion in the study by data collectors, data collectors are advised not to complete data collection sections beyond section C for those patients.
    - Section D is designed to record data on medication reconciliation or equivalent medication entries activity that you identify in patient records during one month post hospital discharge.. Section D in 'Data Collection Form 1', (See figure 4) is designed to record information of medication discrepancies identified, including description of medication discrepancies, severity of discrepancies, and action taken.
    - Regarding the severity of the medication discrepancy, they will be categorized based on national coordinating council for medication error reporting and prevention NCC MERP, the scale has an acceptable validity and reliability (Garfield et al., 2013). Please use the scale developed by NCC MERP summarised below:
    - Category A: circumstances or events that have the capacity to cause error
    - Category B: An error occurred but the error did not reach the patient (An error of omission does reach the patient)
    - Category C: An error occurred that reached the patient but did not cause patient harm
    - Category D: an error occurred that reached the patient and required monitoring to confirm that it resulted in no harm to the patient and/or required intervention to preclude harm
    - Category E: an error occurred that may have contributed to or resulted in temporary harm to the patient and required intervention
    - Category F: An error occurred that may have contributed to or resulted in temporary harm to the patient and required initial or prolonged hospitalization
    - Category G: an error occurred that may have contributed to or resulted in permanent patient harm
    - Category H: An error occurred that required intervention necessary to sustain life
    - Category I: An error occurred that may have contributed to or resulted in the patient's death
- 'Data Collection Form 2' is designed to collect data of the suspected ADE, and is discussed in more detail below (see Part 5 and Figure 5).

Data collection forms (1 and 2)

Figure 3 – Medication discrepancy form, page 1 and 2

Data Collection Form 1 (Medication Discrepancy Form)

Directions:
Please complete one form per individual patient discharge screened during the study.
Please tick the appropriate circle

A. Data collector

Data collector initials	FQ	**Pharmacist type**	◯ Practice employed pharmacist ● NIPPS ◯ Other. Please specify: .....
Data collected relates to which stage of e-referral implementation			◯ Pre-implementation stage ● Post-implementation stage
Date of data collection (dd/mm/yyyy)			30/09/2019
NHS practice number (please see study guide)			II

B. Patient demographics

Patient study number (please see study guide)	005		
Patient age (years)	72	**Patient gender**	● Male ◯ Female
Drug allergies/ drug intolerances	● No ◯ Yes. If yes, what is the medication(s) involved and nature of reaction(s)?		
Ethnic group	● White ◯ Black ◯ Asian ◯ Other. Please specify:		
Setting patient discharged from hospital to	◯ Home ◯ Residential home ◯ Nursing home ◯ Other. Please specify:		
Hospital discharge diagnosis	ACS		
Discharge ward	● Medical ◯ Surgical ◯ Unspecified ◯ Other. Please specify:		
Date of hospital admission (dd/mm/yyyy)			01/05/2019
Date of hospital discharge (dd/mm/yyyy)			07/05/2019

C. Patient eligibility criteria

Patient discharged from an in-patient hospital stay at [redacted]	● Yes ◯ No. **'If 'no' do not proceed further with data collection**
Patient stayed at least 24 hours in [redacted] **hospital**	● Yes ◯ No. **'If 'no' do not proceed further with data collection'**
Patient discharged from emergency department	◯ Yes. **'If 'yes' do not proceed further with data collection'** ● No
Patient have a medication reconciliation or (equivalent activity)	● Yes ◯ No. **'If 'no' do not proceed further with data collection**
Type of hospital admission	● Emergency admission ◯ Planned admission including; e.g. dialysis, day-case surgery, chemotherapy or transfusion-related. **'If 'Planned admission' do not proceed further with data collection'**
Reasons for e-referral (ONLY COMPLETE FOR PATIENTS SCREENED WHO WERE DISCHARGED AFTER E-REFERRAL SERVICE WENT LIVE) (can choose more than one circle)	◯ New MDS ● Recurrent MDS ◯ Needs any additional service. Please specify: ..... ◯ Not referred through e-referral. **If so, do not proceed further with data collection unless collecting data for patient screened before the e-referral system went live**

D. Medication reconciliation (or equivalent) documented activity

Which entry(ies) were used for data collection		● Medication reconciliation. Please specify: *Medication reconciliation using the read code in vision system* ..... ○ Other equivalent medicidation activity (Please see data collection guide). Please specify:	
Please specify the profession of the person who completed the entry(ies)		~~Pharmacist~~	
Date hospital discharge summary was available to practice (dd/mm/yyyy)	22/05/2019	**Date of medication reconciliation (or equivalent activity) (dd/mm/yyyy)**	25/05/2019
Practice electronic health record software used	●Vision ○ EMIS	**Number of medication discrepancies identified**	2
Total number of prescribed medications following medication reconciliation (including PRN)	6	**Number of PRN medications following medication reconciliation**	1

Figure 4 – Medication discrepancy form, page 3

E. Medication discrepancies documented

Patient study number (.....)

Direction: Copy this page if number of medication discrepancies is more than what can be fit within one page

Description of discrepancies **Name, dose, frequency, formulation of medications involved** *(each row represents one discrepancy)*	**Severity of discrepancy** *(NCC MERP)* *(Please see study guide)*	**Actual or potential harm**	**Action taken** *Please specify the nature of the contact* *(can select more than one action)* • Contct GP (Accepted, rejected, unknown) • Contact patient (Successful, unsusseful) • Other. Please specify

End of data collection form 1

5. Data Collection Form 2- Collecting medication related harm (Adverse Drug Event) data

In 'Data Collection Form 2' (See Figure 6), please screen healthcare record and laboratory results and record any suspected drug related harm (adverse drug events) that you identify in patient records during **three months post hospital discharge**, and provide us with a full description of what happened (what is the ADE detected, what is/are trigger identified, and what are the factors that help describe the harm or potential reason(s) it occurred). It is possible that one patient may experience more than one episode of medication related harm (ADE) during the 3 months period post hospital discharge. If you find that your patient has more than one suspected ADE, complete a copy of 'Data Collection Form 2' for each suspected harm episode that you identify and return to the research team together with 'Data Collection Form 1' for that discharged patient. In case the suspected harm involves multiple medications, please describe in detail the medications involved and the reason(s) why the event happened. Please do not use any patient identifiable data in describing the incident in the data collection form.

It is recommended that when in doubt about whether something is an ADE, you should record it anyway and provide as much data as possible as there is going to be an expert panel to assist validating the event.

Data Collection Form 2 comprises three sections, namely section A, section B, and section C.

- In section A, please answer questions 1, 2 and 3 in as much detail as possible regarding the nature of suspected patient ADE, the outcome associated with this ADE (to help us assessing the severity of the reported ADEs) and any history potentially related to the reported ADE (e.g. laboratory result, potential drug-drug interaction, smoking and alcohol use and liver/kidney problems) to help us confirm the presence of ADE.
- Please include details of any drugs involved with the ADE you describe in section B (including name, dose, frequency, route and when the medication has started).
- In section C of 'Data Collection Form 2' (See Figure 6), please describe thoroughly your thoughts on the likelihood that a particular drug(s) is/are the cause of the observed ADE (Question 1) and how avoidable you think the harm is/was (Question 2). This will help us further assessing the causality and avoidability of the reported harm. Additional boxes are provided for information you believe is relevant.

Figure 5- Data collection form 2 , page 1

Data collection form 2 (Suspected Adverse Drug Event Form)

Kindly screen general practice medical record data for a time period of three months following hospital discharge

Kindly be advised that each adverse drug event identified must be completed on separate forms for each patient discharge screened during the study

Patient study number (……)

A. Suspected adverse drug event description

1. Please provide a full description of the suspected drug related harm (adverse drug event): • What is the suspected adverse drug event? **Describe the event/ (e.g. pain, rash, constipation)** • What is/are the potential trigger(s) of this harm? • Are there any factors that help describe the harm or potential reason(s) it occurred? (for example, medication discrepancy, pre-existing medical condition, non-adherence, drug-drug interaction, allergies, smoking and alcohol use, liver/kidney problems, test/laboratory results) • How was the suspected adverse event identified? (for example, change of medication, laboratory results, antidotes use, high clinical priority read code, healthcare utilization, hospital admission, death) • When was the suspected adverse drug event first reported? (for example, dd/mm/yyyy, or how many days-weeks following hospital discharge?
2. Please describe what happened to the patient following the suspected adverse drug event, for example: • Life-threatening consequences or death • Disability or permanent damage of any nature • Hospital admission for any reason, referral to a specialist, contact with primary care health care staff • Other serious medical events that might require intervention to prevent permanent impairment
3. What was the corrective action, if any? (for example, additional monitoring and/or treatment required, drug stopped, changed, continued or dose altered)

Figure 6– Data collection form 2, page 2

B. Details of drug(s) involved in the suspected adverse drug event

Name of drug(s)	Dose & frequency	Route	Comment e.g. new drug (started within last 7 days), changes made to regimen, should not have been continued, discrepancy related, others

C. Causality and preventability assessment

Please describe the likelihood that a particular drug(s) is/are the cause of the observed suspected adverse drug event. For example: • Was the drug(s) initiated/removed/changed before adverse drug event was observed? • Were other potential cause(s) of this harm excluded? • Did removal of the drug(s) improve the patient's condition?	
Do you think the observed suspected adverse drug event could have been avoided by any means? (Do you think that the event was preventable?) Please explain	◯ Preventable ◯ Non-preventable Explain:
Other relevant details about the suspected adverse drug event:	

End of data collection form 2

6. Terminating Data Collection

In the event that a patient had another hospital stay (readmitted) within three months following hospital discharge, please confirm the suspected/actual reason(s) for hospital admission and if medication(s) were involved. If you found cases where patients are re-admitted and then discharged again during your 3 months follow up window please only collect data for that patient up until their hospital admission and do not restart once they are discharged back to the community again. This is because each discharge may be considered a new 'patient' in the study and if they are sent home again as this may start a new TCAM referral if in the post-implementation phase.
In addition, data collection should be stopped in case; patient transfer to another hospital or patient death.

7. Frequently Asked Questions

1. **Does the medication discrepancy have to be identified from pharmacist medication reconciliation notes?**
   No. Whilst medication reconciliation entries are the primary source of this information, if a medicines reconciliation entry is not present medication discrepancies may also be identified from any equivalent medication review activity that was completed in the practice by any practice staff member including; a pharmacist, pharmacy technicians, physician, nurse or administration staff. You can record which type of medicines related note entry was used as the source of discrepancies in 'data collection form 1'.

2. **How long does it take to screen and complete data collection for one patient?**
   Based in pilot work, we estimate that it will take 10-15 minutes to screen and complete data collection forms for one discharged patient.

3. **How do I know if a patient has an ADE? Do I have to read the entire record?**
   Yes, you advised to read the entire record and laboratory results. Look for ADE triggers, however, remember that a positive trigger does not always yield an adverse drug event.

4. **Do medication discrepancies need to be moderate or severe in severity to be reported in data collection form?**
   No, all medication discrepancies need to be reported regardless of their potential or actual severity.

5. **Should I report medication discrepancies even if I am uncertain?**
   Yes, as each medication discrepancy will be further assessed by a multidisciplinary panel who will confirm whether the event is considered a discrepancy or not. Therefore, it is really important that you report as much information as much as you can so the panel can make decision.

6. **Do the medication related harm events (ADEs) that I find need to be severe to be reported on the data collection form?**
   No, all suspected ADEs need to be reported regardless of their severity. If you are not sure whether an ADE has occurred, please report it anyway as all data will be scrutinised by an expert panel to confirm whether an ADE occurred.

7. **Should I report a medication related harm event (ADE) even if I am uncertain whether it is an ADE or not, or I do not have enough information to support my decision that actual harm has occurred?**

   Yes, as each ADE will be further assessed by a multidisciplinary panel who will confirm whether the harm has occurred or not. Therefore, it is really important that you need to record as much information as you can so the panel can make decision.

8. **Should I report medication related harm due to patient non-adherence?**

   Remember, in many cases medications may be altered due to harm because of non-adherence to treatment by the patient – this should be recorded as an ADE. In some cases, non-adherence itself may be related to the presence of one or more additional ADEs associated with medications, for example a patient may suffer side effects and stop taking their medication. So please ensure that you investigate the reason(s) for non-adherence as this may indicate that an additional ADE has occurred. In addition, please record ADE associated with drug overdose whether they are intentional or accidental overdoses.

9. **What if a particular patient is discharged from hospital more than once during the data collection period, what do I do in this situation?**

   Each patient who has been discharged from hospitals more than once within the study data collection period will be counted as new hospital discharge. Therefore, each discharge is evaluated as a separate discharge even though it is the same patient.

10. **What if a particular patient had another hospital stay (readmitted) within three months following hospital discharge, what do I do in this situation?**

    It is recommended to confirm the reason of hospital admission and if medication were involved. If you found cases where patients are re-admitted and then discharged again during your 3 months follow up window. You need to be clear that you should stop collecting data if a paitent is admitted to hospital and not restart if they are sent home again as this may start a new TCAM referral.

11. **What if I encounter cases of medication discrepancy and/or ADE that still a carry risk to patient safety and have not been recognised during the normal care?**

    You need to report this issue to your line management, the clinical team responsible for the care of affected patient(s) and by using local incident reporting systems. Please continue to record these details on the data collection forms for this study.

12. **What if I have encountered cases of malpractice or/and negligence, what should I do in this situation?**

    Any sign of malpractice/negligence that may not have been previously recognised or adequately addressed at the time, you need to report the details to your line manager for follow up investigation.

13. **Where should I store the master patient link code sheet forms?**

    Please store the master patient link code sheet forms in a locked filing cabinet at your practice and ensure only you can access it.

14. **What if I can not collect data myself, can I ask one of my colleagues to collect the data?**

    Please contact project lead; Fatema Alqenae via phone or email as soon as possible to discuss further.

15. **What should I do if I do not want to collect data anymore?**

    Please contact project lead; Fatema Alqenae via phone number or email as soon as possible to discuss further.

16. **What happen if I mentioned any patient identifiable data in the data collection form?**

Please do not mention any patient identifiable data in the data ollection form. If any form received to the research team at University of Manchester with any identifiable data, the team will contact you to send another version and the data will not be used in the analysis.

17. **What should I do if I experience distress when I am screening medical records and recording medication incidents ?**

- In this case we advise you to consider stopping collecting data and go to quiet and comfortable space to disengage from the study.
- Remind yourself that the anonymity of the patient, data collectors and NHS general practice site are preserved.
- Report the distress incident to your line manager and the study lead, Fatema Alqenae.
- In case you require professional counselling services you can contact your local occupational health department, or one of the following services:

1. **Royal Pharmaceutical Society**
   Tel: 0845 257 2570 (member support services)
   Web: http://www.rpharms.com/support/enquiry-service.asp

2. **Pharmacist Support**
   Tel: 0808 168 2233 (free support services)
   Web: http://www.pharmacistsupport.org/

8. ADE trigger tool

The Institute for Healthcare Improvement developed a global "trigger tool" which are clues to help identify possible ADEs. These triggers maybe useful clues or identifiable flags in patient records that could alert you to any potential adverse drug events

Please note that this list is not exhaustive- instead this contains some useful clues for ADEs that may occur and reviewers are also likely to detect ADEs not associated with the 'triggers' provided.

Remember, in many cases medications may be altered due to harm because of non-adherence to treatment by the patient – this should be recorded as an ADE. In some cases, non-adherence itself may be related to the presence of one or more additional ADEs associated with medications, for example a patient may suffer side effects and stop taking their medication. So please ensure that you investigate the reason(s) for non-adherence as this may indicate that an additional ADE has occurred. In addition, please record ADE associated with drug overdose whether they are intentional or accidental overdoses.

Below are three triggers tool:

a. Outpatient adverse event tool (Institute for Healthcare Improvement, 2006)
b. Skilled Nursing Facility Trigger Tool for Measuring ADE (Institute for Healthcare Improvement, 2015)
c. Trigger Tool for Measuring Adverse Drug Events (Institute for Healthcare Improvement, 2004)

A. Outpatient Adverse Event Trigger Tool

- **Nursing Home Placement**

Determine if the placement was the result of an event, such as oversedation causing a fall and hip fracture or a surgical misadventure requiring long-term care.

- **Admission and Discharge from the Hospital**

Determine if the reason for admission was related to an event related to any health care interaction, either inpatient or outpatient.

- **Frequent GP visits in 6 months periodof Review**

Multiple GP visitcan be the result of a medical misadventure. Look for unintended events from other care that required consultation with others afterwards.

- **Surgical Procedure**

Look for evidence of pulmonary embolism, deep vein thrombosis, wound dehiscence, infection, hemorrhage, hematoma, etc. – any of the unintended events that can occur from surgery either while the patient was in the hospital or after discharge.

- **ED Visit**

Look for the reason for the visit, specifically for an adverse event related to other care that required ED care or events related to the ED visit.

- **Greater Than 5 Medications**

Evidence exists that patients taking greater than 5 medications have a high incidence of adverse medication events. Look for drug-drug interactions, particularly oversedation or overmedication, and development of toxicity.

- **Physician Change**

Look for an abrupt change from a mid-level provider to a physician or out of network referral. Was there an abrupt change in the physician in charge? What might that reason be?
Look for adverse events.

- **Complaint Letter**

Look to see if the complaint related to an event (i.e., request for the waiver of co-payment, payment or concern about quality of care).

- **Greater Than 3 Nursing Calls in One Week**

Calls might all be related to one event.

- **Abnormal Lab Value**

Patients with results outside of range have greater risk of experiencing an adverse event. The lab value itself is only a trigger, so look for evidence of harm. Pay particular attention to lab values related to high-risk medications, such as INR >6 or Glucose <50.

- **Additional Triggers (to be used if desired):**

- Abrupt medication stop
- Sudden change in treatment or care plan
- Outpatient code or arrest

B. IHI Skilled Nursing Facility Trigger Tool for Measuring Adverse Events

- **Abnormal electrolytes**

In general, for example, the resident develops hypokalemia or hyponatremia (above or below lower limits of laboratory) without signs and symptoms such as lightheadedness, confusion, EKG changes, low blood pressure, or decrease in urinary output or difficulty breathing are not considered adverse events. Exceptions that may be considered adverse events based on lab values, even without signs or symptoms, are rising serum creatinine and hyperkalemia.

- **Abrupt medication stop**

Although the discontinuation of medications is a common finding in the record, abruptly stopping medications is a trigger that requires further investigation for cause. A sudden change in resident condition requiring adjustment of medications is often related to an adverse event. This trigger is most useful when many medications are suddenly stopped, suggesting something dramatic has occurred to the resident. "Abrupt" is best described as an unexpected stop or deviation from typical ordering practice; for example, discontinuation of an intravenous antibiotic to switch to oral is not unexpected.

- **Antiemetic use**

Nausea and vomiting commonly are the result of drug administrations both in surgical and non-surgical settings. Antiemetics are commonly administered. Nausea and vomiting that interferes with feeding or delayed discharge suggests an adverse event. One or two episodes treated successfully with antiemetics would not suggest an adverse event. Reviewer judgment is needed to determine whether harm occurred.

- **Diphenhydramine use**

Diphenhydramine is frequently used for allergic reactions to drugs, but can also be ordered as a sleep aid or for seasonal allergies. If the drug has been administered, review the record to determine if it was ordered for symptoms of an allergic reaction to a drug administered during the SNF stay. This would indicate an adverse event. Also diphenhydramine use in the elderly may result in adverse events due to its anticholinergic side effects (i.e., delirium, constipation, urinary retention, and hallucinations).

- **Elevated INR**

An elevated International Normalized Ratio (INR) laboratory test is not considered an adverse event unless the elevated INR is associated with signs and symptoms of bleeding. Look for evidence of bleeding due to medications to determine if an adverse event has occurred. Any value above the laboratory normal should be reviewed.

- **Epinephrine use**

Epinephrine use on a SNF resident with a severe allergic (i.e., anaphylactic) reaction is considered an adverse event, regardless of whether it was preventable.

- **Glucose <50mg/dL, glucagon or dextrose supplement given**

Review for symptoms such as lethargy and shakiness documented in nursing notes, and the administration of glucose, orange juice, or other intervention. In addition, an abnormal lab result with no symptoms is considered an adverse event if glucose <50mg/dL because most residents have physiologic changes that may not be

documented or recognized by the resident due to cognitive disorders. If symptoms are present, or blood glucose <50mg/dL, review diabetic flow sheets, glucose monitoring flow sheets, nursing notes, laboratory tests orders, and medication administration record for symptoms, laboratory value, and associated use of insulin or oral hypoglycemic.

- **Abrupt onset hypotension**

Abrupt onset hypotension, defined as systolic blood pressure less than 90mmHg, may be due to the resident's underlying condition, but often may be related to an adverse event secondary to medications, including muscle relaxants, pain medications, sedatives, or diuretics. Review for symptoms such as resident feeling like he/she is going to pass out, has weakness, or has a lack of coherence. Look for actions such as paging the physician, flattening the bed, or starting IVs.

- **Naloxone use**

Naloxone is a powerful narcotic antagonist. Usage likely represents an adverse event since excess narcotic administration may result in a spectrum of clinical signs and symptoms, ranging from oversedation to respiratory failure.

- **Sodium polystyrene administration**

Sodium polystyrene sulfonate is used in the treatment of hyperkalemia and aids in the removal of excess potassium from the body. Look for the reason for hyperkalemia and whether the resident had been receiving potassium. Administration of sodium polystyrene may be in response to an overdose of potassium, which is considered an adverse event. Hyperkalemia should be considered an adverse event for any potassium (K+) greater than or equal to (≥) 6.5, regardless of whether there are associated signs and symptoms.

- **Abnormal drug levels**

If laboratory tests are sub-therapeutic (below therapeutic limit) or supra-therapeutic (above upper therapeutic limit), review the SNF record progress notes for documentation of a potential adverse event. Examples include inadequate seizure medication, serum drug levels leading to a seizure, or an elevated aminoglycoside serum drug level that leads to acute kidney injury.

- **Thrombocytopenia**

Certain medications can cause platelet counts in the blood to drop, placing residents at greater risk for bleeding. Look for adverse events related to bleeding such as strokes, hematomas, and hemorrhage requiring blood transfusions. Look for information about why the platelet count decreased to see if it was as a result of a medication. Usually, a platelet transfusion is an indication that the resident has a low platelet count. Events related to transfusions or bleeding may indicate that an adverse drug event may have occurred.
M13–Total WBC count <3,000 (or >12,000)

Follow the white blood cell (WBC) counts throughout the admission and see if the resident becomes symptomatic due to infection. An elevated WBC count may indicate a new infection or progression of an existing infection. In some cases, a low WBC count will occur in response to drug administration (and is not considered an adverse event, in this case). Infection is most likely to occur if the Absolute Neutrophil Count is less than 1,000. Intentional decrease in leukocyte count as part of planned chemotherapy is also not an adverse event. If a decrease in WBC count occurs in the absence of medications that may cause this, an adverse event related to drugs has not occurred; for example, when due to bone marrow infiltration by cancer, this is not considered an adverse event.

- **Vitamin K administration**

If Vitamin K was used as a response to a prolonged prothrombin time or elevated INR levels, it may signal an adverse event. If either lab value is high, review the resident record for evidence of bleeding. Look in the lab reports for a decrease in hematocrit or for guaiac-positive stools. Check the progress notes for evidence of excessive bruising or gastrointestinal bleeding. Less likely, a hemorrhagic stroke or other internal bleeding may have occurred. If any of these is found, it is likely that an adverse event has occurred.

- **Antibiotics started in SNF**

Review the SNF record for documentation of a SNF-acquired healthcare-associated infection or other signs or symptoms from unintentional medication side effects such as nausea, vomiting diarrhea, elevated serum creatinine, or allergic reactions (e.g., a rash).

- **Increasing pain medication needs**

Increases in pain medications may be required to control SNF residents' pain. However, increases may also signal an adverse event such as a fall with injury, procedural or post-operative complication, prolonged constipation, or worsening pressure ulcers.

C. **IHI Trigger Tool for Measuring Adverse Drug Events**

- **Diphenhydramine (Benadryl)**

Diphenhydramine is frequently used for allergic reactions to drugs. Benadryl may signal a possible ADE, but can also be ordered as a sleep aid, a pre-operative or pre-procedure medication, or for seasonal allergies. If Benadryl has been administered, review the chart to determine if it was ordered for symptoms of an allergic reaction to a drug administered either during the hospitalization or prior to admission.

- **Vitamin K (Aqua-mephyton)**

If Vitamin K was used as a response to a prolonged prothrombin time or elevated International Normalized Ration (INR) levels, it may signal an ADE. If either lab value is high, review the chart for evidence of bleeding. Look in the lab reports for a drop in hematocrit or for guiac-positive stools. Check the progress notes for evidence of excessive bruising or gastrointestinal bleeding. Less likely, a hemorrhagic stroke or other internal bleeding may have occurred. If any of these is found, it is likely that an ADE has occurred.

- **Flumazenil (Romazicon)**

This drug reverses benzodiazepine drugs. Determine why the drug was used. If hypotension or marked, prolonged sedation occurred following benzodiazepine administration, an ADE may have occurred.

- **Anti-emetics (Droperidol (Inapsine); Ondanestron (Zofran); Promethazine (Phenergan); Hydroxyzine (Vistaril); Trimethobenzamide (Tigan); Prochlorperazine (Compazine); or Metoclopramine (Reglan)**

Nausea and vomiting can be the result of drug toxicity or overdose, particularly in patients with impaired renal function. Drugs such as theophylline preparations frequently cause nausea and vomiting when levels get high. Anti-emetics are also commonly administered to patients postoperatively or to patients receiving chemotherapy. Chart reviewers must use professional judgment in these situations to determine if an ADE may have occurred.

- **Naloxone (Narcan)**

This is a powerful narcotic antagonist. Use of Narcan frequently indicates overdosage of narcotics. If Narcan was used and the patient's condition changed, excessive narcotic administration, which is an ADE, probably has occurred.

- **Anti-diarrheals**

Look for antibiotic-caused infections of *Clostridium difficile*. If the *C. difficile* was not ordered and significant diarrhea occurred in a patient receiving multiple antibiotics, it is likely that an ADE has occurred.

- **Sodium Polystyrene (Kayexalate)**

Sodium polystyrene sulfonate is used in the treatment of hyperkalemia. The drug aids in the removal of excess potassium from the body. Look for the reason for hyperkalemia and whether the patient had been receiving potassium. Administration of Kayexalate may be in response to an overdose of potassium, which would be an ADE.

- **Glucose < 50**

Low serum glucose does not necessarily mean an ADE occurred. Look for evidence of symptoms and administration of glucose (orally or IV). Not all patients will be symptomatic. In addition, look for signs or symptoms in the nursing notes about lethargy, shakiness, etc., to determine if an ADE has occurred.

- ***Clostridium difficile* Positive Stool**

If a patient is on multiple antibiotics, a stool positive for *Clostridium difficile* is a likely complication and an indication of an ADE.

- **Partial Thromboplastin Time (PTT) > 100 seconds**

As with Vitamin K, look for evidence of bleeding to determine if an ADE has occurred. High PTT is not an infrequent occurrence when patients are on heparin. Use professional judgment for patients with high PTTs receiving heparin during a surgical procedure.

- **International Normalized Ration (INR) Level > 6**

Again, an elevated INR is not an infrequent occurrence when patients are on warfarin (Coumadin). Look for evidence of bleeding to determine if an ADE has occurred.

- **T12 White Blood Cell (WBC) Count < 3,000**

In some cases, a low WBC count will occur in response to drug administration. Follow the WBC counts throughout the admission and see what has happened. If leukopenia is related to drugs such as Indocin, a drop in WBC should be evident. Don't include patients currently receiving chemotherapy. If a drop in WBC occurs in the absence of medications that may cause this, an ADE has not occurred.

- **Platelet Count < 50,000**

Certain medications can cause platelet counts in the blood to drop, placing patients at greater risk for bleeding. Look for adverse events related to bleeding such as strokes, hematomas, and hemorrhage requiring blood transfusions. Look for information about why the platelet count decreased to see if it was as a result of a medication. Usually, a platelet transfusion is an indication that the patient has a low platelet count. Events related to transfusions or bleeding may indicate that an ADE may have occurred.

- **Digoxin Level > 2 ng/ mL**

This heart medication provides benefits within a continuous therapeutic range depending on the patient and the condition. When the level exceeds this range, some patients get benefits, but in others, toxicity may occur. The toxicity frequently manifests itself as arrhythmias or bradycardia, but may also include nausea, vomiting, anorexia, and vision changes even without cardiac symptoms. If the level is greater than the therapeutic range, look for evidence that the patient had complications related to this drug or required other interventions as signs that an ADE may have occurred.

- **Rising Serum Creatinine**

Certain medications, especially aminoglycosides, diuretics, and anti-hypertensive medications can cause renal toxicity, which may become evident when serum creatinine levels start rising. Look at several sequential results to see if levels rose. If they did, check to see if the patient received medications that are known to be nephrotoxic. If interventions were required to correct renal problems, an ADE may have occurred.

- **Over-sedation, Lethargy, Falls**

Look in the physician progress notes, nursing notes, or multidisciplinary notes for evidence of over-sedation, lethargy, and falls. If any of these triggers appears, look for a relationship between the event and administration of a sedative, analgesic, or muscle relaxant. If oversedation, lethargy, or falls occurred as a result of administration of a sedative, analgesic, or muscle relaxant, an ADE has occurred. Include falls related to an ADE and resulting in the admission. Do not include intentional overdose resulting in sedation.

- **Rash**

There are many causes for a rash. To determine if an ADE has occurred, look for evidence that the rash is related to drug administration. For example, a yeast infection may indicate overuse of antibiotics.

- **Abrupt or Gradual Cessation of Medication**

In the order sets, whenever "hold" or "stop" medication orders appear, look for the reason. These orders frequently indicate that an ADE has occurred.

- **Transfer to a Higher Level of Care**

Transfer to a higher level of care includes transfers within the institution, to another institution from yours, or to your institution from another. Transfer of a patient to a higher level of care is only a trigger, a clue that an ADE may have occurred. A higher level of care is indicated when a patient's clinical condition deteriorates or becomes more serious. This is a result of a change in clinical condition or sometimes following a major procedure. However, in some cases an adverse drug event is the cause of the change in condition. When reviewing this trigger, look for the reasons for the transfer and the change in condition. If the clinical condition can be linked to any medications, this may be an indication that an ADE has occurred. For example, in the case of transfer to intensive care following respiratory arrest and intubation, if the respiratory arrest was a complication of chronic obstructive pulmonary disease (COPD), it would not be an ADE, but if it was caused by use of a narcotic or sedative, it would be an AD

- **Abrupt or gradual reduction of dose of medication**

May indicate that an ADE has occurred but professional judgment is required.

- **Laxatives prescribed**

There are many causes of constipation necessitating the prescription of laxatives. To determine if an ADE is likely to have occurred, look for evidence that the prescription of laxatives is related to drug administration Professional judgment will be necessary.

- **Stat, PRN or regular prescription for antihistamines (e.g., Chlorpheniramine, Promethazine, Diphenhydramine)**

Antihistamines are frequently used for allergic reactions to drugs but can also be ordered as a sleep aid, as a preoperative or pre-procedure medication, or for seasonal allergies. If an antihistamine has been administered, review the record to determine if it was ordered for symptoms of an allergic reaction to a drug administered.

- **Prescription of potassium supplements (e.g. Slow-K® (Alliance), Sando-K® (HK Pharma), and Kay-Cee-L® (Geistlich).**

These medications used in the treatment of hyperkalaemia and aids in the removal of excess potassium from the body. Look for the reason for hyperkalaemia and whether the patient had been receiving potassium. Administration of SPS may be in response to an overdose of potassium, which would be an ADE. Drugs which can cause hyperkalaemia include potassium-sparing diuretics, NSAIDs, and ACE inhibitors.

- **Drug levels**

With any drug level above normal particularly medication with a narrow therapeutic index (e.g. Digoxin level >2 ng/ml, Lidocaine level >5 ng/ml, Gentamicin or tobramycin levels: peak >10 mg/ml, trough >2 mg/ml, Amikacin levels: peak >30 mg/ml, trough >10 mg/ml, Vancomycin level >26 mg/ml, Theophylline level >20 mg/ml, Phenytoin (Free) level > 2 mg/L), look for evidence of ADEs. If any signs or symptoms have occurred, it is considered an ADE. Please note that not all levels above normal will result in an ADE.

9.35 Appendix 35 – Master Patient Link Code Sheet

MANCHESTER 1824
The University of Manchester

Version 3 25.05.2019
IRAS Project ID: 262688

Master Patient Link Code Sheet

Date:	
General practice name:	
General practice number*:	
Data collector:	
Patient NHS number	**Patient link code***

*Guidance on practice number and generating patient link code is in the data collection guide.

Please use multiple sheets if required.

Please store in Masterfile in secure place in the practice.

Master patient link code sheet – [redacted] eTCP evaluation
Lead Researcher (Fatema Alqenae). Tel: 0161 306 0620. Email: fatema.alqenae@postgrad.manchester.ac.uk

9.36 Appendix 36 – Data Collection forms

MANCHESTER 1824
The University of Manchester

Version 11 10.10.2020
IRAS Project ID: 262688

Data Collection Form 1 (Medication Discrepancy Form)

Directions:

Please complete one form per individual patient discharge screened during the study.

Please tick the appropriate circle

A. Data collector

Data collector initials		Pharmacist type	☐Practice employed pharmacist ☐NIPPS ☐Other. Please specify: .....
Data collected relates to which stage of e-referral implementation			☐Pre-implementation stage ☐Post-implementation stage
Date of data collection (dd/mm/yyyy)			Click or tap to enter a date.
NHS practice number (please see study guide)			

B. Patient demographics

Patient study number (please see study guide)			
Patient age (years)		Patient gender	☐ Male ☐Female
Drug allergies/ drug intolerances	☐ No ☐ Yes. If yes, what is the medication(s) involved and nature of reaction(s)?		
Ethnic group	☐White ☐ Black ☐ Asian ☐Other. Please specify:		
Setting patient discharged from hospital to	☐ Home ☐Residential home ☐ Nursing home ☐ Other. Please specify:		
Hospital discharge diagnosis			
Discharge ward	☐Medical ☐Surgical ☐ Unspecified ☐ Other. Please specify:		
Date of hospital admission (dd/mm/yyyy)			Click or tap to enter a date.
Date of hospital discharge (dd/mm/yyyy)			Click or tap to enter a date.

C. Patient eligibility criteria

Patient discharged from an in-patient hospital stay at [redacted]	☐Yes ☐No. 'If 'no' do not proceed further with data collection
Patient stayed at least 24 hours in [redacted] hospital	☐Yes ☐No. 'If 'no' do not proceed further with data collection'
Patient discharged from emergency department	☐Yes. 'If 'yes' do not proceed further with data collection' ☐No
Patient have a medication reconciliation or (equivalent activity)	☐Yes ☐No. 'If 'no' do not proceed further with data collection
Type of hospital admission	☐Emergency admission ☐Planned admission including; e.g. dialysis, day-case surgery, chemotherapy or transfusion-related. 'If 'Planned admission' do not proceed further with data collection'
Reasons for e-referral (ONLY COMPLETE FOR PATIENTS SCREENED WHO WERE DISCHARGED AFTER E-REFERRAL SERVICE WENT LIVE) (can choose more than one circle)	☐New MDS ☐Recurrent MDS ☐Needs any additional service. Please specify: ..... ☐Not referred through e-referral. If so, do not proceed further with data collection unless collecting data for patient screened before the e-referral system went live

Data collection forms, Evaluation of Medication Discrepancies and Adverse Drug Events Following Transition from Secondary to Primary Care Before and After Implementation of Transfers of Care Around Medicines (TCAM) in [redacted] Greater Manchester
Lead Researcher (Fatema Alqenae). Tel: 0161 306 0620. Email: fatema.alqenae@postgrad.manchester.ac.uk

D. Medication reconciliation (or equivalent) documented activity

Which entry(ies) were used for data collection		☐Medication reconciliation. Please specify: …… …… ☐Other equivalent medication activity (Please see data collection guide). Please specify: …… ……	
Please specify the profession of the person who completed the entry(ies)			
Date hospital discharge summary was available to practice (dd/mm/yyyy)		Date of medication reconciliation (or equivalent activity) (dd/mm/yyyy)	
Practice electronic health record software used	☐Vision ☐EMIS	Number of medication discrepancies identified	
Total number of prescribed medications following medication reconciliation (including PRN)		Number of PRN medications following medication reconciliation	

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Version 11 10.10.2020
IRAS Project ID: 262688

E. Medication discrepancies documented

Patient study number (.....)

Direction: Copy this page if number of medication discrepancies is more than what can be fit within one page

Description of discrepancies Name, dose, frequency, formulation of medications involved *(each row represents one discrepancy)*	Severity of discrepancy *(NCC MERP)* *(Please see study guide)*	Actual or potential harm	Action taken *Please specify the nature of the contact* *(can select more than one action)* • Contct GP (Accepted, rejected, unknown) • Contact patient (Successful, unsusseful) • Other. Please specify

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Version 11 10.10.2020
IRAS Project ID: 262688

Data collection form 2 (Suspected Adverse Drug Event Form)

Kindly screen general practice medical record data for a time period of three months following hospital discharge
Kindly be advised that each adverse drug event identified must be completed on separate forms for each patient discharge screened during the study

Patient study number (.....)

A. Suspected adverse drug event description

1. Please provide a full description of the suspected drug related harm (adverse drug event): • What is the suspected adverse drug event? **Describe the event/ (e.g. pain, rash, constipation)** • What is/are the potential trigger(s) of this harm? • Are there any factors that help describe the harm or potential reason(s) it occurred? (for example, medication discrepancy, pre-existing medical condition, non-adherence, drug-drug interaction, allergies, smoking and alcohol use, liver/kidney problems, test/laboratory results) • How was the suspected adverse event identified? (for example, change of medication, laboratory results, antidotes use, high clinical priority read code, healthcare utilization, hospital admission, death) • When was the suspected adverse drug event first reported? (for example, dd/mm/yyyy, or how many days-weeks following hospital discharge?
2. Please describe what happened to the patient following the suspected adverse drug event, for example: • Life-threatening consequences or death • Disability or permanent damage of any nature • Hospital admission for any reason, referral to a specialist, contact with primary care health care staff • Other serious medical events that might require intervention to prevent permanent impairment
3. What was the corrective action, if any? (for example, additional monitoring and/or treatment required, drug stopped, changed, continued or dose altered)

B. Details of drug(s) involved in the suspected adverse drug event

Name of drug(s)	Dose & frequency	Route	Comment e.g. new drug (started within last 7 days), changes made to regimen, should not have been continued, discrepancy related, others

C. Causality and preventability assessment

Please describe the likelihood that a particular drug(s) is/are the cause of the observed suspected adverse drug event. For example: • Was the drug(s) initiated/removed/changed before adverse drug event was observed? • Were other potential cause(s) of this harm excluded? • Did removal of the drug(s) improve the patient's condition?	
Do you think the observed suspected adverse drug event could have been avoided by any means? (Do you think that the event was preventable?) Please explain	☐Preventable ☐Non-preventable **Explain:**
Other relevant details about the suspected adverse drug event:	

End of data collection form 2

9.37 Appendix 37 – Adverse drug events assessment forms

Individual case review					
Case number:			ADE detected:		
Reviewer name:					
Causality assessment					
Causality assessment criteria [Amended Hallas criteria for causality assessment[185]] 1. Known adverse drug reaction, toxic reaction, response to omission of treatment or inadequate treatment. 2. Reasonable temporal relationship between commencement or cessation/omission of treatment and onset of problem 3. Risk of further problems likely to be reduced by dose reduction or increase, discontinuation, closer monitoring or commencement of treatment. 4. Not explained by any other known condition of predisposition to the patient, or this condition/predisposition is likely to be exacerbated by the presence/absence of the drug. 5. For drug toxicity: symptoms re-appeared upon re-exposure; laboratory tests showed toxic drug levels or drug induced metabolic disturbances that explained the symptom; symptoms resolved on dose reduction or discontinuation of the drug. For drug omission: symptoms resolved upon re-introduction of the drug or dose increase. - If 5 criteria fulfilled then definite, if 4 criteria fulfilled then probable, if 3 criteria fulfilled then possible, if 2 or less criteria fulfilled then either, not drug related or unevaluable					
Assessment result	1	2	3	4	5
Comment:					
Preventability assessment					
Preventability assessment criteria [Hepler criteria for preventability assessment [462]] 1. Drug related morbidity (DRM) proceeded by a recognisable drug therapy problem (DRP). 2. Given the DRP, the DRM would have been reasonably foreseeable. 3. The cause of DRM would have been identifiable with reasonable probability (Hallas criteria probable or definite for causality). 4. The cause of the DRM could have been reasonably controllable within the context and objectives of treatment. All four criteria must be fulfilled to confirm preventability					
Assessment result	Preventable □ Yes □ No				
Comment:					
Severity Assessment					
Severity assessment criteria [National Patient Safety Agency criteria for severity assessment (438)] • Low harm (score 1): Any patient safety incident that required extra observation or minor treatment and which cause minimal harm, to one or more person receiving NHS-funded care • Moderate harm (score 2): Any safety patient incident that resulted in moderate increase in treatment and which caused significant but not permanent harm, to one or more person receiving NHS-funded care • Severe harm (score 3): Any safety patient incident that appears to have resulted in permanent harm to one or more person receiving NHS-funded care • Death (score 4): Any safety patient incident that directly resulted in death of one or more receiving NHS-funded care					
Assessment result	Low		Moderate	Sever	Death
Comment:					

9.38 Appendix 38– Variable and outcomes list 'service impact' study

Variable name	Description, type of variable	Example
Date of DC summary received	Date	11/10/2019
Date of medication reconciliation	Date	12/11/2019
Patient age in years	Categories (n=8)	80
Patient gender	Categories (n=2)	Female
Practice size	Categorical (n=3)	
Data collector initial	Categories (n=16)	FA
Data collector grade	Categories (n=3)	6
Discharge location	Categories	Home
Hospital discharge diagnosis	Categories	Heart failure
Discharge ward	Categories	Medical
Practice study number	Categorical, nominal	1
Practice locality (neighbourhood)	Categorical, nominal	2
Practice electronic system	Categorical, nominal	EMIS
Stage of service implementation	Categorical, nominal	Pre-implementation
Ethnic group	Categorical, nominal	White
Medication reconciliation entry and profession	Free text that was coded as categorical, nominal variable	Pharmacist
Total number of prescribed medications	Categorical	8
Number of PRN medication	Number	2
*Data collection form ID	Number	12
*Date of data collection	Date	Date
*Drug allergy	Categories (n=2)	no
*Date of hospital admission/ discharge	Date	Date
Outcomes	**Description, type of variable**	**Example**
Number of medications discrepancy	Numeric	2
Medication involved in discrepancy	Free text	
Description of medication discrepancy	Free text	
Severity of harm of medication discrepancy	Categorical	A
Description of ADE	Free text	
Name, dose & route of medication involved in ADE	Free text was codded as categorical	
Medication involved in ADE (causality, preventability, harm serenity)	Free text was codded as categorical	

**were not used in the analysis*

9.39 Appendix 39- Medication data categories and codes

BNF	1	2	3	4	5	6	Code
1	Anti-infective	Bacterial infection	Antibacterials	Quinolones		Ciprofloxacin	
2	Blood and blood forming organs	Anaemias	Megaloblastic anaemia	Vitamins and trace elements	Vitamin B group	Cyanocobalamine (vitamin b12)	
3	Cardiovascular system	Blood pressure conditions	Hypertension	Beta-adrenoceptor blockers	Beta blocking agents, selective	Bisoprolol	3001
3	Cardiovascular system	Blood pressure conditions	Hypertension	Calcium-channel blockers		Lercanidipine	3002
3	Cardiovascular system	Blood pressure conditions	Hypertension	Drugs acting on the renin-angiotensin system	ACE inhibitors	Ramipril	3022
3	Cardiovascular system	Blood pressure conditions	Hypertension	Drugs acting on the renin-angiotensin system	ACE inhibitors	Lisinopril	3022
3	Cardiovascular system	Blood pressure conditions	Hypertension	Drugs acting on the renin-angiotensin system	ACE inhibitors	Perindopril	3022
3	Cardiovascular system	Blood pressure conditions	Hypertension	Drugs acting on the renin-angiotensin system	Angiotensin II receptor antagonists	Candesartan	3003
3	Cardiovascular system	Blood pressure conditions	Hypertension	Alpha-adrenoceptor blockers		Doxazosin	3023
3	Cardiovascular system	Blood pressure conditions	Hypertension	Diuretics	Thiazides and related diuretics	Bendroflumethiazide	3004
3	Cardiovascular system	Hyperlipidaemia	Lipid modifying drugs	Statins		Atorvastatin	3006
3	Cardiovascular system	Blood clots	Thromboembolism	Antithrombotic drugs	Factor Xa inhibitors	Apixiaban	3008
3	Cardiovascular system	Blood clots	Thromboembolism	Antithrombotic drugs	Antiplatelet drugs	Aspirin / clopidogrel /prasugrel /Dipyridamole	3009
3	Cardiovascular system	Blood clots	Thromboembolism	Antithrombotic drugs	Vitamin K antagonists	Warfarin	3010
3	Cardiovascular system	Blood clots	Thromboembolism	Antithrombotic drugs	Heparins	Tinzaparin (inohep)	3011
3	Cardiovascular system	Arrhythmias	Cardiac glycosides			Digoxin	3013
3	Cardiovascular system	Arrhythmias	Antiarrhythmics	Antiarrhythmics, class III		Amiodarone	3014
3	Cardiovascular system	Myocardial ischaemia	Acute coronary syndromes	Nitrates		Glyceryl trinitrate (GTN)	3015
3	Cardiovascular system	Myocardial ischaemia	Vasodilators	Potassium-channel openers		Nicorandil	3016
5	Endocrine system	Diabetes mellitus and hypoglycaemia	Diabetes mellitus	Insulin		Insulin (rapid, intermediate, long) acting [Tresiba, Humulin, novorapid, abasaglarins, novomix, kwikpen, Humalog, Levemir, flex pen,	5002
5	Endocrine system	Diabetes mellitus and hypoglycaemia	Diabetes mellitus	Blood glucose lowering drugs	Biguanides	Metformin (Glucophage)	5003
5	Endocrine system	Disorders of bone metabolism	Bisphosphonates			Alendronic acid (fosamax)	5004

5	Endocrine system	Sex hormone responsive conditions	Female sex hormone responsive conditions	Oestrogens combined with progestogens		Estradiol with norethisterone (evorel)	5005
5	Endocrine system	Corticosteroid responsive conditions	Corticosteroids			Fludrocortisone	5007
6	Eye	Ocular lubricants				Carbomers	
7	Gastro-intestinal system	Liver disorders and related conditions	Biliary disorders	Bile acids		Ursodeoxycholic acid	7001
7	Gastro-intestinal	Constipation	Laxatives	Stimulant laxatives		Senna	7002
7	Gastro-intestinal	Disorders of gastric acid and ulceration	Gastric and duodenal ulceration	H2-receptor antagonists		Ranitidine	7003
8	Genito-urinary system	Bladder and urinary disorders	Urinary frequency, enuresis, and incontinence	Antimuscarinics	Antimuscarinics, urinary	**Solifenacin**	
12	Musculoskeletal system	Neuromuscular disorders	Spasticity	Muscle relaxants	Muscle relaxants, centrally acting	Baclofen	
12	Musculoskeletal system	Xanthine oxidase inhibitors				Allopurinol	
13	Nervous system	Mental health disorders	Psychoses and schizophrenia	Antipsychotics	Antipsychotics, second generation	Quetiapine (Seroquel)	13001
13	Nervous system	Mental health disorders	Depression	Antidepressants	Serotonin and noradrenaline re-uptake inhibitors	Duloxetine	13003
13	Nervous system	Mental health disorders	Anxiety	Hypnotics, sedatives, and anxiolytics	Benzodiazepines	Diazepam	13004
13	Nervous system	Epilepsy and other seizure disorders	Antiepileptics	Barbiturates		Phenobarbital	13007
13	Nervous system	Nausea and labyrinth disorders	Antihistamines			Cyclizine	13010
13	Nervous system	Pain	Analgesics	Analgesics, non-opioid		Paracetamol (calpol)	13011
13	Nervous system	Pain	Analgesics	Opioids		Morphine (Zomorph) (oramorph)	13012
13	Nervous system	Local anaesthesia				Lidocaine (instillagel)	13013
13	Nervous system	Substance dependence	Nicotine dependence	Nicotinic receptor agonists		Nicotine	13014
15	Nutrition and metabolic disorders	Fluid and electrolyte imbalances				**Sodium chloride**	
18	Respiratory system	Conditions affecting sputum viscosity	Mucolytics			Carbocisteine	
18	Respiratory system	Airway diseases, obstructive	**Antimuscarinics**			Tiotropium (Spiriva)	
18	Respiratory system	Airway diseases, obstructive	**Beta2-adrenoceptor agonists, selective**	Selective beta2-agonists (short acting)		Salbutamol	
18	Respiratory system	Airway diseases, obstructive	**Corticosteroids**			Beclomethasone with formoterol (fostair)	
19	Skin					Doublebase	

9.40 Appendix 40 - TCAM referrals by month of referral, patient gender and age

Characteristics	Number of un- completed referrals (n=955)[a]	Number of completed referrals (n=2,038)[a]	Number of all referrals (n=3,033)
Month*			
March 2019	43	172	215
April 2019	70	162	232
May 2019	89	176	265
June 2019	83	161	244
July 2019	95	174	269
August 2019	101	147	248
September 2019	62	171	233
October 2019	113	197	310
November 2019	83	156	239
December 2019	101	183	284
January 2020	83	169	252
February 2020	72	170	242
Age**			
20-29	6	8	14
30-39	11	29	40
40-49	32	98	130
50-59	79	179	258
60-69	128	268	396
70-79	231	491	722
80-89	362	729	1,091
90-100	146	236	382
Gender* [b]**			
Female	545	1,168	1,713
Male	449	870	1,319

**Pearson chi2(11) = 33.1190, P-value = 0.001*

***Pearson chi2(7) = 11.0743, P-value = 0.135*

****Pearson chi2(1) =1.6748, P-value = 0.196*

[a]This data without 88 completed referrals, which were later provided and added to the dataset, thus the total included dataset was 2,126

[b]This data without one missing one patient with missing data about the gender

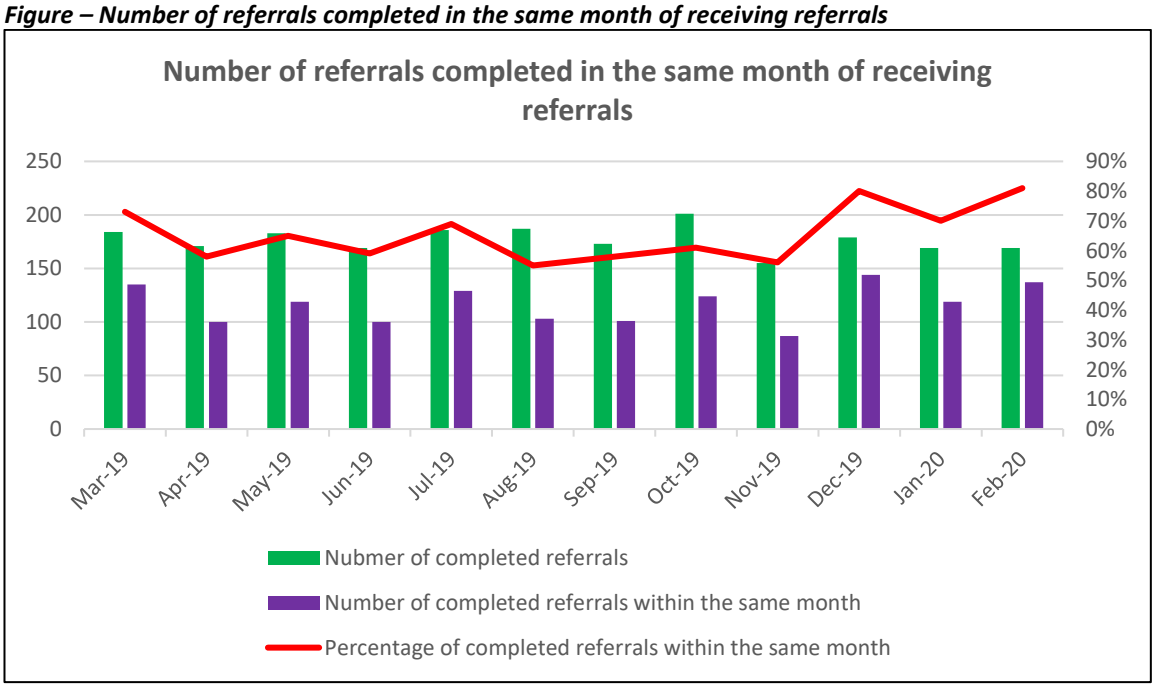
9.41 Appendix 41 - Number of completed TCAM referrals by month of actioning referrals

Table – Number of referrals completed in the same month of receiving referrals

Final date	Month of sending referrals												
	March 2019	April 2019	May 2019	June 2019	July 2019	Aug 2019	Sep 2019	Oct 2019	Nov 2019	Dec 2019	Jan 2020	Feb 2020	Total
March 2019	135 (73%)	0	0	0	0	0	0	0	0	0	0	0	135
April 2019	28	100 (58%)	0	0	0	0	0	0	0	0	0	0	128
May 2019	4	40	119 (65%)	0	0	0	0	0	0	0	0	0	163
June 2019	1	3	31	100 (59%)	0	0	0	0	0	0	0	0	135
July 2019	8	19	20	51	129 (69%)	0	0	0	0	0	0	0	227
Aug 2019	0	0	2	13	41	103 (55%)	0	0	0	0	0	0	159
Sep 2019	0	1	2	1	7	58	101 (58%)	0	0	0	0	0	170
Oct 2019	0	2	3	2	0	2	43	124 (61%)	0	0	0	0	176
Nov 2019	0	0	0	0	0	4	7	41	87 (56%)	0	0	0	139
Dec 2019	0	1	3	0	0	8	4	9	49	144 (80%)	0	0	218
Jan 2020	0	0	0	0	0	0	1	2	7	23	119 (70%)	0	152
Feb 2020	3	0	0	0	3	12	15	21	11	8	49	137 (81%)	259
March 2020	2	0	0	0	0	0	0	0	0	0	0	17	19
April 2020	1	0	0	0	0	0	1	2	1	4	1	6	16
May 2020	1	4	1	1	5	0	1	1	0	0	0	9	23
*	1	1	2	1	1	0	0	1	0	0	0	0	7
Total	184	171	183	169	186	187	173	201	155	179	169	169	2,126

**User errors (final provision date was manually entered by mistake by community pharmacies) – excluded from the analysis here in this table*

Figure – Number of referrals completed in the same month of receiving referrals



9.42 Appendix 42 – Community pharmacy information about the cohort of included patients who received medicines use review (MUR) or new medicines service (NMS) services

Characteristics	Medicines use review (MUR) (n=109)	Medicines use review (NMS) (n=153)
Patient knows the purpose of their medication		
Yes (n=713)	66 (60.5%)	93 (60.7%)
No (n=1,413)	43 (39.4%)	60 (39.2%)
Patient knows how to take/use their medicines		
Yes (n=1,066)	77 (70.6%)	119 (77.7%)
No (n=1,060)	32 (29.3%)	34 (22.2%)
Patient knows when to take/use their medication		
Yes (n=1,312)	78 (71.5%)	121 (79%)
No (n=814)	31 (28.4%)	32 (20.9%)
Respiratory condition		
Yes (n=32)	2 (1.8%)	4 (2.6%)
No (n=2,094)	107 (98.2%)	149 (97.3%)
Diabetes		
Yes (n=38)	3 (2.7%)	5 (3.2%)
No (n=2,088)	106 (97.2%)	148 (96.7%)
Cardiac condition		
Yes (n=165)	5 (4.5%)	4 (2.6%)
No (n=1,961)	104 (95.4%)	149 (97.3%)

9.43 Appendix 43 – Age groups by stage of TCAM service implementation

Age groups	Pre-implementation stage	Post-implementation stage	Total
20-34	3 (1.7%)	3 (1.2%)	6 (1.4%)
35-44	3 (1.7%)	3 (1.2%)	6 (1.4%)
45-54	7 (4.1%)	9 (3.7%)	16 (3.8%)
55-64	16 (9.5%)	26 (10.6%)	42 (10.2%)
65-74	26 (15.4%)	40 (16.4%)	66 (16.0%)
75-84	58 (34.5%)	83 (34.1%)	141 (34.3%)
85-94	46 (27.3%)	67 (27.5%)	113 (27.4%)
95-104	8 (4.7%)	11 (4.5%)	19 (4.6%)
Missing data	1 (0.5%)	1 (0.4%)	2 (0.4%)
Total	**168 (100%)**	**243 (100%)**	**411 (100%)**

9.44 Appendix 44– Hospital discharge diagnosis by stage of TCAM service implementation

Hospital discharge diagnosis (ICD10)	Pre-implementation stage	Post-implementation stage	Total
Symptoms, signs, and lab test (R00- R99)	24 (14.2%)	49 (20.1%)	73 (17.7%)
Disease circulatory system (I00 - I99)	30 (17.8%)	38 (15.6%)	68 (16.8%)
External causes of morbidity (V00 - Y99)	19 (11.3%)	38 (15.6%)	57 (13.8%)
Disease of respiratory system (J00 - J99)	22 (13%)	22 (9.0%)	44 (10.7%)
Diseases of genitourinary system (N00 - N99)	18 (10.7%)	18 (7.4%)	36 (8.7%)
Digestive system (K00 - K95)	14 (8.3%)	14 (5.7%)	28 (6.8%)
Endocrine, nutritional and metabolic diseases (E00-E89)	8 (4.7%)	14 (5.7%)	22 (5.3%)
Injury, poisoning and certain other consequences of external causes (S00-T88)	8 (4.7%)	10 (4.1%)	18 (4.3%)
Nervous system (G00 - G99)	4 (2.3%)	9 (3.7%)	13 (3.1%)
Disease of the musculoskeletal system and connective tissue (M00 - M99)	6 (3.5%)	6 (2.4%)	12 (2.9%)
Mental, Behavioral and Neurodevelopmental disorders (F01-99)	5 (2.9%)	6 (2.4%)	11 (2.6%)
Disease of the skin and subcutaneous tissue (L00-L99)	4 (2.3%)	6 (2.4%)	10 (2.4%)
Certain infection and parasitic diseases (A00-B99)	2 (1.1%)	1 (0.4%)	3 (0.7%)
Factors influencing health status and contact with health services (Z00 - Z99)	1 (0.5%)	2 (0.8%)	3 (0.7%)
Missing data	3 (1.7%)	10 (4.1%)	13 (3.1%)
Total	**168 (100%)**	**243 (100%)**	**411 (100%)**

9.45 Appendix 45- Difference in dates between sending discharge letter from secondary to primary care

Days from sending discharge letter from secondary care to primary care	Pre-implementation stage	Post-implementation stage	Total	%	Cumulative percentage
0	57 (33.9%)	108 (44.4%)	165	40.15	40.15
1	53 (31.5%)	62 (25.5%)	115	27.98	68.13
2	10 (5.9%)	16 (6.5%)	26	6.33	74.45
3	24 (14.2%)	25 (10.2%)	49	11.92	86.37
4	10 (5.9%)	9 (3.7%)	19	4.62	91.00
5	1 (0.5%)	9 (3.7%)	10	2.43	93.43
6	1 (0.5%)	0	1	0.24	93.67
7	2 (1.1%)	3 (1.2%)	5	1.22	94.89
8	1 (0.5%)	0	1	0.24	95.13
9	1 (0.5%)	0	1	0.24	95.38
11	1 (0.5%)	0	1	0.24	95.62
12	0	1 (0.4%)	1	0.24	95.86
19	1 (0.5%)	0	1	0.24	96.11
25	1 (0.5%)	0	1	0.24	96.35
30	0	1 (0.4%)	1	0.24	96.59
123	0	1 (0.4%)	1	0.24	96.84
Missing data	5 (2.9%)	8 (3.2%)	13	3.16	100.00
Total	168 (100%)	243 (100%)	411	100.00	

9.46 Appendix 46 - Profession of staff completing medication reconciliation or related activity

Profession	Data entry		Total
	Medication reconciliation	Other equivalent activity	
Pharmacist / Pharmacy Technician / student Pharmacy technician	278	0	278 (67.6%)
GP / GP trainee / Doctor	0	82	82 (20%)
Practice staff (was not further defined)	0	17	17 (4.1%)
Administrative staff	0	13	13 (3.1%)
More than one staff member (GP and/or practice staff and/or admin staff and/or pharmacist)	0	6	6 (1.4%)
Nurse / Advance nurse practitioner (ANP)	0	4	4 (1%)
Practice manager	0	1	1 (0.2%)
Missing data	7	3	10 (2.4%)
Total	**285**	**126**	**411 (100%)**

9.47 Appendix 47– Unintentional medication discrepancies per data collection forms

➢ Number of unintentional medication discrepancies (X)	➢ Number of data collection forms with (X) unintentional medication discrepancies	➢ Cumulative numbers of forms with at least (X) medication discrepancies
7	2	
5	2	4
3	2	6
2	10	16
1	36	52

9.48 Appendix 48– Demographic of patients affected by unintentional medication discrepancies

Table - Gender and age of patients affected by unintentional medication discrepancies

	Pre-implementation stage		Post-implementation stage		Both stages	
	UMD	Total	UMD	Total	UMD	Total
Gender						
Female	12 (12.3%)	97	18 (12.5%)	144	30 (12.4%)	**241 (100%)**
Male	11 (15.9%)	69	11 (11.2%)	98	22 (13.2%)	**167 (100%)**
Missing data	0	2	0	1	0	**3 (100%)**
Age groups						
<65	5 (21.7%)	29	7 (24.2%)	41	12 (17%)	**70 (100%)**
65+	18 (78.3%)	138	21 (72.4%)	201	39 (11.5%)	**339 (100%)**
Missing data	0	1	1 (3.4%)	1	1 (50%)	**2 (100%)**
Age groups						
20-34	0	3	0	3	0	**6**
35-44	0	3	0	3	0	**6**
45-54	1 (14.2%)	7	2 (22.2%)	9	3 (18.7%)	**16**
55-64	4 (25%)	16	5 (19.2%)	26	9 (21.4%)	**42**
65-74	3 (11.5%)	26	5 (12.5%)	40	8 (12%)	**66**
75-84	9 (15.5%)	58	8 (9.6%)	83	17 (12%)	**141**
85-94	5 (10.8%)	46	7 (10.4%)	67	12 (10.6%)	**113**
95-104	1 (12.5%)	8	1 (9%)	11	2 (10.5%)	**19**
Missing data	0	1	1 (100%)	1	1 (50%)	**2**
Total	**23 (13.6%)**	**168**	**29 (11.9%)**	**243**	**52 (12.7%)**	**411 (100%)**

Table - Hospital discharge diagnosis of patients affected by unintentional medication discrepancies

Hospital discharge diagnosis (ICD10)	Both stages	
	UMDs	Total
Certain infection and parasitic diseases (A00-B99)	0	3
Endocrine, nutritional and metabolic diseases (E00-E89)	2 (9%)	22
Mental, Behavioral and Neurodevelopmental disorders (F01-99)	2 (18%)	11
Nervous system (G00 - G99)	2 (15%)	13
Disease circulatory system (I00 - I99)	10 (15%)	68
Disease of respiratory system (J00 - J99)	5 (11%)	44
Digestive system (K00 - K95)	2 (7%)	28
Disease of the skin and subcutaneous tissue (L00-L99)	2 (20%)	10
Disease of the musculoskeletal system and connective tissue (M00 - M99)	1 (8%)	12
Diseases of genitourinary system (N00 - N99)	2 (5%)	36
Symptoms, signs, and lab test (R00- R99)	8 (11%)	73
Injury, poisoning and certain other consequences of external causes (S00-T88)	3 (17%)	18
External causes of morbidity (V00 - Y99)	11 (19%)	57
Factors influencing health status and contact with health services (Z00 - Z99)	2 (67%)	3
Missing data	0	13
Total	**52 (12.7%)**	**411**

9.49 Appendix 49 – Demographic of patients a*ffected by adverse drug events (ADE) by patient demographics*

	Pre-implementation stage		Post-implementation stage		Both stages	
	ADE	Total	ADE	Total	ADE	Total
Gender						
Female	12 (12.3%)	97	15 (10.4%)	144	27 (11.2%)	241
Male	1 (1.4%)	69	8 (8.1%)	98	9 (5.3%)	167
Missing data	0	2	0	1	0	3
Age group						
20-34	0	3	0	3	0	6
35-44	0	3	1 (33.3%)	3	1 (17%)	6
45-54	0	7	0	9	0	16
55-64	1 (6.2%)	16	1 (3.8%)	26	2 (5%)	42
65-74	0	26	6 (15%)	40	6 (9%)	66
75-84	8 (13.7%)	58	6 (7.2%)	83	14 (10%)	141
85-94	2 (4.3%)	46	9 (13.4%)	67	11 (10%)	113
95-104	2 (25%)	8	0	11	2 (11%)	19
Missing data	0	1	0	1	0	2
Total	**13 (7.7%)**	**168**	**23 (9.4%)**	**243**	**36 (8.7%)**	**411**

9.50 Appendix 50– Patients affected by adverse drug events (ADE) by hospital discharge diagnosis

Hospital discharge diagnosis (ICD10)	Pre-stage		Post-stage		Both stages	
	ADEs	Total	ADEs	Total	ADEs	Total
Symptoms, signs, and lab test (R00- R99)	0	24	6 (12.2%)	49	6 (8.2%)	73
Disease circulatory system (I00 - I99)	4 (13.3%)	30	6 (15.7%)	38	10 (14.7%)	68
External causes of morbidity (V00 - Y99)	1 (5.2%)	19	1 (2.6%)	38	2 (3.5%)	57
Disease of respiratory system (J00 - J99)	3 (13.6%)	22	1 (4.5%)	22	4 (9%)	44
Diseases of genitourinary system (N00 - N99)	1 (5.5%)	18	4 (22.2%)	18	5 (14%)	36
Digestive system (K00 - K95)	1 (7.1%)	14	1 (7.1%)	14	2 (7%)	28
Endocrine, nutritional and metabolic diseases (E00-E89)	0	8	2 (14.2%)	14	2 (9%)	22
Injury, poisoning and certain other consequences of external causes (S00-T88)	0	8	1 (7.1%)	10	1 (5.6%)	18
Nervous system (G00 - G99)	0	4	0	9	0	13
Disease of the musculoskeletal system and connective tissue (M00 - M99)	0	6	0	6	0	12
Mental, Behavioral and Neurodevelopmental disorders (F01-99)	2 (40%)	5	0	6	2 (18.2%)	11
Disease of the skin and subcutaneous tissue (L00-L99)	0	4	1 (16.6%)	6	1 (10%)	10
Certain infection and parasitic diseases (A00-B99)	1 (50%)	2	0	1	1 (33.3%)	3
Factors influencing health status and contact with health services (Z00 - Z99)	0	1	0	2	0	3
Missing data	0	3	0	10	0	13
Total	**13 (7.7%)**	**168**	**23 (9.4%)**	**243**	**36 (8.7%)**	**411**

9.51 Appendix 51 - Previous systematic review of intervention

Reference	Intervention	Outcome	Number of included studies	Conclusion
Motamadi, 2011[273]	• Computer-enabled discharge communication compared with traditional communication for patients discharged from acute care hospitals	• Mortality, readmission, ER visit, adverse events • Timeliness, quality and accuracy of information	• 12 studies	• Intervention groups experienced reductions in perceived medical errors/adverse events, and improvements in timeliness and physician/patient satisfaction.
Kwan, 2013[269]	• Inpatient medication reconciliation • Compared medication reconciliation with "usual care" • Compared 2 forms of medication reconciliation. • Interventions targeted: o Admission to a hospital, discharge home, o In-hospital transfer, o Multiple care transitions.	• 2 outcomes of interest— • Clinically significant unintentional discrepancies • 30-day post discharge hospital utilization, o emergency department visits or hospitalizations • Or evaluated the severity or clinical significance of unintentional discrepancies.	• 18 studies (7 targeted hospital discharge)	• Most unintentional discrepancies identified had no clinical significance. • Medication reconciliation alone probably does not reduce post discharge hospital utilization but may do so when bundled with interventions aimed at improving care transitions.
Mills, 2016 [11]	• Communication of discharge information from hospitals to general practitioners	• Medicines-related discharge information communication • Discharge prescribing error rate	• 15 studies	• Implementation of interim electronic discharge solutions resulted in complete legibility but did not eradicate information and prescribing errors.
Nazar, 2015[661]	• Community pharmacy	• Patient and medication outcomes • Identify intervention characteristics that influenced all reported outcomes	• 14 studies	• Impact not consistent
McNab, 2018[270]	• Pharmacist led medication reconciliation in community after hospital discharge	• Discrepancy identification and resolution, • Clinical relevance of resolved discrepancies • Healthcare utilisation, • Including readmission rates, emergency department attendance and primary care workload.	• 14 studies	• Patient outcome or care workload improvements were not consistently seen.
Redmond, 2018[265]	• Medication reconciliation	• Medication discrepancies, • Patient-related outcomes • Healthcare utilisation	• 25 studies	• The impact is uncertain
Daliri, 2020[264]	• Patient education • Medication reconciliation • Information transfer	• Medication readmission • Medication adherence • Medication related harm • Mortality	• 14 studies	• Reduced readmission