Medication Reconciliation: the primary secondary care interface

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Citation
Medication Reconciliation:  
the primary secondary care interface  

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June 2017
Candidate Thesis Declaration

I declare that this thesis, which I submit to RCSI for examination in consideration of the award of a higher degree of Doctor of Philosophy, is my own personal effort. Where any of the content presented is the result of input or data from a related collaborative research programme this is duly acknowledged in the text such that it is possible to ascertain how much of the work is my own.

I have not already obtained a degree in RCSI or elsewhere on the basis of this work. Furthermore, I took reasonable care to ensure that the work is original, and, to the best of my knowledge, does not breach copyright law, and has been taken from other sources except where such work has been cited and acknowledged within the text.

Signed

Student Number  000954
Date    28th April 2017
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<td>A&amp;E</td>
<td>Accident and Emergency</td>
</tr>
<tr>
<td>ADE</td>
<td>Adverse Drug Event</td>
</tr>
<tr>
<td>ACEI</td>
<td>Angiotensin converting enzyme inhibitor</td>
</tr>
<tr>
<td>ATC</td>
<td>Anatomical Therapeutic Chemical</td>
</tr>
<tr>
<td>BPMH</td>
<td>Best Possible Medication History</td>
</tr>
<tr>
<td>CDS</td>
<td>Chronic Disease Score</td>
</tr>
<tr>
<td>CHF</td>
<td>Congestive heart failure</td>
</tr>
<tr>
<td>CI</td>
<td>Confidence Interval</td>
</tr>
<tr>
<td>CINAHL</td>
<td>Cumulative Index to Nursing and Allied Health Literature</td>
</tr>
<tr>
<td>COPD</td>
<td>Chronic obstructive pulmonary disease</td>
</tr>
<tr>
<td>CP</td>
<td>Community Pharmacist</td>
</tr>
<tr>
<td>CPD</td>
<td>Continuing Professional Development</td>
</tr>
<tr>
<td>DDD</td>
<td>Defined daily doses</td>
</tr>
<tr>
<td>DoH</td>
<td>Department of Health</td>
</tr>
<tr>
<td>DVC</td>
<td>Doctor Visit Card</td>
</tr>
<tr>
<td>ED</td>
<td>Emergency Department</td>
</tr>
<tr>
<td>GMS</td>
<td>General Medical Services</td>
</tr>
<tr>
<td>GP</td>
<td>General Practitioner</td>
</tr>
<tr>
<td>HCP</td>
<td>Healthcare Professional</td>
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<tr>
<td>HIQA</td>
<td>Health Information and Quality Authority</td>
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<tr>
<td>HIT</td>
<td>Health Information Technology</td>
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<tr>
<td>HP</td>
<td>Hospital Pharmacist</td>
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<tr>
<td>HRB</td>
<td>Health Research Board</td>
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<tr>
<td>HSE-PCRS</td>
<td>Health Services Executive – Primary Care Reimbursement Scheme</td>
</tr>
<tr>
<td>ICC</td>
<td>Intra-class correlation coefficient</td>
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<tr>
<td>ICD-10</td>
<td>International Classification of Diseases – Version 10</td>
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<td>ICGP</td>
<td>Irish College of General Practitioners</td>
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<tr>
<td>ICPC-2</td>
<td>International Classification of Primary Care – Second edition</td>
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<tr>
<td>ICT</td>
<td>Information and Communication Technology</td>
</tr>
<tr>
<td>IHI</td>
<td>Institute for Healthcare Improvement</td>
</tr>
<tr>
<td>IPA</td>
<td>International Pharmaceutical Abstracts</td>
</tr>
<tr>
<td>IPCRN</td>
<td>Irish Primary Care Research Network</td>
</tr>
<tr>
<td>JCI</td>
<td>Joint Commission International</td>
</tr>
<tr>
<td>IQR</td>
<td>Inter-Quartile Range</td>
</tr>
<tr>
<td>MAI</td>
<td>Medication Appropriateness Index</td>
</tr>
<tr>
<td>MDT</td>
<td>Multi-disciplinary Team</td>
</tr>
<tr>
<td>MPR</td>
<td>Medication Possession Ratio</td>
</tr>
<tr>
<td>MedRec</td>
<td>Medication Reconciliation</td>
</tr>
<tr>
<td>NAM</td>
<td>National Academy of Medicine (formerly Institute of Medicine)</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Full Form</td>
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<tr>
<td>--------------</td>
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<tr>
<td>NCCMERP</td>
<td>National Coordinating Council for Medication Error Reporting and Prevention</td>
</tr>
<tr>
<td>NCHD</td>
<td>Non-consultant hospital doctor</td>
</tr>
<tr>
<td>NICE</td>
<td>National Institute for Health and Care Excellence</td>
</tr>
<tr>
<td>NPSA</td>
<td>National Patient Safety Agency</td>
</tr>
<tr>
<td>NPSCG</td>
<td>National Patient Safety Goals</td>
</tr>
<tr>
<td>OR</td>
<td>Odds ratio</td>
</tr>
<tr>
<td>PADE</td>
<td>Potential Adverse Drug Event</td>
</tr>
<tr>
<td>PAML</td>
<td>Pre-Admission Medication List</td>
</tr>
<tr>
<td>PDC</td>
<td>Proportion Days Covered</td>
</tr>
<tr>
<td>PHMD</td>
<td>Post-Hospital Medication Discrepancy</td>
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<tr>
<td>PIP</td>
<td>Potentially Inappropriate Prescribing</td>
</tr>
<tr>
<td>PSI</td>
<td>Pharmaceutical Society of Ireland</td>
</tr>
<tr>
<td>RCT</td>
<td>Randomised controlled trial</td>
</tr>
<tr>
<td>RCSI</td>
<td>Royal College of Surgeons in Ireland</td>
</tr>
<tr>
<td>REC</td>
<td>Research Ethics Committee</td>
</tr>
<tr>
<td>SD</td>
<td>Standard Deviation</td>
</tr>
<tr>
<td>STOPP</td>
<td>Screening Tool of Older Person’s Potentially Inappropriate Prescription</td>
</tr>
<tr>
<td>STROBE</td>
<td>Strengthening the Reporting of Observational studies in Epidemiology</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
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Figure 9-8 Systematic Review (Chapter 5) Alternate ICC 0.06 Schnipper 2011

Figure 9-9 Systematic Review (Chapter 5) Alternate ICC 0.2 Schnipper 2011
Summary

Background
The aim of this thesis was to examine medication reconciliation at the primary secondary care interface and to identify the impact of hospitalisation on the continuity of medication post discharge as well as methods to both implement and improve reconciliation.

Methods
A mixed methods research approach was used. A questionnaire was used to gather the opinion of primary care based healthcare professionals (HCPs) on the perceived quality of medication reconciliation both within and between primary and secondary care. A retrospective cohort of general practice patients was recruited to assess the impact of hospitalisation on the continuity of chronic medications post hospitalisation. A systematic review of the literature was performed to report the most effective method of reconciliation (e.g. HCP mediated, Information Communication Technology (ICT), multifaceted). Qualitative techniques were used to gather the opinions of secondary and primary care based HCPs on the barriers and facilitators to implementing effective reconciliation. The findings from all studies were triangulated to provide recommendations on methods to improve medication safety at this transition point.

Results
A total of 897 general practitioners (GPs) and community pharmacists (CPs) responded to the questionnaire – reporting satisfaction with GP/CP communication, mixed quality of communication with secondary care and an extremely common experience of prescribing errors following transitions of care (>80%). Analysis of a cohort of patients (n=19,777) from 44 practices, prescribed chronic medications long-term, reported a proportion of medication discontinuity ranging from 6-12% in the six months post-hospitalisation. There was reduced odds of discontinuity of respiratory inhalers (adjusted odds ratio AOR 0.53 95%CI [0.39, 0.71]) and thyroid medications (AOR 0.54 95%CI [0.33,
in those hospitalised versus those not hospitalised, with no impact of hospitalisation on the continuity of antithrombotics and lipid lowering medication. A systematic review and meta-analysis of reconciliation interventions showed a positive impact on medication discrepancies with a reduction in the relative risk (RR 0.58, 95%CI [0.46 to 0.73], 18 studies) by interventions that were primarily delivered by pharmacists. There is no certainty of this effect due to the low quality of included studies. Thematic analysis, of interviews with thirty-five HCPs, revealed that existing organisational practices, infrastructural deficits and the opinion of HCPs were the main barriers to effective reconciliation with improved communication, multidisciplinary teams and use of information technology listed as facilitators.

Conclusions
There is a frustration with the current standard of medication reconciliation between primary and secondary care with the experience of errors following transitions being commonly reported. This thesis provides evidence on the impact of transitions post hospital discharge on medication continuity, reviews successful reconciliation interventions, and examines the key suggestions of stakeholders in implementing reconciliation.
Acknowledgements

First and foremost, thank you to the participants and general practices who gave so generously of their time in taking part in this thesis’ studies. Several research assistants and undergraduates contributed to this study through data collection and data inputting. I gratefully acknowledge Khalid Munir and Oludare Alabi who conducted interviews and coded patient data, Hailey Carroll who administered the survey database, Janice Sweeney and her nursing colleagues for their hard work in coding clinical data, Paul Dillon for reviewing medication matching, and Dr Fiona Boland, Dr Atieh Zarabzadeh and Prof Carmel Hughes, for their contribution to the systematic and academic reviews.

Thank you to the Health Research Board of Ireland (HRB) who funded my systematic review through a Cochrane Research Training Fellowship (CTF/2012/7), as well as the HRB Centre for Primary Care Research who supported me in undertaking this PhD and the academic and administrative team of the HRB PhD Scholar’s programme in Health Services Research for their support, and for providing a structured environment for this research. I have been very fortunate to receive excellent supervision and mentorship throughout my PhD. Huge thanks to Professor Tom Fahey, Dr Tamasine Grimes and Dr Ronan McDonnell for their direction, reassurance and support. I’m very grateful to Dr Ronald McDowell, who gave so generously of his time and biostatistics expertise. Thank you to my classmates on the HRB PhD Scholars programme and my colleagues at RCSI who were and continue to be a great source of inspiration.

Finally, thank you to my parents for their support throughout, and to Edel and my children, for their constant encouragement and understanding, which made this thesis possible.
Peer reviewed publications and oral presentations

Parts of this thesis have been published as follows:

Peer reviewed publications


Oral & Poster Presentations


2. Redmond P. Cross-sectional survey of general practitioners’ and community pharmacists’ opinions on medication management at transitions of care in Ireland. Association of University Departments of General Practice in Ireland (AUDGPI) Conference, Belfast March 2015


Invited oral presentation:


1 Introduction
1.1 Background

The seminal Institute of Medicine report ‘To Err is Human: Building a Safer Health System’ highlighted medication error as being widely prevalent, costly and contributing to preventable causes of patient harm.(1) In particular, transitions of care, as patients move between different levels and locations of care, lead to medication error and what has been described as the “healthcare (dis)continuum”.(2) Improving and standardising the process of reconciling the transfer of information at these transitions has been advocated as means to improve medication list accuracy and reduce the presumed consequences of these errors.(3–5) This thesis aims to gather the opinions of primary care based healthcare professionals (HCPs) on the quality of medication reconciliation between primary and secondary care, explore the impact of hospitalisation on medication continuity post discharge and investigate the most effective methods by which reconciliation can reduce discrepancies as well as the challenges of implementing reconciliation interventions.

1.2 Medication safety

Prescribing is the most common intervention applied across all areas of the health service with an increasing volume of medications being prescribed to individuals in recent years. (6) Between 2003 and 2013 the average number of prescription items per year for any one person in England increased from 13 (in 2003) to 19 (in 2013).(3) In particular older people are prescribed multiple medications concurrently – polypharmacy - with the number of those over 65 years prescribed five or more medication regularly in Ireland in 2012 over 60%.(7)
Errors are common as medications are procured, prescribed, dispensed, administered, and monitored but, they occur most frequently during the prescribing and administering actions.\(\text{(8,9)}\) The Institute of Medicine report "Preventing Medication Error" in 2006 estimated 1.5 million preventable Adverse Drug Events (ADEs) occurring in the United States (US) alone with an associated cost of $3.5 billion. \(\text{(9)}\) A more recent, controversial study has suggested that over 250,000 deaths a year in the US are due to medical error generally (making it the third most common cause of death).\(\text{(10)}\) Primary care is also affected with a recent systematic review of the literature suggesting errors in medication range from 1 – 90 of a 100 prescriptions with up to 11% of those errors likely to result in harm.\(\text{(11)}\)

1.3 Transitions of care

Errors in recording medication history give rise to discrepancies such as medication omission, commission, and errors in dose, route or frequency. These discrepancies, particularly if initiated at admission to hospital, may perpetuate through to discharge and return to the community. Transitional care provides for the continuity of care as patients move between different stages and settings of care ensuring that an accurate medication use history is collected and transmitted between caregivers.\(\text{(12)}\) The prevalence of medication discrepancies arising at transitions of care have been reported in many different settings (hospital, community and long-term care facilities) and stages of care (admission, transfer and discharge); in particular transitioning between an inpatient and outpatient setting is associated with an increase in medication errors relative to other stages of care.\(\text{(12–15)}\) Prevalence of adverse events post-hospitalisation as high as 19% have been reported with the majority of these related to adverse drug events, which may be the result of medication error.
(16). Medication discrepancies as patients transition to home from hospital have also been linked with increased rehospitalisation rates (17).

The avoidable cost associated with poorly coordinated care transitions, leading to complications and rehospitalisation has been estimated at €45 billion in the US in 2011 alone.(18) This has been recognised by the internationally supported effort of the World Health Organization (WHO) in launching the High 5’s project in 2006, with an emphasis on patient safety with the standard operating procedure – ‘assuring medication accuracy at transitions in care’ focussed on reducing medication discrepancies.(19)

1.4 Medication reconciliation

One way to address the continuity of medicines information when moving from one care sector to another is medication reconciliation - the process of creating the most accurate list of medications at transition points. This takes place in three stages:

- a list of medications the patient was using before transfer is developed,
- the medication and dosage is checked against the new list – with a view to identifying any discrepancies or differences. Discrepancies are determined to be intentional or not, with unintentional discrepancies changed as appropriate and intentional discrepancies documented.
- Finally, this comprehensive new list and information regarding changes is communicated to the next healthcare provider.(20)

Medication reconciliation has been advocated by a number of different professional and accrediting bodies internationally - the Joint Commission, the Institute for Healthcare
Improvement, the National Institute for Health & Care Excellence (United Kingdom), the Canadian Patient Safety Institute (CPSI) and the Institute for Safe Medication Practices (Canada). A consensus statement by key stakeholders described medication reconciliation as a patient safety issue with a need to clearly define the process, address practical and flexible local implementation, identify at-risk patients, and actively promote and disseminate effective methods of reconciliation.(21)

A number of different interventions have been assessed in randomised trials in relation to medication reconciliation including information technology solutions, pharmacist input and reconciliation as part of a more complex multi-faceted care plan.(22,23) Interventions relying heavily on an increased role for pharmacists and targeting the patients most at risk of ADEs have reported the greatest improvement.(24) However, systematic reviews of medication reconciliation have commented not only on the poor quality of studies in the area, notably design flaws and the lack of appropriate comparison groups, but also the difficulty of comparing outcomes across heterogeneous settings and the absence of head-to-head comparisons of different intervention types.(22,23,25)

The difficulty in designing and powering randomised trials to examine ADEs related to re-hospitalisation has led to a shift to the more pragmatic approach of choosing medication discrepancy as a primary outcome.(26) However, this should not neglect the need to explore both the clinical significance and the causal relationship between discrepancies, ADEs, re-hospitalisation, quality of life measures and cost effectiveness, in light of reconciliation being a recommendation of professional organisations and a necessity for accreditation in some countries.(24) More
broadly, research efforts to date have been primarily concerned with in-patient reconciliation neglecting the wider patient journey upon discharge, with transitions between the hospital and long-term care facilities and within the community. Investigating strategies to reduce the potential for error and the practice of reconciliation between these sectors is also necessary.
2 Literature Review
2.1 Introduction

This chapter provides an overview of the literature relating to medication error at transitions of care, an explanation of the medication reconciliation process and discussion of the relevant healthcare policy in Ireland and internationally.

2.2 Background

Errors at transitions of care is an important element of risk relating to medication error and harm to patients. Medication reconciliation is advocated as one important component of mitigating that risk. This chapter summarises the medication management process, medication errors at transitions of care – specifically the primary secondary care divide, medication reconciliation itself, as well as the context of the Irish healthcare system and relevant health policy. It also provides a background for the subsequent chapters in the thesis.

2.3 Data sources used for literature review

The sources used in compiling this literature review are informed by the comprehensive search deployed in preparing Chapter 5 (Appendix T), in addition to being supplemented by keywords and MeSH terms from Google Alerts as well as wide-ranging publications from bodies such UK King’s fund, NICE, IoM (now the National Academy of Medicine) and the WHO. Additional literature was found by reviewing the bibliography of papers identified.

2.4 Medication therapy management and medication errors

Medication therapy management, a complex process, has been defined as including the following – assessing a patient’s health status, formulating a medication treatment plan, selecting/prescribing and administering a medication, monitoring for safety and effectiveness, comprehensive
medication review, documenting care and communicating to other providers, and educating the patient to enhance understanding and appropriate use of medication.\(^{(27)}\) Medication safety has become an increasingly important issue due to the recognition that medication error arises frequently and is both harmful and costly.\(^{(9,28–31)}\) A widely accepted definition of medication error is that used by the National Coordinating Council for Medication Error Reporting and Prevention (NCCMERP) which defines medication error as:

"Any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. Such events may be related to professional practice, health care products, procedures, and systems, including prescribing, order communication, product labelling, packaging, and nomenclature, compounding, dispensing, distribution, administration, education, monitoring, and use."\(^{(32)}\)

Recently a more simplified (and broader definition has been published by the European Medicines Agency:

"A medication error is an unintended failure in the drug treatment process that leads to, or has the potential to lead to, harm to the patient."\(^{(33)}\)

It is reported that 5-8% of unplanned admissions in the UK are due to medication errors,\(^{(28,31)}\) an estimated cost of over €700 million annually,\(^{(31)}\) with 1.5 million people harmed due to medication error annually in the US.\(^{(9)}\) 7.8% of adverse events reported to the Clinical Indemnity Scheme in Ireland (a State body tasked with handling clinical negligence claims against state healthcare employees) in 2012 were medication related, with 21% of those being due to incorrect medication on admission, transfer or discharge to
hospital.(30) Primary care is similarly affected with patient safety incidents not infrequently found in both the prescribing and dispensing of medication.(11,34,35) Across both primary and secondary care 20% of medical negligence cases arise due to medication errors.(36)

It is clear that the prescribing process is one possible source of medication error with a prescribing error being described as:

“A clinically meaningful prescribing error occurs when, as a result of a prescribing decision or prescription writing process, there is an unintentional significant (1) reduction in the probability of treatment being timely and effective or (2) increase in the risk of harm when compared with generally accepted practice” (37)

Examples of this include errors of omission, commission, or errors in the dose, the strength, the route, the quantity, the indication, or in the contraindication to medication. Indeed, the prescribing and administration of medication is the most common element of the medication management process to be associated with error.(29,38)

Many terms, that are both overlapping and which may give rise to confusion, are used in describing the impact on patients related to medications. The terms discussed below are illustrated graphically in Figure 2-1.(39,40) Adverse drug reactions (ADR), defined by the WHO, was one of the earliest terms used to describe the negative impact of medication:

“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.” (41)

A broader term that encompasses adverse events both due to intentional drug use (i.e. ADR) and through error in medication use lead to the wider adoption of the term Adverse Drug Events (ADEs):

“All injury occurring during the patient’s drug therapy and resulting either from appropriate care, or from unsuitable or suboptimal care. Adverse drug events include: the adverse drug reactions during normal use of the medicine, and any harm secondary to a medication error, both errors of omission or commission.” (41)

A variant of the ADE concept is that where the actual event itself did not occur – a potential adverse drug event:

“A serious medication error-one that has the potential to cause an adverse drug event, but did not, either by luck or because it was intercepted and corrected”. (41)

Where harm does occur, and was preventable, this is termed a preventable adverse drug event:

“any adverse drug event that would not have occurred if the patient had received ordinary standards of care appropriate for the time when this event occurred, so that, associated to a medication error”. (41)
Figure 2-1 Relationship between adverse drug events (ADEs), potential ADEs, and medication errors – Adapted from Reckmann 2009(39,40) See Appendix EE for documentation of permission to republish this material.
The severity of the impact of possible medication errors is most commonly categorised according to the NCCMERP classification system listed in Figure 2-2.

The causes of error are multifactorial. In primary care the prescriber, the patient, the team, the working environment, the task, the computer system and the primary/secondary care interface have all been implicated.(42) Similar issues arise in secondary care with factors relating to the individual, the task, teams, environment and the patient all suggested as causative.(43)
Figure 2-2 NCC MERP index for Categorising Errors. See Appendix EE for documentation of permission to republish this material.
Finally, while adverse incidents involving patients are common and relatively easily recorded, a difficulty arises in establishing causality in ADEs; despite the availability of causality assessment scales often the judgement remains a probable/possible cause as opposed to a certainty.\(^{(44,45)}\) A commonly used method to determine causality is the WHO Uppsala Monitoring Centre (WHO-UMC).\(^{(45)}\)

### 2.5 Transitions of care

Transitional care is defined as “a set of actions designed to ensure the coordination and continuity of health care as patients transfer between different locations or different levels of care in the same location”.\(^{(46)}\) These transitions can occur between different settings (e.g. hospital to nursing home) and between levels within the same settings (e.g. emergency department to intensive care). Grimes illustrates the interaction between the medication management process and transitions of care both between and within primary and secondary care in Figure 2-3.

The coordination of care, particularly in those patients with complex medical conditions is a priority of health policy makers.\(^{(47,48)}\)
Figure 2-3 Medication management at transitions of care (49) See Appendix EE for documentation of permission to republish this material
Poor coordination of transitions of care can lead to errors in continuity of prescriptions, lack of adequate follow-up of investigations as well as rehospitalisation.\cite{14,50–54} Discrepancies in prescriptions, both at admission and discharge, are extremely common,\cite{50,55} with errors on discharge prescriptions ranging from a minor to a significant potential for ADEs.\cite{56} The cascade of error arising from suboptimal medication management at all transition points is highlighted in the recommendations arising from a systematic review of studies describing medication errors on admission.

The review underlined the importance of the pre-admission medication list (PAML) – in particular this included distinguishing between both unintentional and intentional discrepancies, judging their clinical importance, and ensuring a number of sources are consulted in generating a PAML.\cite{15,55} Confusingly, this concept of PAML is also varyingly referred to as best possible medication history (BPMH),\cite{57,58} pre-admission medication (PAM), and gold standard preadmission medication list (GSPAML).\cite{59}

The UK Care Quality Commission in a report on the quality of prescribing at discharge to primary care reported more than 80% of GPs who responded as saying discharge summaries as being inaccurate/incomplete.\cite{60} Hospital discharge can almost impact on patient satisfaction with Knight et al., reporting anxiety and confusion around medication in older people at the time of discharge.\cite{61}

A recent systematic review by Michaelsen et al., reported that patients had on average 1.2-5.3 discrepancies on their prescription upon leaving hospital.\cite{62} Grimes et al., in a study of two Irish hospitals, noted that 50% of patient discharges had discrepancies on their discharge medication orders, with more than 60% of these having the potential to result in at least moderate harm.\cite{63} Tam et al., in a study of
hospital admission medication errors reported that 10-67% of patients had one or more errors on their medication history, with 11-59% of those judged to be clinically important.(15) In repeated studies by Forster et al., ADEs were the most common error affecting patients after discharge, with many of them being preventable.(16,64) Most studies of discrepancies at transitions are small and from single centres however the weight of evidence suggests discrepancies are extremely common.

The definition of medication error at transitions varies considerably in reported studies however what is consistent is that errors of omission are the commonest error found both at admission and discharge.(15,25,55,65–68) The chief concern is these discrepancies will continue on to the next healthcare provider and there is some limited evidence that discrepancies at discharge do appear to propagate into the next healthcare setting.(69) In addition, inadequate discharge planning generally has been suggested as a cause for rehospitalisation, which itself ranges from 18% of patients within 30 days in 2013 in the US and 11% in 2012 in Ireland.(70,71)

Age, longer length of time in hospital, increased morbidity, hand written discharge, and increased number of medications have all been found to be associated with discrepancies at discharge.(63,65,68,72–74), however not all of these associations have been found in all settings.(65,73,75–78) In addition inaccuracies in the compiling of preadmission medication histories, limited patient understanding and delegating medication history taking to the most junior staff were all associated with pADEs at hospital discharge.(55) Insurance status does not appear to impact on reconciliation.(65)
One study of two Irish hospitals reported the medications most commonly affected by omission at discharge include endocrine, central nervous system, nutritional and antiplatelet medications.\(^{(63)}\)

To improve the accuracy of medication information transfer between primary and secondary care many organisations have developed essential information requirements templates.\(^{(79,80)}\) Medication reconciliation has been proposed as one of the key elements to improve patient safety by decreasing medication discrepancies at transitions of care.\(^{(3,19,20,81)}\) This reflects the finding that interventions to improve the accuracy of medication management process at transitions of care have been shown to be a successful component of multifaceted interventions to reduce rehospitalisation.\(^{(82)}\)

### 2.6 Medication reconciliation

Medication reconciliation is a process designed to reduce medication errors at transitions of care. The process, including the specific term medication or medicines reconciliation, began to be referred to more frequently in the literature in the early 2000s.\(^{(14,83–85)}\) It has been varyingly described by both regulatory and patient safety organisation as well as reported studies adopting their own variation on the individual components. A selection of the varying definitions as compiled by Urban is shown in Table 2-1.\(^{(84)}\) The most commonly reported elements include:

- Creation of a BPMH of all medication the patient is taking (both prescribed and un-prescribed).
- Comparing this list against updated medication orders at the particular transition of care and resolving any discrepancies.
• Updating the medication list to account for the above and communicating this updated list to the next healthcare provider.

The process of reconciliation is repeated at each transition point. It relies upon the use of multiple sources of medication information to construct a BPMH. The process is illustrated in a figure by Fernandes et al., in Figure 2-4. The number of potential sources of patient prescribing information is numerous – patient’s own drugs, community pharmacist /GP records, previous admission/discharge records etc., any of which may not be available – in particular outside of normal hours, and may be inaccurate when read on its own. (86–88) In fact Foss et al., found agreement in only 8% of patients when comparing across seven paired sources.(89)

Medication reconciliation has strong support from safety and regulatory organisations internationally and has been mainly studied from the perspective of admission and discharge from secondary care with primary care, and long term care less well studied.(90,91)
Figure 2-4 Medication reconciliation at admission and discharge to hospital
Adapted from Pharmacy Practice 2009;25(6):26 by Fernandes et al., 2012 (92)

See Appendix EE for documentation of permission to republish this material
Table 2-1 Definitions of ‘medication reconciliation’ used by government and professional organisations, by Urban 2014(84)

<table>
<thead>
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<th>Organisation</th>
<th>Definition</th>
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| Australian Commission on Safety and Quality in Healthcare | ‘Medication reconciliation is a formal process of obtaining and verifying a complete and accurate list of each patient’s current medicines. Matching the medicines the patient should be prescribed to those they are actually prescribed. Where there are discrepancies, these are discussed with the prescriber and reasons for changes to therapy are documented. When care is transferred (e.g. between wards, hospitals or home), a current and accurate list of medicines, including reasons for change is provided to the person taking over the patient’s care. Points of transition that require special attention are:  
  - Admission to hospital  
  - Transfer from the Emergency Department to other care areas (wards, Intensive Care, or home)  
  - Transfer from the Intensive Care Unit to the ward  
  - From the hospital to home, residential aged care facilities or to another hospital.’ |
| National Patient Safety Agency (NPSA) (UK)         | ‘The aim of medicines reconciliation on hospital admission is to ensure that medicines prescribed on admission correspond to those that the patient was taking before admission. Details to be recorded include the name of the medicine(s), dosage, frequency, and route of administration. Establishing these details may involve discussion with the patient and/or carers and the use of records from primary care. This does not include medicines review.’ |
| Institute for Health Improvement (USA)             | ‘The process of creating the most accurate list possible of all medications a patient is taking — including drug name, dosage, frequency, and route — and comparing that list against the physician’s admission, transfer, and/or discharge orders, with the goal of providing correct medications to the patient at all transition points within the hospital.’ |
| The Joint Commission (USA)4                        | ‘Medication reconciliation is the process of comparing a patient’s medication orders to all of the medications that the patient has been taking. This reconciliation is done to avoid medication errors such as omissions, duplications, dosing errors, or drug interactions. It should be done at every transition of care in which new medications are ordered or existing orders are rewritten.’ |
| Institute for Safe Medication Practices (ISMP) (Canada) | ‘Medication reconciliation is a formal process in which healthcare providers work together with patients, families and care providers to ensure accurate and comprehensive medication information is communicated consistently across transitions of care. Medication reconciliation requires a systematic and comprehensive review of all the medications a patient is taking (known as a BPMH) to ensure that medications being added, changed or discontinued are carefully evaluated. It is a component of medication management and will inform and enable prescribers to make the most appropriate prescribing decisions for the patient.’ |
| High 5’s Project (WHO)                             | ‘Medication reconciliation addresses the prevention of medication errors resulting from incomplete or mis-communicated information at points of transition in the patient care process, such as admission to the hospital, transfers within the hospital, and discharge from the hospital.’ |
| Agency for Healthcare Research and Quality (AHRQ)   | ‘Medication reconciliation is a process to decrease medication errors and patient harm by comparing the patients’ current medication regimen against the physicians’ admission, transfer, and/or discharge orders to identify discrepancies.’ |
| American Pharmacists Association (APhA) & American Society of Health System Pharmacists (ASHSP) | ‘Medication reconciliation is the comprehensive evaluation of a patient’s medication regimen any time there is a change in therapy in an effort to avoid medication errors such as omissions, duplications, dosing errors or drug interactions, as well as to observe compliance and adherence patterns. This process should include a comparison of existing and previous medication regimens and should occur at every transition of care in which new medications are ordered or existing orders are rewritten or adjusted or if the patient has added non-prescription medications to (his or her) self-care.’ |
2.7 Interventions to improve reconciliation

Many studies have examined the overlapping issues of medication discrepancies, transitions of care and interventions to improve medication reconciliation. Following this there have been many attempts by reviews to summarise these findings both narratively and quantitatively.(23,24,62,82,93–131)

Interventional studies often provide limited detail on the process of reconciliation, making assessment of the integrity of the delivery of the intervention as well recreating the intervention difficult. Furthermore, some studies label interventions as reconciliation, that actually involve more complex interventions e.g. medication use review.(106) In general, reconciliation efforts have a positive impact – mainly on process outcomes e.g. documentation. For example, Mueller et al., in a systematic review, found interventions reduced pADEs and ADEs with less clear impact on actual healthcare utilisation.(107) When reconciliation has been combined in a multifaceted intervention including patient education, discharge planning and follow up – a so called ‘bundle of care’ - then an impact on rehospitalisation has been shown.(82,132,133)

Pharmacists are the staff most commonly involved in studies of reconciliation,(24,106,107,110) with a smaller number of studies employing pharmacy technicians,(134,135) student pharmacists,(136,137), nurses(138) and ICT.(23) Hospitals are the setting most commonly studied, with primary care,(105,112,114) and long-term care less commonly researched.(103)

A significant deficit, especially in considering health policy planning, is that there have been few studies that have
attempted an economic analysis of the cost-effectiveness of reconciliation.(106,139,140)

Previously assessed outcome measures used to assess quality of medication reconciliation at discharge from secondary to primary care range from medication error, pADEs, ADEs, drug therapy inconsistencies and omissions (DTIOs), continuity of medication, adherence, clinical significance of pADEs, patient satisfaction, and healthcare utilisation.(14,25,50,51,55,56,64,141–145) Within these studies even the recording of discrepancies is not easy, as an agreed method of determining discrepancies is not available e.g. discrepancies between sources, or between medication list and PAML, (84) categorising discrepancies in dose and form as separate or as a single category, and choosing the appropriate numerator and denominator(55,146) Other studies have counted the number of necessary interventions (e.g. pharmacist intervening to correct an error) as an outcome measure, (147) or the number of drug related problems.(148)

Furthermore, studies generally are limited by issues such as small sample size, lack of randomisation, lack of blinding, retrospective/non-experimental design, unclear intervention definition, contamination, and non-consecutive patient enrolment. This has meant that few reviews have attempted meta-analysis,(95,110,111) and their attempts at combining individual studies effects must be treated with extreme caution.

2.8 Implementation and impact of reconciliation

The challenges of implementing successfully a medication reconciliation programme have been recognised, and studied.(149–158) The WHO in a standard operating protocol
(SOP) implementation guide to accompany their High 5’s initiative highlighted the following:(83,159,160)

- Standardised systems within organisations to collect medication information at each care transitions (prescribed, un-prescribed, check compliance and source information from patient and their primary care provider).
- Reconcile medication changes at each transition to patient’s home medication list – emphasising the importance of accurate reconciliation at the first time point e.g. admission (to occur within specified time frames)(161)
- Document reasons for discrepancies and changes that have occurred and communicate these to the next provider.
- Integration of reconciliation into broader medication management processes.
- All HCPs aware of their roles and responsibilities in this process.
- Pharmacy involvement or availability at each step of the process.
- Training of staff to support this process.
- Involve patients and carers in the process as much as possible.

The barriers to effective reconciliation are likely to revolve around systems, skills, people, organisational, and resources issues.(150,162,163) Complex interventions, as most healthcare service interventions are, require well thought out implementation plans.(164,165) Suggested priorities in implementing reconciliation are adequate time, staff training, early application of reconciliation in a patient’s transition, prioritising higher risk patients, clear delineation of staff roles and consideration of both benefits and potential downsides of ICT in medication management.(149). Examples of
implementation models include ‘Plan, Do, Study, Act (PDSA), (166) Failure Modes and Effects Analysis (FMEA), Six Sigma and the Multi-Centre Medication Reconciliation Quality Improvement Study (MARQUIS) toolkit. (158,167,168) While note is made of pharmacy involvement in the WHO implementation guidelines most organisations do not specify the skills, probable impact on resources, or knowledge required by staff to undertake reconciliation. (24) In fact, there have been conflicting statements about which professions should take the lead in reconciliation efforts. (161,169,170) Nevertheless, most reviews that have reported successful studies are predominately pharmacist delivered interventions. (107)

The limited use of ICT to improve the transfer of information across transitions, including reconciliation interventions, has been recognised with a call to improve the interoperability of proprietary systems. (171–173) The potential benefits of ICT usage – particularly in standardising the recording of information has been noted. (174) This enthusiasm must be tempered by the fact that ICT interventions may introduce errors in to medication ordering. (175)

2.9 Health policy

Patient safety and the recognition of avoidable adverse events in healthcare, including medication error, have come to the fore with influential reports from the US (To Err is Human) and the UK (An Organisation with a Memory; A Spoonful of Sugar; Exploring the costs of unsafe care in the NHS). (1, 28, 176, 177) What followed was an intense interest in medication safety and transitions of care with a focus on the potential impact of medication reconciliation. Thus, reconciliation has been made a requirement of healthcare organisations by many regulatory organisations and strongly recommended in patient safety reports. (3, 5, 161, 178)
In Ireland, there has also been recognition by statutory bodies of patient safety, transitions of care and medication management as important topics. In 2003, the Health Boards Executive published ‘Admissions and discharge guidelines: health strategy implementation project’, which made recommendations about improved links between primary and secondary in arranging transfers of care; this was followed by another HSE report in 2008 (updated in 2014) that made explicit reference to medication management at transitions of care – *Code of Practice for Integrated Discharge Planning*.\(^{179}\) In 2008, the Report of the Commission for Patient Safety and Quality Assurance, commissioned by the Department of Health and Children and chaired by Dr Deirdre Madden, recommended that healthcare organizations prioritise the implementation of formal medication reconciliation systems at all points of transfer of care as well considering the positive impact of ICT in improving the patient journey.\(^{178}\) An implementation group was established to implement the recommendations of this report which led to the forming of the National Patient Safety Advisory Group. The establishment of the Health Information & Quality Authority (HIQA) in 2007 began a raft of reports and recommendations on patient safety pertinent to coordination of care in the healthcare system, ICT and medication management. These included standardising of classification and terminology for interoperability in health ICT (“ability of different information technology systems and software applications to communicate, exchange data, and use the information that has been exchanged”),\(^{180}\) ePrescribing,\(^{181}\) unique health identifiers,\(^{182}\) minimum standards for discharge\(^{80}\) and referral,\(^{183}\) These reports are complemented by strategic initiatives and projects such as the HSE’s eHealth strategy,\(^{184}\) the establishment of the Office of Chief Information Officer, *Healthlink* (an electronic...
messaging standard) and the HSE Medication Safety Programme.

This health policy imperative is not confined to Ireland with the Care Quality Commission (CQC) in the UK calling for an improvement in the quality of discharge summaries, as well as an improvement in the information exchange between primary-secondary care. (60) NICE published recommendations on the optimisation of medicines that specifically includes reconciliation as an organisational responsibility and that it is explicitly necessary upon hospital discharge and return to primary care. (3), and the Scottish Intercollegiate Guidelines Network (SIGN) advises a reconciliation process at discharge that fully accounts for pre-admission medication with onward communication to not only a person’s GP but also their community pharmacist. (79) The profile of reconciliation has been further boosted by Canada’s national patient safety campaign, Safer Healthcare Now!, adopting medication reconciliation in LTC as one of its new patient safety strategies in 2008. The ‘5 million lives’ campaign in the US similarly underlines the importance of implementing medication reconciliation. The WHO’s patient safety drive included medication reconciliation as one of its five areas for improvement. (19)

2.10 Conclusion

Medication reconciliation is one element of safe prescribing and complements other high value issues such as the optimisation of prescribing through the reduction in inappropriate medication, the recognition of under prescribing, avoidance of interactions and encouragement of adherence. (3, 185–188) The vast majority of studies of discrepancies have been focused on admission and discharge from secondary care with very few examining the onward effect of pADEs upon return to primary care. There
have been many reviews comparing different interventions to improve reconciliation at transition of care - most of which are difficult to interpret due to the quality of the included studies, outcome selection and reporting and the non-randomised nature of the study designs. Finally, it is recognised that implementation of complex health care interventions is difficult and must take account of, amongst others, factors related to the user e.g. HCP, patient, organisation, resources and intervention itself.\(^{(164,165,189)}\)

This thesis will address these gaps in the literature in turn.
3 Rationale, context, methods and objectives of this thesis
3.1 Rationale for this thesis

As has been summarised, medication reconciliation is a “conscientious, patient-centred, inter-professional process that supports optimal medicines management”.(21) It contributes to the larger area of medication safety, appropriateness and timeliness. By definition, it crosses professional boundaries and requires interdisciplinary planning and cooperation. This thesis contributes to the body of research on medication reconciliation by quantifying the impact of transitions of care on medication continuity in general practice, gives contextual information to the process at the primary secondary care interface and adds to the evidence on the ideal design and implementation of reconciliation interventions.

The findings of this thesis are relevant at both a national and international level. Regulatory bodies, healthcare institutions, patient safety advocates, healthcare practitioners and the wider public would be receptive audiences for the findings.

3.2 Mixed methods, research paradigm and triangulation of results

Methodology

This thesis employs a mixed methods research enquiry. This has been described as a: (190)

“Methodology of research that advances the systematic integration, or “mixing,” of quantitative and qualitative data within a single investigation or sustained program of inquiry.

The basic premise of this methodology is that such integration permits a more complete and synergistic utilization of data than do separate quantitative and qualitative data collection and analysis”

The opportunities provided by integrating different research methodologies has been recognised in the literature for many
years, originally in sociology but more recently healthcare and in particular primary care research.(191–194) Specific benefits include strengthening the conclusions of research, addressing both confirmatory and exploratory questions and allowing for contrast of divergent opinions/evidence.(195) A number of previous researchers investigating medication reconciliation have employed mixed methods. (26,49,84,173) Some of the core characteristics of a mixed method study as listed by Wisdom et al., include:(190)

- Collecting and analysing quantitative (closed ended) and qualitative (opened ended) data.
- The use of rigorous procedures for data collection and analysis that is consistent with each method’s tradition.
- Integration of data through collection, analysis and discussion.
- Framing the study within a philosophical/theoretical model of research that is appropriate to the topic e.g. social constructionist model.

In a summary of the literature, Greene et al., stated the main purposes for undertaking mixed methods research were to triangulate (seek convergence or corroboration), complement (enhance or illustrate the results from differing methods), develop methods from the results of a differing methods, initiate contradictions and new questions, and expand the breadth of inquiry.(196) Creswell et al., advised in designing mixed methods study that thought should be given to the priority (emphasis more on quantitative, qualitative or equal priority), the implementation (whether data are collected sequentially or concurrently) and the integration (whether data from the differing methods is mixed - either during data collection or as results are reported). Finally, the purpose of mixed methods study should be stated – instrument design (e.g. grounded in the experience of the target population),
triangulation (comparing and contrasting results from different methodologies) or data transformation (transforming qualitatively collected data for the purposes of quantitative analysis).(191)

Research paradigm
The definition of a paradigm has been described in many different ways e.g. “A paradigm is a way of looking at the world. It is composed of certain philosophical assumptions that guide and direct thinking and action”.(197) A critical realist paradigm was chosen for this thesis because it retains an ontological realism (“there is a real world that exists independently of our perceptions, theories, and constructions”) while accepting a form of epistemological constructivism and relativism (“our understanding of this world is inevitably a construction from our own perspectives and standpoint”).(198) In addition this paradigm specifically allows for the influence of both culture, and surrounding structures on human behaviour.(199,200)

Triangulation
Triangulation is defined as "the combination of methodologies in the study of the same phenomenon."(201) This thesis' methodological triangulation ("between method") allows for the convergence/agreement of the results of two methods and may enhance the validity of the findings by relieving the concerns about the limitations of the methods individually.(201,202) Conversely, where findings from differing methods conflict then triangulation allows for moderation of any one single method. Also, it is suggested it increases the richness and comprehensiveness of the study of a topic.
3.3 Research context

3.3.1 Researcher characteristics and reflexivity

The author of this thesis (PR) is a PhD student in Health Services Research. PR’s background is that of a practising male general practitioner (GP) who interacts regularly with the health care organisations (e.g. hospital, pharmacies), as well as some of the research participants (Chapter 7). PR has both quantitative and qualitative training (PhD module teaching) and practical research experience (previous publications). PR is actively engaged in studying the process of medication reconciliation at transitions of care arising from a professional disappointment with the current standard of care provided to patients during transitions in Ireland. By virtue of being a GP, he is particularly interested in reconciliation as it occurs between secondary and primary care. PR conceived the research ideas, defined the objectives and methodology, as well as conducting the data collection, analysis and reporting of results.

3.3.2 Research colleagues and funding

PR for the duration of this thesis was based in the Health Research Board (HRB) Centre for Primary Care Research at the Royal College of Surgeons in Ireland. This Centre consists of a multidisciplinary team of academic clinicians, research pharmacists, postdoctoral researchers and statisticians interested in the topics and interplay of pharmacoepidemiology (in particular, quality in prescribing), vulnerable populations and the utility of ICT in healthcare. These research colleagues were invaluable in providing their expertise and experience in developing this thesis. PR was the recipient of an HRB Cochrane training fellowship to conduct a systematic review on the effectiveness of medication reconciliation. The award of this funding, while providing an opportunity to undertake a review, was also
supportive in undertaking the broader thesis on the topic of medication reconciliation.

3.3.3 The Irish healthcare system

An understanding of the context in which this thesis’ research took place – the Irish healthcare system – is necessary in interpreting the choice of methodology, availability of data sources and conclusions drawn. Ireland has a mixed public and private healthcare system. Public health services include prescribed medications, GP visits, secondary and tertiary care services such as outpatient visits and hospital admission, community services such as public health nurse and physiotherapy and social services. Individuals who meet specified income thresholds are granted a medical card through the General Medical Services (GMS) scheme and are entitled to all public health services free of charge. The exception to this is a fee per prescription item (€2.50 per item to a maximum of €25 per family unit (€2 and €20, respectively, for those over 70 years from 1st March 2017)).

Until 2008, all people aged 70 years and over automatically qualified for a GMS medical card. Since January 2009 a new income threshold for eligibility for the scheme has been applied. Despite this, the vast majority of older people still qualify for free medical care with more than 348,000 people (96%) of the population aged 70 and over eligible for the GMS scheme in 2013.(203)

In 2005, an additional scheme was introduced for individuals not meeting the income thresholds for a full GMS medical card, which provides certain services free of charge. This scheme is called a GP Visit or Doctor Visit Care, which grants the recipient (and their dependents) free access to GP services but fees must be paid for prescriptions and other primary care services. Approximately 2.7% of the population qualifies for this scheme.(203)
The remainder of the population pay for all GP services and prescribed medications (capped at €144 per family monthly) with entitlement to free public health services such as public hospital services (subject to statutory co-payments) and maternity services. Many people, who do not meet the eligibility criteria for a GMS medical card or GP Visit card, and a proportion of those that do, purchase supplementary private health insurance, which typically offers cover for both private care in a public hospital and part-payment of GP fees. An average of 45% of people aged over 60 years were covered by private health insurance in 2013. (204)

The Health Service Executive (HSE) in its role of providing all state funded health services administers a network of public hospitals nationally; it has four administrative regions representing broad geographic regions (Dublin Mid-Leinster, Dublin North East, South and West) with hospitals divided into seven hospital groups (Appendix A). These hospitals all have local management and differing methods of interaction with primary care with for example varying levels of transition services at discharge.(205) In addition to the public network of hospitals are a number of privately run hospitals. These are run on a ‘for profit’ basis and charges apply for admission. Many private health insurance plans subsidise investigations and inpatient stays in these hospitals.

Prescribed medications are funded through the Health Services Executive-Primary Care Reimbursement Service (HSE-PCRS). This service funds the GMS scheme and the excess of the capped payment schemes for individuals not meeting income thresholds for free care, known as the Drugs Payment Scheme. GPs and community pharmacists are self-employed and are contracted by the State through the HSE to provide services (e.g. dispensing of medication,
immunisations etc.). In the case of community pharmacists, the review of medication prior to dispensing is contractually required and includes review for "drug therapy problems e.g. interactions, duplications, dosing issues, allergies, indications, patient counselling on medication, and cost effectiveness". Furthermore, pharmacists may repeatedly dispense many medications, with some exceptions, up to a maximum of six months from the initial prescription date – the potential implications of this will be discussed in Chapter 4.

3.4 Research hypothesis, aims and objectives

The hypothesis of this thesis is that medication reconciliation takes place between secondary and primary care. The aim is to examine the process of reconciliation at this transition, both quantitatively and qualitatively, and to review the most effective methods of reconciliation and the challenges to implementing them.

There are four main objectives:

i. To gather information from general practitioners (GPs) and community pharmacists (CPs) on current practices of medication management at the primary/secondary care interface in Ireland including an assessment of the experience of prescribing errors following transition, identification of medication reconciliation practices, and evaluating the quality of communication/relationship between HCPs.

ii. To determine whether the potentially unintentional discontinuation of common, evidence-based medications for chronic diseases occurs after acute care hospitalisation.
iii. To conduct a systematic review to assess the effect of medication reconciliation interventions on medication discrepancies, patient related outcomes and healthcare utilisation in patients receiving this intervention during transitions of care compared to patients not receiving medication reconciliation.

iv. To gather information from healthcare professionals on the barriers and drivers to the implementation of medication reconciliation both between and within primary and secondary care in Ireland.

The thesis has been divided into eight chapters with a mixed methods approach used in collecting and analysing data. The objectives were met through a number of differing methods. Method one was a national cross-sectional study. Method two a retrospective cohort study of GP prescribing and hospitalisation data. Method three a systematic review. Finally, objective four's method was a qualitative study of semi structured interviews of relevant healthcare professionals. Qualitative and quantitative data were then analysed to illustrate current medication reconciliation practice and highlight areas of concern, opportunities for improvement and potential for further research.

**Timeline**

The individual studies are presented in chronological table 5-1 order of completion as well as illustrating an evolution from contextual information (cross-sectional study, cohort study) through to solutions (systematic review) and their implementation (interviews). While the design, conduct and analysis of these studies did naturally somewhat overlap the final discussion and triangulation of data sequentially followed the end of all data collection.
The thesis chapters are as follows:
Chapter 1 provides an introduction and illustration of key concepts.
Chapter 2 explores the literature, first looking at the issue of medication errors at transitions, then medication reconciliation, as well as relevant healthcare policy. Additional pertinent background information is discussed within each subsequent chapter.
Chapter 3 outlines the rationale, methodology and context in which the research took place. It also sets out the aims and objectives of the thesis.
Chapter 4 describes a national cross-sectional questionnaire administered to GPs and CPs investigating their opinions on the quality of medication reconciliation both within primary care and between primary and secondary care.
Chapter 5 is a retrospective cohort study of GP prescribing and hospitalisation records examining the impact of hospitalisation on the continuity of specific chronic medication in the GP record.
Chapter 6 describes a systematic review of controlled trials of medication reconciliation at transitions of care with the specific primary outcome of medication discrepancies examined.
Chapter 7 reports the findings from a qualitative study gathering information from HCPs, both hospital and community based, on the challenges of implementing medication reconciliation. The findings are reported through a pre-existing implementation framework.
The final chapter (Chapter 8) triangulates and summarises the findings and discusses clinical, research, policy and societal implications of this thesis.
4 Cross-sectional survey of community pharmacists’ and general practitioners’ opinions on medication management at transitions of care in Ireland
4.1 Introduction

This chapter presents the results of a cross-sectional survey of community pharmacists’ and general practitioners’ opinions on medication management at transitions of care in Ireland. It investigates the perceived quality of reconciliation and communication between and within primary and secondary care.

Most existing studies of medication reconciliation have been prevalence studies of discrepancies attempting to identify high risk groups and transitions, or trials of pharmacist and Information Communication Technology (ICT) mediated interventions with only a few studies investigating primary care based healthcare professionals (HCPs) opinions on their role in reducing and preventing errors at transitions(60,156,208). Barriers to effective reconciliation have been grouped as patient, provider and system factors; in considering designing solutions to reconciliation issues it is necessary to examine these factors more closely(163).

4.2 Aims and objectives

The aim of this study was to gather information from general practitioners (GPs) and community pharmacists (CPs) on current practices of medication management at the primary/secondary care interface in Ireland. Specific objectives of the study included an assessment of the experience of prescribing errors following transition, identification of medication reconciliation practices, and evaluating the quality of communication/relationship between HCPs. The methods and results are presented in detail below and are also available in published format.(209)
4.3 Methods

A cross-sectional, self-administered electronic questionnaire which facilitates anonymous completion was devised. The study and results were conducted and reported in line with best practice reporting guidelines.\(^{(210,211)}\)

4.3.1 Setting & Population

Healthcare in the Republic of Ireland, as described in Section 3.1.3.1, is provided through a mixed model of funding. The Health Service Executive (HSE) provides all state funded health services; it has four administrative regions representing broad geographic regions (Dublin Mid-Leinster, Dublin North East, South and West). Almost half (44\%) (July 2013) of the population have their healthcare subsidised by the state (General Medical Services scheme - GMS). GPs operate as private contractors, consulting with both private (self-funding) and public (GMS) patients. CPs are contracted by the HSE to dispense medication, and are typically private contractors also.

4.3.2 Sampling frame

The study aimed to recruit a representative sample from GPs and CPs in Ireland (total population 3439 CPs and 2799 GPs). A sampling frame of potential participants was identified with the permission of the professional representative and regulatory bodies respectively of general practitioners and community pharmacists (Irish College of General Practitioners (ICGP) and the Pharmaceutical Society of Ireland (PSI) who hold up-to-date email addresses for almost all members on their registers). All GPs and GP Registrars on the ICGP register were included in the sample while a simple random sample of CPs was prepared by the PSI from their register to satisfy the sample size requirement.
4.3.3 Survey design, development and testing

There are a limited number of existing questionnaires available on this topic; therefore, a new questionnaire was devised based on information derived from the literature and the input of a panel of academics and the target HCPs. This multidisciplinary group consisting of practising GPs and pharmacists was brought together to devise the items within the questionnaire. The group revised the questionnaire to confirm face validity, identify and refine any ambiguous questions, and to judge the time taken for completion.

Two separate versions of the tool were developed for GPs and CPs – with core questions (allowing for comparison between groups) supplemented by some profession specific questions. The questionnaire had a mix of quantitative (a mix of dichotomous (e.g. yes/no), multiple choice, scaled responses) as well as free text responses – with respondents having an opportunity to clarify reasons with explanations. Core content consisted of basic demographics, details on employment and professional experience. In addition, questions on current medication management practices (specifically medication reconciliation), the quality of communication and relationship with other healthcare providers, as well as the experience and handling of prescribing errors were included. (See Appendix E & F for GP and CP versions of the questionnaire)

The questionnaire was adapted and hosted on an online survey platform (surveygizmo.com). The number of items and screen pages were kept to a minimum to reduce responder fatigue and enhance the completion rate. Adaptive questioning was used (certain items being conditionally displayed based on responses to other items) to reduce the number and complexity of questions. Respondents were
prompted to complete missing items at each step (‘completeness check’) and a review option was allowed whereby respondents could return to previous screens to review/update answers (within the same log in session). Finally, the questionnaire was piloted with a number of the target HCPs that are associated with the HRB Centre for Primary Care Research.

4.3.4 Sample size

In order to attain a statistically representative sample of the target population, allowing for a 15% response rate, a sample size of 346 responses for each profession was calculated (margin of error: 5%, confidence level: 95%). This projected low response rate was a recognition of the widespread reporting in the survey literature of poor response rates to postal and electronic surveys in particular.

4.3.5 Ethical approval and consent

Ethical approval to undertake this study was granted by the Royal College of Surgeons in Ireland Research Ethics Board (ID REC000923) (Appendix B). Completion and return of the questionnaire was taken as indicating consent.

4.3.6 Data collection

The survey was distributed in June 2014 using the PSI and ICGP email lists (2,364 GPs, 311 GP Registrars [complete ICGP mailing list] and 2,382 CPs [PSI random sample]) with a hyperlink to the online survey tool. A reminder email was sent four weeks later. Participants were incentivised, with their consent, to complete the survey (e.g. voluntary participation in a free prize draw for a monetary gift voucher as well as registering the time spent participating in the questionnaire as contributing to their individual requirements for continuing professional development).
4.3.7 Data management

Multiple entries from the same individual were discouraged by requiring the input of name and contact details into the prize draw. This information was entered and held in an independently administered online survey tool that linked from the main survey. Computer internet protocol (IP) addresses were also recorded to review potential duplicate entries.

To encourage 100% completion participants were advised of the prize draw at the beginning on the invitation screen but access to the separate data collection tool for prize draw entry was only available after completing all screens of the survey.

A completeness check was undertaken at the end of data collection. An examination of all respondents’ submissions was done to assess for patterns of non-response.

An undergraduate RCSI medical student (HC), while completing a summer research placement, was responsible for maintaining the survey, liaising with respondent queries, and compiling the initial data extraction prior to analysis. The project adhered to the RCSI Research Ethics Committee (REC) policy on data protection. Upon receiving ethical approval, a unique secure folder was created under the PhD candidate’s name within the local computer drive. Access to the anonymised data provided for the study was granted by the REC convener and this was restricted to specific authorised members of the research team. All information pertaining to the study was stored in this location. The data analysis took place within the HRB Centre for Primary Care Research, RCSI.
Data will not be stored beyond seven years and will be destroyed following this date by the data controller (i.e. the research centre’s principal investigator) or his designated successor.

4.3.8 Statistical and qualitative analysis

Quantitative data were analysed in Stata statistical software, version 14 (215). One researcher (HC) was primarily responsible for survey response management with a second (PR) verifying a random sample of 10% for accuracy and consistency of coding. Summary statistics were used to characterise the sample and compare it to the original proposed population.

Responses were assessed for missing data, in particular patterns of non-response, whether intentional e.g. skip pattern - some questions were presented dependent on the response to the previous question in the series. A standard approach of list wise deletion was undertaken where variables/responses were not available for comparison.

Following this, the distributions of responses to questions concerning key outcomes (medication reconciliation, quality of communication and prescription error) were compared between GP and CP using tabular and graphical means. Means and standard deviations (where appropriate) were computed for continuous outcomes and percentages for categorical outcomes. These data were used to describe the study participants, address the descriptive research questions and to inform further statistical analysis. The sign-test, Chi-squared test and Fisher’s exact test were used as appropriate to examine possible associations between responses to questions of interest and community healthcare provider (GP or CP). Statistical significance was determined by p value of < 0.05.
Given that quality of communication and experience of prescription errors were considered to be outcomes of particular importance, these were explored in greater detail using multivariable modelling. Logistic regression was used to model recall of prescribing error in the previous six months and ordered logistic regression for quality of communication with public hospital, private hospital and between GP and CP. For each model the primary exposure variable was healthcare provider (GP or CP), with adjustments for relevant confounders (HSE region, practice location, age, gender, hours worked per week and distance from the local public hospital). The potential for interactions between exposure variable and confounders was examined using the likelihood ratio test, with the potential for collinearity between predictor variables considered through examination of Variance Inflation Factors (VIF); these were satisfactory. The suitability of the proportionality assumption of ordered logistic regression was explored using generalised ordered logistic regression models; however, deviations from proportionality were rare and had little substantive impact on the clinical conclusions and hence the results from the more parsimonious ordered logistic regression models are presented. Due to low numbers responses to ‘very poor’ and ‘poor’, these were amalgamated when considering opinions on communication of GP and CP of each other.

For the qualitative analysis, all free text responses were reviewed by the PhD candidate (PR) by the inductive method of data driven content analysis within Nvivo software, version 10 (216), developing themes linked to individual participants’ contributions (217). Similar meanings and concepts were coded together into distinct new themes with the creation of no further categories with data saturation. To ensure validity and consistency, a second researcher undertook dual coding.
of 10% of free text. Finally, the central or axial categories were checked against the original data for negative evidence to ensure the themes developed accurately reflected the data.

4.4 Results

4.4.1 Quantitative survey results

In total, 897 out of 5057 questionnaires were returned resulting in an overall response rate of 17.7%; the response rate was 20.7% (n=554) and 14.4% (n=343) for GPs and CPs respectively. Demographic data of respondents are summarised in Table 4-1. There was broad representation from all geographic regions, with more male GP respondents (n=317, 57.2%) but more female CP respondents (n=223, 65%). Most respondents were in full time practice.

4.4.1.1 Missing data

There was a varying response rate to individual items. The demographic questions were the most complete with 20 CPs (5.5%) and 33 GPs (5.6%) not responding. Responses to questions towards the end of the survey were less complete with 122 CPs (33.7%) and 191 (32.5%) failing to answer questions around experiences of errors in the previous six months. Eighty-nine CPs and 145 GPs completed all questions (including potential skip items) with only one CP and GP each failing to answer questions beyond basic demographics.
Table 4-1 Characteristics of GP and CP respondents. GP (n=554) CP (n=343)

<table>
<thead>
<tr>
<th>Key Characteristics</th>
<th>GP (n, %)</th>
<th>CP (n, %)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
<td>554</td>
<td>343</td>
</tr>
<tr>
<td>Female</td>
<td>237 (42.8)</td>
<td>223 (65.0)</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td>554</td>
<td>343</td>
</tr>
<tr>
<td>&lt;=30</td>
<td>27 (4.87)</td>
<td>58 (16.9)</td>
</tr>
<tr>
<td>31-40</td>
<td>187 (33.8)</td>
<td>137 (39.9)</td>
</tr>
<tr>
<td>41-50</td>
<td>124 (22.4)</td>
<td>80 (23.3)</td>
</tr>
<tr>
<td>51-60</td>
<td>149 (26.9)</td>
<td>50 (14.6)</td>
</tr>
<tr>
<td>&gt;61</td>
<td>67 (12.1)</td>
<td>18 (5.3)</td>
</tr>
<tr>
<td><strong>Health Service Executive (HSE)Region</strong></td>
<td>554</td>
<td>342*</td>
</tr>
<tr>
<td>HSE Dublin Mid Leinster</td>
<td>174 (31.4)</td>
<td>102 (29.8)</td>
</tr>
<tr>
<td>HSE Dublin North East</td>
<td>112 (20.2)</td>
<td>69 (20.2)</td>
</tr>
<tr>
<td>HSE West</td>
<td>125 (22.6)</td>
<td>79 (23.1)</td>
</tr>
<tr>
<td>HSE South</td>
<td>143 (25.8)</td>
<td>92 (26.9)</td>
</tr>
<tr>
<td><strong>Hours worked per week</strong></td>
<td>553*</td>
<td>342*</td>
</tr>
<tr>
<td>10 or less</td>
<td>7 (1.3)</td>
<td>12 (3.5)</td>
</tr>
<tr>
<td>11 to 20</td>
<td>41 (7.4)</td>
<td>24 (7)</td>
</tr>
<tr>
<td>21 to 30</td>
<td>46 (8.3)</td>
<td>28 (8.2)</td>
</tr>
<tr>
<td>31 to 40</td>
<td>148 (26.8)</td>
<td>123 (35.9)</td>
</tr>
<tr>
<td>&gt;40</td>
<td>311 (56.2)</td>
<td>155 (45.3)</td>
</tr>
<tr>
<td><strong>Location</strong></td>
<td>554</td>
<td>342</td>
</tr>
<tr>
<td>City Suburbs</td>
<td>187 (33.8)</td>
<td>105 (30.7)</td>
</tr>
<tr>
<td>Large Town</td>
<td>108 (19.5)</td>
<td>88 (25.7)</td>
</tr>
<tr>
<td>Inner City</td>
<td>72 (13.0)</td>
<td>26 (7.6)</td>
</tr>
<tr>
<td>Small Town/Rural</td>
<td>187 (33.6)</td>
<td>123 (35.9)</td>
</tr>
<tr>
<td><strong>Distance from nearest acute public hospital</strong></td>
<td>554</td>
<td>340*</td>
</tr>
<tr>
<td>&lt;5km</td>
<td>255 (46.0)</td>
<td>138 (40.6)</td>
</tr>
<tr>
<td>5-15km</td>
<td>109 (19.7)</td>
<td>86 (25.6)</td>
</tr>
<tr>
<td>6-20km</td>
<td>53 (9.6)</td>
<td>37 (10.9)</td>
</tr>
<tr>
<td>21-40km</td>
<td>93 (16.8)</td>
<td>79 (23.2)</td>
</tr>
<tr>
<td>&gt;40km</td>
<td>44 (7.9)</td>
<td>0 (0.0)</td>
</tr>
</tbody>
</table>

*One missing response
4.4.1.2 Respondent characteristics

The majority of GP respondents were GP principals (n=349, 63%) working with other GPs as part of a larger practice (n=407, 73%), with computerised prescribing records (n=517, 96%), seeing 10-19 individual patients per session/half day (n=430, 78%). A third of CPs (n=119, 35%) held a role as a Supervising Pharmacist, dispensing >3000 prescriptions/month (n=103, 30%); more than half described themselves as employees (n=189, 55%), working in an independently run pharmacy (n=193, 57%).

Views on medication reconciliation

Most GP respondents did not feel they had a formal system for medication reconciliation (n=327, 60%). Nevertheless, three quarters of GPs (n=298, 75.4%) rated the standard of medication reconciliation in their practice as being good to excellent. Most CPs reported they had systems in place to identify omissions (n=213, 74.5%) and newly initiated medications (n=220, 76.9%) in their patients’ prescriptions. Almost all GPs (n=396; 97.8%) agreed or strongly agreed reconciling medication was an important way to both improve medication safety, with both GPs (93%) and CPs (93%) in agreement that it was also an important way to improve medication adherence. Only 22% (n=90) of GPs agreed that reconciliation was best handled by pharmacists. However, the majority (74%) of CPs agreed/strongly agreed that they were best placed to handle reconciliation, with 88% agreeing their time was well-spent updating the patient medication list.

When asked to rank what information they considered most important to include when receiving details of medications from other HCPs, respondents ranked a full list of current medications (GP n=314, 69.6%; CP n=171, 64.5%) followed
by details of any change to long-term medication (GP n=76, 16.6%; CP n=33, 12.2%) as most important. Details of previous adverse effects (GP n=10, 2.2%; CP n=3, 4.1%) and special administration requirements (GP n=10, 3.8%; CP n=11, 3.7%) were considered the least important information. There was no overall difference in the mean rankings given to items selected by GP and CP (p=0.73) (Table 4-2).
Table 4-2 Views of GPs and CPs on medication reconciliation

<table>
<thead>
<tr>
<th>Please rank the following in order of importance when preparing and dispensing prescriptions or updating medication records (from any prescriber). Lists those choosing as most important for each category (GP: min n=450, max n= 486, CP: n= min n=261, max n=271) ¥</th>
<th>GP (N, %)</th>
<th>CP (N, %)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>List of all current medications</td>
<td>314 (69.6)</td>
<td>171(64.5)</td>
<td>p=0.73^</td>
</tr>
<tr>
<td>Change to long term medication</td>
<td>76 (16.6)</td>
<td>33 (12.2)</td>
<td></td>
</tr>
<tr>
<td>Reason for changes to previously used medication</td>
<td>34 (7)</td>
<td>14 (5)</td>
<td></td>
</tr>
<tr>
<td>Allergy status</td>
<td>18 (3.9)</td>
<td>23 (8.8)</td>
<td></td>
</tr>
<tr>
<td>Special requirements of administration</td>
<td>18 (3.83)</td>
<td>10 (3.72)</td>
<td></td>
</tr>
<tr>
<td>Duration of therapy</td>
<td>9 (2)</td>
<td>3 (1.1)</td>
<td></td>
</tr>
<tr>
<td>Previous adverse effects</td>
<td>10 (2.2)</td>
<td>3 (1.1)</td>
<td></td>
</tr>
<tr>
<td>Drug indication</td>
<td>10 (2.2)</td>
<td>11 (4.1)</td>
<td></td>
</tr>
</tbody>
</table>

What is your opinion on the standard of medication reconciliation that occurs in your practice? (GP: n=395)

| Excellent | 9 (2.3) | |
| Very good | 96 (24.3) | |
| Good | 193 (48.9) | |
| Fair | 86 (21.8) | |
| Poor | 11 (2.8) | |

^ Sign test of difference in mean rankings of items between groups
¥ The number of available responses varied due to non-completion of all items in questionnaire

Communication and relationship between GP, CP, hospital pharmacist, public and private hospitals

There were mixed views amongst GPs and CPs regarding communication with their local publicly funded hospital, with approximately a third describing it as poor/very poor and a similar proportion describing it as good to very good. Most GPs did not receive communication electronically about prescriptions from their local hospitals (n=348, 64%). There were differences in satisfaction levels between HSE regions. Respondents in Dublin North East were, on average, 40% less likely, and those in the West 34% less likely, to report higher levels of satisfaction in communication with public hospitals than their counterparts in Dublin Mid-Leinster,
adjusted odds ratio (AOR): 0.59, 95%CI [0.41-0.87], p=0.01; AOR: 0.66, 95%CI [0.45-0.95], p=0.03 respectively. These effects did not vary between GPs and CPs (p=0.53).

Differences in levels of satisfaction between HSE regions in satisfaction of communication with private hospitals were not apparent. CPs were less likely to rate communication with private hospitals favourably compared to GPs (AOR: 0.66, 95%CI [0.48-0.90], p=0.01). (Appendix G)

The opinion of GPs and CPs on their relationship with each other was generally positive, with 62% (n=311) of GPs and 52.5% (n=150) of CPs describing the relationship as very good (Table 4-3 and Appendix H).

Regarding hospital pharmacists (HP), nearly 40% of GPs described the quality of communication as poor/very poor. Adjustment for age, gender, location, hours worked and distance from a public hospital had no significance. Both CPs (86%) and GPs (87%) were in favour of expanding the role for HPs in identifying and preventing prescribing errors as patients experienced care transitions. Similarly, GPs (74%) and CPs (82%) felt the role of the community pharmacist should be expanded in the identification and prevention of prescribing errors following a transition.

*Experience of prescribing errors*

Almost 84% (n=320) and 87.2% (n=205) of GPs and CPs respectively reported (of those who answered this question) that they could remember mistakes in patients’ prescriptions, which may have been due to poor transfer of information following a care transition (e.g. delayed or no discharge prescription available, omission of long-term medications) in the past six months (p=0.27; Table 4-4). Although in-patient
discharge prescriptions were selected by both respondent groups as being the single largest source of prescription error (GP 21.6%, CP 16.8%), all sources of prescriptions including out-patients, emergency departments, in-patient discharges and private hospitals were implicated. There was evidence (p<0.001) of an overall significant difference in the sources of mistakes in prescribing errors identified between GPs and CPs. GP transcription of hospital prescriptions was identified as also being a source of error with 67.7% (n=153) of CPs stating it was likely/very likely for an error to arise. In general, managing identified errors was recognised as being complicated with most respondents (CP n=170, 79.4%; GPs n=253, 88.1%) finding it difficult or impossible to contact hospital prescribers.
Table 4-3  Quality of communication between GP/CP and Primary/Secondary Care (GP n=498; CP n=286*)

<table>
<thead>
<tr>
<th>How would you rate the quality of communication you have with...?</th>
<th>GP (n, %)</th>
<th>CP (n, %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Between GP &amp; CP</td>
<td>498</td>
<td>286</td>
</tr>
<tr>
<td>• Very good</td>
<td>311 (62.4)</td>
<td>150 (52.4)</td>
</tr>
<tr>
<td>• Good</td>
<td>138 (27.7)</td>
<td>109 (38.1)</td>
</tr>
<tr>
<td>• Neutral</td>
<td>24 (4.8)</td>
<td>18 (6.3)</td>
</tr>
<tr>
<td>• Poor</td>
<td>4 (0.8)</td>
<td>7 (2.4)</td>
</tr>
<tr>
<td>• Very Poor</td>
<td>10 (2.0)</td>
<td>2 (0.7)</td>
</tr>
<tr>
<td>• N/A</td>
<td>11 (2.2)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Public Hospital</td>
<td>498</td>
<td>286</td>
</tr>
<tr>
<td>• Very good</td>
<td>16 (3.2)</td>
<td>18 (0.6)</td>
</tr>
<tr>
<td>• Good</td>
<td>173 (34.7)</td>
<td>68 (23.8)</td>
</tr>
<tr>
<td>• Neutral</td>
<td>148 (29.7)</td>
<td>95 (33.2)</td>
</tr>
<tr>
<td>• Poor</td>
<td>104 (20.9)</td>
<td>71 (24.8)</td>
</tr>
<tr>
<td>• Very Poor</td>
<td>55 (11.0)</td>
<td>31 (10.8)</td>
</tr>
<tr>
<td>• N/A</td>
<td>2 (0.4)</td>
<td>3 (1.0)</td>
</tr>
<tr>
<td>Private Hospital</td>
<td>498</td>
<td>285</td>
</tr>
<tr>
<td>• Very good</td>
<td>41 (8.2)</td>
<td>14 (4.9)</td>
</tr>
<tr>
<td>• Good</td>
<td>195 (39.8)</td>
<td>73 (25.6)</td>
</tr>
<tr>
<td>• Neutral</td>
<td>140 (28.1)</td>
<td>83 (29.1)</td>
</tr>
<tr>
<td>• Poor</td>
<td>71 (14.3)</td>
<td>44 (15.4)</td>
</tr>
<tr>
<td>• Very Poor</td>
<td>20 (4.0)</td>
<td>21 (7.4)</td>
</tr>
<tr>
<td>• N/A</td>
<td>31 (6.2)</td>
<td>50 (17.5)</td>
</tr>
</tbody>
</table>
Table 4-4: Comparison of GPs and CPs experience and handling of prescribing errors. (GP n=381; CP n=235)

<table>
<thead>
<tr>
<th></th>
<th>GP (n, %)</th>
<th>CP (n, %)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>In the past 6 months, can you remember a time where mistakes have happened in patients’ prescriptions?</strong> (GP: n=381, CP: n=235)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>320 (83.9)</td>
<td>205 (87.2)</td>
<td>p=0.27*</td>
</tr>
<tr>
<td>No</td>
<td>61 (16.0)</td>
<td>30 (12.8)</td>
<td></td>
</tr>
<tr>
<td><strong>Which sources account for the mistakes you see?</strong> (GP: n=320, CP: n=203)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Out patients Department</td>
<td>16 (5.0)</td>
<td>8 (3.9)</td>
<td>p&lt;0.001**</td>
</tr>
<tr>
<td>Emergency Department</td>
<td>5 (1.6)</td>
<td>4 (1.9)</td>
<td></td>
</tr>
<tr>
<td>Inpatient</td>
<td>69 (21.6)</td>
<td>34 (16.8)</td>
<td></td>
</tr>
<tr>
<td>Private</td>
<td>2 (0.6)</td>
<td>1 (0.5)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>7 (2.2)</td>
<td>17 (8.4)</td>
<td></td>
</tr>
<tr>
<td>Mixture of sources</td>
<td>204 (63.7)</td>
<td>111 (54.7)</td>
<td></td>
</tr>
<tr>
<td>No preference</td>
<td>17 (5.3)</td>
<td>28 (13.8)</td>
<td></td>
</tr>
<tr>
<td><strong>If you do attempt to contact the hospital prescriber, how easy is it to do?</strong> (GP: n=287, CP: n=214)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Very Easy</td>
<td>0 (0.0)</td>
<td>1 (0.5)</td>
<td>p=0.07**</td>
</tr>
<tr>
<td>Easy</td>
<td>9 (3.1)</td>
<td>14 (6.5)</td>
<td></td>
</tr>
<tr>
<td>Neutral</td>
<td>25 (8.7)</td>
<td>29 (13.6)</td>
<td></td>
</tr>
<tr>
<td>Difficult</td>
<td>215 (74.9)</td>
<td>146 (68.2)</td>
<td></td>
</tr>
<tr>
<td>Impossible</td>
<td>38 (13.2)</td>
<td>24 (11.2)</td>
<td></td>
</tr>
<tr>
<td><strong>In those patients whom you have received a prescription transcribed by their GP how likely is it that an error from an original hospital prescription – how likely is it, in your opinion that a potential error will arise?</strong> (CP: n=226)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Very likely</td>
<td>N/A</td>
<td>40 (17.7)</td>
<td>N/A</td>
</tr>
<tr>
<td>Likely</td>
<td></td>
<td>113 (50.0)</td>
<td></td>
</tr>
<tr>
<td>Neutral</td>
<td></td>
<td>49 (21.7)</td>
<td></td>
</tr>
<tr>
<td>Unlikely</td>
<td></td>
<td>24 (10.6)</td>
<td></td>
</tr>
</tbody>
</table>

*Pearson’s chi-squared test  **Fisher’s exact test
4.4.2 Free text content analysis survey results

The examination of free text responses generated four broad categories representing a number of subthemes:

1. Organisational/Infrastructural issues
2. Relationship and quality of communication between HCPs
3. Role of the patient/vulnerable patients
4. Prescribing errors

4.4.2.1 Organisational/Infrastructural issues

Many CPs were frustrated by the lack of clinical information available to them about their patients.

“The current role is an impossible guessing game where community pharmacists don’t have the information to do any more than prevent the most gross of errors. More subtle but equally dangerous errors can and do go unmissed”

Female Superintendent/Supervising Pharmacist, 51-60, Small town/rural, HSE West

An expanded role for CPs was also highlighted by some respondents:

“Currently the only official recognition of the pharmacist’s intervention in patient care is via the ‘not-dispensed’ category in dispensing of GMS [General Medical Services] only prescriptions. This should be expanded to all State Schemes and an electronic communication mechanism should be put in place to allow pharmacists to directly contact the prescriber and record details of their discussion on medication changes”
Male Superintendent/Supervising Pharmacist, 51-60, City Suburb, HSE Dublin North East

The clinical guidance given to junior hospital doctors in preparing discharge summaries and prescriptions was also raised as an issue:

“There needs to be accountability by consultant/senior team member so that scripts and letters written by inexperienced interns and SHOs [Senior House Officers] are reviewed at time of discharge or at the very least post discharge a chart review in a timely fashion. It is impossible to expect a junior doctor to understand the importance of this crucial step unless he/she is taught this by their seniors”

Male GP Principal, 31-40, Large Town, HSE South.

CPs underlined the role that HPs could play in improving safe and appropriate prescribing by providing an additional layer of review in the transition process for patients.

“Hospital pharmacists have the knowledge and access to current clinical in-patient notes and determine which medications have been adjusted and to communicate this to the team/GP on discharge. The main reason that this is not happening across the country is due to poor resourcing of pharmacists in hospital and inadequate staffing levels so that they do not have time to perform this function in all wards etc. I have worked in hospitals/units before where the pharmacist played a key role in reviewing medication lists on discharge and there is no doubt that this prevented many prescribing/transcribing errors”

Male GP Principal, 31-40, Large Town, HSE South
Finally, the fragmented nature of the healthcare system itself was also noted. There were issues regarding the lack of printed or computerised discharge letters/prescriptions, interoperability of hospital/pharmacy and GP software systems, a 'safety net' for some categories of patients, and resources:

“Every 2-year-old is computerised...my first PC was a 386 in 1994....so WHY are we still receiving illegible hand written prescriptions from hospitals????!!!”

Female GP Principal, 41-50, Large Town, Dublin Mid Leinster

“Medicine reconciliation is often complex...while updating medication lists is professionally fulfilling it is time-consuming and must be suitably remunerated”

Female Superintendent/Supervising Pharmacist, 51-60, Small Town/Rural, HSE West

“...patients can go straight to any pharmacy in any town with a prescription - lots of scope for errors and misunderstandings to occur and in relation to private patients, they may not attend at GP at all and in some cases prescriptions are dispensed by pharmacies without any medical check being done”

Male GP Principal, 51-60, Small Town/Rural, HSE West

4.4.2.2 Relationship and quality of communication between HCPs

A good relationship was reported between the two groups of HCPs by respondents. The strength of this relationship in terms of improving patient safety was highlighted:
“In all instances, no harm came to [the] patient as between the GP and pharmacy any problems were identified and rectified—benefit of having a working relationship”

Female CP <=30, Small group pharmacy, HSE South

The specific skills of the CP were recognised and valued by GPs, even when correcting GP prescribing or seeming to be particularly fastidious:

“An essential professional in helping to minimise drug errors. I will always take phone call queries from pharmacists, even being very careful and ‘OCD’ nearly about my prescribing, we are all human and mistakes can happen. Also, pharmacists’ pharmacology knowledge I feel is superior to doctors in general…I”

Male GP Assistant, <=30, Large Town, HSE South

A significant theme in terms of contributions from respondents was disappointment with the quality of communication within the health system, particularly when attempting to contact hospital prescribers to resolve identified problems or ambiguities with prescriptions outside of normal working hours:

“Difficult to impossible. Signatures are always illegible. Bleep numbers are often incorrect or missing. Entire teams can be unavailable”

Male Superintendent/Supervising Pharmacist, 31-40, Small/Town, HSE Dublin Mid-Leinster

“Incomplete list of meds no mention of specific meds to be stopped. Medication prescribed that patients have already been
on and found ineffective or intolerable. Delay in the discharge letter and script. Patients often present with a script but no discharge letter so no information as to what was or wasn’t done or why.”

GP Principal, 31-40, Inner City, HSE South

4.4.2.3 Role of the patient/vulnerable patients

Respondents highlighted the need for involvement of patients in ensuring correct prescribing information was transmitted. Some respondents felt patients contributed to the lack of clarity:

“Have found in the past that patients sometimes are reluctant to tell their GP that they have stopped taking a medication, yet do not get it dispensed every month and leave it on the prescription indefinitely. Is problematic for GP’s as they do not have the full picture from patients…”

Female Pharmacist <=30, employee, City Suburb HSE South

Comments also indicated that patients should be respected and engaged when making changes to their prescriptions:

“Patient’s own personal responsibility and education. Paramount [to] educate them to hold their own drug (and indication) records and encourage them to chase all to update them”

Male GP Principal, 51-60, City Suburbs, HSE Dublin North East

Respondents highlighted patients with multi-morbidity and those with mental health issues as having the greatest risk of
medication error due to frequent transitions of care and specialist review without a global view of their medications:

“… Quite often the hospital specialist is only concerned about his area of expertise (e.g. cardiac) and is not aware of the other medicines taken by the patient. This can lead to errors in prescribing. The pharmacist is concerned with the total drug therapy”

Female supervising pharmacist, 51-60, employee, Small town/rural, HSE Dublin North East

4.4.2.4 Prescribing errors

The majority of participants recalled that they had seen any errors in their patients’ prescriptions over the past six months. There was almost universal agreement, with many examples given of errors:

“… This is a genuine problem, and it'll blow up for some individual. I'm amazed it doesn't frequently blow up actually given the amount of prescribing errors I see”

Male Superintendent Pharmacist, 31-40, Inner City, Employer, Dublin Mid Leinster

“Multiple errors. Nearly a daily occurrence. Can be very stressful trying to ensure safe prescribing”

Male GP Assistant, <=30, Large Town, HSE South
4.5 Discussion

4.5.1 Principal findings and context in comparison with previous research

Internationally, patient safety incidents are relatively common in primary care and prescribing incidents are those most likely to cause avoidable harm to the patient.\(^{(11)}\) The main findings of this study, while weakened by a low response rate, highlighted almost unanimous experience among respondents of prescribing errors following transitions, an absence of formalised medication reconciliation practices in GP practices, dissatisfaction with the current standard of communication between primary and secondary care, and support for a greater role for both HPs and CPs in medication management.

Implementing formal systems of medication reconciliation was a key recommendation in terms of medication safety in a Department of Health & Children, Ireland report in 2008.\(^{(178)}\) Despite this and the fact that both responding GPs and CPs were positive about the benefits of medication reconciliation in terms of prescribing safety and adherence, formal systems of medication reconciliation were not in place in most GP practices. A greater understanding is needed as to why improvements in medication reconciliation have not been adopted by the majority of GPs.

The results of this study are in-keeping with barriers and potential solutions identified internationally to medication management at transitions of care.\(^{(60)}\) In terms of provider and organisational issues, concerns with poor communication across the primary/secondary interface were highlighted, with many examples of errors arising. While the reason for the reported geographic difference in opinion on the quality of
communication is not clear from this study, a discrepancy between regions in terms of the in-patient clinical pharmacy services provided has been recorded previously. Furthermore, many respondents highlighted a deficit in the limited use of ICT to improve communication, as well as its possible role in reconciliation. GPs reported having limited contact with CPs and both groups felt HPs could play a greater role in interacting with primary care HCPs. This lack of contact between HPs and community HCPs has been confirmed previously with a majority of hospitals having no arrangement for HPs involvement or communication to primary care based HCPs upon patient discharge.

Conversely the relationship between GPs and CPs was rated positively by the majority of both groups. However, there was a frustration from some CPs that they could not contribute more in the management of medications. Indeed high quality trials of CPs effectiveness in medication management, while limited in number, are generally favourable. Furthermore, 22% of GPs agreed that reconciliation was best handled by pharmacists while 74% of CPs agreed/strongly agreed that they were best placed to handle reconciliation. This highlights a possible ambiguity around ‘ownership’ of outpatient medications and the difficulty in developing a community of HCPs to coordinate care for patients as recommended in the King’s Fund and subsequent commissioner reports in the UK. This is further compounded by the majority of GP respondents’ view that CPs role in medication management could be enhanced. This apparent conflict in findings is perhaps representative of the legal underpinning of prescribing authority in Ireland – CPs can contribute to the process, but do not have prescribing authority.
The majority of both groups noted that they were exposed to errors in prescriptions in the past 6 months, following a transition of care. These findings are consistent with international experience, particularly omission of chronic medications and possible subsequent re-hospitalisation and mortality.\(^{15,218}\) The fact that respondents also expected more ADEs to occur than is the case is also supported by previous reviews that found that most unintentional discrepancies had no apparent clinical significance.\(^{24}\)

Respondents also highlighted a lack of funding to dedicate time and staff to reconciliation – an issue likely impacting development of additional services in secondary care too (e.g. HP availability for discharge reconciliation). Finally, a theme which resonates with much of the literature around multi-morbidity was the lack of patient involvement in the process of coordinating transitions for complex patients.

### 4.5.2 Strengths and limitations

There are some limitations to the study. Firstly, and most damagingly, the response rate (17.7 %), similar to many electronic surveys, was low. This weakens the generalisability of the findings of this survey – therefore while the findings are in keeping with the results of previous surveys published internationally we cannot be certain these results are representative of the target population. In addition, the possibility of responder bias needs to be taken into consideration. Furthermore, the number of questions unanswered rose towards the end of the questionnaire – making the results of later questions perhaps less representative. Nevertheless, despite these weaknesses, the demographics of GP and CP responders were comparable to data published in two national reports, giving confidence that the respondents comprise a representative sample.\(^{219–222}\)
Secondly, although the questionnaire enabled the collection of data from a large number of respondents, it may have been limited in its ability to gain rich in-depth information on behaviours and feelings. Finally, with self-report questionnaires, the issue of socially desirable responding (i.e. the tendency for participants to present a favourable image of themselves) should be considered.

4.5.3 Future clinical and research implications

The findings of this study are relevant to those directly involved in medication reconciliation as well as health care policy makers in Ireland; there is a need to address the concern expressed by most respondents about the current quality of reconciliation and communication between primary and secondary care. Future research efforts should aim to confirm this study's findings by achieving a greater response rate of the target groups, further explore the suggested geographic variation in satisfaction with communication (and its possible link with hospital discharge service provision); and further explore the possibility of a greater role for community pharmacists (noted by both groups) in the reconciliation process.

4.6 Conclusion

The findings from this study, while interpreted with caution due to a limited response rate, are consistent with previous research highlighting HCPs’ recognition of prescribing errors as being a common event at transitions of care. Poor communication between primary care HCPs and secondary care, as well as the call for a more “structured seamless care programme” linking primary and secondary care, were also highlighted. A suggestion of geographical variation in satisfaction with communication also emerged. The results of
this study confirm that while there is enthusiasm for the benefits of medication reconciliation, there are limited formal structures in primary care to support it, despite it being a stated aim of regulatory agencies. Additionally, CPs have limited opportunity to contribute in medication reviews and the role of HPs in coordinating transitions could, in the respondents’ view, be expanded. In the following chapters the perceived level of prescribing errors will be explored quantitatively and the major thematic issues identified will be investigated through an in depth qualitative study.
Does the potentially unintended discontinuation of chronic medication occur following hospitalisation? A retrospective cohort study.
5.1 Background

This chapter presents the results of a retrospective cohort study examining whether the unintended discontinuation of common, evidence based, long-term medication occurs after hospitalisation and whether the quality of documentation of medication at discharge is associated with subsequent discontinuity of medication.

Poor coordination of transitions of care is associated with error, ADEs, rehospitalisation and in particular discrepancies in medication lists.(14,46,142,223–225) Disruptions in medication continuity following hospitalisation have previously been reported.(218,226–228) Omissions of medication are one of the most common discrepancies noted in prescribing errors at discharge.(51,90,229–231)

Previous studies have reported an increased risk of medication discontinuity post hospitalisation. These studies have primarily examined large dispensing and/or administrative databases post hospitalisation to record the outcome of ‘discontinuity’. (218,226–228,232) There has been limited specialised study of the immediate impact of hospitalisation and/or medication error at hospital discharge propagating forward into general practice prescribing records.(69,233–236) In a small study of post-hospital medication discrepancy (PHMD) reviewing the GP, pharmacist and patient account of medications, more than 50% of patients had at least one error that had continued into primary care records.(69) These studies have suffered from issues such as small sample size, and bias in enrolment. (69,233–236)

Older patients are more likely to be prescribed multiple medications, have multiple chronic conditions, and experience
increasing number of transitions of care. (7, 17, 237) Adherence to clinically appropriate evidence-informed therapies are important for lowering the risk of progression and complications related to their underlying chronic conditions. There is a strong evidence base for prescribing in certain chronic diseases, with a clear role for statins in both primary and secondary prevention (238), anticoagulants/antiplatelets in atrial fibrillation (239), thyroid disease treatment (hypo and hyper) (240, 241) and respiratory inhalers in chronic obstructive pulmonary disease. (242)

While studies have shown an increased risk of medication discontinuity post hospitalisation it is unclear where and why this discontinuity arises. Hospitalisation giving rise to discontinuity may be attributable to prescribing errors at discharge (e.g. omissions, communication issues), disruption in the prescribing process at the GP level, failure or error in dispensing at the pharmacy level or the multitude of reasons for patient non-adherence. This study examines the GP prescribing record of patients prescribed evidence based medication long-term who have been hospitalised and compares medication continuity with those who have not been hospitalised. This study will address the relationship between hospitalisation and disruption of prescriptions at the GP level.

5.2 Aim and objectives

The aim of this study is to determine whether the potentially unintentional discontinuation of common, evidence-based medications for chronic diseases occurs after hospitalisation.

- The primary objective was to describe the discontinuation of prescriptions in the GP record of patients 65 years of age and older being prescribed at least one of the following four medication groups regularly: statins,
antiplatelet or anticoagulants, thyroid medication, respiratory inhalers in the six months post hospitalisation. The odds of discontinuation in those hospitalised was compared to the odds of discontinuation in those not experiencing hospitalisation.

The main predictor variable of interest for the primary objective, hospitalisation, was examined both dichotomously (hospitalised v not hospitalised) and continuously (repeated hospitalisations). Other important covariates that were examined included age, number of medications, insurance status, morbidity and the possible variation of hospitalisation’s association with the outcome between different hospitals.

- The secondary objective was to determine the odds of discontinuation in the GP record of the specified medications in those patients where the medication was not listed on the hospital discharge summary. The odds of discontinuation was compared to those where the medication was listed in the discharge summary.

5.3 Methods

The methods are reported using the Strengthening and Reporting of Observational Studies in Epidemiology (STROBE) statement for reporting observational studies (243). (Appendix I).

5.3.1 Study design

This was a retrospective cohort study, reported adhering to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement, examining the association between hospitalisation and the discontinuation of specific chronic medications (Table 5-1) in the GP prescribing record of
a cohort of GP patients aged 65 years of age and older in Ireland from 2012 to 2016. Data were gathered using the general practice patient management system (Socrates (Figure 5-4)) which includes prescribing, demographic and clinical records, and hospital supplied (Healthlink (Figure 5-3)) hospitalisation records. Project approval was received from the Irish Primary Care Research Network (IPCRN – Section 5.3.6) in 2014 and ethical approval was granted from the Irish College of General Practitioners in 2015 (See Appendix J).

5.3.2 Setting

This was a primary care based study, set in Ireland, using GP clinical and prescription records with anonymous data extracted via an electronic research network. Figure 5-1 outlines the study timeline.

This methods section describes:

- Development and pilot of an electronic finder/extractor tool
- Ethical approval
- Patient and practice eligibility
- Practice recruitment
- Exposure and covariates
- Sample size
- Analysis methods.

5.3.3 Electronic record finder/extractor development and piloting

The principal researcher worked with the general practice patient management system software company Socrates (http://www.socrates.ie) to design a software tool for extracting the relevant study information from the GP electronic record. The researcher had regular meetings with two software developers, the company’s head of communications and the chief executive officer. The software went through an
iterative process of testing with refinements to ensure accuracy and ease of use for the study’s purposes. The anonymised patient data were derived at the primary care level with the prescribing information being extracted from the general practitioner’s record from the 1st January 2011 to the extraction date (See Appendix N for a full list of variables extracted).

Patients from participating practices, who met the eligibility criteria outlined in Section 5.3.12, were identified by the program running within the vendor software. All Healthlink (Section 5.3.5) notification message headers (pre-specified tags or identifiers within the electronic message) were inspected by the software, with message types referring to 'discharge summary' (also known as referral type message) and 'discharge notification' of specific interest, as this indicated discharge from a hospital setting. For these specific message types only, the message bodies were examined to identify the discharging hospital and discharge date. A simple text parser looked for keywords such as ‘discharge’, ‘hospital’ or the names of the hospitals. Admission/discharge date, discharge diagnosis and discharge medications were also extracted from the message content. No further information was extracted from these message bodies. Additionally, where hospitalisation episodes were manually coded (Section 5.3.4) the coders manually created “investigations” tabs within the software. These ‘tabs’ were pre-specified to be coded to contain the detail listed in Appendix N. These were then uploaded through the same method as described below.

The software tool extracted all the data as described above and an anonymised version of the data was uploaded securely to a server run by the IPCRN. The tool removed any identifiers (patient names, addresses, and contact details prior to the data being sent) and assigned patient IDs instead of patient names.
prior to uploading the file to the secure server. No patient recorded clinical notes were uploaded. All dates of births were converted to age only (in whole years – due to ethics committee restrictions as explained in Section 5.3.7). The completed data set was converted by the IPCRN into a MYSQL database and subsequently CSV file for further analysis (Figure 5-4).

5.3.4 Manual Coding

Four practices (Two from Cork hospitals catchment area, two from Dublin hospital catchment area) engaged with the HRB Centre for Primary Care Research to code hospital discharge notifications manually (including length of state, diagnosis, specialty, hospital and discharge medication).

Two third year medical students from the RCSI undertook a six-week summer research elective with the Department of General Practice, RCSI and were involved in chart medical record review. All medical students completed training in research design, planning and organisation skills, systematic recording of patient data, data quality and completeness, patient confidentiality and data security. Four practice nurses were similarly trained in clinical record review and correct procedures around data management and security. Training involved standardising the recording of information by prioritising important medical conditions, and identification of hospitalisation records. Four practices were recruited (Section 5.3.9) to have their records manually reviewed. Nurses and medical students were attached to practices and signed practice level agreements to function as members of the practice – in particular respecting patient confidentiality. GPs remained the data controllers and no practice data left the practice at this stage. All chart review took place within the
practice electronic record system and GPs were provided with reports of the coding process. Coders were not aware of the study hypothesis.

5.3.5 Healthlink

The hospital discharge alert is delivered by Healthlink, the national body charged with coordinating electronic message delivery between secondary and primary care; this was used to establish exposure to hospitalisation.(245) Forty-seven hospitals participate in the Healthlink service, with nine hospitals currently contributing to the discharge summary communication service. More than 90,000 messages were sent to GPs in 2012 on inpatient admissions from seven hospitals. A Health Level-7 (HL7) messaging standard is used that has fixed fields for data entry but the contents of those fields is free text.(246) Different message types may be sent by the hospital upon discharge, depending on local arrangements (e.g. discharge summary; discharge notification (not prepared by a clinician – automated message)). These messages, varying in completeness between hospitals, contain information on discharge diagnosis, length of stay and discharge medications. 3836 GPs and 1491 practices were registered with the Healthlink service as of June 2016 (Figure 5-3).(245)

5.3.6 Irish Primary Care Research Network (IPCRN)

The HRB Centre for Primary Care Research has developed secure methods of deriving patient data from each of the GP software vendors operating in Ireland via the Irish Primary Care Research Network, a “national network of GP practices (214 practices, approx. 75% of whom are Socrates users) whose purpose is to participate in clinical research for the benefit of their patients and to enhance the discipline of general practice through research training and activity” (www.ipcrn.ie).(247) It is
a collaboration between the Irish College of General Practitioners (ICGP), the HRB Centre for Primary Care Research (based in RCSI) and WestRen (based in NUI Galway). The network has previously worked with GP software vendors to create quality indicator tools for audit and research e.g. a recently completed study into the resistance patterns of urinary tract infections (UTIs) in Ireland.(248) As the data were anonymised by the data controller (the GP by initiating the IPCRN extraction tool) before being sent, individual patient consent is not necessary for this data to be used in research. The IPCRN approached the Data Protection Commissioner and their data extraction technique is compliant with data protection legislation. The Network operates an ‘opt out’ system within practices that have joined the IPCRN. These practices display posters in their waiting rooms to make patients aware that some of their anonymised data may be used for audit and research purposes. Any patient who wishes to opt out is tagged in their electronic record and their data is not uploaded to the IPCRN server when the extraction tool is run (the number opting out is not reported by the IPCRN when reporting the data). Additional posters, explaining the specifics of this particular study and details for opting out of the study, were displayed in each participating practice. The IPCRN website and the IPCRN research data are located on two separate password protected servers in separate data centres. The data centres have achieved ISO27001:2005 Security Management Standards. Data on the servers are managed by the Health Research Board Galway Clinical Research Facility. (Figure 5-2)

5.3.7 Ethical approval

Ethical approval for the project was requested from the Irish College of General Practitioners (ICGP) Research Ethics Committee in March 2014. This was granted subject to removal
of date of birth as a variable (replaced with age in whole years) and demonstration of a proof of concept pilot study in advance of reapplying for full study approval. Similarly, an application was made to the IPCRN board explaining the importance of the project and contribution to research. This was approved in the spring of 2014.

5.3.8 Pilot

The finder/extractor tool was piloted to ensure accuracy and to fulfil the ICGP ethics committee requirement of demonstrating proof of concept. Two practices, one each from Galway and Dublin, were recruited to represent possible variations in different message types and differing hospital systems. The pilot extracted data over the summer months in 2014. Following this the extractor was completed and the pilot results presented to the ethics committee for approval for a larger national study. This was granted in May 2015.
August 2013 - April 2014:
Planning, design of extractor, ethical approval for pilot

May 2014 - February 2015:
Pilot, revision of electronic extractor

March - May 2015:
Pilot study results, full study ethical application

May 2015 - January 2016:
Data collection

May-September 2015:
Practice coding

May 2015 - January 2016:
GP invitation to participate and consent

September 2015 - March 2016:
Data cleaning and preparation

January - June 2016:
Data analysis

Figure 5-1 Study Timeline
Figure 5-2 Irish Primary Care Research Network (IPCRN)(247) See Appendix A for documentation of permission to republish this material
Figure 5-3 Healthlink discharge notification message, Grimes 2011(381) See Appendix A for documentation of permission to republish this material
Figure-5-4 – Diagram of Data Sources for Electronic finder
5.3.9 Practice recruitment

Following completion of the pilot and granting of ethical approval for the larger study GP practices based in the catchment areas of Dublin, Galway and Cork hospitals were invited to take part in the study (Section 5.3.12). Forty-four GP practices (response rate 91%) provided consent to take part in the study. Thirty practices were in the catchment area of the Dublin hospitals, with one in the North-East of Ireland. Eleven practices were in the catchment area of the Galway hospitals and two in the catchment area of the Cork hospitals (see Appendix A for list of HSE Regions and Acute hospitals). A sample GP letter of invitation, information sheet and consent form are included in Appendices K-N. Participating GPs were awarded continuing professional development points for their participation.

5.3.10 Medication classes

Four distinct cohorts were created based on the four medication classes (Table 5-1). All of these medications are commonly prescribed in older populations and have a strong evidence base in terms of efficacy. In addition, these medications, once commenced, are usually continued on a long-term basis. Furthermore, the continuity of these medications in prescribing and dispensing records has been the subject of study internationally – allowing for comparison of results. The inclusion criteria allowed for the broad number of drugs within ‘classes’ of medications to be included and in addition allowed for within class substitution during the study period (Section 5.3.11). Finally, as this was a proof of concept study, these medications classes were chosen as a pragmatic choice prior to broadening to all classes of long-term medications (238,239,249–254) Each participant could be enrolled into more than one cohort dependent on their eligibility. The four cohorts were analysed independently. The
first three characters of the World Health Organization - Anatomical Therapeutic Chemical (WHO-ATC) code were used to define medication class. (255) The WHO-ATC classification system divides medications into different groups according to the organ or system on which they act and according to their pharmacological and therapeutic properties.

For convenience, throughout the rest of the chapter the four cohorts will be referred to by the first three figures of their ATC grouping (Table 5-1).
<table>
<thead>
<tr>
<th>World Health Organization Anatomical Therapeutic Chemical (WHO - ATC) Classification System Code*</th>
<th>Drug class/name</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>C10</td>
<td>Lipid modifying agents</td>
<td>Statins, ezetimibe etc.</td>
</tr>
<tr>
<td>B01 (includes N02BA01)</td>
<td>Antithrombotics (antiplatelet or anticoagulant agents)</td>
<td>Aspirin, clopidogrel, warfarin, novel oral anticoagulants (NOACs) etc.</td>
</tr>
<tr>
<td>H03</td>
<td>Thyroid medication</td>
<td>Levothyroxine, carbimazole etc.</td>
</tr>
<tr>
<td>R03</td>
<td>Respiratory inhalers</td>
<td>Inhaled anticholinergics, short &amp; long acting beta agonists, inhaled steroids</td>
</tr>
</tbody>
</table>

*ATC code groupings (as above) were used to ensure all component drugs within a class were included (e.g. prasugrel, tecagrelor etc.)

This chapter refers to each cohort by the first three figures of the ATC group.
5.3.11 Study, enrolment and follow-up period criteria

Study Period:
The possible study period for each patient ranged from the 1\textsuperscript{st} of January 2012 to the date of extraction. This differed for each practice, ranging from May 2015 to the 7th January 2016). This study period included the one-year enrolment period, the follow-up period post the index/discharge date (Section 5.3.13 for details on the primary explanatory variable - hospitalisation exposure) and beyond to the date of extraction. The maximum possible study period was four years. The minimum study period was eighteen months (Figure 5-5).

Enrolment Period:
The relationship between enrolment period and follow-up periods is illustrated in Figure 5-5. The enrolment period for each medication class was the earliest one-year period over which a patient was continuously prescribed medication from that class. Patients could not be enrolled before 65 years and could be enrolled into more than one of the medication groups. Where a patient was enrolled into more than one of these medication groups, the enrolment periods did not necessarily overlap. The data were analysed as four distinct cohorts with no patient being counted twice within anyone cohort.

Enrolment criteria:
- Two or more scripts of specified medication classes (Table 5-1) over a one-year period.
- 1-year enrolment period.
- First prescription from within the specified medication class initiated a twelve-month enrolment period with at least one other prescription issued between 6 and 12 months after the enrolment period commenced (this reflects the legal
situation in Ireland which allows private patients to get medications dispensed for up to a total of 6 months with one prescription).

- No hospitalisations were allowed during the enrolment period to avoid misclassifying patients according to exposure.
- Differences within medication classes between prescriptions were acceptable e.g. a participant could be prescribed atorvastatin on the first prescription and rosuvastatin on the second prescription. This allowed for the normal occurrence of generic substitutions, tolerance issues, preferences etc.

Index date:
The index date for those hospitalised was assigned as the discharge date. For those individuals not experiencing hospitalisation the index date was randomly assigned within the study period (from the end of the enrolment period to the date of extraction). This method of generating a comparison group has been used previously and is in line with assuming the medications are long-term and unlikely to be discontinued.(218)

Follow-up period:
The follow-up period comprised a six-month (180-day) period following the index date, plus an additional period of time dependent on the exposure status of the patient.
For those who had been admitted to hospital after enrolment the 180-day follow-up period was extended to take account of their length of stay of the appropriate admission (reflecting the possibility that patients may have supplies of long-term medication at home). A median length of stay for those hospitalised was added to the unexposed group follow-up period.
Participants were assessed for a second and third follow-up period, depending on whether they were re-hospitalised following the first follow-up period (and met all the criteria as outline above).

Finally, any patients who were categorised as deceased/inactive at the extraction date or who had no consultations after each follow-up period were excluded from the analyses. This avoided misclassifying a patient who may, for example, have died in hospital or was discharged to a long-term care facility etc. and was not under the care of their previous GP.

The primary outcome was calculated over all relevant follow-up periods (Section 5.3.15).
**Figure 5-5** Study, enrolment and follow-up period
Discharge date = Random date in those not hospitalised (see text); ** median length of stay in those not hospitalised
5.3.12 Participants

Eligibility
Practice Inclusion Criteria:
Practices were considered eligible if they fulfilled the following:

- Practices using Socrates GP patient management software and subscribed to the Healthlink service AND

EITHER

- Practices identifying at least one of the tertiary hospitals currently contributing discharge notifications via Healthlink (Seven Dublin hospitals and two Galway hospitals) as their primary destination of referral. See Appendix A for geographic spread of hospitals in Ireland)

OR

- Practices involved in manual coding of hospitalisation data via trained HRB Centre for Primary Care Research coders.

Patient Exclusion Criteria:

- Patients less than 65 years old on the date of the enrolment period.

- Patients with no prescriptions of the specified medication classes over consecutive five and seven-month periods in the one-year enrolment period (Table 5-1).

- Inadequate follow-up time over which to assess whether medications had been prescribed.

- Patients with less than eighteen months follow-up time between enrolment and the date of data extraction.

- Patients with less than six months follow-up (+ median length of stay) data post-hospitalisation or index date.
5.3.13 Primary explanatory variable (exposure to hospitalisation)

Hospitalisation was the main exposure/explanatory variable of interest for the primary analyses. Hospitalisation was coded in two different ways. Healthlink provided discharge messages were used in 41 practices to signal a hospitalisation. These records of hospitalisation are generated by hospital based medical staff upon preparing a patient for discharge. They are electronically documented, containing demographic details, admission/discharge dates, discharge diagnosis and discharge medications – including medication changes and discontinuations. The message quality in terms of completeness of all data fields is both operator and hospital dependent with a high degree of variability between messages (varying from all fields completed to only hospital and admission date recorded e.g. ‘discharge referral’ v ‘discharge summary’ message types). The notifications may include day procedure admissions (e.g. angiogram) as well as longer in-patient stays. Outpatient and Emergency Department (ED) visits are not included in this message type (Figure 5-3).

Hospitalisation was coded manually by HRB Centre trained coders in four practices by examining the clinical record directly – including paper discharge letters and prescriptions. The coders were trained to include a broader range of hospital interactions including day procedures, inpatient stays and ED attendances. In addition, they recorded the contents of all discharge prescriptions.

For the primary analyses, the exposure was hospitalisation. For analyses in which hospitalisation was treated as a dichotomous variable, the value 0 denoted that the person had not been in hospital at the index date, 1 if they had been. For analyses in
which it was treated as a count variable, hospitalisation was the number of times a person had been admitted to the hospital prior to the index date.

Following collection of the data, additional variables for length of stay, unique hospital ID, Health Services Executive Region, and length of stay greater than one day were generated. For the secondary analysis, the exposure was whether the specific medication was documented on the discharge summary or not (0= listed on summary, 1=not listed on summary).

5.3.14 Comparison (Unexposed) group

As detailed in Section 5.3.11, a comparator group was defined comprising those who did not experience hospitalisation post enrolment in that cohort. An index date was randomly generated after enrolment, and the follow-up period comprised of 180 days after this index date (extended to include the median length of stay in the hospitalised group of the appropriate medication class).

5.3.15 Outcome variables

Primary outcome (medication continuity)

The primary outcome, failure to renew medication (discontinuity), was defined as an absence of specific medication class prescription renewal within the GP record over the appropriate follow-up period.

Failure to renew specified medication was recorded as a dichotomous variable, with the value of 0 if medication was renewed over the follow-up period and 1 if medication was not renewed i.e. discontinuity occurred, over the follow-up period. The unit of analysis was per patient. For each cohort, the primary outcome was compared between those who had been
hospitalised and those who had not, with the non-hospitalised group being the reference group. For each subsequent follow-up period the primary outcome was calculated for all eligible patients comparing hospitalisation exposure at that time point.

Traditional measures of assessing medication continuity in prescription databases (e.g. Medication Possession Ratio MPR), Proportion of Days Covered (PDC)) were considered and trialled in the pilot dataset. These have been widely applied to dispensing databases where there is, for example, a strong link between recording Daily Dose Dispensed (DDD) and reimbursement. In this dataset, because the quality of the information recording duration of prescription and DDD differed substantially between and within practices it was not considered appropriate to use these measures.

Figure 5-6 displays the comparison of the primary outcome in each cohort for those who had been hospitalised post enrolment and those who were not hospitalised for the first follow-up period.

**Figure 5-6** – Patient flow diagram highlighting the exposure (hospitalisation) and the primary objective of discontinuation for each medication class
Secondary outcome (association between discharge summary documentation and medication continuity)

The secondary outcome, which was limited to hospitalised patients only, was defined as the absence of specific medication class prescription renewal in the GP record during the follow-up period. This variable was coded as 0 if the medication class was present in the GP record over the follow-up period, 1 if it was absent. For each cohort, the secondary outcome was compared between those patients where the medication class was not explicitly referred to on their discharge summary notes and those where it could be identified, with the latter group being the reference group (Figure 5-7). This analysis was undertaken on those patients who had a single hospitalisation only before the first follow-up period.

Table 5-2 Main explanatory variables and covariates

<table>
<thead>
<tr>
<th>Primary outcome explanatory variable</th>
<th>Hospitalisation:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Dichotomous (Hospitalised v not hospitalised)</td>
</tr>
<tr>
<td></td>
<td>Continuous (0, 1, 2, 3 etc.)</td>
</tr>
<tr>
<td>Secondary outcome explanatory variable</td>
<td>Medication documented on discharge summary (Present v not present)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Covariates</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Years</td>
</tr>
<tr>
<td>Gender</td>
<td>Female v Male</td>
</tr>
<tr>
<td>Insurance Type</td>
<td>Private v GMS/DVC</td>
</tr>
<tr>
<td>Number of repeat drugs</td>
<td>0, 1, 2, 3 etc.</td>
</tr>
<tr>
<td>Charlson score</td>
<td>≥1 v 0</td>
</tr>
<tr>
<td>RxRisk</td>
<td>0, 1, 2, 3 etc.</td>
</tr>
<tr>
<td>Number of consultations in enrolment period</td>
<td>0, 1, 2, 3 etc.</td>
</tr>
</tbody>
</table>

GMS= General Medical Services; DVC=Doctor Visit Card
Figure 5-7 Patient flow diagram highlighting (in hospitalised patients only) the explanatory variable (absence of medication documentation in discharge summaries) and the secondary outcome of discontinuation in the GP record (for each medication class)
5.3.16 Covariates

Potential confounders were determined from the literature prior to statistical analysis and were either directly recorded from the GP record (age, gender, insurance type, number of GP consultations) or were generated based on data derived from the GP record (polypharmacy: number of repeat drug classes, co-morbidity: Charlson co-morbidity index/RxRiskV) (Table 5-2). (63,65,68,72–74) All covariates were measured during the enrolment period. Confounders fulfil the following criteria (Figure 5-8):

- be a risk factor for the outcome (discontinuation of medication)
- be associated with the exposure (hospitalisation)
- not be an intermediate step in the causal pathway between hospitalisation and discontinuation of medication

![Figure 5-8 Relationship between confounders, exposure and outcome](image)

For the primary outcome of discontinuation, the following variables were adjusted for in the final analysis - gender, age, insurance type, Charlson co-morbidity index, number of repeat drugs, and number of GP visits in the enrolment period. Age, number of repeat drug classes, and number of practice visits
were included as continuous variables. Gender (male=0, female=1), insurance type (General Medical Services (GMS)/Doctor Visit Card (DVC) = 0, private/other=1), and Charlson (No condition=0, one or more conditions=1) were included as categorical variables.

5.3.16.1 Demographic variables

Gender, age and insurance category were extracted from the patients’ medical records. Only age (in whole years) at extraction was recorded thus requiring age at study enrolment to be estimated. Insurance category (GMS, DVC, private or other) was extracted from the medical record. Details on these categories are provided previously in Section 3.3.1. Insurance category was subsequently reclassified as DVC/GMS=0 and Private/Other=1.

5.3.16.2 Co-morbidity

Co-morbidity was measured using the Charlson co-morbidity index (CCI) and RxRiskV.

The CCI includes 17 diseases which have been selected and weighted on the basis of the strength of their association with mortality (Appendix S).(256) The CCI has been applied in numerous studies and both test-retest and interrater reliability are good.(257–259) Predictive validity of the index has been demonstrated by associations with various outcomes such as mortality, disability, readmission to hospital, length of stay and short term mortality in older populations.(260,261) The CCI was calculated over the appropriate enrolment period for each medication class separately using a patient’s medical record information – the GP recorded International Classification of Disease (ICD) version 10 and/or International Classification of Primary Care (ICPC-2) disease coding systems for the respective Charlson disease.(262,263) The Charlson co-
morbidity weights were reclassified into two groups of weights (0= no weights) or (≥1 weight) in the analysis based on the cumulative frequency distribution.

RxRisk was developed from the Chronic Disease Score (CDS), a risk assessment instrument based on outpatient pharmacy dispensing data.(264) RxRisk is an algorithm that classifies prescription drug refills into chronic disease classes for adults and children based on the WHO ATC classification system.(255) RxRisk-V was developed specifically for older populations and included 45 condition categories (Appendix R).(265) RxRisk-V has good reliability and criterion validity against ICD diagnoses and has been shown to predict costs of care, mortality and healthcare utilisation.(260,266–269) As with the CCI the RxRisk was calculated over the appropriate enrolment period for each medication class separately using a patient’s prescribing history. The original RxRisk required only one prescription to indicate a chronic condition (e.g. H2 antagonist or proton pump inhibitor indicating peptic ulcer disease). For this study, each chronic condition was assumed to be present if two prescriptions were identified during the enrolment period, one within the first 5 months of the enrolment period and the second within the last 7 months of the enrolment period. This modified approach has been used previously to reflect the more chronic nature of disease categories in RxRiskV (270), and mirrors how prescription information was used in determining the enrolment periods.

The measurement of co-morbidity using diagnosis information (CCI) or dispensed medication (RxRisk) can be viewed as complementary measures of co-morbidity (e.g. oral hypoglycaemic for diabetes will produce the same RxRisk score as CCI). However, the absence of prescriptions (e.g. likely in early type 2 diabetes mellitus) or disease coding
(reliant on GP review and updating) may impact on the accuracy of the RxRisk and CCI, respectively.

5.3.16.3 **Number of different repeat drug classes**

The number of different repeat drug classes was measured over the one-year enrolment period. The first five characters of the WHO ATC code were chosen to represent a unique drug class. The number of repeat drug classes was calculated over the appropriate enrolment period for each medication class separately using a patient’s prescribing history. Each patient was required to receive at least one prescription per drug class in consecutive five and seven-month periods - as with the RxRisk – to be included as a measure of a repeat drug class. The number of different medications has been shown to be a good predictor of medication discrepancies, mortality, future physician visits, and expenditures. (7,72,73,185,271–275)

5.3.16.4 **Number of consultations in the enrolment period**

The number of face-to-face GP visits by each patient was measured over the one-year enrolment period. This measure was chosen as it is likely associated with morbidity, the continuity of medication on the basis of greater contact with the GP practice, and it has been used elsewhere in the literature. (218,276)

5.3.17 Risk of bias

In addition to the STROBE statement, The Critical Appraisal Skills Programme (CASP) cohort study checklist was utilised to assess the methodological quality of the study as well as the usefulness of the study results. The checklist asks 12 questions addressing three broad areas – ‘Are the results valid; what are the results; will the results help locally?’ (277) In addition, the Bradford-Hill criteria were applied to explore the various issues
around establishing causality in observational research, for example temporal relationship, strength of the observed association, plausibility, and consideration of alternate hypotheses.(278)

5.3.18 Funding

This study was funded by the HRB Centre for Primary Care Research. Socrates Healthcare Company were contracted to develop a computer application to run on their software to upload the relevant results to the IPCRN. They provided the necessary programmer’s time under contract.

5.3.19 Sample size

The pilot study and previous international studies in this area informed the ability to detect the absolute difference in the proportions of patients continuing medications.(218) A previous Canadian study of unintended medication discontinuation suggested an adjusted odd ratio (AOR) varying from 1.18 (95% confidence interval (CI) [1.14-1.23]) to 1.86 (95%CI [1.77-1.97]) depending on medication classes in those experiencing hospitalisation versus no hospitalisation.(218)

For this study, the sample size calculation was based on 90% power to detect a 3% difference in the proportion of patients experiencing discontinuity in medications. This effect size was chosen as being a pragmatic balance between the findings of previous research and maximum likely number of participants that could be recruited based on the pilot study. We assumed 11% of non-hospitalised patients have medications unintentionally discontinued. Additionally, a 4:1 ratio of non-hospitalised to hospitalised patients (based on experience from the pilot study) with a statistical significance of 5% was
used. This gave a total requirement of 8410 participants in any one medication cohort group.

5.3.20 Data cleaning

Data were received from the IPCRN in comma separated values (.csv) files for each practice individually, containing separate files for demographics, consultations, hospitalisation information, disease coding and prescriptions. These were combined to obtain one file containing all demographic information across the forty-four practices, another file with all consultation information etc. Each participant had a unique identifier that was present across all files. Duplicate or missing data were checked against IPCRN records however it was not possible, by design, to check against original practice records.

A number of queries were run to examine the initial dataset for unrealistic data (e.g. data outside a normally considered range for a variable) or missing data. Duplicate entries of Healthlink messages were removed manually at this point. No further unusual data were removed at this stage (prior to running the cohort enrolment criteria).

5.3.21 Missing data

ATC codes (~5%)
The prescription file included the tradename, generic name and ATC code for each prescription issued. Less than 5% (300,000) of prescriptions had no recorded ATC codes. Using the tradename and generic names a matching algorithm was run to input missing ATC codes (relying on an Irish Pharmacy Union master dataset containing all available medications and their corresponding ATC codes). The matching output was manually reviewed and any remaining missing values were coded manually.
Hospital discharge dates (~30%)
The Healthlink message data (dates of admission and discharge, medical diagnoses and discharge medication) were of varying quality with the discharge date sometimes missing (Table 5-3). Prior to applying the enrolment criteria, it was necessary to estimate the discharge date. Where a hospital discharge date was missing, a conservative approach was taken to estimate this date. The missing discharge date was replaced by the next GP prescription (of any medication). If none was recorded it was replaced by the next hospital admission date. If neither of these were available, the discharge date was replaced with the admission date.

<table>
<thead>
<tr>
<th>Table 5-3 Number of recorded hospitalisations with missing discharge dates</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antithrombotics (B01)</strong></td>
</tr>
<tr>
<td>Number of hospitalised patients eligible for enrolment*</td>
</tr>
<tr>
<td>Missing Discharge date</td>
</tr>
<tr>
<td>Date N (%)</td>
</tr>
</tbody>
</table>

*After application of enrolment criteria

No patients had missing data across all of the outcome, exposure and confounder variables.

5.3.22 Statistical methods

5.3.22.1 Plan of analysis

Statistical software
Descriptive statistics and multilevel logistic regression was performed in Stata Version 14.(215) The ‘xtmelogit’ command was used for logistic regression models.
5.3.22.1.1 Descriptive statistics

Enrolment descriptives
The number of patients at each stage of the study is reported, including those potentially eligible, those enrolled into each of the four cohorts, and those available for analysis at each of the follow-up periods. Reasons for removal are documented at each stage. The number of practices and hospitals as well as their broad geographic location is also reported. Additionally, a reference group is reported of patients prior to application of the enrolment criteria. This group was created to allow comparison of the participants within the broader dataset to previously conducted studies to ensure external validity and representativeness.

Patient descriptives
Demographic characteristics of patients are presented for the reference group and each of the four cohorts. Descriptive statistics (means (SDs), median (IQR) and numbers (%)) for the exposure variable (hospitalisation) and the confounder variables (gender, age, insurance type, co-morbidity (Charlson Index and RxRisk), number of repeat drugs, and number of practice visits in the enrolment period) are reported. The relationship between hospitalisation and the confounder variables is also reported.

Outcome descriptives
The number and percentage of those participants experiencing the primary and secondary outcomes are reported at each follow-up time point.

5.3.22.1.2 Multilevel analysis
A multilevel model was used to analyse the data. This is an analytical approach to investigate clustered data.(279) The
individual patient, in this study, is at the lowest level of this hierarchical model with the practice being the highest, giving rise to a (two level) multilevel model. Multilevel analysis is appropriate for this study due to fact that patients within any given practice could reasonably be expected to have more in common with each other than with those from a different practice (e.g. individual prescriber patterns).

Firstly, a multilevel model without any explanatory variables (the ‘null’ model) was fitted. The likelihood ratio statistic testing the null hypothesis that there was no significant difference between practice variation was examined. The intracluster correlation coefficient (ICC) was used to report the proportion of variability in the outcome variable that was due to differences between clusters (practices).

Primary outcome (medication discontinuity) – Follow-up period 1

The association between hospitalisation post-enrolment and the primary outcome was assessed using a two-level logistic regression model in which a random intercept was incorporated to model differences in the primary outcome between practices.

Additional models were also fitted in which the exposure was the number of admissions post enrolment (0, 1, 2, 3, 4, ≥5) prior to calculation of the primary outcome.

Where there was a significant effect associated with hospitalisation and the primary outcome the models were rerun with the effects associated with individual hospitals relative to the non-hospitalised being treated as fixed effects.(205) These unadjusted models were fitted individually for the four medication cohorts.
Finally, for each cohort, a multivariable model was fitted in which the exposure variable was adjusted for patient variables (age, gender, insurance type, Charlson score, number of repeat drug classes, and number of enrolment period GP visits). In all instances, Odds Ratios (OR) and 95% Confidence Intervals (CI) were calculated for each predictor variable.

Continuous independent variables were examined for non-linearity. In the final model age was treated as a continuous variable (having initially been explored for non-linearity by including an additional quadratic term in addition to age). The multivariable regression models were assessed for collinearity by examining the correlations between the estimated parameters.

Primary outcome (medication discontinuity) - Follow-up period 2

At follow-up period two, the association between exposure status (hospitalised v not hospitalised) and discontinuity of medication at second follow-up was explored (Figure 5-9). Patients within each cohort may have belonged to one of three states:

1. those who had never experienced hospitalisation between the end of enrolment and the extraction date,
2. those who had a hospitalisation before the first follow-up period but had no further hospital admissions before the extraction date, and
3. those who had two eligible follow-up periods, both of which followed a hospital discharge.

The second time point in the latter group was the next available uninterrupted six-month (plus length of stay) period post discharge that followed the first follow-up period. For the other
two groups a second random date was generated between the end of the first follow-up period and the extraction date.
Figure 5-9 Possible relationship between exposure status and the discontinuity of medication at follow-up period one and two.
Univariate and multivariate models were fitted analogous to the follow-up period one analyses; however, in the multivariable model adjustment was also made for discontinuity of medication at follow-up time one as well as the exposure status at follow-up period one.

Figure 5-9 illustrates the suspected relationship between the primary explanatory variable (hospitalisation at time one) and the outcome (discontinuity at time one). Hospitalisation at time one is likely associated with hospitalisation at time two and discontinuity at time two. Discontinuity at time one is similarly on the causal pathway of hospitalisation at time two and discontinuity at time two – therefore all of these variables were included in the final adjusted models.

Secondary outcome (association between discharge summary documentation and medication continuity)

The secondary outcome was examined using multilevel random intercept logistic models to compare absence of the specified medications in the GP record post hospitalisation between those for whom medication was listed on the discharge summary and those for whom it was not listed. Those patients where the discharge summary explicitly stated medication was to be discontinued were excluded from this analysis (an extremely small number of individuals). Both unadjusted and adjusted models were fitted. Effects associated with hospital of discharge were also explored.

5.3.22.2 Model checking and goodness of fit

Deviance residuals, defined as the square root of the contribution to the likelihood-ratio test statistic of a saturated model versus the fitted model, were generated for the final
model in each of the four cohorts. The following were also considered in assessing the validity of the final model:

- Re-examination of the data to identify possible errors
- Examination of the residuals
- Suitability of the logit link function, as opposed to other link functions (e.g. probit)
- Additional confounders (e.g. level two effects)
- Interaction terms between predictor and covariates
- Continuous variables requiring transformation
- Outlying individuals and practices
- Consideration as to whether it was clinically appropriate to allow the effects associated with confounders variables to vary between practices (random slope models)
- Additional features of the study design

### 5.3.22.3 Subgroups

Subgroups of interest were identified in advance.

- Length of stay greater than one day

Patients transitioning to and from the hospital over less than 24 hours will have less opportunity for their medication regime to be reviewed, or changed with subsequently less opportunity for unintentional omissions (e.g. day case surgery, procedures – angiogram). This group was examined separately.

### 5.3.22.4 Sensitivity analysis

The dataset developed for this study is novel and required a number of assumptions in generating the data for analysis. The validity and robustness of the findings were explored through sensitivity analysis of key decision areas:
• Estimating missing discharge date
Missing discharge dates were conservatively estimated (Section 5.3.21). An alternative approach of replacing all missing dates with the date of admission was considered.

• Exposed group confined to one hospitalisation only
Approximately 30% of patients within each cohort had more than one admission following the enrolment period and prior to the first eligible follow-up period. This sensitivity analysis confined the primary outcome calculation to those with a single hospitalisation prior to the follow-up period.

• Practices with possible misclassification of exposure
Some practices are located on the periphery of the catchment area of Healthlink enabled hospitals and refer patients to non-Healthlink hospitals. This analysis excluded these practices to consider whether the exposure (hospital) was misclassified.

• Manually coded hospitalisations
The manually coded practices were examined separately to determine whether manual coding of hospital provided discharge communications would alter the primary outcome.

• Alternate primary outcome calculation
180 days was chosen as the time period in the primary analysis over which discontinuity of medication was examined. In this analysis, the time period was extended to 270 days post the index date to assess whether varying the time limit allowed more participants to renew prescriptions and therefore avoid discontinuation.
5.4 Results

5.4.1 Descriptive statistics

5.4.1.1 Enrolment period

A total of 91,866 records were extracted from the 44 recruited practices, of which 62,653 (68.20%) were removed immediately due to insufficient data (33,941 - no data available beyond age, gender, insurance type), no consultations (23,693) or prescriptions (5,019) beyond the 1st of January 2012. (Figure 5-10)

Subsequently 9,436 patients were removed due to not being prescribed a medication of interest or having less than 12 months of follow-up data available to enable enrolment. This left 19,777 patients on which the enrolment criteria were applied.

The enrolment criteria were applied to the 19,777 patients described above creating four cohorts, one for each of the distinct medication classes - antithrombotics (B01) n=10,517, lipid-lowering medications (C10) n=10,884, thyroid meds (H03) n=2,740, and respiratory inhalers (R03) n=4,160). Table 5-4 shows the numbers of participants enrolled into each cohort and available at each follow-up time.

To establish the external validity of the dataset, a reference group was defined (24,363 patients) which included all patients having sufficient data following the initial removal of records prior to 1st January 2012 and sociodemographic records only, and who had at least one-year of follow-up time.
Figure 5-10 Cohort Patient Flow Diagram  *Reference Group: Follow-up time of one year available. No specified medication exclusions
<table>
<thead>
<tr>
<th>Individual Cohort Enrolment</th>
<th>Available at 1st follow-up *</th>
<th>Available at 2nd follow-up *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number Enrolled * 19,777</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antithrombotics (B01): 10,517</td>
<td>6,516</td>
<td>2,250</td>
</tr>
<tr>
<td>Lipid-Lowering (C10): 10,884</td>
<td>6,890</td>
<td>2,395</td>
</tr>
<tr>
<td>Thyroid Meds (H03): 2,740</td>
<td>1,686</td>
<td>586</td>
</tr>
<tr>
<td>Respiratory Inhalers (R03): 4,160</td>
<td>2,348</td>
<td>752</td>
</tr>
</tbody>
</table>

*See text for enrolment and follow-up period criteria*
5.4.1.2 Practice level descriptives

44 practices were recruited. 30 practices were in the catchment area of the Dublin hospitals, with one practice in the North-East of Ireland. Eleven practices were in the catchment area of the Galway hospitals and two in the catchment area of the Cork hospitals. Following the enrolment criteria being applied, the numbers of participants enrolled from each practice ranged from 32 to 755 with a median of 414 participants per practice.

5.4.1.3 Patient level descriptives

Demographic characteristics are provided for the reference group as well as each of the cohorts (Table 9-4, Table 5-5).

Cohort participants:

The demographics of the participants within the four cohorts of those available at the first follow-up period are presented in Table 5-5. The breakdown of covariates according to exposure (hospitalisation) is also presented. In addition, tables for each cohort at the end of enrolment as well as exploration of the main covariates graphically for outliers is displayed in Appendix P. Of those hospitalised following enrolment approximately three quarters experienced a single hospitalisation before the first follow-up period. Of those participants who experienced multiple hospitalisations prior to the first follow-up period, nearly all admissions were to the same hospital. In the antithrombotics (B01) group 24 (4.86%) participants who experienced more than one hospitalisation had been hospitalised in different hospitals prior to the first follow-up period. This figure was similarly low across the other medication groups – lipid-lowering (C10) (35
participants, 7.32%), thyroid meds (4 participants, 4.55%) and respiratory inhalers (R03) (14 participants, 6.25%) (not shown in Table 5-5).

Reference group:
To establish the validity of the data source a reference group was created, prior to running the enrolment code and creating the four cohorts, of patients who had a full year of prescribing data available (n=24,363). The summary statistics for the demographic variables, number of medications, RxRisk, and Charlson index are reported in Table 9-4 (Appendix P).
Table 5-5 Table of participant characteristics of individual cohorts

<table>
<thead>
<tr>
<th>Number enrolled</th>
<th>Antithrombotics (B01) (N=10,190)</th>
<th>Lipid-lowering (C10) (N=10,585)</th>
<th>Thyroid meds (H03) (N=2,644)</th>
<th>Respiratory inhalers (R03) (N=3,933)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number at follow-up time point 1</td>
<td>H (N=1,970)</td>
<td>NH (N=4,546)</td>
<td>H (N=1,892)</td>
<td>NH (N=4,998)</td>
</tr>
<tr>
<td>Age (years) Mean (SD)</td>
<td>78.53 (6.98)</td>
<td>75.39 (7.01)</td>
<td>77.16 (6.70)</td>
<td>73.75 (6.46)</td>
</tr>
<tr>
<td>Female n (%)</td>
<td>1,042 (52.89)</td>
<td>2,404 (52.88)</td>
<td>1,041 (55.02)</td>
<td>2,843 (56.88)</td>
</tr>
<tr>
<td>Insurance Type: GMS/DVC n (%)</td>
<td>1,824 (92.59)</td>
<td>4,095 (90.08)</td>
<td>1,763 (93.18)</td>
<td>4,494 (89.92)</td>
</tr>
<tr>
<td>No. of Consultations in enrolment period Mean (SD)</td>
<td>8.76 (6.89)</td>
<td>6.96 (6.03)</td>
<td>8.54 (6.59)</td>
<td>6.76 (5.51)</td>
</tr>
<tr>
<td>No. of repeat drugs classes during enrolment Mean (SD)</td>
<td>8.35 (4.01)</td>
<td>7.21 (3.63)</td>
<td>8.14 (4.02)</td>
<td>6.69 (3.67)</td>
</tr>
<tr>
<td>RxRisk during enrolment Mean (SD)</td>
<td>5.03 (2.05)</td>
<td>4.52 (1.89)</td>
<td>4.97 (2.07)</td>
<td>4.27 (1.99)</td>
</tr>
<tr>
<td>Charlson Index during enrolment Mean (SD)</td>
<td>1.03 (1.34)</td>
<td>0.77 (1.14)</td>
<td>1.02 (1.33)</td>
<td>0.72 (1.13)</td>
</tr>
<tr>
<td>No. experiencing one hospitalisation only before follow-up time one n (%)</td>
<td>1476 (74.9%)</td>
<td>-</td>
<td>1414 (74.7%)</td>
<td>-</td>
</tr>
</tbody>
</table>

H: Hospitalised; NH: Not Hospitalised
GMS = General Medical Services; DVC=Doctor Visit Card
5.4.1.4 Hospital/Practice descriptive statistics

Table 9-5 in Appendix P presents selected data from the geographic distribution of practices and hospitals available in the final dataset at follow-up period one. Using the B01 group as an example, most participants were located in the Dublin region (B01 – 4602, 70.63%), with most hospitalisations taking place in Dublin (B01 – 1360, 69.04%) and one hospital in particular accounting for 33.5% of all hospitalisations at follow-up period one in the B01 group. Fifteen practices had hospitalisation information from one hospital only and nineteen from only two hospitals. Conversely 11 hospitals were associated with a single GP practice and eight hospitals with only two. There were 25 unique hospitals recorded at the first follow-up period. These were then reduced to categories as in Table 9-5 (Appendix P).

5.4.1.5 Outcomes variables

Primary outcome (medication discontinuity)

The number and percentage of those participants experiencing the primary outcome are reported for each cohort in Table 5-6.
Table 5-6 Breakdown of patients by medication group, follow-up period and discontinuity of medication *

<table>
<thead>
<tr>
<th>Numbers enrolled initially</th>
<th>Antithrombotics B01 (N=10,517)</th>
<th>Lipid Lowering C10 (N=10,855)</th>
<th>Thyroid Meds H03 (N=2,740)</th>
<th>Respiratory Inhalers R03 (N=4,161)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>H  NH</td>
<td>H  NH</td>
<td>H  NH</td>
<td>H  NH</td>
</tr>
<tr>
<td>No. in each group at 1st follow-up</td>
<td>1970  4546</td>
<td>1892  4998</td>
<td>419  1267</td>
<td>767  1581</td>
</tr>
<tr>
<td>No. discontinued at 1st follow-up N (%)</td>
<td>224 (11.37%)  549 (12.08%)</td>
<td>221 (11.68%)  539 (10.78%)</td>
<td>26 (6.21%)  119 (9.39%)</td>
<td>79 (10.29%)  277 (17.52%)</td>
</tr>
<tr>
<td>No. in each group at 2nd follow-up</td>
<td>254  1,996</td>
<td>226  2,169</td>
<td>47  539</td>
<td>102  650</td>
</tr>
<tr>
<td>No. discontinued at 2nd follow-up N (%)</td>
<td>26 (10.24%)  286 (14.33%)</td>
<td>30 (13.27%)  271 (12.49%)</td>
<td>4 (8.51%)  51 (9.46%)</td>
<td>11 (10.78%)  117 (18.00%)</td>
</tr>
<tr>
<td>3rd follow-up ‡</td>
<td>14</td>
<td>12</td>
<td>1</td>
<td>10</td>
</tr>
</tbody>
</table>

H = Hospitalised post enrolment; NH = Not Hospitalised post enrolment

See appendix P for individual cohort’s participant flow diagrams

† See text for follow-up criteria

‡ Outcome not calculated at 3rd follow-up due to small number of patients
5.4.1.5.1 Discontinuity of medication

Follow-up period one
The percentage of participants experiencing discontinuation at follow-up period one ranged from 9.39% (thyroid meds – H03 group) to 17.52% (respiratory inhalers - R03 group) in those not hospitalised; and from 6.21% (thyroid meds – H03 group) to 11.68% (lipid-lowering - C10 group) in those who were hospitalised. Levels of discontinuity were noticeably higher among those who had not been hospitalised than those who had been hospitalised for both the H03 group and the R03 group (Table 5-6).

Follow-up period two
Three categories of patients were available for analysis at follow-up period two:
1. those who had never experienced hospitalisation following enrolment,
2. those who had another hospitalisation following the first time point and
3. those who had experienced hospitalisation only prior to the first-time point.

Table 5-6 reports levels of discontinuity at follow-up period two. The percentage of patients whose medication had been discontinued at the end of the second follow-up period ranged from 8.51% (thyroid meds – H03) to 13.27% (lipid-lowering - C10) in those who experienced hospitalisation again following the first follow-up period. The percentage of patients whose medication was discontinued in the non-hospitalised group, following application of a second random date, ranged from 9.46% (n=51) in the H03 group to 18.00% (n=117) in the R03
group. Again, levels of discontinuity were similar to the previous follow-up period.

**Secondary outcome (documentation of medication on discharge summary and discontinuity of medication)**

The secondary outcome was calculated for those patients who had a single hospitalisation following enrolment and had a follow-up period uninterrupted by further hospitalisation. The numbers experiencing the secondary outcome are presented in Table 5-7.

Recording of the chronic medication on the discharge summary was low. It was not listed in approximately half of all discharge summary notes regardless of medication group. Patients for whom the chronic medication was not listed on their discharge summary tended to be less likely to receive a prescription within this group in the follow-up period after discharge than those for whom the medication was listed in the discharge summary notes. The numbers discontinued ranged from seven patients (8.81%) in the thyroid meds (H03) group to 41 patients (13.18%) in respiratory inhalers (R03) group.
Table 5-7 Breakdown of patients by medication group, documentation of medication on discharge summary, and discontinuity of medication

<table>
<thead>
<tr>
<th></th>
<th>Antithrombotics (B01) (N=1,475)</th>
<th>Lipid-lowering (C10) (N=1,407)</th>
<th>Thyroid meds (H03) (N=331)</th>
<th>Respiratory inhalers (R03) (N=543)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Medication listed on discharge summary</td>
<td>Medication not listed on discharge summary</td>
<td>Medication listed on discharge summary</td>
<td>Medication not listed on discharge summary</td>
</tr>
<tr>
<td>Number of patients</td>
<td>750</td>
<td>725</td>
<td>792</td>
<td>615</td>
</tr>
<tr>
<td>No. (%) of patients with no relevant prescriptions over 1st follow-up period</td>
<td>67 (8.93%)</td>
<td>88 (12.14%)</td>
<td>52 (8.46%)</td>
<td>99 (12.50%)</td>
</tr>
</tbody>
</table>
5.4.2 Analysis

5.4.2.1 Null Model

The likelihood ratio test in the null model was significant (p<0.05) in all cohorts thus rejecting the null hypothesis that there were no differences between practices in discontinuity of medication (primary outcome) over follow-up period one. The ICC for the practice level variation for each cohort was 0.045 (antithrombotics (B01) and lipid lowering (C10) groups), 0.50 (respiratory inhalers (R03) group) and 0.12 (thyroid meds (H03) group), between 5% and 12% of the variation observed in lack of continuity of medications at follow-up period one was attributable to differences between practices.

5.4.2.2 Follow-up period one

5.4.2.2.1 Unadjusted and adjusted models

Table 5-8 presents the association of the primary explanatory variable (hospitalisation) and covariates in those experiencing the primary outcome (medication discontinuity) for each of the four cohorts.

Hospitalisation (dichotomous variable)

Hospitalisation, recorded dichotomously (0 = no hospitalisation following enrolment and 1 for at least one hospitalisation), had no significant association with discontinuity of medication at follow-up period one for both the antithrombotics (B01) (p=0.428) and lipid-lowering (C10) (p=0.154) groups. For the other two chronic medication groups, patients who had been hospitalised following enrolment were less likely to experience discontinuity of medication during the follow-up period than those who had not been hospitalised. This only attained formal statistical significance in the respiratory inhalers
(R03) group, where those who had been hospitalised where almost half as likely as those who had not been hospitalised to experience discontinuation (OR 0.55, 95%CI [0.42, 0.72], p<0.001.

Following adjustment for confounding variables, hospitalisation was significantly associated with discontinuity of medication over follow-up period one in both the thyroids meds (H03) group (Adjusted Odds Ratio (AOR) 0.56, 95%CI [0.33, 0.89], p=0.016) and the respiratory inhalers (R03) group (AOR 0.53, 95%CI [0.39, 0.71], p<0.001). In both groups, those who were hospitalised were almost half as likely as those not hospitalised to experience discontinuation of medication.

**Covariates**

In the unadjusted models (with hospitalisation exposure coded as both categorical and continuous -Table 5-8, Table 5-9), increasing age (ranging from p<0.001 to p=0.015), and private insurance type (p<0.001) were associated with an increased odds of discontinuation of medication; while the presence of at least one Charlson condition was associated with decreased odds in discontinuity of medication in the antithrombotics (B01) (p=0.005) group. Patients who had more face-to-face visits with their GP during the enrolment period were significantly less likely to experience discontinuity of medication in the antithrombotics (B01) (p<0.001), thyroid meds (H03) (p=0.001) and respiratory inhalers (R03) (p=0.029) groups. RxRisk was not significant (p>0.05 in all groups – odds ratio not shown in table) and following discussion was not included in the final model. An increasing number of repeat drug classes was associated with a reduction in the odds of discontinuity of medication in the respiratory inhalers (R03) group only (OR 0.95, 95%CI [0.91, 0.99], p=0.01.
As with the unadjusted models, increasing age (p<0.05), and private insurance type (p<0.05) were associated with increased odds of discontinuation of medication in all chronic medication groups in the adjusted model. The effect associated with the Charlson index on discontinuity of medication was no longer significant in any group. An increasing number of consultations in the enrolment period was still associated with decreased odds in discontinuity of medication though this was only formally of statistical significance in the antithrombotics (B01) (p=0.029) and thyroid meds (H03) (p=0.021) groups. Increasing number of medication was still associated with decreased odds in discontinuity of medication in the adjusted analysis in the respiratory inhalers (R03) group only (p=0.037)
### Table 5-8: Association between hospitalisation and medication discontinuation at follow-up period one – Hospitalisation (Dichotomous)

<table>
<thead>
<tr>
<th></th>
<th>Antithrombotics (B01) (6,516)</th>
<th>Lipid-lowering (C10) (6,890)</th>
<th>Thyroid meds (H03) (1,686)</th>
<th>Respiratory inhalers (R03) (2,348)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Unadjusted OR (95%CI)</td>
<td>Adjusted OR (95%CI)</td>
<td>Unadjusted OR (95%CI)</td>
<td>Adjusted OR (95%CI)</td>
</tr>
<tr>
<td>Hospitalised=1 (v non-hospitalised=0)</td>
<td>0.93 (0.79, 1.11)</td>
<td>1.13 (0.95, 1.34)</td>
<td>0.64 (0.41, 1.01)</td>
<td>0.54 (0.42, 0.72)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>1.02 (1.00, 1.03) *</td>
<td>1.04 (1.02, 1.05) *</td>
<td>1.03 (1.01, 1.06) *</td>
<td>1.06 (1.00, 1.04) *</td>
</tr>
<tr>
<td>Female (v Male)</td>
<td>0.87 (0.74, 1.02)</td>
<td>0.87 (0.87, 1.20)</td>
<td>0.68 (0.45, 1.04)</td>
<td>0.96 (0.75, 1.21)</td>
</tr>
<tr>
<td>Insurance Type (Private v GMS/DVC patients)</td>
<td>4.61 (3.78, 5.62) *</td>
<td>4.52 (3.71, 5.49) *</td>
<td>8.22 (5.31, 12.72) *</td>
<td>4.03 (2.89, 5.64) *</td>
</tr>
<tr>
<td>Number of repeat drugs classes</td>
<td>0.98 (0.95, 1.01)</td>
<td>1.01 (0.98, 1.03)</td>
<td>0.97 (0.92, 1.03)</td>
<td>0.95 (0.91, 0.99)</td>
</tr>
<tr>
<td>Charlson score (21 v 0)</td>
<td>0.89 (0.84, 0.97) *</td>
<td>1.07 (0.99, 1.14)</td>
<td>1.05 (0.89, 1.23)</td>
<td>0.94 (0.85, 1.03)</td>
</tr>
<tr>
<td>No of consultations in enrolment period</td>
<td>0.97 (0.96, 0.98) *</td>
<td>0.99 (0.97, 1.00)</td>
<td>0.94 (0.90, 0.97) *</td>
<td>0.98 (0.96, 0.99)</td>
</tr>
</tbody>
</table>

* p value <0.05; OR – Odds Ratio

Adjusted model included gender, age, insurance type, Charlson index, number of repeat drugs, and number of practice visits in the enrolment period.

GMS = General Medical Services; DVC=Doctor Visit Card
Hospitalisation (continuous variable)

Hospitalisation, recorded as a continuous measure and capped at 5 or more visits due to small numbers, was significantly associated with discontinuity of medication at follow-up period one in both the lipid-lowering (C10) and respiratory inhalers (R03) cohorts (Table 5-9). The odds of discontinuation increased by 15% with each additional visit to hospital prior to the first follow-up period in the lipid-lowering (C10) group (OR 1.15. 95%CI [1.05, 1.26], p=0.003) however the odds of being discontinued fell by 22% for each additional hospital visit prior to the first follow-up period in the respiratory inhalers (R03) group (OR 0.77. 95%CI [0.65, 0.91], p=0.002).

Following adjustment, hospitalisation was significantly associated with discontinuity of medication in three of the four cohorts (C10, H03 and R03). The odds of discontinuation increased by 11% for each additional visit to hospital prior to follow-up period one in the lipid-lowering (C10) group (AOR 1.11, 95%CI [1.00, 1.22], p=0.047), whereas the odds of being discontinued decreased for every additional visit to hospital prior to the follow-up period for both the thyroid meds (H03) group (AOR 0.65, 95%CI [0.44, 0.95], p=0.025) and the respiratory inhalers (R03) group (AOR 0.77, 95%CI [0.65, 0.91], p=0.003).
Table 5-9 Association between hospitalisation and medication discontinuation at follow-up period one– Hospitalisation (Continuous)

<table>
<thead>
<tr>
<th></th>
<th>Antithrombotics (B01) (N=6,516)</th>
<th>Lipid-lowering (C10) (N=6,890)</th>
<th>Thyroid meds (H03) (N=1,686)</th>
<th>Respiratory Inhalers (R03) (N=2,347)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Unadjusted OR (95%CI)</td>
<td>Adjusted OR (95%CI)</td>
<td>Unadjusted OR (95%CI)</td>
<td>Adjusted OR (95%CI)</td>
</tr>
<tr>
<td>Hospitalisation (Continuous)**</td>
<td>1.04 (0.95, 1.15)</td>
<td>1.06 (0.96, 1.17)</td>
<td>1.15 (1.05, 1.26) *</td>
<td>1.11 (1.00, 1.22) *</td>
</tr>
<tr>
<td></td>
<td>1.04 (1.00, 1.03) *</td>
<td>1.03 (1.02, 1.04) *</td>
<td>1.04 (1.02, 1.05) *</td>
<td>1.05 (1.04, 1.06) *</td>
</tr>
<tr>
<td>Age (years)</td>
<td>1.02 (0.78, 1.07)</td>
<td>1.03 (0.74, 1.03)</td>
<td>0.91 (0.87, 1.18)</td>
<td>0.87 (0.88, 1.21)</td>
</tr>
<tr>
<td>Female (v Male)</td>
<td>0.91 (0.78, 1.07)</td>
<td>0.87 (0.74, 1.03)</td>
<td>1.01 (0.87, 1.18)</td>
<td>1.03 (0.88, 1.21)</td>
</tr>
<tr>
<td>Insurance Type (Private v GMS/DVC patients)</td>
<td>4.61 (3.78, 5.62) *</td>
<td>4.72 (3.86, 5.78) *</td>
<td>4.52 (3.71, 5.49) *</td>
<td>5.41 (4.39, 6.66) *</td>
</tr>
<tr>
<td>Number of repeat drugs classes</td>
<td>0.98 (0.95, 1.01)</td>
<td>0.99 (0.97, 1.03)</td>
<td>0.99 (0.98, 1.03)</td>
<td>0.99 (0.98, 1.03)</td>
</tr>
<tr>
<td>Charlson score (21 v 0)</td>
<td>0.89 (0.84, 0.97) *</td>
<td>0.91 (0.84, 0.98)</td>
<td>1.07 (0.99, 1.14)</td>
<td>1.06 (0.99, 1.14)</td>
</tr>
<tr>
<td>No. of consultations in enrolment period</td>
<td>0.97 (0.96, 0.98) *</td>
<td>0.98 (0.97, 0.99) *</td>
<td>0.99 (0.97, 1.00)</td>
<td>0.99 (0.99, 1.01)</td>
</tr>
</tbody>
</table>

*p <0.05; OR – Odds Ratio
** Capped at 5 or more hospitalisations; hospitalisation as recorded at the first follow-up time point
Adjusted model included gender, age, insurance type, Charlson index, number of repeat drugs, and number of practice visits in the enrolment period.
GMS = General Medical Services; DVC=Doctor Visit Card
Hospitalisation (Regional Differences)

The individual hospital association with discontinuity was examined in the thyroid meds (H03) and respiratory inhalers (R03) groups (the only groups showing a notable association between exposure and the primary outcome at follow-up period one). Patients who had been discharged from two of the Dublin hospitals and Galway hospitals were significantly less likely to experience discontinuity of medication at follow-up period one than those who had not been admitted to hospital following enrolment (Table 5-10). For the other hospitals in Dublin and in other regions, there was no significant difference in the odds of discontinuity between patients who had been admitted to hospital and those who had not.

Table 5-10 Individual hospitals effect on the primary outcome (discontinuation) in H03 & R03 groups

<table>
<thead>
<tr>
<th>Medication cohort</th>
<th>Thyroid meds (H03) (N=1,686) OR (95%CI)</th>
<th>Respiratory inhalers (R03) (N=2,348) OR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dublin Hospital 1</td>
<td>0.78 (0.38, 1.58)</td>
<td>0.55 (0.35, 0.85) *</td>
</tr>
<tr>
<td>Dublin Hospital 2</td>
<td>0.73 (0.29, 1.81)</td>
<td>0.52 (0.28, 0.94) *</td>
</tr>
<tr>
<td>Dublin Hospital 3</td>
<td>0.64 (0.14, 2.91)</td>
<td>0.98 (0.41, 2.35)</td>
</tr>
<tr>
<td>Dublin Hospitals (other)</td>
<td>1.92 (0.39, 9.33)</td>
<td>0.93 (0.39, 2.19)</td>
</tr>
<tr>
<td>Galway Hospital</td>
<td>0.44 (0.18, 1.06)</td>
<td>0.44 (0.26, 0.72) *</td>
</tr>
<tr>
<td>Others</td>
<td>Not Estimable**</td>
<td>0.49 (0.14, 1.77)</td>
</tr>
</tbody>
</table>

*p value < 0.05; OR – Odds Ratio

** Not estimable due to very small numbers

Unadjusted analyses presented
5.4.2.3 Follow-up period two

5.4.2.3.1 Unadjusted and adjusted analyses

Hospitalisation (dichotomous variable)
Hospitalisation, recorded dichotomously, following the first follow-up period and prior to second follow-up period, was not significantly associated (p>0.05) with discontinuity of medication at follow-up time two and this remained so following adjustment for confounders (Table 5-11).

Covariates
Patients who experienced discontinuity of medication at follow-up time one were significantly more likely to experience discontinuity at follow-up time two than those who did not experience discontinuity at follow-up time one (p<0.001) in all groups.

As with follow-up period one, increasing age (p<0.05), and private insurance type (p<0.001) were associated with increased odds of discontinuation of medication at time point 2 in all groups.

The more consultations a person had with their GP during the enrolment period, the less likely they were to experience discontinuity of medication at time point 2, but this was only of statistical significance in the antithrombotics (B01) group (OR 0.95, 95%CI [0.93, 0.98], p<0.001) and the thyroid meds (H03) group (OR 0.93, 95%CI [0.88, 0.99], p=0.032.

Following adjustment for confounding variables, age (<0.013), and private insurance type (p<0.001) continued to be strongly associated with increased odds of discontinuation of medication at the second follow-up period.
Table 5-11 Association between hospitalisation and medication discontinuation at follow-up period two (dichotomous exposure)

<table>
<thead>
<tr>
<th></th>
<th>Antithrombotics (B01) (2,250)</th>
<th>Lipid-lowering (C10) (2,395)</th>
<th>Thyroid meds (H03) (586)</th>
<th>Respiratory inhalers (R03) (752)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Unadjusted OR (95%CI)</td>
<td>Adjusted OR (95%CI)</td>
<td>Unadjusted OR (95%CI)</td>
<td>Adjusted OR (95%CI)</td>
</tr>
<tr>
<td>Hospitalised (v non-hospitalised before 2nd follow-up)</td>
<td>0.69 (0.45, 1.06)</td>
<td>0.66 (0.38, 1.17)</td>
<td>1.12 (0.74, 1.69)</td>
<td>1.06 (0.61, 1.85)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>1.06 (1.04, 1.08) *</td>
<td>1.07 (1.05, 1.09) *</td>
<td>1.08 (1.03, 1.10) *</td>
<td>1.08 (1.01, 1.11) *</td>
</tr>
<tr>
<td>Female (v Male)</td>
<td>0.98 (0.77, 1.25)</td>
<td>0.82 (0.60, 1.11)</td>
<td>0.88 (0.69, 1.13)</td>
<td>0.73 (0.54, 0.99) *</td>
</tr>
<tr>
<td>Insurance Type (Private vs GMS/DVC)</td>
<td>7.95 (5.64, 11.21) *</td>
<td>6.03 (3.93, 9.25) *</td>
<td>6.25 (4.48, 8.72) *</td>
<td>4.87 (3.16, 7.50) *</td>
</tr>
<tr>
<td>Number of repeat drugs classes</td>
<td>1.01 (0.96, 1.06)</td>
<td>1.01 (0.95, 1.08)</td>
<td>0.99 (0.95, 1.04)</td>
<td>0.99 (0.93, 1.05)</td>
</tr>
<tr>
<td>Charlson index (≥1 v 0)</td>
<td>0.93 (0.71, 1.20)</td>
<td>1.15 (0.84, 1.58)</td>
<td>0.88 (0.68, 1.15)</td>
<td>0.88 (0.63, 1.22)</td>
</tr>
<tr>
<td>No. consultations in enrolment period</td>
<td>0.95 (0.93, 0.98) *</td>
<td>0.98 (0.95, 1.05)</td>
<td>0.99 (0.96, 1.01)</td>
<td>0.99 (0.97, 1.03)</td>
</tr>
<tr>
<td>Hospitalised before 1st follow-up</td>
<td>0.99 (0.76, 1.29)</td>
<td>0.97 (0.67, 1.42)</td>
<td>1.18 (0.89, 1.54)</td>
<td>1.01 (0.69, 1.49)</td>
</tr>
</tbody>
</table>

*p value <0.05

Adjusted model included gender, age, insurance type, Charlson index, number of repeat drugs, discontinuity status at follow-up period one, hospitalisation prior to follow-up period one and number of practice visits in the enrolment period.

GMS = General Medical Services; DVC=Doctor Visit Card
Hospitalisation (continuous variable)

Similarly, hospitalisation recorded continuously in the time prior to the second follow-up period was not associated with medication discontinuity in either the unadjusted or adjusted analyses (Table 5-12).
Table 5-12 Association between hospitalisation and medication discontinuation at follow-up period two (continuous exposure)

<table>
<thead>
<tr>
<th></th>
<th>GMS = General Medical Services</th>
<th>DVC=Doctor Visit Card</th>
<th>Antithrombotics (B01) (N=2,250)</th>
<th>Lipid-lowering (C10) (N=2,395)</th>
<th>Thyroid meds (H03) (N=586)</th>
<th>Respiratory Inhalers (R03) (N=752)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hospitalisations prior to 2nd follow-up period (Continuous)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unadjusted OR</td>
<td>0.75</td>
<td>0.82</td>
<td>1.01</td>
<td>1.26</td>
<td>1.44</td>
<td>0.68</td>
</tr>
<tr>
<td>(95%CI)</td>
<td>(0.56, 1.03)</td>
<td>(0.60, 1.11)</td>
<td>(0.96, 1.06)</td>
<td>(1.01, 1.50)</td>
<td>(1.01, 2.06)</td>
<td>(0.43, 0.76)</td>
</tr>
<tr>
<td>Adjusted OR</td>
<td>0.72</td>
<td>0.88</td>
<td>0.99</td>
<td>1.09</td>
<td>0.98</td>
<td>0.68</td>
</tr>
<tr>
<td>(95%CI)</td>
<td>(0.49, 1.06)</td>
<td>(0.69, 1.13)</td>
<td>(0.95, 1.04)</td>
<td>(0.98, 1.22)</td>
<td>(0.93, 1.08)</td>
<td>(0.42, 0.76)</td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unadjusted OR</td>
<td>1.06</td>
<td>1.07</td>
<td>1.05</td>
<td>1.08</td>
<td>1.07</td>
<td>1.05</td>
</tr>
<tr>
<td>(95%CI)</td>
<td>(1.04, 1.08)</td>
<td>(1.03, 1.10)</td>
<td>(1.03, 1.07)</td>
<td>(1.05, 1.10)</td>
<td>(1.03, 1.11)</td>
<td>(1.02, 1.08)</td>
</tr>
<tr>
<td>Adjusted OR</td>
<td>0.98</td>
<td>0.88</td>
<td>0.99</td>
<td>0.99</td>
<td>0.93</td>
<td>1.14</td>
</tr>
<tr>
<td>(95%CI)</td>
<td>(0.77, 1.25)</td>
<td>(0.69, 1.13)</td>
<td>(0.95, 1.04)</td>
<td>(0.93, 1.05)</td>
<td>(0.93, 1.01)</td>
<td>(0.64, 1.78)</td>
</tr>
<tr>
<td><strong>Female (v Male)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unadjusted OR</td>
<td>0.98</td>
<td>0.99</td>
<td>0.99</td>
<td>0.99</td>
<td>0.93</td>
<td>0.98</td>
</tr>
<tr>
<td>(95%CI)</td>
<td>(0.71, 1.20)</td>
<td>(0.84, 1.15)</td>
<td>(0.95, 1.04)</td>
<td>(0.93, 1.05)</td>
<td>(0.93, 1.01)</td>
<td>(0.90, 1.09)</td>
</tr>
<tr>
<td>Adjusted OR</td>
<td>0.93</td>
<td>0.88</td>
<td>0.99</td>
<td>0.99</td>
<td>0.93</td>
<td>0.98</td>
</tr>
<tr>
<td>(95%CI)</td>
<td>(0.71, 1.20)</td>
<td>(0.84, 1.15)</td>
<td>(0.95, 1.04)</td>
<td>(0.93, 1.05)</td>
<td>(0.93, 1.01)</td>
<td>(0.90, 1.09)</td>
</tr>
<tr>
<td><strong>Insurance Type (Private v GMS/DVC patients)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unadjusted OR</td>
<td>7.95</td>
<td>6.07</td>
<td>6.25</td>
<td>4.86</td>
<td>17.46</td>
<td>14.55</td>
</tr>
<tr>
<td>(95%CI)</td>
<td>(5.64, 11.21)</td>
<td>(3.95, 9.31)</td>
<td>(4.48, 8.72)</td>
<td>(3.16, 7.49)</td>
<td>(8.75, 34.84)</td>
<td>(7.56, 28.03)</td>
</tr>
<tr>
<td>Adjusted OR</td>
<td>1.01</td>
<td>1.02</td>
<td>0.99</td>
<td>0.99</td>
<td>0.93</td>
<td>1.14</td>
</tr>
<tr>
<td>(95%CI)</td>
<td>(0.96, 1.06)</td>
<td>(0.96, 1.08)</td>
<td>(0.95, 1.04)</td>
<td>(0.93, 1.05)</td>
<td>(0.93, 1.03)</td>
<td>(0.67, 1.83)</td>
</tr>
<tr>
<td><strong>Number of repeat drugs classes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unadjusted OR</td>
<td>0.93</td>
<td>1.16</td>
<td>0.88</td>
<td>0.88</td>
<td>1.11</td>
<td>0.78</td>
</tr>
<tr>
<td>(95%CI)</td>
<td>(0.71, 1.20)</td>
<td>(0.84, 1.58)</td>
<td>(0.84, 1.15)</td>
<td>(0.84, 1.22)</td>
<td>(0.61, 1.99)</td>
<td>(0.52, 1.18)</td>
</tr>
<tr>
<td>Adjusted OR</td>
<td>0.93</td>
<td>1.16</td>
<td>0.88</td>
<td>0.88</td>
<td>0.84</td>
<td>0.78</td>
</tr>
<tr>
<td>(95%CI)</td>
<td>(0.71, 1.20)</td>
<td>(0.84, 1.58)</td>
<td>(0.84, 1.15)</td>
<td>(0.84, 1.22)</td>
<td>(0.84, 1.18)</td>
<td>(0.52, 1.18)</td>
</tr>
<tr>
<td><strong>Charlson score (≥1 v 0)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unadjusted OR</td>
<td>0.95</td>
<td>0.98</td>
<td>0.99</td>
<td>0.99</td>
<td>0.93</td>
<td>0.98</td>
</tr>
<tr>
<td>(95%CI)</td>
<td>(0.93, 0.98)</td>
<td>(0.95, 1.01)</td>
<td>(0.96, 1.01)</td>
<td>(0.97, 1.03)</td>
<td>(0.95, 1.01)</td>
<td>(0.90, 1.06)</td>
</tr>
<tr>
<td>Adjusted OR</td>
<td>0.95</td>
<td>0.98</td>
<td>0.99</td>
<td>0.99</td>
<td>0.93</td>
<td>0.98</td>
</tr>
<tr>
<td>(95%CI)</td>
<td>(0.93, 0.98)</td>
<td>(0.95, 1.01)</td>
<td>(0.96, 1.01)</td>
<td>(0.97, 1.03)</td>
<td>(0.95, 1.01)</td>
<td>(0.90, 1.06)</td>
</tr>
<tr>
<td><strong>No. of consultations in enrolment period</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unadjusted OR</td>
<td>26.92</td>
<td>23.59</td>
<td>28.68</td>
<td>26.44</td>
<td>35.57</td>
<td>20.29</td>
</tr>
<tr>
<td>(95%CI)</td>
<td>(19.48, 37.21)</td>
<td>(16.73, 33.26)</td>
<td>(20.63, 39.87)</td>
<td>(18.61, 37.56)</td>
<td>(15.33, 82.56)</td>
<td>(12.39, 33.24)</td>
</tr>
<tr>
<td>Adjusted OR</td>
<td>0.96</td>
<td>0.97</td>
<td>1.13</td>
<td>1.06</td>
<td>1.44</td>
<td>0.95</td>
</tr>
<tr>
<td>(95%CI)</td>
<td>(0.81, 1.13)</td>
<td>(0.77, 1.21)</td>
<td>(0.96, 1.33)</td>
<td>(0.85, 1.34)</td>
<td>(1.01, 2.06)</td>
<td>(0.74, 1.22)</td>
</tr>
</tbody>
</table>

*p <0.05; OR – Odds Ratio

** Capped at 5 or more hospitalisations; hospitalisation as recorded at the first follow-up time point
Adjusted model included gender, age, insurance type, Charlson index, number of repeat drugs, discontinuity status at follow-up period one, hospitalisation prior to follow-up period one and number of practice visits in the enrolment period.

GMS = General Medical Services; DVC=Doctor Visit Card
5.4.2.4 Secondary outcome (association between absence of medication on discharge summary and medication continuity in GP record)

These analyses examine the association between absence of the specified medication on the patient’s discharge notes and lack of continuity of medication over the follow-up period. For these analyses the exposure variable was coded 0 (medication explicitly listed on the discharge summary), 1 (medication not listed on the discharge notes). The outcome variable was coded 0 (if the specified medication group was present within the GP record within the follow-up period) and 1 (if it was absent). The results of these analyses are reported in Table 5-13.

5.4.2.4.1 Unadjusted analyses

In all medication groups the absence of the medication on the discharge summary note was significantly associated with an increase in the odds of the medication not being present in the GP record over the follow-up period after discharge. These odds ratios ranged from 1.41, (95%CI [1.01, 1.97], p=0.046) in the antithrombotics (B01) group to 2.36 (95%CI [1.26, 4.45], p=0.08) in the respiratory inhalers (R03) group.

Consequently, an individual was on average was at least 40% more likely not to receive a prescribed medication in the follow-up period after discharge if the medication was not named on their discharge summary notes than if it was named.

5.4.2.4.2 Adjusted analyses

In the adjusted models (which included all covariates from the primary analyses - gender, age, insurance type, Charlson index, number of repeat drugs, number of practice visits in the enrolment period as well as hospital cluster), the absence of
the named medication in the discharge summary notes was still significantly associated with an increase in the odds of a patient not receiving the chronic medication in the follow-up period post discharge for two medication groups - the lipid-lowering group (C10) (AOR 2.23, 95%CI [1.47, 3.39], p<0.001) and the respiratory inhalers group (R03) (AOR 3.44, 95%CI [1.67, 7.06], p=0.001).

The relationship between specific hospitals and discontinuity in the follow-up period was examined with generally no differences seen between hospitals, except in one case where in Dublin hospital 1 the odds of discontinuation were greater than Dublin hospital 2 in the lipid-lowering (C10) group (AOR 2.23 [1.19, 4.16], p=0.012).
Table 5-13 Association between medication continuity and medication being present on discharge summary

<table>
<thead>
<tr>
<th>Medication group</th>
<th>Antithrombotics (B01) (1,475)</th>
<th>Lipid-lowering (C10) (1,407)</th>
<th>Thyroid meds (H03) (331)</th>
<th>Respiratory inhalers (R03) (543)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Unadjusted OR (95%CI)</td>
<td>Adjusted OR (95%CI)</td>
<td>Unadjusted OR (95%CI)</td>
<td>Adjusted OR (95%CI)</td>
</tr>
<tr>
<td>Medication not named on discharge summary (v medication named on discharge summary)</td>
<td>1.41 (1.01, 1.97) *</td>
<td>1.46 (0.99, 2.17)</td>
<td>1.63 (1.12, 2.37) *</td>
<td>2.23 (1.47, 3.39) *</td>
</tr>
<tr>
<td>Age (years)</td>
<td>1.02 (0.99, 1.04)</td>
<td>1.02 (0.99, 1.04)</td>
<td>1.04 (1.02, 1.07) *</td>
<td>1.05 (1.02, 1.07) *</td>
</tr>
<tr>
<td>Female (v Male)</td>
<td>0.99 (0.71, 1.39)</td>
<td>1.05 (0.74, 1.50)</td>
<td>0.93 (0.66, 1.31)</td>
<td>0.99 (0.69, 1.43)</td>
</tr>
<tr>
<td>Insurance Type (Private v GMS/DVC patients)</td>
<td>5.83 (3.78, 8.99) *</td>
<td>5.90 (3.79, 9.20) *</td>
<td>4.73 (2.89, 72) *</td>
<td>4.91 (2.94, 8.18) *</td>
</tr>
<tr>
<td>Number of repeat drugs classes</td>
<td>0.95 (0.89, 1.01)</td>
<td>0.96 (0.89, 1.03)</td>
<td>0.99 (0.93, 1.06)</td>
<td>0.98 (0.91, 1.06)</td>
</tr>
<tr>
<td>Charlson score (≥1 v 0)</td>
<td>0.82 (0.58, 1.14)</td>
<td>0.91 (0.63, 1.31)</td>
<td>1.51 (1.06, 2.16) *</td>
<td>1.65 (1.12, 2.42) *</td>
</tr>
<tr>
<td>No. of consultations in enrolment period</td>
<td>0.96 (0.93, 0.99) *</td>
<td>0.97 (0.94, 0.99) *</td>
<td>0.98 (0.95, 1.01)</td>
<td>0.99 (0.95, 1.02)</td>
</tr>
<tr>
<td>Hospitals:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dublin Hosp 2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Dublin Hosp 1</td>
<td>0.73 (0.45, 1.17)</td>
<td>1.08 (0.62, 1.89)</td>
<td>1.24 (0.74, 2.08)</td>
<td>2.23 (1.19, 4.16) *</td>
</tr>
<tr>
<td>Dublin Hosp -Other</td>
<td>1.07 (0.62, 1.87)</td>
<td>1.43 (0.79, 2.62)</td>
<td>1.23 (0.67, 2.27)</td>
<td>1.66 (0.85, 3.25) **</td>
</tr>
<tr>
<td>Galway Hosp</td>
<td>0.97 (0.61, 1.54)</td>
<td>1.31 (0.79, 2.17)</td>
<td>1.06 (0.62, 1.81)</td>
<td>1.46 (0.79, 2.68) **</td>
</tr>
<tr>
<td>Others</td>
<td>0.77 (0.31, 1.90)</td>
<td>1.05 (0.39, 2.74)</td>
<td>1.24 (0.52, 2.99)</td>
<td>1.83 (0.67, 4.97) **</td>
</tr>
</tbody>
</table>

* p value <0.05; OR: Odds Ratio
** Clusters collapsed due to small numbers

Adjusted model included gender, age, insurance type, Charlson index, number of repeat drugs, hospital cluster, and number of practice visits in the enrolment period.

GMS = General Medical Services; DVC=Doctor Visit Card
5.5 Model checking and goodness of fit

The methods outlined in section 5.3.22.2 were used to assess the fit of the final models examining the association between hospitalisation and discontinuity of medication at follow-up period one as follows:

a. Deviance Residuals

Plots of the residuals for each group are displayed in Appendix Q. These plots were visually inspected, with no obvious patterns present and data points appearing to be randomly scattered.

b. Obvious errors in the data

The data were extracted anonymously which precluded the possibility of being able to, for example, verify the data by examining the primary source (the GP record). Nevertheless, the lengthy pilot project ensured a rigorous examination of the data extraction process and discussion with software engineers about the data quality. Following extraction, the all data fields were examined and both variables which were extracted as well as newly generated were plotted and examined for unusual data patterns (see Appendix P). No consistently obvious deviations in the data were uncovered.

c. Logit link function

The linktest was used to assess the suitability of the logit link function in the multilevel models. Models were refitted using both the linear predictor and the square of the linear predictor as independent variables. The squared variable was not found to be significant in any of the groups (p>0.05), suggesting the chosen models were appropriate in this respect.
d. *Additional confounders (e.g. level two effects)*

The only additional cluster level variable that could be considered was the geographical distribution of the practices (e.g. Dublin = 0, West = 1, Cork = 2, North-East = 3). A model was fitted to incorporate this covariate. None of these effects were found to be significant (p>0.05) and therefore were omitted.

e. *Interaction terms between predictor and covariates*

For each chronic medication group, the adjusted model was compared with a model in which interaction terms between hospitalisation and each covariate were added. The likelihood ratio test for each of these comparisons confirmed that the addition of these interactions did not significantly improve the model fit (p>0.05 in all cases). Consequently, no interaction terms were added to the final models.

f. *Continuous variables requiring transformation*

There are a number of continuous variables included in the final model (age, number of drugs, Charlson index, and number of consultations). The possible non-linear effect of age on the primary outcome was explored through including a quadratic term for age in addition to the linear term. Although of statistical significance, the appreciable difference was not deemed clinically significant or appropriate. Other variables were explored graphically for outliers and capped rather than transformed. No obvious transformations for the continuous variables were identified in the literature and hence were not explored further.

 g. *Outliers*
Covariates were examined for unusually large or small values (See Appendix P). The models included a small number of patients whose age was considerably higher than the rest of the cohort (e.g. age 115 years in two observations). Models were rerun removing these older patients as well as those more than 90 years of age with no difference in the overall results. In one practice the odds of discontinuity were considerably higher than average across all four cohorts however removing this practice from the analysis made no difference to the overall result.

h. Effects of covariates varying between clusters
No clinically sound reason could be given in testing whether effects associated with confounding variables on the outcome variables could be expected to vary between clusters (practices).

i. Additional features of the study design
The validity of the study design as examined in Section 5.8 (Risk of bias). Other issues such as three level models (involving hospital clusters) or practice level covariates were explored and not deemed appropriate.

None of the above affected the original results or improved the fit of the multivariable models as reported.
5.6 Subgroup analysis

Subgroup analysis was undertaken to explore whether the findings were replicated when patients whose length of stay in hospital had been less than one day were removed from the analyses. The findings of this analysis are displayed in Table 5-14. As with the primary analysis only patients who were long term users of respiratory inhalers (R03 group) who had been admitted to hospital were less likely to experience discontinuity of medication during follow-up than those who had not been admitted to hospital (AOR 0.61 [0.45, 0.81]).
Table 5-14 Subgroup analysis: Odds of discontinuity at follow-up time one - Length of stay of less than one day excluded

<table>
<thead>
<tr>
<th></th>
<th>Antithrombotics (B01) (n=6567)</th>
<th>Lipid-lowering (C10) (n=6974)</th>
<th>Thyroid meds (H03) (n=1705)</th>
<th>Respiratory inhalers (R03) (n=2392)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Unadjusted OR (95%CI)</td>
<td>Adjusted OR (95%CI)</td>
<td>Unadjusted OR (95%CI)</td>
<td>Adjusted OR (95%CI)</td>
</tr>
<tr>
<td>Hospitalisation V No</td>
<td>1.03 (0.86, 1.22)</td>
<td>1.03 (0.86, 1.24)</td>
<td>1.18 (0.99, 1.39)</td>
<td>1.08 (0.89, 1.30)</td>
</tr>
<tr>
<td>Hospitalisation (Dichotomous)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Unadjusted OR (95%CI)</td>
<td>Adjusted OR (95%CI)</td>
<td>Unadjusted OR (95%CI)</td>
<td>Adjusted OR (95%CI)</td>
</tr>
<tr>
<td></td>
<td>0.69 (0.44, 1.09)</td>
<td>0.62 (0.38, 1.03)</td>
<td>0.61 (0.46, 0.80) *</td>
<td>0.61 (0.45, 0.81) *</td>
</tr>
</tbody>
</table>

*p value <0.05; OR: Odds Ratio
5.7 Sensitivity analysis

Sensitivity analysis was undertaken to assess whether the methods by which the data were collected, prepared and analysed could substantively affect the results (as pre-specified in Section 5.3.22.4)

The results of the various sensitivity analyses are tabulated in Table 5-15, with a summary of the findings of the analyses described here. The direction of the association between hospitalisation and discontinuity at time one remained the same as the primary analyses in all cases.

Consistent with the primary analysis long-term users of respiratory inhalers (the R03 group) and thyroid medication (the H03 group) who had been admitted to hospital were significantly less likely to experience discontinuity of medication over the first follow-up period than those who had not been admitted to hospital in nearly all analyses. Within the manually coded practices, the lipid-lowering (C10) group who were admitted to hospital were significantly more likely to experience discontinuity of medication over the follow-up period than those who had not been admitted to hospital (AOR 2.73, 95%CI [1.52, 4.93]). In the primary analysis, this association was not significant (Table 5-8). Increasing the outcome assessment to 9 months (from the original of 6 months) did not affect the original conclusions substantively. It was deduced that the assumptions which had been made in preparing and analysing the data had not invalidated the initial findings.
Table 5-15 Sensitivity analysis: Odds of non-reconciliation at follow-up time one (Analyses 1-5)

<table>
<thead>
<tr>
<th>Sensitivity Analysis Method – Effect of hospitalisation</th>
<th>Antithrombotics (B01)</th>
<th>Lipid-lowering (C10)</th>
<th>Thyroid meds (H03)</th>
<th>Respiratory inhalers (R03)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unadjusted OR (95%CI)</td>
<td>Adjusted OR (95%CI)</td>
<td>Unadjusted OR (95%CI)</td>
<td>Adjusted OR (95%CI)</td>
<td>Unadjusted OR (95%CI)</td>
</tr>
<tr>
<td>#1</td>
<td>0.97 (0.82, 1.14)</td>
<td>0.97 (0.81, 1.16)</td>
<td>1.19 (1.00, 1.41) *</td>
<td>1.09 (0.90, 1.30)</td>
</tr>
<tr>
<td>#2</td>
<td>0.85 (0.70, 1.04)</td>
<td>0.85 (0.69, 1.05)</td>
<td>1.05 (0.86, 1.27)</td>
<td>0.96 (0.78, 1.18)</td>
</tr>
<tr>
<td>#3</td>
<td>0.90 (0.74, 1.09)</td>
<td>0.89 (0.73, 1.09)</td>
<td>1.17 (0.97, 1.42)</td>
<td>1.03 (0.84, 1.27)</td>
</tr>
<tr>
<td>#4</td>
<td>1.23 (0.71, 2.13)</td>
<td>1.57 (0.86, 2.86)</td>
<td>2.86 (1.65, 4.97) *</td>
<td>2.73 (1.52, 4.93) *</td>
</tr>
<tr>
<td>#5</td>
<td>1.04 (0.85, 1.27)</td>
<td>0.99 (0.79, 1.23)</td>
<td>1.43 (1.17, 1.76) *</td>
<td>1.24 (0.99, 1.54)</td>
</tr>
</tbody>
</table>

*p<0.05; OR: Odds Ratio; CI: Confidence Interval
1. Estimation of the missing discharge date
2. Only one hospitalisation permitted before calculation of follow-up period
3. Practices with potential misclassification of exposure removed
4. Manually coded hospitalisations only
5. Primary outcome was calculated over a nine-month period
5.8 Risk of bias of the retrospective cohort study

The CASP cohort study checklist was adapted to assess the overall risk of bias of this retrospective cohort study. A summary is presented in Table 5-16. Overall risk of bias was low.
Table 5-16 Risk of bias in the cohort study

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Yes</th>
<th>Can’t tell</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are the results of the study valid?</td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Did the study address a clearly focussed issue?</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Was the cohort recruited in an acceptable way?</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Is it worth continuing?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Was the exposure accurately measured to minimise bias?</td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Was the outcome accurately measured to minimise bias?</td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Have the authors identified all important confounding factors?</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Have they taken account of the confounding factors in the design and/or analysis?</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Was the follow up of subjects complete enough?</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Was the follow up of subjects long enough?</td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>What are the results?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>What are the results of this study?</td>
<td></td>
<td>See text</td>
<td></td>
</tr>
<tr>
<td>How precise are the results?</td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Do you believe the results?</td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Will the results help locally?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>------------------------------</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Can the results be applied to the local population?</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Do the results of this study fit with other available evidence?</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>What are the implications of this study for practice?</td>
<td>See text</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Each criterion is addressed individually with the overall judgement and rational for the judgement below.

Are the results of the study valid?

1. **Did the study address a clearly focused issue?**
   
   Overall judgement: Yes
   
   Rationale: The study methodology clearly states the population, risk factors and outcomes that were proposed to study. The plan of analysis is constructed to detect a beneficial or harmful effect.

2. **Was the cohort recruited in an acceptable way?**
   
   Overall judgement: Probably yes
   
   Rationale: Both the exposed and unexposed study participants were drawn from the same population i.e. older community dwelling people attending 44 general practices in Ireland. Both exposed and unexposed were present in the same practices across different hospital regions. Is it worth continuing?

3. **Was the exposure accurately measured to minimise bias?**
   
   Overall judgement: Can’t tell
   
   Rationale: The risk of bias for this methodological quality criterion depends on the exposure of interest. Ascertainment of hospitalisation was via both hospital provided electronic discharge summaries and a subgroup of manually coded discharge summaries. Any participant hospitalised during the enrolment period was automatically excluded until a hospitalisation free period of one year was defined.

4. **Was the outcome accurately measured to minimise bias?**
   
   Overall judgement: Can’t tell
   
   Rationale: The outcome measure chosen was a necessary compromise due to the nature of the data. No prescription of the specified medication within 180 days of the index date was chosen
was synonymous with an unintentional discontinuation of prescription. There are limitations with using this outcome e.g. appropriate discontinuation; handwritten prescriptions are not recorded, reliant on up to GP prescribing record. In addition, a sizeable number of patients who were initially recruited to the cohorts were not included in the final analysis due to the inability to calculate the primary outcome. Nonetheless, the emphasis on establishing a prescribing history for each patient in the enrolment period gives confidence in using the same data for comparison in the follow-up period. Furthermore, the chosen outcome was interrogated through sensitivity analysis e.g. alternate time periods of 270 days and a random date (with subsequent censoring of individuals) was applied in the unexposed group ensuring bias was limited between those experiencing and not experiencing the exposure of interest.

5. Have the authors identified all important confounding factors??
Overall judgement: Yes
Rationale: Confounding variables were chosen based on literature review and clinical relevance.
The GP medical record was utilised to record diagnoses, consultations and prescribing. The manual coding process of a subgroup ensured these details were correct. Through the IPCRN upload of the majority of practices it was not possible to validate the GP records.

6. Have they taken account of the confounding factors in the design and/or analysis?
Overall judgement: Yes
Rationale: Each statistical model adjusted for a range of relevant covariates. All analyses presented both the unadjusted and adjusted coefficients.

7. **Was the follow up of subjects complete enough?**
   Overall judgement: Yes
   Rationale: This was a retrospective cohort study, where loss to follow-up was not an issue. In calculating the primary outcome, it was necessary to remove participants who did not have adequate follow-up time or an insufficient hospitalisation free period. Detailed reasons for removal at each stage of the study are given.

8. **Was the follow up of subjects long enough?**
   Overall judgement: Yes
   Rationale: A predefined outcome was measured requiring a specific follow-up period – this was measured for each individual.

What are the results?

9. **What are the results of this study?**

   A detailed description and analysis of the results is reported in Section 5.4. Model checking, subgroup and sensitivity analysis are presented in Sections 5.5 – 5.7. The predefined outcome in both the exposed and unexposed groups with unadjusted and adjusted odds ratio as well as confidence intervals are all reported. The strength of the association is reported in the Bradford Hill criteria discussion below.

10. **How precise are the results?**
The precision of the results as indicated by the odds ratio and confidence intervals is reported for all analyses. In those who were hospitalised their medication was more likely to be continued in the GP record if they were prescribed thyroid meds (AOR 0.54, 95%CI [0.33, 0.89]) and respiratory inhalers (R03) group (AOR 0.53, 95%CI [0.39, 0.71]).

11. Do you believe the results?

Overall judgement: Yes
Rationale: The adjusted odds ratio is large in both the thyroid and respiratory inhalers group indicating hospitalisation is associated with less odds of medication being discontinued. There were detailed steps taken in both the study design and analysis for possible confounding factors, analysis of the possible effect of certain design features (e.g. outcome selection, data collection methods) and discussion in the context of the Bradford Hill criteria.

Will the results help locally?

12. Can the results be applied to the local population?

Overall judgement: Yes
Rationale: The choice of a retrospective cohort study design was both a pragmatic and appropriate decision in light of the available data sources and the explanatory variable being studied (hospitalisation). The population studied is representative of older patients prescribed at least one medication continuously in Ireland and is not dissimilar to pharmacoepidemiological cohort studies of older people published internationally examining this clinical question. The results are quantifiable at a local level in terms of benefits and harms of the exposure.
13. Do the results of this study fit with other available evidence?

Overall judgement: Can’t tell
The results of this study differ in the direction of the effect from some international studies – this is discussed further in Section 5.9.2.

14. What are the implications of this study for practice?

This is an observational study with certain constraints due to the nature of the available data and decisions made in designing the study. The limitations are discussed in more detail in Section 5.9.3. The healthcare policy and future research implications are discussed in Section 5.9.4 and 5.9.5.

Examining the issue of a causal relationship between exposure (hospitalisation) and outcome (discontinuation of medication)

When examining the longitudinal association between hospitalisation and unintentional discontinuation of medication the issue of causality is particularly important. The Bradford-Hill criteria include several factors which should be present if a causal link is to be established between an exposure and outcome.(278) These factors are addressed as follows:

Temporal relationship
The measurement of the exposure of interest preceded the outcome in this study. Hospitalisation was recorded after the enrolment period and before the follow-up period.
**Strength of association**

The stronger or larger the size of the association between an exposure and outcome the more likely it is causal. There was neither a significantly positive nor negative effect of hospitalisation on any medication type, except thyroid medication and respiratory inhalers – where those who were hospitalised their medication was more likely to be continued in the GP record thyroid meds (AOR 0.54, 95%CI [0.33, 0.89]) and respiratory inhalers (R03) group (AOR 0.53, 95%CI [0.39, 0.71]).

The association between lack of medication documentation at discharge on discontinuity was strong in both lipid-lowering (C10) (AOR 2.23, 95%CI [1.47, 3.39]) and respiratory inhalers (R03) (AOR 3.44, 95%CI [1.67, 7.06]) groups, albeit there were smaller numbers of participants available in assessing this outcome.

**Dose-response relationship**

This criterion notes that if with increasing exposure there is an increased risk of the outcome then it is likely there is a causal relationship. This study did not find a negative association between hospitalisation and discontinuity of medication – in fact with some medication types hospitalisation meant a participant was less likely to be discontinued. Hospitalisation was recorded as dichotomous exposure in the main analysis. Where hospitalisation was applied as a continuous measure (Table 5-9), the odds of discontinuation remained less in the thyroid meds and respiratory inhalers (R03) group. Conversely lipid-lowering (C10) became significant for discontinuation in the post hospitalisation period (AOR 1.11, 95%CI [1.00, 1.22]).

**Consistency of the relationship**
There is a lack of evidence for the negative impact in terms of continuity of chronic medication in the GP record post hospitalisation. While small numbers were involved there does appear to be an association between documentation of medication on discharge and continuity in the GP record (lipid-lowering (C10) and respiratory inhalers (R03) groups only).

**Plausibility**
This refers to a causal relationship that is in agreement with currently accepted understanding. The likelihood that documentation of medication upon discharge, and not the transfer of care itself as causative is plausible.

**Consideration of alternate explanations**
The inclusion of a large number of confounding variables is a strength of this study. It allows exploration of alternate explanations for this study’s findings. In particular, the inclusion of age and insurance type, for example, in the statistical modelling and the establishment of a one-year enrolment period lend credence to the findings. However, the study design and outcome measurement did require a number of assumptions that may impact on the validity of the findings. Nevertheless, these assumptions were explored in the sensitivity analysis.

**Coherence**
The findings reported in this study are consistent with the unclear relationship between hospitalisation and long-term continuity of medication.

**Specificity**
This is established when a single putative cause is linked to the outcome. Hospitalisation does not meet this criterion.

5.9 Discussion

5.9.1 Principal findings

The principal findings are as follows:
Discontinuation of chronic medication, in the GP record, in those who have been recently hospitalised ranges from a relatively low 6% in those on thyroid medication to approximately 11% in those prescribed antiplatelets, anticoagulants and statins (Table 5-6).

There was no statistical difference, in antithrombotics and lipid lower medications, of the odds of discontinuation between those who have been hospitalised and those who have not been hospitalised when adjustment has been made for a number of different confounding variables (p>0.05) (Table 5-8).

Respiratory inhalers were statistically less likely to be discontinued in those who have been hospitalised compared to those have not been hospitalised (AOR 0.53, 95%CI [0.39, 0.71]); those prescribed thyroid medications were also less likely to be discontinued (AOR 0.54, 95%CI [0.33, 0.89]) (Table 5-8).

Regarding covariates, insurance status played a significant role in the likelihood of medication being discontinued with the odds of discontinuation significantly higher in all groups where the patient was listed as ‘private’. Increasing age was also associated with increased odds of discontinuation in all medication groups (Table 5-8).
The variation of the association of hospitalisation and the primary outcome was explored between hospitals. While there were statistical differences between some hospitals in the odds of discontinuation of respiratory inhalers post discharge none of these reversed the effect of the exposure (Table 5-10).

Finally, in considering the impact of medication documentation on discharge summaries the association between documentation and subsequent discontinuation was explored. Omission of statins and inhalers on electronically provided discharge summaries was associated with those medications being discontinued on the GP record in the 6 months post hospitalisation. There was little difference between hospitals in the effect of the omissions on the discharge summary on the GP record following discharge (Table 5-13).

5.9.2 Context of this research in comparison with previous literature

Bell et al., reported a higher discontinuation rate in their study, with a significant increase in discontinuation in those experiencing hospitalisation, using pharmacy dispensing data post hospitalisation – 12% in a thyroid medication cohort, and 19% in those prescribed antithrombotics.(218) Stall et al., in 2015 reported discontinuation rates more in line with our study with 4% of nursing home participants discontinued from thyroxine at 7 days post discharge.(227) Increasing age, as has been in shown in many previous studies, is associated with an increased discontinuity post discharge.(232) In contrast to previous studies there was no association between the exposure of hospitalisation generally and an increased risk of
discontinuation of chronic medication – in fact discontinuity was higher in those not hospitalised in some groups.\(^{(227,228,232)}\)

Sensitivity analysis of length of stay greater than one day in this study did not have any impact on the significance of relationship to our primary outcome. This is in contrast to previous studies that have suggested increased hospitalisation time increases risk of discontinuity.\(^{(232)}\) It is noteworthy that many of these studies have examined administrative/dispensing databases to assess continuity of medication post-hospitalisation and did not have access to the GP prescribing record as in this study.

Conflicting with previous studies, increased number of drugs was not associated with discontinuation; in fact in the respiratory inhalers group patients were less likely to be discontinued if they had increased numbers of medications.\(^{(64,68,72–74,283,284)}\) However some studies, small in number, have also not reported a relationship.\(^{(75,76,78)}\). Neither has gender been found to be predictive of continuity.\(^{(68,73,146)}\) Similarly those who had increased contact with their GP (assessed by the number of GP visits in the enrolment year) were less likely to be discontinued across all groups – which has also been previously reported.\(^{(285)}\)

A particular concern is the marked difference between GMS and private patients, with the latter having a very large increase in the odds of discontinuation in the 6 months post hospitalisation. There are many possible explanations for this, some of which were addressed through sensitivity analysis, with the most benign being that private patients are not required to have their hospital discharge prescription transcribed by their GP and may proceed directly to the pharmacy – thereby appearing as if they have been
discontinued by our method of outcome calculation. Nevertheless, this raises concern about validity of the information the GP has at their disposable when assessing private patients if their prescription file is not up to date. There have been a limited number of studies conducted in Ireland examining the influence of eligibility for free care on the use of GP services – with those eligible for free care appearing to utilise the service more often.\(^{286,287}\) While some studies have reported on the impact of prescriptions charges on dispensing continuity no study has examined eligibility for free care and continuity of medication in the GP record.\(^{288}\)

Many previous studies have found an association between increasing morbidity and increased risk of medication error at transitions; however, this was not replicated in this study.

In keeping with findings from other studies the quality of prescribing information contained in discharge communications is poor with the omission of essential medications extremely common (Table 5-7).\(^{51,63}\) Furthermore this lack of reconciliation upon discharge communication is perpetuated through discharge back into general practice records.\(^{69}\) These omissions at discharge may, based on previous research, be due to a failure of reconciliation at admission or throughout the hospital stay emphasising the need that reconciliation must take place at all transitions of care.\(^{15,51,55}\)

The discharge summary used to determine discharge prescriptions in this study is only one element of the information normally given to patients at discharge from hospitals in Ireland – normally a handwritten discharge prescription is provided also.\(^{63}\)
Therefore a discrepancy may arise between the summary and prescription, as hospital doctors make judgements about what to include/exclude from discharge prescriptions. This is a cause for concern as GPs may be acting upon the information provided upon one or the other without knowledge of discrepancies between them. Judgements about which medications to include and omission of ‘less risky’ medications has been reported previously.

While lack of reconciliation following hospital discharge may be one possible explanation for the reported discontinuity there are other possibilities – most obviously patient adherence. A recent large UK study of statin adherence reported discontinuation rates of 27% at one year in those prescribed statins (notably this was examining primary non-adherence as distinct from what may be secondary non-adherence in this cohort). The factors that influence adherence may be patient, therapy, physician or health system related. While this study was able to control for some of these factors (e.g. demographics, comorbidities, insurance status) others were not recorded (e.g. socioeconomic status, side-effects, individual physician behaviour and access to healthcare).

Inadequate adherence (and the related terms non-compliance and non-concordance) may take many forms e.g. non-filling of prescriptions, altering doses, stopping/starting. This study reported a varying discontinuity rate across the four drug classes (lower in antithrombotics and higher in thyroid meds and respiratory inhalers). This variation may be explained by disease specific issues (e.g. altering doses of thyroxine replacement meaning repeat prescriptions are not required; undulating severity of disease – if a patient is asymptomatic they are less likely to take
the medication regularly), evolving diagnoses/clinical considerations (e.g. risk benefit profile of antithrombotic in a patient with a high risk of falls) to patient beliefs about the effectiveness or benefits of the therapy and/or their own susceptibility to illness.(292)

5.9.3 Strengths and limitations

This retrospective primary care based cohort study is the largest Irish study to date to examine the effect of hospitalisation on the continuity of chronic medication in the GP prescribing record. It is also the first study to systematically use GP prescribing records (as opposed to pharmacy dispensing records) via a new data collection technique (the IPCRN) to examine this issue. This study was carefully conducted and adhered to the STROBE guidelines for observational research. The risk of bias of the study, as assessed by the CASP checklist, was low. The study methodology developed a novel data source of prescribing and clinical data from GP clinical records. This rich database allowed greater assessment of the interaction of clinical factors (e.g. codified chronic disease) in relation to discontinuity. The recruitment of GP practices was not confined geographically and the inclusion of multiple hospitals allowed comparison of messaging standards and their impact on prescribing continuity, enhancing the generalisability of the findings.

There are several limitations to this study. The medication groups were specifically chosen to be evidence based and long-term in their usage and the establishment of an enrolment period of continuous usage over one year further ensures the pattern of chronic use. However, the primary outcome of discontinuation of
medication was applied to a prescribing database and therefore is devoid of the understanding of a possible therapeutic intent e.g. intentional discontinuation of statins in older/end-of-life individuals or appropriate discontinuation of antiplatelets/anticoagulants following a gastrointestinal bleed. The construction of adjusted models to cater for confounding partially compensate for this, as well the sensitivity analysis.

The nature of data collection and the dataset itself also incur limitations. For example, the anonymity of the data collection did not allow review of individual participants’ records to uncover clinical intent. The recording of information by GPs – both chronic disease and prescribing may also have contributed to error. Hand written prescriptions were not captured by this data collection technique. Furthermore, the recording of prescriptions did not lend itself to employing traditional metrics such as MPR. This meant the adoption of a particular outcome measure for this study and did not allow direct comparison with many similar dispensing database studies. However, the recruitment of a subset of GP practices whose records were then manually coded contributed to the robustness of the calculation of the exposure and confounder variables - such as disease coding.

The follow-up of participants from enrolment through to outcome calculation also required certain assumptions to made in preparing the data for analysis. The requirement of adequate follow-up time (6 months post index date) and censoring of those without sufficient time may have introduced a bias. The calculation of an index date, using a random date, within the unexposed group to allow comparison with the exposed group is also artificial. This method has been used previously, and is in line with the
underlying hypothesis that there should be no difference within groups with both having 100% persistence of the medication in the GP record.

The recording of the exposure is likely to be variable within practices (with the Healthlink service employed differently by hospitals) with the possibility of misclassification of exposed individuals as being unexposed. This was explored in the sensitivity analysis with no change in the summary findings. The manual coding process also allowed comparison of this issue. The study failed to achieve the planned sample size in any of the groups. This was a combination of the higher than expected loss of data due to so called ghost patients as well as the restricted years over which the data were collected. Additionally, the criteria used to calculate the primary outcome meant a significant proportion of patients who were originally enrolled did not enter the final analysis. However, the observed difference, in two of the groups, between the exposed and unexposed in the primary outcome was less than the 3% estimated in section 5.3.19, with a statistical difference detected in the other two groups. Differences of less than 3% are likely to be of questionable clinical importance.

The number of medications examined by the four cohorts is limited. While they are of importance, due to the known benefit accrued to patients if their continuous usage is uninterrupted, the effect of hospitalisation needs to be explored on all medications types.

The nature of the private public health system in Ireland may also contribute to a misattribution of both the exposure and the outcome. Patients paying for healthcare out-of-pocket (private
patients) are less tied to a single GP practice and likely have greater access to private secondary care also. Furthermore, the categorising of insurance type GMS/DVC v private is worthy of discussion. Those patients holding a Doctor Visit Card (DVC), while entitled to free GP care, are treated similarly to private patients in medication dispensing at the pharmacy (i.e. payment is required, and have a longer dispensing duration of six months). Private hospital usage (and the possible miscategorising of the exposure) was explored in the manual coding of practice data – ensuring private hospital discharge data were also collected. Finally, this was a retrospective cohort study and is by definition at risk of bias and confounding with the inability to infer causation but merely articulate associations.

5.9.4 Future clinical, research and healthcare policy implications

This study suggests that the previously reported discontinuation of medication seen post hospitalisation is not present when examining the GP prescribing record. In attempting to further explore the continuum of care and source of disruption the contrasting findings of this study need to be confirmed and the alternative causes for the reported discontinuity need to be postulated and researched.

Future efforts should focus on identifying particularly high-risk individuals and medications that would be the best targets for reconciliation studies and interventions. Recent efforts in this regard to develop a consensus of high risk medications and methods of assessing the potential severity of omission are helpful.(293) Also the corollary of discontinuation, inappropriate
continuation or commission errors, may be explored in this study population e.g. proton pump inhibitors, hypnotics for short term illness inappropriately continued post discharge.(294) Exploring ways to improve utilisation, documentation and operation of the electronic medication information transfer systems should be targets for further research.

The quality of electronic discharge communication received by general practices and the possible association with inappropriate discontinuation of chronic medication suggests more emphasis needs to be placed on improving the quality of discharge communication. Reports have been issued calling for the standardisation and improvement of the interoperability of messaging standards and electronic communication in Ireland.(80,180,181) The HSE’s ePrescribing initiative and eScript pilot projects are efforts to improve the transfer of medication information.(184) Possible differences in the effect of hospitalisation on the primary outcome between hospitals suggest larger studies of this potential for variation are needed – particularly considering the known variation in practices and staffing availability at hospital admission and discharge.(205)

The large effect size seen with private patients is worth further exploration. While the limitations of this study to examine this patient type specifically have been noted the magnitude of the effect means the group requires further attention. Whether private patients suffer from a greater lack of coordination of their care, with increased risk of discontinuity or whether they receive medications outside of the GP which handles their hospitalisation records this is not a satisfactory or coordinated arrangement.
5.10 Conclusion

The findings of this study contribute to the understanding of the medication management process and transitions of care between primary and secondary care in Ireland. It adds to the relatively limited evidence based on the impact of hospitalisation and discharge summary prescription omissions on the continuity of medication in the GP record specifically.

The study reports relatively low rates of discontinuity of chronic medication (albeit with variability between different medications) and unexpectedly found no increased odds of discontinuity in those who had experienced hospitalisation. Furthermore, there were no consistent differences between hospitals in this association. Age and private insurance type were significantly associated with discontinuity – independent of hospitalisation. The impact of not recording medication on discharge summaries did appear to increase the risk of discontinuity in some medication groups.

Discrepancies in medication are known to be common at transitions of care with a large emphasis from regulatory and healthcare safety organisations to ensure accurate transmission of medication information. This study indicates that, for specified chronic medication, hospitalisation itself does not contribute to discontinuation but the quality of the medication information communicated may more likely be causative.
6 Interventions to improve medication reconciliation at transitions of care – a systematic review
6.1 Introduction
This chapter presents a systematic review of interventions to improve medication reconciliation at transitions of care. The importance and regulatory impetus for medication reconciliation has been explained in Chapter 2. Despite this high level of interest in implementing medication reconciliation the most effective process of conducting reconciliation remains unclear. A consensus statement from key stakeholders has called for further efforts to identify the best practices surrounding medicine reconciliation and their wider dissemination (21).

6.2 Aims and objectives
The aim of this study was to perform a systematic review to assess the effect of medication reconciliation interventions on medication discrepancies, patient related outcomes and healthcare utilisation in patients receiving this intervention during transitions of care compared to patients not receiving medication reconciliation.

Important factors of interest, including polypharmacy, increasing age and the transition of care at which the intervention may be applied were also examined.

6.3 Methods
The Cochrane Collaboration handbook and reporting guidelines were used in conducting this systematic review (295) The Cochrane Collaboration software programme Review Manager (RevMan) V5.3 was used in drafting this review (296) RevMan’s inbuilt meta-analysis software as well as additional functions provided in Stata Version 14 were deployed for statistical analysis purposes (215)
The Cochrane Collaboration stipulation requiring dual assessment/review of documents at all stages of the review process required the creation of a systematic review authorship team. TF, CH, FB, RMcD and TG were involved in screening titles/abstracts, reading full text articles, data extraction and statistical analysis. PR conceived the aims and objectives of the review, led and coordinated all stages of the process, analysed and wrote the results.

The review protocol was published with the Cochrane Collaboration Effective Practice and Organisation of Care (EPOC) review group and the methodology stated below reflects that.(297)

6.3.1 Criteria for considering studies for this review

6.3.1.1 Types of studies

We included randomised controlled trials (RCTs) only. Studies were eligible for inclusion, irrespective of language or publication status. Non-RCTs, controlled before after studies, interrupted time series studies and repeated measures studies were not included. We did not include case series, cohort studies, studies using historical controls or cross-sectional studies.

6.3.1.2 Types of participants

We included all studies involving patients experiencing a transition of care. Transitions of care referred to changes in the level, location, or providers of care as patients move within the health care system.(46,298) This included but was not limited to hospital admission/discharge, acute and sub-acute facilities/units/wards, primary and speciality care, long term care institutions and patients' homes. Transition could have been in either direction e.g.
admission and/or discharge to an intensive care unit from a
general ward.
There was no restriction on age, gender, ethnicity, location or
patient population.

6.3.1.3 Types of interventions

We included studies where the intervention was broadly compliant
with the process of medication reconciliation as outlined by the
Institute for Healthcare Improvement (20): "the process of creating
the most accurate list possible of all medications a patient is taking
- including drug name, dosage, frequency, and route — and
comparing that list against the physician's admission, transfer,
and/or discharge orders, with the goal of providing correct
medications to the patient at all transition points...". Medication
reconciliation involves three steps.(20):
1. create an accurate and complete list of current medications
   (verify);
2. check appropriateness of medication regimes (clarify);
3. document the reason for medication changes and communicate
   this complete list (reconcile).

The intervention must have been applied as patients transition
from different levels and/or locations of care.
Medication reconciliation interventions must have been aligned to
a number of broad interventional categories including professional
interventions, financial, organisational and regulatory.(299) These
could include pharmacist delivered reconciliation (300–303),
complex multi-faceted interventions (304), and information
technology solutions.(145,305) Interventions were grouped
according to the original EPOC taxonomy of intervention types
(professional, financial, organisational or regulatory).(306)
We excluded trials investigating interventions to improve the quality of prescribing during transitions of care, with no medication reconciliation focus.

The comparator group was those patients receiving no intervention or "usual care" as provided by the relevant healthcare provider.

6.3.1.4 Types of outcome measures

The outcomes chosen reflected the Cochrane EPOC Group guidance as those being important to the population of interest as well as decision makers in healthcare (307). We excluded studies reporting secondary outcomes only. We included process measures, patient related outcomes and healthcare utilisation.

Primary outcomes

Discrepancies in prescription per:
- Patient;
- Medication (e.g. drug/dose/name/mode of administration/frequency).

Medication discrepancies have previously been defined as unexplained differences in documented medication regimes across different sites of care.(22)

Secondary outcomes

Patient related and process outcomes:
- medication discrepancy with the potential for adverse drug events, which have been previously described as "incidents with potential for injury related to a drug" (308);
- adverse drug events;
- mortality.

Health care utilisation:
- primary care visits;
- emergency department visits;
• unplanned re-hospitalisation;
• length of stay.

Additional outcomes:

• adverse effects of interventions (e.g. unanticipated increased workload, health worker attrition);
• resource use (dependent on studies of effectiveness selected for inclusion in the review, a narrative summary of the characteristics of economic analysis undertaken may be possible e.g. comparisons of study design, methodology and outcome, measures of incremental resource use, cost and cost effectiveness etc. These results may be useful in future full economic evaluations).

The order of the chosen outcomes (with a process measure being identified as the primary outcome) was a reflection of the current efforts in the study of medication reconciliation. The majority of completed and planned interventional studies in this area have chosen medication discrepancy as their primary outcome. Indeed, many trials reporting clinical measures such as re-hospitalisations are underpowered to adequately report such findings. In addition, reporting potential for adverse drug events acknowledges previously-raised concerns that some discrepancies may have little or no impact on patient safety.(24)

6.3.2 Search methods for identification of studies

The following databases were searched for primary studies: See the Appendix T for the full search string and results for each database.

Electronic searches

• Database of Abstracts of Reviews of Effects (DARE)
• Cochrane Database of Systematic Reviews (CDSR)
- Cochrane EPOC Group Specialised Register
- Cochrane Central Register of Controlled Trials (CENTRAL), The Cochrane Library
- MEDLINE and MEDLINE In-Process and other non-indexed citations, OvidSP
- EMBASE, OvidSP
- PsychINFO, OVIDSP
- CINAHL (Cumulative Index to Nursing and Allied Health Literature), EbscoHost
- Dissertations and Theses Database, ProQuest
- Science Citation Index, ISI Web of Knowledge
- Web of Science, Conference Proceedings Citation Index-Science, ISI Web of Knowledge
- Pharmline, National Electronic Library for Medicines
- International Pharmaceutical Abstracts (IPA), ProQuest

The MEDLINE syntax was used to develop a search strategy and then adapted to other databases using appropriate syntax and vocabulary for those databases. The strategy included medical subject headings and synonyms for medication reconciliation and transitions of care. We limited results using the "Cochrane Highly Sensitive Search Strategy for identifying randomised trials in MEDLINE: sensitivity- and precision-maximising version (2008 revision); Ovid format", to identify RCTs, as well as the Cochrane EPOC Group methodology filter to identify RCTs.

**Searching other resources**

We conducted a grey literature search to identify studies not indexed in the databases listed above. Sources included the sites listed below.

- Open Grey (http://www.opengrey.eu/).
• Agency for Healthcare Research and Quality (AHRQ) (http://www.ahrq.gov/).
• National Research Register (NRR) Archive (http://www.nihr.ac.uk/Pages/NRRArchive.aspx).
• Joanna Briggs Institute (http://joannabriggs.org/).
• National Institute for Health and Care Excellence (NICE) (http://www.nice.org.uk/).
• NHS Evidence Search (https://www.evidence.nhs.uk/).

We searched the following Registries:
• International Clinical Trials Registry Platform (ICTRP) search portal, WHO (http://apps.who.int/trialsearch/);
• ClinicalTrials.gov, US National Institutes of Health (NIH) (http://clinicaltrials.gov/).

We also:
• screened individual journals and conference proceedings;
• reviewed reference lists of all included studies, relevant systematic reviews/primary studies/other publications;
• contacted authors of relevant studies or reviews to clarify reported published information/seek unpublished results/data;
• contacted researchers with expertise relevant to the review topic/Cochrane EPOC Group interventions.

6.3.3 Data collection and analysis
6.3.3.1 Selection of studies

A combination of two authors (PR, TG, RMcD, FB) independently screened titles and abstracts to decide which studies satisfied the inclusion criteria as well as identifying multiple reports from single studies. Any papers not meeting the inclusion criteria were excluded at this stage. If there was uncertainty, consensus was
reached by discussion with another co-author. If agreement could not be reached, we involved a Cochrane EPOC Group editor to resolve it. Following this, two authors (PR, TG) independently assessed the full text articles to ensure the studies still fulfilled the inclusion criteria.

6.3.3.2 Data extraction and management

A combination of two authors (PR, TG, RMcD, FB) independently undertook data abstraction using a modified version of the Cochrane EPOC Group data collection checklist to include: study design, study population, intervention, usual care, outcome measures used and length of follow-up data.(299) Any disagreement was resolved by discussion between the co-authors. Where necessary, we contacted authors for missing information or clarification. Information from data extraction forms guided the extraction of numerical data for meta-analysis in the Cochrane Collaboration's statistical software, Review Manager 2013.(296)

6.3.3.3 Assessment of risk of bias in included studies

The criteria against which the risk of bias in a study was judged was based on the following domains (299,309):

1. sequence generation;
2. allocation concealment;
3. baseline characteristics;
4. baseline outcome measurement;
5. blinding;
6. incomplete outcome data;
7. protection against contamination;
8. selective outcome reporting;
9. other biases.
We tabulated the description of the domains for each included study, along with a judgement on the risk of bias (low, high or unclear), using one key domain of a study-level entry (allocation concealment) and one key domain of an outcome-level entry (incomplete outcome data) based on the *Cochrane Handbook for Systematic Reviews of Interventions*. We undertook a summary assessment of the risk of bias for the primary outcome across the studies. For each study, we provided a summary assessment of risk of bias as shown below:

1. low risk when there is a low risk of bias across all key domains;
2. unclear risk of bias when there is an unclear risk of bias in one or more of the key domains;
3. high risk of bias when there is a high risk of bias in one or more of the key domains.

A combination two authors (PR, TG, RMcD, FB, CH, TF) independently performed the quality assessment. We resolved disagreements by discussion and, if needed, arbitration by a third author.

6.3.3.4 **Measures of treatment effect**

We reported outcomes for each study in natural units. We calculated, where possible, absolute change from baseline with 95% confidence intervals. We reported estimates for dichotomous outcomes (e.g. adverse drug events) as risk ratios. We reported estimates for continuous outcomes as mean differences if they were measured on the same scale, if continuous outcomes were measured on multiple scales, we reported the standardised mean difference. We reported pre-intervention and post-intervention means or proportions where baseline results were available for both intervention and control groups from RCTs.
For RCTs, we combined findings from independent studies using standard meta-analysis techniques, provided enough study data were obtained and taking account of heterogeneity between studies. The size of the study determined the study's weight and an overall treatment effect was estimated.

We tabulated all relevant information of studies included in the review. This included all pre- and post-intervention results (sample sizes, means, proportions, 95% confidence intervals, etc.) for each group for each outcome of interest. Additionally, we examined the pre- and post-intervention difference for each group for each outcome of interest as well as the differences across groups. We conducted a meta-analysis combining the results of the individual studies.

6.3.3.5 Unit of analysis issues

Cluster-randomised trials selected for inclusion were assessed in order to ensure that appropriate analysis was carried out to address cluster effects and to avoid overestimating the significance of differences. In cluster randomised studies where the analysis was carried out ignoring the effect of clustering, efforts were made to obtain the data needed to correct for this. If the data was not forthcoming, we used the intra cluster correlation coefficient (ICC) from external sources to inflate the standard error so as to account for clustering as described in the Cochrane Handbook for Systematic Reviews of Interventions.(309)

6.3.3.6 Dealing with missing data

We contacted lead study investigators or corresponding authors for any missing trial data or data missing from published reports or
for additional clarification. If there was any missing data from a study, we explicitly stated this. Sensitivity analyses was undertaken as per the Cochrane Handbook for Systematic Reviews of Interventions to assess how sensitive results are to reasonable changes in the assumptions that are made. We commented on the potential impact of missing data on the review findings in the Discussion section.

6.3.3.7 Assessment of heterogeneity

We assessed contextual heterogeneity on the basis of information collected on the context in which the intervention was implemented. We assessed for variability in the participants, interventions and outcomes studied to identify clinical heterogeneity, and for variability in study design to describe methodological diversity. Statistical heterogeneity was identified and measured as recommended by the Cochrane Handbook for Systematic Reviews of Interventions. The following was used as a guide for interpretation:

- 0% to 40%: might not be important;
- 30% to 60%: may represent moderate heterogeneity;
- 50% to 90%: may represent substantial heterogeneity;
- 75% to 100%: considerable heterogeneity.

6.3.3.8 Assessment of reporting biases

We examined asymmetry in funnel plots of the primary outcome to assess the potential for study effects such as publication bias. We conducted formal statistical tests for funnel plot asymmetry, namely the Harbord’s and Peter’s methods. Furthermore, we assessed reporting bias by scrutinising the study results using the Risk of Bias tables (e.g. selective outcome
reporting). Where there was a possibility of publication bias and small-study effects, we undertook a sensitivity analysis as described below. In addition to searching trial registries for relevant trials not identified in our main database searches, we also searched for protocols of studies selected for inclusion, to compare planned with actual methods, interventions and outcomes. Furthermore, a thorough search of the grey literature and contact with known experts in the field also reduced the influence of publication bias on our review.

6.3.4 Data synthesis

We performed statistical analysis using Review Manager 2013 (and Stata version 14 software where necessary).(215,296) Pooled estimates (risk ratios (RRs) with 95% confidence intervals (CIs)) of the evaluated outcome measures were calculated by the generic inverse variance method and random effects model. Results were not depicted as 'not statistically significant' or 'non-significant', instead we reported the CIs together with the exact P value. The $I^2$ statistic was examined to describe the proportion of variability in the results that reflects real differences in effect size. Studies were likely to vary, with respect to populations, interventions, outcomes and settings, therefore a random-effects model was chosen to perform a meta-analysis.

Where it was not possible to synthesise the data from the included studies, we provided a narrative synthesis of the results, grouping together studies that used similar interventions and provided a comparison of different approaches. The data were eventually synthesised using a 'Summary of Findings' table that provides key information concerning the quality of evidence, the magnitude of effect of the interventions examined, and the sum of available data.
on all primary outcomes for a given comparison. We conducted quality assessment of the results using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach, which specifies four levels of quality (high, moderate, low and very low) where the highest quality rating is for a body of evidence based on randomised trials. Quality was assessed separately for each outcome.

6.3.4.1 **Subgroup analysis, investigation of heterogeneity and sensitivity analysis**

We pursued subgroup analyses and investigation of heterogeneity (via meta-regression) with sufficient data. Attention was given to characteristics with strong pre-existing biological support in the literature.(312) A priori, the following areas were considered important:

- Patients with polypharmacy (≥5 long-term medications)
- Older patients and/or chronic illnesses
- Reconciliation applied at different transitions/settings of care.

The following criteria were considering in reviewing the results of subgroup analysis:

- The possibility of chance accounting for the result
- The consistency of effect across studies
- The subgroup difference was a pre-specified hypothesis
- Biological rationale supporting the apparent subgroup effect
- The subgroup difference suggested by comparisons within rather than between studies?

We also conducted a sensitivity analysis to calculate the effect of risk of bias (including missing data) within studies on effect size,
by calculating the effect of excluding or including studies with a higher risk of bias.

6.4 Results

6.4.1 Results of the search

Electronic searches identified 10,596 potentially relevant citations (Figure 6-1). Through searches of other sources, such as relevant reviews, clinical trials registries and grey literature an additional 5,265 records were retrieved. Following de-duplication 10,155 records had their titles and abstracts reviewed. Following this process, 481 full-text records (including publications, conference presentations, reports etc.) were retrieved for more detailed assessment.

Of these, 20 studies met all inclusion criteria (including study design, study population, appropriate comparison group, types of interventions and outcome measurement) and were included in the review.

The PRISMA flow diagram documents the number of studies excluded with accompanying reasons. (Figure 6-1)

Based on identified conference abstracts, published protocols and trial registry listings, sixteen ongoing studies were identified (see Characteristics of ongoing studies in Appendix Y).
6.4.2 Included studies

There were a total of 20 studies meeting the inclusion criteria. Seven of the studies required contact with the authors to attain data relevant for this
Following this 19 of the studies had data that was suitable for meta-analysis. One study, despite contacting the author, did not have data available to allow pooling of results. Three studies were available as conference abstracts only. Of these three, one study author provided an unpublished manuscript for analysis. All study details are provided in the Characteristics of included studies table (Appendix W) and are briefly summarised below.

### 6.4.3 Study design

Included studies consisted of 19 RCTs and one cluster RCT. Two studies had two intervention arms as well as one control arm.

### 6.4.4 Settings

All of the studies were conducted in hospital or immediately related settings. Three studies in surgical pre-admission assessment clinics, one at the hospital/long term care interface, two at hospital/primary care interface, one in a hospital outpatient clinic setting and four primarily at admission, four studies spanned participants entire hospital stay from admission to discharge, and five studies focused interventions primarily on discharge.

The included studies were carried out in eight countries: USA (6 studies), Australia (5 studies), Canada (4 studies) and Colombia, Egypt, Netherlands, Singapore and Ireland (one study each).
6.4.5 Participants

Age, gender, ethnicity
A total of 6007 participants (3106 intervention, 2901 control) were included in this review. The mean age of the intervention group participants was 63.3 years and of the control group participants was 63.7 years. Two studies did not report the age of study participants (321,327). All studies included adults (> 18 years old) participants only. Some by design (age limits) or setting (medicine for the elderly ward) recruited older participants only (≥50 (328); ≥ 55 (315,327); ≥60 (318); ≥70 (314)). Three studies did not report the proportion of participants by gender (320,321,327), of those that did 1284 of the participants in the intervention group were female and 1156 of the control group were female. Ethnicity was not reported in most of the studies; in the 2 studies (314,323) (943 participants) that did report this 73.7 % of participants were white.

Prescribed medications
Most studies recruited participants prescribed multiple medications (>1 medication (318,324,325,329); > 3 medications (313,315,328); ≥5 medications (316,327); >8 medications). (320) Four studies did not report the number of medications prescribed to participants (317,320,321,327), of those that did (n=16) the participants were prescribed a mean of 5.1 (intervention) and 6.1 (control) medicines.

Co-morbidities
Many studies recruited participants with chronic conditions (Diabetes Mellitus, Chronic Obstructive Pulmonary Disease, Cardiovascular disease, Hypertension, Stroke). Some focused on
specific conditions (e.g. Oncology (329); Acute coronary syndrome/Heart failure (316,323) or specific patient types (e.g. surgical patients).(300,318,325) Nine studies reported morbidities of participants in varying ways including Charlson comorbidity index (91,144), with a mean of 2.7 for intervention patients and 3.7 for control patients, and individual counts of varying lists of chronic conditions.(313,316–318,323,326,328)

6.4.6 Interventions

A completed description of each study's intervention is contained in the Characteristics of included studies tables (Appendix W). A summary of their characteristics is given below.

EPOC Taxonomy of interventions

In all of the studies the interventions were classified as 'organisational' according to EPOC definitions; none of the included studies were classified as professional, financial or regulatory.

Organisational

- Provider orientated
  - Eighteen studies were complex, multifaceted interventions within the EPOC 'organisational' sub classification of 'provider orientated interventions'.(91,144,300,313–323,325,326,328,329) Studies were a mix of 'continuity of care', 'skills mix changes', 'revision of professional roles', 'clinical multidisciplinary teams', 'formal integration of services' and 'communication of case discussions between distant health professionals'.
  - Structural
Two studies were classified as 'structural' interventions. One of these studies, sub-classified as 'changes in physical structure, facilities and equipment', examined the availability of an electronic reconciliation tool built into the electronic medical record of a network of primary care practices within an integrated healthcare system.\(^{(327)}\) The tool reconciled discharge prescriptions with preadmission medication lists.

One study, sub-classified as 'changes in medical records system', examined the inclusion of a 'medication discharge plan' ("a completed report of a patient's pharmacotherapy...specifying the status of each medication used before hospitalisation" e.g. continued, discontinued) at the time of discharge.\(^{(324)}\)

**Provider(s) of intervention**

In eighteen studies the intervention was delivered primarily by clinical pharmacists \((144,300,313,314,316,318-323,325,328,329)\), also variously labelled as transitional care pharmacists \((320)\), pharmacist transition coordinators \((91)\), seamless care pharmacists \((326)\), community liaison pharmacists \((315)\), and pharmacist case managers.\(^{(317)}\) Distinguishing between the varying use of these labels was not clear. One study's intervention was primarily the provision of a 'medication discharge plan' but this again was verified by the hospital clinical pharmacy service.\(^{(324)}\) The final study was provided through an ICT reconciliation tool linking secondary and primary care.\(^{(327)}\)

Medication reconciliation was commonly provided by pharmacists working closely with other HCPs in a variety of settings. In hospital settings, pharmacists worked as part of a team of HCPs in surgical
pre-admission assessment clinics (PAC) (300,318,319), at admission with medical officers (328), during hospital stay and discharge with consultant physicians, medical officers and nurses.(316,322,324,329) At transfer to long term care facilities, multidisciplinary case conferences combined with staff education was provided by pharmacists.(91)

Timing of Intervention and Transition of care

Hospital (Setting)

- Preadmission:
  - Three studies targeted their intervention in surgical pre-admission assessment clinics.(300,318,319)

- Admission:
  - Four studies primarily at admission.(313,314,325,328)

- During hospitalisation
  - Four studies provided interventions that spanned participants’ entire hospital stay from admission to discharge.(315,317,323,324)

- Discharge
  - Five studies focused interventions primarily on discharge.(144,316,322,326,329)

- Post discharge:
  - Three studies involved interventions targeted at participants as they were discharged from hospital to a long term care facility (91), or primary care offices.(320,327)

- Hospital outpatient clinic setting.(321)

Format of reconciliation intervention

Information gathering
All study interventions included an attempt to construct a 'best possible medication list' or 'gold standard medication list'. This was constructed with various levels of intensity with almost all including patient interview and some variation of: review of previous prescriptions, patient's own drug (PoD) review, carer/family member interview, General Practitioner (GP) referral letters, contacting GP or community pharmacist, and reviewing medication changes during hospitalisation. Some intervention protocols specifically mentioned recording over the counter (OTC), herbal medications, supplements, as needed and non-prescribed medications in addition to regular prescribed medications. (313)

In seventeen of the studies the intervention was conducted face to face, in two studies (321,324) it was not clear and in one study the intervention was ICT mediated. (327)

Post transition communication
Nine studies specifically included a provision within the intervention to communicate the output of reconciliation to receiving HCPs. (91,144,315–317,324,326,327,329) Four studies included a follow-up telephone call to participants post transition to clarify medication regimes, assess adherence etc. (144,317,322,323)

Resources
Six studies provided personalised medication information sheets to patients (315,317,318,320,323,324), with one study developing low literacy aids specific to its population. (323) One required the development and integration of an electronic reconciliation tool into an existing functioning linked electronic medical record (327), while another used an electronic link with community pharmacists to gather pre-admission medication information. (328) In addition to
the four interventions which performed follow-up telephone calls
one study established a medication help line for post-transition
patients.\textsuperscript{(315)}

Additional interventions beyond medication reconciliation

- \textit{Medication review}
Six studies included an additional element in the intervention that
could be described as 'medication review'.\textsuperscript{(91,144,315,316,322,326)} This was described as
"assessment and management of the patients own drugs brought
into hospital and rationalization of these against discharge
medication" \textsuperscript{(315)}, "evidence based medication review...providing
information on medication use and appropriateness" \textsuperscript{(91)};
checking of discharge prescriptions for "prescription errors", which
had a broad definition of "dosing errors, dosage form errors,
contra-indications, drug–drug interactions and double-medication"
\textsuperscript{(316)}; screening of prescriptions for "previous Drug Related
Problems (DRPs), including non-adherence, lack of efficacy, and
side effects" \textsuperscript{(144,322)}; "comprehensive pharmaceutical care work
up" \textsuperscript{(326)} and "reviewed the indications, directions for use, and
potential adverse effects of each discharge medication".\textsuperscript{(144)}

- \textit{Participant counselling}
Participant education was provided as part of the medication
reconciliation intervention in nine of the 17 studies in which the
intervention was conducted face to face, these participants were
given 'directive guidance' and in one case low literacy adherence
aids \textsuperscript{(323)} to encourage adherence to their prescribed medication
regimes.\textsuperscript{(144,315–317,320,322–324,326)} Directive guidance
describes pharmaceutical care activities such as provision of
information about medications, their administration and their adverse effects.\(^{(330)}\)

- **Prescriber education**
  
  Education was provided to prescribers and other HCPs included in the multidisciplinary team as part of the intervention in only one of the studies (\(^{(91)}\)); this occurred at a case conference following transfer of patients to a long term care facility.

- **Prescribing**
  
  In two of the 20 studies an additional role as a prescriber was taken on by the intervention pharmacist. In one study prescribing was limited to "continuing or withholding regular medications and prescribing VTE prophylaxis according to local and national guidelines, following a risk and contraindication assessment" in a PAC clinic.\(^{(319)}\) In the second study one intervention arm contained a pharmacist functioning as a "supplementary prescriber" who prescribed the regular medications for participants who were admitted electively for surgery. Protocols for prescribing "were developed before the study in consultation with surgeons and anaesthetists and approved by the hospital’s drug and therapeutics committee".\(^{(325)}\)

6.4.7 **Comparison group**

Eighteen studies reported the control group's intervention to consist of usual care in the context in which the study took place. This meant there was a large variation in the care provided to different control groups between studies (ranging from physician only conducted reconciliation to pharmacist and ICT involvement). Two studies, in addition to a usual care control group had two intervention arms.\(^{(317,325)}\) The control group interventions are
described in detail in the Characteristics of included studies table (Appendix W).

6.4.8 Outcomes

6.4.8.1 Primary outcome

The primary outcomes of interest in this review were discrepancies in prescription per patient and/or medication (defined as unexplained differences in documented medication regimes across different sites of care). All included studies must have reported this outcome.

No validated measure of the primary outcome was used by any of the included studies. Eight studies clearly reported an outcome of unexplained unintentional discrepancy, where the discrepancy between medication lists could not be accounted for either through reviewing medical records, order forms or discussion with treating physicians. (144,300,317,320,322,327–329) Three studies reported an outcome of discrepancy but did not clearly define or investigate whether that discrepancy was intentional or not. (313,314,316) Three studies reported discrepancies as a mismatch in a direct comparison of two lists e.g. discharge prescription and home medication (315), medication summary sent to a long care facility and actual medication sent (91) and a medication discharge planner and community pharmacy records. (324) One study recorded the outcome as whether reconciliation took place or not. (318) Four studies recorded the outcome in various ways ("Omissions, prescribing and communication errors" (319); "medication discrepancies with potential ADEs" (323); "missed and incorrect dose and frequency of medications" (325); "Drug therapy inconsistency and omission"
and one study did not report how the outcome was defined.(321)

Seven study authors were successfully contacted for additional study data or for a re-analysis of published data.(317–319,323–325,328)

Outcome assessment was done by the study pharmacist (300,314,316,317,320,326,328,329) or other members of the research team (144,313,315,318,319,322,323,325,327) and in three studies it was unclear who had performed the outcome assessment.(91,321,324) Blinding of outcome assessors was specifically mentioned in only six studies.(144,313,317,319,322,323)

Eighteen studies reported a dichotomous outcome of at least one discrepancy per patient.(91,144,300,313,314,316,318–329) Two studies reported a dichotomous outcome of any discrepancy per medication.(316,319) Three studies reported discrepancies per patient as a continuous outcome (313,317,323) and one study reported discrepancies per medication as a continuous outcome (324). In those studies reporting discrepancies as a continuous outcome, all studies reported means and standard deviation. However, only two studies reported median figures per group (313,323), these additional data are useful in highlighting the baseline prevalence of discrepancy in intervention and control arms e.g. 57.2% and 61% had no discrepancies in control and intervention group respectively, with reported means of 0.94 and 0.76 and median of 0 and 0 per patient in the control and intervention group respectively.(323) This highlights the limitations in interpreting the continuous outcome of discrepancies without
being aware of the distribution of the baseline prevalence – in this case the majority of patients in the study had no discrepancies.

6.4.8.2 Effect of the intervention on the primary outcome

- At least one medication discrepancy per patient:
  - Eighteen of the 20 included studies had sufficient data to pool results for the dichotomous outcome of 'at least one medication discrepancy' per patient. A total of 4285 patients (2369 intervention and 2456 control) of the 6007 patients included in this review were included in this comparison. The analysis found in favour of the intervention - those receiving the intervention had 0.58 times the risk of any discrepancy compared to the control group (RR 0.58, 95%CI [0.46, 0.73]; participants = 4825; studies = 18) (Figure 6-2). Marked heterogeneity was noted between studies ($I^2 = 92\%$, $P$ value <0.00001). This heterogeneity is explored further in the "Other potential sources of bias" section via meta-regression of potentially important variation in pre-defined study characteristics.

- Number of discrepancies per patient:
  - Discrepancies per patient was reported as a continuous outcome by three of the twenty studies.(313,317,323) There was no evidence found either for or against reconciliation (MD -0.68, 95%CI [-1.79, 0.43]; participants = 1685; studies = 3); with a high degree of statistical heterogeneity ($I^2 = 86\%$).

- Discrepancies per medication:
This outcome was reported as both a dichotomous and a continuous measure. Two of the 20 studies reported this outcome as a dichotomous measure and showed no difference between groups in discrepancies per medication (RR 0.13, 95% [CI 0.01, 1.29]; participants = 3595; studies = 2). There was a high degree of statistical heterogeneity in the pooled odds ratio of these studies ($I^2 = 98\%$). Only one study reported discrepancies per medication continuously with no difference in effect seen between groups (MD -2.10, 95%CI [-9.64, 5.44]; participants = 82; studies = 1). One study did not report the outcome of discrepancies in a directly comparable way. The study authors when contacted were unable to provide the original data. The study reported the mismatch between discharge prescriptions and home medication upon discharge in 171 participants based on three criteria - drug name ($p<0.005$), dose ($p<0.07$) and frequency ($p<0.004$). No further details, including number of participants per groups etc. were available.
### Figure 6-2 Forest Plot of Primary outcome – At least one medication discrepancy (dichotomous) at any time point/setting

CI: Confidence Interval; IV: Inverse variance method; df: degrees of freedom

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Reconciliation Events Total</th>
<th>Control Events Total</th>
<th>Risk Ratio IV, Random, 95% CI</th>
<th>Risk Ratio IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.1.1 Reconciliation at any time point</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Becerra-Carnargo 2013</td>
<td>71</td>
<td>117</td>
<td>117</td>
<td>125</td>
</tr>
<tr>
<td>Beckett 2012</td>
<td>12</td>
<td>41</td>
<td>21</td>
<td>40</td>
</tr>
<tr>
<td>Crotty 2004</td>
<td>35</td>
<td>55</td>
<td>26</td>
<td>54</td>
</tr>
<tr>
<td>Eggink 2010</td>
<td>16</td>
<td>41</td>
<td>30</td>
<td>44</td>
</tr>
<tr>
<td>George 2011</td>
<td>15</td>
<td>62</td>
<td>17</td>
<td>172</td>
</tr>
<tr>
<td>Hale 2013</td>
<td>13</td>
<td>194</td>
<td>136</td>
<td>190</td>
</tr>
<tr>
<td>Hawes 2014</td>
<td>6</td>
<td>12</td>
<td>19</td>
<td>21</td>
</tr>
<tr>
<td>Heng 2013</td>
<td>3</td>
<td>20</td>
<td>12</td>
<td>20</td>
</tr>
<tr>
<td>Ibrahim 2012</td>
<td>81</td>
<td>125</td>
<td>84</td>
<td>125</td>
</tr>
<tr>
<td>Kripalani 2012</td>
<td>165</td>
<td>423</td>
<td>183</td>
<td>428</td>
</tr>
<tr>
<td>Kwan 2007</td>
<td>41</td>
<td>202</td>
<td>86</td>
<td>214</td>
</tr>
<tr>
<td>Lalonde 2008</td>
<td>27</td>
<td>41</td>
<td>28</td>
<td>41</td>
</tr>
<tr>
<td>Marchi 2011</td>
<td>22</td>
<td>239</td>
<td>41</td>
<td>118</td>
</tr>
<tr>
<td>Nickerson 2005</td>
<td>1</td>
<td>28</td>
<td>67</td>
<td>119</td>
</tr>
<tr>
<td>Schnipper 2008</td>
<td>44</td>
<td>72</td>
<td>43</td>
<td>66</td>
</tr>
<tr>
<td>Schnipper 2011</td>
<td>293</td>
<td>380</td>
<td>296</td>
<td>379</td>
</tr>
<tr>
<td>Tompason 2012</td>
<td>56</td>
<td>203</td>
<td>234</td>
<td>284</td>
</tr>
<tr>
<td>Yau 2006</td>
<td>3</td>
<td>13</td>
<td>10</td>
<td>15</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td><strong>2369</strong></td>
<td><strong>2456</strong></td>
<td><strong>100.0%</strong></td>
<td><strong>0.58 [0.46, 0.73]</strong></td>
</tr>
</tbody>
</table>

Total events: 304
1450

Heterogeneity: $\phi^2 = 0.16; \chi^2 = 218.94, df = 17 (P < 0.00001); \phi = 92%$

Test for overall effect: $Z = 4.63 (P < 0.00001)$
6.4.8.3 **Secondary outcomes**

The following secondary outcomes were reported by the studies listed.

**Patient related and process outcomes:**

- Medication discrepancy with the potential for adverse drug events (pADEs):
  - Only one study reported potential ADEs; defining potential ADEs as due to discrepancies or non-adherence. It reported an adjusted incidence rate ratio between groups of 0.79 (95%CI [0.61, 1.01]).
  - Three studies described an outcome of preventable or ameliorable ADEs calculated using the Bates methodology to retrospectively identify medication related ADEs. There was no evidence of an overall effect on preventable ADEs with a high degree of heterogeneity (RR 0.37, 95%CI [0.09, 1.57]; participants = 1253; studies = 3, $I^2 = 84\%$) (Figure 6-3). Note that Kripalani's methodology lists secondary outcomes of preventable and potential ADEs but reports ADEs and potential ADEs.

- Adverse drug events:
  - Four studies reported ADEs as an outcome with no evidence of an overall effect of the intervention (RR 1.09, 95%CI [0.91, 1.30]; participants = 1363; studies = 4) (Figure 6-4). There was no statistical heterogeneity reported between the studies ($I^2 = 0\%$).

- Mortality:
  - Not reported in any of the studies
A classification of the clinical significance/severity of discrepancies/ADEs and/or the necessity of clinical pharmacist intervention was undertaken by 11 studies.\(^{300,313,315–319,323,324,326,329}\) The classification systems used were varied (as well as independently devised criteria) and did not allow for pooling of results.\(^{76,331,332}\)

Medication Appropriateness Index (MAI) was reported by one study \(^{91}\), showing a significant difference between groups in favour of the intervention (mean MAI 2.5, 95%CI [1.4, 3.7] vs the control group (mean MAI 6.5, [3.9, 9.1]) \(^{76}\) \(P=0.007\)). Medication adherence was reported by 3 studies.\(^{144,316,322}\) The Brief Medication Questionnaire - Regime Screen (BMQ) was used by one of the studies, with no difference found between groups (RR: 1.07, 95%CI [0.47, 2.44]).\(^{316}\) Two studies directly asked participants about adherence to medication, reporting a dichotomous outcome of those who were not adherent to at least one medication (RR 0.76, 95%CI [0.41, 1.42]; participants = 379; studies = 2).\(^{144,322}\) However, Schnipper 2006 was only able to report this outcome on \(~70\)% of all participants originally randomised.

**Health care utilisation:**

Eight studies reported an outcome fitting the description of healthcare utilisation. These were often listed as secondary or composite outcomes and the trial(s) was not powered to detect a significant difference between groups.

- Primary care visits:
  - "Scheduled/unscheduled office visits" stated as an outcome measure in one study but not actually reported.\(^{144}\)
Emergency department visits:
- Crotty 2004; Hawes 2014; Kripalani 2012; Schnipper 2006; Ibrahim 2012.(91,144,320,322,323)
  - Only one study reported actual individual visit rates, finding reduced rates in the intervention group (RR 0.07, 95%CI [0.00, 1.07]; participants = 61; studies = 1).(320)

Unplanned re-hospitalisation:
- Bolas 2004; Crotty 2004; Hawes 2014; Kripalani 2012; Schnipper 2006; Tompson 2012; Ibrahim 2012.(91,144,315,320,322,323,328)
  - Two studies reported a positive effect on unplanned re-hospitalisation of study participants (RR 0.11, 95%CI [0.02, 0.58]; participants = 548; studies = 2).(320,328)
  - One other study reported a non-significant difference in hospitalisation at three months between groups (p >0.05) but did not report the actual number of participants in each group nor the confidence interval.(315)

Composite measure:
- Four studies reported a combined measure (hospitalisation and emergency department attendance) of healthcare utilisation with no consistent evidence of an effect (RR 0.78, 95%CI [0.50, 1.22]; participants = 597; studies = 4) (Figure 6-5).(91,144,320,322) There was some evidence of heterogeneity between these studies (I² = 48%).

Length of stay:
- Bolas 2004; George 2011; Tompson 2012.(315,318,328)
  - Three studies reported a non-significant difference in length of stay between groups, p=0.77, p=0.75, p=0.7 respectively, but did not provide any further information to allow data to be pooled.(315,318,328)
Figure 6-3 Preventable Adverse Drug Events
CI: Confidence Interval; IV: Inverse variance method; df: degrees of freedom
### Figure 6-4

Adverse Drug Events CI: Confidence Interval; IV: Inverse variance method; df: degrees of freedom

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Reconciliation</th>
<th>Control</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Weight</td>
</tr>
<tr>
<td>Crofty 2004</td>
<td>9</td>
<td>56</td>
<td>6</td>
</tr>
<tr>
<td>Ibrahim 2012</td>
<td>25</td>
<td>125</td>
<td>23</td>
</tr>
<tr>
<td>Ktpalani 2012</td>
<td>133</td>
<td>423</td>
<td>125</td>
</tr>
<tr>
<td>Schnipper 2006</td>
<td>14</td>
<td>79</td>
<td>12</td>
</tr>
</tbody>
</table>

**Total (95% CI)**

<table>
<thead>
<tr>
<th>Events</th>
<th>Total</th>
<th>Weight</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>683</td>
<td>680</td>
<td>100.0%</td>
<td>1.09 [0.91, 1.30]</td>
</tr>
</tbody>
</table>

**Total events:**

- Reconciliation: 131
- Control: 156

**Heterogeneity:**

- Tau² = 0.30; Ch² = 0.35; df = 3 (P = 0.96); I² = 0%
- Test for overall effect: Z = 0.93 (P = 0.35)
Figure 6-5 Hospitalisation (Composite measure of re-hospitalisation and Emergency Department visits)

CI: Confidence Interval; IV: Inverse variance method; df: degrees of freedom

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Reconciliation</th>
<th>Control</th>
<th>Risk Ratio</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Events</td>
<td>Total</td>
</tr>
<tr>
<td>Hawes 2014</td>
<td>0</td>
<td>24</td>
<td>15</td>
<td>37</td>
</tr>
<tr>
<td>Crotty 2004</td>
<td>9</td>
<td>56</td>
<td>15</td>
<td>54</td>
</tr>
<tr>
<td>Ibrahim 2012</td>
<td>30</td>
<td>125</td>
<td>35</td>
<td>125</td>
</tr>
<tr>
<td>Schnipper 2006</td>
<td>28</td>
<td>92</td>
<td>25</td>
<td>84</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>297</strong></td>
<td><strong>300</strong></td>
<td><strong>100.0%</strong></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 67 / 90

Heterogeneity: $\hat{\tau}^2 = 0.09$; $\chi^2 = 5.76$, df $= 3$ (P = 0.12); I² = 48%

Test for overall effect: $Z = 1.09$ (P = 0.27)
6.4.8.4 **Unintended consequences**

The adverse effects of interventions were not reported by any of the studies.

6.4.8.5 **Resource use/Economic cost**

Only one study reported on resource requirements as one of their outcomes. The study reported the median time spent with patients to deliver the intervention and extrapolated possible Full Time Equivalent (FTE) pharmacists required to implement the intervention in their organisation – reporting that two FTEs would be required (or 88 hours per week) to provide medication reconciliation to all admitted patients in the study centre. (314)

6.4.9 **Subgroups**

Consideration was given, a priori, to reporting of specific subgroups that may be of specific interest, in particular for future development and implementation of interventions (i.e. specific transition points). Number of medications, and age differences between groups was explored by meta-regression (Section 6.4.12 for more detail). It was agreed that the proportions of chronic illnesses in studies was less clearly reported and therefore not appropriate to examine further. The intervention in eighteen of the twenty studies was primarily delivered by pharmacists therefore there was little value in sub grouping between different intervention types. Finally, interventions often concentrated on a specific transition point (e.g. hospital admission) therefore studies reporting the primary outcome were further sub grouped into the transition point primarily focused on in their intervention (Figure 6-6). A test for subgroup differences (fixed effects meta-analysis conducted in ReviewManager) was significant (p=0.005) with substantial heterogeneity reported ($I^2=76.6\%$).
- Reconciliation at admission:
  - Four studies, representing 1167 participants, focused on admission with a positive effect on discrepancies (RR 0.43, 95%CI [0.27, 0.68]; participants = 1167; studies = 4).(313,314,325,328)

- Reconciliation at discharge:
  - Five studies, representing 649 participants, focused on discharge with no evidence of an effect on discrepancies (RR 0.71, 95%CI [0.50, 1.02]; participants = 649; studies = 5).(144,316,322,326,329)

- Reconciliation throughout hospital stay:
  - Two studies, representing 933 participants, focused on reconciliation from admission throughout the hospital stay to discharge, with no difference between intervention and control groups (RR 0.92, 95%CI [0.80, 1.07]; participants = 933; studies = 2).(323,324) One further study, despite describing the intervention as being discharge focused, provided reconciliation at admission and discharge but reported a continuous outcome.(317)

- Reconciliation at PreAdmission Clinic (PAC):
  - Three studies, representing 1082 participants, reported the effect of a pharmacist involved in reconciliation in a preadmission clinic; with no difference between groups (RR 0.38, 95%CI [0.13, 1.11]; participants = 1082; studies = 3).(300,318,319)
### Figure 6-6 Reconciliation applied at different transition points (At least one medication discrepancy (dichotomous))

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Reconciliation Events</th>
<th>Control Events</th>
<th>Risk Ratio IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>Total</td>
<td>Weight</td>
</tr>
<tr>
<td><strong>1.1.2 Reconciliation at admission</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recerra-Camargo et al. 2013</td>
<td>71</td>
<td>117</td>
<td>125</td>
</tr>
<tr>
<td>Beckel 2012</td>
<td>12</td>
<td>41</td>
<td>21</td>
</tr>
<tr>
<td>Marolt 2011</td>
<td>22</td>
<td>239</td>
<td>41</td>
</tr>
<tr>
<td>Tompsett 2012</td>
<td>68</td>
<td>263</td>
<td>234</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>688</td>
<td>567</td>
<td>190.0%</td>
</tr>
<tr>
<td></td>
<td>161</td>
<td>413</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Heterogeneity Tau² = 0.16, Chi² = 30.00, df = 3 (P = 0.00001), I² = 69%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Test for overall effect Z = 3.61 (P = 0.0003)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| **1.3 Reconciliation at discharge** |                       |                |                               |
| Egger et al. 2010                  | 18                    | 41             | 44                            | 23.9% | 0.57 [0.37, 0.86] |
| Ibrahim et al. 2012                | 61                    | 126            | 125                           | 33.4% | 0.86 [0.66, 1.13] |
| Nickerson 2006                     | 1                     | 26             | 27                            | 3.2%  | 0.06 [0.01, 0.44] |
| Schneipen 2006                     | 44                    | 72             | 43                            | 26.8% | 0.50 [0.37, 0.73] |
| Yau et al. 2006                    | 3                     | 13             | 10                            | 8.0%  | 0.37 [0.13, 1.07] |
| **Subtotal (95% CI)**              | 279                   | 370            | 100.0%                        | 0.71 [0.50, 1.02] |
|                                    | 145                   | 234            |                               |
|                                    | Heterogeneity Tau² = 0.08, Chi² = 14.74, df = 4 (P = 0.085), I² = 73% |
|                                    | Test for overall effect Z = 1.36 (P = 0.08) |

| **1.4 Reconciliation throughout hospital stay** |                       |                |                               |
| Krippioni et al. 2013              | 165                   | 420            | 438                           | 72.8% | 0.61 [0.78, 1.07] |
| Lalonde 2006                       | 27                    | 41             | 41                            | 22.2% | 0.61 [0.71, 1.31] |
| **Subtotal (95% CI)**              | 464                   | 469            | 100.0%                        | 0.92 [0.80, 1.07] |
|                                    | 162                   | 211            |                               |
|                                    | Heterogeneity Tau² = 0.00, Chi² = 10.00, df = 1 (P = 0.75), I² = 0% |
|                                    | Test for overall effect Z = 1.00 (P = 0.31) |

| **1.5 Reconciliation at PreAdmission Clinic** |                       |                |                               |
| Öberg 2011                          | 15                    | 162            | 172                           | 31.9% | 0.04 [0.46, 1.61] |
| Halla 2013                          | 13                    | 149            | 136                           | 53.2% | 0.12 [0.07, 0.21] |
| Iken et al. 2007                    | 41                    | 202            | 214                           | 35.0% | 0.51 [0.37, 0.68] |
| **Subtotal (95% CI)**               | 513                   | 569            | 100.0%                        | 0.38 [0.13, 1.11] |
|                                    | 69                    | 236            |                               |
|                                    | Heterogeneity Tau² = 0.04, Chi² = 29.28, df = 2 (P = 0.00001), I² = 93% |
|                                    | Test for overall effect Z = 1.76 (P = 0.08) |
6.4.10 Excluded studies

Excluded publications that were read in full are summarised along with the reason for exclusion in the Characteristics of excluded studies table (Appendix Z).

Studies of unsuitable design were excluded from this review (316 citations). Three studies were excluded because the population was not in transition. Thirty-three studies were excluded because the intervention as described did not fit this review's definition of medication reconciliation. One study was excluded because its control group was not deemed to have experienced usual/standard care. Fifty-eight studies were excluded because they did not report this review's primary outcome measure (medication discrepancies).

A further thirty-four citations consisting of news articles, commentary or editorial pieces were excluded because of the absence of appropriate data.

6.4.11 Summary of findings and GRADE

As shown in the summary of findings for the main outcome (at least one discrepancy per patient), the quality of evidence presented in this review, as described by the GRADE approach, was almost universally very low (Table 6-1). Despite inclusion of data exclusively from randomised trial designs in the meta-analyses, the quality of the body of evidence was subsequently downgraded when each of the GRADE considerations (e.g. imprecision, indirectness, study limitations) was taken into account. This severely limits our confidence in the pooled effect estimates. Based on observed heterogeneity in the pooled effect estimate ($I^2 = 92\%$) the findings of the meta-analysis related to improved number of discrepancies should be treated cautiously, as the interventions did not seem
to work consistently across all studies. Potential factors accounting for this heterogeneity were explored further with no obvious pattern emerging (Section 6.5).

Table 6-1 Summary of findings – Primary outcome of any medication discrepancy (all transition points/setting)

**Summary of findings:**

Medication Reconciliation compared to standard care for all patients at any transition of care

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Anticipated absolute effects* (95%CI)</th>
<th>Relative effect (95%CI)</th>
<th>No of participants (studies)</th>
<th>Quality of the evidence (GRADE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>At least one discrepancy per patient assessed with multiple time points and locations reported. (One-time point per study reported here to coincide with end of intervention)</td>
<td>RR 0.58 (0.46 to 0.73)</td>
<td>4825 (18 RCTs)</td>
<td>⬤ ◯◯ ◯</td>
<td>VERY LOW 1,2,3,4,5</td>
</tr>
<tr>
<td>Study population</td>
<td>594 per 1,000</td>
<td>338 per 1,000 (267 to 427)</td>
<td>662 per 1,000</td>
<td>377 per 1,000 (298 to 476)</td>
</tr>
</tbody>
</table>

**GRADE Working Group grades of evidence**

**High quality:** We are very confident that the true effect lies close to that of the estimate of the effect

**Moderate quality:** We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

**Low quality:** Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

**Very low quality:** We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

---

1. Serious limitations in terms of allocation concealment, incomplete baseline outcome data, baseline characteristics, attrition bias, knowledge of allocated intervention and protection against contamination
2. No large variation in effect, confidence intervals do overlap, statistical test for heterogeneity is p>0.05 and I squared is low
3. Significant variation in population and intervention limiting generalisability
4. Optimal Information Size (OIS) requirements not met
5. >50% risk reduction
6.4.12 Risk of bias in included studies

Details of the risk of bias are presented in Figure 6-7, Figure 6-8 and in the Characteristics of included studies tables (Appendix W). No major differences were noted in the risk of bias of studies included in the review.
Figure 6-7 Risk of Bias graph of included studies
Figure 6-8 Risk of Bias summary of included studies
6.4.12.1 **Allocation concealment (selection bias)**

*Key Domain*
Seventeen trials reported adequate sequence generation (91,144,300,313,315–326,328), and 11 reported concealment of allocation.(91,144,300,318,319,322–327)

6.4.12.2 **Blinding (performance bias and detection bias)**

In nine studies, the risk of performance and detection bias was deemed low as either blinded measurement of outcomes had taken place to ensure that primary outcome assessors had no knowledge of the intervention received by participants or the outcomes were deemed to be objective.(144,313,314,316,317,319,322,323,325)

6.4.12.3 **Incomplete outcome data (attrition bias)**

*Key Domain*
Incomplete outcome data were adequately addressed in 11 studies. In one study 35 participants were consented but only 29 were included in the analysis, six patients were removed with no explanation.(329) Another study (144) randomised 92 and 84 participants to intervention and control group respectively. Due to loss to follow-up only 79 and 73 were included in their primary analysis. No imputation of missing data were undertaken when reporting the results.

6.4.12.4 **Selective reporting (reporting bias)**

One study, as a sub-study of a larger trial, did not report identified outcomes of the larger trial.(317)
6.4.12.5 Other potential sources of bias

Two studies had no information beyond a conference abstract so there was little methodological detail to assess (321,327), with one study author providing an unpublished manuscript for additional detail (329). Five studies had possible selection bias issues by not including certain wards or pre-specifying a large number of conditions/requirements for exclusion.(300,324,326,328) In two studies patients were only recruited when the intervention pharmacist was scheduled to work in the clinic or between certain hours.(318,326) Furthermore, the inclusion criteria were changed significantly in the second year of recruitment for one study.(320)

Contamination bias (when members of the control group are inadvertently exposed to the intervention) was an important limitation in many of the included studies in this review. Fifteen studies were judged to be at high risk of contamination, with a further two where it was unclear whether protection against contamination had been provided.

Publication bias

A funnel plot of the post intervention estimates of the primary outcome for eighteen studies was constructed. Visual inspection of the plot showed a mildly asymmetrical plot suggesting the possible presence of bias (e.g. potentially smaller studies of lower methodological quality producing an exaggerated intervention effect estimates) (Figure 6-9). However, considering the dichotomous nature of the outcome, this was further tested using the Harbord's modified test for small-study effects (p=0.559) as well as the Peter's test (p=0.639); neither of which showed evidence of a publication bias (Figure 6-10).
Figure 6-9 Funnel Plot of small study effects (e.g. Publication bias)

Figure 6-10 Harbord’s test for small study effects
6.5 Unit of analysis error, sensitivity analysis and metaregression

Unit of analysis error

One study, a cluster RCT, did not appear to take account of clustering at the practice level. Adjustment of the reported incident rate and subsequent effect size was undertaken to allow for this. Firstly, an appropriate ICC was chosen. Values of ICC can range from 0 to 1 in human studies. In the theoretical case where $\rho = 1$, all responses within a cluster are identical. In that case the effective sample size is reduced to the number of clusters. A very small value for ICC implies that the within-cluster variance is much greater than the between-cluster variance, and an ICC of 0 shows that there is no correlation of responses within a cluster. Usually, values of ICC are between 0.01 and 0.02 in human studies.

A range of ICCs have been reported in a number of studies. However, it is difficult to obtain an appropriate ICC value for this study from the published ICC estimates. Kul et al., looked at binary outcome measures in hospital and found they ranged between 0.001 and 0.203. In this study, taking a conservative value, we used an ICC of 0.02 and in the sensitivity analysis used values of 0.06 and 0.2 (A range of values were tested - not shown here). None of the range of possible ICC values influenced the pooled point estimate and confidence intervals in considering the primary comparison where the study was included (Appendix V).

Sensitivity analysis

The primary comparison (Figure 6-2) reported a high degree of statistical heterogeneity ($RR = 0.58$, $95\% CI [0.46, 0.73]$; $I^2 = 92\%$). A sensitivity analysis was undertaken to investigate the effect of
those studies with a high risk of bias on the primary comparison. Five studies reported a high summary risk of bias.\(^{(314,322,324,328,329)}\) Upon excluding these studies there was no appreciable difference in the pooled estimate or CI of the primary outcome (RR 0.57, 95%CI [0.43, 0.74]; participants = 3896; studies = 13). There was also no improvement in the reported statistical heterogeneity ($I^2 = 92\%$).

Furthermore, a meta-analysis of the 18 studies included in the primary outcome was undertaken to investigate the influence of any one single study on the overall meta-analysis estimate. This was done via the `metainf` command in Stata statistical software. Inspection of the graphical output showed no undue influence of any one study.\(^{(337)}\)

**Metaregression**

Metaregression was used to formally investigate the potential cause(s) of the observed heterogeneity of the primary outcome analysis (Table 6-2). Caution was exercised undertaking this analysis e.g. more than 10 studies were available for each covariate and the covariates were identified in the protocol as being important clinically. Variables were chosen relating to:

- study population (number of medication, age)
- study quality (summary risk of bias)
- intervention (transition point at which an intervention was applied)

Difficulties encountered included using mean age for studies in which there may have been a large intra-study age range which would not be recognised in comparing means between studies (aggregation bias). Two studies did not report mean number of
medication per participants, however due to the presumed importance of this variable to the primary outcome a mean number of medications was generated based on the studies’ individual eligibility criteria. 18 studies were included in the meta-regression (91,144,300,313,314,316,318–329), with one study (321) not reporting enough information on the number of medications analysis and two studies not included at all due to the lack of a comparable effect estimate.(315,317)

- Number of medications
Mean number of medications was tested in 17 studies as a continuous and categorical (≥5 medications - polypharmacy, ≥10 medications - excessive polypharmacy) variable. Neither continuous (β =0.14, 95%CI [-0.15, 0.44]) nor categorical (Polypharmacy β =1.24, 95%CI [-0.23, 2.72], Excessive polypharmacy β =1.12, 95%CI [-1.11, 3.34]) variables proved to be significant (Figure 6-11).

- Age
Mean age of study participants was tested in 18 studies with no significance found (β=0.03, 95%CI [-0.08, 0.15]) (Figure 6-12).

- Risk of bias
A summary risk of bias measure was tested for 18 studies with no significant result found e.g. low risk of bias compared to unclear risk of bias (β=0.56, 95%CI [-0.94, 2.06]).

- Transition point
Eighteen studies were included in comparing the transition point at which the study intervention was applied (preadmission clinic, admission, throughout hospital stay, discharge and others) with none reporting significant differences.

- Control event rate (Baseline risk)
One potentially important source of heterogeneity among a series of studies is when the underlying average risk of the outcome event varies between the studies. It might be postulated that participants with a higher risk status (e.g. greater medication discrepancies) would be more likely to benefit from an intervention. However, this is difficult to interpret as baseline risk represents a summary of both known and unknown risk factors. Baseline risk was explored via meta-regression of the rate of discrepancies in the control group. Analysis was undertaken as continuous and categorical (low (<0.3), medium (0.3 - 0.75) and high (>0.75)) outcomes. Neither the continuous nor categorical outcomes showed any significant relationship.

Figure 6-11 Metaregression using categorical polypharmacy variable (≥ 5 medications) i.e. ('bubbleplot')
Figure 6-12 Metaregression using continuous variable of age ('bubbleplot')
### Table 6-2 Metaregression output

<table>
<thead>
<tr>
<th>Explanatory Variable</th>
<th>Slope (Coef.)</th>
<th>95% Confidence Interval</th>
<th>Proportion of variation explained</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medication (Number of drugs)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Continuous</td>
<td>0.14</td>
<td>(-0.15, 0.44)</td>
<td>2.27%</td>
<td>No evidence of an effect on the outcome</td>
</tr>
<tr>
<td>Categorical</td>
<td>1.25</td>
<td>(-0.23, 2.72)</td>
<td>14%</td>
<td></td>
</tr>
<tr>
<td>Polypharmacy (≥5 v none)</td>
<td>1.12</td>
<td>(-1.11, 3.34)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Excessive Polypharmacy (≥10 v none)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>0.03</td>
<td>(-0.08, 0.15)</td>
<td>4.98%</td>
<td>No evidence of an effect on the outcome</td>
</tr>
<tr>
<td>Risk of Bias</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medium (v low)</td>
<td>1.17</td>
<td>(-0.27, 2.61)</td>
<td>8.49%</td>
<td>No evidence of an effect on the outcome</td>
</tr>
<tr>
<td>High (v low)</td>
<td>0.61</td>
<td>(-0.97, 2.18)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transition point</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Admission</td>
<td>-1.36</td>
<td>(-3.23, 0.50)</td>
<td>11.89%</td>
<td>No evidence of an effect on the outcome</td>
</tr>
<tr>
<td>Discharge</td>
<td>-0.37</td>
<td>(-2.21, 1.46)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Throughout Hospital Stay</td>
<td>0.59</td>
<td>(-1.66, 2.83)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PreAdmission Clinic</td>
<td>-0.81</td>
<td>(-2.09, 1.18)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline event (continuous)</td>
<td>-0.83</td>
<td>(-2.01, 0.35)</td>
<td>7.20%</td>
<td>No evidence of an effect on the outcome</td>
</tr>
</tbody>
</table>
6.6 Discussion

6.6.1 Summary of main results

The types of interventions included in this review of medication reconciliation were primarily pharmacist delivered – 18 of the 20 included studies (e.g. deploying a pharmacist in a new role, location or with a new skill set). Only one trial involved using an electronic reconciliation tool. The interventions are complex and mostly multifaceted with notable variability between studies in how they were applied locally.

The presence of at least one medication discrepancy per participant, at any transition following reconciliation, was the main outcome used in the included studies to measure the effectiveness of reconciliation. Eighteen of the 20 studies were pooled in a meta-analysis of this dichotomous outcome (Table 6-1). The pooled effect showed almost half the relative risk in the intervention group (RR 0.58, 95%CI [0.46, 0.73]). There was a high degree of heterogeneity in the effect of the interventions on the presence of discrepancies ($I^2 = 92\%$). This was investigated via both meta-regression and sensitivity analysis with no obvious influence of a single study, or study characteristic (number of medications, age, transition point, risk of bias). Furthermore, a probable unit of analysis error in a single study (327) was adjusted for with no appreciable difference in the pooled effect estimate.

Subgroup analysis was undertaken to investigate the effect of reconciliation on specific transitions (Section 6.4.9), with studies were grouped via hospital admission, discharge, throughout the hospital stay and pre-admission clinics. Of the four studies where interventions were applied primarily at hospital admission, they showed a positive pooled effect (RR
0.43, 95%CI [0.27, 0.68]), again with a high degree of heterogeneity ($I^2 = 90\%$). However, the direction of the effect of the individual studies within this subgroup was consistent, the effect and characteristic (transition point) were pre-specified in the studies’ design, the effect size is large, the between subgroup differences is greater than a chance effect ($p=0.005$), and the effect has good biological plausibility. We may have ‘moderate confidence’ in the beneficial effect of medication reconciliation at admission on medication discrepancies, however this should be treated with caution as already stated a metaregression analysis of the differences between interventions at transition point did not show a significant difference (Table 6-2).(338) None of the other transitions showed a consistently positive or negative effect.

The primary outcome of discrepancies was also reported both as a continuous measure per patient and per medication as well as a dichotomous outcome per medication. None of these reported outcomes showed a consistently positive or negative effect of the intervention.

Secondary outcomes of pADEs, ADEs, healthcare utilisation (EDs, re-hospitalisation), and medication adherence showed no consistently positive or negative effect of the intervention. Of note, the potential adverse effects of interventions were not reported in any of the included studies and only one study briefly mentioned the economic cost involved.

6.6.2 Context of this review in comparison with previous reviews

We identified 45 relevant previously published reviews (both narrative and systematic reviews as well as meta-analyses) and reports (Appendix U). The conclusions were similar, that is mixed results were obtained from several intervention types.
tested in heterogeneous studies of limited methodological quality.

Many reviews included non-randomised study designs, a reflection of the commonest method by which reconciliation efforts are studied (e.g. control before and after study, interrupted time series). Most studies included in reviews were conducted in developed countries. Hospital based care was the most commonly studied transition, with primary care (105,114), and long term care (103) less so.

Medication discrepancies are extremely common (3.4% to 98.2% of patients).(117) However, there is limited evidence of the potential for harm from these discrepancies.(24) Most studies have found an improvement in process measures (127), but disagreed on the impact of interventions on ADEs, hospital re-admissions and medication adherence.(24,107,110,111) There was significant study population, intervention and outcome heterogeneity. In addition, most studies were underpowered to examine clinical outcomes. No review carried out formal cost benefit analysis of interventions, this is an underexplored area with limited publications generally.(139) Meta-analysis was often not undertaken due to the dissimilarity of studies. Pharmacist conducted reconciliation (e.g. transition pharmacist coordinator) was the most commonly studied intervention, with ICT interventions less commonly tested.(23) Measures that worked included pharmacist involvement, patient education, counselling, improved HCP communication and targeting high risk populations.

Reviews call for further research on high risk populations, multi-centre designs and adequate sample size to evaluate clinical outcomes.
6.6.3 Overall completeness, applicability and quality of the evidence

The considerable local variability of the interventions studied in this review limits the generalisability of effects to settings beyond the original study environments.

Although a promising result was obtained suggesting that the interventions described in this review were successful in improving the presence of discrepancies per participant, the clinical impact of this is not known. The various endpoints of medication discrepancies and pADEs considered in this review are surrogate markers. Only five of the included studies reported healthcare utilisation, with the outcome variously reported. Of note, other non-included studies have focused on this outcome but this review limited included studies to those reporting the outcome of discrepancies. Future studies should focus on designing studies adequately powered to investigate clinical outcomes such ADEs, emergency department visits and hospital (re)admissions.

Finally, many of studies were affected by incomplete outcome data with nine studies classed as high or unclear risk of attrition bias. This impacts on the quality of the evidence as reported in the GRADE process of the summary of findings table (Table 6-1).

Of 481 studies originally identified for full text review, many were excluded due to poor design, an intervention inconsistent with the review protocol and/or the choice of outcome measures used. The studies included in this review were limited by their small sample sizes and poor quality.
Different definitions, data collection procedures, and follow-up duration make comparison to other studies difficult. The variation in heterogeneity between studies included in this review, should be treated cautiously as the interventions did not seem to work consistently across all studies. Factors contributing to this heterogeneity included variation in types, intensity and duration of interventions, or differences in timing of follow-up measurements. This is perhaps because of differences in how the interventions were provided, background practice and culture and variable processes in delivery of care.

Furthermore, the variation in study-specific factors such as the individual quality of studies. The method sections of the studies provided little detail about how complex interventions were developed, the design of the trials and how staff were trained in the delivery of the intervention.

Finally, the quality of the evidence across all outcomes and the subsequent recommendations that may be drawn from the results is also unclear due the very low rating according to the GRADE approach (Section 6.4.11).

6.6.4 Strengths and limitations

There was evidence of potential bias in some studies, for example only 11 studies reported adequate concealment of allocation and only three reported appropriate protection from contamination, both of which may have influenced the effect estimate in these studies and therefore the overall pooled estimate.

A limited number of the possible studies testing reconciliation as an intervention were included in this review as many of them
did not report the primary outcome of this review - medication discrepancies. This limits the relevance of this review in commenting on the effects of reconciliation on long term patient focused outcomes e.g. ADEs, re hospitalisation. However, in considering the causal pathway of ADEs arising from transitions of care it was deemed that the process measure of medication discrepancies was the most likely starting point and therefore most worthwhile studying. Nevertheless, in considering clinicians, patients and health care funders and the relative importance of clinically relevant outcomes, the focus of this review on a process measure limits its impact and credibility.

No language restrictions were placed on the search strategy, but all of the included trials were published in English. Note however that the study intervention sites were confined to economically developed countries. Funnel plots and formal tests of publication bias showed no apparent cause for concern. Finally, two review authors independently screened titles and abstracts, assessed studies for eligibility, evaluated risk of bias and extracted data.

6.6.5 Future clinical, research and healthcare policy implications

Overall, the quality of the studies in this review was poor and further research should attend to the rigour of study design. The term "medication discrepancies" has no uniform definition, making objective comparison between studies difficult. Further work is required to develop a consensus in identifying, defining, measuring and reporting discrepancies. Future studies should utilise clear definitions of discrepancies as well as objective measurement techniques and appropriate choice of time points attendant to the transition point at which the intervention is
applied. Similarly, the method by which "gold standard" medication lists are compiled is not uniform and therefore the subsequent identification of discrepancies is entirely dependent on this process. Standardising both the nomenclature and processes surrounding medication reconciliation is important not only in research but in clinical practice also.

To ensure the accurate replication of successful study interventions there should be careful documentation of the development of interventions and the training and background of the providers. Documentation of intervention processes utilised would enable identification of the critical elements for successful interventions. Many of the studies included in this review lacked sufficient detail in how these processes were conducted.

The lack of economic analysis of the interventions included in this review is also important. Policy makers require cost benefit analysis information in deciding to fund interventions - future studies should include this as an outcome or process evaluation.

The prioritisation of patient level outcomes (e.g. hospitalisations, ADEs) is also an important consideration. The link between discrepancies and subsequent increased healthcare utilisation, while plausible, is not clear. Therefore, planning studies of sufficient power to test these hypotheses is important as well as attending to the noted biases of this review's included studies - e.g. concealment of allocation, protection from contamination etc. These issues present particular challenges to health service researchers who are often embedded within healthcare organisation and involved in ongoing service provision. Disentangling the effect of the intervention deliverer, the need for objective measurement, the
compromise of service improvement interventions (generally observational or quasi experimental in design) and the rigour of randomised study design is complex.

The heterogeneity of the healthcare systems of the studies included in this review is such that findings from one study are not immediately generalisable to all settings. Therefore, the translation of successful complex interventions will likely require retesting in new populations.

The adoption of interventions, successful or otherwise, including the specific processes and critical elements of success needs investigation that may not be possible through quantitative processes. Use of qualitative methodology may uncover reasons why interventions were not acceptable (e.g. timing of intervention not sensitive to local processes) or indeed the importance placed in reconciliation by study HCPs. The challenges of implementing reconciliation, specifically in an Irish context, will be explored through this methodology in the next chapter using an implementation science theoretical framework.

6.7 Conclusion

The interventions implemented in the studies in this review reduced the likelihood of any medication discrepancy by almost half in patients at transitions of care – however the quality of the evidence was judged to be very low and no recommendation either in favour or against the intervention could be made. The majority of studies implemented reconciliation via pharmacist mediated efforts. Only two studies showed a reduction in unplanned re hospitalisation, again with only moderate certainty of the evidence. We are also uncertain about the effect of the included studies on any other patient focused outcome (e.g. Emergency Department visits, ADEs) as
the certainty of the evidence was assessed as very low. Considering specific transitions - interventions delivered at admission to hospital appeared to be consistently beneficial, again with no certainty of the reported effect due to the low quality of evidence. Surprisingly, increasing number of drugs and age had no impact on the effect of the intervention. However, there was significant clinical and statistical heterogeneity in the included studies limiting the impact of the findings. This dearth of high quality evidence (in particular due to the risk of bias) and subsequent inability to draw conclusions needs to be addressed in improved design of future experimental research of reconciliation interventions. Future research should concentrate on both improved intervention and outcome definition and reporting.
The opinions of healthcare professionals of the barriers and facilitators to effective medication reconciliation at transitions of care in Ireland
7.1 Introduction

This chapter presents a qualitative study on the opinions of healthcare professionals of the barriers and facilitators of medication reconciliation in Ireland.

The systematic review (Chapter 5), as well as previous research has identified many different types of medication reconciliation interventions, most commonly pharmacist delivered interventions.(22,24) However, as discussed in the previous chapter generalising interventions beyond their original setting may prove difficult due to the need to adapt to local specific issues.

A number of previous studies have examined the experience of healthcare professionals (HCPs) - including physicians, nurses, pharmacists - and hospital administrators in managing medications at transitions of care as well as describing the barriers and facilitators to effective implementation of medication reconciliation.(150–153,155,157,339) These studies used a variety of data collection techniques and analytical models to describe behaviour. There were many similarities in the findings regarding the barriers identified in these studies including competing clinical tasks, unreliable patient provided information, time pressures, lack of available clinical rationale, ICT issues, inconsistent/poor communication between secondary and primary care and role confusion in reconciliation responsibility.

While regulatory organisations may require reconciliation, they are not specific in the steps required to undertake this. This failure to translate research findings into practically useful outcomes, ambiguity in intervention requirements or an unpreparedness for local circumstances suggests the need to
explore current practice and implementation of medication reconciliation specific to Ireland. (165,340)

7.2 Aims and objectives

The aim of this study was to gather information from healthcare professionals on the barriers and drivers to the implementation of medication reconciliation both between and within primary and secondary care in Ireland. The objective was to investigate factors which influence the implementation process of reconciliation according to the individual perceptions of the persons involved and align these factors with an existing implementation science theory to support more successful reconciliation efforts. We conducted face-to-face interviews with a wide range of HCPs involved with medication management at transitions of care.

7.3 Methods

7.3.1 Qualitative approach

A qualitative study was undertaken, data were collected via face-to-face semi-structured interviews and participants’ responses were coded to an existing theoretical framework. The method of interpreting the data was through deductive thematic analysis. (199) Standardised reporting frameworks for qualitative, and in particular interview-based studies, i.e. consolidated criteria for reporting qualitative research (COREQ), were used. (341,342)

7.3.2 Theoretical framework

Many differing examples of implementation theories for healthcare interventions have previously been published. Greenhalgh et al., conducted an extensive review of the literature summarising the findings of almost 500 sources in their ‘Conceptual model for considering the determinants of diffusion, dissemination, and implementation of innovations in
health service delivery and organisation’ (Figure 7-1). (164) The theories attempt to describe the complex and multiple influences on the success or failure in adopting a new process. These influences are summarised graphically to include – the innovation itself (e.g. its complexity), the reaction and receptivity of actors within the system, organisational or system adoption of the innovation (e.g. receptiveness to change), networks of dissemination, and extra organisational issues (e.g. socio-political). A number of subsequent efforts to develop theories have drawn from this summary of the literature. (165, 189) There are a limited number of studies of medication reconciliation that have adopted formal theoretical frameworks to examine reconciliation specifically. (150–152, 156) For the purposes of this study a theoretical framework was used that was developed by Sluisveld et al., for the particular purpose of categorising the barriers and drivers to implementation of medication reconciliation. The framework is an adaptation of two existing theories - ‘the implementation model’ of Grol and ‘the framework for improvement’ of Cabana. (150, 340, 343). According to this framework, the implementation of medication reconciliation can be hindered or facilitated by factors related to:

- **Innovation**
  - The advantages/disadvantages of the new intervention – e.g. its feasibility, complexity and/or usefulness.

- **Health care professionals**
  - The motivation to accept change, the attitude and awareness of individuals to the new intervention.

- **Patients**
  - What is the level of knowledge of the patient, their engagement, concordance with the intervention?

- **Social context**
  - Opinion of colleagues, collaboration, leadership and social learning e.g. observational learning

- **Organisation**
Existing care processes and structures, funding issues, and resources.
- **Political, legal, and economic context**
  - Regulations, policies and economic constraints.

This model’s thematic structure is broadly similar to previously derived implementation models and allows easy comparison of our results with its application in previous studies’ settings – both those specific to reconciliation and to healthcare interventions more generally. (150,164,165,340) An interview data collection method, in contrast to participatory/non-participatory observation was chosen as this was the most feasible option considering the diverse clinical environments of interest, HCPs’ availability and the sampling method, ethical and access considerations, and the time constraints of the study. Furthermore, interviews allowed the necessary in-depth exploration of the attitudes and perceptions of HCPs regarding reconciliation.
Figure 7-1 Conceptual model for considering the determinants of diffusion, dissemination, and implementation of innovations in health service delivery and organisation. Greenhalgh et al., (164) See Appendix A for documentation of permission to republish this material.
7.3.3 Context

Healthcare in Ireland, as described in Chapter 2, has a mixed model of funding as well as provision of care. A sizeable minority of patients have their healthcare paid for by the State. The majority of acute hospitals are publicly funded by the Health Service Executive (HSE); this organisation’s service delivery is divided over four geographic regions (HSE Dublin-Mid Leinster, North East, South and West). Hospital specialists (consultants) in many cases practise in private and publicly funded institutions. Community pharmacists (CPs) and general practitioners (GPs) are private contractors who see patients who are publicly funded as well as self-paying. Many different HCPs are involved in coordinating the care of patients both within and between primary and secondary care e.g. hospital based physicians (both specialist and in training – non-consultant hospital doctors - NCHDs), hospital pharmacists (HPs), CPs, and GPs. There is currently no unique health identifier in Ireland. While computerisation is almost 100% in general practice there is little interoperability between primary and secondary care systems. No institution provides completely electronic prescribing and only a minority provides electronic communication for referral and discharge information. It is recommended all healthcare organisations undertake a process of medication reconciliation. This is variably applied across the Irish system and medication errors at transitions of care continue to be a common occurrence.(63,205) The complexity of this system underpinned the choice of a theoretical framework that encompasses an array of influences and the broad sampling strategy adopted as described below.
7.3.4 Sampling strategy

The target population was all doctors and pharmacists directly involved with medication reconciliation between primary and secondary care in Ireland. To ensure maximum variation in participants and their perceived barriers and drivers, the principles of ‘purposive sampling’ was applied.(344,345) In order to achieve a wide exploration of the probable diversity of factors, both in primary and secondary care, influencing implementation, we invited GPs, CPs, HPs, NCHDs and hospital consultants who were involved in the implementation of medication reconciliation in their daily routine. HCPs were invited to participate by letter with an accompanying study information sheet, consent form, and return address envelope. (Appendix DD). Sixty-one invitations were sent to a broad list of HCPs nationally representing the specialties of interest.

There were no exclusions in terms of clinical commitment, location, type or practice etc. The number of interviews conducted depended on reaching saturation - that is when no new barriers or drivers had been identified (346). Thirty-five individuals responded with a completed consent form and 34 HCPs were eventually interviewed. One HCP, despite having initially agreed was uncontactable for the duration of the study.

7.3.5 Researcher profile

The PhD candidate’s profile and reflexivity is described in Section 3.3.2. OA and KM are undergraduate medical students who undertook research placements. They have an early stage experience of clinical environments with no previous contact with any of the study participants. PR, KM and OA conducted the interviews. PR trained and initially supervised KM and OA to later conduct interviews independently. The research team identified the initial participants as per the sampling strategy.
(see below), with some participants known to the research team in advance. Beyond declaring an interest in the area of medication reconciliation, neither personal goals nor future research agendas were discussed with participants by the interview team.

7.3.6 Ethical issues

Ethical approval was received for this project through the Research Ethics Committee (REC) of the Royal College of Surgeons in Ireland (REC 1112 Appendix AA). Return of completed consent forms was taken as consent (Appendix BB and CC). Data management and confidentiality were adherent to the REC policy. Participants were incentivised by registering the time spent participating in the questionnaire as contributing to their individual requirements for Continuing Professional Development (CPD), or including in a CPD cycle (pharmacists).

7.3.7 Data collection methods & instruments

Data were collected between July and December 2015. Interviews, 30 - 60 minutes in length, were conducted using a semi-structured interview guide (Appendix DD), and an audio recorder. Interviews took place in or near the respondents’ own offices/homes or by telephone at the discretion of the interviewee. The interview guide was devised by the research team to ensure validity and conciseness with the questions and prompts being iteratively revised to ensure alignment with the theoretical framework. At the beginning of the interview, the interviewees re-confirmed their willingness to participate (and record interviews) by giving verbal informed consent. The interview questions consisted of both closed-ended and open-ended questions (e.g., “Are adverse drug events a significant cause of morbidity/mortality for your patients?”; “What does medication reconciliation mean to you?”). Probing questions were available to the interviewer and improvised during the
interview to enrich providers’ responses. Three members of the research team conducted the interviews (PR, OA, and KM). All HCPs were interviewed alone. Field notes may have been taken by the interviewer but these were not the basis for analysis. Interviewers were debriefed after each interview to identify additional potential areas of exploration, focus for subsequent interviews and data saturation. Only one author (PR) had access to the file linking transcripts with respondents’ identities.

7.3.8 Data processing

Voice recordings were transcribed verbatim. The transcription was checked against the recording to ensure an accurate transcription was made. All transcriptions were checked to ensure anonymisation and de-identification of any third party inadvertently mentioned. Transcriptions were returned to participants for comments and/or correction. Three participants returned transcripts with corrections – consisting of spelling corrections, abbreviations explained, and/or elaborating on answers. Following this all transcripts were imported into NVivo software for analysis.(216)

7.3.9 Data analysis

One researcher (PR) was primarily responsible for data entry and management with an additional researcher (BC) verifying a random sample of 10% for accuracy and consistency of coding (using a shared NVivo database). A process of line by line deductive coding was undertaken according to the chosen theoretical framework (example given in Figure 7-2). The coded transcripts were entered into NVivo software to facilitate sorting of passages.(216) Research team members compared codes within and across interviews to elucidate themes. Where data represented more than one theme, dual or multiple coding was possible. Where novel themes in the data were uncovered that
could not be placed within the existing framework, new codes were developed to capture this. A coding tree used during analysis is displayed in Figure 7-3. The coded responses were then explored via tree maps. These maps are a set of nested rectangles of varying size and colour, constructed based on the frequency of coded responses at each subtheme heading – this allowed graphical exploration of most commonly coded themes.(347) (Figure 7-4, Figure 7-5)
"I think they're painfully aware. I think they're harassed. I think they have a high level of performance anxiety around this issue. I think most of us know that we're not doing an adequate job and I think there's a high level of demoralisation and frustration around this as it's recognised as an important cause of medicolegal concern and injury to patients".

General Practitioner Respondent 1, Dublin Mid Leinster

Figure 7-2 Example of deductive coding
Figure 7-3 Coding Tree for theoretical model of implementation of medication reconciliation
7.4 Results

7.4.1 Participants

There were 35 participants interviewed. This group included eleven CPs, eight HPs, nine hospital consultants, five GPs, and two NCHDs. There were two or more representatives from each of the HSE’s geographic regions. Interview length ranged from 13 to 38 minutes. See Table 7-1 for the characteristics of the sample.

7.4.2 Thematic analysis

The relative importance of the coded responses was explored by the frequency with which particular themes were coded - this is represented by tree maps in Figure 7-4, and Figure 7-5. Note some subthemes have been omitted due to space restrictions and to more clearly represent those themes coded most and least often.

In coding barriers to medication reconciliation, organisational and HCPs themes were to the fore – issues such as current care processes, ICT infrastructure and the attitude and knowledge of HCPs were coded most commonly.

Regarding the potential drivers to implementing MedRec, the themes most commonly came under the social heading e.g. collaboration, social networks, opinion of colleagues with ICT infrastructure again mentioned.

Illustrative quotes from participants are listed below as examples of barriers and drivers under each of the framework’s six main themes. It was not necessary to create additional main themes. The main points for each theme are summarised in Table 7-2 categorised under barriers and drivers.
### Table 7-1 Characteristics of participants (n=35)

<table>
<thead>
<tr>
<th>Key Characteristics</th>
<th>N (%)*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total Participants</strong></td>
<td>35</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>18 (51)</td>
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<tr>
<td>• Medical</td>
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<td>o Neurology</td>
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<td>o Nephrology</td>
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<td>o General Medicine</td>
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<td>o Cardiology</td>
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<td>o Medicine for the Elderly</td>
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<td>• Emergency Medicine</td>
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<td>• Acute Medical Assessment</td>
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<td>• Anaesthetics</td>
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<td>• Surgery</td>
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<td>o Ear Nose and Throat</td>
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<tr>
<td>Non-prescriber</td>
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* Rounded to the nearest whole number
### Figure 7-4 Barriers to medication reconciliation

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<th>Organisation of care processes</th>
<th>Attitude</th>
<th>ICT Infrastructure</th>
<th>Time</th>
<th>Resources</th>
<th>Political developments</th>
<th>Knowledge</th>
<th>Complexity</th>
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<td>Culture of social network</td>
<td>Awareness</td>
<td>Financial support</td>
<td>Attitude</td>
<td>Feasibility</td>
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### Figure 7-5 Drivers to medication reconciliation

<table>
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<th>ICT Infrastructure</th>
<th>Opinion of colleagues</th>
<th>Policies</th>
<th>Knowledge</th>
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<td>Task Reallocation</td>
<td>Organisation of care</td>
<td>Awareness</td>
<td>Resources</td>
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7.4.2.1 Theme 1 - Innovation

The innovation theme addresses the complexity, feasibility and usefulness of the intervention. Implementing medication reconciliation was described by most contributors as a potentially complex process. The complexity of the reconciliation intervention and the complexity of the healthcare system itself was often overlapping and difficult to disentangle in the interviewees responses. This was highlighted in responses that listed the number of HCPs and sources (e.g. GP, carer, community pharmacy) that need to be consulted to conduct a comprehensive reconciliation of medication:

“It is complex because of the number of people involved. So, you have invariably got the patient and their wider carers and family etc. You’ve got the community pharmacy, you’ve got the GP, you can have other services…say for example, psychiatric services, so it’s not just one source and I mean we have to go to multiple sources” HP Respondent 3, Dublin Mid Leinster

The established communication pathways between HCPs, and their failings were underlined as barriers:

“It’s poor [medication reconciliation], because often there are multiple prescribers involved in the care of a complex co-morbid patient. Often there are substantial delays in effective communication from one prescriber to the next and the information coming back from hospitals is not infrequently late, not infrequently illegible, not infrequently contains inaccuracies and all of that is a challenge” GP Respondent 3, Dublin Mid Leinster.

The drivers in implementing medication reconciliation included tailoring the process to locally available resources:
“I think it’s something that has to have a certain degree of fluidity to it and perhaps has to be a little bit localised in some centres … that’s appropriate to their resources, to their patient cohort and to the different interfaces they have with the community”. Hospital Pharmacist Respondent 5, Dublin Mid Leinster

The particular strengths of certain staff in adapting to new procedures were also recognised:

“One of the key things to ours [local reconciliation initiative] was that it was nurse-led. We put a huge resource into nursing. Because nurses understand processes and they want to be told, 'This is a standard operating procedure.' You tell doctors that, they just think - They haven't a clue what you're talking about'” Hospital Consultant Respondent 4, Dublin Mid Leinster

7.4.2.2 Theme 2 - Healthcare professionals

The Healthcare professional theme encompasses issues of attitudes, motivation to change, knowledge and education. Indeed, staff training, across different disciplines and with the transient nature of some staff (e.g. NCHDs) was recognised as being important but challenging to implement:

“A lot of it, obviously, is education and trying to get education across to layers and layers of people in a healthcare setting. So, you've got nursing staff, medical staff, all who are changing over very frequently” Hospital Consultant Respondent 2, Dublin Mid Leinster

One participant felt supervision for doctors in training was a safety issue:
“The very fact that so many junior hospital doctors are put into a position where they are prescribers and you have to question the level of supervision…Sometimes the consultant isn’t even there so their ability to advice around issues is far less good. So, that’s a huge concern” GP Respondent 3, Dublin Mid Leinster.

Beyond training, the actual culture specific to professionals was also raised as being a barrier to effective teamwork between differing HCPs:

“We have a medical culture at the moment that imbues a certain level of autonomy to doctors …so they don’t want to be told by a pharmacist or a nurse that they’re doing the wrong thing… And nobody feeds back to them because they’re at the top of the profession” Hospital Consultant Respondent 4, Dublin Mid Leinster

HCPs responses were often not limited to reconciliation and broadened out to discussions about patient safety and the medication management more generally. The level of interest and attention given by HCPs to reconciliation and medication management in general was also listed as a reason why it was not implemented:

“The thing that frustrates me is my colleagues’ ambivalence towards medication safety. And it needs to be from the top down. So, if the clinician leading out in an area doesn't think it's important, then their team is going to feel that it's even less important” Hospital Consultant Respondent 1, Dublin Mid Leinster

Despite institutional efforts to highlight medication safety, this did not seem to rank as highly for doctors in training:
“Medication errors are definitely highlighted and adverse events are highlighted and we get monthly emails about adverse events and medication errors so it’s certainly high on the hospital list and it’s certainly something that is flagged to us frequently but medical staff I don’t think care about it that much. It’s kind of not on their priority; it’s something they think somebody else will fix…. For me personally, very low [medication reconciliation as a priority]. I think for a hospital system, it is very high but for me personally it’s very low” NCHD Respondent 2, Dublin Mid Leinster

Medication reconciliation was deemed to be somebody else’s responsibility:

“I think they’re [doctors] all aware it’s important but I think they often see it as somebody else’s problem, particularly in regard to where I work, which is an emergency department” Hospital Consultant Respondent 5, Dublin Mid Leinster

The time pressure felt by HCPs and prioritising of what seemed to be more urgent issues also detracted from reconciliation:

“Well, there’s self-preservation…the problems that you’re immediately faced with are going to be a bigger problem than problems that are theoretically going to occur, which is - making sure that medication reconciliation happens properly. That's more of a preventative method. So, it's never going to be as high a priority…” Hospital Pharmacist Respondent 7, Dublin Mid Leinster

To address these barriers, participants recommended a number of corresponding solutions. For example, empowering doctors in training to acknowledge a deficit in
knowledge/training (or an opportunity for professional development) in prescribing was seen as important:

“A cultural change embodies a whole load of things. So, in other words, you'll know you've succeeded when somebody's entering their Day 1 as an intern and the intern goes, ‘Excuse me, I just feel totally unprepared to address the prescribing issues in this hospital…” Hospital Consultant Respondent 4, Dublin Mid Leinster

Another contributor continued the theme of challenging established practice and to upskill in prescribing:

“But I do think that specifically when it comes to…the avoidance of error in the future and in cultivating a culture of really good prescribing practices, you really should spend your money on people, I think” Hospital Consultant Respondent 3, Dublin Mid Leinster

Other respondents highlighted the responsibility and need for institutional initiatives both to increase the profile of medication reconciliation as a patient safety issue and to garner patient interest also:

“Increased awareness at an organisational level. So, if there was, like, a promotional thing, like, as we had with hand hygiene…You know, it's very heavily advertised everywhere, posters everywhere…. If there was such a campaign for medicines reconciliation, just to make everyone aware - nursing staff, doctors, pharmacists - of the importance of it all, why we're doing it and what each of the steps actually are, that would help…. Because all of that would make it easier to get the list right earlier” Hospital Pharmacist Respondent 2, Dublin Mid Leinster
“The Director of Quality, Safety and Improvement here is a consultant and the fact that medication reconciliation is included in those guidelines means it is seen as more of a high-profile issue within the hospital which you would hope would help direct resources in that direction” Hospital Pharmacist Respondent 1, Dublin Mid Leinster

These final two responses touch on the challenge of behaviour change and what may influence established practices.

7.4.2.3 Theme 3 - Patients

The patients theme related to issues experienced, or with direct input from, patients e.g. polypharmacy, multimorbidity, medication knowledge, attitude and concordance. Many of the contributions in this theme were an interplay between the input of patients and the organisational provisions for patients (e.g. patient own drug schemes, medicines information provision etc.).

Many participants underlined the lack of interest taken by patients in their own medication as being a key issue:

“I think we have to try and get patients to be responsible for their own medications and I know with elderly patients it’s difficult but there’s a lot of people in between that that just don’t take responsibility, just don’t know what their tablets are for” CP Respondent 11, Dublin Mid Leinster

Health literacy relating to medications was also raised as an issue:

“There’s definitely, like, a patient empowerment issue, in that more better-off patients would come in with a very clear list …
While other patients would come in and they would have blister packs and… they wouldn’t have much knowledge beyond that.” Hospital Pharmacist Respondent 7, Dublin Mid Leinster

Some participants attributed the responsibility for this lack of health literacy as something HCPs (and organisational policy) were obliged to address:

“Generally, there is very little done at the hospital level or the doctor level to educate them about what medicines do and what they’re for” CP Respondent 5, Dublin Mid Leinster

This tension between the responsibility expected of patients and the control required by HCPs was further explored in discussing medication errors arising from the ‘Patients’ Own Drugs’ (POD) scheme operating for patients while in hospital. This respondent felt the POD scheme in their hospital led to difficulties for staff in confirming patient medication adherence (giving control to patients), which needed to be balanced against the reality that the patient would be managing their own medication following discharge:

“I think there’s quite a bit of work to be done on understanding the control that the patient needs to be in, in order to function independently when they go home versus the level of control you need to have when the patient is in hospital” Hospital Consultant Respondent 3, Dublin Mid Leinster

Consequently, many participants talked about empowering patients by educating them about their list of medications and the indications for them:

“We’re sending patients out of the hospital … and we’re not saying to them, ‘here’s a personal list of your medication and
you have control over them... if you go anywhere show it to the
doctor and if he makes changes say doctor ‘I’m sorry but can
you write what you’re doing on my little list’. We empower the
patient” Hospital Pharmacist Respondent 6, Dublin Mid Leinster

Targeting those patients more at risk, through morbidity or
multiple medication use, was also deemed to be important.
Specific issues included patients with cognitive decline and the
subsequent challenge of capacity issues in terms of medication
management. Suggested strategies included involving family
members in medication management, and risk stratifying on
admission to hospital, ICT/smart card solutions:

“You’ve got the impaired cognitive function crowd and their
ability to take medication. You’ve got to be vigilant about that…
we encourage them to relinquish control of their own
medication and encourage a named individual within the circle
of care to help them with medication compliance” GP
Respondent 3, Dublin Mid Leinster

“We try to risk-score our patients when they come in based on
the amount of drugs that they take and the types of drugs that
they take. The lower risk ones tend to have a much simpler
MedRec process so the process is as complicated as the
patient.” Hospital Pharmacist Respondent 4, HSE West

“I suppose if patients were given more responsibility across the
board that say they all had to hold a drug card or an app with
all their medications or something electronic, like a swipe card
where medications come up straight away, as regards time and
effort, everything would work so much more efficiently at every
level” GP Respondent 1, Dublin Mid Leinster
7.4.2.4 Theme 4 - Social Context

The social context theme describes issues such as collaboration between colleagues, leadership, the opinion of colleagues and social learning. The many possible combinations of HCPs involved in a patient’s care, and their lack of communication, was raised as a barrier to effective reconciliation:

“Historically I suppose the GP was very much in control of prescribing everything for a patient, whereas now they are being referred to different disciplines you know, they will maybe be seeing a diabetic centre. They will see a neurologist, they will see a pain clinic, they will be going to a vascular clinic” CP Respondent 6, Dublin Mid Leinster

The partitioning of responsibility and lack of a feedback on activities, successful or otherwise, for patients at transition were clearly illustrated by these responses:

“So you find difficulties arise when the patients would transition, say, from here [hospital] back into the community, to a nursing home, to another care facility etc.?“ - Interviewer

“To be honest, I'm largely unaware of what happens [once the patient leaves the hospital]” Hospital Pharmacist Respondent 2, Dublin Mid Leinster

“We have never measured; we’ve never asked community pharmacies and GPs about how they rate our service, which we probably should” Hospital Pharmacist Respondent 7, Dublin Mid Leinster

Multidisciplinary teams were proposed as a better method in hospitals of conducting reconciliation:
“You have such a high turnover of doctors, you’ve just trained them and they’re gone. There’s no point, in my eyes, asking them unsupervised, on their own to be performing that task. They should be working closely with senior pharmacists who are not rotating, who are not going anywhere.” Hospital Pharmacist Respondent 4, HSE West

The difficulty in building effective multidisciplinary teams was discussed. Different training, staff hierarchies or beliefs around healthcare delivery were seen as entrenched, especially between doctors and other HCPs:

“I know the other consultants I work with; they don’t take kindly to anybody telling them what to do…It’s far better for the patient when we work together; it’s actually a far healthier dynamic …you know there’s a huge issue with all of that. There’s a sort of self-righteousness there” Hospital Consultant Respondent 6, HSE South

This led to difficulty especially when trying to integrate pharmacists into medication reviews:

“Pharmacists are not empowered to metaphorically body-check the doctors off a problem. They’re seeing this stuff being written that’s incorrect. And even if they’re picking that up, they’re very politely, you know, informing them, ‘Oh, you see, you’ve written that…” Hospital Consultant Respondent 4, Dublin Mid Leinster

The possibility of task shifting and sharing of responsibility between allied HCPs left some HCPs unclear about where overall responsibility lay:
“People sometimes think that only they can be legally responsible, nobody else could do it. And I think that's probably a little bit arrogant” Hospital Consultant Respondent 5, Dublin Mid Leinster

The lack of multidisciplinary care and effective communication was raised by many contributors:

“There’s no discussion of the medication between the pharmacist and the doctors. We’re not a primary care team here...we never sit down to discuss medication that certain patients are on so communication could be better” CP Respondent 8, HSE North East

“I’m a great believer in meetings between hospitals and GPs working in the community like a meeting of stakeholders getting together. It doesn’t happen, that never happens and that should be the case for all aspects of primary/secondary interface and not just MedRec” GP Respondent 5, Dublin Mid Leinster

Organisational and social context themes overlapped when the lack of communication extended to sharing of medication records, the lack of interoperability and the self-contained nature of HCPs records was a source of frustration for respondents:

“Why do we have silos of information? So, why can't community pharmacy access my team's discharge summary to see what I sent the patient home? So, I spent, and my team, spent a lot of time seeking out information that is held in other sites that, if we had more rapid access to it, would increase patient safety, reduce workload and increase efficiency ...” Hospital Consultant Respondent 1, Dublin Mid Leinster

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The proposed solutions under this theme emphasised communication between HCPs on either side of a transition:

“We would frequently say to our pharmacists, 'Look, I'm worried about this patient and compliance. I wouldn't mind if you go through this prescription’” Hospital Consultant Respondent 1, Dublin Mid Leinster

“We rely hugely on them [Community pharmacists]. We’d have a very good relationship with the pharmacists in this area and we’d always try to be contactable” GP Respondent 1, Dublin Mid Leinster

Encouraging teamwork between different disciplines and building truly multidisciplinary teams was seen as important:

“We have a slightly different culture that’s what I suppose we’re kind of proud of here. It’s much more a team culture and we don’t just pay lip service to that we actually do it so they’re [Hospital pharmacists] a valued part of the team when they’re here” Hospital Consultant Respondent 6, HSE South

Collaboration and benefiting from the opinion of colleagues were underlined as the positive of multidisciplinary teams:

“It's got to be a process of communication. And I think, actually, we have been beaten into submission by our pharmacists to communicate well with them and it's really paid dividends, I have to say. When people understand what they've been saved from, what disaster could have befallen them, they're usually a lot more willing to communicate the next go out... So, it's really collaborative” Hospital Consultant Respondent 3, Dublin Mid Leinster
Hardwiring these lines of communication, to make them routine procedures in the transition coordination process was seen as essential:

“The system doesn’t allow for consistency … for instance occasionally … the hospital will actually give us a call and say, ‘look they are going home this evening, will you try and get that medicine in,’ …really the issue is that the system isn’t robust enough or consistent enough and its different hospital settings or for the system to be stronger than the individuals who are actually doing it” CP Respondent 7, HSE South

Social learning and leading by example were listed as good practice.(348) This could be seen in involving all staff in the challenge of medication reconciliation:

“…we’ve gotten the consultants on board … the new service that we’re providing have bought into medicines reconciliation and recognise it as an important part of the admission, and look for it and ask for it in their patients” Hospital Pharmacist Respondent 2, Dublin Mid Leinster

Disseminating good practice both within and beyond an institution was also seen as helpful:

“Most people are abutting against the same set of healthcare providers around their catchment area, be it their GPs, their pharmacists, their nursing homes and their other allied or affiliated institutions. And, really, you need to create a permissible environment for that level of outreach…extend that hand in a very collaborative manner about medicines management. Good institutions can do that, by making their good policies available, and their good practices available, and
taking time to have the mentorship role over the institutions that have less capacity” Hospital Consultant Respondent 3, Dublin Mid Leinster

7.4.2.5 Theme 5 - Organisation

The organisation theme gathers issues relating to existing care processes/structures, resources (time, staff, and capacity) and particularly in the case of reconciliation – ICT infrastructure. Frustration with ICT issues was extremely commonly reported. Numerous examples were presented including the clash of handwritten and electronic systems, inaccurate electronic records, and lack of interoperability or coordination between and within settings. For example, even where an electronic prescribing system was in place – where it was deployed in a single department of this hospital created a further unintended danger:

“So, we go from an electronic prescribing system in ITU [Intensive Treatment Unit] to hand-written Kardex on the ward. You can imagine it's fraught with disaster” Hospital Consultant Respondent 1, Dublin Mid Leinster

There was a perceived lack of a coordinated national strategy to utilise electronic solutions to improve medication management:

“The way IT systems have been developed in hospitals has been a complete and utter disaster because everybody has bought a bit of equipment here and a bit of equipment there but none of the equipment talks to each other” Hospital Consultant Respondent 2, Dublin Mid Leinster

Handwritten and paper based systems were also singled out as source of error:
“...the system has got too complex to be operating at this level. We have complex medicines and we’re using a paper based system and paper communication and paper everything. It’s nonsense” Hospital Pharmacist Respondent 6, Dublin Mid Leinster

The unique challenges posed by different settings and patient types were also discussed. In this example an emergency admission to hospital did not allow for planning of the transition:

“Where we have problems are with what we call ‘unscheduled care’... where a large number of people either are too ill to tell you what they're on, don't have anybody with them or just really don't know what they’re taking, in a reliable fashion” Hospital Consultant Respondent 4, Dublin Mid Leinster

Service availability did not always reflect the need:

“Then I talk about the things we don’t want to talk about and that’s we work 8:30am-5:30pm. We actually need an 8am-8pm because you have late discharges and we also possible need a clinical pharmacy service at weekends” Hospital Pharmacist Respondent 6, Dublin Mid Leinster

Even where an admission may have been planned, it appeared the discharge process was often not planned:

“The difficulties for the pharmacist are people can be discharged at any time of the day and if you have to have a review of the discharge summary or discharge script by the pharmacist, they may not be on the ward at that time...so the discharges are not planned terribly well” Hospital Pharmacist Respondent 1, Dublin Mid Leinster
Funding was also an extremely common topic in relation to staff education, ICT systems, and local initiatives:

“Resources are the bane of everybody's life. I think they're a huge problem. There have been enormous cutbacks in every hospital...And I think that's a safety issue. I think there's only so far you can cut it back and still be safe. So, I think we've kind of got to that stage now” Hospital Consultant Respondent 2, Dublin Mid Leinster

This resource issue extended into the community in the lack of remuneration to focus on more advanced medication management:

“I'm terribly sorry but if you need me to manage a new scheme...and it's going to have a time requirement, then unfortunately something else is going to have to give. Either we have to stop doing something else in order to do this or we have to be given the resources with which to deliver it” CP Respondent 3, HSE South

Specifically, in discussing staff training, contributors identified NCHDs in the hospital system as raising challenges. It was recognised that they undertook most of the prescribing and problems arose because by their very nature, NCHDs were in training positions:

“I suppose the other things that add to complexity - It's the perfect storm, really, of novice doctors, junior doctors, bearing a lot of the burden of prescribing” Hospital Consultant Respondent 3, HSE Dublin Mid Leinster

They often had limited or no supervision:
“I’m just thinking back to when I was a junior doctor I mean I just used to transcribe the drug Kardex and send people off home with their laxatives and their paracetamol and their sleeping tablets because I didn’t know whether I should stop them or not because you don’t have a clue when you’re an intern and you were the one doing the discharge prescription usually” GP Respondent 4, Dublin Mid Leinster

The relative priority of medication reconciliation was negatively impacted by time pressures:

“If I have to make 5 calls outside…that’s time I don’t have. There’s never been enough time to do those kinds of things” NCHD Respondent 1, Dublin Mid Leinster

HP involvement at hospital discharge was seen as helpful in reducing the potential for medication error:

“Sometimes if there’s a pharmacist involved at discharge, we tend to get less problems…. If there isn’t a pharmacist involved at secondary care, it tends to be a complete mess” CP Respondent 3, HSE South

However, HPs were rarely involved at discharge, based on the experience of many of the respondents interviewed:

“We’re very aware at corporate level that there’s a need for MedRec at the point of discharge, not just at the point of admission. We just simply don’t have the resources to provide that at the minute” Hospital Pharmacist Respondent 1, Dublin Mid Leinster
This lack of HP at discharge was linked to the theme of funding:

“Discharge, we don’t do for a very good reason: if you were to compare our capacity to perform clinical duties with Dublin hospitals or any other hospitals in the UK, you’d find the number of pharmacists we have is far less compared to the amount of work we have so we cannot stretch ourselves to discharge. We know that there’s a huge gap” Hospital Pharmacist Respondent 4, HSE West

Many respondents discussed the creation of new roles or the shifting of necessary tasks away from the traditional providers of that care e.g. pharmacy technicians, prescribing pharmacists:

“There needs for a modern hospital pharmacy structure to be put in place… we need a third-tier of semi-skilled labour if you like so that technicians can do more at the bedside and then the pharmacists can do more” Hospital Pharmacist Respondent 4, HSE West

“…there’s too much rework and it’s all a complete waste of time. If you have experienced pharmacists in A&E writing the admission prescription, so the doctors could simply review that and sign off on administration, it would be a far safer system” Hospital Pharmacist Respondent 4, HSE West

The separation of clinical information from prescribing information was frustrating for many respondents:

“When someone comes through my door I don’t know what their clinical conditions are… most of the time we just try to make a professional judgement on it. So, we have no idea at
all. We’re just given a prescription to sort” CP Respondent 11, Dublin Mid Leinster

This discrepancy in the transmission of intrinsically linked information was recognised:

“We have computerised discharge summaries but the summary can often be written after the patient has gone. So, the patient has often left the hospital with their handwritten discharge prescription. I think there is an opportunity for us to combine the discharge prescription and summary” Hospital Pharmacist Respondent 1, Dublin Mid Leinster

Additional funding and new roles for staff combined led to this successful example of medication management expansion:

“So, we went from 5.5 nurses nationally in 2010 who were dealing with epilepsy up to 26. 16 of those are being trained to advanced nurse practitioner level. They have prescribing, all that sort of stuff. They are very, very comfortable with this” Hospital Consultant Respondent 4, Dublin Mid Leinster

Many participants made arguments for more funding to re-orientate the current service to provide more comprehensive reconciliation service:

“I think what I would like to see is that we have reconciliation at entry. What we actually have is reconciliation the following working day, on the ward. And I think that that leaves a fairly significant gap that could be filled in very sensibly. It can't be filled in 24 hours a day, 7 days a week because we can't afford pharmacists at that level” Hospital Consultant Respondent 5, Dublin Mid Leinster
“We probably need more staff in the hospital here in the pharmacy department to make sure that we are seeing every patient on admission. And obviously then if we had more staff we could do a review of discharge prescription” Hospital Pharmacist Respondent 8, Dublin Mid Leinster

ICT was seen, by many contributors, as a major component of an effective reconciliation programme.

“… in a country of this size, we should be looking at a global, national prescription database where everybody knows what the patient is taking” Hospital Pharmacist Respondent 4, HSE West

A linked accessible prescribing database was described by one contributor:

“The thing that frustrates me most is information held in pockets. When I worked in Toronto, we had an electronic patients’ record… I could link into their dispensing pharmacy and see what they had been dispensed and link it to compliance” Hospital Consultant Respondent 1, Dublin Mid Leinster

Many units were progressing with independent initiatives in this area, focussing on generating disease specific patient registers with prescribed medications:

“We have an electronic record, which is trans-institutional, goes across geographic and institutional lines, and is web-based. So, every interaction is documented online. So, every time the nurses talk to a patient, change of medicine - So we have real-time information of the medicines” Hospital Consultant Respondent 4, Dublin Mid Leinster
More advanced ICT solutions incorporating decision support around prescribing were also described by contributors:

“I also think that hospital prescriptions should have to be computerised and that there would be systems where you wouldn’t be able to go through the process of the prescription without clicking ‘did you stop any medications? Yes, or no? And, if yes, what did you stop? Did you change the doses of any medications and, if so, what did you change?” GP Respondent 4, Dublin Mid Leinster

Another example given was the possibility of using ICT to share clinical information in addition to prescribing information to CPs:

“It would be great to have access to the patient’s notes, from the point of view of the indication of why they are on the medicine and maybe some laboratory stats and maybe some access to maybe some letters between GPs and consultants, you know so you can understand the train of thought” CP R7, HSE South

7.4.2.6 Theme 6 - Economic, political and legal issues

This theme covered political, social, legal and regulatory issues. The barriers to reconciliation listed under this theme presented conflicting views from respondents. In particular, when asked to discuss guidelines in this area respondents broadened their responses to reflecting on guidelines and legal responsibilities in general:

“There isn't any really um......formal guidelines that we, you know, have to adhere to. I suppose that may be part of the issue. So, I do think it is all a little bit ad hoc. CP R6, Dublin Mid Leinster
Other participants felt there were too many guidelines:
“There’s just far too bloody many of them [guidelines], and too
detailed. I think if you come back a step and get people to
focus on what needs to be done and doing it properly, as
opposed to how exactly they would do every single bit of it”
Hospital Consultant R5, Dublin Mid Leinster

Some felt the profile of reconciliation needed to be increased:

“It's less prioritised in terms of safety…Reconciliation per se I
don't think is emphasised enough at all actually… I really do
think it should have seen far greater prominence because it is
very dramatic when it all goes to pot” Hospital Consultant R3,
Dublin Mid Leinster

The disconnect between policy and actual practice was felt by
a number of contributors:

“I think part of the problem with it is that to have a meeting in
the hospital, a specific group of people, and everybody pats
everybody on the back and says that they're great. But the
people who are on the ground who are actually most involved
in it and are not doing it. And they're not involving them
enough” Hospital Consultant R2, Dublin Mid Leinster

This disconnect created resentment, particularly in deciding
what areas should be priorities:

“The answer back is you decide the priorities to the hospital.
So, senior management in the HSE can wash their hands and
say oh we left it to the hospital manager or, hospital
management team to decide their priorities. So, they have a
A consequence of Ireland’s mixed private-publicly funded healthcare is the difference in which prescribing information for self-paying patients is handled e.g. GMS patients have their hospital prescriptions transcribed by the GP prior to dispensing whereas private patients do not have this restriction. This discrepancy in prescription handling has been discussed previously in Chapter 4 but arises here also:

“There are plenty of private patients where you have no idea what medication they’re on because they don’t come to us very often as they don’t need to come to us to get the prescriptions done so we really wouldn’t have a notion what medication they’re on whereas at least with GMS patients they have to come back to you to have it transferred over to GMS” GP R4, Dublin Mid Leinster

Contractual issues and funding overlapped in this theme also. Deregulation of community pharmacy, with increased competition between pharmacies was a cause of concern for CPs:

“[Community] Pharmacists have been deregulated so you can have ten pharmacies in a small area and everyone is doing a little bit but GPs could easily have 2000 patients” CP R1, Dublin Mid Leinster

This linked with calls for remuneration for any extra work load involved:

“If you wanted to implement medicine management, they would have to include it as part of the contract and pharmacists
would have to be compensated for that service” CP R8, HSE North East

Interestingly, this direct relationship between remuneration and activity in primary care was perceived to be not as influential in secondary care and overlapped with the lack of feedback to secondary care on the outcome of their activities downstream:

“I think it’s very hard to incentivise in hospitals because there’s no direct relationship between an NCHD and what they’re doing on a day-to-day basis and their own salary… most NCHDs are not aware of the errors they make on discharge prescriptions because it’s never highlighted for them …somebody else just sorts it out” GP R4, Dublin Mid Leinster

Data protection concerns around sharing of electronic information were also raised:

“The obvious challenge would be that it would have to be watertight to prevent hacking and to adhere to the Data Protection Act. We’d have a number of professionals sharing private, sensitive information. But this can be done. I don’t think this is really a barrier if you were to spend the money on it” CP R5, Dublin Mid Leinster

Positive steps being taken by HSE were commended, in particular the appointment of a lead in health ICT:

“Information technology resources that are shared between doctors, nurses and pharmacists. That, I think, would be the key thing that would improve medicines reconciliation. I think the fact that the HSE now have a Chief Information Officer, that ideas like that are going to have to start to be implemented” Hospital Pharmacist R7, Dublin Mid Leinster
Finally, putting in place systems to support HCPs in quality prescribing was suggested as a positive intervention:

“I do think there’s an element of needing to create systems to say this is how things should be done, in accordance with the guidelines, not that you have to learn off the guidelines and implement them yourself, just that the system is set up that the guidelines are implemented automatically”

GP R4, Dublin Mid Leinster

7.5 Discussion

This study presents the opinions of key healthcare professionals on the barriers and drivers to medication reconciliation in Ireland, and analyses them against an implementation science theoretical framework. The most frequently mentioned barriers were organisation of care issues (e.g. ICT infrastructure), and the attitude and awareness of healthcare professionals. The most frequently mentioned drivers to effective medication reconciliation were coded under the theme of social context (e.g. collaboration) and organisational issues such as the availability of ICT infrastructure (Figure 7-4, Figure 7-5).

7.5.1 Principle findings

A summary of the main findings under each heading of the theoretical framework is present in Table 7-2.

Organisation

The limitations in the current organisation of care were the most commonly reported reasons for why reconciliation was not carried out effectively. This theme covered a wide variety of issues from the lack of electronic prescription databases, reliance on handwritten records, and no interoperability
between primary and secondary care ICT systems to human resource issues including junior doctor specific issues and lack of funding to consider expanding service availability or new roles e.g. pharmacist prescribing.

**Social context**

Social issues were listed most commonly in considering solutions to reconciliation. These issues described the relationship between individuals and groups of individuals (i.e. teams, communication, and local leadership) as distinct from the hard infrastructure (i.e. ICT) or legal responsibilities. Frustrations arose when describing communication between primary and secondary care, with respondents identifying issues such as truly multidisciplinary teams and changes in established culture with better collaboration between medical and non-medical staff.

**Healthcare professionals**

Healthcare professional themes included awareness of reconciliation, and the attitude in particular of NCHDs with competing priorities and time pressures meaning effective reconciliation was threatened. The concept of existing hierarchal structures inhibiting effective reconciliation practice also arose here with unclear lines of responsibility between different HCPs (pharmacists, physicians) and increasingly specialist care meaning non-relevant medications may have been ignored.

**Other themes**

Less commonly reported themes were discussions around patient health literacy, patients’ responsibility for their own medication lists, HCPs’ responsibility to educate patients on their medications and discussion around the *innovation* (reconciliation) itself. Respondents felt some patients were
more at risk of lack of reconciliation and should be targeted with scarce available resources. The disconnect between primary and secondary care in terms of their funding sources (independent contractors versus publicly funded employees respectively) meant that while most respondents mentioned funding as an issue the likely solutions in this area will be different with CPs, for example, mentioning contractual negotiations to engage in medicines use reviews.
Table 7-2 Summary of themes describing barriers and driver to medication reconciliation

<table>
<thead>
<tr>
<th>Barriers</th>
<th>Drivers</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Innovation</strong></td>
<td></td>
</tr>
<tr>
<td>Complex - many different healthcare providers</td>
<td>Tailoring processes to local needs</td>
</tr>
<tr>
<td>Poor existing communication pathways</td>
<td>Standard operating procedures and staff adoption of same</td>
</tr>
<tr>
<td><strong>Healthcare Professionals</strong></td>
<td></td>
</tr>
<tr>
<td>Staff training and supervision</td>
<td>Institutional effort to boost profile of reconciliation</td>
</tr>
<tr>
<td>Existing culture and hierarchies</td>
<td>Teaching prescribing</td>
</tr>
<tr>
<td>Interest and awareness of reconciliation</td>
<td>Culture change</td>
</tr>
<tr>
<td>Unclear lines of responsibility</td>
<td></td>
</tr>
<tr>
<td>Time pressures and prioritization</td>
<td></td>
</tr>
<tr>
<td><strong>Patients</strong></td>
<td></td>
</tr>
<tr>
<td>Lack of health literacy</td>
<td>Empowering patients</td>
</tr>
<tr>
<td>Responsibility of prescribing information – patient vs HCP</td>
<td>Risk stratifying/targeting those most at risk</td>
</tr>
<tr>
<td>HCP commitment to patient education</td>
<td>Involving patient supports e.g. family members, ICT, multi-compartment compliance aids</td>
</tr>
<tr>
<td><strong>Social context</strong></td>
<td></td>
</tr>
<tr>
<td>Multiple prescribers not communicating</td>
<td>Clear, effective, systematic lines of communication</td>
</tr>
<tr>
<td>Lack of effective multidisciplinary care (not supporting new roles, not sharing information)</td>
<td>Teamwork culture</td>
</tr>
<tr>
<td></td>
<td>Local leaders and disseminating good practice</td>
</tr>
<tr>
<td><strong>Organisation</strong></td>
<td></td>
</tr>
<tr>
<td>Lack of a coordinated ICT strategy</td>
<td>Funding to increase staff/service capability e.g. 8am-8pm, more FTEs</td>
</tr>
<tr>
<td>Fallible paper based systems</td>
<td>ICT solutions – linked prescribing databases, decision support systems</td>
</tr>
<tr>
<td>System not robust enough to accommodate different patient presentations e.g. elective vs non-elective</td>
<td>Greater involvement of pharmacists e.g. pharmacist prescribing, medicines use reviews</td>
</tr>
<tr>
<td>Service availability not reflecting need</td>
<td></td>
</tr>
<tr>
<td>Lack of funding/remuneration to expand activities</td>
<td></td>
</tr>
<tr>
<td>Training, supervision, capacity of NCHDs all limited</td>
<td></td>
</tr>
<tr>
<td>HPs absent from hospital discharge</td>
<td></td>
</tr>
<tr>
<td>Clinical and prescribing information not intrinsically linked</td>
<td></td>
</tr>
<tr>
<td><strong>Political, legal and economic</strong></td>
<td></td>
</tr>
<tr>
<td>Ambiguity around official ‘MedRec’ policy</td>
<td>Positive steps by health authority appointing health informatics lead</td>
</tr>
<tr>
<td>Disconnect between policy and practice</td>
<td>Putting in place systems to support good prescribing practice</td>
</tr>
<tr>
<td>Discrepancy between private and publicly funded patients</td>
<td>Feedback on good/bad practice</td>
</tr>
<tr>
<td>Contractual/remuneration concerns</td>
<td></td>
</tr>
<tr>
<td>Data protection concerns</td>
<td></td>
</tr>
</tbody>
</table>

HCP: Healthcare Professional; ICT: Information Communication Technology; FTE: Full Time Equivalent; NCHD: Non-consultant Hospital Doctor; HP: Hospital Pharmacist
The results of this study are similar to previously reported studies internationally. Organisational issues, including task substitution and the greater involvement of non-traditional HCPs in the prescribing process is increasingly common and shown to be effective. However coupled with this is the need to have functioning multidisciplinary teams – through openness to the opinion of others and willingness to compromise.

The difficulty of staff engagement and training regarding medication safety, where there is a fluid and constant changing staff profile (e.g. NCHDs), has been raised previously.

Designing ICT systems to support good practice was seen as key by many respondents e.g. decision support systems, connected prescribing databases and health information exchanges. This has good face validity and study evidence. The realisation that ICT solutions may also be a cause of error, particularly if incorrect medication information is recorded, has been noted previously. There is also a recognition that the implementation of Health Information Technology (HIT) is slow, dependent on local circumstances/complex communication arrangements, unrealistic expectations that are often hindered by conflicting strategic initiatives, and lack of immediately discernible benefits.

Effective reconciliation may also be hampered by increasing specialisation, where in some cases physicians have regard only to their own specialist medication, this can have the effect of making it difficult to clarify with a prescriber the intent of
prescription changes. Coupled with the difficulty in integrating non-medical professionals into multidisciplinary teams can make questioning prescribing decisions difficult and reduce the effectiveness of the team.

The experience of respondents that some patients had little knowledge of their medications is common. Finally, in keeping with the experience of many institutional reconciliation interventions internationally, respondents discussed the disconnect between policies and local practices with the need for interventions to be tailored to locally available resources.

7.5.3 Strengths and limitations

A methodological strength of this study is that we applied qualitative methods to explore, in-depth, all possible barriers and drivers of implementing reconciliation. Interviews have proven to be a useful method of providing in-depth information on barriers and drivers with regard to implementation while at the same time exploring and understanding the motivations underlying behaviour. Our analysis of barriers provided detailed information for professionals or organisations, regionally or nationally, to develop multifaceted implementation strategies for improving the implementation process of medication reconciliation. Even so, several limitations should be considered when interpreting our findings. The sampling strategy in selecting interviewees, while purposive, was limited in the number of different kinds and geographic location of health care professionals who participated and this may limit the transferability of our findings. The results are, however, consistent with previous studies on this subject. Indeed, a strength of this study in comparison to previous studies was the broad range of participants involved including hospital and community based HCPs. Nevertheless, future research should
consider the inclusion of other interested and relevant individuals – patients, nurses, carers/family members, healthcare managers/administrators etc.

A further limitation is that interviewees may be subject to social desirability bias e.g. it is possible that respondents exaggerated their issues because they knew the study was examining barriers and facilitators for reconciling medications. To help overcome social desirability bias, both direct and indirect questions regarding medication reconciliations were asked. Indirect questioning involved, as part of the semi-structured interview process, asking the respondent to describe their perceptions of the process as opposed to pinpointing exact issues. Additionally, due to the interpretative nature of qualitative research, the research team may have introduced confirmation bias into the analysis and classification of the themes derived from the interviewees narratives – favouring information that supports our belief. (354) The choice of data collection method, while allowing comparison with previous published studies, may have been improved by triangulating the findings though alternative techniques such as participant observation research.(199,354) Finally, the use of a pre-identified theoretical framework may have limited the potential breadth of responses. Nevertheless, the chosen model’s thematic structure is broadly similar to previously derived implementation models, the primary aim of this study, and thus allows easy comparison of our results with its application in previous studies’ settings.(150,164,165,340)

7.5.4 Future clinical, research and healthcare policy implications

This study, through an implementation science framework, synthesises some key areas for clinicians and healthcare policy makers to focus on to improve the reconciliation process. A
consistency of the findings in comparison with previous international research lends further weight to their validity. Future reconciliation interventions could be implemented through process mapping and feedback studies (e.g. Plan-Do-Study-Act(PDSA)) to specifically target the areas identified in this study.

7.6 Conclusion

Medication reconciliation is advocated as a solution to the known problem of medication discrepancies at transitions of care. Despite the requirement of many regulatory organisations for healthcare organisations to implement reconciliation practices the perception that medication errors are common and dissatisfaction with management of medications at transitions remains common. This study presents the key challenges and potential solutions health policy makers, managers and HCPs in Ireland should consider in reviewing implementation of medication reconciliation in their own organisations. Key areas to focus on include staff support and training, supporting effective multidisciplinary teams, greater involvement of pharmacists in medication reconciliation, ICT solutions (linked prescribing/dispensing databases, decision support systems) and increased funding to provide additional (e.g. admission and discharge reconciliation) and more advanced services (e.g. dedicated CP delivered medication reconciliation and medication use review).
8 Discussion and recommendations
8.1 Introduction

In this chapter, the findings from chapters two, three, four, five and six are triangulated and the thesis is summarised via a widely-cited research impact framework. The methodological difficulties and limitations of the study are discussed. The context of these findings within the existing evidence base and their contribution as well as the proposed direction of future research efforts is also discussed.

8.2 Summary of methods

In this thesis, a mixed methods approach to research was employed to assess medication reconciliation between primary and secondary care in Ireland. This method was appropriate due to the complex nature of this process with the many possible influences both at an individual and organisational or system level. Quantitative methods were used to both survey the perceived quality of reconciliation and describe the actual continuity of medication post hospitalisation. Various qualitative methods were used to explore the views of a diverse group of HCPs on the quality of medication reconciliation as well as to gather opinions on the influences on implementing reconciliation successfully. Equal priority was given to both research methodologies, data were collected sequentially, with integration of data taking place at the time of the reporting of results and the primary purpose was triangulation of the data of the varying sources and methods.

8.3 Summary chapter two

There is a high risk of miscommunication and errors at transitions of care with medication error, in particular omission of appropriate medication, being commonly reported. Medication errors – including medication discrepancies at transitions - have been linked to ADEs, rehospitalisation and increased costs. A number of different factors have been
associated with discrepancies with increased age, number of medications, length of time in hospital and increased morbidity being reported as increasing the risk of discrepancies on medication lists. Despite the wealth of evidence of poor documentation and potential for ADEs, the actual propagation of errors into the next healthcare setting is unclear.

Medication reconciliation is proposed as a solution to ensure the accuracy of medication information transfer between settings and HCPs. While there is strong regulatory support for reconciliation, the definition and assessment of the effectiveness of reconciliation is not uniform, furthermore the most effective method of reconciliation is unclear.

The implementation of reconciliation has received attention with previous research and standard operation procedures published. Effective implementation is likely to revolve around knowledge of and appreciation for local organisational and user issues, resources, and skills/training.

The Irish health care system is fragmented with public and private provision of services. There is a varying level of intensity and specialisation of service provision within hospitals across the country. Self-paying or private patients avail of services differently from hospitals, community pharmacists and GPs.

There are an increasing number of regulatory and patient safety organisations both nationally and internationally advocating for medication reconciliation. Nationally, HIQA and the HSE have published guidance and strategic documents advising on improved transitions of care, medication and information management at transitions, and a greater role for ICT.
8.4 Summary chapter four

The aim of this study was to gather the views of GPs and CPs on the current practices of medication management at the primary/secondary care interface – in particular the objectives were to explore the standard of medication reconciliation, the quality of communication between HCPs and the perceived level of prescribing errors (Table 8-1).

This was undertaken by means of an online questionnaire of GPs and CPs nationally. A total of 897 (of 5057) questionnaires were returned – a 17.7% response rate. The profile of respondents was relatively consistent with the makeup nationally of both professions.

The most alarming finding was that most respondents (both GPs and CPs) reported experiencing prescribing errors following transitions in the previous 6 months.

Despite almost unanimous support for medication reconciliation as a positive intervention for both patient safety and medication adherence most GP practices (60%) did not have formal reconciliation systems in place.

The opinion of respondents on the quality of communication between primary and secondary was mixed with a third of GPs and CPs rating it as poor/very poor. This opinion of the quality of communication varied significantly across the country – with those outside the Dublin Mid-Leinster region more likely to rate communication with secondary care poorly. Conversely GPs/CPs were positive about the relationship between each other with more than half rating it as very good.
Both groups were supportive of an expanded role for hospital pharmacists as well as community pharmacists in the identification and prevention of prescribing errors following a transition.

Content analysis of free text generated four broad categories - organisational/infrastructural issues, relationship and quality of communication between HCPs, the role of the patient and prescribing errors.

This study, while weakened by a poor response rate, highlighted the experience of prescribing errors as being a common event at transitions of care. Poor communication between primary care HCPs and secondary care with a possible geographical variation in satisfaction with communication. The findings of this study indicated the need to investigate quantitatively the onward impact of medication errors at discharge.
Table 8-1 Summary of the questionnaire of GPs and CPs (Chapter 4)

<table>
<thead>
<tr>
<th>Aim</th>
<th>Methods</th>
<th>Data management</th>
<th>Key findings</th>
<th>Limitations and difficulties</th>
<th>Recommendations</th>
</tr>
</thead>
</table>
| To gather information from GPs and CPs on current practices of medication management at the primary/secondary care interface in Ireland. Specific objectives of the study included:  
- Experience of prescribing errors following transition,  
- Medication reconciliation practices,  
- Quality of communication/relation between HCPs. | Nationwide online questionnaire of GPs and CPs. | Data were entered into Stata where descriptive and inferential statistics were generated. Multilevel logistic regression was undertaken of the effect of hospitalisation on medication continuity. |  
- 17.7% response rate.  
- Experience of prescribing errors following transitions extremely common in both groups (>84%).  
- Minority of GP practices with formal medication reconciliation procedures.  
- Almost unanimous support for medication reconciliation as a way to improve medication safety.  
- Dissatisfaction with communication between primary and secondary care.  
  - With significant variation in satisfaction between HSE regions.  
- Support for a greater role for both hospital and community pharmacists in medication management.  
- Limited engagement or education of patients regarding medication management. |  
- Non-validated questionnaire limited internal validity.  
- Small response rate limits external validity.  
- Possible responder bias e.g. social desirability. |  
- Greater role for interaction between hospital pharmacists and GP/CPs as patients transition.  
- Exploration of geographic variation needed e.g. systematic, related to service provision.  
- Improved interoperability of ICT systems between primary and secondary care.  
- Harness positive relationship between GP and CP e.g. Both GPs and CPs felt pharmacists could have more of a role in reducing and preventing medication errors at transitions. |
8.5 Summary chapter five

The aim of this study was to examine the impact of hospitalisation on the continuity of common, evidence based medication following hospitalisation. Specific objectives were to compare discontinuation of medication in the GP record between those who were hospitalised and not hospitalised who had been prescribed statins, antiplatelets/anticoagulants, thyroid medication or respiratory inhalers continuously for a year prior to hospitalisation. Additionally, the impact of electronic discharge summary documentation on the continuity of medication in the GP record was assessed (Table 8-2).

91,866 records were initially extracted from 44 GP practices, with four cohorts being created (with enrolment and follow up criteria) aligned to the four medication classes (6,516 participants prescribed antiplatelets/anticoagulants, 6,890 prescribed statins, 1,686 prescribed thyroid medications and 2,348 prescribed respiratory inhalers).

The rate of discontinuation in the GP record at 6 months post hospitalisation ranged from 6% in those prescribed thyroid medication to 11% in those prescribed statins or antiplatelets/anticoagulants.

The recording of the specified medication in the discharge summary was poor with the proportion of messages where the medication was missing ranged from 44% (statins) to 57% (respiratory inhalers).

Hospitalisation (recorded dichotomously) was significant in two groups only (thyroid medication and respiratory inhalers) with both of these groups likely to have less odds of discontinuation
compared to those not hospitalised - respiratory inhalers (AOR 0.53 (0.39, 0.71)) and thyroid medication (AOR 0.54 (0.33, 0.89)).

Where the exposure was recorded continuously (i.e. increasing number of hospitalisations), the direction of the effect remained the same for the groups prescribed thyroid medication and inhalers - (AOR 0.65, [0.44, 0.95]) and (AOR 0.77, [0.65, 0.91]) respectively. In the cohort where patients were prescribed statins, the odds of discontinuation increased with each further hospitalisation (AOR 1.11, [1.00, 1.22]).

There was no clinically important difference between hospitals in terms of the effect of hospitalisation. Various subgroup and sensitivity analyses had no impact on the principal findings. Private or self-paying status as well as increasing age were both associated with increased odds of discontinuation of medication across all groups. Surprisingly, number of drugs was not significant in most groups; in fact, an increasing number of drugs was associated with reduced odds of discontinuation in the respiratory inhalers groups (AOR 0.95, [0.91, 0.99]).

In exploring the impact of the lack of documentation of medication on the discharge summary, the absence of medication was associated with an increased odds of medication discontinuation 6 months post hospitalisation in those prescribed lipid lowering medication (AOR 2.23, [1.47, 3.39]), and respiratory inhalers (AOR 3.44 [1.67, 7.06]).

This study adds to the evidence base on the impact of transitions of care on the continuity of medication post discharge – in particular within the GP record. Having explored the perceived quality of medication reconciliation and the actual
continuity of medication at the primary secondary care divide
the next study investigates, via a systematic review, the most
effective method of delivering medication reconciliation.
### Table 8-2 Summary of the cohort study of medication discontinuation post discharge (Chapter five)

<table>
<thead>
<tr>
<th>Aim</th>
<th>Methods</th>
<th>Data management</th>
<th>Key findings</th>
<th>Limitations and difficulties</th>
<th>Recommendations</th>
</tr>
</thead>
</table>
| Examine the impact of hospitalisation on the continuity of common,  | Retrospective cohort study using GP prescribing records and hospital   | Quantitative data – Stata (descriptive and inferential statistics) | • 44 GP practices recruited (91,866 patient records extracted).                | • Limited to only four medication classes  
• Assumed unintentional discontinuation in the absence of clinical information (internal validity).  
• Prescribing not dispensing database.  
• Non-traditional outcome measure limits ability to compare to previous studies.  
• Data limitations may impact on patient follow-up, exposure recording and outcome calculation (internal validity).                                                                                           | • The impact of transitions of care on GP prescription records, for specific medication classes, does not increase medication discontinuity and is in contrast to previous studies of dispensing records post hospitalisation – this needs further study.  
• The quality of documentation on hospital provided discharge summaries is poor and may impact on the continuity of medication post discharge – this needs to be addressed.  
• ‘Private’ patients appear to be at particularly increased risk of discontinuation in the GP record. This needs to be considered in performing reconciliation between primary and secondary care. |
| evidence based medication following hospitalisation. Specific    | provided hospitalisation notifications to examine discontinuity of    | Qualitative data – Nvivo (inductive content analysis) | • Discontinuation in the GP record in the 6 months post hospitalisation ranges from 6% (thyroid medications) to 11% (antiplatelets/anticoagulants and statins)  
• Those prescribed respiratory inhalers (AOR 0.53 (0.39, 0.71)) and thyroid medication (AOR 0.54 (0.33, 0.89)) were significantly less likely to be discontinued compared to those who did not experience hospitalisation.  
• Increasing age increased the odds of medication being discontinued.  
• Private or self-paying patients were much more likely to be discontinued.  
• Lack of documentation of medications on the discharge summary increased the odds of medication being discontinued in the GP record post discharge in both statin and respiratory medication groups. | • Prescribing not dispensing database.  
• Non-traditional outcome measure limits ability to compare to previous studies.  
• Data limitations may impact on patient follow-up, exposure recording and outcome calculation (internal validity).                                                                                           |                                                                                                                                                                                                                             |
| objectives were to compare discontinuation of medication in the  | medication post-hospitalisation.                                       |                                   | • Those prescribed respiratory inhalers (AOR 0.53 (0.39, 0.71)) and thyroid |                                                                                                                                                                                                                             |                                                                                                                                                                                                                             |
| GP record between those who were hospitalised and not hospitalised |                                                                        |                                   | medication (AOR 0.54 (0.33, 0.89)) were significantly less likely to be    |                                                                                                                                                                                                                             |                                                                                                                                                                                                                             |
| who had been prescribed:                                            |                                                                        |                                   | discontinued compared to those who did not experience hospitalisation.       |                                                                                                                                                                                                                             |                                                                                                                                                                                                                             |
| • statins,                                                          |                                                                        |                                   | • Increasing age increased the odds of medication being discontinued.         |                                                                                                                                                                                                                             |                                                                                                                                                                                                                             |
| • antiplatelets/anticoagulants,                                     |                                                                        |                                   | • Private or self-paying patients were much more likely to be discontinued.  |                                                                                                                                                                                                                             |                                                                                                                                                                                                                             |
| • thyroid medication                                               |                                                                        |                                   | • Lack of documentation of medications on the discharge summary increased the odds of medication being discontinued in the GP record post discharge in both statin and respiratory medication groups. |                                                                                                                                                                                                                             |                                                                                                                                                                                                                             |
| • respiratory inhalers                                            |                                                                        |                                   | • Those prescribed respiratory inhalers (AOR 0.53 (0.39, 0.71)) and thyroid |                                                                                                                                                                                                                             |                                                                                                                                                                                                                             |
8.6 Summary chapter six

The aim of this chapter was to conduct a systematic review of the most effective methods of medication reconciliation. The Cochrane Collaboration methodology and reporting guideline was adhered to in conducting this review. The Effective Practice Organisation of Care (EPOC) review group taxonomy and classification of interventions was used in reporting the review. Randomised control trials, reporting the outcome of medication discrepancies only were included, with no other restrictions applied (Table 8-3).

10,155 records were screened, with 481 of these undergoing full text review. Of these, 20 studies were included in the review.

All of the included studies were conducted in hospital or immediately related settings, with most studies being from economically developed countries and including older patients, prescribed multiple medications. Eighteen of the 20 studies were classified as provider orientated within the organisational intervention type (according to EPOC taxonomy), with pharmacists being involved in all of these. Only one study was ICT focused with an electronic reconciliation tool available to a network of primary care practices following discharge. While all interventions had some element of information gathering to generate a PAML, there was much variation in other elements with some studies specifically providing for onward communication of medication information, others conducting medication review, counselling, education or added skills e.g. pharmacist prescribing. This lead to a high degree of heterogeneity between the studies. This was compounded by varying definitions of study outcomes and significant risk of bias issues (e.g. non-blinding of outcome assessors).
Eighteen studies were pooled in a meta-analysis of the primary outcome of at least one medication discrepancy per participant (RR 0.58 95% [CI 0.46, 0.73]), with a high degree of heterogeneity in the effect ($I^2 = 92\%$), which was further limited by a GRADE assessment of evidence as being ‘very low’. Secondary outcomes (pADEs, ADEs, healthcare utilisation) showed no consistent effect – neither positive nor negative. No studies undertook an economic evaluation of their intervention.

The findings of this review was that there is no certainty as to the effect of medication reconciliation on the process measure of medication discrepancies due to the very low quality of evidence. Pharmacists are the HCP most commonly involved in reconciliation interventions. The definition of discrepancies, the integrity and fidelity of interventions and the blinding of outcome assessment need to be improved in intervention studies. There needs to be a greater focus on economic evaluation as part of the reporting of interventions.

Furthermore, future intervention studies should include relevant patient focussed outcomes and be adequately powered to detect clinically significant differences.

In Chapter six, the final study examined the views of key HCPs on the implementation of reconciliation.
### Table 8-3 Summary of the systematic review of medication reconciliation interventions (Chapter six)

<table>
<thead>
<tr>
<th>Aim</th>
<th>Methods</th>
<th>Data management</th>
<th>Key findings</th>
<th>Limitations and difficulties</th>
<th>Recommendations</th>
</tr>
</thead>
</table>
| To perform a systematic review to assess the effect of medication reconciliation interventions, on patients experiencing a transition of care, on the outcomes:  
- medication discrepancies,  
- patient related outcomes  
- healthcare utilisation | Systematic review (adherent to Cochrane Collaboration guidelines) of randomised control trials. | Data were entered and managed in the Cochrane Collaboration’s Review Manager software. Additional statistical analysis, including meta-analysis was performed in Stata. | - 20 studies included (following screening of 10,155 and full text review of 481 records)  
- All included studies were conducted in hospital or immediately related settings, with most studies from developed countries including older patients (mean age 63 years) prescribed multiple medications.  
- Most studies (18/20) were classified as provider orientated within the organisational intervention type (according to EPOC taxonomy), with pharmacists being involved in all of these.  
- Eighteen studies were pooled in a meta-analysis of the primary outcome of at least one medication discrepancy per participant (RR 0.58 95%CI [0.46, 0.73]), with a high degree of heterogeneity in the effect ($I^2 = 92\%$)  
- Secondary outcomes (pADEs, ADEs, healthcare utilisation) showed no consistent effect – either positive or negative  
- No studies undertook an economic evaluation of their intervention. | - High degree of clinical and statistical heterogeneity  
- Significant risk of bias across a number of criteria.  
- Limited inclusion criteria to those studies with an outcome of discrepancies.  
- GRADE assessed as ‘very low’. | - No certainty as to the effect of medication reconciliation on the process measure of medication discrepancies.  
- Pharmacists are most commonly involved in reconciliation interventions  
- The definition of discrepancies, the integrity and fidelity of interventions and the blinding of outcome assessment need to be improved in intervention studies.  
- There needs to be a greater focus on economic evaluation as part of intervention studies.  
- Future intervention studies should include relevant patient focussed outcomes and be adequately powered to detect clinically significant differences (with the caveat of this review’s inclusion criteria). |
8.7 Summary chapter seven

The aim of this study was to gather the opinions of both primary and secondary care based HCPs on the barriers and supports to implementing medication reconciliation. An existing theoretical framework was used to deductively code participants’ responses (Table 8-4).

Thirty-five participants were interviewed, a mix of hospital consultants, non-consultant hospital doctors, hospital and community pharmacists and GPs. All HSE geographic regions were represented.

In depth interviews with HCPs involved at a management, training and service provision level of medication reconciliation were useful in gathering information on the success or otherwise of implementation and comparing their experience to existing evidence.

Use of an existing implementation framework facilitated data collection and comparison. Data were coded under the themes innovation, healthcare professionals, social context, organisation and political, legal and economic issues. Participants’ responses were concentrated under the thematic headings of organisational, social and healthcare professional issues.

Organisational issues were listed as among the most common reasons challenging effective medication reconciliation. The topics here were wide ranging from limited training/supervision of doctors in training, paper based records, limited take up of the opportunities offered by ICT, funding of current and added activities, and a mismatch between service needs and
provision e.g. pharmacists not being available at hospital discharge.

The social context comprised of issues such as poorly functioning multidisciplinary teams, with a missed opportunity to fully integrate pharmacists. Participants mentioned local leaders prioritising reconciliation would inspire colleagues to reconsider the importance of the issue. Many participants struggled with ineffective or absent communication – especially between primary and secondary care. This communication issue abutted with roles and responsibilities - this was particularly highlighted in the responses of some hospital based individuals that they did not consider the impact of decisions beyond discharge.

The healthcare professionals theme included the view of participants that effective reconciliation suffered due to existing hierarchies, a culture that didn't allow other voices to question or contribute to prescribing/medication management. Younger doctors in training also described the compromise between the importance of reconciliation with more pressing activities.

The results of this study highlighted many areas that could improve reconciliation implementation efforts - institutional and local leader support, true multidisciplinary teams, ICT links (GP & dispensing records, inpatient records of prescribing), and expanding services to underserved transition points (e.g. discharge).
<table>
<thead>
<tr>
<th>Aim</th>
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| To gather information from healthcare professionals on the barriers and drivers to the implementation of medication reconciliation both between and within primary and secondary care in Ireland. | Face-to-face interviews with a wide range of HCPs involved with medication management at transitions of care using an existing implementation science theoretical framework to support more successful reconciliation efforts. | Qualitative data – Nvivo (deductive thematic analysis according to an existing theoretical framework)                                                                 | • 35 participants were interviews (a mix of hospital consultants, ‘junior’ doctors, hospital and community pharmacists, and GPs.  
• The most frequently mentioned barriers to successful reconciliation were organisation of care issues (e.g. ICT) as well as the attitude and awareness of HCPs  
• Drivers most commonly mentioned were coded under the social context theme (e.g. collaboration) and organisational issues – ICT.  
• Additional barriers described included:  
  o Paper based systems; lack of interoperability and the silo like nature of information within the health service.  
  o Poor communication between prescribers  
  o Minimal support of junior staff; greater training/emphasis on reconciliation required.  
  o Lack of functioning multidisciplinary teams with minimal integration of non-medical staff (e.g. pharmacists).  
  o Time pressures and resource issues. | • Sampling, while purposive, was limited to participants’ geographic and professional backgrounds.  
• No patient, nurse or healthcare management involvement.  
• Possibility of social desirability bias.  
• Constrained by the use of a pre-existing theoretical framework. | • Consideration of local needs in implementing reconciliation interventions.  
• Institutional support of the profile of reconciliation.  
• Greater support for prescribing training.  
• Tackle existing cultures and hierarchal arrangements  
• Greater involvement of patients in medication management.  
• Functioning multidisciplinary teams – especially pharmacists seen as contributing member of the team.  
• Funding to expand existing or new services (e.g. pharmacist discharge reconciliation).  
• ICT – linked databases, decision support systems. |
8.8 Triangulation of results in context of previous research

The hypothesis of this thesis is that medication reconciliation takes place between secondary and primary care.

The findings of the thesis both refute and support this hypothesis. There is a widespread experience of prescribing errors among HCPs based in primary care however the discontinuity of medication in the GP prescribing record, for specific medication, was relatively low and the unexpected direction of effect in the association between hospitalisation and the continuity of medication was surprising. ‘Private’ insurance status had a significant impact on the continuity of medication independent of hospitalisation. Not unexpectedly pharmacists were the most commonly studied HCPs in the delivery of reconciliation interventions. The obstacles to implementing reconciliation were consistent with previous international experience and revolved around ICT, funding, definitions and evolution of professional roles and interprofessional relationships.

In this section the findings from the various methodologies employed in the thesis’ studies will be triangulated to highlight the main factors impeding reconciliation, the impact of transitions of care and future research opportunities.

8.8.1 Factors impeding effective reconciliation

Many studies have examined errors arising in medication management and reconciliation, using different theoretical perspectives in the attribution of the causes of error and implementation theories to identify the factors likely to help successful adoption of reconciliation. (26,49,84,150,355,356)
The ‘at risk behaviours’ and organisational factors impeding effective reconciliation identified in this thesis are similar to those reported both nationally and internationally. The roles and responsibilities of HCPs, greater involvement of patients, supervision and training of the different healthcare professionals in the reconciliation process, improved communication and remuneration/resources themes received attention in the various studies included in this thesis.

8.8.1.1 Roles and responsibilities

There is disagreement internationally on the role to be played by different HCPs in reconciliation – with contrasting statements from different professional organisations. (27,28) However, the value of pharmacists as part of a functioning multidisciplinary team was noted by interview participants who had experienced this in their work. The survey respondents were supportive of the idea of hospital pharmacists being more involved in the medication management/error identification process (~86% - Section 4.4.1.2).

The systematic review found that pharmacists were the HCP most commonly involved in interventions (18 of the 20 studies included – Section 6.4.6) – successfully adopting new skills such as prescribing. This task shifting was raised by interviewees in suggestions that pharmacists could replace or supplement doctors in gathering medication histories at transition points – reducing duplication.

Doctor conducted medication histories tend to document less medications and uncover less discrepancies than pharmacist history taking. (357–360) Previous studies have suggested that doctors place less emphasis on medication history taking during clerking, relying on other elements of the systems to clarify/gather comprehensive medication lists. (84,361) Some
interviewees illustrated this by describing their opinion of the standard of medication history clerking in the emergency department:

“I think they’re all aware it’s important but I think they often see it as somebody else’s problem, particularly in regard to where I work, which is an emergency department”

Hospital Consultant Respondent 5, Dublin Mid Leinster

The relative priority given to reconciliation also played a role according to one participant:

“You know, while you want to do the best job you can and reduce risk, unless you see the direct impact of it like most NCHDs are not aware of the errors they make on discharge prescriptions because it’s never highlighted for them, it’s just picked up somewhere down the food chain and it never gets said back to them that this was an error but somebody else just sorts it out”

GP R4, Dublin Mid Leinster

A noteworthy element in this discussion of task shifting and substitution is the limited discussion of other healthcare staffs’ possible contribution. Some interviewees mentioned the risk of inaccuracies with non-medical staff (e.g. GP receptionists) preparing prescriptions. This danger was echoed in responses to the survey in which it was revealed most GPs do not have any formal system in place for reconciliation (Section 4.4.1.2). One interviewee mentioned the promise of involving nurses in the reconciliation process.

Some of the interviewees based in community pharmacy mentioned having SOPs in place for pharmacy staff, while
hospital based staff talked about the transfer of routine work to ancillary staff.

In contrast to these suggestions none of the included studies in the systematic review prioritised the possible role of nurses, pharmacy technicians etc. despite these being the subject of some previous publications. However, some studies did include nurses as part of a more multidisciplinary reconciliation intervention.

8.8.1.2 Communication

Communication, the corner stone of good teamwork, was consistently rated as inadequate across the studies. Frustrations with poor communication between primary and secondary care was shown in the questionnaire results (Table 4-3). The theme emerged that some HCPs felt their responsibility ended when/began once the patient transitioned, not considering the onward impact of their actions.

The social context element to this information and task sharing is likely to be beneficial in problem solving, as collaboration was highlighted by contributors in both interviews and the questionnaire. Poor information sharing in an organisation leading to poor performance and error is recognised in the literature.

The impact of poor information sharing was also revealed in the analysis of the cohort study in which increased odds of discontinuity of medication was reported where discharge summaries omitted medications (Table 5-13). Indeed, poor quality and inconsistent communication between secondary and primary has been previously reported with for example community pharmacists not receiving updates on medication changes.
A bright spot of the questionnaire results was the positive relationship reported between GPs and CPs – leading, in the opinion of some contributors, to the avoidance of medication errors (Table 4-3).

Of note, few of the included studies in the review focused on the secondary primary care transition with none investigating transitions of care taking place exclusively within primary care (e.g. nursing home transitions). Furthermore, none explicitly mentioned communication as a key target of the intervention – rather introduction of new skills, or reorganisation of existing services was the main intervention.

8.8.1.3 Training/Education

Training and supervision of doctors in training was deemed as inadequate by some of the respondents to the survey and interviewees.

Focusing on education and inclusion of the topic of prescribing at undergraduate level was mentioned by some of the interviewees as a method of improvement. This focus on education has merit based on positive results in the literature, (364–366) and is line with recommendations to develop a competency framework in medication management.(178)

The existing culture was also blamed by interview participants as inhibiting progress – e.g. ignoring other HCPs input, priorities of senior medics negatively impacting on more junior staff (e.g. medication management receiving the least attention).
Negative longstanding cultural norms lead to problems around attitudes and behaviours of HCPs to patient safety, and have been previously highlighted. The use of audit and other feedback mechanism was mentioned by participants in this thesis and is accepted as an important element of process improvement, and organisational culture change in previous studies.

8.8.1.4 Remuneration and service provision

The services provided by hospital pharmacy departments varied nationwide. Interviewees confirmed the struggle with funding and the recognised gaps in certain areas (e.g. 9-5 only, no discharge service). Noteworthy, many of the included studies in the review (Section 6.4.2) listed as a limitation the lack of availability of the intervention (pharmacist) outside of normal working hours – as was also noted by a senior hospital pharmacist during the interviews.

However, while this variation in service availability is known, in examining this in the cohort study, reassuringly no consistently significant differences between hospitals in the discontinuation of the specified medications post discharge was noted (Table 5-10). While no statistical difference was seen between the hospitals, the quality of information (in terms of comprehensiveness of messages) did vary (Section 5.3.5).

Community pharmacists have been shown to effectively provide services beyond dispensing including medication counselling. Contributors were open to providing enhanced services but funding and remuneration were raised as an issue.
8.8.1.5 ICT and written records

Errors associated with transcribing were noted by interviewees – both from poor handwriting, to direct transcription of discharge prescriptions without reconciling medications (Table 4-3 - likely/very likely 67%). Transcribing has long been recognised as a source of error. (370)

ICT is seen as a solution to these issues and was raised by contributors from both the questionnaire and interviews.

Commentators have suggested that health information technology (e.g. ICT interventions, Computerised Physician Order Entry (CPOE)) could reduce errors at transition points. (49,84,351) The experience of the cohort, with the lack of medication documentation on electronic discharges, would suggest this isn’t necessarily a complete solution (Table 5-13). There are differing practices within and across Irish hospitals with varying use of electronic discharge summaries and employment of CPOE – despite this no differences between hospitals was seen in the impact on discontinuity post-hospitalisation. Furthermore, only one study in the review was based on an ICT intervention (327), suggesting there is a lack of high quality ICT studies focussed on improving medication discrepancies. (131)

Role of the patient

Discrepancies between HCPs and patients in accounts of medication, recollection of counselling and adherence has been previously reported. (371,372) An increase in patient involvement was called for in both interview and questionnaire related data.
Likewise, in some of the studies included in the review there were targeted interventions to patients as part of medication reconciliation package (Appendix W). (144, 315–317, 320, 322–324, 326)

Private patients in the cohort study appeared to be at greater risk of discontinuity (Table 5-8). This was a concerning result and suggests a fragmented, unequal medication management system between private and public patients.

Finally, a greater involvement and education of patient’s may improve experiences and reporting of ADEs and is in line with advice from patient safety organisations (including the WHO guidance on implementation of medication reconciliation). (159, 373, 374)

8.8.2 Frequency and severity of errors at transition

Medication reconciliation receives a lot of attention – both in the publication of research studies (observational, interventional, reviews and editorials) and guidelines/reports. Many studies have been published documenting the severity of discrepancies at transitions, especially at hospital discharge – which is of particular relevance to this thesis.

However, the impact of these documented discrepancies on the future care of patients is unclear. Most studies have reported the potential for ADEs, with actual ADEs (e.g. rehospitalisation) much less commonly reported. (225) The findings of this thesis’ studies are conflicting. The qualitative research added to the alarm felt by HCPs on the scale of errors at transitions of care. There was unanimous experience of prescribing errors following transition (Section 4.4.1.2) with some contributors questioning the actual translation of errors into clinical impact.
The quantitative exploration of the impact of transitions of care on medications, undertaken through the cohort, addresses this viewpoint somewhat. The primary outcome of the cohort, discontinuation of medication in the GP record, in those who were hospitalised is relatively low ~6-11% (Table 5-7). When compared to those who did not experience the exposure of hospitalisation the odds of discontinuation are actually significantly lower in some groups (thyroid and inhalers) (Table 5-8).

The documentation of medication on electronic discharge summaries is extremely poor and this did seem to be associated with discontinuation (albeit with small numbers and limitations in recording/retrieval of data for this outcome in the study) (Table 5-13). Discrepancies upon discharge in Irish hospitals are known to be high and yet this study suggests this is not being translated through as discontinuity. (63) This lack of a negative impact of hospitalisation on medication continuity may suggest that reconciliation is occurring appropriately for patients upon return to primary care. Of course, the cohort study in this thesis included only four medication classes and the findings would need to be replicated across other, higher risk, drug classes (e.g. insulin). Efforts at identifying higher risk medications and the impact of discrepancies has already begun with examples of medications and algorithm of severity assessment developed by Doerper et al. (293)

8.8.3 Standardisation of definitions

A continuing issue of confusion is the lack of a standardised definition of medication reconciliation. This has been raised by commentators before and is illustrated by Urban’s work (Table 2-1) where there is a multiplicity of definitions – not all inclusive of the same actions.
This confusion was seen in the results of the various studies within this study. GPs in their responses to the questionnaire were very supportive of the idea of reconciliation, but then did not have formal systems to support it (Table 4-2). Many contributors when interviewed discussed problems around prescribing more generally and overlapped with the process of medication review when asked specifically about reconciliation. Further ambiguity was found in the screening and selection of studies for inclusion in the systematic review (Figure 6-1). These studies, empirical studies of the effect of reconciliation, did not have any homogeneity in the process of conducting reconciliation and quite often provided additional interventions (e.g. medication review) as part of a package described as reconciliation.

This lack of clarity hinders the effective implementation of the process – making it difficult to clarify the roles and responsibilities of HCPs. The confusion as to what constitutes core elements of reconciliation is also troubling – for example – the onward communication of medication information is not uniformly agreed as part of the process. The confusion has its origins, somewhat, in the fact that reconciliation arose as standardised operation procedure in secondary care – requiring that it be adapted to facilitate primary care usage (receiving patients from hospital discharge, CP/GP communication, nursing home etc.).

Urban addressed this directly by devising a new definition that encompassed all possible settings where reconciliation might be performed:(84)

“The retrospective assessment and evaluation of the patient’s recent medicines (e.g. inpatient medication chart or discharge
prescription) at specific transition points in care and the resolution of any discrepancies found. The aim is to ensure the information transferred accurately reflects the patient’s current treatment requirements (including drug, dose/strength, form, route, frequency).”

Noteworthy in this definition however is the failure to mention onward communication.

Studying the effectiveness of a process requires the selection of valid, reliable outcome measures (e.g. COMET (Core Outcome Measures in Effectiveness Trials).(375) Here again, the study of reconciliation suffers due to the lack of both an agreed taxonomy and prioritisation of outcomes. The systematic review suffered due to this heterogeneity of collection, assessment and reporting of outcomes (Section 6.6.3).

Difficulty in interpreting outcomes commonly occur for example due to inconsistent recording of discrepancies (intentional, unintentional, undocumented intentional etc.), sources selected for comparison, the review of dosing, frequency, strength, and the incorrect attribution of prescribing errors as errors of reconciliation. The ambiguity of outcome measures in this field has been the subject of a recent systematic review by Almanasreh.(25) Almanasreh et al., highlighted the lack of a gold standard medication list, the limited involvement of patients and the lack of agreement on current terms in use as being stumbling blocks to effective outcome based research in medication reconciliation.(25) Finally, in practice choosing outcome measures that are practical, easily recorded, collected and compared will be necessary to facilitate adoption to clinical practice.
Triangulation of the findings suggests that the medication reconciliation between primary and secondary is poor, with communication between HCPs being fragmented. Knowledge sharing through multidisciplinary teams was not widespread. Responsibility for medication management was not collaborative with little concern for the onward care of patients. Private patients in particular appeared to be at risk of medication disruption during transitions of care. Reconciliation as a key patient safety target was not recognised in all settings. Finally, ICT developments across settings were heterogeneous, limited in use and quite possibly adding to the possibility of error.

8.9 Strengths and limitations of this thesis

A major strength of this study is the mixed methods research undertaken, with data being collected sequentially, and within and between methods triangulation used in discussing the results. The studies explored the experience of the quality of reconciliation between primary and secondary care, the impact of transitions on the continuity of medication, the most effective methods of reconciliation and the experience of key HCPs on the challenges in implementing reconciliation.

The generalisability of the findings beyond the various study populations may impact on the external validity (e.g. the low response rate to the questionnaire) however sampling for the questionnaire and interviews was wide-ranging and broadly representative. The cohort study recruited GP practices nationally and the systematic review had few study exclusion criteria to include the broadest ranges of studies. Nevertheless, particular settings were not studied – paediatric, maternity and private hospitals. These groups deserve more attention, which is particularly important in view of the findings of this study around the care provided to private patients.
The qualitative research was strengthened by inter-method triangulation of results between the questionnaire and interviews, as well as the broad sampling strategy that recruited participants nationally. Nevertheless, there are possible limitations. The use of an existing theoretical framework and the fact that coding was primarily undertaken by one researcher may have influenced the coding and attribution of meaning.

The impact of the systematic review is lessened by the methodological quality of the included studies, the significant heterogeneity of the results of the meta-analysis, the lack of economic analysis and limited focus on clinically relevant patient outcomes.

Finally, the cohort’s internal validity is challenged by the use of a new data source with distinct limitations requiring pragmatic decisions on the preparation and analysis of the data. These limitations were countered by robust interrogation and sensitivity analysis of assumptions and comparison with existing literature.

8.10 Considering the impact of this thesis

According to Kuruvilla et al., the impact of health research can be measured across four domains:(376)

- Research related impact
- Policy impact
- Health service impact
- Societal impact

8.10.1 Research impact (including implications for future research)

There are a number of ways in which this thesis has had a research impact.
This is the largest primary care based study ever conducted in Ireland to examine discontinuity of medication post hospitalisation. In addition, the cohort study that accomplished this used a novel data collection method that required an innovative collaboration between industry and academic research. This provides a natural partnership for future research efforts.

The systematic review is the first review to apply the rigour of the Cochrane methodological process to the area of medication reconciliation. It provides evidence on the impact (or lack thereof) of interventions (avoiding quasi experimental and observational studies) on the reconciliation process and highlights clear deficits in the literature to date and provides goals for future interventional studies (e.g. selection of more clinically relevant outcomes, economic analysis, outcome and intervention definition clarity). Future Cochrane registered reviews of the reconciliation literature should expand outcome selection to include patient related outcomes (ADEs, rehospitalisation) and continue to underline the lack of certainty in the effectiveness of reconciliation due to the poor quality of the evidence to date.

The cohort study demonstrated a proof of concept of developing an electronic finder tool within the umbrella of the IPCRN to harness GP prescribing records and hospital provided hospitalisation records. This novel data source will allow comparison with other administrative data sources, allowing a closer inspection of the data available to clinicians as they make prescribing decisions. Plans are in place to continue following this cohort, with further recruitment, and to examine additional outcomes such as other classes of
medications, and potentially inappropriate prescribing pre and post hospitalisation.

The unexpected association of reduced discrepancies in those hospitalised, in certain medication groups, needs to be further investigated by continuing follow up of this cohort. It also challenges pharmacoepidemiological researchers to consider the potential for variation between the well examined administrative/dispensing databases and (this study’s) doctor (GP) records.

The qualitative studies identified key areas for future implementation research and quality improvement strategies to consider. For example, plan-do-study-act (PDSA) actions and process mapping exercises could be targeted at issues identified in this thesis—such as multidisciplinary teams, ICT usage and reconciliation, as well as communication at discharge.

The studies in the thesis benefited from the involvement of a number of undergraduate medical students who were upskilled in research methods (e.g. study design, data collection/management, and ethics) as well co-authoring output from the research.

This thesis contributed to a broader package of work, within the HRB Centre for Primary Care Research, examining the quality of prescribing. The studies recruited interested participants and established a network of 44 GP practices enthusiastic about contributing data to examine the issue of medication reconciliation.

Importantly in terms of dissemination and increased impact this research has resulted in three publications to date, with further
publications planned, and has been presented at both national and international health services research and primary care conferences.

The PhD student was recognised for his development as researcher by being invited to address an audience of new and prospective researchers at the Irish College of General Practitioners Research & Audit conference (2015) as well as being awarded a travel bursary to attend the WONCA Young Researcher of the Year finalists’ competition (2015).

8.10.2 Policy impact

The HSE’s eHealth strategic initiatives and appointment of a Chief Information Officer is welcome. The requirement for standardised datasets and future introduction of a unique health identifier are also important. These are necessary steps as ICT infrastructure was continually highlighted by participants in this thesis’s research as being important for successful medication reconciliation (e.g. shared databases, and decision support systems).

Service provision and remuneration issues were an important theme in the output from this thesis. The staffing levels, in particular the provision of pharmacists at hospital discharge is a clear gap in reconciliation provision currently. The service provision is known to vary throughout the country and may be impacting on quality of the service experienced by patients at transitions. Evidence from this thesis shows that there is support for an increased role for hospital pharmacists and that there is an evidence base that they can reduce medication discrepancies. This needs to be considered at a national level as a quality of care issue.
Community pharmacists are positive about taking more of a role in medication review and avoidance of error (which is supported by GP respondents). This expanded role needs to be considered against the current contractual agreements and possible increased remuneration requirements.

The possibility of expanded roles for community and hospital pharmacist necessitates clarity on role definition and greater acceptance of these HCPs as part of multidisciplinary teams. This cultural and organisational change may be helped by training, institutional support and support from senior clinicians/management (as has been seen in other jurisdictions). (48, 377)

The coordination of private patients’ medication is more unclear, with primary care providers often unsure of what medications have been reconciled. This obviously gives rise to concern in terms of drug to drug interactions, monitoring and drug allergies. The unequal treatment of these two patient groups needs to be considered at a policy level.

Medication reconciliation is an element of the broader quality in prescribing initiative. The PhD candidate is a member of the Quality in Practice committee of the Irish College of General Practitioners and has continuously fed back output from the thesis and supported publications from the College on medication review, potentially inappropriate prescribing etc.

8.10.3 Health service impact

This thesis highlights a number of areas that impact on health service delivery.

Greater adoption of cross setting HIT/ICT solutions (shared medication databases) and decision support in CPOE have
been recommended by HCPs (Sections 4.4.2.1 and 7.4.2.5) This is urgently needed – especially considering the quality of information exchanged through electronic discharge summaries seen in this thesis. Similar to the impact in policy, greater attention needs to be given to an expanded role for pharmacists in medication error identification and prevention – including recognising the current uneven distribution of pharmacy services nationwide. Neither of these initiatives has undergone a cost benefit analysis – which should be considered in any evaluation of implementation. Finally, the fragmented medication management care provided to private patients needs to be addressed.

8.10.4 Societal impact

The number of older Irish people is growing, with an increasing number of people taking multiple medications regularly. Interactions with difference healthcare providers are common and medication errors at these transitions of care are also known to be extremely common, with the most vulnerable patients often the most likely to be affected. This thesis provides a clear list of areas that may facilitate the implementation of medication reconciliation. Improved management of medications at transitions of care will have an impact on the quality of prescribing, with possible reductions in healthcare costs and ADEs. It highlights the deficits in attitudes and behaviours of HCPs around medication reconciliation. It acknowledges the reasons for poor patient involvement in reconciliation (e.g. health literacy) as well as recognising the patient’s role as essential in improving the service. The thesis uncovers a disparity in the care received between private and public patients – which hopefully can be addressed through policy and health service changes.
8.11 Conclusion

This thesis adds to the body of evidence on medication management in Ireland and adheres to The “Building a Culture of Patient Safety” report recommendation that national standards for transitional care should be a multidisciplinary effort with contributions from both primary and secondary care.(49,178)

The principal findings from this thesis are that the reported experience of prescribing errors post transitions is extremely common among primary care based HCPs. However, discontinuity of medication, in those prescribed specific long-term medication, is relatively low, with no increased risk of discontinuity in those who’ve experienced hospitalisation. The documentation of medication on electronic discharge summaries is poor and does appear to be associated with discontinuity in the post-hospitalisation period.

Interventions to reduce discrepancies through reconciliation are successful, particularly at admission to hospital, and are predominately delivered by pharmacists. However, the certainty of this effect is unclear due to the low quality of the evidence – therefore no recommendation can be made for or against reconciliation in reducing discrepancies. In addition, their impact on more clinically orientated outcomes is also uncertain.

The implementation of reconciliation is supported by concentrating on some key areas including staff training, effective multidisciplinary teams, greater involvement of pharmacists, ICT solutions, and increased funding.

This thesis provides clear aims for future research efforts including - better design of experimental trials of reconciliation;
opportunity to examine a large cohort of electronically collected primary care based prescribing and clinical data on reconciliation practices; challenges the heretofore accepted link between transitions and discrepancies and provides a list of key areas for implementation research of medication reconciliation.

Medication reconciliation is known to be a complex process prone to error and is considered important in the safe transition of patients between different healthcare providers and settings. Identifying the key areas of concern, such as the patients and medications most at risk, the strategies most likely to reduce errors and the task, and the individual and organisational factors likely to play a role is of crucial importance. This thesis adds to the literature in this area by addressing each of these areas and provides firm evidence on the impact of transitions post hospital discharge on medication continuity, explores successful reconciliation interventions, and lists the key suggestions of stakeholders in implementing reconciliation.
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Appendices
Appendix A Location of Health Service Executive’s (HSE) four regions and 50 acute care hospitals (378)

Location of HSE’s Four Regions & 50 Acute Care Hospitals
Appendix B Questionnaire - Ethical Approval

Royal College of Surgeons in Ireland
The Research Ethics Committee
121 St. Stephen's Green, Dublin 2, Ireland.
Tel: +353-1-6027700 Email: research@rcsi.ie

Dr. David Smith, Acting Chair
Dr. Niamh Clarke, Convenor
4th June 2014

Dr. Patrick Redmond
Dept. of General Practice,
RCSC, Inner Ward Street,
Dublin 2

<table>
<thead>
<tr>
<th>Reference No.</th>
<th>R13923</th>
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<td>Project Title</td>
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Researchers/Investigating Team

<table>
<thead>
<tr>
<th>Principle investigator</th>
<th>Prof. Fiona Galvin, Professor of General Practice, RCSI</th>
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<tbody>
<tr>
<td></td>
<td>Dr. Patrick Redmond (Dept of General Practice, RCSI)</td>
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<tr>
<td></td>
<td>Dr. Tamsin Grimes (School of Pharmacy, UCD)</td>
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<td></td>
<td>Dr. Emily Connolly (Dept of Health Services Research, RCSI)</td>
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<td>Dr. Fiona Boland, Statistical Advisor, RCSI</td>
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<td></td>
<td>Prof. James Barry, Professor of Primary Care Pharmacy, University of Sheffield</td>
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<td></td>
<td>Dr. Helen Carroll (Dept of General Practice, RCSI)</td>
</tr>
<tr>
<td></td>
<td>Dr. Aisling O'Sullivan (HRB Centre for Primary Care, RCSI)</td>
</tr>
</tbody>
</table>

Dear Dr. Redmond,

Thank you for your Research Ethics Committee (REC) application. We are pleased to advise that ethical approval has been granted by the committee for this study.

This letter provides approval for data collection for the time requested in your application and for an additional 6 months. This is to allow for any unexpected delays in proceeding with data collection. Therefore, this research ethics approval will expire on 4th April 2015.

Where data collection is necessary beyond this point, approval for an extension must be sought from the Research Ethics Committee.

This ethical approval is given on the understanding that:

- All personnel listed in the approved application have read, understand and are thoroughly familiar with all aspects of the study.
- Any significant change which occurs in connection with this study and which may alter its ethical consideration must be reported immediately to the REC, and an ethical amendment submitted where appropriate.
- Please submit a final report to the REC upon completion of your project.

We wish you all the best with your research.

Yours sincerely,

[Signature]

[Name]

[Title]
Appendix C  Questionnaire Participant Information Leaflet

Study Information Sheet
Study Title:
Cross-sectional survey of general practitioner and community pharmacists' opinions on medication management at transitions of care in Ireland
Principal Investigator’s Name: Patrick Redmond
Principal Investigator’s Title: Dr
Telephone No. of Principal Investigator: +353 1 402 2722

You are being invited to take part in a research study carried out by The HRB Centre for Primary Care Research, Royal College of Surgeons in Ireland (RCSI). This document provides information about the study so that you can make an informed decision about whether or not you would like to participate in this project. Your participation in the study is completely voluntary. If you decide you do not want to take part, you are free to withdraw from the study at any time without explanation.

You should clearly understand the risks and benefits of taking part in this study so that you can make a decision that is right for you.

You do not have to take part in this study. You can change your mind about taking part in the study any time you like.

Why is this study being carried out?
The study includes a brief questionnaire to pharmacists and GPs interacting with patients as a routine part of their clinical work. The registers of the Pharmaceutical Society of Ireland and the Irish College of General Practitioners have been used to compile a representative sample of community pharmacists and general practitioners. The questionnaire seeks to learn about medication management as patients experience transitions in care. This information will help to better describe suspected issues of poor information transfer and disruption of appropriate chronic medication as patients move between different health care professionals.

Who is organising and funding this study?
This study is organised by a team of researchers from the HRB Centre for Primary Care Research based in the Royal College of Surgeons in Ireland (RCSI). It is being led by a doctoral researcher (Patrick Redmond) for the purposes of a PhD degree. This study is funded by the HRB Centre for Primary Care Research.

The research group comprises of:
Professor Tom Fahey, Head of Department of General Practice, RCSI and the HRB Centre for Primary Care Research, RCSI
Dr Tamasine Grimes, TCD School of Pharmacy
Dr Fiona Boland, Statistician, RCSI
Professor Carmel Hughes, Professor of Primary Care Pharmacy, School of Pharmacy, QUB, Belfast
Dr Ronan McDonnell, Post-doctoral researcher, RCSI.
Dr Patrick Redmond, General Practitioner & Lecturer in RCSI and PhD student
Dr Rose Galvin, HRB Centre Research Manager, RCSI

How will the study be carried out?
The study includes a brief questionnaire to pharmacists and GPs interacting with patients as a routine part of their clinical work. The questionnaire seeks to learn about medication management as patients experience transitions in care. This information will help to better describe suspected issues of poor information transfer and disruption of appropriate chronic medication as patients move between different health care professionals.

What will happen to me if I agree to take part?
You will be asked a brief series of questions on your experiences and attitudes on around the issues of medication management. The questionnaire should take no longer than 5-10 minutes of your time. Your responses to the survey will be uploaded to be collected by the study administrators.

What are the benefits?
Disruption of medication regimens and lack of continuity in appropriate long term medication usage is a problem that has not been described in Ireland before. This study will analyse community healthcare professionals’ experience of potentially
unintentional discontinuation of medication in the transfer between secondary and primary care. In considering the long-term goal of the HRB Centre for Primary Care Research to develop a shared medication record to improve transitions of care for vulnerable patients, this observational study is essential in describing the clinical problem at a national level. Participating in this study and using the opportunity to engage in reading around the topic of medication reconciliation may be recorded for professional competence purposes e.g. personal CPD points for the ICGP scheme.

**What are the risks?**
The potential for risks from taking part in this study are minimal as it is essentially attitudinal information that is being collected. Patient treatment will continue as normal.

**Is the study confidential?**
The survey is anonymous and confidential. Individual results will be aggregated anonymously and research reported on aggregate results. Aggregated anonymous study data will be stored separately on a secure password protected server in RCSI. Study data will be subject to the strict data management policy of RCSI. Analysis of the study data will be presented at conference(s) and published in appropriate peer reviewed journals.

**Where can I get further information?**
If you have any further questions about the study, or if you wish to withdraw from the study you may do so without justifying your decision and your future interaction with the study team will not be affected, please contact:

<table>
<thead>
<tr>
<th>Name</th>
<th>T:</th>
<th>Email</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dr Patrick Redmond</td>
<td>+355 14072722</td>
<td><a href="mailto:predmond@rcsi.ie">predmond@rcsi.ie</a></td>
</tr>
<tr>
<td>Professor Tom Fahey</td>
<td>+353 14022305</td>
<td><a href="mailto:tomfahey@rcsi.ie">tomfahey@rcsi.ie</a></td>
</tr>
</tbody>
</table>

Thank you for your time and interest.
Appendix D  Questionnaire Participant Consent Form

Title of Study:
Cross-sectional survey of general practitioner and community pharmacists’ opinions on medication management at transitions of care in Ireland
By completing and returning this survey you are agreeing to the following:

- I am 18 years or older and am competent to provide consent
- I am working as a pharmacist/general practitioner in Ireland
- I understand that I have been invited to participate in an internet based survey
- I am aware of the potential risks of this research study
- I agree that my data is used for scientific purposes and I have no objection that my data is published in scientific publications in a way that does not reveal my identity
- I freely and voluntarily agree to be part of this research study, though without prejudice to my legal and ethical rights
- I understand that I may refuse to answer any question and that I may withdraw at any time
- I understand that my participation is fully anonymous and that no personal details about me will be recorded
- I have read and I understand this consent form. I understand the description of the research that has been provided to me in the study information page preceding this consent page. I have opportunity to ask questions via email

Storage and future use of information:
I give my permission for information collected about me to be stored or electronically processed for the purpose of scientific research and to be used in related studies or other studies in the future but only if the research is approved by a Research Ethics Committee.

PLEASE DO NOT NAME THIRD PARTIES IN ANY OPEN TEXT FIELD OF THE QUESTIONNAIRE. ANY SUCH REPLIES WILL BE ANONYMISED

Thank you for reading this far, the questionnaire will begin on the next page
Medication Reconciliation Questionnaire – Demographics:

1. Gender:
   - Male
   - Female

2. Age
   - ≤30
   - 31-40
   - 41-50
   - 51-60
   - >61

3. Please identify the term that most accurately describes your role as a pharmacist?
   - Superintendent pharmacist
   - Supervising pharmacist
   - Other

4. Which of the following would you describe yourself as?
   - Employee
   - Employer
   - Locum

5. How would you describe your place of work?
   - Inner city
   - City suburbs
   - Large town
   - Small town/rural

6. Which one of the following HSE regions do you primarily practice within?
   - HSE Dublin North East
   - HSE Dublin Mid Leinster
   - HSE West
   - HSE South

7. What is the average number of hours you work per week?
   - 10 or less
   - 11-20
   - 21-30
   - 31-40
   - >40

8. On average, how many prescriptions in total does the pharmacy (in which you work most often) currently dispense per month? (Please tick the appropriate option below)
   - <1000
   - 1000-3000
   - >3000

9. Which one of the following best describes the community pharmacy in which you work?
   - An independent pharmacy
   - A small group pharmacy
   - A large chain pharmacy

10. How close to your pharmacy are the following?

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<tr>
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<th>&lt;5km</th>
<th>5-15km</th>
<th>16-20km</th>
<th>21-40km</th>
<th>&gt;40km</th>
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</tbody>
</table>
11. On average, what percentage of your monthly prescription volume are General Medical Services (GMS) Scheme prescriptions? *in the pharmacy in which you work most often*

- <25%
- 26-50%
- 51-75%
- 76-100%

12. Is your pharmacy computerised?
- Yes
- No

13. If computerised, what software package (if any) do you use in your pharmacy?
- System Solutions QicScript
- System Solutions QicScript Windows
- McLernons DoS
- McLernons MPS
- Ocuco Prometheus
- Other *(please specify below)*

**Description of Medication Management Systems**

14. When dispensing medications to a patient who has experienced a care transition, who regularly uses your pharmacy, do you have a system to identify the following?

<table>
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<tr>
<th></th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omission of a regularly prescribed medication</td>
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<td></td>
</tr>
<tr>
<td>Newly commenced medication</td>
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<td></td>
</tr>
</tbody>
</table>

Please provide any additional information you feel is worthwhile e.g. description of systems, gaps in care

**Medication accuracy**

15. In general, how would you rate the quality of communication you have with the following? *(From very good to very poor or not applicable)*

<table>
<thead>
<tr>
<th></th>
<th>Very good</th>
<th>Good</th>
<th>Neutral</th>
<th>Poor</th>
<th>Very Poor</th>
<th>Not applicable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local General Practitioner</td>
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<tr>
<td>Local public hospital</td>
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<td>Local private hospital</td>
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</tbody>
</table>

Please provide any additional information you feel is worthwhile about the quality of the communication you have with the sources identified above.

16. What is the extent of your agreement that changes made to a patient’s medication (e.g. stopping a medication) are adequately communicated to you by the following sources? *(From strongly agree to strongly disagree)*

<table>
<thead>
<tr>
<th></th>
<th>Strongly agree</th>
<th>Agree</th>
<th>Neutral</th>
<th>Disagree</th>
<th>Strongly disagree</th>
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<td>Local General Practitioner</td>
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<tr>
<td>Local Private Hospital</td>
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</tbody>
</table>
17. Thinking of your practice - When preparing and dispensing prescriptions or updating medication records (from any prescriber), how important is it that the following information is provided to you? (From very important to unimportant)

<table>
<thead>
<tr>
<th>Information</th>
<th>Very Important</th>
<th>Important</th>
<th>Moderately important</th>
<th>Of little importance</th>
<th>Unimportant</th>
</tr>
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<tr>
<td>List of all current medications the patient uses</td>
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<tr>
<td>Drug indication</td>
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<tr>
<td>Duration</td>
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<tr>
<td>Details of allergy status</td>
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<td>Details of known previous adverse effects to medication</td>
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<td>Special requirements of administration</td>
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<tr>
<td>Change to long term medication list</td>
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<tr>
<td>Reason for changes made to previously used medication</td>
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Are there other pieces of information that you consider important to document on a prescription?

18. Which one of the following best completes the following sentence?

“The community pharmacist’s role in identifying and preventing prescribing errors in prescriptions as patients experience care transitions should be...

- expanded from what it currently is”
- Remain the same”
- ...Be less than what it currently is”

Please provide any additional information you feel is worthwhile about the role of community pharmacists in identifying/preventing prescribing errors at transitions.

19. Which one of the following best completes the following sentence?

“The hospital pharmacist’s role in identifying and preventing prescribing errors in prescriptions as patients experience care transitions should be...

- expanded from what it currently is”
- ...Remain the same”
- ...Be less than what it currently is”

Please provide any additional information you feel is worthwhile about the role of hospital pharmacists in identifying/preventing prescribing errors at transitions.

The following is an accepted definition of the concept of medication reconciliation:

Medication reconciliation is a means of compiling a highly accurate list of medicines which a patient may be currently taking and comparing this list to medicines listed in the patient notes or in prescriptions issued to them, especially in relation to the care of patients being transferred from one care setting to another. The process is also about ensuring that any changes made to medications in one setting are communicated when the patient moves to another healthcare setting.

20. Please rate the following statements in terms of your agreement in relation to medication reconciliation (from strongly agree to strongly disagree)

<table>
<thead>
<tr>
<th>Statement</th>
<th>Strongly agree</th>
<th>Agree</th>
<th>Neutral</th>
<th>Disagree</th>
<th>Strongly Disagree</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reconciling medication at the...</td>
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</table>
Community pharmacy is an important way to improve medication safety

Reconciling medication lists with the patient is an important way to improve medication adherence

A community pharmacist’s time is well spent with the patient updating the patient medication list

Reconciling medication is a responsibility best handled by community pharmacists

The Irish Commission on Patient Safety and Quality Assurance in their report – “Building a culture of patient safety” recommended in 2008 that:

“As part of the safety and quality governance framework, healthcare organizations must prioritise the implementation of formal medication reconciliation systems. This would include regular tracking audits and the deployment of suitable resources for this purpose”.

Please answer the following questions in light of the above statement

21. How clear do you find this recommendation?
   - Not clear at all
   - Somewhat unclear
   - Undecided
   - Somewhat clear
   - Completely clear

22. Do you feel this recommendation applies to you?
   - Yes
   - No

Please provide any additional information you feel is worthwhile about the regulatory impetus behind medication reconciliation

Experience of Prescribing Errors/Issues

23. In the past 6 months, can you remember a time where mistakes have happened in patients’ medications which may have been due to poor transfer of information following a care transition (e.g. delayed or no discharge prescription available, omission of long-term medications)?
   - Yes
   - No

24. If you answered yes to question 24, then please give one example.
   (N.B. please do not name any third party or organisation)

25. If you have experienced such mistakes, in your experience, which source (s) account for these mistakes? Please tick all that apply

361
Outpatient Department (OPD) Prescriptions
Emergency Department (ED) Prescriptions
Inpatient hospital discharge prescriptions
Private hospital prescriptions
Other

Please provide any additional information you feel is worthwhile about the quality of information from different sources of prescriptions.

26. In those patients who have experienced a transition of care, that you have dealt with in the past six months, what if any problems have you encountered? Please tick all that apply:
- Patient’s previously known medication apparently missing from prescription
- Dose or frequency error
- Illegibility
- Duplication of therapy
- No clear indication/reason for initiating therapy
- Interactions
- Prescription of a known allergen
- No problems
- Other

27. In those patients whom you have received a prescription transcribed by their GP from an original hospital prescription – how likely is it to encounter errors?
- Very likely
- Likely
- Neutral
- Unlikely
- Very unlikely

Please provide any additional information you feel is worthwhile on errors you may have encountered.

28. In general, if you encounter potential mistakes in prescriptions from the hospital, how are they handled? Please tick all that apply:
- I attempt to contact the hospital prescriber
- I attempt to contact the patient’s GP
- I attempt to correct the problem myself and don’t contact the prescriber
- Other

29. If you do attempt to contact the hospital prescriber, how easy is this to do?
- Very easy
- Easy
- Neutral
- Difficult
- Very difficult

Please provide any additional information/experience you may have about the ease of contacting prescribers.

Thank you for completing the questionnaire. Your responses are anonymous. Please return the questionnaire in the envelope provided.

If you require further information on the topics being discussed here, feel free to contact Patrick Redmond at predmond@rcsi.ie
Appendix F  Questionnaire – GP Copy

Demographics:
30. Gender:
   o Male
   o Female

31. Age
   o ≤30
   o 31-40
   o 41-50
   o 51-60
   o >61

32. Are you a:
   o GP Registrar
   o GP within 5 years of attaining specialist training qualification
   o GP beyond 5 years of attaining specialist training qualification

33. Do you work as:
   a) Independent GP
   b) With other GPs in a larger practice
   c) In a healthcare centre with other healthcare professionals

34. If you answered (c), please specify the other healthcare professional groups you work with (Please tick all that apply):
   o Public health nurse
   o Occupational therapist
   o Physiotherapist
   o Psychologist
   o Psychiatry
   o Other ____________________

35. How would you describe your employment status?
   o Employee
   o Employer

36. Is your place of work:
   o Inner city
   o City suburbs
   o Large town
   o Small town/rural

37. Which one of the following HSE regions do you primarily practice within?
   o HSE Dublin North East
   o HSE Dublin Mid Leinster
   o HSE West
   o HSE South

38. What is the average number of hours you work per week?
   o 10 or less
   o 11-20
   o 21-30
   o 31-40
   o >40

39. How many patients do you see in an average session? (a session being a half day or approximately 4 hours)
   o <10
   o 10-14
   o 15-19
   o 20-25
   o >26

40. How close to your practice are the following?

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<th>&lt;5km</th>
<th>5-15km</th>
<th>16-20km</th>
<th>21-40km</th>
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363
Description of Current Medication Management Practice

41. Do you have a formal system of managing medication prescriptions as patients are discharged from hospital?
   - Yes
   - No

Please provide any additional information you feel is worthwhile (e.g. description of practices prescription management system)

42. In general, would describe your system of managing patients' prescriptions as being "computerised"?
   - Yes
   - No

43. Do you receive discharge messages electronically that include information on patient’s medication list upon discharge?
   - Never
   - Yes – Some hospitals I communicate with
   - Yes – All hospitals I communicate with

44. If you answered 'Yes' to Q.14 – If the hospital communicates electronically to you changes made to a patient’s long term medication, are these changes easy to incorporate in to your prescribing records?
   - Yes
   - No

If you answered 'No' please provide details as to why changes may not be incorporated easily:

Medication Accuracy

45. On referral letters that you receive from other healthcare providers, how important is it to include the following information regarding the patient's medication? (rated from very important to unimportant)

<table>
<thead>
<tr>
<th>Information Provided</th>
<th>Very Important</th>
<th>Important</th>
<th>Moderately important</th>
<th>Of little importance</th>
<th>Unimportant</th>
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Please provide any additional information you feel would be useful to receive on patients’ prescriptions:

46. Do you think the indication for medications should be included on prescriptions from the hospital/consultant?
   - o Yes
   - o No

47. Thinking of your practice - When transcribing hospital/consultant prescription requests or updating medication details, if the indication has not been made clear to you, how likely are you to proceed with the transcription? (From very likely to very unlikely)
   - o Very Likely
   - o Likely
   - o Neutral
   - o Unlikely
   - o Very unlikely

Please provide any additional information you feel is worthwhile on adhering to other prescribers’ instructions

**Relationship with other prescribers**

48. In general, how would you rate the quality of communication you have with the following regarding medications? (From very good to very poor or not applicable)

<table>
<thead>
<tr>
<th></th>
<th>Very good</th>
<th>Good</th>
<th>Neutral</th>
<th>Poor</th>
<th>Very Poor</th>
<th>Not applicable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Public Hospital</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Community Pharmacist</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospital Pharmacist</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Private Hospital</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

49. Which one of the following best completes the following sentence?
   “The community pharmacist’s role in identifying and preventing prescribing errors in prescriptions as patients experience care transitions should be...
   - o ...expanded from what it currently is”
   - o ...Remain the same”
   - o ...Be less than what it currently is”

Please provide any additional information you feel is worthwhile about the role of community pharmacists in identifying/preventing prescribing errors at transitions.

50. Which one of the following best completes the following sentence?
   “The hospital pharmacist’s role in identifying and preventing prescribing errors in prescriptions as patients experience care transitions should be...
   - o ...expanded from what it currently is”
   - o ...Remain the same”
   - o ...Be less than what it currently is”

Please provide any additional information you feel is worthwhile about the role of hospital pharmacists in identifying/preventing prescribing errors at transitions.

The following is an accepted definition of the concept of medication reconciliation:

*Medication reconciliation is a means of compiling a highly accurate list of medicines which a patient may be currently taking and comparing this list to medicines listed in the patient notes or in prescriptions issued to them, especially in relation to the care of patients being transferred from one care setting to another. The process is also about ensuring that any changes made to medications in one setting are communicated when the patient moves to another healthcare setting.*

51. Please rate the following statements in terms of your agreement in relation to medication reconciliation (from strongly agree to strongly disagree)

---

Please provide any additional information you feel is worthwhile on medication reconciliation.
<table>
<thead>
<tr>
<th>Statement</th>
<th>Strongly agree</th>
<th>Agree</th>
<th>Neutral</th>
<th>Disagree</th>
<th>Strongly Disagree</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reconciling medication during clinic is an important way to improve medication safety</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>It is valuable for the patient to complete a medication history at each visit to the practice</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reconciling medication lists with the patient is an important way to improve medication adherence</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A GP’s time with the patient is well spent updating the patient medication list</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>The GP should take responsibility for reconciling all medications</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I cannot assume responsibility for reconciling medications that other providers prescribe</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reconciling medication is a responsibility best handled by pharmacists</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The Irish Commission on Patient Safety and Quality Assurance in their report – “Building a culture of patient safety” recommended in 2008 that:

“As part of the safety and quality governance framework, healthcare organizations must prioritise the implementation of formal medication reconciliation systems. This would include regular tracking audits and the deployment of suitable resources for this purpose.”

Please answer the following questions in light of the above statement:

52. How clear do you find this recommendation?

  o  Not clear at all
53. Do you feel this recommendation applies to you?
   - Yes
   - No
   Please provide any additional information you feel is worthwhile about the regulatory impetus behind medication reconciliation.

54. What is your opinion on the standard of medication reconciliation that occurs in your place of work?
   - Poor
   - Fair
   - Good
   - Very good
   - Excellent

55. Experience of Prescribing Errors/Issues
   In the past 6 months, can you remember a time where mistakes have happened in patients' medications due to poor transfer of information following a care transition (e.g. delayed or no discharge prescription available, absent long-term medications?).
   - Yes
   - No

56. If you answered yes to question 26 then please give one example.
   (N.B. please do not name any third party or organisation)

57. If you have experienced such mistakes, in your experience, which source(s) account for these mistakes? Please tick all that apply
   - Outpatient Department (OPD) Prescriptions
   - Emergency Department (ED) Prescriptions
   - Inpatient hospital discharge prescriptions
   - Private hospital prescriptions
   - Other
   Please provide any additional information you feel is worthwhile about the quality of information from different sources of prescriptions.

58. What problems on prescriptions have you encountered? Please tick all that apply
   - Patient’s previously known medication apparently missing from prescription
   - Dosing error
   - Illegibility
   - Duplication of therapy
   - No clear indication/reason for initiating therapy
   - Interactions
   - Prescription of a known allergen
   - Other
   Please provide any additional information you feel is worthwhile on errors you may have encountered.

59. In general, how do you handle potential mistakes in prescriptions from the hospital? Please tick all that apply
   - I contact the hospital prescriber
   - I correct the problem myself and don’t contact the prescriber
   - I don’t alter the prescription
   - Other

60. If you do attempt to contact the original prescriber, how easy is this to do?
   - Very easy
   - Easy
   - Neutral
   - Difficult
Impossible
Please provide any additional information/experience you may have about the ease or otherwise of contacting prescribers
Thank you for completing the questionnaire. Your responses are anonymous.
If you require further information on the topics being discussed here, feel free to contact Patrick Redmond at predmond@rcsi.ie
## Ordered logistic regression of responses to communication between secondary care and GP/CP communication

### Table 9-1
Ordered logistic regression of responses to communication between secondary care and GP/CP communication

<table>
<thead>
<tr>
<th>HEALTHCARE PROVIDER</th>
<th>Adjusted odds ratios (95% CI, p-value) **</th>
<th>With Public Hospital (n=779) †</th>
<th>With Private Hospital (n=702) †</th>
</tr>
</thead>
<tbody>
<tr>
<td>GP</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>CP</td>
<td>0.98 (0.73, 1.31) p=0.87</td>
<td>0.66 (0.48, 0.90) p=0.01</td>
<td></td>
</tr>
<tr>
<td>AGE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;30 years</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>31-40 years</td>
<td>1.48 (0.92, 2.39) p=0.11</td>
<td>1.27 (0.77, 2.09) p=0.37</td>
<td></td>
</tr>
<tr>
<td>41-50 years</td>
<td>1.94 (1.16, 3.24) p=0.01</td>
<td>1.14 (0.66, 1.95) p=0.647</td>
<td></td>
</tr>
<tr>
<td>51-60 years</td>
<td>2.16 (1.28, 3.64) p=0.004</td>
<td>1.81 (1.04, 3.14) p=0.037</td>
<td></td>
</tr>
<tr>
<td>61+</td>
<td>4.08 (2.18, 7.62) p&lt;0.001</td>
<td>3.43 (1.75, 6.71) p&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>GENDER</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Female</td>
<td>1.03 (0.78, 1.35) p=0.83</td>
<td>1.05 (0.79, 1.41) p=0.72</td>
<td></td>
</tr>
<tr>
<td>LOCATION</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>City Suburbs</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Large Town</td>
<td>1.26 (0.86, 1.87) p=0.23</td>
<td>0.77 (0.53, 1.13) p=0.18</td>
<td></td>
</tr>
<tr>
<td>Inner City</td>
<td>1.31 (0.83, 2.07) p=0.25</td>
<td>0.87 (0.54, 1.39) p=0.55</td>
<td></td>
</tr>
<tr>
<td>Small town/Rural</td>
<td>1.43 (0.93, 2.19) p=0.10</td>
<td>0.83 (0.58, 1.18) p=0.30</td>
<td></td>
</tr>
<tr>
<td>Dublin/ Mid Leinster</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Dublin/ North East</td>
<td>0.59 (0.41, 0.87) p=0.01</td>
<td>0.75 (0.49, 1.11) p=0.15-</td>
<td></td>
</tr>
<tr>
<td>West</td>
<td>0.66 (0.45, 0.95) p=0.03</td>
<td>1.21 (0.82, 1.81) p=0.32</td>
<td></td>
</tr>
<tr>
<td>HSE REGION</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>South</td>
<td>0.81 (0.57, 1.16) p=0.26</td>
<td>1.21 (0.84, 1.75) p=0.30</td>
<td></td>
</tr>
<tr>
<td>HOURS WORKED PER WEEK</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10 or less</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>11-20</td>
<td>1.24 (0.48, 3.21) p=0.65</td>
<td>0.83 (0.29, 2.34) p=0.72</td>
<td></td>
</tr>
<tr>
<td>21-30</td>
<td>0.89 (0.35, 2.28) p=0.82</td>
<td>0.83 (0.30, 2.30) p=0.73</td>
<td></td>
</tr>
<tr>
<td>31-40</td>
<td>1.19 (0.51, 2.78) p=0.68</td>
<td>0.93 (0.37, 2.36) p=0.88</td>
<td></td>
</tr>
<tr>
<td>&gt;40</td>
<td>0.94 (0.41, 2.18) p=0.89</td>
<td>0.74 (0.29, 1.86) p=0.52-</td>
<td></td>
</tr>
<tr>
<td>DISTANCE TO PUBLIC HOSPITAL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;5km</td>
<td>1</td>
<td>N/A</td>
<td>1</td>
</tr>
<tr>
<td>5-15km</td>
<td>0.89 (0.62, 1.29) p=0.56</td>
<td></td>
<td></td>
</tr>
<tr>
<td>16-20km</td>
<td>0.73 (0.44, 1.23) p=0.24</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21-40km</td>
<td>0.70 (0.45, 1.10) p=0.12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;40km</td>
<td>0.66 (0.33, 1.33) p=0.23</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

** Respondents choosing "non-applicable" removed from calculation
N/A: not applicable
†: 5 possible response options ranked very poor, poor, neutral, good, very good
## Appendix H  Ordered logistic regression of the quality of communication between GP and CP

### Table 9-2  Ordered logistic regression of the quality of communication between GP and CP (n=773) ††

<table>
<thead>
<tr>
<th>HEALTHCARE PROVIDER &amp; GENDER</th>
<th>MALE GP</th>
<th>1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male CP</td>
<td>0.40 (0.25,0.62) p&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Female GPs</td>
<td>0.60 (0.41,0.89) p=0.01</td>
<td></td>
</tr>
<tr>
<td>Female CPs</td>
<td>1.55 (0.97,2.49) p=0.07</td>
<td></td>
</tr>
<tr>
<td>MALE GP</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Male CP</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Female GPs</td>
<td>1.55 (0.97,2.49) p=0.07</td>
<td></td>
</tr>
<tr>
<td>Female CPs</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>AGE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;30 years</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>31-40 years</td>
<td>1.26 (0.75,2.12) p=0.38</td>
<td></td>
</tr>
<tr>
<td>41-50 years</td>
<td>1.63 (0.93,2.88) p=0.09</td>
<td></td>
</tr>
<tr>
<td>51-60 years</td>
<td>1.52 (0.86,2.69) p=0.15</td>
<td></td>
</tr>
<tr>
<td>61&gt;</td>
<td>1.09 (0.54,2.18) p=0.81</td>
<td></td>
</tr>
<tr>
<td>LOCATION</td>
<td></td>
<td></td>
</tr>
<tr>
<td>City Suburbs</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Large Town</td>
<td>0.77 (0.51,1.14) p=0.19</td>
<td></td>
</tr>
<tr>
<td>Inner City</td>
<td>0.62 (0.38,1.01) p=0.06</td>
<td></td>
</tr>
<tr>
<td>Small town/Rural</td>
<td>1.09 (0.75,1.59) p=0.65</td>
<td></td>
</tr>
<tr>
<td>HSE REGION</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dublin/ Mid Leinster</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Dublin/ North East</td>
<td>0.84 (0.56,1.26)</td>
<td></td>
</tr>
<tr>
<td>West</td>
<td>1.05 (0.69,1.60) p=0.82</td>
<td></td>
</tr>
<tr>
<td>South</td>
<td>1.28 (0.87,1.89) p=0.22</td>
<td></td>
</tr>
</tbody>
</table>

††: 4 possible response options ranked very poor/poor, neutral, good, very good: the bottom two categories were collapsed due to low numbers.
### Appendix I  STROBE Statement—checklist of items that should be included in reports of observational studies

<table>
<thead>
<tr>
<th>Item No</th>
<th>Recommendation</th>
</tr>
</thead>
</table>
| **Title and abstract** | (a) Indicate the study’s design with a commonly used term in the title or the abstract  
(b) Provide in the abstract an informative and balanced summary of what was done and what was found |
| **Introduction** | |
| Background/rationale | 2 Explain the scientific background and rationale for the investigation being reported |
| **Objectives** | 3 State specific objectives, including any pre-specified hypotheses |
| **Methods** | |
| Study design | 4 Present key elements of study design early in the paper |
| Setting | 5 Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection |
| Participants | 6*(a) Cohort study—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up  
Case-control study—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls  
Cross-sectional study—Give the eligibility criteria, and the sources and methods of selection of participants  
(b) Cohort study—For matched studies, give matching criteria and number of exposed and unexposed  
Case-control study—For matched studies, give matching criteria and the number of controls per case |
| Variables | 7 Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable |
| Data sources/measurement | 8* For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group |
| **Bias** | 9 Describe any efforts to address potential sources of bias |
| Study size | 10 Explain how the study size was arrived at |
| Quantitative variables | 11 Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why |
| Statistical methods | 12*(a) Describe all statistical methods, including those used to control for confounding  
(b) Describe any methods used to examine subgroups and interactions  
(c) Explain how missing data were addressed  
(d) Cohort study—if applicable, explain how loss to follow-up was addressed  
Case-control study—if applicable, explain how matching of cases and controls was addressed  
Cross-sectional study—if applicable, describe analytical methods taking account of sampling strategy  
(e) Describe any sensitivity analyses |
| **Results** | |
| Participants | 13* (a) Report numbers of individuals at each stage of study—e.g. numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed  
(b) Give reasons for non-participation at each stage  
(c) Consider use of a flow diagram |
| **Descriptive data** | 14* | (a) Give characteristics of study participants (e.g., demographic, clinical, social) and information on exposures and potential confounders |
| | | (b) Indicate number of participants with missing data for each variable of interest |
| | | (c) **Cohort study**—Summarise follow-up time (e.g., average and total amount) |
| **Outcome data** | 15* | **Cohort study**—Report numbers of outcome events or summary measures over time |
| | | **Case-control study**—Report numbers in each exposure category, or summary measures of exposure |
| | | **Cross-sectional study**—Report numbers of outcome events or summary measures |
| **Main results** | 16 | (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included |
| | | (b) Report category boundaries when continuous variables were categorized |
| | | (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period |
| **Other analyses** | 17 | Report other analyses done—e.g. analyses of subgroups and interactions, and sensitivity analyses |

**Discussion**

| **Key results** | 18 | Summarise key results with reference to study objectives |
| **Limitations** | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias |
| **Interpretation** | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence |
| **Generalisability** | 21 | Discuss the generalisability (external validity) of the study results |

**Other information**

| **Funding** | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based |

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.*
13th May, 2015

Dr. Patrick Redmond
Royal College of Surgeons in Ireland
Lower Mercer Street,
Dublin 2

Medication Reconciliation - Unintentional discontinuation of long term medication post hospitalisation

Dear Dr. Redmond,

I wish to confirm that I have reviewed your clarifications and I am now happy to grant the above named study ethical approval.

If you have any further questions please contact Sally-Anne O’Neill – sallyanne.o’neill@icgp.ie

Yours sincerely,

Sent on behalf of Dr. Kieran Doran
Chair Research Ethics Committee
12th June, 2014

Dr. Patrick Redmond
Department of General Practice
Royal College of Surgeons
Lower Mercer Street
Dublin 2

Dear Dr. Redmond,

We would like to inform you that the IPCRN Board approved your application on May 27th for 10 months storage of data from the MED-REC project.

Please contact sallyanne.o’neill@icgp.ie to agree timeframes and payment structure and Sally Anne will then issue a contract to you.

Yours sincerely,

[Signature]

Dr. Claire Collins
ICGP Director of Research
IPCRN Acting Manager
Appendix K Cohort Study Practice Invitation Letter

24th March 2015
Dear Dr,
We would like to invite your practice to participate in the Medication Reconciliation study, a research study being conducted via the Irish Primary Care Research Network (IPCRN) for the HRB Centre for Primary Care Research, a collaboration led by the Department of General Practice, RCSI Medical School, with Department of Public Health and Primary Care, TCD and School of Pharmacy, QUB (http://www.hrbcentreprimarycare.ie/).
The study aims to examine the transition of care that vulnerable older patients undertake at the primary secondary care interface. This is an observational study to understand the disruption in patients’ medications as they transition in and out of hospital. Unintentional discontinuation of appropriate long term medication is a recognised hazard of care transitions however it has never been studied in the transition between primary and secondary care in Ireland.
We would like to invite your practice to take part in this study which is a retrospective cohort study primarily examining prescribing records of patients over the age of 65. The study will involve using the facility of the IPCRN to collect data at the practice level (from the prescribing record and Healthlink notification of discharges), anonymise it and then analyse the data to determine who are the patients most at risk of disruption of their medications. Feedback will be given to each practice regarding prescribing and hospitalisation patterns in your patients (e.g. chronic medication use, numbers of hospitalisations and levels of potentially inappropriate prescribing).
We will support GPs participating in the study to undertake an audit which will satisfy internal CME accreditation and Professional Competence requirements from the ICGP and Medical Council.
A practice information sheet (detailing the full study) is attached. We will contact you in a week to ten days after you receive this letter to discuss the study with you. If you have any questions in the meantime, please contact Dr Patrick Redmond (GP & PhD scholar) or Professor Tom Fahey using the contact details below.
Thank you for your time and interest,
Dr Patrick Redmond
GP, Lecturer and PhD Scholar in Health Services Research, RCSI (01 402 2722)

Professor Tom Fahey
Head of Division of Population Health Sciences / PI HRB Centre for Primary Care Research, RCSI
Appendix L Cohort Study Practice Information Leaflet

**Study Title:** Medication Reconciliation - Unintentional discontinuation of long term medication post hospitalisation – Pilot Study

**Principal Investigator’s (PI) Name:** Dr Patrick Redmond

**Telephone No. of Principal Investigator:** 087-9583108  **Email:** predmond@rcsi.ie

You are being invited to take part in a research study carried out by The HRB Centre for Primary Care Research, Royal College of Surgeons in Ireland (RCSI). This document provides information about the study so that you can make an informed decision about whether or not your practice would like to participate in this project.

Your practice’s participation in the study is completely voluntary. If you decide you do not want the practice to take part, you are free to withdraw from the study at any time without explanation.

You should clearly understand the risks and benefits of your practice taking part in this study so that you can make a decision that is right for your practice. This process is known as ‘Informed Consent’.

You do not have to take part in this study. You can change your mind about taking part in the study any time you like. Even if the study has started, you can still opt out. You do not have to give us a reason. Any uploaded data will remain on the system even if the patient has chosen to opt out of the study. If you do opt out, it will not affect the quality of treatment received by your patients or any future interaction with the IPCRN

**WHY IS THIS STUDY BEING DONE?**

The use of medications in older patients is arguably one of the most important interventions in modern medicine. People aged over 65 years old are the most active consumers of healthcare. At present 11% of the Irish population are aged 65 years and over.

As patients move from home to hospital and back again, their prescribed medications are prone to disruption and the long-term medicines used to treat chronic conditions may be stopped either inappropriately or inadvertently and unintentionally. Older patients prescribed multiple medications are most associated with this disruption in medication regimens.

This observational study will use the existing and proven data collection tool of the Irish Primary Care Research Network (IPCRN) to describe the potentially unintentional discontinuation of chronic medications following discharge from hospital.

**WHO IS ORGANISING AND FUNDING THIS STUDY?**

This study is organised by a team of researchers from the HRB Centre for Primary Care Research based in the Royal College of Surgeons in Ireland (RCSI). It is being carried out by a doctoral researcher (Patrick Redmond) for the purposes of a PhD degree. This study is funded by the HRB Centre for Primary Care Research and uses the now firmly established data collection method of the Irish Primary Care Research Network (IPCRN) to securely and anonymously collect data. This study is building on previous research in the area conducted by the HRB Centre for Primary Care Research.

The research group comprises of:

Professor Tom Fahey, Head of Department of General Practice, RCSI and the HRB Centre for Primary Care Research, RCSI

Dr Tamasine Grimes, Associate Professor in Practice of Pharmacy, Trinity College Dublin.

Dr Fiona Boland, Lecturer in Biostatistics and Research Methods, Division of Population Health Sciences, RCSI.

Professor Carmel Hughes, Professor of Primary Care Pharmacy, School of Pharmacy, Queens University Belfast.

Dr Ronan McDonnell, Post-Doctoral Researcher in ICT, HRB Centre for Primary Care Research, RCSI.

Dr Patrick Redmond, General Practitioner, Lecturer in RCSI and PhD student

**HOW WILL IT BE CARRIED OUT?**

This study is an observational retrospective cohort study – a study where a defined group of people is followed and outcomes of interest are recorded as they have already happened in the past. We will use the existing and proven data collection tool of the Irish Primary Care Research Network (IPCRN) to describe the potentially unintentional discontinuation of chronic medications following discharge from hospital. The IPCRN operates at two levels; it allows GPs to generate patient specific data held within the practice for audit and quality improvement and this function facilitates GPs in maintaining the medical council’s requirements for professional
competence. It also allows the export of anonymous data to the IPCRN secured server, which allows each gp practice to be benchmarked against evidence based standards, for comparative clinical purposes. This project uses these functions of the IPCRN network and is a form of clinical audit with a research component. The IPCRN have been involved in running a number of research projects including diabetes and urinary tract infections (www.ipcrn.ie). We will invite GP practices to participate in this study. A cohort of patients ≥65 years will be identified. Data on prescribing, explanatory variables and hospitalisations will be collected. The primary outcome will be potentially unintentional discontinuation of long term medications. This will be identified by reviewing discontinuation of chronic medications before and after an index date comparing hospitalised to non-hospitalised patients. Data will be gathered locally at practice level by a GP initiated electronically run IPCRN report tool within the practice patient management system (Socrates). This tool will anonymise data and submit the report to the IPCRN centrally. In analysing our chosen primary outcome (the number of people who are hospitalised who experience disruption of their appropriate long-term medications) we have estimated we will need 41,363 patients.

The study is due to commence early 2015 and will last 12 months.

**WHAT WILL HAPPEN TO ME IF I AGREE TO TAKE PART?**

By giving your consent to participate, you are agreeing that your practice will submit a computer-generated report via the IPCRN.

If your practice agrees to participate you will be asked to:
- Sign the consent form and place study information leaflets in the practice – available for patients.
- Run the electronic tool provided by the IPCRN within Socrates Patient Management System. No further steps are required on behalf of the practice. The electronic tool will do the following:
- Patients, from participating practices, who meet the eligibility criteria outlined below, will be identified by the software tool within Socrates.
- Healthlink message headers (pre-specified tags or identifiers within the electronic message) will be inspected by the vendor software, with message types referring to 'discharge summary' (also known as referral type message) and 'discharge notification' of specific interest, as this indicates discharge from a hospital setting.
- For these specific message types only, the message bodies will also be examined to identify the discharging hospital and discharge date. A simple text parser will look for keywords such as 'discharge', 'hospital' or the names of the hospitals. Length of stay, discharge diagnosis and medications may also be extracted from the message content. No further information will be extracted from these message bodies.
- All patients (including those who were the subject of a Healthlink 'discharge summary' or 'discharge notification') will have their prescription details from specific time points before and after the index date (discharge date) extracted by the program from the GP prescribing record. Additionally, the age, sex, insurance category, allergy status, number of consultations and diagnoses of patients will be extracted.
- The software tool will submit an anonymised version of the data to be uploaded securely to a server run by the IPCRN. The procedure has already been validated for a number of audit and research tools (www.ipcrn.ie). The tool will remove any identifiers (patient names, addresses, ethnicity and contact details prior to the data being sent) and assign patient IDs instead of patient names prior to upload of file to the secure server. No patient recorded clinical notes will be uploaded. For example, all dates of births will be converted to age only.
- The completed and anonymised data set will be converted by the IPCRN into a MYSQL database for further analysis in RCSI. The IPCRN tool will at the time of submission of anonymous data to the IPCRN server also generate a report for use locally in the GP practice. This will contain details on prescribing patterns, number of hospitalisations and summary record of hospitalisations diagnoses. This report may prove useful in conducting quality improvement audits for the practice as part of the medical council professional competence scheme requirements.

No patients will be contacted and no identifiable individual patient data will be available beyond the practice in this study.

**BENEFITS:**

The study aims to find beneficial ways of assisting GPs optimising prescribing practices for older patients by enhancing prescribing continuity and safety especially following hospitalisation. By participating in this study, information on prescribing in your older patients will be sent directly to
your practice. Disruption of medication regimens and lack of continuity in appropriate long term medication usage is a problem that has not been described in Ireland before. This study will analyse the level of potentially unintentional discontinuation of medication in the transfer between secondary and primary care. It will further describe the incidence of potentially inappropriate prescribing arising from hospitalisation. In considering the long-term goal of the HRB Centre for Primary Care Research to develop a shared medication record to improve transitions of care for vulnerable patients this observational study is essential in describing the clinical problem at a national level.

Participation in this study may be useful in fulfilling continuing professional development (CPD) by review of practice procedures and clinical case management. The research team will support all participants by providing useful localised reports through IPCRN generated reports of practice activity (e.g. prescribing, hospitalisations etc.). The electronic report builder developed for this study will remain available to all participating GPs as part of the IPCRN suite of tools, free of charge.

**RISKS:**
The potential for risks from taking part in this study are minimal as it is a retrospective study involving the submission of anonymised data only. Patient treatment will continue as normal.

**CONFIDENTIALITY ISSUES**
GPs will remain the data controller for their own practice data. Neither the IPCRN nor RCSI will have access to clinical consultation details. Individually identifiable patient data will not be available beyond practice level. Patients will be given a study ID, and identifiable details such as exact date of birth, address or contact details will not be uploaded. Aggregated anonymous study data will be stored separately on a secure password protected server in RCSI following processing in the secure IPCRN server. Study data will be subject to the strict data management policy of RCSI. Individual patients will remain anonymous to the research team; patient confidentiality will remain secure. The IPCRN will collect the anonymous data and subsequently package it into a database format for the research team at the HRB Centre for Primary Care Research for analysis. Data will only be accessible by the named individuals of the study team listed above.

Analysis of the study data will be presented at conference(s) and published in appropriate peer reviewed journals. Upon completion of this study, anonymised data may be accessed by contacting the PI; aggregated anonymous data may be published to the open access resource Irish Social Science Data Archive (ISSDA). A repository for many publicly funded longitudinal studies e.g. Growing Up in Ireland.

**IF YOU REQUIRE FURTHER INFORMATION**
If you have any further questions about the study, or if you wish to withdraw from the study you may do so without justifying your decision and your future treatment will not be affected, please contact:

- Dr Patrick Redmond T: +355 (0) 87 9583108 predmond@rcsi.ie (office hours)
- Professor Tom Fahey T: +353 1 4022305 tomfahey@rcsi.ie (office hours)
Appendix M  Cohort Study Practice Agreement Form

Title of Study:
Medication Reconciliation study – Unintentional discontinuation of long term medication post hospitalisation

Please tick the appropriate answer.
I confirm that I have read and understood the study information leaflet attached, and that I have had ample opportunity to ask questions all of which have been satisfactorily answered. ☐Yes ☐No
I understand that my practice’s participation in this study is entirely voluntary and that I may withdraw at any time, without giving reason. ☐Yes ☐No
I understand that my study related data (prescribing and clinical data for participant patients) following anonymisation may be viewed by individuals with delegated authority from The Royal College of Surgeons. ☐Yes ☐No
I have been given a copy of the Information Leaflet and this completed consent form for my records. ☐Yes ☐No

FUTURE USE OF ANONYMOUS DATA:
I agree that I will not restrict the use of the results for research purposes. I give my approval that unidentifiable data concerning my patients may be stored or electronically processed for the purpose of scientific research and may be used in related or other studies in the future. ☐Yes ☐No
Participant Name (Block Capitals): _______________________
Participant Signature: _______________________
Date: _______________________

To be completed by the Principal Investigator or his nominee.
I the undersigned have taken the time to fully explain to the above participant the nature and purpose of this study in a manner that he/she could understand. I have explained the risks involved, as well as the possible benefits and have invited him/her to ask questions on any aspect of the study that concerned them.
Name: _______________________
Signature: _______________________
Date: _______________________

3 copies to be made: 1 for participant, 1 for PI and 1 for practice records (if relevant).
### Table 9-3 Cohort Study Data Collection Form

<table>
<thead>
<tr>
<th>Anonymised GP id</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Anonymised patient id</td>
<td></td>
</tr>
<tr>
<td>Year of Birth</td>
<td>Year only</td>
</tr>
<tr>
<td>Gender</td>
<td>Male/Female</td>
</tr>
<tr>
<td>Age (extracted, not calculated)</td>
<td></td>
</tr>
<tr>
<td>Number of GP interactions within study period</td>
<td>Quantity</td>
</tr>
<tr>
<td>Active Diagnoses</td>
<td>Quantity</td>
</tr>
<tr>
<td>Social/Past Medical history</td>
<td>Quantity</td>
</tr>
<tr>
<td>Medical Card Status</td>
<td>GMS/None/DVC</td>
</tr>
<tr>
<td>Insurance category</td>
<td>None/Private e.g. VHI/other</td>
</tr>
<tr>
<td>Allergies</td>
<td>Yes/No</td>
</tr>
<tr>
<td>Printed Medication (extract all issues from study start date)</td>
<td>Quantity</td>
</tr>
<tr>
<td>Healthlink Discharge Notification</td>
<td>Quantity</td>
</tr>
<tr>
<td>Practice Coded Hospital Discharge (where available)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Note all above are terms/codes used within the software package*
Appendix O  Cohort Study Patient Flow Diagrams

Figure 9-1  Cohort study – B01 participant flow diagram
Figure 9-2 Cohort study - C10 participant flow diagram
Figure 9-3 Cohort study – H03 participant flow diagram
Figure 9-4 Cohort study – R03 participant flow diagram
### Table 9-4: Descriptive statistics for Reference Group participants (n=24,363) prior to application of the enrolment criteria

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>Mean (SD) 74.51 (7.69)</td>
</tr>
<tr>
<td>Female</td>
<td>n (%) 13,958 (57.29)</td>
</tr>
<tr>
<td>GMS + DVC</td>
<td>n (%) 19,344 (79.39)</td>
</tr>
<tr>
<td>No. of repeat drugs classes</td>
<td>Mean (SD) 4.89 (4.35)</td>
</tr>
<tr>
<td>RxRisk</td>
<td>Mean (SD) 2.91 (2.59)</td>
</tr>
<tr>
<td>Charlson Index</td>
<td>Mean (SD) 0.63 (1.09)</td>
</tr>
</tbody>
</table>

GMS = General Medical Services, DVC=Doctor Visit Card
### Antithrombotics (B01) Group

<table>
<thead>
<tr>
<th>Total (n=10190)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
</tr>
<tr>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Median (IQR)</td>
</tr>
<tr>
<td>Female n (%)</td>
</tr>
<tr>
<td><strong>GMS/DVC n (%)</strong></td>
</tr>
<tr>
<td>Mean (SD)</td>
</tr>
<tr>
<td><strong>Number of Consultations</strong></td>
</tr>
<tr>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Median (IQR)</td>
</tr>
<tr>
<td><strong>Number of Drugs</strong></td>
</tr>
<tr>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Median (IQR)</td>
</tr>
<tr>
<td><strong>RxRisk</strong></td>
</tr>
<tr>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Median (IQR)</td>
</tr>
<tr>
<td><strong>Charlson Index</strong></td>
</tr>
<tr>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Median (IQR)</td>
</tr>
</tbody>
</table>

#### B01 Group (Variables Per Practice)

- **Age**
- **Repeat Drugs**
- **RxRisk Score**
- **Charlson Index**
- **PIP Score**
- **Consultations**
<table>
<thead>
<tr>
<th>Lipid-lowering (C10) Group</th>
<th>Total (n=10585)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>74.64 (6.94)</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>74 (10.59)</td>
</tr>
<tr>
<td>Female n (%)</td>
<td>5914 (55.87)</td>
</tr>
<tr>
<td>GMS/DVC n (%)</td>
<td>9303 (87.89)</td>
</tr>
<tr>
<td><strong>Number of Consultations</strong></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>7.22 (5.99)</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>6 (7)</td>
</tr>
<tr>
<td><strong>Number of Drugs</strong></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>7.22 (4.02)</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>7 (5)</td>
</tr>
<tr>
<td><strong>RxRisk</strong></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>4.51 (2.09)</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>4 (3)</td>
</tr>
<tr>
<td><strong>Charlson Index</strong></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>0.83 (1.22)</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>0 (1)</td>
</tr>
<tr>
<td>Thyroid meds (H03) Group</td>
<td>Total (n=2644)</td>
</tr>
<tr>
<td>-------------------------</td>
<td>----------------</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>75.63 (7.68)</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>75 (12.02)</td>
</tr>
<tr>
<td><strong>Female n (%)</strong></td>
<td>2155 (81.51)</td>
</tr>
<tr>
<td><strong>GMS n (%)</strong></td>
<td>2303 (87.10)</td>
</tr>
<tr>
<td><strong>Number of Consultations</strong></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>7.49 (6.19)</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>6 (7)</td>
</tr>
<tr>
<td><strong>Number of Drugs</strong></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>7.49 (4.39)</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>7 (6)</td>
</tr>
<tr>
<td><strong>RxRisk</strong></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>4.61 (2.34)</td>
</tr>
<tr>
<td>Median</td>
<td>4 (3)</td>
</tr>
<tr>
<td><strong>Charlson Index</strong></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>0.69 (1.12)</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>0 (1)</td>
</tr>
</tbody>
</table>

**H03 Group (Variables Per Practice)**

![Graphs showing variables per practice](image-url)
<table>
<thead>
<tr>
<th>Respiratory inhalers (RO3) Group</th>
<th>Total (n=3933)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>75.39 (7.37)</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>74 (11.54)</td>
</tr>
<tr>
<td>Female n (%)</td>
<td>2329 (59.22)</td>
</tr>
<tr>
<td>GMS n (%)</td>
<td>3496 (88.89)</td>
</tr>
<tr>
<td>Number of Consultations</td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>8.36 (7.03)</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>7 (7)</td>
</tr>
<tr>
<td>Number of Drugs</td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>8.90 (4.62)</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>8 (6)</td>
</tr>
<tr>
<td>RxRisk</td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>5.01 (2.39)</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>5 (4)</td>
</tr>
<tr>
<td>Charlson Index</td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>1.09 (1.32)</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>1 (2)</td>
</tr>
</tbody>
</table>

R03 Group (Variables Per Practice)
Table 9-5 GP Practice & Hospital Region distribution at follow-up period one

<table>
<thead>
<tr>
<th>Total No. of participants at follow-up time 1</th>
<th>Antithrombotics (B01) (N=6,516)</th>
<th>Lipid-lowering (C10) (N=6,890)</th>
<th>Thyroid meds (H03) (N=1,686)</th>
<th>Respiratory Inhalers (R03) (N=2,348)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location of Participants</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Dublin Region</td>
<td>4602</td>
<td>4702</td>
<td>1113</td>
<td>1626</td>
</tr>
<tr>
<td>• West of Ireland</td>
<td>1580</td>
<td>1751</td>
<td>486</td>
<td>614</td>
</tr>
<tr>
<td>• Cork/South-west</td>
<td>265</td>
<td>362</td>
<td>77</td>
<td>79</td>
</tr>
<tr>
<td>• North-East</td>
<td>69</td>
<td>75</td>
<td>10</td>
<td>29</td>
</tr>
<tr>
<td>Location of hospitalisations</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Dublin Region</td>
<td>1360</td>
<td>1261</td>
<td>280</td>
<td>524</td>
</tr>
<tr>
<td>• West of Ireland</td>
<td>534</td>
<td>536</td>
<td>121</td>
<td>214</td>
</tr>
<tr>
<td>• Cork/South-west</td>
<td>74</td>
<td>94</td>
<td>18</td>
<td>28</td>
</tr>
<tr>
<td>• Other</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Individual Hospitals*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Dublin Hospital 1</td>
<td>660</td>
<td>563</td>
<td>150</td>
<td>297</td>
</tr>
<tr>
<td>• Dublin Hospital 2</td>
<td>450</td>
<td>457</td>
<td>87</td>
<td>145</td>
</tr>
<tr>
<td>• Dublin Hospital 3</td>
<td>150</td>
<td>144</td>
<td>29</td>
<td>37</td>
</tr>
<tr>
<td>• Dublin Hospitals (other)</td>
<td>97</td>
<td>95</td>
<td>14</td>
<td>45</td>
</tr>
<tr>
<td>• Galway Hospital</td>
<td>534</td>
<td>536</td>
<td>121</td>
<td>214</td>
</tr>
<tr>
<td>• Others</td>
<td>79</td>
<td>97</td>
<td>18</td>
<td>29</td>
</tr>
</tbody>
</table>
Appendix Q  Cohort Study Residuals

Figure 9-5 Cohort Study residuals
<table>
<thead>
<tr>
<th>RxRisk No. of conditions</th>
<th>N (%)</th>
<th>Number of repeat drug classes</th>
<th>N (%)</th>
<th>Charlson co-morbidity index *</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>6010  (24.67)</td>
<td>0</td>
<td>4718 (19.37)</td>
<td>0</td>
<td>16088 (66.03)</td>
</tr>
<tr>
<td>1</td>
<td>3115 (12.79)</td>
<td>1</td>
<td>1965 (8.07)</td>
<td>1</td>
<td>4035 (16.56)</td>
</tr>
<tr>
<td>2</td>
<td>3104 (12.74)</td>
<td>2</td>
<td>2016 (8.27)</td>
<td>2</td>
<td>2478 (10.17)</td>
</tr>
<tr>
<td>3</td>
<td>2863 (11.75)</td>
<td>3</td>
<td>2129 (8.74)</td>
<td>3</td>
<td>1099 (4.51)</td>
</tr>
<tr>
<td>4</td>
<td>2698 (11.07)</td>
<td>4</td>
<td>2065 (8.48)</td>
<td>4</td>
<td>396 (1.63)</td>
</tr>
<tr>
<td>5</td>
<td>2263 (9.29)</td>
<td>5</td>
<td>2080 (8.54)</td>
<td>5</td>
<td>135 (0.55)</td>
</tr>
<tr>
<td>6</td>
<td>1763 (7.24)</td>
<td>6</td>
<td>1772 (7.27)</td>
<td>6</td>
<td>85 (0.35)</td>
</tr>
<tr>
<td>7</td>
<td>1212 (4.97)</td>
<td>7</td>
<td>1608 (6.60)</td>
<td>7</td>
<td>33 (0.14)</td>
</tr>
<tr>
<td>8</td>
<td>673 (2.77)</td>
<td>8</td>
<td>1311 (5.38)</td>
<td>8</td>
<td>11 (0.05)</td>
</tr>
<tr>
<td>9 (≥10)</td>
<td>353 (1.45)</td>
<td>9</td>
<td>1076 (4.42)</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>≥10</td>
<td>309 (1.27)</td>
<td>≥10</td>
<td>3623 (14.87)</td>
<td>10</td>
<td>1 (0.00)</td>
</tr>
<tr>
<td>RxRisk No. of conditions</td>
<td>N (%)</td>
<td>Number of repeat drug classes</td>
<td>N (%)</td>
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Appendix R  RxRisk Veterans

1. Alcohol dependence
2. Allergies
3. Anti-coagulation therapy
4. Anti-platelet therapy
5. Anxiety
6. Arrhythmia
7. Benign prostate hypertrophy
8. Bipolar disorder
9. Chronic heart failure
10. Dementia
11. Depression
12. Diabetes
13. End stage renal disease
14. Epilepsy
15. Gastric-oesophageal reflux disorder & Peptic ulcer
16. Glaucoma
17. Gout
18. Hepatitis C
19. HIV
20. Hyperkalaemia
21. Hyperlipidaemia
22. Hypertension
23. Hypothyroidism
24. Angina
25. Ischaemic heart disease/hypertension
26. Inflammatory bowel disease
27. Liver failure
28. Malignancies
30. Osteoporosis/Paget's
31. Pain - OPIATES
32. Inflammation/pain
33. Pancreatic insufficiency
34. Parkinson's disease
35. Psoriasis
36. Psychotic illness
37. Chronic airways disease
38. Smoking cessation
39. Steroid responsive disease - Systemic corticosteroid use
40. Transplant
41. Tuberculosis
42. Neurogenic Bladder and Urinary Incontinence
43. Ostomy
Appendix S Charlson Index

Charlson comorbidity index any time before initiation:
Low (0)
Medium (1-2)
High (>2)

Scoring: Comorbidity Component (Apply 1 point to each unless otherwise noted)

Myocardial Infarction
Congestive Heart Failure
Peripheral Vascular Disease
Cerebrovascular Disease
Dementia
COPD
Connective Tissue Disease
Peptic Ulcer Disease
Diabetes Mellitus (1 point uncomplicated, 2 points if end-organ damage)
Moderate to Severe Chronic Kidney Disease (2 points)
Hemiplegia (2 points)
Leukaemia (2 points)
Malignant Lymphoma (2 points)
Solid Tumour (2 points, 6 points if metastatic)
Liver Disease (1-point mild, 3 points if moderate to severe)
AIDS (6 points)

Age Reweighting Scoring
Age <50 years: 0 points
Age 50-59 years: 1 points
Age 60-69 years: 2 points
Age 70-79 years: 3 points
Age 80-89 years: 4 points
Age 90-99 years: 5 points
Age 100-109 years: 6 points
110 -max years: 7 points
**Appendix T Search strategies**

**Medline (OVID)**

Date of Search: March 20, 2015
1. Medication Reconciliation/ (402)
2. ((medication? or medicine? or drug or drugs or pharmacist? or pharmacy or pharmacies or formulary or formularies or prescription? or prescrib$) adj3 (reconcili$ or review or reviewing)).ti, ab. (9665)
3. ((medication? or medicine? or drug or drugs or pharmacist? or pharmacy or pharmacies or formulary or formularies or prescription? or prescrib$) adj3 (assess$ or audit?)).ti,ab. (14763)
4. (stopp or beer's criteria).ti,ab. (387)
5. (medication? adj2 discrepanc$).ti,ab. (191)
6. (medication? or prescribing) adj2 error?).ti,ab. (4209)
7. stewardship.ti,ab. (2115)
8 or/1-7 [Medication Reconciliation] (30370)
9. Medication Systems, Hospital/ [ML] (3182)
10. Pharmacy service, hospital/ [ML] (9989)
11. ((PHARMACEUTICAL CARE or PHARMACY or PHARMACIES or PHARMACIST? or PRESCRIBING) and (inpatient? or hospital$ or WARD? or UNITE or UNITS)).ti. (3320)
12. ((PHARMACEUTICAL CARE or PHARMACY or PHARMACIES or PHARMACIST? or PRESCRIBING) adj2 (inpatient? or hospital$ or WARD? or UNITE or UNITS)).ab. (2976)
13. ((medication? or prescribing or prescription? or dispensing) adj2 system?).ti,ab. and (hospital$ or WARD or WARDS or (CARE adj2 UNIT?) or INPATIENT?).ti,hw. (576)
14 or/9-13 [Med systems/Pharm service hospitals] (15218)
15. Pharmacists/ or Pharmacists' Aides/ [ML] (11482)
16. Pharmaceutical Services/ or Drug Information Services/ or Clinical Pharmacy Information Systems/ (8887)
17. Drug Monitoring/ or Medication Therapy Management/ or Drug Therapy/ or Drug Therapy, Computer-Assisted/ (44876)
18. Prescriptions/ or Pharmaceutical Preparations/ or Drug Therapy/ or Drug Dosage Calculations/ or Electronic Prescribing/ or Medication Systems/ (94933)
19. medication errors/ or polypharmacy/ or inappropriate prescribing/ (13783)
20. Drug utilization review/ (3180)
21. (pharmacy or pharmacies or pharmacist? or prescription? or prescribing).ti. (45730)
22. (pharmacist-led or pharma$ initiated or ((driven or lead or led) adj2 pharmacist?)).ab. (375)
23. (PRESCRIBING adj2 PATTERN?).ab. (1688)
24. ("physician-pharmacist?" or "doctor-pharmacist?").ti,ab. (161)
25. ((IMPROV$ or OPTIMI?ING or OPTIMI?E? or OPTIMAL$) and (DOSING or DOSAGE or PHARMAC$ or PRESCRIB$ or PRESCRIPT$)).ti. or ((IMPROV$ or OPTIMI?ING or OPTIMI?E? or OPTIMAL$) adj2 (PHARMACEUTICAL CARE or PHARMACY or PRESCRIB$ or PRESCRIPT$)).ab. (5678)
26. ((pharmaceutical adj (care or consult$)) or (pharmacist? adj2 (care or consult$ or intervention? or managed))).ab. (2803)
27. ((drug therapy or drug regime? or medication? or medicineS or pharmacy or pharmacist? or pharmaceutical or PRESCRIB$ or prescription?) adj2 (audit$ or monitor$ or RECONCIL$ or review$)).ti,ab. (5849)
28. ((medication? or prescrib$ or pharmac$) adj2 (manage? or manage$ or service? or system$)).ti,ab. (15716)
29. ("(drug therapy or dosage? or dose? or medication? or PRESCRIPTION? or PRESCRIB$ or PHARMACIST? or PHARMACEUTICAL CARE) adj2 (managing or management or monitor$)).ti,ab. (7596)
30. ("drug utili?ation" adj2 (review? or reconcili$ or audit?)).ab. or ("drug utili?ation" and (review? or reconcili$ or audit$)).ti. (302)
31. (inappropriate$ adj2 (medicine? or medication? or prescrib$ or drug$)).ab. or ("drug utili?ation" adj2 (review? or reconcili$ or audit$)).ab. and ("drug utili?ation" and (review? or reconcili$ or audit$)).ti. (302)
32. Drug utilization/ (17302)
33. or/15–32 [Drug use/misuse. Pharmacy services] (189417)
34. ((care or patient?) adj3 transition$).ti,ab. (5745)
35. (hospital adj3 releases$).ti,ab. (505)
36. "hospital to home",ti,ab. (1930)
37. Patient admission/ or Patient discharge/ or Patient readmission/ or Patient transfer/ [ML] (49965)
38. (patient? or hospital$/ or medical centre or medical centres or medical center?).ti,hw. and (discharg$ or admission? or admitting or readmission? or readmit$ or transfer or transferred or transferring).ti. (28017)
39. ((patient? or care facility or medical facility or hospital? or medical centre or medical centres or medical center? or emergency or ward or wards or unit or units or (intensive adj2 care) or ICU or acute care or (hospital? adj2 department?) adj2 (discharg$ or admission? or admitting or readmission? or transfer? or transferring or transferred$)).ab. (96318)
40. (exp Academic Medical Centers/ or exp Hospital Units/ or exp Hospitals/ or exp Ambulatory Care Facilities/) and (transfer or transferred or discharge or admission? or readmission? or re-admission?).ti. (6889)
41. (earli$ or early) adj2 discharg$.ab. (3329)

399
1 Medication therapy management/ (3889)
2 ((medication? or medicine? or drug or drugs or pharmacist? or pharmacy or pharmacies or formulary or formularies or prescription? or prescrib$) adj3 (reconcil$ or review or reviewing)).ti,ab. (14949)
3 (medication? or medicine? or drug or drugs or pharmacist? or pharmacy or pharmacies or formulary or formularies or prescription? or prescrib$) adj3 (error?).ti,ab. (6496)
4 stewardship.ti,ab. (2682)
5 or/1-7 [Medication Reconciliation] (48179)
6 9 (PHARMACEUTICAL CARE or PHARMACY or PHARMACIES or PHARMACIST? or PRESCRIBING) and (inpatient? or hospital$ or WARD? or UNIT or UNITS)).ti,ab. (6084)
7 (PHARMACEUTICAL CARE or PHARMACY or PHARMACIES or PHARMACIST? or PRESCRIBING) adj2 (inpatient? or hospital$ or WARD? or UNIT or UNITS)).ab. (6111)
8 (medication? or prescribing or prescription? or dispensing) adj2 system?).ti,ab. (1128)
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<th>AB time series</th>
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405
S56 S48 OR S49 OR S50 OR S51 OR S52 OR S53 OR S54 OR S55

S55 TI controlled AND TI ( trial or trials or study or experiment* or intervention )

S54 AB ( (multicent* n2 design*) or (multicent* n2 study) or (multicent* n2 studies) or (multicent* n2 trial* ) ) or AB ( (multi-cent* n2 design*) or (multi-cent* n2 study) or (multi-cent* n2 studies) or (multi-cent* n2 trial* ) )

S53 TI multicentre or multicenter or multi-centre or multi-center

S52 TI ( cluster N2 trial* or cluster N2 study or cluster N2 group or cluster N2 groups or cluster N2 cohort or cluster N2 design or cluster N2 experiment* ) OR AB ( cluster N2 trial* or cluster N2 study or cluster N2 group or cluster N2 groups or cluster N2 cohort or cluster N2 design or cluster N2 experiment* )

S51 TI ( control group or control groups OR control* experiment* or control* design or controlled study ) OR AB ( control group OR control groups or control* cohort* or controlled experiment* controlled design or controlled study)

S50 TI random* or AB random*

S49 TI ( "clinical study" or "clinical studies" ) or AB ( "clinical study" or "clinical studies" )

S48 (MM "Clinical Trials+")

S47 (S31 AND S44) NOT (S45 OR S46)

S46 (S14 AND S44) NOT S45
S45 S8 AND S44

S44 S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41 OR S42 OR S43

S43 TI (discharge N3 (medication# or prescription# or communication# or (information N2 exchange*)))

S42 TI ( (hospital N8 (transfer# or transferred)) OR AB ( (hospital N8 (transfer# or transferred)))

S41 TI (transfer* N3 emergency) OR AB (transfer* N3 emergency)

S40 TI ( ( ICU or intensive N2 care or acute care or unit or units or ward or wards or department ) N3 transition*) OR AB ( ( ICU or intensive N2 care or acute care or unit or units or ward or wards or department ) N3 transition*)

S39 AB ((early* or early) N2 discharge*)

S38 ( MH "Academic medical centers*" or MH "Hospital Units*" or MH "Hospitals*" or MH "Ambulatory Care Facilities*" ) AND TI ( (transfer or transferred or discharge or admission# or readmission# or re- admission#) )

S37 AB ((patient# or care facility or medical facility or hospital# or medical centre or medical centres or medical center# or emergency or ward or wards or unit or units or (intensive N2 care) or ICU or acute care or (hospital# N2 department#) ) N2 (discharge* or admission# or admitting or readmission# or transfer# or transferring or transferred))

S36 ( TI ((patient# or hospital* or medical centre or medical centres or medical center#) ) OR MW ((patient# or hospital* or medical centre or medical centres or medical center#) ) ) AND TI ( (discharge* or admission# or admitting or readmission# or readmit* or transfer# or transferring or transferred) )

S35 MH Patient admission OR MH Patient discharge OR MH readmission OR MH transfer, discharge

S34 TI "hospital to home" OR AB "hospital to home"
S33 TI (hospital N3 releas*) OR AB (hospital N3 releas*)

S32 TI ( ((care or patient#) N3 transition*) ) OR AB ( ((care or patient#) N3 transition*) )

S31 S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30

S30 MH drug utilization

S29 AB ( (inappropriate* N2 (medicine# or medication# or prescrib* or drug#)) ) OR TI ( (inappropriate* N2 (medicine# or medication# or prescrib* or drug#)) )

S28 AB ( ("drug utilizat#ion" N2 (review# or reconcil* or audit#)) ) OR TI ( ("drug utilisat#ion" and (review# or reconcil* or audit#)) )

S27 TI ( ("drug therapy" or dosage# or dose# or medication# or PRESCRIPTION# or PRESCRIB* or PHARMACIST# or PHARMACEUTICAL CARE) N2 (managing or management or monitor*)) OR AB ( ("drug therapy" or dosage# or dose# or medication# or PRESCRIPTION# or PRESCRIB* or PHARMACIST# or PHARMACEUTICAL CARE) N2 (managing or management or monitor*))

S26 TI ( ((medication# or prescrib* or pharmac*) N2 (manage# or management or service# or system#)) ) OR AB ( ((medication# or prescrib* or pharmac*) N2 (manage# or management or service# or system#)) )

S25 TI ( ((drug therapy or drug regime# or medication# or medicineS or pharmacy or pharmacist# or pharmaceutical or PRESCRIB* or prescription#) N2 (audit* or monitor* or RECONCIL* or review#)) ) OR AB ( ((drug therapy or drug regime# or medication# or medicineS or pharmacy or pharmacist# or pharmaceutical or PRESCRIB* or prescription#) N2 (audit* or monitor* or RECONCIL* or review#))

S24 AB ((pharmaceutical N1 (care or consult*)) or (pharmacist# N2 (care or consult* or intervention# or managed)))

S23 TI ( ( (IMPROV* or OPTIMI#ING or OPTIMI#E# or OPTIMAL*) and (DOSING or DOSAGE or PHARMAC* or PRESCRIB* or PRESCRIPTION*)) ) OR AB ( ( (IMPROV* or OPTIMI#ING or OPTIMI#E# or OPTIMAL*) and (DOSING or DOSAGE or PHARMAC* or PRESCRIB* or PRESCRIPTION*)) )

S22 TI ( ("physician-pharmacist#" or "doctor-pharmacist#") ) OR AB ( ("physician-pharmacist#" or "doctor-pharmacist#") )
S21 AB (PRESCRIBING N2 PATTERN#)

S20 AB (pharmacist-led or pharma* initiated or ((driven or lead or led) N2 pharmacist#))

S19 TI (pharmacy or pharmacies or pharmacist# or prescription# or prescribing)

S18 MH prescription, drugs OR prescriptions OR pharmaceutical preparations OR MH medication errors OR MH polypharmacy OR MH drug utilization OR inappropriate prescribing

S17 MH Drug Monitoring OR MH Drug Therapy OR MH Drug Therapy, Computer-Assisted OR Medication Therapy Management OR MH dosage calculations OR MH Medication Systems OR Electronic Prescribing

S16 MH drug information services OR MH clinical pharmacy information systems OR pharmaceutical services

S15 MH Pharmacists OR MH Pharmacy technician

S14 S9 OR S10 OR S11 OR S12 OR S13

S13 ( TI ( ((medication# or prescribing or prescription# or dispensing) N2 system#) ) OR AB ( ((medication# or prescribing or prescription# or dispensing) N2 system#) ) ) AND ( TI ( (hospital* or WARD or WARDS or (CARE N2 UNIT#) or INPATIENT#) ) OR MW ( (hospital* or WARD or WARDS or (CARE N2 UNIT#) or INPATIENT#) ) )

S12 AB ((PHARMACEUTICAL CARE or PHARMACY or PHARMACIES or PHARMACIST# or PRESCRIBING) N2 (inpatient# or hospital* or WARD# or UNIT or UNITS))

S11 TI ((PHARMACEUTICAL CARE or PHARMACY or PHARMACIES or PHARMACIST# or PRESCRIBING) and (inpatient# or hospital* or WARD# or UNIT or UNITS))
S10 MH pharmacy service AND hospital

View Results
(822)
View Details
Edit

S9 MH Medication Systems AND hospital

View Results
(387)
View Details
Edit

S8 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7

View Results
(10,257)
View Details
Edit

S7 TI stewardship OR AB stewardship

View Results
(630)
View Details
Edit

S6 TI ( ((medication# or prescribing) N2 error#) ) OR AB ( ((medication# or prescribing) N2 error#) )

View Results
(3,028)
View Details
Edit

S5 TI (medication# N2 discrepanc*) OR AB (medication# N2 discrepanc*)

View Results
(78)
View Details
Edit

S4 TI ( (stopp or beer's criteria) ) OR AB ( (stopp or beer's criteria) )

View Results
(37)
View Details
Edit

S3 TI ( ((medication# or medicine# or drug or drugs or pharmacist# or pharmacy or pharmacies or formulary or formularies or prescription# or prescrib*) N3 (assess* or audit#)) ) OR AB ( ((medication# or medicine# or drug or drugs or pharmacist# or pharmacy or pharmacies or formulary or formularies or prescription# or prescrib*) N3 (assess* or audit#)) )

View Results
(3,336)
View Details
Edit

S2 TI ( ((medication# or medicine# or drug or drugs or pharmacist# or pharmacy or pharmacies or formulary or formularies or prescription# or prescrib*) N3 (reconcil* or review or reviewing)) ) OR AB ( ((medication# or medicine# or drug or drugs or pharmacist# or pharmacy or pharmacies or formulary or formularies or prescription# or prescrib*) N3 (reconcil* or review or reviewing)) )

View Results
(3,385)
View Details
Edit

S1 MH medication reconciliation

EPOC Specialised Register, Reference Manager 12
Date of Search: March 23, 2015

Connector Field Parameter Results

View
Results
(822)
View
Details
Edit

View
Results
(387)
View
Details
Edit

View
Results
(10,257)
View
Details
Edit

View
Results
(630)
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View
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(3,028)
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View
Results
(37)
View
Details
Edit

View
Results
(3,336)
View
Details
Edit

View
Results
(3,385)
View
Details
Edit

# 177
22
indexes=SCI-EXPANDED, CPCI-S Timespan=2014-2015

# 107
(#18 or #19 or #20) not (#17 or TI=placebo* or TS=placebo* or TI=animal or TS=animal)

21
indexes=SCI-EXPANDED, CPCI-S Timespan=2014-2015
TI=((medication? NEAR/2 discrepancy* or TI=((medication? or prescribing) NEAR/2 error?) or TI=stewardship)
Indexes=SCI-EXPANDED, CPCI-S Timespan=2014-2015

PsycINFO (OVID)
Date of Search: March 20, 2015
1 ((medication? or medicine? or drug or drugs or pharmacist? or pharmacy or pharmacies or formulary or formulations or prescription? or prescrib$) adj3 (reconcil$ or review or reviewing)).ti,ab. (1857)
2 ((medication? or medicine? or drug or drugs or pharmacist? or pharmacy or pharmacies or formulary or formulations or prescription? or prescrib$) adj3 (assess$ or audit?)!).ti,ab. (3598)
3 (stop or beer's criteria).ti,ab. (87)
5 (medication? or prescribing) adj2 error?).ti,ab. (450)
6 stewardship.ti,ab. (517)
7 or/1-6 [Medication Reconciliation] (6378)
8 ((PHARMACEUTICAL CARE or PHARMACY or PHARMACIES or PHARMACIST? or PRESCRIBING) and (inpatient? or hospital$ or WARD? or UNIT or UNITS)).ti. (170)
9 ((PHARMACEUTICAL CARE or PHARMACY or PHARMACIES or PHARMACIST? or PRESCRIBING) adj2 (inpatient? or hospital$ or WARD? or UNIT or UNITS)).ab. (196)
10 ((medication? or prescribing or prescription? or dispensing) adj2 system?).ti,ab. and (hospital$ or WARD or WARDS or (CARE adj2 UNIT?) or INPATIENT?).ti,hw. (30)
11 or/8-10 [Med systems/Pharm service hospitals] (358)
12 (pharmacy or pharmacies or pharmacist? or prescription? or prescribing).ti. (5440)
13 (pharmacist-led or pharmacist$ initiated or ((driven or lead or led) adj2 pharmacist?)!).ab. (47)
14 (PRESCRIBING adj2 PATTERN?).ab. (307)
15 ("physician-pharmacist?" or "doctor-pharmacist?").ti,ab. (15)
16 (IMPROV$ or OPTIMI?ING or OPTIMI?E? or OPTIMAL$) and (DOSING or DOSAGE or PHARMAC$ or PRESCRIB$ or PRESCRIPT$).ti. or (IMPROV$ or OPTIMI?ING or OPTIMI?E? or OPTIMAL$) adj2 (PHARMACEUTICAL CARE or PHARMACY or PRESCRIB$ or PRESCRIPT$).ab. (545)
17 ((pharmaceutical adj (care or consult$)) or (pharmacist? adj2 (care or consult$ or intervention? or managed))).ab. (236)
18 ((drug therapy or drug regime? or medication? or medicine$ or pharmacy or pharmacist? or pharmaceutical or PRESCRIB$ or prescription?) adj2 (audit$ or monitor$ or RECONCIL$ or review?).ti,ab. (1298)
19 ((medication? or prescrib$ or pharmacist$) adj2 (manage? or management or service? or system?)!).ti,ab. (3235)
20 ("drug therapy" or dosage? or dose? or medication? or PRESCRIPTION? or PRESCRIB$).ti. and (PHARMACEUTICAL CARE adj2 (review? or reconcil$ or audit?))).ab. (2179)
21 ("drug utili?ation" adj2 (review? or reconcil$ or audit?)!).ab. or ("drug utili?ation" and (review? or reconcil$ or audit?)).ti. (45)
22 (inappropriateness adj2 (medicine? or medication? or prescrib$ or drug$)).ti,ab. (372)
23 or/12-22 [Drug use/misuse Pharmacy services] (10268)
24 ((care or patient?) adj3 transition?).ti,ab. (1400)
25 (hospital adj3 releas$).ti,ab. (233)
26 "hospital to home".ti,ab. (274)
27 (patient? or hospital$ or medical centre or medical centres or medical center?).ti,hw. and (discharg$ or admission? or admitting or readmission? or readmit$ or transfer? or transferred or transferring).ti. (4167)
28 ((patient? or care facility or medical facility or hospital? or medical centre or medical centres or medical center? or emergency or ward or wards or unit or units or (intensive adj2 care) or ICU or acute care or (hospital? or department?)) adj2 (discharg$ or admission? or admitting or readmission? or transfer? or transferred or transferring)).ab. (11633)
29 (Academic Medical Centers or Hospital Units or Hospitals or Ambulatory Care Facilities).ti,ab. and (transfer or transferred or discharge or admission? or re-admission?).ti. (629)
30 ((earlier$ or early) adj2 discharg$).ab. (294)
31 ((icu or (intensive adj2 care) or acute care or unit or units or ward or wards or department) adj3 transition$).ti,ab. (127)
32 (transfer$ adj3 emergency).ti,ab. (45)
33 (hospital adj8 (transfer? or transferred)).ti,ab. (547)
34 discharge.ti. (2088)
35 (discharge adj3 (medication? or prescription? or communication? or (information adj2 exchang$))).!ab. (232)
36 or/24-35 [Discharge/transition care] (17338)
37 7 and 36 [Medication Reconciliation & Transition of Care] (139)
38 (11 and 36) not 37 [Hospital Med Systems & Transition of Care] (41)
39 (23 and 36) not (37 or 36) [Drug Use/Misuse Pharm services & Transition of Care] (157)
40 double-blind.tw. (18654)
41 random$ assigned.tw. (26025)
42 control.tw. (26025)
44 intervention? adj6 (intervention? or collaborat$ or complex or DESIGN$ or doctor? or educational or family doctor? or family physician? or family practitioner? or financial or GP or general practice? or hospital? or impact? or improv$ or individual$ or individual? or interdisciplin$ or multicomponent or multiple-component or multidisciplin$ or multi-disciplin$ or multifacet$ or multiframe$ or multimodal$ or multi-modal$ or personal$ or personal! or pharmacists or physician? or pharmacy? or practitioner? or prescrib$ or prescription? or primary care or professional$ or provider? or regulatory or regulatory or tailor$ or target$ or team$ or usual care!).ab. (97399)
45 (pre-intervention? or preintervention? or "pre intervention?" or post-intervention? or postintervention? or "post intervention?").ti,ab. [added 2.4] (5867)
46 (hospital$ or patient?).hw. and (study or studies or care or health$ or practitioner? or provider? or physician? or nurse? or nursing or doctor?).ti,hw. (45330)
47 demonstration project?.ti,ab. (1007)
48 (pre-post or "pre test$" or pretest$ or posttest$ or "post test$" or (pre adj5 post)).ti,ab. (39602)
49 (pre-workshop or post-workshop or (before adj3 workshop) or (after adj3 workshop)).ti,ab. (450)
50 trail.ti. or ((study adj3 aim?) or "our study").ab. (86672)
51 (before adj10 (after or during)).ti,ab. (54268)
52 ("quasi-experiment$" or quasieperiment$ or "quasi random$" or quasirandom$ or "quasi control$" or quasicontrol$ or ((quasi$ or experimental) adj3 (method$ or study or trial or design$))).ti,ab,hw. (46888)
53 ("time series" adj2 interrupt$).ti,ab,hw. (488)
54 (time points adj3 (over or multiple or three or four or five or six or seven or eight or nine or ten or eleven or twelve or month$ or hour? or day? or "more than")).ab. (2718)
55 pilot.ti. (11636)
56 (multicentre or multicenter or multi-centre or multi-center).ti. (1957)
57 random$.ti,ab. or controlled.ti. (145446)
58 (control adj3 (area or cohort? or compare? or condition or design or group? or intervention? or participant? or study)).ab. not (controlled clinical trial or randomized controlled trial).pt. (93610)
59 "comment on",cm. or review.ti,pt. or randomized controlled trial.pt. (120084)
60 review.ti. (120084)
61 (rat or rats or cow or cows or chicken? or horse or horses or mice or mouse or bovine or animal?).ti. (109066)
62 or/44-58 or experimental design/ or between groups design/ or quantitative methods/ or quasi experimental methods/ (502713)
63 exp animals/ or animal?.ti,id,hw. (307154)
64 62 not (or/60-61,63) [EPOC Methods Filter 2.4 PsycINFO] (457861)
65 (or/37-39 and 43) not placebo$.ti,ab,hw. [RCT Results] (37)
66 (2015$ or 2014$).dp,yr. (196949)
67 65 and 66 [RCT 2015 results] (3)
Dissertations & Theses (ProQuest)
Date of Search: March 23, 2015
(subject("Prescription drugs") AND subject("Reconciliation")) OR (((ti,ab((medication* OR medicine* OR drug or drugs or OR pharmacist* OR pharmacy OR pharmacies OR formulary OR formularies OR prescription* OR prescrib*) NEAR/3 (reconcil* OR review OR reviewing)) OR ((medication* OR medicine* OR drug or drugs or OR pharmacist* OR pharmacy OR pharmacies OR formulary OR formularies OR prescription* OR prescrib*) NEAR/3 (assess* OR audit*)) OR (stopp OR beer's criteria) OR (medication* NEAR/2 discrepanc*) OR (medication* OR prescribing) NEAR/2 error*) OR (stewardship)) OR su(medication reconciliation) AND ti,ab(patient* OR "care facility" OR "medical facility" OR hospital* OR "medical centre" OR "medical centres" OR "medical center"") OR emergency OR ward OR wards OR unit OR units OR (intensive NEAR/2 care) OR ICU OR "acute care" OR (hospital* NEAR/2 department*)) NEAR/2(discharge* OR admission* OR admitting OR readmission* OR transfer* OR transferring OR transferred))) OR ((ti(medication OR medicine OR drug OR drugs OR prescription*) AND ti(reconcil*))
Joanna Briggs Institute Library
Date of Search: July 21, 2015
1 "medication management"
2 "medication reconciliation"
3 "medication systems"
4 "medicines reconciliation"
5 "medicines discrepancies"
6 "medication discrepancies"
7 or/1-6
NHS Evidence Search
Date of Search July 21, 2015
filter AHRQ/Care Quality Commission/Centre for Reviews and Dissemination Health Technology Assessment/ National Institute for Health and Care Excellence (includes National electronic Library for Medicines)/National Patient Safety Agency – National Reporting and Learning Service/ National Prescribing Centre/ UKMi (includes Pharmline)/
1 "Medicines Management"
2 "Medication Reconciliation"
3 "Medicines Reconciliation"
4 "Medication systems"
5 or/1-4
Agency for Healthcare Research and Quality
Date of Search July 22, 2015
1 "Medication Reconciliation"
2 "Medicines Reconciliation"
3 "Medication Systems"
4 "Medicines Management"
or/1-4
National Research Register Archive (2000-2007)
Date of Search August 28, 2013
1 "medication management"
2 "medication reconciliation"
3 "medication systems"
4 "medicines reconciliation"
5 "medicines discrepancies"
6 "medication discrepancies"
7 or/1-6

International Pharmaceuticals Abstract
Date of Search July 21, 2015
1 "medication reconciliation"
2 "medicines reconciliation"
3 "medication management"
4 "medication discrepanc*"
5 "medicines discrepanc*"
6 "medication systems"
7 or/1-6

Open Grey
Date of Search July 21, 2015
1 "medication reconciliation"
2 "medication management"
3 "medicines reconciliation"
4 "medication systems"
5 "medicines discrepancies"
6 "medication discrepancies"
7 or/1-6

National Institute for Health and Care Excellence (NICE)
Date of Search July 22, 2015
1 "Medication Reconciliation"
2 "Medicines Reconciliation"
3 "Medication Systems"
4 "Medicines Management"
5 or/1-4

Grey Literature Report
Date of Search July 21, 2015
1 "medication reconciliation"
2 "medicines reconciliation"
3 "medication systems"
4 "medicines management"
5 "medication discrepancies"
6 "medicines discrepancies"
7 or/1-6

World Health Organization (WHO) - International Clinical Trials Registry Platform (ICTRP)
Date of Search July 22, 2015
1. "medication reconciliation"
2. "medication management"
3. "Medication Systems"
4. "Medication Therapy Management"
5. "medication errors"
6. "Pharmacy service"
7. "Pharmacist"
8. "Pharmacy"
9. "Pharmacies"
10. "Medication discrepanc*"
11. "Prescrib*"
12. "Pharmaceutical Services"
13. "inappropriate prescribing"
14. "polypharmacy"
15. "Patient admission"
16. "Patient discharge"
17. "Patient readmission"
18. "Patient transfer"
19. or/ 1-18

Clinical Trials.gov, US National Institutes of Health (NIH)
Date of Search March 31, 2015
1 "medication reconciliation"
2 "medicines reconciliation"
3 "medication errors"
4 "medication discrepancy"
5 or/1-4

Google Alerts (https://www.google.ie/alerts)
"medication reconciliation"
Appendix U

Reviews screened for included studies


Appendix V Systematic Review Alternate Intra-cluster correlation coefficients

Figure 9-6 Systematic Review (Chapter 5) Alternate ICC 0.02
Schnipper 2011

Figure 9-7 Systematic Review (Chapter 5) Alternate ICC 0.04
Schnipper 2011
Figure 9-8 Systematic Review (Chapter 5) Alternate ICC 0.06 Schnipper 2011

Figure 9-9 Systematic Review (Chapter 5) Alternate ICC 0.2 Schnipper 2011

419
Appendix W  Characteristics of included studies

Becerra-Camargo 2013

Methods
Study design: A multi-centre, double-blind, randomised and controlled parallel-group trial study
Unit of allocation: Patients and doctors were randomly assigned to the intervention or standard care arm
Unit of analysis: individual patient
Follow-up: Outcome recorded at admission
Duration: admission interface, first 24 hours

Participants
Setting/participants:
270 participants (134 intervention and 136 control). Intervention group 17 lost to follow-up, usual care 11 lost to follow-up.
The study was conducted from October 26th to November 30th 2012 at 3 large teaching hospitals in Bogota, Colombia. All consecutive patients (18 years or older) who had been admitted to an Emergency Department (ED), taking at least one medication or had been prescribed a minimum of one prescription medication before admission, who had been assessed as triage I and II on admission and who had been hospitalised for at least 24 hours were eligible for inclusion. (Fundacion Cardio Infantil, 60% Hospital Samaritana and 50% at Hospital San Carlos - 3 large teaching hospitals in Bogota, Colombia).
Transition of care: Admission through the emergency department
Age (mean +-SD): 59 +- 18 years intervention, 58 +- 20 years control
Female: 59.8% intervention, 56% control
Ethnicity: No information given

Interventions
Organisational
"The intervention consisted of a pharmacist-acquired medication history in an ED focusing on a patient’s current home medication regimen documented on the admission medication order form which was available to be used by a doctor when consulting in an ED. Doctors verified the data with patients and indicated which home medications were to be reordered, suspended or discontinued. This resulted in an accurate and comprehensive history of a patient’s current home medication regimen, called medication order form verified with patient.
Patients in the control group received standard care; this included doctors documenting medication histories in admission notes and nurses reviewing medication orders for appropriateness. Doctors wrote in-patient orders during consultation without having access to F1. The medication information was entered on each medical chart forming part of a hospital’s electronic health records. Pharmacists were not routinely involved in documenting patient admission medication histories; this function is primarily the admitting resident doctor or medical student’s responsibility at the institutions involved in the present study”

Outcomes
Patients having at least 1 admission medication discrepancy: “Admission discrepancies were defined as any medication clarification related to current home medication made whilst being cared for in an ED. They could have been associated with any of the following: drug, dosage, frequency, administration route, appropriateness of restarting medication, therapeutic duplicity and/or medications lacking indication. Discrepancies were identified using a systematic approach (i.e. MedRec)."
Characteristics of discrepancy: Definition not recorded
Clinical severity of discrepancy: The degree of effect for each medication discrepancy was defined as follows (76). Class 1 discrepancies were classified as being those unlikely to cause patient discomfort or clinical deterioration, Class 2 those having the potential to cause moderate discomfort or clinical deterioration and Class 3 discrepancies had the potential to result in severe discomfort or clinical deterioration.

Notes

Risk of bias table

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>Allocation by each randomisation manager was daily and depended on the number of patients, doctors and residents per shift. The combined coded numbers concerning intervention allocation were concealed in sequentially-numbered, sealed, opaque envelopes and kept by the clinical trials group at the Universidad Nacional de Colombia (UNALCO, Bogota). The assignments were also concealed in sequentially numbered containers, according to the allocation sequence. It was ensured that all envelopes were numbered in advance and that they were equal in weight and similar in appearance. It was guaranteed that the envelopes were opened sequentially and only after a participant’s name and other details had been written on the assignation list. (See Page 5)</td>
</tr>
</tbody>
</table>

420
Allocation concealment (selection bias) | Low risk
---|---
Were baseline outcome measurements similar? | Low risk
---|---
Unclear risk | Table 1 gives patients' baseline demographic and clinical characteristics regarding the intervention and standard care arms. There were no statistically significant differences between both treatment arms.
---|---
Low risk | Number lost to follow-up in intervention was 17 and 11 in control group - mainly due to non-adherence to protocol (i.e. discharged before 24-hour follow-up). Fig 2 Page 7
---|---
Low risk | The primary outcome measure is objective. Secondary outcomes: the authors state that "The clinical severity of medication discrepancies was independently assessed by two clinical pharmacists blinded to the patient data collection forms". Page 3
---|---
Low risk | Patients and doctors were randomised. The doctors were assigned to receive only patients in the intervention or control group during their shifts to ensure blinding. The forms used were made to look the same as the forms used in the hospitals, the logo, colours and fonts being exactly alike so it seemed that the doctor was filling in just another new form. All statistical analysis involved maintaining the masking. Analysis was completed before the randomisation code was broken at the end of the completed trial. Each researcher sent the data online via an information system link provided by the statistics office. All records were checked.
---|---
Low risk | No issues
---|---
Low risk | All outcomes mentioned in methodology are present in the results section. Page 3 - Outcomes; Page 5 - Results
---|---
Low risk | No evidence of any other bias.
---|---
Unclear risk | Unclear
---|---

Methods
Study design: Described as a randomised non-blinded trial but randomisation was based on the last digit of their medical card number (i.e. quasi randomised). Controls odds; intervention evens. Discussed with EPOC Contact - Editor (JW) and advised to keep in with note of possible bias.
Unit of allocation: patient
Unit of analysis: patient
Follow-up: 48 hours post admission
Duration: Admission to 48-hour post pharmacist medication review.
Providers: Pharmacists, no information provided regarding their credentials

Participants
Setting/participants: 81 participants (41 intervention and 40 control). Patients more than 70 years of age were eligible for inclusion if they were admitted to 1 of the 2 general medicine floors or 1 general surgery floor during the study period (December 1, 2009 through March 31, 2010). These floors were selected in order to obtain a broad population of patients in terms of disease states and home medications. Patients were excluded from the study if their expected duration of hospital stay was less than 48hours as indicated by their admission to a designated short-stay service or if they were admitted to a primary service rounding with a clinical pharmacist. Rush University Medical Centre, Chicago, IL, USA, a 676-bed tertiary care medical centre with 1500 monthly admissions to medicine and surgery. 1 of the 2 general medicine floors or 1 general surgery floor during the study period. These floors were selected in order to obtain a broad population of patients in terms of disease states and home medications.
Transition of care: comprehensive medication reconciliation performed by a pharmacist within 24 hours of admission
Age (mean ± SD): 80 ± 6.7 years intervention, 79 ± 7.1 years control
Female: 63.4% intervention, 62.5% control
Ethnicity: Intervention: Caucasian 46.3%; African American 43.9%; Hispanic 9.8%; Asian American 0%. Control: Caucasian 55%; African American 32.5%; Hispanic 7.5%; Asian American 5%.

Interventions
Organisational
"Pharmacist-led medication reconciliation was defined as comprehensive admission medication reconciliation performed by a pharmacist within 24 hours of inpatient admission. Pharmacists were required to use at least one source of information apart from the patient's electronic medical record and interviewed every patient when feasible. There were situations when a full patient interview by the pharmacist was not conducted, but these were limited to patients unable to participate in an interview for medical, psychological, or social reasons. Other sources of information included, but were not
Medication reconciliation in the control group was defined as medication reconciliation per existing standard hospital practice; at our institution, at the time of the study, primarily the admitting medical resident or intern performed medication reconciliation. This was typically done at the time of admission or as soon as the family could be contacted for any necessary input. Additionally, as part of the existing hospital practice, staff pharmacists review medication orders for appropriateness and agreement with the electronic home medication list completed by the admitting medical resident; however, they do not have significant opportunity for direct patient contact and rely on that list to be accurate. Our control patients received this standard practice, followed by additional quality assurance performed by a pharmacist at 48 hours after admission, to determine whether the original medication list was reconciled correctly and to allow for comparison to the intervention group.

Outcomes

The primary end point assessed was medication profile appropriateness at 48-hour pharmacist review. For a medication profile to be deemed as “appropriate,” it required all discrepancies from medication reconciliation to be resolved and all medication use to be appropriate as documented by the reviewing pharmacist. Secondary endpoint included type of discrepancies - Table 2 and Table 3

Notes

Included based on advice from EPOC contact editor. However, note possible bias because randomisation was based on the last digit of their medical card number (i.e. quasi randomised). Odds numbers were controls and even number into the intervention. Limited to patients aged 70+, e.g. potential bias with regard to comorbidity, polypharmacy, susceptibility to drug-related harm.

Risk of bias table

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>High risk</td>
<td>All patients were randomly assigned to either control or pharmacist-led medication reconciliation based on the last digit of their medical record number (i.e. controls; odds; intervention, evens). p137. Discussed with EPOC Contact - Editor (JW) and advised to keep in with note of possible bias</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>High risk</td>
<td>All patients were randomly assigned to either control or pharmacist-led medication reconciliation based on the last digit of their medical record number (i.e. controls; odds; intervention, evens). p137</td>
</tr>
<tr>
<td>Were baseline outcome measurements similar?</td>
<td>Unclear risk</td>
<td>No baseline measure of outcome</td>
</tr>
<tr>
<td>Were baseline characteristics similar?</td>
<td>High risk</td>
<td>Baseline characteristic were similar between the 2 groups except that 37% of patients had altered mental status per pharmacist assessment in the intervention group compared to 23% in the control group (Table 1). Analysis was not adjusted for any differences. p138</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Unclear risk</td>
<td>Not specified in the paper</td>
</tr>
<tr>
<td>Was knowledge of the allocated interventions adequately prevented during the study?</td>
<td>Low risk</td>
<td>Outcomes are objective.</td>
</tr>
<tr>
<td>Was the study adequately protected against contamination?</td>
<td>High risk</td>
<td>Patients were randomised and intervention conducted by pharmacist and control by admitting medical resident or intern.</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>All outcomes mentioned in methodology are present in the results section. p137 and 138</td>
</tr>
<tr>
<td>Other bias</td>
<td>Low risk</td>
<td>No evidence of any other bias.</td>
</tr>
<tr>
<td>Summary Risk of Bias</td>
<td>High</td>
<td>High</td>
</tr>
</tbody>
</table>

Bolas 2004
Methods

Randomised Trial
Study design: RCT (cluster)
Unit of allocation: Participant
Unit of analysis: Participant
Follow-up: Following discharge, at patient's home
Duration: Full inpatient episode, from initial presentation through to discharge
Providers: Liaison pharmacist, no information provided regarding credentials

Participants

Setting/participants: 243 participants (119 intervention, 124 control). A total of 162 patients completed the full protocol. Patients were recruited after emergency or unplanned admission to the medical admissions unit at Antrim Area Hospital. Patients were considered suitable for inclusion if they were aged 55 years or over and receiving more than 3 drugs, which were taken regularly not on an as required basis. The Antrim Area Hospital is a 426-bed district general hospital in Northern Ireland. Patients in the area are registered with one general practitioner and admitted to Antrim Hospital on a geographical basis. Patients were excluded from the study if they were: transferred to another hospital, admitted or transferred to a nursing home, patient or carer unable to communicate with pharmacist, any mental illness or alcohol related admission or home visit or follow up was declined on admission.

Transition of care: Admission and discharge
Age (average, years): 73 intervention, 75 control
Female: 41/81 intervention, 39/81 control
Ethnicity: No information given

Interventions

Organisational
A full medication history was taken by comparing the GP referral letter, the initial inpatient prescription, the GP surgery record, the community pharmacy PMR, the patient’s own drugs brought into hospital and the patient or carer as sources of information. Unintentional discrepancies were recorded. A record of prescribed medication and OTC and herbal product use was made. The final correct version of the drug history verified by the liaison pharmacist was used as the gold standard to compare the other sources for accuracy.

* Daily contact with the patient to explain changes made to their treatment as they happened.
* Preparation of the discharge letter which was then signed by the junior doctor (currently signed off by the clinical pharmacists).
* Preparation of a pharmaceutical discharge letter which was faxed with the discharge prescription to the GP and community pharmacist on the day of discharge.
* Preparation of a personalized medicines record sheet and discharge counselling.
* Provision of a medicines help line which was advertised by a card given to all patients enrolled in the study inviting them to request further information if required after discharge.
* Assessment and management of the patients own drugs brought into hospital and rationalization of these against discharge medication when the patient was going home.

Control patients received the standard clinical pharmacy service, which at the time of study, did not include discharge counselling. Little further details provided.

Outcomes

Not clear what the primary outcome is. Outcomes include: 1. Eadon Scores (for intervention only) 2. Name of drug, dose & frequency of complete drug history compared to other sources (intervention only) 3. Mismatch between GP prescription and hospital discharge letter 4. Patient recall of drugs 5. Emergency re-admission rates 6. Rate of reconciliation of patients own drugs with discharge medications.

Notes

Contacted authors for original data to reanalysis of the mismatch data (presented as %) for our primary outcome. No response as yet.

Risk of bias table

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>Computer generated random number. p115</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>not specified, computer generated number but was the computer on site? p115</td>
</tr>
<tr>
<td>Were baseline outcome measurements similar?</td>
<td>Unclear risk</td>
<td>No baseline measurements. pages 116 &amp; 117</td>
</tr>
<tr>
<td>Were baseline characteristics similar?</td>
<td>High risk</td>
<td>characteristics only for those who finished the protocol, not all those randomised. p116</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low risk</td>
<td>Table 1 - similar numbers in each group. p117</td>
</tr>
<tr>
<td>Was knowledge of the allocated interventions adequately prevented during the study?</td>
<td>Unclear risk</td>
<td>Not all outcomes are objective.</td>
</tr>
<tr>
<td>Was the study adequately protected against contamination?</td>
<td>High risk</td>
<td>patients were randomised however 11 patients received counselling and were excluded. pages 115 &amp; 116</td>
</tr>
</tbody>
</table>
Selective reporting (reporting bias)   
Low risk  ▼
All outcomes mentioned in the methods are reported in the results. p 116 and 117

Other bias   
Low risk  ▼
The primary outcome is not clearly specified

Summary Risk of Bias   
Unclear risk  ▼
Unclear

Crotty 2004

Methods
Study design: RCT
Unit of allocation: participant
Unit of analysis: participant
Follow-up: 3 months
Duration: 2 case conferences 6 to 12 weeks apart. Prior to transfer through to 28 days after transfer
Providers: Pharmacist transition coordinator, who also worked with the community pharmacist, and who coordinated a case conference with the family physician, community pharmacist and nurse at the long term care facility

Participants
Setting/participants:
110 participants (56 intervention, 54 control) from 10 high-level residential aged care facilities (nursing homes). Between October 2002 and July 2003, older adults making a first-time transition from hospital to a long-term residential care facility were recruited from the 3 metropolitan public hospitals in southern region of Adelaide. Patients were eligible if they or their caregiver gave consent and they had a life-expectancy of >=1 month as assessed by their medical team. Residents were prescribed more than 5 medications
Transition of care: Discharge from hospital and admission to the long term care facility
Age (years, CI): 82 years (95% CI 80.2 to 83.7) intervention, 83.4 years (95% CI 81.7 to 85.1) control
Female (%): 58.9% intervention, 63% control
Ethnicity: "Non English Speaking Background" 8.9% intervention, 5.6% control

Interventions
Summary:
Medication Information Transfer Fax, Medication Review 10-14 days post discharge.
Multidisciplinary Case conference
The intervention focused on transferring information on medications to case providers in the long term care facilities, including the nursing staff; the family physician, and the accredited community pharmacist. On the patient's discharge from the hospital to the long term care facility, both the family physician and the community pharmacist were faxed a medication transfer summary compiled by the transition pharmacist and signed by the hospital medical officer. This communication supplemented the usual hospital discharge summary and included specific information on changes to medications that had been made in file hospital and aspects of medication management that required monitoring. After transfer of the patient to the long term care facility, the transition pharmacist coordinated evidence based medication review that was to be performed by the community pharmacist contracted to the facility within 10 to 14 days of the transfer. The transition pharmacist also coordinated a case conference involving him or herself, the family physician, the community pharmacist, and a registered nurse at the facility within 14 to 28 days of the transfer. At this case conference, the transition pharmacist provided information concerning medication use and appropriateness.
A half-day training workshop examining use of a toolkit in the management of challenging behaviours was provided to all facilities in the study, including control facilities.
The usual hospital discharge process received by the control group included a standard hospital discharge summary. In Australia, community pharmacists are paid to perform an annual medication review for residents of long term care facilities. This review is usually independent of the general practitioner and is not necessarily coordinated with first time transfer.

Outcomes
Appropriateness of patients’ medication plans as assessed using the Medication Appropriateness Index (MAI). All regular and as-needed medications prescribed as of the date of hospital discharge (baseline) and 8 weeks after discharge (follow-up) were included in the MAI assessment. Change in MAI was reported. All residents had their medication charts reviewed before and after the intervention by an independent pharmacist. The Nursing Home Behaviour Problem Scale (NHBPS) was used to assess the effect of the intervention on residents’ behaviour Monthly drug costs for all regular medications on the government’s pharmaceutical benefits scheme were calculated for all residents in the intervention and control groups
Other outcomes included unplanned visits to the emergency department or hospital readmissions (grouped together as hospital usage), adverse drug events, falls, worsening mobility, worsening behaviours, increased confusion, and worsening pain.
Discrepancies do not seem to be recorded. However, in Table 2 it lists - "discrepancy between medication summary and medication sent" although this is not listed in outcomes.

Notes
Discrepancies do not seem to be recorded. However, in Table 2 it lists - "discrepancy between medication summary and medication sent" although this is not listed in outcomes.
<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation</td>
<td>Low risk</td>
<td>A computer generated allocation sequence that used block randomisation and was stratified by hospital. P 258</td>
</tr>
<tr>
<td>Allocation concealment</td>
<td>Low risk</td>
<td>Randomisation was coordinated by a centralised hospital pharmacy service.</td>
</tr>
<tr>
<td>Were baseline outcome</td>
<td>Low risk</td>
<td>There were no significant differences in the primary outcome - Table 1. P 259</td>
</tr>
<tr>
<td>Were baseline characteristics similar?</td>
<td>Low risk</td>
<td>There were no significant differences in characteristics between treatment groups with the exception of the number of medications discontinued during hospitalisation. However, the analysis controlled for this difference. Page 259, results paragraph 2 and statistical analysis paragraph 2</td>
</tr>
<tr>
<td>Incomplete outcome data</td>
<td>Low risk</td>
<td>12 patients in intervention and 10 in control group died or did not complete the study, follow up. High risk data available on 44 patients for control and same for intervention. Page 259, results paragraph 1</td>
</tr>
<tr>
<td>Was knowledge of the allocated interventions adequately prevented during the study?</td>
<td>Unclear risk</td>
<td>Does not indicate who assessed the outcomes. Pharmacists blinded but does not state if they did assessment. Page 258 and 259 - study assessments</td>
</tr>
<tr>
<td>Was the study adequately protected against contamination?</td>
<td>High risk</td>
<td>Patients were randomised. Page 258 study intervention paragraph 1</td>
</tr>
<tr>
<td>Selective reporting</td>
<td>Low risk</td>
<td>All outcomes mentioned in the methods are reported in the results (Page 263 Table IV).</td>
</tr>
<tr>
<td>Other bias</td>
<td>Low risk</td>
<td>No evidence of any other bias.</td>
</tr>
</tbody>
</table>

Summary Risk of Bias: Low

**Eggink 2010**

**Methods**

Study design: RCT  
Unit of allocation: Patient  
Unit of analysis: Patient  
Follow-up: OPD visit <=6 weeks post discharge  
Duration: Discharge from the hospital + post discharge clinic visit - This included an outpatient visit within 6 weeks after hospital discharge and an additional visit to the heart failure nurse if necessary.  
Providers: Clinical Pharmacist + Cardiologist + Hospital Physician. Provided by a single pharmacist only - no credentials provided.

**Participants**

Setting/participants:  
89 participants (41 intervention, 48 control). The study was conducted at the department of cardiology of a teaching hospital in Tilburg, the Netherlands between May 2007 and July 2008. Eligible patients were adults (aged over 18 years) admitted with a diagnosis of heart failure and prescribed five or more medicines (from any class) at discharge. Excluded patients included those living in a nursing home or unable to give informed consent, due to mental incapacity or terminal illness.  
Transition of care: Discharge from hospital  
Age (years +/- SD): 74 +/-12 years intervention, 72 +/- 10 years control  
Male (%): 59% intervention, 75% control  
Ethnicity: No information provided

**Interventions**

Summary:  
Prescription error check, medication knowledge update for patient, updated medication list generated, fax of updated medication list to community pharmacy + GP  
The intervention consisted of the clinical pharmacist identifying potential prescription errors in the discharge medication and discussing them with the cardiologist. This resulted in the final discharge medication. Patients received both verbal and written information about (side) effects of, and changes in, their in hospital drug therapy from a clinical pharmacist upon hospital discharge. In addition to this, the clinical pharmacist made a discharge medication list which contained additional information related to dosage changes and discontinued items. After physician approval, the list was faxed to community pharmacist and given as written information to patient with instruction to hand it to their GP.  
All patients (both regular care and intervention) collected medication at their community pharmacy and received usual routine management by their cardiologist after discharge.
This included an outpatient visit within 6 weeks after hospital discharge and an additional visit to the heart failure nurse if necessary.

Outcomes

The primary endpoint was the frequency of prescription errors in the discharge medication and medication discrepancies after discharge combined. Discrepancies were classified as: re-start of discontinued medication, discontinuation of prescribed discharge medication, use of higher or lower dose, more or less frequent use than prescribed and incorrect time of taking medication.

A prescription error was defined as an error which occurs in the process of prescribing medication, namely dosing errors, dosage form errors, contra-indications, drug–drug interactions and double-medication. All prescription errors identified by the clinical pharmacist and agreed upon by the cardiologist were collected.

The clinical relevance of prescription or discrepancy error was assessed by the NCCMERP Index

Brief Medication Questionnaire—Regimen Screen (BMQ) a measure of adherence

Notes

Risk of bias table

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>All patients who provided written informed consent were randomised using a random number table, to receive intervention or regular care. Page 761 - setting and study population - 3rd paragraph</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Not specified in the paper</td>
</tr>
<tr>
<td>Were baseline outcome measurements similar?</td>
<td>Unclear risk</td>
<td>No baseline measure of outcome</td>
</tr>
<tr>
<td>Were baseline characteristics similar?</td>
<td>Low risk</td>
<td>Patient characteristics are represented in Table 3. The characteristics of both groups did not differ. Page 763 - Table 3</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low risk</td>
<td>Four (2 lost to follow-up and 2 died in the control group) and all were followed up in the intervention group. Figure 1 page 736</td>
</tr>
<tr>
<td>Was knowledge of the allocated interventions adequately prevented during the study?</td>
<td>Low risk</td>
<td>Primary outcome measure is objective - the primary endpoint was the frequency of prescription errors in the discharge medication and medication discrepancies after discharge combined. See data collection (paragraphs 3, 4, 5 and 6) Page 761</td>
</tr>
<tr>
<td>Was the study adequately protected against contamination?</td>
<td>High risk</td>
<td>All patients who provided written informed consent were randomised using a random number table, to receive intervention or regular care.</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>All outcomes mentioned in methodology are present in the results section. Pages 763 and 764 - Results</td>
</tr>
<tr>
<td>Other bias</td>
<td>Low risk</td>
<td>No evidence of any other bias.</td>
</tr>
<tr>
<td>Summary Risk of Bias</td>
<td>Unclear risk</td>
<td>Unclear</td>
</tr>
</tbody>
</table>

Farley 2014

Methods

Study design: RCT
Unit of allocation: patient
Unit of analysis: patient
Follow-up: Up to 90 days post-discharge
Duration: Admission to discharge from hospital
Providers: “Pharmacist Case Manager”

Participants

This study was conducted at the University of Iowa Hospitals and Clinics (UIHC), a large, tertiary care, academic medical centre in the USA 592 participants (enhanced intervention n = 195, minimal intervention n = 199, and control n = 198). The ICOC study enrolled patients that were admitted to the cardiology, internal medicine, family medicine or orthopaedic services at the UIHC. Subjects were at least 18 years old, spoke English or Spanish and had at least 1 of the following diagnoses: hypertension, hyperlipidaemia, heart failure, coronary artery disease, myocardial infarction, transient ischaemic attack, stroke, diabetes, asthma, chronic obstructive pulmonary disease or require anticoagulation. Subjects could not have hearing impairments, life expectancy of less than 6 months, cognitive impairments, substance abuse problems or severe psychiatric conditions.

Transition of care: Admission and discharge from hospital
Age (mean ± CI): 60 ± 12.7 years control, 59.8 ±12.8 years minimal intervention, 61.1 ± 12.8 enhanced intervention.

Female (%): 44.9 % control, 51.7% minimal Intervention, 49.2% enhanced intervention
Ethnicity: No information available
Interventions

Summary:
Reconciliation at admission and again at discharge by a clinical pharmacist case manager.

Enhanced:
Clinical pharmacist case managers (PCMs). Patients received the minimal model PLUS having the discharge care plan prepared and faxed to their community physician and community pharmacy. The plan focused on medication issues and changes that happened during the hospitalisation and highlighted which medications had been added, changed or stopped. They also received a follow-up phone call from the PCM 3-5 days after discharge to address any medication related issues that had developed since discharge.

Minimal:
Patients received a visit from a PCM to counsel them on their medications after admission to hospital. PCM took a detailed medical history, including interview patient, calling the pharmacy and an update medical record. This was followed by medication reconciliation where the PCM compared the inpatient medications to the patient's home list to identify any discrepancies and bring them to the attention of the prescriber. The medication reconciliation process was repeated at discharge and a teaching session covering the important aspects of the patient's current medications and making sure new medications were fully understood by the patient. The discharge medication reconciliation focused on comparing the medications a patient was currently taking in the hospital with the patients prior to admission (home) medication list and making sure all medications were addressed and active medications were appropriate for the patient and consistent with practice guidelines. The patient also received a discharge medication list listing all discharge medication and their purpose.

Control:
The control group received only usual hospital care without any involvement of the PCM. All of the patients in the study received the exposure to the usual hospital medication list collection process, which was most often done by the patient's floor nurse on admission. They also received the typical discharge summaries from the University of Iowa Hospitals and Clinics sent to primary care physicians for their records.

Outcomes

Medication discrepancies:
A discrepancy was deemed present if (a) medications that documentation indicated should be active were not on the list (unintended omission), (b) medications were on list without documentation (unintended addition) or (c) medications were found with different dose or frequency.

Clinical significance of discrepancies:
The clinical research pharmacists determined the clinical significance of each discrepancy by giving a low, moderate or high designation based on the potential for patient harm. The following definitions were used by CRP in the evaluation of medication discrepancy significance:

- Low unlikely to impact any therapeutic outcome, little/no risk of harm to patient, most over the counter medication discrepancies.
- Moderate may impact therapeutic outcome and/or possibility of harm to patient.
- High likely to adversely affect outcome, medications with narrow therapeutic index, medications on Institute for safe medication practices (ISMP) high alert list and/or impending risk to patient.

Notes

This is a sub-study from the Iowa Continuity of Care (ICOC) study, funded by the National Institutes of Health (NIH). The study was a randomised, controlled trial to determine if introducing clinical pharmacist case managers (PCMs) into the inpatient care team could reduce medication underutilization, adverse drug events, and readmissions. Additional outcomes are listed in the ICOC protocol paper but were not reported in this study. Retrieved additional data and recalculations from author. Data now available includes mean discrepancies per patient for each group recorded from physician notes and pharmacists notes. Also reported at 30 and 90 days. Outcome chosen for comparison is combined discrepancies from both records at 30 days. A pooled mean of the two intervention groups was calculated for meta-analysis.

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>That the randomisation was developed using pseudo-random number generation via SAS statistical software to ensure the probabilities of assignment to each treatment group are equal. It states in Carter et al. that the randomisation was developed using pseudo-random number generation via SAS statistical software to ensure the probabilities of assignment to each treatment group are equal. Definition of pseudo-random is a process that appears to be random but is not. However, it was done using a statistical package and hence allocation was likely concealed. Page 4 of Carter et al. (reference 10) - Farley methods and background publication</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Specifies 'sealed envelopes' but were they opaque? Page 4 of Carter et al. (reference 10) - Farley methods and background publication</td>
</tr>
</tbody>
</table>
Were baseline outcome measurements similar?  Unclear risk  not measured
Were baseline characteristics similar?  Low risk  No significant differences. Table 1 and demographics in results section
Incomplete outcome data (attrition bias)  Unclear risk  No mention of loss to follow-up.
Was knowledge of the allocated interventions adequately prevented during the study?  Low risk  For the primary outcome measure, blinded, clinical research pharmacists (CRP) evaluated and compared the discharge medication lists from the hospital (updated to reflect intended changes since discharge) to 30- and 90-day post-discharge medication lists found in the community physician and community pharmacy records evaluating the lists for medication discrepancies. Methods - Data collection
Was the study adequately protected against contamination?  High risk  Patients randomised
Selective reporting (reporting bias)  High risk  Farley et al refer to another paper, Carter et al. (reference 10), for the background and methods. All the outcome measures mentioned in Carter paper are not reported in Farley paper. Carter et al, page 7 - 9
Other bias  Low risk  No evidence of any other bias.
Summary Risk of Bias  Unclear Risk

George 2011

Methods
Study design: RCT
Unit of allocation: Participant
Unit of analysis: Participant
Follow-up: Preadmission clinic to discharge
Duration: Preadmission to admission
Providers: 2 pharmacists on rotation 3 days each week. They had 2 and 8 years clinical pharmacy experience, although no previous experience in Pre-Admission Clinic (PAC).

Participants
Setting/participants: 401 participants (192 intervention, 209 control). Patients were eligible if they attended the surgical preadmission clinic (PAC) at a large metropolitan teaching hospital in Melbourne prior to orthopaedic, colorectal and vascular surgery. Patients were eligible if they were either aged 60 years or over, with or without co morbidities or current medication use, or under 60 years of age, with at least one pre-existing comorbidity and taking regular prescribed medication. Patients for non-elective, day and other surgical procedures and those unable to give written informed consent were excluded.
Transition of care: Preadmission clinic to admission
Age (median, IQR): 68, 61-75 years intervention; 67, 60-76 years
Female (%): 54% intervention, 51% control
Ethnicity: Not reported but Non-English speaking:17% intervention, 10% control

Interventions
Intervention group:
Standard PAC care plus assessment by a Pre Admission Clinic (PAC) pharmacist including patient interview in a dedicated consulting room in PAC, consisted of taking a history of the patient’s regular and PRN medications, including self- and doctor- prescribed medications, on the hospital’s dedicated form. Details were corroborated with at least one other source, e.g. patient’s own, GP, community pharmacist. Patient’s medication supply requirements on discharge were also noted on the form for attention following admission. Given a medication management plan detailing medications to cease and medications to continue or start up to and including the day of admission. The completed form was filed in the medical record for reference by hospital staff when prescribing admission medications. The PAC pharmacist contacted the intervention group patients during the pre-op period to confirm they understood the drug plan, and to document & advise on any changes since their PAC visit. Patients were also asked to contact the PAC pharmacist if there were any changes to their medication regimen during the pre-operative period.
Control:
Standard care saw allied health staff when appropriate. Both groups received standard inpatient care on admission, including clinical pharmacy services from the rostered clinical pharmacist. Important to note that standard care involved a ward pharmacist involved in building the pre-admission medication list.

Outcomes
Interventions:
Pharmacist interventions were any actions that resulted in a change in medication management or therapy
Intervention severity assessment:
Visual analogue scale (0 = no potential adverse effect to 10 = potential for causing death or lasting impairment).
Medication reconciliation:
The process of checking that the medicines the patient was taking prior to hospital admission correlated with medicines prescribed during the admission and on discharge, and any discrepancies were intentional. Further communication with the author clarified exactly what this outcome reported: "It means the percentage [of patients] that had accurate medications as an outcome assessment... inaccurate meaning at least one unintended medication discrepancy".

Notes
Medication reconciliation outcome was reported at admission and discharge. Discharge outcome recording was chosen for comparison data.

Study had a selected population, reasoning given as: "Patients from these surgery types were selected as they would benefit from a PAC pharmacist's input, due to their age, length of inpatient stay, potential for co morbidities and complex medication regimens."

Also the study hospital has a well-established PAC, where patients are assessed by nurses, surgeons and anaesthetists, approximately 2 weeks prior to surgery. Important to note that standard care involved a ward pharmacist involved in building the pre-admission medication list.

Original published data re-analysed by author following communication

Risk of bias table

<table>
<thead>
<tr>
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<th>Support for judgement</th>
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<tr>
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<td>Low risk</td>
<td>Computer-generated randomisation numbers and group assignments were pre-sealed in sequentially numbered, opaque envelopes held by the pharmacy technician. Page 213</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>Computer-generated randomisation numbers and group assignments were pre-sealed in sequentially numbered, opaque envelopes held by the pharmacy technician. Page 213</td>
</tr>
<tr>
<td>Were baseline outcome measurements similar?</td>
<td>Unclear risk</td>
<td>Outcomes measurements are not clear and some measurements appear to have no baseline information collected (e.g. medication documentation). Page 214, 215</td>
</tr>
<tr>
<td>Were baseline characteristics similar?</td>
<td>Low risk</td>
<td>It appears that in Table 1 there is no difference in baseline characteristics of patients between the intervention and control group. Note that Table 1 shows differences in medication documentation but I think this is an outcome. Table 1 page 215.</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low risk</td>
<td>In Figure 1 it shows that 21 were ineligible for analysis in the intervention group and 25 in the control group. However, reviewers noted that in the paragraph on medication reconciliation on page 215 it is unclear if all the patients were followed up. It gives denominator figures for admission but not for follow-up. Follow up to discharge is not clear. Figure 1 page 214. Following contact with the study authors loss to follow-up was confirmed: There were 12 (6.5%) and 9 (5.3%) missing in control and intervention groups respectively</td>
</tr>
<tr>
<td>Was knowledge of the allocated interventions adequately prevented during the study?</td>
<td>Unclear risk</td>
<td>Does not specify if outcomes were assessed blindly. Page 213</td>
</tr>
<tr>
<td>Was the study adequately protected against contamination?</td>
<td>High risk</td>
<td>The PAC, pharmacy and ward staff were aware a study was underway, but were not privy to the study protocol or patient allocation. Randomised by patient. Page 213</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>All outcomes mentioned in methodology are present in the results section. Page 214-215</td>
</tr>
<tr>
<td>Other bias</td>
<td>High risk</td>
<td>Patients were only recruited on certain days - 'Eligible patients attending clinic days when the PAC pharmacist was in attendance were invited to participate. Page 213</td>
</tr>
<tr>
<td>Summary Risk of Bias</td>
<td>Low risk</td>
<td>Low</td>
</tr>
</tbody>
</table>

Hale 2013

Methods
Study design: RCT
Unit of allocation: Participant
Unit of analysis: Participant
Follow-up: Peri-operatively
Duration: Pre Admission Clinic (PAC) attendance to admission
Providers: Nurse, prescribing pharmacist, Resident Medical Officer (RMO) and anaesthetist

Participants
Setting/participants: 400 participants - 200 intervention, 200 control. Following cancelled surgeries 190 in control group, 194 intervention group. Surgical PAC at Princess Alexandra Hospital, a 750-bed tertiary teaching hospital in Queensland. All patients who attended PAC and could provide written informed consent were considered for participation. Patients were excluded if they were under 18 years of age, unable to communicate due to language difficulties or
undergoing day surgery. Urology and renal transplant patients were excluded (N=43 control, N=34 intervention) from VTE prophylaxis prescribing as the director of urology was unavailable to confirm the scope of the project, and the director for transplant requested exclusion on the grounds that VTE prophylaxis in these patients was driven more by consultant discretion as opposed to being driven by guidelines.

Transition of care: PAC attendance, admission to hospital
Age (Mean, Range) - 57.6 (18-89) control, 55.8 (18-86) intervention
Male (%): - 58% control; 59% intervention
Ethnicity: No information provided

Interventions

Intervention: Patients were seen by a nurse, prescribing pharmacist, Resident Medical Officer (RMO) and anaesthetist. Patients had to be seen by the pharmacist before they were seen by the RMO to allow usual RMO duties and a countersignature of the pharmacist prescriptions, a site requirement. The pharmacist undertook all pharmacist duties as per usual care, as well as prescribing medications on the medication chart. The scope of prescribing was continuing or withholding regular medications and prescribing VTE prophylaxis according to local and national guidelines, following a risk and contraindication assessment.

Control: Patients were seen by all four healthcare professionals in clinic, in no particular order, as per usual care. Either pharmacist in the clinic saw control patients for documentation of medication history. The prescribing of the medication chart was the responsibility of the RMO. In both arms, review and monitoring were undertaken, both by RMOs in clinic at countersignature and by RMOs and clinical pharmacists at the ward level, once the patient was admitted. Changes made by RMOs to intervention patient medication charts in clinic were recorded.

Outcomes

The primary endpoint for the study was the accuracy of medication charts, with regard to concordance of the medication chart with the medication history, the plan for medications perioperatively and the quality of the individual orders related to legality and safety for administration purposes.

Prescribing errors:
- Anomaly in drug name, strength, dose, frequency or route, with no documentation in patient chart
- Communication errors: Unclear prescription in terms of name, route, dose, frequency, slow release medication notification or intermittent order prescribing

VTE Prophylaxis Prescribing:
- VTE-risk assessment, contraindication assessment and VTE prescribing
- Assessment of clinical significance of omissions:
  An expert panel, comprising a surgeon, a clinical pharmacologist, an anaesthetist, a RMO, a pharmacist and a nurse, was convened to assess the clinical significance of omissions in a randomly selected 5% sample of the total cohort of patients from both arms (N=10 control, N=9 intervention). Panel members were blinded to randomisation.

Notes

Original data from author retrieved and re-analysed, combining both prescribing and communication errors. Both regular and PRN medications summarised together. Only one pharmacist in the PAC, with 3 years’ experience as a hospital pharmacist and having a postgraduate diploma in clinical pharmacy, was trained to be a prescriber. The pharmacist attended a prescribing course which was accredited by the General Pharmaceutical Council, UK as an Independent Pharmacist Prescribing Course. Training included a minimum of 12 days of ‘period of learning in practice’ under a ‘designated medical practitioner’ (DMP), who was the consultant anaesthetist for PAC. The training included case studies and sessions on venous thromboembolism (VTE) prophylaxis with a consultant vascular physician and the clinical nurse consultant (CNC) for VTE prophylaxis at PAH. The DMP endorsed the pharmacist’s competency to prescribe before the study could start. For the pilot, an amendment was facilitated to the Queensland Health (Drugs and Poisons) Regulation 1996 to allow ‘Pharmacists registered in Queensland who are employed or contracted to Queensland Health and working in the Pharmacist Prescribing Pilot’ to prescribe controlled drugs, restricted drugs and schedule 2 and 3 poisons.

Risk of bias table

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>After consent, patients were randomised using a computer generated randomisation list, in blocks of 10 (Microsoft Excel). Sealed envelopes (not prepared by the recruiting researcher) contained a zero or one as per the computer list; the next envelope was opened after consent to determine whether a patient entered the control or intervention arm, respectively. Page 3</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
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</tr>
</tbody>
</table>
Were baseline outcome measurements similar? Unclear risk
 Were baseline characteristics similar? High risk
 Incomplete outcome data (attrition bias) Unclear risk
 Was knowledge of the allocated interventions adequately prevented during the study? Low risk
 Was the study adequately protected against contamination? High risk
 Selective reporting (reporting bias) Low risk
 Other bias Unclear risk
 Summary Risk of Bias Unclear

Methods
Study design: RCT
Unit of allocation: Participant
Unit of analysis: Participant
Follow-up: 30 days post discharge
Duration: 72 hours post discharge
Providers: Transition pharmacist + clinical pharmacy service

Participants
Setting/participants: 61 participants (24 intervention, 37 control) conducted at an 804-bed academic medical centre from October 2009 to April 2011. Patients with risk factors for rehospitalisation admitted to the family medicine inpatient service (FMIS) who also received primary care at the health care system’s outpatient family medicine centre were eligible for inclusion.
Inclusion Criteria:
Year 1: Patient must meet 1 of the 3 criteria below:
- Heart Failure
- COPD
- Hyperglycaemic crisis
- Stroke
- NSTEMI/UA
More than 3 hospitalizations in the past 5 years
8 or more scheduled medications anticipated at discharge
Year 2:
Inclusion criteria: 8 or more scheduled medications anticipated at discharge.
Exclusion criteria: Inability to speak in English, incarceration, no telephone access, transferring to another medical service/skilled nursing facility/rehabilitation facility/hospice, no transportation to follow up clinic, decisionally impaired individuals, < 18 years, not receiving care from PCP involved with research institution. Year 2 removed most of these restrictions except number of medications.

Transition of care: Hospital discharge to Primary Care Physician
Age (mean): 62.8 year - no breakdown given
Female (%): 61% - no breakdown given
Ethnicity: 59% African American, 41% Caucasian - no breakdown given

Interventions
Summary:
Transition pharmacist visit 72 hours post discharge. Clinical pharmacy service while inpatient.
Intervention:
Patients were scheduled for a care transitions clinic visit with a clinical pharmacist approximately 72 hours post discharge, and prior to the post hospitalisation primary care provider (PCP) visit. The visit involved performing a complete medication history, identifying and resolving medication discrepancies, creating a current medication list for both the medical record and the patient, and counselling on appropriate medication use. During these visits, the pharmacist identified discrepancies between the Best Possible
Medication Discharge List (BPMDL) and the discharge summary and characterized medication discrepancies using predefined categories.

Control:
Patients were scheduled to see their PCP for a post hospitalisation visit with no interim pharmacist intervention. Medication discrepancies of study subjects not attending care transitions visits were identified and characterized by study personnel in the same manner as those in the intervention group.

At the study institution, pharmacists provide clinical pharmacy services for the FMIS and outpatient family medicine clinic. Inpatient clinical pharmacists round with the medical team daily, review and monitor medications for effectiveness and safety, and make recommendations to the physician staff to optimise medications. Subjects in both groups received this usual care from the inpatient pharmacist. The role of the inpatient pharmacist in the study was to collaborate with the inpatient medical team to create a Best Possible Medication Discharge List (BPMDL) for all study subjects just prior to discharge.

Outcomes
The 3 prespecified primary outcomes of this study were a composite of the occurrence of a hospital admission or an emergency room visit within 30 days after hospital discharge and the resolution of medication discrepancies before the PCP visit. Secondary outcomes include the individual rates of rehospitalisation and ED visits within 30 days after discharge.

Composite of the occurrence of a hospital admission or an emergency room visit within 30 days after hospital discharge
We counted no more than one rehospitalisation and ED visit for each study subject. If patients were admitted to the hospital from the ED, they were not considered to have both an ED visit and a hospital admission.

Resolution of medication discrepancies before the PCP visit:
Best Possible Medication Discharge List (BPMDL) used to generate list of medication discrepancies. Reported as "medication discrepancies resolved or not resolved" having reviewed discrepancies present at discharge, prior to transition visit. Only patients who were noted to have a discrepancy at discharge were included for discrepancy analysis at 30 days

Individual rates of rehospitalisation within 30 days after discharge:
We counted no more than one rehospitalisation and ED visit for each study subject. If patients were admitted to the hospital from the ED, they were not considered to have both an ED visit and a hospital admission.

Individual rates of ED visits within 30 days after discharge
During the first year of the study, 30 patients were enrolled and a random number generator was used for randomisation. Because of unequal allocation of patients to the study arms, block randomisation with a block size of 4 was used for the second year of the study, during which 31 patients were enrolled. Also there was a significant change in the inclusion criteria in the second year of the study.

Notes
During the first year of the study, 30 patients were enrolled and a random number generator was used for randomisation. Because of unequal allocation of patients to the study arms, block randomisation with a block size of 4 was used for the second year of the study, during which 31 patients were enrolled. Change in methodology as other risk of bias. Page 2

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</tr>
<tr>
<td>(selection bias)</td>
<td></td>
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<td></td>
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<tr>
<td>Allocation concealment</td>
<td>Unclear risk</td>
<td>Not specified in paper.</td>
</tr>
<tr>
<td>(selection bias)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Were baseline outcome</td>
<td>Unclear risk</td>
<td>No baseline measure</td>
</tr>
<tr>
<td>measurements similar?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Were baseline characteristics</td>
<td>Unclear risk</td>
<td>there were no statistically significant differences in baseline characteristics</td>
</tr>
<tr>
<td>similar?</td>
<td></td>
<td>between groups but actual data presented.</td>
</tr>
<tr>
<td>Incomplete outcome</td>
<td>Low risk</td>
<td>All patients reported on</td>
</tr>
<tr>
<td>data (attrition bias)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Was knowledge of the</td>
<td>High risk</td>
<td>Although a medication discrepancy identification tool was used and discrepancies were</td>
</tr>
<tr>
<td>allocated interventions</td>
<td></td>
<td>categorized into prespecified groups to reduce subjectivity, clinician judgment was</td>
</tr>
<tr>
<td>adequately prevented during</td>
<td></td>
<td>required, which could introduce bias. All other outcomes were objective.</td>
</tr>
<tr>
<td>the study?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Was the study</td>
<td>Low risk</td>
<td>Patients randomised but unlikely that control received intervention or vice versa.</td>
</tr>
<tr>
<td>adequately protected</td>
<td></td>
<td></td>
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<tr>
<td>against contamination?</td>
<td></td>
<td>Page 3</td>
</tr>
<tr>
<td>Selective reporting</td>
<td>Low risk</td>
<td>All outcomes mentioned in methodology are present in the results section.</td>
</tr>
<tr>
<td>(reporting bias)</td>
<td></td>
<td>Page 3 and Table 2 on page 4</td>
</tr>
</tbody>
</table>
Other bias

High risk

In year 2 of study the inclusion criteria changed (from that of year 1). Unequally sized groups (i.e. control / intervention). A lot of intervention group did not attend the clinic visit. Page 2 - study design, page 3 - results (paragraph 2), page 4 - discussion (paragraph 2). Also discrepancies outcome was decided based on discrepancies at discharge, after randomisation and < 50% of enrolled patients

Summary Risk of Bias

Unclear risk

Heng 2013

Methods

Study design: RCT
Unit of allocation: Participant
Unit of analysis: Participant
Follow-up: Unclear
Duration: Immediately prior to clinic appointment
Providers: Pharmacist + Doctor

Participants

Setting/participants: 40 participants (20 intervention, 20 control). Endocrine outpatient clinic in Tan Tock Seng Hospital, Singapore. Inclusion and exclusion criteria not specified.
Transition of care: Endocrine hospital outpatient clinic visit
Age: No information provided
Gender: No information provided
Ethnicity: No information provided

Interventions

Summary: Pharmacist medication reconciliation (MR) passed to doctor at clinic visit.
Intervention: Pharmacist performed medication reconciliation done before consultation, and the MR list was passed to the doctor
Control: Pharmacist performed medication reconciliation done before consultation, but the MR list was not passed to the doctor.

Outcomes

Discrepancies between doctor’s orders and pharmacist’s medication reconciliation (MR) list.
No further detail given.

Notes

Endocrine clinic only

Risk of bias table

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<tr>
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<tr>
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<td>Low risk</td>
<td>Computer generated random number</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>not specified</td>
</tr>
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<td>Were baseline outcome measurements similar?</td>
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<td>no outcome measurement</td>
</tr>
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<td>Not specified in the paper</td>
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<td>Was knowledge of the allocated interventions adequately prevented during the study?</td>
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<td>not specified.</td>
</tr>
<tr>
<td>Was the study adequately protected against contamination?</td>
<td>High risk</td>
<td>Patients were randomised.</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Unclear risk</td>
<td>outcomes not clearly specified</td>
</tr>
<tr>
<td>Other bias</td>
<td>High risk</td>
<td>There is not enough information given and contact details for authors cannot be found.</td>
</tr>
<tr>
<td>Summary Risk of Bias</td>
<td>Unclear risk</td>
<td>Unclear</td>
</tr>
</tbody>
</table>

Ibrahim 2012

Methods

Study design: RCT
Participants

Setting/participants: 250 participants (125 intervention, 125 control). Conducted at a major teaching hospital in Cairo, Egypt during the period from April 2009 till end of March 2010. Patients eligible for the study were patients admitted to the general medicine service then being discharged home and who could be followed up by phone 30 days after discharge. Exclusion criteria not listed.

Transition of care: Hospital Discharge

Age (mean): 62.7 (18.3) years; 59.8 (16.8) years
Female: 47.2% intervention, 44.8% control
Ethnicity: No information provided

Interventions

Summary: Medication review by pharmacist (including reconciliation with admission medications) with medical team’s help and a follow up phone call in which a medicines review/monitoring was also done.

Intervention:
Pharmacist review on the day of discharge consisted of several parts. First, Drug Related Problems (DRP) including therapeutic failure and regimens and all discrepancies were reconciled with the medical team’s help. Patients were screened for previous DRPs, including non-adherence, lack of efficacy, and side effects. The pharmacist reviewed the indications, directions for use, and potential adverse effects of each discharge medication with the patient. The intervention group also received a telephone follow-up 3-4 days after discharge during which the clinical pharmacist asked about medication adherence, possible ADEs, and adherence with scheduled follow-up visits and laboratory appointments.

Control:
Patients assigned to usual care received routine review of medication orders by a ward-based pharmacist at the time of discharge. Discharge counselling typically focused on directions to use medications and may have included a discussion of indications or potential side effects, especially for new medications.

Outcomes

Presence of a preventable ADE in patients 30 days after hospital discharge:
Preventable ADEs were assessed with a modified version of the method developed by Bates et al. Patients were asked a screening question for new or worsening symptoms since hospital admission. In the case of an affirmative response, follow-up questions to uncover details about these symptoms and their relation to medications. Case summaries were prepared from these answers and they also include medication lists at admission and discharge, the hospital discharge summary, any available outpatient visit notes, discharge summaries from ED visits or hospital readmissions, and any available laboratory test results in the month since discharge. From these summaries, a clinical pharmacist who is blinded to treatment group determined whether an ADE had occurred, using the Naranjo algorithm which is a validated scoring system to assess causality. The clinical pharmacist also evaluated ADE severity and preventability. For all hospital admissions or ED visits, the blinded clinical pharmacist assessed any relationship to medication use or preventability. Preventable medication-related ED visits or readmissions were considered to be preventable ADEs. If patients could not be contacted by telephone 30 days after discharge but had been readmitted to the hospital or visited the ED, case summaries were prepared and ADEs assessed as described in the previous paragraph but without the patients’ responses.

Patient satisfaction:
Satisfaction with hospitalisation and discharge processes was assessed using a standard questionnaire.

Medication adherence:
Assessed by asking patients whether they had taken each medication exactly as prescribed during the previous day and on how many days during the previous week.

Medication discrepancies
Determined by comparing the discharge medication regimen with the medications reported by each patient at 30 days. Differences not attributable to a physician’s order or completion of a prescribed course of treatment were considered discrepancies.

Healthcare utilisation:
Emergency department visit or readmission. Assessed as per primary outcome

Notes

Risk of bias table

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Page 1 - Methods (2nd paragraph)
Allocation concealment (selection bias)  Low risk  Randomization was performed through a computer-generated algorithm, and treatment assignments kept in sealed opaque envelopes which were opened after patient consent was obtained. Page 1 - Methods (2nd paragraph)

Were baseline outcome measurements similar?  Unclear risk  No baseline measure of outcome

Were baseline characteristics similar?  Low risk  At baseline, there were no significant differences between patients in the 2 study arms. Page 2 - Statistical Analysis paragraph 2

Incomplete outcome data (attrition bias)  High risk  15 lost to follow-up in intervention and 21 in the control. Effect size low so could be affected by loss to follow up. Figure 1 page 2

Was knowledge of the allocated interventions adequately prevented during the study?  Low risk  Although patients and clinical pharmacists were not blinded to the treatment assignment, outcomes were assessed by research assistants who were blinded to treatment assignment. A clinical pharmacist who is blinded to treatment group determined whether an ADE had occurred, using the Naranjo algorithm which is a validated scoring system to assess causality [19, 20]. The clinical pharmacist also evaluated ADE severity and preventability. For all hospital admissions or ED visits, the blinded clinical pharmacist assessed any relationship to medication use or preventability. Preventable medication-related ED visits or readmissions were considered to be preventable ADEs. Page 1 - Methods (paragraph 2 and paragraph 6)

Was the study adequately protected against contamination?  High risk  Patients were randomised

Selective reporting (reporting bias)  Low risk  All outcomes mentioned in methodology are present in the results section. Page 1 - methods (paragraph 5) and page 3 - Table 3

Other bias  Low risk  none obvious

Summary Risk of Bias  High risk  High

Kripalani 2012

Methods
Study design: RCT
Unit of allocation: Participant
Unit of analysis: Participant
Follow-up: 25-35 days post discharge
Duration: Hospital admission to 1-4 days post discharge
Providers: Clinical pharmacist (Note “pharmacist-led”, but importantly collaborative with inpatient and outpatient physicians)

Participants
Setting/participants:
862 participants (430 Intervention, Control 432). Adults hospitalised at Vanderbilt University Hospital or Brigham and Women’s Hospital, USA for acute coronary syndromes or acute decompensated heart failure were enrolled between May 2008 and September 2009. Patients were excluded if they were being discharged within 3 hours; were too ill to participate; could not communicate in English or Spanish; had active psychosis, bipolar disorder, delirium, or severe dementia; had hearing or vision impairment; did not manage their own medications; were unlikely to be discharged to home; lacked a telephone; or were in police custody.

Transition of care: Admission & Discharge from hospital
Age (mean, SD): 59 (14) years control; 61 (14) years intervention
Male (%): 58.2% control, 59.1% intervention
Ethnicity (%): White 78.3% control 75.4% intervention. Black 16.6% control 18.2% intervention. Other 5.1% control 6.4% intervention

Interventions
Summary:
Reconciliation at admission and discharge, inpatient medication counselling, patient information leaflet, adherence improvement and follow up phone call.

Intervention:
The intervention consisted of 4 components: pharmacist assisted medication reconciliation, tailored inpatient counselling by a pharmacist, provision of low-literacy adherence aids, and individualized telephone follow-up after discharge. Eleven study pharmacists performed medication reconciliation at the time of enrolment, discharge, and in-hospital transfers. They communicated with the treating physicians to resolve any clinically relevant, unintentional medication discrepancies. Intervention counselling was sensitive to the patient’s health literacy and cognition. It was typically provided during 2 sessions, or during a single session when discharge occurred on the day of enrolment. During the initial meeting, the pharmacist assessed the patient’s baseline understanding of medications and prescription labels, barriers to adherence, and social support. The second meeting generally occurred at discharge and included tailored counselling on the discharge medication regimen and the patient’s needs, as previously identified. The pharmacist focused on changes between the preadmission and discharge regimen; strategies to
promote adherence and minimize adverse effects; and high-risk medications, such as insulin or warfarin. Pharmacists confirmed understanding by using “teach back” and provided low-literacy adherence aids, including a pill box and illustrated daily medication schedule. Within 1 to 4 days after discharge, an unblinded research coordinator called intervention patients and used a structured interview to identify medication-related problems. As needed, pharmacists then called to address any identified issues in collaboration with the treating inpatient and responsible outpatient physicians.

Control:
The patients’ treating physicians and nurses performed medication reconciliation and provided discharge counselling. At each hospital, medication reconciliation was facilitated by electronic records from the hospital and affiliated clinics, as well as internally developed interfaces to construct a pre-admission medication list. At Brigham and Women’s Hospital, the program had additional features (such as reminders to complete a preadmission medication list and integration with order entry) and required providers to continue, stop, or change each preadmission medication at admission; this application, combined with process redesign, was previously shown to reduce potential ADEs. Patients assigned to usual care were not routinely provided with a pill box, illustrated medication schedule, or telephone follow-up.

Outcomes
The primary composite outcome was the number of clinically important medication errors per patient within 30 days after hospital discharge. This included preventable or ameliorable ADEs and potential ADEs due to medication discrepancies or non-adherence. Clinical important medication errors per patient within 30 days post discharge:

- For each medication discrepancy or episode of non-adherence, adjudicators graded the potential for harm if left uncorrected; if the likelihood of potential harm exceeded 50%, it was counted as a potential ADE. A drug implicated in an ADE was not eligible to be adjudicated as a potential ADE in the same patient. For each ADE and potential ADE, adjudicators categorized the severity as significant, serious, or life-threatening, following rules and examples from an adjudication manual. Disagreements between the independent adjudicators about whether or not a medication was implicated in a study outcome were uncommon (approximately 3% for ADEs and 5% for potential ADEs) and occurred with similar frequency at each site. Disagreements were resolved by discussion or, in about 5% of cases, with assistance from a third adjudicator.

- Preventable or ameliorable ADEs;
- Potential ADEs due to discrepancies or non-adherence.

Preventable or ameliorable ADEs judged to be serious, life-threatening, or fatal were determined by 2 independent clinician adjudicators, blinded to treatment assignment. Each adjudicator reviewed all available medical records during the 30 days after discharge and the results of a patient follow-up phone interview conducted by research staff 25-35 days after discharge.

Notes
Data on all discrepancies retrieved through direct contact with author. Additional data and analysis received through contact with the author.

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</tr>
<tr>
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<td>randomisation was stratified by site and diagnosis, in permuted blocks of 2-6 patients, by a computer program that maintained allocation concealment. methods, R&amp;I, p2</td>
</tr>
<tr>
<td>Were baseline outcome measurements similar?</td>
<td>Unclear risk</td>
<td>not possible to do, as the outcomes were discrete events occurring after discharge. Page 3 - “Outcomes”</td>
</tr>
<tr>
<td>Were baseline characteristics similar?</td>
<td>Low risk</td>
<td>similar for most characteristics, with the exception of age, higher by 2 years (59 v 61) in the intervention group. Extensive reporting of other characteristics, and no differences identified. Last sentence p 4, and table 1</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low risk</td>
<td>Very little attrition, balanced between the two groups. Fig 1 and table 2</td>
</tr>
<tr>
<td>Was knowledge of the allocated interventions adequately prevented during the study?</td>
<td>Low risk</td>
<td>Outcomes were determined by 2 independent clinician adjudicators who were blinded to treatment assignment. p3, outcomes, para 2</td>
</tr>
<tr>
<td>Was the study adequately protected against contamination?</td>
<td>Unclear risk</td>
<td>Patients were randomised. However, HCPs delivered care commonly to both groups, although the pharmacist intervention was restricted to the intervention group. Also, at each hospital, med reconciliation was facilitated electronically. methods, R&amp;I</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>All outcomes mentioned in methodology are present in the results section. Page 3 - outcomes and follow-up; Page 6 - Tables 2 &amp; 3</td>
</tr>
</tbody>
</table>
Other bias  High risk  Not all patients received the full intervention as intended, although the vast majority did (see the discussion). Figure 1, Page 9 - discussion

Summary Risk of Bias  Low risk  Low

Kwan 2007

Methods

Study design: RCT
Unit of allocation: Participant
Unit of analysis: Participant
Follow-up: Preadmission clinic assessment to post-surgical unit
Duration: Surgical preadmission clinic appointment to surgical procedure
Providers: Hospital based pharmacists (no mention of specific training)

Participants

Setting/participants: 464 participants (227 intervention, 237 control). Tertiary care university, affiliated teaching hospital in Toronto, Ontario, Canada. All consecutive patients who had a surgical preadmission clinic visit before undergoing surgical procedures from the urology, plastic surgery, general surgery, thoracic surgery, gynaecology oncology, and ear, nose, and throat services were eligible for inclusion. Patients were excluded if they were scheduled for discharge on the same day as their surgery.
Transition of care: Pre-surgical admission clinic (orders prepared for review at post-operative surgical review also)
Age (median, range): 57 (18-89) years intervention; 57 (16-86) years control
Male: 52.5% intervention, 54.7% control
Ethnicity: No information provided

Interventions

Summary: Structured pharmacist medication history interviews with assessments in the surgical preadmission clinic and the use of a postoperative medication order form.

Intervention: Provider orientated interventions
The model uses a combined intervention of the pharmacist as part of the multidisciplinary team completing structured medication assessments and a postoperative medication order form in the surgical preadmission clinic. The intervention consisted of pharmacists in the preadmission clinic conducting a standardized comprehensive medication history interview and assessment focusing on the patient’s current home medication regimen. This was documented in the health record, and the results were used by the pharmacist to generate a pre-printed postoperative medication order form for preoperative home medications. Through the use of check boxes, the surgeon indicated on this medication order form after surgery which home medications were to be reordered. Home medications that required further clarification before being ordered on hospital admission (e.g., conflicting information between patient report vs medication vials) or that required special management in the postoperative setting (e.g., anticoagulants, antiplatelets, analgesics, and hypoglycaemic agents) were listed in the bottom section of the form. A detailed description of the issue was written in the medical record to be considered by the surgeon at hospital admission. On reassessment, the continuation of medications listed in this section required that the physician write a separate medication order. Pharmacists conducted telephone interviews with patients they were unable to see in the clinic. If needed, the pharmacist contacted the patient’s community pharmacy or family physician to clarify the medication regimen. After postoperative admission, the pharmacist also attempted to verify with the patient if any medication changes had been made since the clinic assessment. Before study implementation, nurses and participating physicians were instructed on the proper use of the new medication order form.

Control: Standard care consisted of nurses conducting medication histories with patients at the surgical preadmission clinic or occasionally over the telephone. Medication history information was entered in the hospital electronic health record and printed. Surgeons could refer to this printout to generate their postoperative medication orders. The patient’s community pharmacy or family physician was contacted for additional medication clarifications if needed. It was not standard practice to routinely follow-up after surgery to clarify medication changes since the clinic assessment.

Outcomes

Postoperative medication discrepancy: Defined as any medication clarification related to home medications that was made during the postoperative period. Medication discrepancies could be associated with any of the following: drug, dosage, duration, frequency, formulation, route of administration, appropriateness of restarting medications, orders requesting the pharmacist to clarify medications, illegible orders, and miscellaneous items. On admission of study patients to the participating surgical inpatient units, the pharmacists prospectively identified patients’ medication discrepancies. Medication discrepancies were detected using a systematic approach whereby the patients’ home medications were compared with the admission medication orders. If an in congruency was detected and the reason was not documented in the medical record, this was clarified with the medical team and patient. Medication discrepancies included unintentional and undocumented intentional discrepancies.
undocumented intentional discrepancy is one in which the physician has made an intentional choice to add, change, or discontinue a medication but is not clearly documented. These discrepancies were recorded because they can lead to confusion for the health care team and to potential medication errors.

Characteristics and clinical severity of postoperative medication discrepancies:
The clinical effect of the postoperative medication discrepancies was assessed independently by 3 pharmacy clinician evaluators. For each postoperative medication discrepancy, the degree of effect was based on the potential that the discrepancy could result in “unlikely,” “possible,” or “probable” patient discomfort and/or clinical deterioration if the discrepancy was not identified and addressed. This ranking system was adapted from the method used by Cornish et al. Each evaluator independently reviewed blinded patient data collection forms, pharmacy patient profiles if available, and medical record orders if needed. The reviewers then rated the medication discrepancies and voted; if disagreements occurred, discussion ensued until a consensus was reached.

Notes

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>p1035</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>The treatment assignments were sealed in sequentially numbered, identical, opaque envelopes according to the allocation sequence. p1035</td>
</tr>
<tr>
<td>Were baseline outcome measurements similar?</td>
<td>Unclear risk</td>
<td>Baseline outcome reporting not reported, per protocol method used and sensitivity analysis also undertaken. p 1037</td>
</tr>
<tr>
<td>Were baseline characteristics similar?</td>
<td>Low risk</td>
<td>Table 1 gives baseline patient characteristics in the intervention and standard care arms. There were no statistically significant differences between the 2 treatment arms except for the number of home medications. Patients in the intervention arm vs the standard care arm had a greater number of home medications (4 vs 3, P=.001). Table 1, p 1037</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low risk</td>
<td>Forty-seven patients had their plan of care changed after randomisation and were not admitted to a postsurgical unit participating in the study during the study period; therefore, they were excluded from the main study analysis. One same-day-discharge patient was incorrectly randomised into the study and was also excluded from the main study analysis. p1037</td>
</tr>
<tr>
<td>Was knowledge of the allocated interventions adequately prevented during the study?</td>
<td>High risk</td>
<td>On admission of study patients to the participating surgical inpatient units, the pharmacists prospectively identified patients’ medication discrepancies. Medication discrepancies were detected using a systematic approach whereby the patients’ home medications were compared with the admission medication orders. If an in congruency was detected and the reason was not documented in the medical record, this was clarified with the medical team and patient. Medication discrepancies included unintentional and undocumented intentional discrepancies. An undocumented intentional discrepancy is one in which the physician has made an intentional choice to add, change, or discontinue a medication but is not clearly documented. Although every effort was made to conceal the treatment arms during the clinical assessment, the assignment of the patient was unblinded if the independent assessors thought they needed to look into the medication discrepancy in more detail. p 1037</td>
</tr>
<tr>
<td>Was the study adequately protected against contamination?</td>
<td>High risk</td>
<td>All patients attended the preadmission clinic. Both control and pharmacist’s interventions taking place within same clinic. p 1035</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>Both a priori outcomes were identified - discrepancies and clinical impact</td>
</tr>
<tr>
<td>Other bias</td>
<td>High risk</td>
<td>A per protocol analysis was performed instead of an intention-to-treat analysis. Patients admitted to inpatient units not participating in this study were not formally assessed for medication discrepancies - a possible selection bias. p 1040</td>
</tr>
</tbody>
</table>

Summary Risk of Bias | Low

Lalonde 2008

Methods

Study design: RCT
Interventions

Structural interventions - changes in the medical record system (medication discharge plan)

Summary:
Pharmacist reconciliation at admission and discharge, Medication discharge plan creation and onward communication to health care professionals in the community

Intervention:
After discussions with Laval hospital pharmacists, the Medication Discharge Plan (MDP) was adapted from MDPs in current use in other hospitals and at the Cité de la Santé de Laval hospital. The MDP included patient information (name, address, telephone numbers) and contact information (names, telephone numbers) for the hospital physician and pharmacist. It also included the patient’s clinical information (weight, height, allergies, intolerances) as well as pharmacotherapy information (drug name, dose, route, frequency, duration) and the pharmacist’s recommendations. All medications reported at admission were listed along with their current status at discharge (re prescribed without changes, re prescribed with changes, discontinued) and new medications added during hospitalisation.

At the time of hospital admission, ward pharmacists were responsible for documenting medication history. If necessary, the patient’s community pharmacy was contacted to complete or confirm the medication history. Medication changes during hospitalisation were documented from the hospital pharmacy medication administration records, physicians’ prescriptions, and pharmacists’ notes. All patients received the comprehensive pharmaceutical care routinely provided by hospital pharmacists during their hospital stay and at discharge. This includes obtaining medication history, chart documentation, case discussion with physicians, and patient counselling at discharge. An MDP was completed for each patient in the intervention group. If discrepancies were observed between the MDP and the discharge prescription, pharmacists were responsible for reconciling the information. However, on rare occasions, MDPs were completed before the discharge prescriptions were finalized. MDP patients received a copy of the MDP, and a copy was faxed to their treating physician and pharmacy or long-term care pharmacist.

Control:
All patients assigned to the control group received similar pharmaceutical care during their hospital stay and at discharge. An MDP was completed for each control patient; however, a copy of the MDP was not given to patients and was not sent to their treating physician and community pharmacy. Patients received a conventional hospital discharge prescription and, if relevant, a medication administration schedule with or without medication information leaflets.

Outcomes
Comparisons of Medication Discrepancies in Community Pharmacy Dispensing Records and Patient Self-Report v MDP.

Clinical Severity of Discrepancies:
Severity was assessed as not clinically significant, clinically significant but not life threatening, serious (i.e., life threatening or may cause major clinical problem or hospitalisation), not enough information to judge, or not applicable (discrepancy judged to be due to an MDP error).

Notes
Clustering by discharge unit (geriatric, psychiatric, family medicine, other), and pharmacies. No mention of this in the analysis.
Contacted author for original data on patients with "at least one discrepancy" between MDP and discharge prescription.

### Risk of bias table

<table>
<thead>
<tr>
<th>Bias</th>
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<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk ▼ ▼</td>
<td>Block Randomisation: &quot;The randomisation, blocked in groups of 10, was stratified by medical ward. Group allocation was deter-mined using a computer-generated, random-number table and placed in numbered, sealed envelopes to be opened in strict sequence.&quot; p.1452</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk ▼ ▼</td>
<td>The randomisation, blocked in groups of 10, was stratified by medical ward. Group allocation was deter-mined using a computer-generated, random-number table and placed in numbered, sealed envelopes to be opened in strict sequence. p.1452</td>
</tr>
<tr>
<td>Were baseline outcome measurements similar?</td>
<td>Unclear risk ▼ ▼</td>
<td>No recording of outcome measures prior to randomisation</td>
</tr>
<tr>
<td>Were baseline characteristics similar?</td>
<td>Low risk ▼ ▼</td>
<td>Presented as table. No obvious differences between groups. p.1454 Table 3</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>High risk ▼ ▼</td>
<td>Copies of the discharge prescriptions were obtained for 65 patients and copies of the community pharmacy dispensing records were obtained for all patients but 1. Six patients could not be contacted for the telephone interview. Data were missing for 18 patients because they left the hospital with their discharge prescription before the researchers could record it. Table 2</td>
</tr>
<tr>
<td>Was knowledge of the allocated interventions adequately prevented during the study?</td>
<td>High risk ▼ ▼</td>
<td>A pharmacist systematically interviewed patients by telephone approximately one week after discharge. Patients were asked when and where they had their discharge prescription filled and the name and dosage taken of each of their medications (medication, dosage, route of administration, duration of use). The patient’s community pharmacy was then contacted to obtain a listing of the patient’s active medications available from the dispensing records. Clinical severity was assessed by blinded assessors.</td>
</tr>
<tr>
<td>Was the study adequately protected against contamination?</td>
<td>Unclear risk ▼ ▼</td>
<td>Randomisation by individual patient but allocated to medical wards. Also intervention was a physical reminder of MDP so unlikely to be contaminated</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk ▼ ▼</td>
<td>Both outcomes reported on</td>
</tr>
<tr>
<td>Other bias</td>
<td>High risk ▼ ▼</td>
<td>A lot of a priori exclusion criteria - including not being available to take a phone call or being transferred to a nursing home</td>
</tr>
<tr>
<td>Summary Risk of Bias</td>
<td>High</td>
<td>High</td>
</tr>
</tbody>
</table>

### Methods

**Study design:** RCT  
**Unit of allocation:** Participant  
**Unit of analysis:** Participant  
**Follow-up:** From presentation to the unit on day of surgery. Control patients were contacted following discharge to construct pre admission medication list.  
**Duration:** Patients admitted on day of surgery, medication history acquired pre-surgery, prescribing perioperatively  
**Providers:** Group 1 & 2: Pharmacist and Resident Medical Officer (RMO). Control: RMO

### Participants

**Setting/participants:** 357 participants (119 Pharmacist history taking group, 118 Pharmacist prescribing group, 118 Control). All adult elective surgery patients admitted to the John Hunter Hospital on the day of surgery were candidates for inclusion in the study. John Hunter Hospital is a 750-bed regional tertiary referral hospital in Newcastle, New South Wales, Australia. Approximately 92% of elective surgery patients staying at least one night are admitted on the day of surgery. Higher risk patients (approximately 62% of all surgical patients who stay at least one night) are seen by a nurse and a doctor in a preoperative assessment and preparation clinic before admission. Surgery types included general, cardiothoracic, gynaecology, vascular, urology, ear nose and throat, facio maxillary and transplant surgery. Orthopaedic surgery patients were excluded due to local process differences. Patients were excluded from the trial if they took no regular medications, were unable to provide consent, had medications charted during a preoperative clinic visit or were admitted as a day-only patient.  
**Transition of care:** Hospital admission  
**Age (Median, IQR):** 65 (54-75) years control, 62 (52-71) years pharmacist history only, 64 (47-75) years pharmacist history and supplementary prescribing
Interventions
Organisational - Provider orientated intervention - Revision of professional roles
Summary:
Pharmacist acquired medication history/Pharmacist acquired medication history and perioperative prescribing
Intervention Group 1 (Preoperative pharmacist medication history only):
The pharmacist interviewed patients at the time of admission on the day of surgery and documented a regular medication list.
Intervention Group 2 (Preoperative pharmacist medication history and supplementary prescribing on the day of surgery):
The pharmacist interviewed patients at the time of admission on the day of surgery and documented a regular medication list. The pharmacist also prescribed their regular medicines on the medication chart. Pharmacist prescribing was guided by protocols advising which medications should be withheld and for how long, for each type of surgery. These were developed before the study in consultation with surgeons and anaesthetists and approved by the hospital’s drug and therapeutics committee.
Control:
‘Usual care’ involved no clinical pharmacist consultation prior to surgery. These patients had their medications charted immediately prior to surgery or postoperatively by the medical officer in the normal time frame. New medications required perioperatively were charted by a medical officer in the usual way, for all three groups.

Outcomes
Missed doses of regular medication (itemised to missed dose or incorrect dose/frequency):
To determine whether the number of missed doses of regular medication were significantly different between one of three allocated interventions. Patient’s regular medication list was compared with their inpatient medication chart to determine number of missed doses during their inpatient stay. Comparisons were based on hospital protocols for regular medication management. Decisions to change medicines and cease medicines that were clearly documented were also taken into consideration. In the control group the patient’s regular medication list was obtained from the patient post discharge by the trial pharmacist over the phone. A combination of the preoperative questionnaire filled out by the patient, the admission and progress notes and lists faxed from the community pharmacy and community doctor were used to prompt the patient on their regular medication prior to admission. The final list was then used as the patient’s regular medication list for the purpose of comparison with their inpatient orders.
Incorrect dose, frequency, or missed medication doses postoperatively of significant medications such as beta blockers, 3-hydroxy-3-methyl-glutaryl-CoA reductase inhibitors, anti-platelets and anticoagulants.

Notes
Contacted author for original data to re-analyse for primary outcome. Re-analysed original data with the reported outcomes “different dose or frequency per participant” to equal "any discrepancy per participant".

Risk of bias table
<table>
<thead>
<tr>
<th>Bias</th>
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<th>Support for judgement</th>
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</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>Patients were randomised via a computer generated list, held by an independent investigator to ensure allocation concealment. Randomisation was done in permuted blocks of 60 to ensure balance of numbers in each group. p1065</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>held by an independent investigator to ensure allocation concealment. p1065</td>
</tr>
<tr>
<td>Were baseline outcome measurements similar?</td>
<td>Unclear risk</td>
<td>Not recorded</td>
</tr>
<tr>
<td>Were baseline characteristics similar?</td>
<td>Low risk</td>
<td>Table 1. p1066</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low risk</td>
<td>fig 1</td>
</tr>
<tr>
<td>Was knowledge of the allocated interventions adequately prevented during the study?</td>
<td>Low risk</td>
<td>Outcome measures were collected after discharge by an independent technician through retrospective chart review and patient administration system records. p1066</td>
</tr>
<tr>
<td>Was the study adequately protected against contamination?</td>
<td>High risk</td>
<td>Intervention groups were unable to be blinded from the patient, pharmacist or the clinicians, introducing the opportunity for bias. It is also recognised that medication history taking post-discharge over the phone is not an ideal method of taking an accurate medication history and may have resulted in medications being omitted from the medication history. For this reason, other secondary sources were utilised in prompting the patient to gain as accurate a list as possible. It was also possible that the presence of a pharmacist in the perioperative...</td>
</tr>
</tbody>
</table>
service highlighted the importance of prescribing regular medications for patients. Each of these factors may have artificially improved the results for the control group.

Selective reporting (reporting bias) | Low risk
Other bias | Unclear risk States it was an ITT analysis and meta-analysis now done with original study numbers
Summary Risk of Bias | Low

Nickerson 2005

Methods
Study design: RCT
Unit of allocation: Participant (But clustered by two inpatient units, not clear if adjusted for this)
Unit of analysis: Participant
Follow-up: From admission to discharge
Duration: Hospital discharge
Providers: Hospital pharmacist

Participants
Setting/participants:
253 participants (119 control, 134 intervention). Family practice patients discharged from two family practice patient units. The study was conducted at The Moncton Hospital, South-East Health Regional Health Authority, Moncton, NB, Canada. The Moncton Hospital is a 381-bed regional hospital that provides tertiary care services. Inclusion criteria included being discharged between 8h00 and 14h00, not discharged to another hospital, prescribed at least one prescription medication at discharge, completion of informed consent form, patient's community pharmacy had signed study participation agreement, and no previous enrolment in the study from a prior admission. Patients were excluded from the study if they were not able to answer the questions needed to complete the study (i.e., the surveys) or if they would not be available for follow-up after their discharge.
Transition of care: Hospital discharge
Age (mean): 67.3 intervention, 61.8 control
Female (%): 69% intervention, 68% control
Ethnicity: No information provided

Interventions
Organisational interventions - Provider orientated interventions
Summary: Clinical Pharmacist medication review, reconciliation, medication counselling and communication to Primary Care Physician (PCP)
Intervention:
The "seamless care pharmacist" carried out the medication reconciliation process by reviewing discharge prescriptions (as written by a physician) and compared these with the Medication Administration Record (MAR) and the patient’s medical chart to identify any discrepancies in the discharge orders. This pharmacist also reviewed the intervention patient’s drug regime at discharge as part of a comprehensive pharmaceutical care work-up. The pharmacist also identified problems with drug therapy and communicated these to the patient’s community pharmacy, hospital staff and family physician(s). Additionally, the seamless care pharmacist performed the medication discharge counselling to all intervention patients and provided them with a medication compliance chart.
Control:
Patients in the control group received the hospital’s standard of care at discharge. The standard of care at this facility is for a nurse on the unit to perform the discharge counselling and manually transcribe the discharge notes from the patient’s medical chart

Outcomes
Frequency and potential clinical impact of drug-therapy problems for seamless monitoring (DTPsm) as identified by a seamless care pharmacist at the time of discharge and frequency and potential clinical impact of drug therapy inconsistencies and omissions (DTIOs) in hospital discharge medication orders as identified by the seamless care pharmacist as part of the medication reconciliation process.
Frequency and potential clinical impact of drug-therapy problems for seamless monitoring (DTPsm):
A drug-therapy (related) problem (DTP) can be defined as an event or circumstance involving drug treatment that actually or potentially interferes with the patient experiencing an optimum outcome of medical care. The DTPs were classified into one of the categories previously established by Strand and colleagues. To facilitate the community pharmacist in monitoring the patient’s progress, each DTP was individually supplemented with additional relevant information such as laboratory findings, diagnosis and general patient notes. This provided the community pharmacist with a more complete picture of the patient’s drug therapy and medical conditions. With this additional information provided to the community pharmacist for follow-up, the DTP was termed a Drug Therapy Problem for Seamless Monitoring (DTPsm) to better reflect its true composition. The complete list of DTPsm was generated for each patient and faxed to their community pharmacist and copied to the family physician at the time of discharge
Frequency and potential clinical impact of drug therapy inconsistencies and omissions (DTIOs):
The seamless care pharmacist also carried out a medication reconciliation process by reviewing the intervention patient’s discharge medication list as prepared by the physician and/or hard copies of discharge prescriptions and comparing these with the hospital’s computerized MAR for the day of discharge, and progress and consultation notes. Variations between the discharge medication list and the MAR and patient’s medical chart were identified and recorded as either a drug-therapy inconsistency or omission. An inconsistency was defined as an alteration in a drug order component occurring between the MAR and discharge medication list. An omission was defined as a deletion of a drug order component occurring between the MAR and the discharge medication list. All variations were further classified into sub-groupings according to the nature of the variation. The sub-groupings are: dose, drug, duration, frequency, and legal. These sub-groupings were chosen based on a previous pilot project.

Notes

Very broad exclusion criteria of "they would not be available for follow-up after their discharge."

Possible unit of analysis error

The DTIO recorded at discharge in the intervention group was actually recording done as part of the intervention. The recording done in the chart review post discharge only looked at a small sample (28/134 individuals) - This was chosen as the intervention group outcome because it post-dates the intervention and was not recorded while the intervention was being delivered.

<table>
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<tr>
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<tbody>
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<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>&quot;The patient was then randomised to the intervention or control group using computer generated random numbers produced by the hospital’s Information technology services&quot;. P 66</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>not recorded</td>
</tr>
<tr>
<td>Were baseline outcome measurements similar?</td>
<td>Unclear risk</td>
<td>Differences between intervention group and control group, not allowed for analysis. Table 1</td>
</tr>
<tr>
<td>Were baseline characteristics similar?</td>
<td>High risk</td>
<td>No loss to follow up</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low risk</td>
<td>Spot checking only and not done blindly by 2nd pharmacist. Study pharmacist was the intervention and reported the primary outcome. p68</td>
</tr>
<tr>
<td>Was knowledge of the allocated interventions adequately prevented during the study?</td>
<td>High risk</td>
<td>Possibility of contamination and no mention made of the risk</td>
</tr>
<tr>
<td>Was the study adequately protected against contamination?</td>
<td>Low risk</td>
<td>Study pharmacist conducted the intervention and recorded the outcome at the same time. Also patients only selected between house of 8am to 2pm. Broad exclusion categories including those &quot;who would not be able available for follow up after their discharge&quot;</td>
</tr>
</tbody>
</table>

Summary Risk of Bias

Low

Schnipper 2006

Methods

Study design: RCT
Unit of allocation: Participant
Unit of analysis: Participant
Follow-up: Admission to outcome assessment at 30 days following discharge (+-3 days)
Duration: Discharge from hospital to 3-5 days later
Providers: Pharmacist

Participants

Setting/participants:
176 participants (92 intervention, 84 control). Patients admitted to 1 of 4 teams on the general medicine service, Brigham and Women’s Hospital, Boston, Mass, USA. Inclusion criteria: patients who were being discharged home and who could be contacted 30 days after discharge, spoke English, and were cared for by a BWH primary care physician or internal medicine resident. Exclusion criteria not listed.
Transition of care: Hospital discharge
Age (Mean/SD): 60.7 (17.2) years intervention, 57.7 (15.9) year control
Female: 67% intervention, 65% control
Ethnicity: No information provided
Interventions

Summary: Pharmacist medication review (with advice from the medical team), reconciliation and telephone follow up to ensure adequate monitoring, discrepancies etc.

Intervention:
The pharmacist intervention on the day of discharge consisted of several parts. First, discharge medication regimens were compared with preadmission regimens and all discrepancies were reconciled with the medical team’s help. Patients were screened for previous Drug Related Problems (DRPs), including non-adherence, lack of efficacy, and side effects. The pharmacist reviewed the indications, directions for use, and potential adverse effects of each discharge medication with the patient and discussed significant findings with the medical team. During the follow-up telephone call, the pharmacist compared the patient’s self-reported medication list with the discharge list, exploring any discrepancies. The pharmacist also asked about medication adherence, possible ADEs, and adherence with scheduled follow-up and laboratory appointments. Significant findings were entered into the electronic medical record used by all BWH outpatient practices and communicated to the patient’s primary care physician via a standard e-mail template.

Control:
Patients assigned to usual care received routine review of medication orders by a ward-based pharmacist and medication counselling by a nurse at the time of discharge. Nursing discharge counselling typically focused on medication directions and may have included a discussion of indications or potential side effects, especially for new medications. These sessions sometimes included informal medication reconciliation, such as comparing discharge medications with those currently prescribed in the hospital.

Outcomes

The primary outcome was the presence of a preventable ADE in patients 30 days after hospital discharge. Secondary outcomes were all ADEs (preventable or not), patient satisfaction, health care utilization, medication adherence, and medication discrepancies.

Presence of a preventable ADE in patients 30 days after hospital discharge:
Preventable ADEs were assessed with a modified version of the method developed by Bates and colleagues and their group. Patients were asked a screening question for new or worsening symptoms since hospital admission. In the case of an affirmative response, follow-up questions elicited details about these symptoms and their relation to medications. Case summaries were prepared from these responses, medication lists at admission and discharge, the hospital discharge summary, any available outpatient visit notes, discharge summaries from ED visits or hospital readmissions, and laboratory test results in the month since discharge. For all hospital admissions or ED visits, blinded physician adjudicators assessed any relationship to medication use or preventability. Preventable medication-related ED visits or readmissions were considered to be preventable ADEs. If patients could not be contacted by telephone 30 days after discharge but had been readmitted to the hospital or visited the ED, case summaries were prepared and ADEs assessed as described in the preceding paragraph but without the patients’ responses. This improved our ability to detect serious and preventable ADEs while minimizing bias due to loss to follow-up. Because ADE assessment without patient responses is less well established than assessment using patient interview, all ED visits or readmissions that were at least possibly medication related were automatically reviewed by an independent, blinded expert in drug safety at BWH.

All ADEs (preventable or not):
2 of 3 physician adjudicators blinded to treatment group independently determined whether an ADE had occurred, using the Naranjo algorithm.

Patient satisfaction:
Satisfaction with hospitalisation and discharge processes was assessed with a standard questionnaire.

Health care utilization:
Health care utilization measures, including scheduled and unscheduled office visits, urgent care and ED visits, and hospital admissions, were assessed by survey questions and hospital administrative data. Administrative data from BWH were subsequently chosen as the gold standard for hospital admission and ED visits because we found evidence of patient underreporting and minimal evidence of readmissions to other hospitals (i.e. no hospital readmissions and only 3 self-reported ED visits, all in the intervention group, that could not be confirmed by BWH administrative data).
Medication adherence: Medication adherence was assessed by asking patients whether they had taken each medication exactly as prescribed during the previous day and on how many days during the previous week. We collected pharmacy refill data for a subset of patients who used the hospital outpatient pharmacy, to confirm the validity of this approach.

Medication discrepancies: Medication discrepancies were determined by comparing the discharge medication regimen with the medications reported by each patient at 30 days. Differences not attributable to a physician’s order or completion of a prescribed course of treatment were considered discrepancies.

Notes

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<tr>
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</tr>
<tr>
<td>Were baseline outcome measurements similar?</td>
<td>Unclear risk</td>
<td>Not Recorded</td>
</tr>
<tr>
<td>Were baseline characteristics similar?</td>
<td>Low risk</td>
<td>Increased hospitalisation in the control group. The characteristics were measured and reported. The cut off for statistical significance was 10%, however, this seems reasonable for the sample size. Reviewing the data provided in Table 1, the variables that might cause concern at a 5% significance level are [Hospitalised in the past year] and [Someone to help when patient returns home]. Table 1</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low risk</td>
<td>The proportion of missing data was similar in the intervention and control groups. The losses seem balanced across the two groups, and the effect size for primary outcome and for discrepancy was non-significant. Additionally, it seems to be per-protocol analysis in the paper (even though the stated statistical analysis claims to follow the intention-to-treat principal). Flowchart p567</td>
</tr>
<tr>
<td>Was knowledge of the allocated interventions adequately prevented during the study?</td>
<td>Low risk</td>
<td>All patients in the trial were contacted 30 days after discharge (±3 days) by a research assistant blinded to treatment assignment. p 566</td>
</tr>
<tr>
<td>Was the study adequately protected against contamination?</td>
<td>High risk</td>
<td>Allocation between medical teams, may have been opportunity for contamination between HCPs</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td></td>
</tr>
<tr>
<td>Other bias</td>
<td>Low risk</td>
<td></td>
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</tbody>
</table>
Methods

Study design: RCT (cluster)
Unit of allocation: Primary care practice
Unit of analysis: Per Patient
Follow-up: Admission and 30 days post discharge
Duration: Pre-admission to readmission to primary care (post discharge)
Providers: ICT Tool

Participants

Setting/participants:
759 participants, clustered by 19 primary care sites and two secondary care facilities (380 participants in intervention practices, and 379 in usual care). Primary-care practices affiliated with Brigham and Women’s Hospital (BWH) and Massachusetts General Hospital (MGH), Mass, USA. Inclusion criteria: Inpatients belonging to these practices, over age 55, and on 5 or more medications were recruited to participate. Exclusion criteria not listed.
Transition of care: Post hospital discharge, readmission to primary care
Age (mean): No information provided
Female: No information provided
Ethnicity: No information provided

Interventions

Organisational - structural intervention - a novel tool built into an ambulatory electronic medical record (EMR).
Summary: Electronic medication list builder and comparison tool
Intervention:
A novel tool built into an ambulatory electronic medical record (EMR). The tool compares the preadmission medication list in the ambulatory EMR to the hospital discharge medication list, highlights all changes, and allows the EMR medication list to be updated.
Control:
"Usual care" in "primary care practice", no more information provided.

Outcomes

Proportion of concordant medications (exact matches in medication, dose, and frequency).
Accuracy of EMR medication list:
Thirty days after discharge, patients were contacted by phone, and a research assistant obtained the "gold-standard" post-discharge medication regimen by including all discharge medications, removing any planned completions in therapy, and incorporating any reported changes made by patients' physicians since discharge. The documented ambulatory EMR medication list at the time of the call was compared to this gold-standard regimen and the proportion of concordant medications (exact matches in medication, dose, and frequency) was calculated.

Notes

Outcome of discrepancies seems to be averaged across practices.
Contacted author, but did not provide more information.
Unit of analysis error - allocation is by practice, analysis by individual. Therefore, adjustment made with ICC (See investigations of potential bias section)

Risk of bias table

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Unclear risk</td>
<td>&quot;[Practices] matched and randomised to receive the tool or usual care&quot;. No further details provided.</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>Allocation by practice at start of study</td>
</tr>
<tr>
<td>Were baseline outcome measurements similar?</td>
<td>Unclear risk</td>
<td>Not reported</td>
</tr>
<tr>
<td>Were baseline characteristics similar?</td>
<td>High risk</td>
<td>Not reported</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Unclear risk</td>
<td>Not reported</td>
</tr>
</tbody>
</table>
Was knowledge of the allocated interventions adequately prevented during the study? Unclear risk

Was the study adequately protected against contamination? Low risk

Selective reporting (reporting bias) Low risk

Other bias High risk

Summary Risk of Bias Unclear risk

Tompson 2012

Methods
Study design: RCT
Unit of allocation: Patient
Unit of analysis: Patient
Follow-up: Admission to discharge only
Duration: Up to 24 hours post hospital admission

Providers: Hospital pharmacist, communication with Community Pharmacist (CP), and Resident Medical Officer (RMO)

Participants
Setting/participants:
487 participants (203 intervention, 284 control). “High risk” patients of 5 Australian hospitals (2 Tasmania, 2 in Western Australia and 1 Victoria). Inclusion criteria: aged 50 years or older, with at least two chronic conditions (at least one of which was cardiovascular, diabetes mellitus or COPD; and were taking at least three chronic medications. Patients had to be able to nominate a regular GP and community pharmacy, not live in a residential aged care facility and were able to provide informed consent.

Transition of care: Hospital admission
Age (Mean/SD): 70.7 (10.3) years intervention, 73.8 (9.5) control
Female (%): 46.8% intervention, 52.5% control
Ethnicity: No information provided.

Interventions
Summary:
Hospital pharmacist compiled a medication list from different sources (including faxed or electronically sent community pharmacist list of medications) and discussed discrepancies on initial drug chart with the RMO.

Intervention:
A hospital based trial pharmacist utilised the following to construct a reconciled list of medication: community pharmacy’s 6 months dispensing history, comprehensive interview with patient, review of the patient’s own medication, information obtained from the GP, the hospital doctor’s initial medication history. CP records were transferred by secure electronic web site or fax. Reconciled and initial drug charts were compared for discrepancies.

Discrepancies for intervention patients were discussed with the attending doctor.

Control:
Control patients received usual care, which was building of the reconciled list as described in the intervention but did not communicate discrepancies to their attending doctor.

Outcomes
Drug discrepancies:
For intervention patients the reconciled admission medication list and the initial drug chart were compared and discrepancies between the two identified and documented. Discrepancies were classified as omissions of medications, wrong medications and dosing errors, those discussed with doctor (in the intervention group) and if deemed to be intentional were removed from the total. To decide if they were intentional in the control group a chart review was done by the trial pharmacist. The hospital based trial pharmacist observed the management of each patient’s medication regimen for the duration of their stay. Progress of the resolution of identified discrepancies was assessed for all patients at number of time points: admission, within 48 hours, over 48 hours, before discharge. For intervention patients the discrepancies were actively followed up with staff, whereas for control patients the process was purely observational.

The outcome time point recorded in the forest plot of this review is the discrepancy rate “not resolved during the hospital stay”.

Readmission:
Defined as within 5 days of discharge
**Notes**

Figures of the primary outcome "one or more discrepancies per patient" were reported as percentages in published paper. Author was contacted and provided the original absolute figures. Conducted in a number of sites? clustering effect - although randomisation was at patient level. "patients randomised centrally" Possible major bias with all discrepancies in the intervention group discussed with the doctor and removed if deemed to be intentional. The same process was not undertaken in the control and may have led to misclassification. Instead they relied on chart review to decide if intentional or not.

**Risk of bias table**

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>Computer generated randomisation tables. p 641</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>High risk</td>
<td>See Ronan’s justification p.645</td>
</tr>
<tr>
<td>Were baseline outcome measurements similar?</td>
<td>Unclear risk</td>
<td>Not reported</td>
</tr>
<tr>
<td>Were baseline characteristics similar?</td>
<td>High risk</td>
<td>Difference in baseline details on age only. Table 2</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>High risk</td>
<td>Withdrawn/Death/Discharge with no additional details. p 642</td>
</tr>
<tr>
<td>Was knowledge of the allocated interventions adequately prevented during the study?</td>
<td>High risk</td>
<td>No blinding of outcome assessors to group allocation. p 641</td>
</tr>
<tr>
<td>Was the study adequately protected against contamination?</td>
<td>High risk</td>
<td>Same physicians and pharmacists managing usual and intervention groups.</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>Discrepancies was selected outcome and it was reported</td>
</tr>
<tr>
<td>Other bias</td>
<td>High risk</td>
<td>Selection bias - no nursing home residents nor those without a GP or pharmacist were not included</td>
</tr>
</tbody>
</table>

**Summary Risk of Bias**

<table>
<thead>
<tr>
<th></th>
<th>High risk</th>
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</thead>
</table>

**Methods**

Study design: RCT  
Unit of allocation: Participant  
Unit of analysis: Participant  
Follow-up: Admission to inpatient ward until follow up 3 days following discharge  
Duration: Hospital discharge  
Providers: Resident pharmacist

**Participants**

Setting/participants:  
29 participants (13 intervention, 16 control). Inpatient wards at the Cross Cancer Institute hospital in Edmonton, Alberta, Canada. The Cross Cancer Institute inpatient wards consist of 59 beds that provide specific care for cancer patients. Patients included in the study were required to be greater than 18 years of age, had to have more than one home medication or herbal medication, and were under the care of one of the three clinical associate physicians that agreed to participate in the study. Patients that were excluded were inpatients that were radioactive such as selectron patients and patients that were to remain in hospital less than 72 hours. Other exclusion criteria included language barrier such as unable to speak English, and patients that were readmitted into the hospital but had already been enrolled on the study.  
Transition of care: Hospital discharge  
Age (mean): 50.6 years intervention, 54.9 years control  
Female (%): 53.8% intervention, 25% control  
Ethnicity: No information provided, but English speakers only being a recruitment requirement

**Interventions**

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td></td>
<td>Residence pharmacist provided medication reconciliation at discharge.</td>
</tr>
<tr>
<td>Intervention</td>
<td></td>
</tr>
</tbody>
</table>
Patients in the study group received standard care and pharmacist discharge medication reconciliation. Discharge medication reconciliation entailed a pharmacist conducted patient interview, phone calls to community pharmacies, phone calls to a patient’s general practitioner, and a review of medication list from the Alberta Electronic Health Record to obtain a best possible medication history of a subject’s home medications. In addition, the last 24-hour hospital Medication Administration Record (MAR) was reviewed and documented. A discharge medication reconciliation tool was created showing the patient’s home medications (including over the counter drugs and herals), medications on last MAR, and medication changes. The pharmacy resident acted as the pharmacist in this study arm. The discharge medication reconciliation tool acted as a resource for the physician and discharge nurse to help in the assessment of prescribing discharge medications. Afterwards, a medication list for health professionals was created and sent out to the patient’s community pharmacy and family physician for information purposes. A patient discharge medication list was also provided for the patient.

Control:
Current standard of care involves the physician or nurse asking the patient if they have medications on the last hospital medication administration record (MAR) at home. The physician would then write a prescription for medications that they believe the patient needs and does not have at home. Standard care involves medication reconciliation by the pharmacist at admission. At discharge, standard care involved review of patient medication administration record (MAR) and an interview with the patient regarding home medications by the physician or nurse. The clinical associate physician assessed which medications to prescribe to the patients at discharge. Discharge counselling was done by either discharge nurse or physician. No discharge medication reconciliation was done by a pharmacist.

Outcomes
Unintentional discrepancies: For both control and study patients, baseline discharge medication lists were created by the investigator after patient has been discharged from the hospital. The baseline discharge medication list represented what the physician believed the patient was taking when discharged to home. This list was then verified by the physician. Three days after discharge, patients received a phone interview by the pharmacist, at home or discharge facility, regarding what medications and herbal medications they are currently taking. Medications taken at home/or transferred facility was compared to the baseline discharge medication list to identify any medication discrepancies. The investigator classified each discrepancy in accordance to the Safer Health Care Now campaign guidelines as “Intentional Documented Discrepancy”, “Intentional Undocumented Discrepancy”, or “Unintentional Discrepancy”.

Clinical importance of discrepancies: A panel of investigators, which included 1 physician, 1 pharmacist and 1 pharmacy resident, analysed the discrepancies for harm. Severity of discrepancies were also determined by the same panel of investigators as either “Unlikely to cause harm”, “Potential to cause moderate harm”, or “Potential to cause severe or serious harm” based on adapted criteria set by Cornish et al. Unlikely to cause harm would result in little to no effect on the patient. Potential to cause moderate harm would result in moderate discomfort to the patient such as an adverse side effect. Potential to cause severe or serious harm would cause significant morbidity to the patient requiring immediate medical attention or hospitalisation.

Notes
Unpublished. Conference poster only, author supplied unpublished manuscript.

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
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<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Unclear risk</td>
<td>No detail described</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>No detail described</td>
</tr>
<tr>
<td>Risk of Bias</td>
<td>Description</td>
<td></td>
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<tr>
<td>-------------</td>
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<td></td>
</tr>
<tr>
<td>Unclear risk</td>
<td>Not Recorded</td>
<td></td>
</tr>
<tr>
<td>Low risk</td>
<td>At least 6 patients lost to follow up with no reason why</td>
<td></td>
</tr>
<tr>
<td>High risk</td>
<td>Study pharmacist recorded outcome and was applied intervention too</td>
<td></td>
</tr>
<tr>
<td>High risk</td>
<td>&quot;As the prescribers knew they were part of the study, prescribers may have been more attentive to the patient's home medications when discharging the patient.&quot;</td>
<td></td>
</tr>
<tr>
<td>Low risk</td>
<td>All specified outcomes were reported</td>
<td></td>
</tr>
<tr>
<td>High risk</td>
<td>Unpublished study, small sample size</td>
<td></td>
</tr>
</tbody>
</table>

Summary Risk of Bias: High
### Characteristics of studies awaiting classification

**Corbett 2011**

**Methods**
- RCT

**Participants**
- Inclusion criteria:
  - Age 50 and older
  - Diagnosed with at least 1 of 6 chronic illnesses
  - Receipt of home care skilled nursing post-hospital discharge.

**Interventions**
- Protocol-trained nurse interventionist delivers home care. The protocol included receipt of an electronic discharge medication list from the hospital and use of an electronic version of the Medication Discrepancy Tool® (MDT) to facilitate identification of medication discrepancies and planning for medication discrepancy resolution.

**Outcomes**
- Medication discrepancies

**Notes**
- Conference presentation. No further information, including actual results provided by author.
- Subset of partial intervention group reported on here: doi: 10.1016/j.gerinurse.2010.03.006
### Characteristics of ongoing studies

<table>
<thead>
<tr>
<th>Study name</th>
<th>Effect of Medication Reviews Performed in High Risk Patients</th>
<th>Methods</th>
<th>RCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>Inclusion Criteria:</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Acutely admitted</td>
<td></td>
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<tr>
<td></td>
<td>&gt;17 years</td>
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<tr>
<td></td>
<td>Patients being treated with at least one drug at admission</td>
<td></td>
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<tr>
<td>Exclusion Criteria:</td>
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<tr>
<td></td>
<td>Dying patients</td>
<td></td>
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<tr>
<td></td>
<td>Suicidal patients</td>
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<td></td>
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<tr>
<td></td>
<td>Intoxicated patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interventions</td>
<td>A medication review will be performed in patients with high medication error risk. Patients in the highest risk will receive the medication review from a clinical pharmacologist whereas patients assessed in lesser risk will receive the medication review from a clinical pharmacist.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Outcomes</td>
<td>Medication errors</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hospital readmissions (all-cause)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Starting date</td>
<td>April 2013</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Contact information</td>
<td>Dorthe K Bonnerup, Aarhus University Hospital, Aarhus, Denmark</td>
<td></td>
<td></td>
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<table>
<thead>
<tr>
<th>Study name</th>
<th>Medication Reconciliation in Comparison to an Extensive Medication Safety Check</th>
<th>Methods</th>
<th>RCT</th>
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</thead>
<tbody>
<tr>
<td>Participants</td>
<td>Inclusion Criteria:</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>Patient 65 years and older</td>
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<tr>
<td></td>
<td>written informed consent patient or the legal representative</td>
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<tr>
<td></td>
<td>existing medication therapy at hospitalisation</td>
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<tr>
<td></td>
<td>admission to one of the project wards via emergency department (non-elective)</td>
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<tr>
<td>Exclusion Criteria:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>patients included in the study previously</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interventions</td>
<td>Pharmacist take the best possible medication history (BPMH), comparison of the BPMH with the admission order (AMO), clarify and solve all discrepancies between the BPMH and the AMO.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Outcomes</td>
<td>Incidence of adverse drug events</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Assessment of the clinical relevance of medication related problems as determined by the French Society of Clinical Pharmacy</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Assessment of the clinical relevance of discrepancies as determined by the French Society of Clinical Pharmacy</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>number of medication related problems</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>number of discrepancies</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>duration of taking the best possible medication history</td>
<td></td>
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<tr>
<td>Starting date</td>
<td>January 2015</td>
<td></td>
<td></td>
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<tr>
<td>Contact information</td>
<td>Albrecht Eisert, University Hospital Aachen, Aachen, Germany</td>
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<table>
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<tr>
<th>Study name</th>
<th>What is the impact of a centralized provincial drug profile viewer on the quality and efficiency of patient admission medication reconciliation?</th>
<th>Methods</th>
<th>RCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>Tertiary care teaching hospital pre-admission clinics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interventions</td>
<td>Centralized provincial medication database</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Outcomes</td>
<td>Unintentional BPMH medication discrepancy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Starting date</td>
<td>2011</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Hammad, 2013

Study name: Medication errors: Do they persist in primary care and can they be identified?
Methods: "Pilot RCT" - no further information provided
Participants: Hospital patients at discharge - no further information provided
Interventions: Pharmacist - no further information provided
Outcomes: Medication errors: Comparing the inpatient chart, discharge letter and the GP medication list.
Starting date: Unclear
Contact information: Eman Hammad, University of East Anglia/School of Pharmacy, Norwich, UK
Notes: Conference presentation.

Juanes 2012

Study name: Randomized Clinical Trial of a Pharmaceutical Care Program in Chronic Patients Users of an Emergency Department
Methods: RCT
Participants: Decompensated heart failure/COPD in the Emergency Department
Interventions: Pharmaceutical care program
Outcomes: Drug Related Problems (DRP)
          Mortality
          Average length of the hospital stay
          Readmissions
          Average cost of hospital stay
Starting date: January 2012
Contact information: Ana Juanes, Fundació Institut de Recerca de l'Hospital de la Santa Creu i Sant Pau, (Barcelona, Spain)
Notes: Clinicaltrials.gov/show/NCT02368548

Kao, 2015

Study name: A Pilot Randomized Trial of a Comprehensive Transitional Care Program for Colorectal Cancer Patients
Methods: RCT
Participants: Inclusion Criteria:
          Diagnosis of colorectal cancer
          Adults, Age 18 years or older
          Undergoing surgery for either palliative cure or palliation
Exclusion Criteria:
          Patients not expected to survive hospital based on the operating surgeon's opinion
          Children under the age of 18 years
Interventions: Patient education: One-on-one visit Discharge planning: Assessment of barriers to discharge Medication reconciliation: Patient medication review Appointment before discharge: Additional measure to ensure awareness of next clinic visit Transition coach Patient-centred discharge instructions: Enhanced Provider continuity: Specific surgeons responsible for coordinating care with medical/radiation oncology Timely follow-up: Barriers to clinic follow-up visits will be discussed Timely PCP communication Follow-up telephone call Patient hotline: 24 hour follow-up following call to Ask My Nurse number
Outcomes: Number of post-operative ER visits and readmissions
Starting date: February 2015
Contact information: Lillian S Kao, Lyndon B. Johnson General Hospital, Houston, Texas, United States
**Kristeller, 2014**

**Study name**
Improving Medication Adherence Through a Transitional Care Pharmacy Practice Model

**Methods**
RCT

**Participants**
Inclusion Criteria:
- admitted to hospital with a primary or secondary diagnosis of heart failure or COPD
- anticipated eventual discharge to home
- agreeable to participate in monthly counselling sessions (if randomised to intervention group) from a participating community pharmacist

Exclusion Criteria:
- presence of cognitive impairment or dementia that would significantly prevent effective patient education and counselling
- non-English-speaking
- anticipated discharge to a long-term care or skilled nursing facility on a permanent basis
- permanent long-term care facility residents
- surgical patients
- hospice patients
- patients who die within 30 days of initial study hospitalisation

**Interventions**
Pharmacist Counselling
The hospital pharmacist will meet with the patient and complete medication reconciliation, assess the patient's understanding of the medications, and identify medication-related problems. The hospital pharmacist will complete a pharmacist discharge care plan and a copy will be sent to the participating community pharmacist. The patients will be scheduled for the first meeting with their community pharmacist within 1 week of hospital discharge. The community pharmacist will interview the patient about their general health and any current symptoms of heart failure or COPD, identify any additional medication-related problems, follow-up on any issues as described in the pharmacist discharge care plan, and provide patient education. The patients will then meet with their community pharmacist for counselling and patient education at monthly intervals for 6 months following hospital discharge.

**Outcomes**
Medication Adherence
Medication related problems
Patient Satisfaction
Hospital readmissions or ED visits

**Starting date**
January 2014

**Contact information**
Judith L. Kristeller, Associate Professor, Wilkes University, Pennsylvania, United States

**Notes**
https://clinicaltrials.gov/show/NCT02202096

---

**Lassere, 2010**

**Study name**
Portable Health Files Improve Quality of Care and Health Outcomes: a Randomized Controlled Trial (PHF-RCT)

**Methods**
RCT

**Participants**
Inclusion Criteria:
- Subjects must be of age 60 or greater
- Patients living independently in the community. Hostel care is acceptable, but patients that are not independent requiring full nursing home care are excluded.
- Subjects must have had six medical practitioner visits in the previous 12 months
- Subjects must have at least two of the following confirmed chronic diseases that require prescription oral or parenteral drug treatment or surgery and requiring at least annual specialist consultation: cardiovascular, respiratory, endocrine, renal, neurologic, gastrointestinal, hepatic, genitourinary, hematologic, infective, rheumatic, inflammatory, immunologic or neoplastic disease.
- Subject's GP must have access to a computer during the consultation visit. 7. Subjects must have at least two medical specialists at least one of whom has access to a computer during the consultation visit.
Subjects must be able to understand the purpose of the trial and undergo full and valid informed consent. Exclusion Criteria:

- Life expectancy of less than 12 months.
- Inability to carry a paper PHF or e-PHF and having no care-giver willing and able to accomplish same.
- Mentally unable to undertake valid informed consent.
- Patients who are not independent in the community, that cannot mobilise to see a specialist or requiring full nursing home care

**Interventions**

Patients randomised to this arm of the trial will be given a USB memory device that contains the Portable Health File (PHF) software. The portable health files contained core medical data which functions as a subset of a comprehensive medical record. The portable health file is updated by the health care provider at each visit and could also be updated by patient between visits if necessary.

**Outcomes**

Combined endpoint of deaths, hospitalisations Quality of Life health service utilisation and health care costs medication errors, duplicative investigations clinical workflow subject and health care provider acceptability and satisfaction with portable health files (PHF) guidelines uptake and documentation health literacy information technology and computer expertise adverse events

**Starting date**

March 2010

**Contact information**

Marissa ND Lassere, St George Hospital, Kogarah, New South Wales, Australia

**Notes**

https://clinicaltrials.gov/show/NCT01082978

---

**Lesselroth 2012**

**Study name**

Medication review software to improve the accuracy of outpatient medication histories

**Methods**

RCT

**Participants**

Inclusion Criteria:
- Veteran with Primary Care appointment at Portland VA
- Three or more medications in medication profile

Exclusion Criteria:
- Visual impairment
- Upper extremity neuromuscular impairment
- Cognitive impairment
- Unable to speak and read English
- Never been seen at a VA

**Interventions**

Medication review software with pictures

The intervention is a self-service software program that displays each prescription on screen along with an image of the pharmaceutical product. Patients must use response buttons to describe adherence patterns and to advance through the questionnaire items.

**Outcomes**

Number of medication discrepancies from the reference standard

**Starting date**

May 2014

**Contact information**

Blake Lesselroth, Director, Portland Patient Safety Centre of Inquiry, Portland VA Medical Centre

**Notes**

https://clinicaltrials.gov/show/NCT02135731

---

**Persell 2013**

**Study name**

North-western University and Access Community Health Network Medication Education Study (NAMES)

**Methods**

Cluster RCT

**Participants**

Inclusion Criteria:
- age is 18 years or older
- at least 3 medications are prescribed by their physician
standardized mean blood pressure measurement ≥130 mm Hg systolic or ≥ 80 mm Hg diastolic if they are diabetic or mean blood pressure measurement ≥ 135 mm Hg systolic or ≥ 85 mm Hg diastolic if they are not a Mini-Cog Exam score of ≥ 3
the patient is the person primarily responsible for administering their medication
the patient does not intend to move or change their usual source of medical care during the next year.
Exclusion Criteria:
the patient's usual source of medical care is not a participating ACCESS Community Health Centre
is non-English language speaking
does not meet mean blood pressure criteria
has a Mini-Cog Exam score of < 3
is not the person primarily responsible for administering medication
intends to move or change their usual source of medical care during the next year.
Is not prescribed at least 3 medications

Interventions
EHR-based medication management tools alone, or EHR tools plus nurse-led medication therapy management.

Outcomes
Systolic Blood Pressure
Effectiveness of the Electronic Health Record-based Health Literacy Medication Therapy management strategy (EHML), with and without a nurse educator, compared to standard care.
Effects of these strategies by patients' literacy skills

Starting date
April 2012
Contact information
Stephen Persell, North-western University, Chicago, Illinois, United States
Notes
https://clinicaltrials.gov/ct2/show/NCT01578577

PictureRx, 2015
Study name
PictureRx: Improving Medication Safety in Health Disparity Populations
Methods
RCT
Participants
Inclusion Criteria:
Prescribed one or more prescription medications
Exclusion Criteria:
Too ill to complete informed consent process
Interventions
PictureRx medication history platform
Tablet PC-based tool to take more complete and accurate medication history
Outcomes
Accuracy of medication history
Patient understanding
Starting date
April 2015
Contact information
PictureRx, LLC, University of Cincinnati
Notes
https://clinicaltrials.gov/show/NCT02289469

Pourrat, 2014
Study name
Communication Between Hospital and Community Pharmacists: Impact on Drug Management at Discharge (REPHVIM)
Methods
Cluster RCT
Participants
Inclusion Criteria:
patients over 18
patients attending to the same CP for at least 3 months
patients speaking French
Exclusion Criteria:
patients with a length stay over 21 days (too many therapeutic modifications),
patients who do not return to home,
palliative patients and/or expected end of life
patients that will not give their informed consent
Interventions
Medication reconciliation at discharge and communication of this intervention to patient's community pharmacist
<table>
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<tr>
<th>Study name</th>
<th>The Secure Messaging for Medication Reconciliation Tool (SMMRT) Trial 2015</th>
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<tbody>
<tr>
<td>Methods</td>
<td>RCT</td>
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<tr>
<td>Participants</td>
<td>Inclusion Criteria: 1) Veterans age 18 years or older, 2) having a VA primary care provider (PCP) at any VA facility in VISN-1, 3) planned discharge home (as opposed to another facility), 4) computer and Internet access, and 5) anticipated to be discharged with at least 5 medications. Having a VA PCP will be defined as having seen the provider within the past two years. Planned discharge home will be ascertained from the Veteran's nurse; approximately 75% of VA Boston discharges are to home. The nurse will also provide number of anticipated discharge medications.</td>
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<tr>
<td>Interventions</td>
<td>Secure Messaging for Medication Reconciliation Tool (SMMRT), with a pharmacist communicating with Veterans to review medications and reconcile discrepancies after hospital discharge via Secure Messaging (SM), within My HealtheVet (MHV), VA's patient portal.</td>
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<td>Outcomes</td>
<td>Medication discrepancies Hospital Utilization</td>
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<tr>
<td>Starting date</td>
<td>September 2015</td>
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<tr>
<td>Contact information</td>
<td>Steven R Simon, MD MPH BS VA Boston Healthcare System Jamaica Plain Campus, Jamaica Plain, MA</td>
</tr>
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<td><a href="https://clinicaltrials.gov/show/NCT02482025">https://clinicaltrials.gov/show/NCT02482025</a></td>
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Simon, 2015  

<table>
<thead>
<tr>
<th>Study name</th>
<th>Pharmaceutical Care and Clinical Outcomes for the Elderly Taking Potentially Inappropriate Medication 2009</th>
</tr>
</thead>
</table>
| Methods                          | RCT  

Wei, 2009
Weiner 2012

**Study name**
Medication Reconciliation Technology to Improve Quality of Transitional Care (MedMatch)

**Methods**
RCT

**Participants**
Inclusion Criteria:
Patients admitted to the Medicine Service during a 12-month period
Physicians who provide inpatient or ambulatory care for participating patients.
Pharmacists who provide care for participating patients.

Exclusion Criteria:
Patients admitted but not seen in a primary-care clinic within the preceding 12 months
If an enrolled subject is determined to be a prisoner or pregnant woman, then the study will discontinue the subject for research purposes or will submit an amendment at that time

**Interventions**
Electronic medication reconciliation
A new, computer-based application will be used to document and prescribe outpatient medications in the inpatient setting.

**Outcomes**
Reconciliation of outpatient medications
Measurement of potential for harm and potential severity of harm
Measurement and analysis of providers’ perspectives
Measurement and analysis of patients’ perspectives
Reportable financial and organizational dimensions
Utilization of intervention
Measurement and analysis of drug-related medical errors
Measurement of adverse drug events and near misses
Medication discrepancies between pre-admission and ambulatory follow up

Starting date
November 2010

**Contact information**
Michael Weiner, MD, MPH
Indiana University School of Medicine, Department of Medicine

**Notes**
http://clinicaltrials.gov/show/NCT01195051

Williams, 2013

**Study name**
Project impact: Improving patient adherence through communication at transition

**Methods**
RCT

**Participants**
Patients with HIV/AIDS being discharged from the university hospital

**Interventions**
An accurate list of discharge medications is identified by a pharmacy team. This pharmacy team will (1) compare the discharge medication list to patients’ pre-hospitalisation list of medications; (2) identify any medication errors and communicate these with the appropriate health care provider; (3) conduct a face-to-face consultation with intervention patients, counselling them on the discharge medications; and (4) call patients 3 to 5 days post-discharge to review discussion and identify problems. The discharge medication list is communicated to patients’ health care providers and community pharmacies.

**Outcomes**
Rate of perfect discharge
Patient and provider satisfaction
Readmission rates.

Starting date
March 2013

**Contact information**
M Williams, University of Cincinnati, USA

**Notes**
### Appendix Z Characteristics of excluded studies

<table>
<thead>
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<th>Study</th>
<th>Reason for exclusion</th>
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<td>Unsuitable control group</td>
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<td>Abdelaziz 2012</td>
<td>Unsuitable study design</td>
</tr>
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<td>Adams, 2013</td>
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<td>Agrawal 2009</td>
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Varkey 2006
Reason for exclusion Unsuitable study design
Varkey 2007
Reason for exclusion Unsuitable study design
Varkey 2007a
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Vasileff 2009
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Vathonne 2003
Reason for exclusion Unsuitable study design
Vigod 2013
Reason for exclusion Unsuitable study design
Voirol 2004
Reason for exclusion No measure of discrepancies
Vuong 2008
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Wadsworth 2012
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Wahlstrom 2007
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Waizy 2011
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Walberg 2008
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Walker 2009
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Wang 2012a
Reason for exclusion Unsuitable study design
Weingart 2007
Reason for exclusion Unsuitable study design
Wernick 1996
Reason for exclusion Unsuitable study design
Whittington 2004
Reason for exclusion Unsuitable study design
Wilkinson 2011
Reason for exclusion Unsuitable study design
Williams 2012
Reason for exclusion No measure of discrepancies
Willoch 2012
Reason for exclusion Intervention not as per review protocol. No measure of discrepancies
Witting 2012
Reason for exclusion Unsuitable study design
Wingard 2013
Reason for exclusion Unsuitable study design
Wish 2014
Reason for exclusion Commentary only
Wo 2008
Reason for exclusion Unsuitable study design
Wolff 2013
Reason for exclusion Population not in transition
Wong 2007
Reason for exclusion Unsuitable study design
Wong 2013
Reason for exclusion Unsuitable study design
Wood 1998
Reason for exclusion Intervention not as per review protocol. No measure of discrepancies
Wortman 2008
Reason for exclusion Unsuitable study design
Xie 2009
Reason for exclusion Unsuitable study design
Zhang 2012
Reason for exclusion Intervention not as per review protocol.
Zhang 2013
Reason for exclusion Unsuitable study design
Zoni 2012
Reason for exclusion Unsuitable study design
Appendix AA

Interviews Project – Ethical approval

<table>
<thead>
<tr>
<th>Ethics Reference No:</th>
<th>REC 1112 (amendment to REC 1036)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Project Title:</td>
<td>Opinions of key stakeholders on medication management at transitions of care in Ireland</td>
</tr>
<tr>
<td>Researchers Name (lead applicant):</td>
<td>Dr Patrick Redmond</td>
</tr>
<tr>
<td>Principal Investigator on the project:</td>
<td>Prof Tom Fahy, (RCSI, Dept of General Practice)</td>
</tr>
<tr>
<td>Other Individuals Involved:</td>
<td>Dr Tamasine Grimes (School of Pharmacy TCD); Dr Ronan McDonnell (HRB Centre for Primary Care Research, RCSI); Dr Fiona Boland (RCSI, Department of Population Health Sciences); Prof Carmel Hughes (School of Pharmacy Queens University Belfast); Medical Students: Khalid Munir &amp; Cludare Olabi (Dept of General Practice, RCSI); and Dr Rose Galvin (HRB Centre for Primary Care Research, RCSI).</td>
</tr>
</tbody>
</table>

Dear Dr Redmond,

Thank you for your amendment to Research Ethics Committee (REC) application REC1112. We are pleased to advise that ethical approval has been granted by the committee for this amendment.

Content of Amendment:
- To expand the interview group to include consultant and non-consultant hospital doctors, focusing on those who have a high turnover of patients and are actively involved in the discharge and admission process.

This letter provides approval for data collection for the time requested in your original application and for an additional 6 months to allow for any unexpected delays in proceeding with data collection. Therefore this research ethics approval will expire on 2nd February 2016. Where data collection is necessary beyond this point, approval for an extension must be sought from the Research Ethics Committee.

This ethical approval is given on the understanding that:
- All personnel listed in the approved application have read, understand and are thoroughly familiar with all aspects of the study.
- Any significant change which occurs in connection with this study and/or which may alter its ethical consideration, must be reported immediately to the REC, and an ethical amendment submitted where appropriate.
- Please submit a final report to the REC upon completion of your project.

We wish you all the best with your research.

Yours sincerely,

[Signature]
PP Dr Niamh Clarke (Convenor)
Dr David Smith (Acting Chair)
Study Title:
Opinions of key stakeholders on medication management at transitions of care in Ireland
Principal Investigator’s Name: Patrick Redmond
Principal Investigator’s Title: Dr
Telephone No. of Principal Investigator: +353 (0)879583108

You are being invited to take part in a research study carried out by The HRB Centre for Primary Care Research, Royal College of Surgeons in Ireland (RCSI). This document provides information about the study so that you can make an informed decision about whether or not you would like to participate in this project.

Your participation in the study is completely voluntary. If you decide you do not want to take part, you are free to withdraw from the study at any time without explanation.

You should clearly understand the risks and benefits of taking part in this study so that you can make a decision that is right for you.

You do not have to take part in this study. You can change your mind about taking part in the study any time you like.

Why is this study being carried out?
The study involves a brief interview of patients, pharmacists, hospital doctors and GPs interacting with patients as a routine part of their clinical work. The interview seeks to learn about medication management as patients experience transitions in care. This information will help to better describe suspected issues of poor information transfer and disruption of appropriate chronic medication as patients move between different health care professionals.

Who is organising and funding this study?
This study is organised by a team of researchers from the HRB Centre for Primary Care Research based in the Royal College of Surgeons in Ireland (RCSI). It is being led by a doctoral researcher (Patrick Redmond) for the purposes of a PhD degree. This study is funded by the HRB Centre for Primary Care Research.
The research group comprises of:
Professor Tom Fahey, Head of Department of General Practice, RCSI and the HRB Centre for Primary Care Research, RCSI
Dr Tamasine Grimes, TCD School of Pharmacy
Dr Fiona Boland, Statistician, RCSI
Professor Carmel Hughes, Professor of Primary Care Pharmacy, School of Pharmacy, QUB, Belfast
Dr Ronan McDonnell, Post-doctoral researcher, RCSI.
Dr Patrick Redmond, General Practitioner & Lecturer in RCSI and PhD student
Dr Rose Galvin, HRB Centre Research Manager, RCSI
Mr Khalid Munir (Medical student)
Mr Oludare Alabi (Medical student)

How will the study be carried out?
The study includes a brief interview of patients, pharmacists, hospital doctors and GPs interacting with patients as a routine part of their clinical work. The interview seeks to learn about medication management as patients experience transitions in
care. This information will help to better describe suspected issues of poor information transfer and disruption of appropriate chronic medication as patients move between different health care professionals.

**What will happen to me if I agree to take part?**
You will be asked a brief series of questions on your experiences and attitudes on around the issues of medication management. The interview should take no longer than 20-30 minutes of your time. Your interview will be recorded and transcribed by the study researchers (including an undergraduate medical student). You will have the opportunity to review and revise your transcript prior to final submission.

**What are the benefits?**
Disruption of medication regimens and lack of continuity in appropriate long term medication usage is a problem that has not been described in Ireland before. This study will analyse healthcare professionals’ experience of potentially unintentional discontinuation of medication in the transfer between secondary and primary care. In considering the long-term goal of the HRB Centre for Primary Care Research to develop a shared medication record to improve transitions of care for vulnerable patients, this study is essential in describing the clinical problem at a national level.

Participating in this study and using the opportunity to engage in reading around the topic of medication reconciliation may be recorded for professional competence purposes e.g. personal CPD points for the ICGP scheme.

**What are the risks?**
The potential for risks from taking part in this study are minimal as it is essentially attitudinal information that is being collected. Patient treatment will continue as normal.

**Is the study confidential?**
The interview results will be anonymous and confidential. Individual results will be aggregated anonymously and research reported on aggregate results. Aggregated anonymous study data will be stored separately on a secure password protected server in RCSI. Study data will be subject to the strict data management policy of RCSI. Analysis of the study data will be presented at conference(s) and published in appropriate peer reviewed journals.

**Where can I get further information?**
If you have any further questions about the study, or if you wish to withdraw from the study you may do so without justifying your decision and your future interaction with the study team will not be affected, please contact:
Dr Patrick Redmond  T: +353 0879583108
(office hours)  predmond@rcsi.ie
Professor Tom Fahey  T: +353 1 4022305
(Office hours)  tomfahey@rcsi.ie
Thank you for your time and interest.
Appendix CC Interview Project Participant Consent Form

Opinions of key stakeholders on medication management at transitions of care in Ireland

Please tick the appropriate answer.

- I am 18 years or older and am competent to provide consent
- I understand that I have been invited to participate in an interview
- I am aware of the potential risks of this research study
- I agree that my data is used for scientific purposes and I have no objection that my data is published in scientific publications in a way that does not reveal my identity
- I freely and voluntarily agree to be part of this research study, though without prejudice to my legal and ethical rights
- I understand that I may refuse to answer any question and that I may withdraw at any time
- I understand that my participation is fully anonymous and that no personal details about me will be recorded
- I have read and I understand this consent form. I understand the description of the research that has been provided to me in the study information page preceding this consent page. I have opportunity to ask questions via email.
- I understand that I will have an opportunity to review and or edit my transcript prior to final submission

Storage and future use of information:
I give my permission for information collected about me to be stored or electronically processed for the purpose of scientific research and to be used in related studies or other studies in the future but only if the research is approved by a Research Ethics Committee.
Interview Script

Introduction:
"The overall goal of this research study is to improve medication reconciliation (MEDREC). If you have not had time to read the study information sheet, please do so now. Following this please review the consent sheet and, if you are happy to proceed, please sign it. MEDREC is often defined as the processes that are used to ensure that patients and those who care for them have a good idea of what medications the patient is actually taking. This is particularly relevant when patients move between different healthcare providers and different intensities of health care provision, for example between hospital and their GP or between the ward and the ICU. The purpose of this project is to provide both a wide and a detailed exploration of the barriers and drivers to the implementation of MEDREC between primary and secondary care in Ireland. We are looking for your honest feelings and opinions; there are no right or wrong answers in this interview and all your responses will be confidential. In any reports of these interviews, we will never mention your name, practice, or any other personal information. We would also ask that you do not mention any third parties by name, like patient names etc.

Do you have any questions before we begin?"

Organisation & Healthcare professionals:
So, to begin, would you like to tell me a little bit about the environment you work in and your experience in dealing with the MEDREC process? [E.g. hospital admission, discharge; re-admission to community or information transfer b/w GP/CP etc.]

“What does medication reconciliation mean to you?”
Do you care for patients who experience a transition of care (TOC)? Listen for description of complexity/good management. Is this a complex process? What kinds of issues arise? What type of errors have you seen?
So, in your practice, are there any facilities like computers or regular audits that enable a more efficient reconciliation process or is anyone in particular assigned to making this process more efficient? [Does somebody collect all prescription scripts and sort them or is this down to individual GPs/pharmacists etc.?]
What to you are the barriers to effective MEDREC? And conversely what supports it?
Do you actively involve yourself with reconciling patients’ medication?
Are adverse drug events a significant cause of morbidity/mortality for your patients?”
Have you seen errors in patients’ medication at points of transitions of care? How dangerous, in your opinion, were these errors? Is it a serious issue?
What do you see as the role of the... (Discharging doctor/pharmacist/community pharmacist/patient/GP)?
Do you think your role in the reconciliation process helps in preventing hospital admissions? Or providing for a safe admission? Or supports safe medication use after discharge?
Are adverse drug events a significant cause of morbidity/mortality for your patients, especially when thinking of MEDREC? [If gives an example - “How dangerous or severe in your opinion?”]
Do you note that certain medications are subject to errors more than others?
Social context:
What is the importance placed on reconciliation where you work?
Do you liaise with other GPs or pharmacists?
What support do you receive in managing patients’ medications? Is this something that is discussed amongst your fellow GPs/pharmacists/nurses?
Do you think, in your role and practice location, you are best placed to help patients in organising their medications? Do you feel that patients feel this is a necessary component of their care?
What, if any, are the unique challenges you face because of the socioeconomic factors, of where you work? E.g. literacy, income, chronic disease, attendance/follow-up issues?
Economic context:
Do you feel MEDREC is a big part of your job? If so, do you feel like this affects already limited time constraints and billing practices? [For example, Doctor-Patient interaction; private/public; practice requires seeing a certain no. of patients.]
Do you think remuneration would help to implement MEDREC?
Do you think you have sufficient resources to effectively carry out MEDREC? [Staff; Computers; Time; Funding]
What are the constraints economically? Are there issues that supersede reconciliation in your practice? [E.g. are there commercial or human resource issues that are more pressing?]
Political and legal context:
I would now like to discuss the role of health regulatory or government agencies in the area of MEDREC, in particular any guidelines you may be aware of or responsibilities you may have as a healthcare provider.
Are you aware of any guidelines relating to MEDREC? Are you aware of any responsibilities you may have as a healthcare provider?
The HSE quality and patient safety guidelines and HIQA have noted the importance of implementing MEDREC. Do you feel that this information is freely available?
Do you think there is much support from the HSE/Department of Health/Local Health authority for this issue?
Do you feel under any legal obligation to perform activities to make medication use safer at care transitions? Can you tell me about that?
Innovation:
How would you improve the process of MEDREC in your area? Do you feel it requires communication with too many parties? Do you think can be an efficient system for HCPs?
“Thank you. Is there anything else you would like to say about anything we discussed today? Thank you for your time and participation. Your input is extremely valuable; you will have an opportunity to review your transcript prior to final submission”
Appendix EE

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- Figure 2-1

- Figure 2-2
  - NCC MERP Index for categorising errors

- Figure 2-3
  - Medication management at transitions of care. By personal permission of T Grimes.

- Figure 2-4
  - Medication reconciliation at admission and discharge to hospital. By permission of Pharmacy Practice

- Figure 5-2
  - Irish Primary Care Research Network illustration. By permission of Dr Claire Collins

- Figure 7-1

- Figure 7-3

- Table 2-1

Definitions of ‘medication reconciliation’ used by government and professional organisations. By permission of R Urban.
Appendix FF Publications arising from the thesis

Title: Tackling transitions in patient care: the process of medication reconciliation

Article category: Editorial

Authors: Patrick Redmond¹, Tamasine Grimes², Ronan McDonnell¹, Fiona Boland¹, Carmel Hughes³, Tom Fahey¹
¹HRB Centre for Primary Care Research, Royal College of Surgeons in Ireland, Dublin, Ireland
²School of Pharmacy, Trinity College Dublin, Dublin, Ireland
³School of Pharmacy, Queen’s University Belfast, Belfast, Northern Ireland

The (Dis)continuum

Errors in the prescribing and administration of medication are frequent, costly and harmful. The seminal Institute of Medicine report *To Err is Human: Building a Safer Health System* highlighted medication error as being widely prevalent, costly and contributing to preventable causes of patient harm. In particular, transitions of care, as patients move between different levels and locations of care, lead to medication error and what has been described as the “healthcare (dis)continuum”.(2) As much as 50% of medication errors and 20% of adverse drug events (ADEs) take place as a result of poor communication during these transitions - admission, transfer and discharge of patients.(20)

The errors in transition cascade

A core component of managing care transitions is ensuring that an accurate medication use history is collected and transmitted between caregivers. Errors in recording medication history give rise to discrepancies such as medication omission, commission, and errors in dose, route or frequency. These discrepancies, particularly if initiated at admission to hospital, may perpetuate through to discharge and return to the community. They have been linked to potential ADEs as well as higher re-hospitalisation rates.(17) The avoidable cost associated with poorly coordinated care transitions, leading to complications and rehospitalisation has been estimated at €45 billion in the United States (US) in 2011 alone.(18) This has been recognised by the internationally supported effort of the World Health Organization (WHO) in launching the *High 5’s* project in 2006, with an emphasis on patient safety with the standard operating procedure – ‘assuring medication accuracy at transitions in care’ focussed on reducing medication discrepancies.(19) Furthermore, reforms introduced by the Patient Protection and Affordable Care Act in the US will allow financial penalties to be imposed upon hospitals to avoid re-hospitalisations.

The reconciliation process

One way to address the continuity of medicines information when moving from one care sector to another is medication reconciliation - the process of creating the most accurate list of medications at transition points. This takes place in three stages: a list of medications the patient was using before transfer is developed, the medication and dosage is checked against the new list – with a view to identifying any discrepancies or differences. Discrepancies are determined to be intentional or not, with unintentional discrepancies changed as appropriate and intentional discrepancies documented. Finally, this comprehensive new list and information regarding changes is communicated to the next healthcare provider.(20) Medication reconciliation has been advocated by a number of different professional and accrediting bodies internationally - the Joint Commission, the Institute for Healthcare Improvement, the National Institute for Health & Clinical Excellence (United Kingdom), the Canadian Patient Safety Institute and the Institute for Safe Medication Practices (Canada). A consensus statement by key stakeholders described medication reconciliation as a patient safety issue with a need to clearly define the
process, address practical and flexible local implementation, identify at-risk patients, and actively promote and disseminate effective methods of reconciliation. (21)

**How to measure success?**

A number of different interventions have been assessed in randomised trials in relation to medication reconciliation including information technology solutions, pharmacist input and reconciliation as part of a more complex multi-faceted care plan. (22, 23) Interventions relying heavily on an increased role for pharmacists and targeting the patients most at risk of ADEs have reported the greatest improvement. (24) However, systematic reviews of medication reconciliation have commented not only on the poor quality of studies in the area, notably design flaws and the lack of appropriate comparison groups, but also the difficulty of comparing outcomes across heterogeneous settings and the absence of head-to-head comparisons of different intervention types. (22, 23) Reconciliation interventions are often assessed by comparing medication regimens across transitions and reporting discrepancy reduction as the primary outcome. However, this is a process measure and what may be of more use is identifying those discrepancies that are considered clinically significant and which may give rise to harm. (24) This failing in undertaking appropriate comparisons and selection of relevant outcomes is seen by the fact that while reported interventions have a positive effect on reducing the prevalence of medication discrepancies, the evidence for the presumed subsequent reduction in healthcare utilisation is equivocal. (22)

**The electronic records panacea?**

Future challenges for research entail identifying which patients are most likely to benefit from the reconciliation process and how discharge co-ordination plans should incorporate reconciliation. (21) The growing adoption of electronic health records, patient portals and shared medication records all may support the implementation and evaluation of the reconciliation process. Whilst Information and Communications Technology (ICT) has the potential to deliver a medical record that is universally accessible across care settings to support reconciliation, consideration should be given to organisational, ethical and social issues developing such systems in order to achieve successful and sustainable uptake. (379)

**Being pragmatic and deciding what’s important**

Interestingly the difficulty in designing and powering randomised trials to examine ADEs related to re-hospitalisation has led to a shift to the more pragmatic approach of choosing medication discrepancy as a primary outcome. (26) However, this should not neglect the need to explore both the clinical significance and the causal relationship between discrepancies, ADEs, re-hospitalisation, quality of life measures and cost effectiveness, in light of reconciliation being a recommendation of professional organisations and a necessity for accreditation in some countries. (24) More broadly, research efforts to date have been primarily concerned with in-patient reconciliation neglecting the wider patient journey upon discharge, with transitions between the hospital and long-term care facilities and within the community. Investigating strategies to reduce the potential for error and the practice of reconciliation between these sectors is also necessary.

**The broader agenda**

In summary, medication reconciliation is a conscientious, patient-centred, inter-professional process that supports optimal medicines management. (21) Reconciliation contributes to the larger area of medication safety, appropriateness and timeliness. By definition, it crosses professional boundaries and requires interdisciplinary planning and cooperation. More research is required to define its ideal design, implementation and assessment.
Title:
Interventions for improving medication reconciliation across transitions of care (Cochrane Protocol)

Background
Errors in the prescribing and administration of medication are frequent, costly and harmful (Bates 2007). More than 40% of medication errors take place as a result of inadequate reconciliation of medications at transitions of care (Barnsteiner 2008). Transitional care provides for the continuity of care as patients move between different stages and settings of care (Coleman 2004). The prevalence of medication discrepancies arising at transitions of care have been reported in many different settings (hospital, community and long-term care facilities) and stages of care (admission, transfer and discharge); in particular transitioning from an inpatient to an outpatient setting is associated with an increase in medication errors relative to other stages of care (Tam 2005; Boockvar 2006; Coleman 2004; Moore 2003). Prevalence of adverse events post hospitalisation as high as 19% have been reported with the majority of these related to adverse drug events (ADE), which may be the result of medication error (Forster 2003). Medication discrepancies as patients transition to home from hospital have also been linked with increased re hospitalisation rates (Coleman 2005).

"Medication reconciliation is a conscientious, patient centred, inter-professional process that supports optimal medicines management" (Greenwald 2010). It is an attempt to prevent medication errors at patient transition points. It is intended to be the process of creating the most accurate list of medications at all transition points, with the goal of providing the correct medications to the patient (Karapinar-Carkit 2011). Different patient groups and locations have been subject to study. A variety of intervention types have been trialled in the reconciliation of medicines including information technology (Kramer 2007; Schnipper 2009), pharmacist led (Gillespie 2009) and more complex multi-faceted interventions (Koehler 2009). The benefits of medication reconciliation interventions are often assessed by comparing medication regimens across transitions and reporting discrepancy reduction as the primary outcome. Challenges arise in identifying those discrepancies that are considered clinically significant and which may give rise to patient harm (Kwan 2013). The recognised difficulty in undertaking appropriate comparisons and selection of relevant outcome measures is seen by the fact that while reported interventions have a positive effect on reducing the prevalence of medication discrepancies, the evidence for the presumed subsequent reduction in patient harm or healthcare utilisation is equivocal (Mueller 2012).

Therefore despite reconciliation being recognised as a key aspect of patient safety there remains a lack of consensus and evidence as to the most effective methods of implementing reconciliation and calls have been made to strengthen the evidence base prior to wider spread adoption (Greenwald 2010).

Description of the condition
Transitional care describes the care provided to patients to ensure the coordination and continuity of healthcare as they transfer between different settings and/or different stages of care within the same settings (Coleman 2003a). Examples of care settings include locations such as hospitals, subacute and long term nursing facilities, patients' homes, primary care offices, and assisted living facilities (Coleman 2003a). Stages of care within these care settings may include admission, transfer and discharge. Transitions of care are associated with medication errors and patient harm. Greater coordination and attention to care transitions have been incentivised by regulatory changes and financial penalties for "hospital-acquired conditions" (Jenq 2012). Furthermore improved continuity of prescribed medication via medication reconciliation for patients at transitions of care is recommended by national standard setting bodies and internationally led initiatives e.g. World Health Organization's High 5's project. (IHI 2011; NICE 2007; WHO 2006). However the most effective method of conducting reconciliation remains unclear.
Description of the intervention
Medication reconciliation consists of three steps (IHI 2011):

1. Verification: A current medication list is developed using one or more sources of information (e.g. general practitioner medical records, patient's own supply, pharmacy records)

2. Clarification: Medication and dosages are checked for appropriateness. Here appropriateness means ensuring that there are no unintentional changes, rather than a medication review leading to optimal medication appropriateness).

3. Reconciliation: Newly prescribed medications are compared to old and any changes made are documented.

Medication reconciliation is incorporated into the National Patient Safety Goal of the Joint Commission under the umbrella of improving the safety of using medications (Joint Commission 2012).

How the intervention might work
Failure to reconcile medications can result in medication error and subsequent adverse drug events (IHI 2011). Interventions to improve medication reconciliation may work by improving the communication between all those involved in the medication use process (dispensing, administration, monitoring across settings and stages of care), including the patient. Additionally these interventions may well help in reducing transcribing errors, improved monitoring of prescriptions, information technology systems and reorganisation of care delivery.

Why it is important to do this review
Medication reconciliation was adopted as a National Patient Safety Goal (NPSG) by the Joint Commission in the US in 2005. The National Institute for Health and Clinical Excellence (NICE) in collaboration with the National Patient Safety Agency (NPSA) in the UK encouraged the standardisation of reconciliation processes within healthcare organisations (NICE 2007). The Canadian Patient Safety Institute and the Institute for Safe Medication Practices (Canada) have advocated for medication reconciliation and the World Health Organization launched the High 5’s project in 2006, with an emphasis on patient safety with the standard operating procedure – ‘assuring medication accuracy at transitions in care’ focused on reducing medication discrepancies (WHO 2006). Despite the high level of interest in implementing medication reconciliation the most effective process of conducting reconciliation remains unclear. A consensus statement from key stakeholders has called for further efforts to identify the best practices surrounding medicine reconciliation and their wider dissemination (Greenwald 2010).

The seminal Institute of Medicine report To Err is Human: Building a Safer Health System highlighted medication error as being widely prevalent, costly and contributing to preventable causes of patient injury (IOM 1999). The findings of this proposed review are relevant at both a national and international level. Regulatory bodies, healthcare institutions, patient safety advocates, healthcare practitioners and the wider public would be receptive audiences for the findings from a systematic review of the most effective method of medicines reconciliation.

Objectives
To assess the effect on medication discrepancies, patient related outcomes and healthcare utilisation in patients receiving medication reconciliation during transitions of care compared to patients not receiving medication reconciliation.

To assess the effect of medication reconciliation on medication discrepancies, patient related outcomes and healthcare utilisation in patients receiving this intervention during transitions of care compared to patients not receiving medication reconciliation.

Methods
Criteria for considering studies for this review
Types of studies
We will include the following types of studies:

- Randomized controlled trials (RCT)
• Non-randomized controlled trials (NRCT)
• Controlled before after studies (CBA)
• Interrupted time series study (ITS)
• Repeated measures study (RMS)

Studies will be eligible for inclusion, irrespective of language or publication status. NRCT, CBA, ITS and RMS will be eligible for inclusion, subject to the criteria stated in the Cochrane Handbook and inclusion criteria developed by the Cochrane EPOC group (Higgins 2011). It was felt necessary to include these types of studies due to the potentially small number and difficulty of designing randomised controlled trials in the area of medication safety.

Case series, cohort studies, studies using historical controls or cross sectional studies will be excluded.

Results from randomised studies will be reported separately.

**Types of participants**

All studies involving patients experiencing a transition of care will be included. Transitions of care refer to changes in the level, location, or providers of care as patients move within the health care system (Kim 2013; Coleman 2003). This may include but is not limited to hospital admission/discharge, acute and sub acute facilities/units/wards, primary and speciality care, long term care institutions and patients’ homes. Transition may be in either direction e.g. admission and/or discharge to an intensive care unit from a general ward. There will be no restriction on age, gender, ethnicity, location or patient population.

**Types of interventions**

Studies will be selected where the intervention is broadly compliant with the process of medication reconciliation as outlined by the Institute for Healthcare Improvement (IHI): (IHI 2011) “the process of creating the most accurate list possible of all medications a patient is taking — including drug name, dosage, frequency, and route — and comparing that list against the physician’s admission, transfer, and/or discharge orders, with the goal of providing correct medications to the patient at all transition points...”

Medication reconciliation involves three steps: 1) create an accurate and complete list of current medications (verify); 2) check appropriateness of medication regimes (clarify); 3) document the reason for medication changes (reconcile) (IHI 2011).

The intervention must be applied as patients transition from different levels and/or locations of care.

Medication reconciliation interventions may be aligned to a number of broad interventional categories including professional interventions, financial, organisational and regulatory (EPOC 2012). Examples of these, following a brief search of trials targeting reconciliation, reveals pharmacist delivered reconciliation (Kwan 2007; Makowsky 2009; Nazareth 2001; Walker 2009), complex multi-faceted interventions (Scullin 2007) and information technology solutions (Jack 2009; Schnipper 2009) all being applied. It may be possible within the review to perform subgroup analysis to compare different approaches within these categories of interventions.

Trials investigating interventions to improve the quality of prescribing during transitions of care, with no medication reconciliation focus, will not be included.

The comparator group will be those patients receiving no intervention or “usual care” as provided by the relevant healthcare provider.

**Types of outcome measures**

The outcomes chosen reflect EPOC review group guidance as those being important to the population of interest as well as decision makers in healthcare (EPOC 2012a). Studies reporting secondary outcomes only will not be included in the review. We will include process measures, patient related outcomes and healthcare utilisation.

**Primary outcomes**

Discrepancies in prescription per:

- patient
- medication (e.g. drug/dose/name/mode of administration/frequency)
Medication discrepancies have previously been defined as unexplained differences in documented medication regimes across different sites of care (Mueller 2012).

**Secondary outcomes**

**Patient Related & Process Outcomes:**
- Medication discrepancy with the potential for adverse drug event (PADE). PADEs have been previously described as “incidents with potential for injury related to a drug” (Bates 1995)
- Adverse Drug Events (ADE)
- Mortality

**Health care utilisation:**
- Unplanned re-hospitalisation
- Emergency department visits
- Primary care visits
- Length of stay

**Additional outcomes:**
- Adverse effects of interventions (e.g. unanticipated increased workload, health worker attrition)
- Resource use
  - Dependent on studies of effectiveness selected for inclusion in the review, a narrative summary of the characteristics of economic analysis undertaken may be possible e.g. comparisons of study design, methodology and outcome, measures of incremental resource use, cost and cost effectiveness etc. These results may be useful in future full economic evaluations.

**Search methods for identification of studies**

The search strategy has been written by Michelle Fiander, EPOC Trials Search Coordinator (TSC), in consultation with the authors. The TSC will search the Cochrane Database of Systematic Reviews and the Database of Abstracts of Reviews of Effects (DARE) for related systematic reviews and the following databases for primary studies.

**Electronic searches**

**Databases:**
- EPOC Group, Specialised Register, Reference Manager
- Cochrane Central Register of Controlled Trials (CENTRAL), Wiley
- MEDLINE and MEDLINE In-Process and other non-indexed citations, OvidSP
- EMBASE, OvidSP
- PsychINFO, OVIDSP
- CINAHL (Cumulative Index to Nursing and Allied Health Literature), EbscoHost
- Dissertations and Theses Database, ProQuest
- Science Citation Index, ISI Web of Knowledge
- Web of Science, Conference Proceedings Citation Index- Science, ISI Web of Knowledge
- Pharmline, National Electronic Library for Medicines (NHS, UK)
- International Pharmaceutical Abstracts (IPA), ProQuest

The MEDLINE search strategy (Appendix 1) will be translated for other databases using appropriate syntax and vocabulary for those databases. The strategy includes Medical Subject Headings and synonyms for medication errors, hospitals, and children. Results will be limited by two methodological filters: the Cochrane Highly Sensitive Search Strategy (sensitivity- and precision-maximizing version - 2008 revision), to identify randomized trials, and an EPOC methodology filter to identify non-RCT designs.

**Searching other resources**

**Grey Literature:**
We will conduct a grey literature search to identify studies not indexed in the databases listed above. Sources will include the sites listed below. Additional sources, if any, will be documented in the review.
Trial Registries:
We will search the following Registries:
- International Clinical Trials Registry Platform (ICTRP), Word Health Organization (WHO) http://www.who.int/ictrp/en/
- ClinicalTrials.gov, US National Institutes of Health (NIH) http://clinicaltrials.gov/

We will also:
- Screen individual journals and conference proceedings
- Review reference lists of all included studies, relevant systematic reviews/primary studies/other publications.
- Contact authors of relevant studies or reviews to clarify reported published informationseek unpublished results/data.
- Contact researchers with expertise relevant to the review topic/EPOC interventions.

Data collection and analysis
Selection of studies
Two review authors will independently screen titles and abstracts to decide which studies satisfy the inclusion criteria as well as identification of multiple reports from single studies. Any papers not meeting the inclusion criteria will be excluded at this stage. If there is uncertainty, consensus will be reached by discussion with another co-author. If agreement cannot be reached, we will involve an EPOC Group editor to resolve it. Following this, two review authors will independently assess the full text articles to ensure the studies still fulfil the inclusion criteria.

Data extraction and management
Two review authors will independently undertake data abstraction using a modified version of the EPOC data collection checklist to include: study design, study population, intervention, usual care, outcome measures used and length of follow-up data. Any disagreement will be resolved by discussion between the co-authors. Where necessary, we will contact authors for missing information or clarification. Information from data extraction forms will guide the extraction of numerical data for meta-analysis in RevMan.

Assessment of risk of bias in included studies
The criteria against which the risk of bias in a study is judged will depend upon study design. The domains by which studies with a control group (RCTs, CCTs and CBAs) will be assessed will include (EPOC 2011; Higgins 2009):
1. sequence generation;
2. allocation concealment;
3. baseline characteristics;
4. baseline outcome measurement;
5. blinding;
6. incomplete outcome data;
7. protection against contamination;
8. selective outcome reporting.

We will tabulate the description of the domains for each included study, along with a judgement on the risk of bias (low, high or unclear), based on the Cochrane Handbook for Systematic Reviews of Interventions 5.0.2 (Higgins 2009). We will undertake a summary assessment of the risk of bias for the primary outcome across the studies (Higgins 2009).

For each study, we will provide a summary assessment of risk of bias as shown below:
1. low risk when there is a low risk of bias across all key domains;
2. unclear risk of bias when there is an unclear risk of bias in one or more of the key domains;
3. high risk of bias when there is a high risk of bias in one or more of the key domains.
The criteria for ITS will consider whether (EPOC 2011):
1. the intervention was independent of other changes;
2. the shape of the intervention effect was pre-specified;
3. the intervention was unlikely to affect data collection;
4. incomplete outcome data were adequately addressed;
5. the study was free from selective outcome reporting.
Two review authors will independently perform the quality assessment. We will resolve disagreements by discussion and, if needed, arbitration by a third person.

Measures of treatment effect
Randomised and non-randomised studies will be reported separately. We will report outcomes for each study in natural units. We will calculate, where possible, absolute change from baseline with 95% confidence intervals. We will report estimates for dichotomous outcomes (e.g. adverse drug events) as risk ratios. We will report estimates for continuous outcomes as mean differences if they are measured on the same scale, if continuous outcomes are measured on multiple scales, we will report the standardised mean difference. We will report pre-intervention and post-intervention means or proportions where baseline results are available for both intervention and control groups from RCTs, quasi-RCTs and CBAs.

Randomised Controlled Trials
The findings from independent studies will be combined and standard meta-analysis techniques will be used to combine the results provided enough study data is obtained and taking account of heterogeneity between studies. The size of the study will determine the study’s weight and an overall treatment effect will be estimated.

Non- Randomised Studies
Interrupted Time Series Studies (ITS)
For interrupted time series design studies, we will extract the difference in slope and the difference in pre to post-intervention levels. We will analyse the post- versus pre-intervention difference (adjusted for trends) at specific time points (three months, six months and six-monthly thereafter). If the differences are not available in the primary reports, we will attempt re-analysis using data from graphs or tables.

Studies ignoring secular changes and performing simple pre-post analyses will not be included unless re-analysis is possible. Re-analysis, to estimate the effect of an intervention, will include a segmented time-series regression analysis, taking into account secular time trends and any autocorrelation between any individuals observations. This allows the change in level and change in trend, after the intervention, to be estimated.

Meta-analysis will be performed for the changes in level and changes in trend using the generic inverse variance method in RevMan.

Controlled Before-After Studies (CBA)
For studies included in the review all relevant information will be tabulated. This will include all pre and post invention results (sample sizes, means, proportions, 95% confidence intervals, etc.) for each group for each outcome of interest. Additionally, the pre-post intervention difference for each group for each outcome of interest and the differences across groups will be examined. A meta-analysis will be carried out combining the results of the individual studies. Care will be taken when interpreting the results.

Unit of analysis issues
Cluster randomised trials selected for inclusion will be assessed in order to ensure that appropriate analysis was carried out to address cluster effects and to avoid overestimating the significance of differences. In cluster randomised studies where the analysis was carried out ignoring the effect of clustering, efforts will be made to obtain the data needed to correct for this. Should the data not be forthcoming we will use the intra cluster correlation coefficient (ICC) or design effect from external sources (other trials included in the review ) to inflate the standard error so as to account for clustering as described in
section 16.3.4 of the Cochrane Handbook (Higgins 2011). As stated above, all NRCT, CBA, ITS and RMS studies selected for inclusion will also be assessed to ensure that the appropriate analysis was carried out and, as for the cluster randomised trials efforts, will be made to obtain the data if necessary.

**Dealing with missing data**

Lead investigators or corresponding authors will be contacted for any missing trial data or data missing from published reports or for additional clarification. If there are any missing data from a study, we will explicitly state this. Sensitivity analyses will be undertaken as per the Cochrane Handbook Chapter 9, Section 9.7 to assess how sensitive results are to reasonable changes in the assumptions that are made. Finally the potential impact of missing data on the review findings will be included in the Discussion section.

**Assessment of heterogeneity**

We intend to assess contextual heterogeneity on the basis of information collected on the context in which the intervention was implemented. We will assess for variability in the participants, interventions and outcomes studied to identify clinical heterogeneity, and for variability in study design to describe methodological diversity. Statistical heterogeneity will be identified and measured as recommended by the Cochrane Handbook for Systematic Reviews of Interventions (section 9.5.2) (Higgins 2011). The following will be used as a guide for interpretation:

- 0% to 40%: might not be important;
- 30% to 60%: may represent moderate heterogeneity;
- 50% to 90%: may represent substantial heterogeneity;
- 75% to 100%: considerable heterogeneity.

**Assessment of reporting biases**

Assymetry in funnel plots of the primary outcome will be examined to assess the potential for study effects such as publication bias, if a sufficient number of trials are available. We will conduct formal statistical tests for funnel plot asymmetry, namely the Begg's and Egger's methods (Handbook Table 10.4.b), again if a sufficient number of trials are available. Furthermore we will assess reporting bias by scrutinising the study results using the 'risk of bias' tables provided in RevMan (e.g. selective outcome reporting). Where there is a possibility of publication bias and small-study effects a sensitivity analysis will be undertaken as described below. In addition to searching trial registries for relevant trials not identified in our main database searches, we will also search for protocols of studies selected for inclusion, to compare planned with actual methods, interventions and outcomes. Furthermore a thorough search of the grey literature and contact with known experts in the field will also reduce the influence of publication bias on our review.

**Data synthesis**

We will perform statistical analysis using the Review Manager software (RevMan 5.1). We will conduct the meta-analysis of included randomised controlled trials and observational trials separately. Pooled estimates (RR with 95% CIs) of the evaluated outcome measures will be calculated by the generic inverse variance method. Results will not be depicted as ‘not statistically significant’ or ‘non significant’, but we will report the CI together with the exact P value. In the absence of statistical and clinical heterogeneity we will apply a fixed-effects model to pooled data. The $I^2$ statistic will be examined to describe the proportion of the variability in the results that reflects real differences in effect size. However variation in studies with respect to populations, interventions, outcomes and settings is likely. Thus, the true effect is likely to be related, but not the same for all studies. We will therefore choose the random-effects model or choose not to perform a meta-analysis (if the populations, settings, etc differ too much).

If it is not possible to synthesise the data from the included studies, we will provide a narrative synthesis of the results, grouping together studies that used similar interventions and provide a comparison of different approaches. The data will eventually be synthesised using a 'Summary of Findings' table that will provide key information concerning the quality of evidence, the magnitude of effect of the interventions examined, and the sum of available data on all primary outcomes for a given comparison. Quality assessment of the
results will also be carried out using the GRADE approach, which specifies four levels of quality (high, moderate, low and very low) where the highest quality rating is for a body of evidence based on randomised trials. Quality will be assessed separately for each outcome.

**Subgroup analysis and investigation of heterogeneity**

Additional subgroup analysis, dependent on availability of data, will be undertaken. Exploratory search results suggest the following subgroup analysis may be possible:

- Patients with polypharmacy (≥4 long-term medications), older (>65), and/or chronic illnesses as these groups are known to suffer more errors in prescribing ([Gleason 2010](#); [Grimes 2011](#)).
- Comparison of different approaches to medication reconciliation (e.g. ICT, pharmacist delivered, integrated medicines management) may be undertaken, particularly where the methods are supported by the literature and are of interest in developing and implementing reconciliation interventions.
- Patients admitted to or discharged from acute hospital care (hospital admission and discharge are well studied transitions of care for applying medication reconciliation interventions).

The number of subgroups will be kept to a minimum and priority will be given to subgroups that are of specific interest to the potential implementation of any future intervention.

**Sensitivity analysis**

A sensitivity analysis will be conducted to calculate the effect of risk of bias (including missing data) within studies on effect size, by calculating the effect of excluding or including studies with a higher risk of bias.
Title:
General practitioners’ and community pharmacists’ opinions on medication management at transitions of care in Ireland

Authors:
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Introduction:
Medication discrepancies during transitions of care can occur as a result of incomplete or inaccurate communication as responsibility shifts between healthcare providers or back to the patient. These discrepancies are common, reported in up to 67% of hospital admissions, and have been linked to potential as well as actual adverse drug events (ADEs)(15,24,380). The coordination of care, in particular improved systems of transfer of medication information at transitions, especially for those with complex chronic illnesses is essential(48). Policy recommendations in the area have been numerous, with reports recommending coordinated care delivered by community based multi-professional teams, mandating all healthcare providers deliver medication reconciliation (A 3 step process - verification of a current medication list, clarification of directions and appropriateness; and documentation of changes(20)); as well as minimum datasets and safe modes of transfer of patient information on referral and discharge.(3,48,178)

Medication reconciliation has been promoted by many statutory and safety focused organizations and a number of studies have explored the most effective method of medication reconciliation(5,22–24,105,114). Most existing studies have been prevalence studies of discrepancies attempting to identify high risk groups and transitions, or trials of pharmacist and Information Technology (IT) mediated interventions with only a few studies investigating primary care based healthcare professionals (HCPs) opinion on their role in reducing and preventing errors at transitions(60,156,208). Barriers to effective reconciliation have been grouped as patient, provider and system factors; in considering designing solutions to reconciliation issues it is necessary to examine these factors more closely(163).

The aim of this study was to gather information from general practitioners (GPs) and community pharmacists (CPs) on current practices of medication management at the primary/secondary care interface in Ireland. Specific objectives of the study included an assessment of the experience of prescribing errors following transition, identification of medication reconciliation practices, and evaluating the quality of communication/relationship between HCPs.

Methods:
A cross sectional, self-administered electronic questionnaire which facilitates anonymous completion was devised based on the literature and the input of a group of relevant GPs and CPs. The questionnaire had a mix of quantitative response options as well as free text responses. Core content consisted of basic demographics, details on employment and professional experience. In addition, questions on current medication management practices (specifically medication reconciliation), the quality of communication and relationship with other healthcare providers, as well as the experience and handling of prescribing errors were included.

Setting & Population:
Healthcare in the Republic of Ireland is provided through a mixed model of funding. The Health Service Executive (HSE) provides all state funded health services; it has four administrative regions representing broad geographic regions (Dublin Mid-Leinster, Dublin North East, South and West). Almost half (44%) (July 2013) of the population have their healthcare subsidised by the state (General Medical Services scheme - GMS). GPs operate as private contractors, consulting with both private (self-funding) and public (GMS) patients. CPs are contracted by the HSE to dispense medication, and are typically private contractors also. The study aimed to recruit a representative sample in Ireland (total population 3439 CPs and 2799 GPs). A sampling frame of potential participants was identified with the permission of the Irish College of General Practitioners (ICGP) and the Pharmaceutical Society of Ireland (PSI). The survey was distributed in June 2014 via these email lists (2364 GPs, 311 GP Registrars [complete ICGP mailing list] and 2382 CPs [PSI random sample]) with a hyperlink to the online survey tool.  A reminder email was sent four weeks later.

In order to attain a statistically representative sample of the target population, allowing for a 15% response rate, a sample size of 346 for each profession was calculated (margin of error: 5%, confidence level: 95%). Participants were incentivized, with their consent, to complete the survey (voluntary participation in a prize draw for a gift voucher).

Analysis:
One researcher (HC) was primarily responsible for data entry with a second (PR) verifying a random sample of 10% for accuracy and consistency of coding. Summary statistics were used to characterize the sample and compare it to the original proposed population. Responses were assessed for missing data, in particular patterns of non-response.

The distributions of responses to questions concerning key outcomes (medication reconciliation, quality of communication and prescription error) were compared between GP and CP. The sign-test, Chi-squared test and Fisher's exact test were used as appropriate. Logistic regression was used to model recall of prescribing errors following a care transition in the previous six months and ordered logistic regression for quality of communication with public hospital, private hospital and between GP and CP. For each model the primary exposure variable was healthcare provider (GP or CP), with adjustments for relevant confounders (HSE region, practice location, age, gender, hours worked per week and distance from the local public hospital). Due to the low number of responses to ‘very poor’ and ‘poor’, these were amalgamated when considering opinions on communication of GP and CP of each other.

All free text responses were reviewed by the inductive method of data-driven content analysis, developing themes linked to individual participants’ contributions.

Results
Quantitative survey results
In total, 949 out of 5057 questionnaires were returned resulting in an overall response rate of 17.7%; the response rate was 20.7% (n=554) and 14.4% (n=343) for GPs and CPs respectively. Demographic data of respondents are summarised in Table 1. There was broad representation from all geographic regions, with more male GP respondents (n=317, 57.2%) but more female CP respondents (n=223, 65%).

Respondent characteristics
The majority of GP respondents were GP principals (n=349, 63%) working with other GPs as part of a larger practice (n=407, 73%), with computerised prescribing records (n=517, 96%), seeing 10-19 individual patients per session/half day (n=430, 78%). A third of CPs (n=119, 35%) held a role as a Supervising Pharmacist, dispensing >3000 prescriptions/month (n=103, 30%); more than half described themselves as employees (n=189, 55%), working in an independently run pharmacy (n=193, 57%).
Views on medication reconciliation

Most GP respondents did not feel they had a formal system for medication reconciliation (n=327, 60%). Nevertheless, three quarters of GPs (n=298, 75.4%) rated the standard of medication reconciliation in their practice as being good to excellent. Most CPs had systems in place to identify omissions (n=213, 74.5%) and newly initiated medications (n=220, 76.9%) in their patients’ prescriptions.

Almost all GPs (n=396; 97.8%) agreed or strongly agreed reconciling medication was an important way to both improve medication safety, with both GPs (93%) and CPs (93%) in agreement that it was also an important way to improve medication adherence. Only 22% (n=90) of GPs agreed that reconciliation was best handled by pharmacists. However, the majority (74%) of CPs agreed/strongly agreed that they were best placed to handle reconciliation, with 88% agreeing their time was well-spent updating the patient medication list.

When asked to rank what information they considered most important to include when receiving details of medications from other HCPs, respondents ranked a full list of current medications (GP n=314, 69.6%; CP n=171, 64.5%) followed by details of any change to long-term medication (GP n=76, 16.6%; CP n=33, 12.2%) as most important. Details of previous adverse effects (GP n=10, 2.2%; CP n=3, 4.1%) and special administration requirements (GP n=10, 3.8%; CP n=11, 3.7%) were considered the least important information. There was no overall difference in the mean rankings given to items selected by GP and CP (p=0.72).

Communication and relationship between GP, CP, hospital pharmacist, public and private hospitals

There were mixed views amongst GPs and CPs regarding communication with their local publicly funded hospital, with approximately a third describing it as poor/very poor and a similar proportion describing it as good to very good. Most GPs did not receive communication electronically about prescriptions from their local hospitals (n=348, 64%). There were differences in satisfaction levels between HSE regions. Respondents in Dublin North East were, on average, 40% less likely, and those in the West 34% less likely, to report higher levels of satisfaction in communication with public hospitals than their counterparts in Dublin Mid-Leinster, [adjusted odds ratio (AOR):0.60, 95%CI: 0.41-0.87, p=0.01; AOR: 0.68, 95%CI: 0.45-0.95, p=0.03 respectively]. These effects did not vary between GPs and CPs (p=0.53). Differences in levels of satisfaction between HSE regions in satisfaction of communication with private hospitals were not apparent. CPs were less likely to rate communication with private hospitals favourably compared to GPs (AOR: 0.66, 95%CI: 0.48-0.90, p=0.01).

The opinion of GPs and CPs on their relationship with each other was generally positive, with 62% (n=311) of GPs and 52.5% (n=150) of CPs describing the relationship as very good (Table 2).

Regarding hospital pharmacists (HP), nearly 40% of GPs described the quality of communication as poor/very poor. Adjustment for age, gender, location, hours worked and distance from a public hospital had no significance. Both CPs (86%) and GPs (87%) were in favour of expanding the role for HPs in identifying and preventing prescribing errors as patients experienced care transitions. Similarly, GPs (74%) and CPs (82%) felt the role of the community pharmacist should be expanded in the identification and prevention of prescribing errors following a transition.

Experience of prescribing errors

Almost 84% (n=320) and 87.2% (n=205) of GPs and CPs respectively reported that they could remember mistakes in patients’ prescriptions, which may have been due to poor transfer of information following a care transition (e.g. delayed or no discharge prescription available, omission of long-term medications) in the past six months (p=0.27; Table 3). Although in-patient discharge prescriptions were selected by both respondent groups as being the single largest source of prescription error (GP 21.6%, CP 16.8%), all sources of prescriptions including out-patients, emergency departments, in-patient discharges and private hospitals were implicated. There was evidence (p<0.001) of an overall significant
difference in the sources of mistakes in prescribing errors identified between GPs and CPs. GP transcription of hospital prescriptions was identified as also being a source of error with 67.7% of CPs stating it was likely/very likely for an error to arise. In general, managing identified errors was recognised as being complicated with most respondents (CP n=170, 79.4%; GPs n=253, 88.1%) finding it difficult or impossible to contact hospital prescribers.

**Free text content analysis survey results (Quotes summarised in Table 4):**

The examination of free text responses generated four broad categories representing a number of subthemes.

1. Organisational/Infrastructural issues
2. Relationship and quality of communication between HCPs
3. Role of the patient/vulnerable patients
4. Prescribing errors

**Organisational/Infrastructural issues**

Many CPs were frustrated by the lack of clinical information available to them about their patients (I). An expanded role for CPs was also highlighted by some respondents (II): The clinical guidance given to junior hospital doctors in preparing discharge summaries and prescriptions was also raised as an issue (III): CPs underlined the role that HPs could play in improving safe and appropriate prescribing by providing an additional layer of review in the transition process for patients (IV). Finally, the fragmented nature of the healthcare system itself was also noted. There were issues regarding the lack of printed or computerised discharge letters/prescriptions, interoperability of hospital/pharmacy and GP software systems, a ‘safety net’ for some categories of patients, and resources (V-VII):

**Relationship and quality of communication between HCPs**

A good relationship was reported between the two groups of HCPs by respondents. The strength of this relationship in terms of improving patient safety was highlighted (VIII). The specific skills of the CP were recognised and valued by GPs, even when correcting GP prescribing or seeming to be particularly fastidious (IX).

A significant theme in terms of contributions from respondents was disappointment with the quality of communication within the health system, particularly when attempting to contact hospital prescribers to resolve identified problems or ambiguities with prescriptions outside of normal working hours (X-XI).

**Role of the patient/vulnerable patients**

Respondents highlighted the need for involvement of patients in ensuring correct prescribing information was transmitted. Some respondents felt patients contributed to the lack of clarity (XII). Comments also indicated that patients should be respected and engaged when making changes to their prescriptions (XIII).

Respondents highlighted patients with multi-morbidity and those with mental health issues as having the greatest risk of medication error due to frequent transitions of care and specialist review without a global view of their medications (XIV).

**Prescribing errors**

The majority of participants recalled that they had seen any errors in their patients’ prescriptions over the past six months. There was almost universal agreement, with many examples given of errors (XV-XVI).

**Discussion**

Internationally, patient safety incidents are relatively common in primary care and prescribing incidents are those most likely to cause avoidable harm to the patient(11). The main findings of this study highlighted a high level of experience of prescribing errors following transitions, an absence of formalised medication reconciliation practices in GP practices, dissatisfaction with the current standard of communication between primary and secondary care, and support for a greater role for both HPs and CPs in medication management.
Implementing formal systems of medication reconciliation was a key recommendation in terms of medication safety in a Department of Health & Children, Ireland report in 2008(178). Despite this and the fact that both responding GPs and CPs were positive about the benefits of medication reconciliation in terms of prescribing safety and adherence, formal systems of medication reconciliation were not in place in most GP practices. A greater understanding is needed as to why improvements in medication reconciliation have not been adopted by the majority of GPs.

Our results are in-keeping with barriers and potential solutions identified internationally to medication management at transitions of care(60). In terms of provider and organisational issues, concerns with poor communication across the primary/secondary interface were highlighted, with many examples of errors arising. While the reason for the reported geographic difference in opinion on the quality of communication is not clear from this study, a discrepancy between regions in terms of the in-patient clinical pharmacy services provided has been recorded previously (205). Furthermore, there is a deficit in the limited use of IT to improve communication, as well as its possible role in reconciliation. GPs reported having limited contact with CPs and both groups felt HPs could play a greater role in interacting with primary care HCPs. This lack of contact between HPs and community HCPs has been confirmed previously with a majority of hospitals having no arrangement for HPs involvement or communication to primary care based HCPs upon patient discharge (205).

Conversely the relationship between GPs and CPs was rated positively by the majority of both groups. However, there was a frustration from some CPs that they could not contribute more in the management of medications. Indeed high quality trials of CPs effectiveness in medication management, while limited in number, are generally favourable (114). Furthermore, 22% of GPs agreed that reconciliation was best handled by pharmacists while 74% of CPs agreed/strongly agreed that they were best placed to handle reconciliation. This highlights a possible ambiguity around ‘ownership’ of outpatient medications and the difficulty in developing a community of HCPs to coordinate care for patients as recommended in the King’s Fund and subsequent commissioner reports in the UK(47,48). This is further compounded by the majority of GP respondents’ view that CPs role in medication management could be enhanced. This apparent conflict in findings is perhaps representative of the legal underpinning of prescribing authority in Ireland – CPs can contribute to the process, but do not have prescribing authority.

The majority of both groups noted that they were exposed to errors in prescriptions in the past 6 months, following a transition of care. These findings are consistent with international experience, particularly omission of chronic medications and possible subsequent re-hospitalisation and mortality (15,218). The fact that respondents also expected more ADEs to occur than is the case is also supported by previous reviews that found that most unintentional discrepancies had no apparent clinical significance (24).

Respondents also highlighted a lack of funding to dedicate time and staff to reconciliation – an issue likely impacting development of additional services in secondary care too (e.g. HP availability for discharge reconciliation). Finally, a theme which resonates with much of the literature around multi-morbidity was the lack of patient involvement in the process of coordinating transitions for complex patients.

Limitations

There are some limitations to the study. Firstly, the response rate (17.7 %), similar to many electronic surveys, was low and the possibility of responder bias needs to be taken into consideration. Nevertheless, the demographics of GP and CP responders were comparable to data published in two national reports, giving confidence that the respondents comprise a representative sample. Additionally, many of the findings were consistent with international literature. Secondly, although the questionnaire enabled the collection of data from a large number of respondents, it may have been limited in its ability to gain rich in-depth information on behaviours and feelings. Finally, with self-report
questionnaires, the issue of socially desirable responding (i.e. the tendency for participants to present a favourable image of themselves) should be considered.

**Conclusion**
The findings from this study are consistent with previous research highlighting HCPs’ recognition of prescribing errors as being a common event at transitions of care. Poor communication between primary care HCPs and secondary care, as well as the call for a more “structured seamless care programme” linking primary and secondary care, were also highlighted. A suggestion of geographical variation in satisfaction with communication also emerged. The results of this study confirm that while there is enthusiasm for the benefits of medication reconciliation, there are limited formal structures in primary care to support it, despite it being a stated aim of regulatory agencies. Additionally, CPs have limited opportunity to contribute in medication reviews and the role of HPs in coordinating transitions could, in the respondents’ view, be expanded. Future research should focus on the barriers identified in this study in implementing medication reconciliation and improving medication management at transitions.