Medication Reconciliation as a Medication Safety Initiative

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A thesis submitted in fulfilment of the requirements for the degree of Doctor of Philosophy

Faculty of Pharmacy

The University of Sydney

July 2017

Declaration

This thesis is submitted to the University of Sydney in fulfilment of the requirements for the degree of Doctor of Philosophy within the Faculty of Pharmacy.

The work presented in this thesis is, to the best of my knowledge, original except as acknowledged in the text. I hereby declare that I have not submitted this material, either in full or in part, for a degree at this or any other institution.

Alemayehu B. Mekonnen

4th July 2017

Acknowledgements

This thesis could not have been possible without the support and input of many people whom I would like to acknowledge and sincerely thank, and this PhD journey is just as much as their encouragement vested on me.

First and foremost, I would like to express my deepest gratitude to my two wonderful supervisors, Professors Jo-anne E Brien and Andrew J McLachlan for their ongoing guidance, support and mentorship throughout this long journey. Jo, it is because of you whom I am successful with my PhD; on top of your expertise, your patience is incredible. It is also worth working with Andrew, and very much thanks for your dedication to the high-quality work and valuable advice for all those PhD years.

My sincere appreciation also extends to my Ethiopian collaborators, Drs Desalew Mekonnen and Zenahbezu Abay for being very generous with their time and serving as an inspiring and supportive mentor throughout the research process.

I would also like to thank the pharmacists from Ethiopia—Feser Dula, Abaynesh Fentahun, Melka Abdisa, Tamerat Befekadu—for their help for the collection and categorization of data, and all staffs at the emergency ward who were keen to work with us during the implementation phase of this research. The contribution of Misganaw Semagn, focal personnel for drug information service, Gondar university hospital is highly acknowledged.

The technical support from the clinical director of Gondar university hospital (Ethiopia), and other departments (Internal medicine department, Hospital pharmacy department) are gratefully acknowledged.

A big thank you goes to all my fellow postgrads at the Faculty of Pharmacy, University of Sydney, both past (Tariq, Hanni, Saleh, Vania) and present (Hadi, Mohammed, Andi, Jeff) for their friendship, intellectual and moral support. Outside the faculty, I am very grateful for my

friends in Sydney (Tadesse, Yezih, Zewedeneh, Abebe, Wedu, Addis)—you are truly my energies, and my stay in Sydney has been enjoyable because of you.

Special thanks to my father, my brothers (Dessalew, Adugnaw), my uncle (Addisu) and to my lovely wife (Mebrat) for their unreserved support, inspiration, firm belief in my work and confidence in me, and their patience during my time of intense work where without this, this PhD would never have been completed.

Last but not least, I would like to acknowledge the generous support from the University of Sydney International Students' Scholarship without which I could not have undertaken this project nor achieved my PhD. Part of this thesis was also funded by the University of Sydney through the Postgraduate Research Support Scheme (PRSS).

Preface

The research presented in this thesis was a project carried out by the author (Alemayehu Mekonnen) under the supervision of Professors Jo-anne Brien and Andrew McLachlan in the Faculty of Pharmacy, The University of Sydney, Australia. Part of the work presented in this thesis (Chapters 6 to 10) was also undertaken in collaboration with Ethiopian staffs at the Universities of Gondar and Addis Ababa, Ethiopia.

The thesis is structured as a PhD by publication; however, some of the chapters form an individual manuscript that has been submitted for publication. Chapters 2 to 7 have been accepted as publications and are displayed as copies. Because it was crucial to discuss the literature and brief the rationale for the research in each manuscript (both published and unpublished), there may be some common ideas in the introductory and methodology sections among the chapters when reading consecutively.

In relation to this thesis, we employed both the terms ‘pharmacist-led’ and ‘pharmacy-led’ equally, but when we intended to refer other supportive staffs such as pharmacy technicians as well, we adhered to the latter terminology. In chapters 9 and 10, the term ‘hospital pharmacist’ is predominantly utilized to suit the local situation, and to make a distinction between pharmacists involved in clinical services and those engaged in dispensing roles.

All of the empirical research included in this thesis has been approved by both The University of Sydney Human Research Ethics Committee (approval No: 2015/818), and the Institutional Review Board of the University of Gondar, Ethiopia (O/V/P/RCS/05/624/2016). Ethics approvals and associated documentations are supplied as appendices.

Abstract

Medication errors and their adverse outcomes are the most common cause of patient injuries in hospitals globally and have important clinical, economic and humanistic consequences. A number of medication safety strategies are available for preventing medication misadventures. Medication reconciliation is the safety strategy usually called for, to prevent medication errors that occur at care transitions. This strategy has been adopted as a standard practice in many developed countries. However, in Ethiopia, there were no published studies on medication reconciliation, nor evidence-based interventions aimed to tackle the burden of medication errors and subsequent patient harm. This thesis explores the journey to medication reconciliation service implementation as a medication safety strategy in Ethiopian public hospitals. Before the journey, however, given the lack of consistent reports regarding the impact of this strategy overall, we synthesized the evidence supporting the effectiveness of this intervention as a medication safety strategy.

Pharmacists play a role in providing medication reconciliation. Therefore, the overarching aim of this thesis was to evaluate the impact of pharmacist-led medication reconciliation intervention and to determine whether this strategy is feasible in resource-limited settings or not. Implementation of medication reconciliation is not an ultimate end but sustainability is an issue, and this should be corroborated by corresponding changes in attitudes, teamwork, communication, culture, and leadership. For this purpose, this thesis was informed by a sequence of four separate but inter-related studies. It uses methods from both safety and implementation sciences for successful implementation of the medication reconciliation program. System approaches to patient safety, such as patient safety culture has been explored, and patients' experiences of medication-related adverse events have been discussed followed by an implementation of a theory informed medication reconciliation intervention at hospital

admission. This thesis thus, utilized a multi-method exploration of patient safety issues to develop, implement and evaluate a medication safety program designed to reduce the burden of unintentional medication discrepancies at care transitions.

Chapter 1 Provides the technical background and the rationale from which the present body of work is built up on. A brief explanation of the various medication safety strategies and the current evidence for the effectiveness of medication reconciliation interventions have been presented. This chapter also elaborates the rationale for conducting this research and a description of the overall structure of the thesis.

Chapter 2 reports the results of a systematic review and meta-analysis that investigated the effectiveness of pharmacist-led medication reconciliation interventions on some of the clinical outcomes studied, including all-cause mortality, hospital readmissions, emergency department hospital visits and composite outcomes, and adverse drug event-related hospital visits. This study has demonstrated a significant impact from involving pharmacists in the medication reconciliation, and most importantly, it helps to cut adverse drug event-related hospital revisits (RR 0.33; 95% CI: 0.20–0.53), subsequent emergency department hospital visits (RR 0.72; 95% CI: 0.57–0.92) and hospital readmissions (RR 0.81; 95% CI: 0.70–0.95). However, this review reveals no evidence that such interventions have an impact on mortality and composite all-cause readmission and/or ED visits.

Chapter 3 presents a systematic review and meta-analysis of the impact of pharmacy-led medication reconciliation programs on the burden of unintentional medication discrepancies at hospital transitions. Medication reconciliation is a resource-intensive process and it was also important to identify areas which suited the best for pharmacists. Of the 1,832 articles screened for title and abstract, nineteen studies which involved a total of 15,525 adult patients were included. Pharmacy-led medication reconciliation intervention usually revealed a trend towards reduction in medication discrepancies, compared with usual care. Compared with

usual care, single medication reconciliation interventions at transitions in care (either admission or discharge) showed a significant reduction of 66% in patients with medication discrepancies (RR 0.34; 95% CI: 0.23–0.50) in favour of the intervention. But, there was no difference between groups for interventions targeting multiple transitions (RR 0.88; 95% CI: 0.77–1.02). Subgroup analyses showed that there were no differences for the target of transition (admission vs. discharge), type of intervention (multi-faceted intervention vs. medication reconciliation), and setting (single center vs. multicenter), nor pharmacists versus pharmacy technicians. Importantly, more clinically relevant and discrepancies of higher impact were easily identified through pharmacy-led medication reconciliation programs.

Chapter 4 is also a systematic review and meta-analysis and addresses the impact of an electronic tool on the occurrence of medication discrepancies identified through the medication reconciliation process. Medication reconciliation process aided with an electronic tool was able to minimize the incidence of medications with an unintended discrepancy, mainly drug omissions. However, there was no significant reduction in either the proportion of patients with medication discrepancies or the mean number of discrepancies per patient. The clinical impact of electronic interventions is also less clear. There was a lack of rigorous designs that ascertain these findings, however. Effective medication reconciliation likely requires a multi-faceted approach involving people, process, technology and that technology intervention alone may not consistently reduce errors.

Chapter 5 presents a systematic review, and it was a broad exploration of the African medication safety literature to have an understanding of the burden of medication errors (MEs) and adverse drug events (ADEs) in the African hospital setting. Of the 1,316 articles extracted from the various databases searched using a systematic search strategy, fifty-one studies met the inclusion criteria; of these, 33 focused on MEs, 15 on ADEs and three studies on MEs and ADEs. These studies were conducted in nine (of the 54) African countries. The median (IQR)

percentage of patients reported to have experienced ADE-related hospital admissions was 2.8% (0.7–6.4 %) in the general population, ranging to as high as 5.5% (1.8–8.0%) in the adult population. In these studies, it was reported that many ADEs were deemed preventable. The most commonly reported types of MEs were prescribing errors. No studies specifically assessing medication history or documentation errors in African hospitals were retrieved. Major contributing factors for MEs reported in these studies were individual practitioner factors (e.g. fatigue and inadequate knowledge/training), and environmental factors, such as workplace distraction and high workload.

Chapter 6 discusses the study protocol for an Ethiopian study, which aimed to implement a new pharmacy service (i.e. medication reconciliation) in public hospitals in one of the regions, and describes the methodological approach employed to achieve our primary objectives. The project was divided into three phases. The first was a mixed-methods study which was undertaken to investigate health care professionals' perspectives of patient safety and patients' experiences of medication-related adverse events. A cross sectional study, utilizing the 'Hospital Survey on Patient Safety Culture' (Chapter 7) questionnaire was conducted among health care professionals working in ten Ethiopian public hospitals. This was complemented by semi-structured interviews—along with the qualitative findings from the patient's interview, it is presented in Chapter 8. The second phase was a focus group study, designed according to the twelve domains from the Theoretical Domains Framework (TDF), to explore the barriers and facilitators to medication safety activities delivered by hospital pharmacists (Chapter 9). Lastly, a single center, before and after study to evaluate the impact of pharmacist-conducted admission medication reconciliation in an emergency ward had been conducted (Chapter 10).

Chapter 7 describes the results of the hospital survey. Of the 480 questionnaires, a total of 410 were returned (response rate, 85.4%). Patient safety culture in the studied hospitals has been

found lower than the benchmark studies. Importantly, understaffing followed by problems during handoffs and care transitions and punitive response to error were identified as major safety problems. Particularly, handoffs and care transitions were largely affected by the lack of teamwork across units, punitive response to error reporting and managerial inaction for promoting patient safety.

In addition to system factors presumed to affect patient safety (also presented in Chapter 7), the findings in **Chapter 8** identified other factors such as individual HCPs, patient and task factors that have been identified as challenges to achieve an optimal patient safety in Ethiopian public hospitals. Resource limitations (e.g. material deficiencies, poor infrastructure) have been indicated as the greatest barriers for patient safety, and these have been scarcely or not reported at all in other similar studies elsewhere. Patients expressed a range of perceived experiences related to their medication, and a number of strategies required to improve patient safety practices have been suggested. Changes in practice, processes, structure, and systems were believed to help improve patient safety in the Ethiopian health care system. For example, engaging pharmacists in the multidisciplinary team have been one of the suggestions to improve medication safety.

Chapter 9 presents a range of factors that may influence the uptake of medication safety interventions delivered by hospital pharmacists. The results of this study demonstrated that hospital pharmacists were very much enthusiastic for medication safety activities and were positive towards the future of the profession; however, there were many factors that likely influenced their behaviour in the clinical practice. For example, dispensing was thought to be a core business by the majority of health managers, and thus, hospital pharmacists were reinforced for other competing priorities. There was no remuneration schemes or incentives arranged for these clinical services delivered by hospital pharmacists, and because of this, most pharmacists preferred dispensing to clinical services, which at the time of this study, entitled

for duty payment. Theory-based identification of behavioural determinants affecting hospital pharmacists' engagement in medication safety activities were predominantly related to 'Knowledge', 'Skills', 'Environmental constraints', 'Motivation and goals', 'Social influences' and 'Social/professional role'.

Chapter 10 presents a single center investigation of the impact of pharmacist-led medication reconciliation intervention on the incidence of unintentional medication discrepancies before and after the implementation of this service. While unintentional medication discrepancies were highly prevalent at the time of hospital admission, this study also found that pharmacist-led medication reconciliation intervention was able to minimize the occurrence of discrepancies significantly. Thus, implementation of medication reconciliation as a medication safety strategy is feasible, and pharmacists may be regarded as key resource personnel for the safe use of medications at the time of hospital admission.

Chapter 11 contextualizes the main findings from the preceding chapters and proposes future research directions. Overall, our intervention has an important clinical implication in the Ethiopian health care system where medication history taking are purely assigned to physicians or physician interns. Notably, pharmacists may be important resource personnel aiding busy physicians in availing complete medication histories important for therapeutic decision at the time of hospital admission. However, the sustainability of this service utilization is highly dependent on other behavioural determinants, such as knowledge and skill, competing priorities, role recognition and reimbursement for clinical services.

Publications and Communications

Peer-reviewed publications

1. Mekonnen AB, McLachlan AJ, Brien JE. Effectiveness of pharmacist-led medication reconciliation programmes on clinical outcomes at hospital transitions: a systematic review and meta-analysis. BMJ Open. 2016; 6(2):e010003.
2. Mekonnen AB, McLachlan AJ, Brien JE. Pharmacy-led medication reconciliation programmes at hospital transitions: a systematic review and meta-analysis. J Clin Pharm Ther. 2016; 41(2): 128–44.
3. Mekonnen AB, Abebe T, McLachlan AJ, Brien JE. Impact of electronic medication reconciliation on medication discrepancies at hospital transitions: a systematic review and meta-analysis. BMC Med Inform Decis Mak. 2016; 16(1):112.
4. Mekonnen AB, Alhawassi TM, McLachlan AJ, Brien JE. Adverse drug events and medication errors in African hospitals: a systematic review. Drugs Real World Outcomes. 2017 Nov 14. doi: 10.1007/s40801-017-0125-6.
5. Mekonnen AB, McLachlan AJ, Brien JE, Mekonnen D, Abay Z. Medication reconciliation as a medication safety initiative in Ethiopia: a study protocol. BMJ Open. 2016; 6(11): e012322.
6. Mekonnen AB, McLachlan AJ, Brien JE, Mekonnen D, Abay Z. Hospital survey on patient safety culture in Ethiopian public hospitals: a cross sectional study. Safety in Health 2017; 3:11.

Letter to editor

1. Mekonnen AB, Welch SA, Medeiros C, Sandaradura I, Nair P, McLachlan AJ, Brien JE. Documenting antibiotic use in transition from intensive care unit to wards. J Pharm Pract Res. 2016; 46(1): 91–2.

Manuscripts under-review

1. Mekonnen AB, McLachlan AJ, Brien JE, Mekonnen D, Abay Z. Health care professionals' perspectives of patient safety and patient's experiences of medication related adverse events: a qualitative study from Ethiopia. BMC Health Serv Res.
2. Mekonnen AB, McLachlan AJ, Brien JE, Mekonnen D, Abay Z. Barriers and facilitators to hospital pharmacists' engagement in medication safety activities: a qualitative study using the Theoretical Domains Framework. J Pharm Policy Pract (Revision submitted).
3. Mekonnen AB, McLachlan AJ, Brien JE, Mekonnen D, Abay Z. Evaluation of the impact of pharmacist-led medication reconciliation intervention: a single center pre-post study from Ethiopia. Int J Clin Pharm.

Conference presentations

1. Medication reconciliation as a medication safety initiative presented at the Pharma-bridge session of the FIP in the 2016 FIP congress held in Buenos Aires, Argentina in August 28 – September 2, 2016 [Invited presentation].
2. Mekonnen AB, McLachlan AJ, Brien JE. Effectiveness of pharmacist-led medication reconciliation programmes on clinical outcomes at hospital transitions: a systematic review and meta-analysis; presented at the 5th Annual Conference of Public Health Officers Association of Ethiopia, held in March 4–5, 2016.
3. Mekonnen AB, McLachlan AJ, Brien JE. Pharmacy-led medication reconciliation programmes at hospital transitions: a systematic review and meta-analysis. Accepted abstract (Value in Health, Volume 19, Issue 3, A34) at the 21st ISPOR conference, Washington, DC, USA).
4. Mekonnen AB, McLachlan AJ, Brien JE. Adverse drug events and medication errors in African hospitals: a systematic review. Accepted abstract (J Pharma Care Health Sys.) at the 4th African Pharma Congress, Cape Town, South Africa.

Author Attributions

The PhD candidate (Alemayehu Mekonnen), referred to as I, has made a substantial contribution to the following published papers presented in the main body of this thesis. The candidate is the corresponding author for all of the listed publications below.

Chapter 2 of this thesis is published as "Mekonnen AB, McLachlan AJ, Brien JE. Effectiveness of pharmacist-led medication reconciliation programmes on clinical outcomes at hospital transitions: a systematic review and meta-analysis. BMJ Open. 2016; 6:e010003. doi: 10.1136/bmjopen-2015-010003".

I conceptualized and designed the study with my co-authors. I conducted the literature search, abstract screening, and data extraction with further confirmation from JEB and AJM. I carried out the initial analysis and drafted the first manuscript. JEB and AJM critically reviewed and revised the manuscript. The final manuscript was approved by all authors.

Chapter 3 of this thesis is published as "Mekonnen AB, McLachlan AJ, Brien JE. Pharmacy-led medication reconciliation programmes at hospital transitions: a systematic review and meta-analysis. J Clin Pharm Ther. 2016; 41(2): 128–44. doi: 10.1111/jcpt.12364".

I designed the study with co-authors. I conducted the literature search, abstract screening, and data extraction with further confirmation from JEB and AJM. I carried out the initial analysis and drafted the first manuscript. JEB and AJM critically reviewed and revised the manuscript. The final manuscript was approved by all authors.

Chapter 4 of this thesis is published as "Mekonnen AB, Abebe T, McLachlan AJ, Brien JE. Impact of electronic medication reconciliation on medication discrepancies at hospital transitions: a systematic review and meta-analysis. BMC Med Inform Decis Mak. 2016; 16:112. doi: 10.1186/s12911-016-0353-9".

I designed the study with co-authors. I and TBA undertook literature searching, abstract and title screening and data extraction. I carried out the initial analysis and drafted the first manuscript. JEB and AJM critically reviewed and revised the manuscript. The final manuscript was approved by all authors.

Chapter 5 of this thesis is published as "Mekonnen AB, Alhawassi TM, McLachlan AJ, Brien JE. Adverse drug events and medication errors in African hospitals: a systematic review. Drugs Real World Outcomes. 2017. doi: 10.1007/s40801-017-0125-6".

I designed the study with co-authors, conducted literature searching, abstract and title screening and data extraction. I carried out the initial analysis and drafted the first manuscript. AJM, JEB and TMA critically reviewed and revised the manuscript. The final manuscript was approved by all authors.

Chapter 6 of this thesis is published as "Mekonnen AB, McLachlan AJ, Brien JE, Mekonnen D, Abay Z. Medication reconciliation as a medication safety initiative in Ethiopia: a study protocol. BMJ Open. 2016; 6(11): e012322. doi: 10.1136/bmjopen-2016-012322".

All authors conceptualized the study. I designed the content of the protocol, which was then revised by AJM and JEB. DM and ZA provided an input in the methodology of the protocol. I drafted the first manuscript. JEB and AJM critically reviewed and revised the manuscript. The final manuscript was approved by all authors.

Chapter 7 of this thesis is published as "Mekonnen AB, McLachlan AJ, Brien JE, Mekonnen D, Abay Z. Hospital survey on patient safety culture in Ethiopian public hospitals: a cross sectional study. Safety in Health 2017; 3:11. doi: 10.1186/s40886-017-0062-9".

All authors conceptualized the study. ABM, AJM, JEB, DM, and ZA have all made significant contributions to the scientific content of this manuscript. ABM carried out data collection and analysis. ABM carried out the initial analysis and drafted the first manuscript. AJM, JEB, DM, and ZA critically reviewed and revised the manuscript. The final manuscript was approved by all authors.

Chapter 8 of this thesis has been submitted for publication as "Mekonnen AB, McLachlan AJ, Brien JE, Mekonnen D, Abay Z. Health care professionals' perspectives of patient safety and patient's experiences of medication related adverse events.

All authors conceptualized the study. ABM, AJM, JEB, DM and ZA have all made significant contributions to the scientific content of this manuscript. ABM carried out data collection and analysis. ABM carried out the initial analysis and drafted the first manuscript. AJM, JEB, DM and ZA critically reviewed and revised the manuscript. All the authors have read and approved the final manuscript.

Chapter 9 of this thesis has been submitted for publication as "Mekonnen AB, McLachlan AJ, Brien JE, Mekonnen D, Abay Z. Barriers and facilitators to hospital pharmacists' engagement in medication safety activities: a qualitative study using the Theoretical Domains Framework.

All authors conceptualized the study. ABM, AJM, JEB, DM and ZA have all made significant contributions to the scientific content of this manuscript. ABM carried out data collection and analysis. ABM carried out the initial analysis and drafted the first manuscript. AJM, JEB, DM and ZA critically reviewed and revised the manuscript. All the authors have read and approved the final manuscript.

Chapter 10 of this thesis has been submitted for publication as "Mekonnen AB, McLachlan AJ, Brien JE, Mekonnen D, Abay Z. Evaluation of the impact of pharmacist-led medication reconciliation intervention: a single center pre-post study from Ethiopia.

All authors conceptualized the study. ABM, AJM, JEB, DM and ZA have all made significant contributions to the scientific content of this manuscript. ABM carried out data collection and analysis. ABM carried out the initial analysis and drafted the first manuscript. AJM, JEB, DM and ZA critically reviewed and revised the manuscript. All the authors have read and approved the final manuscript.

Supervisor Attestation

As the primary supervisor for the candidature upon which this thesis is based, I can confirm that the authorship attribution statements above are correct.

Supervisor: Professor Jo-anne Brien

Signature: 

Date: 5th July 2017

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List of Abbreviations

ADE	Adverse Drug Event
ADR	Adverse Drug Reaction
ART	Antiretroviral Therapy
ASHP	American Society of Health-System Pharmacists
BPMH	Best Possible Medication History
CEO	Chief Executive Officer
CNS	Central Nervous System
COPD	Chronic Obstructive Pulmonary Disease
CP	Clinical Pharmacy
CPT	Co-trimoxazole Preventive Therapy
CPOE	Computerized Physician Order Entry
CT	Computed Tomography
ED	Emergency Department
FGD	Focus Group Discussion
GUH	Gondar University Hospital
HCP	Health Care Professional
HSOPSC	Hospital Survey on Patient Safety Culture
ICU	Intensive Care Unit
IOM	Institute of Medicine
IPT	Isoniazid Preventive Therapy
IT	Information Technology
IV	Intravenous
ME	Medication Error

MedRec	Medication Reconciliation
NCC MERP	National Coordinating Council for Medication Error Reporting and Prevention
OTC	Over the Counter
PRISMA	Preferred Reporting Item for Systematic Reviews and Meta-analyses
RVI	Retroviral Infection
SOP	Standard Operating Procedure
TDF	Theoretical Domains Framework
UD	Unintentional Discrepancy
UK	United Kingdom
USA	United States of America
USD	United States Dollar
WHO	World Health Organization

PART A: BACKGROUND

- **Introduction and Thesis Structure (Chapter 1)**
- **Literature Reviews (Chapters 2 – 5)**

Chapter 1

Introduction and Thesis Structure

1.1 Overview

"To err is human, to cover up is unforgivable, and to fail to learn is inexcusable".

– Sir Liam Donaldson, WHO Envoy for Patient Safety

Unsafe medication practices and errors are the leading cause of injury and avoidable harm in both developed and developing countries [1]. By coincidence, in March 2017, the World Health Organization (WHO) launched a global initiative to minimize the incidence of preventable medication-related adverse events in all countries by 50% over the next 5 years. This is the third global patient safety challenge endorsed by the WHO, following the Clean Care is Safe Care challenge in 2005 and the Safe Surgery Saves Lives challenge in 2008. The aim is to address the weaknesses in health systems that lead to medication errors and their resulting harm. It is believed that most medication harms arise from system failures, mainly in the way that care is organized and coordinated, especially when patients going through transitions of care. Many of these events occur as a result of poor communication and documentation when care is transferred [1].

Medication reconciliation is recognized as an important approach to the Quality Use of Medicines. Quality Use of Medicines generally refers to the judicious selection and appropriate choice of medicines, as well as the safe and effective use of medicines that are appropriately indicated [2]. Medication reconciliation is a process of effectively communicating changes to medication regimens during the transitions in care, and is one of the guiding principles to achieve continuity in medication management for the Australian hospitals [2]. Since the last decade, this strategy is also being effectively implemented across care transitions in many other developed countries and endorsed among various patient safety organizations [3-5]. However, implementation approaches varied from place to place, and there were no consistent protocols urging service utilization. It has been 10 years since the WHO and collaborators have

prioritized medication reconciliation as one of the top patient safety strategies, and it is only recently that the medication reconciliation standard operating procedure (SOP) was released to the public after it has been tested for its success [4]. Although the WHO encourages member countries to adopt medication reconciliation SOP, the impact on patient safety in a resource-limited setting is not yet explored. Notwithstanding, it is also important to take cognizance of the fact that, evidence for effectiveness might not be enough for sustainable patient safety, but also highly depends on creating a positive culture for patient safety [4, 6]. Successful medication reconciliation implementation requires a culture change within the health care organization and works best when patients are actively involved in the process [4, 6]. Prior to medication reconciliation implementation, however, it is also imperative to understand the existing processes that might affect its success.

Overall, this thesis is a result of a medication safety initiative that has addressed how medication reconciliation interventions effectively optimize patient safety at care transitions. The journey to this quality improvement approach was based on a single experience from an Australian public hospital and was initiated whether this strategy would be feasible in the Ethiopian hospital setting. Specifically, this chapter is a brief introduction of the various approaches to medication reconciliation practice and highlights a review of medical literature regarding the importance of medication reconciliation when patients transfer across hospital care transitions. This chapter also elaborates the rationale for conducting this research and a description of the overall structure of the thesis.

1.2 Definitions and Terminologies in Patient Safety

Patient safety as a discipline has emerged in response to the high burden of avoidable adverse events [7]. Patient safety is an overarching umbrella for which a diverse range of safety issues resides in the health care, and it has been defined variously. According to the Institute of

Medicine (IOM), patient safety is an important aspect of quality of care and is defined as "freedom from accidental injury" [8]. The WHO also defined patient safety as "the absence of preventable harm to a patient during the process of health care" [9]. Yet, Vincent 2010 [10] provides a broadest, but simplest, definition widely used in the international literature.

"The avoidance, prevention and amelioration of adverse outcomes or injuries stemming from the process of health care" [10].

Given the scope of medication use in patient care and the frequency and severity of potential harm, medication safety—defined as the freedom from accidental injury due to medical care/errors during the medication-use process—is also equally important, and is an essential organizational priority [11].

The above definitions go some way, but what is most distinct are the variations in which subsets of patient safety issues, such as adverse events, medication errors and adverse drug events are defined. For example, an adverse event is defined as an unintended injury that is caused by medical management (e.g. injuries resulting from improper or delayed diagnosis, or occurring during an operation), and that resulted in measurable disability [12]. Medications are the main cause of adverse events, and if such injuries arose, they also termed as adverse drug events (ADEs) [12, 13]. However, there are yet various terms employed in patient safety related to medication [14]; such terms included medication errors, adverse drug reactions, and potential and preventable adverse drug events. Although these terms are inconsistently used in the literature, some authors have proposed the relationship between these safety issues related to medications (Figure 1.1) (adapted from Morimoto et al 2004 [15]). Briefly, medication errors (MEs) may or might not cause patient harm. The term ADE included both adverse drug reactions (ADRs), in which harm occurs as a result of intrinsic nature of a medication, as well as complications from MEs [13, 15]. The WHO definition of ADR is "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 functions" [16]. An injury that is the result of ME is classified as preventable ADE whereas a non-preventable ADE is an injury other than an error—for example, the occurrence of anaphylactic reactions in a patient with no known previous history of drug allergy. A potential ADE is a medication error with the potential to cause an injury but which does not actually cause any injury, either because of specific circumstances, chance, or because the error is intercepted and corrected [13, 15].

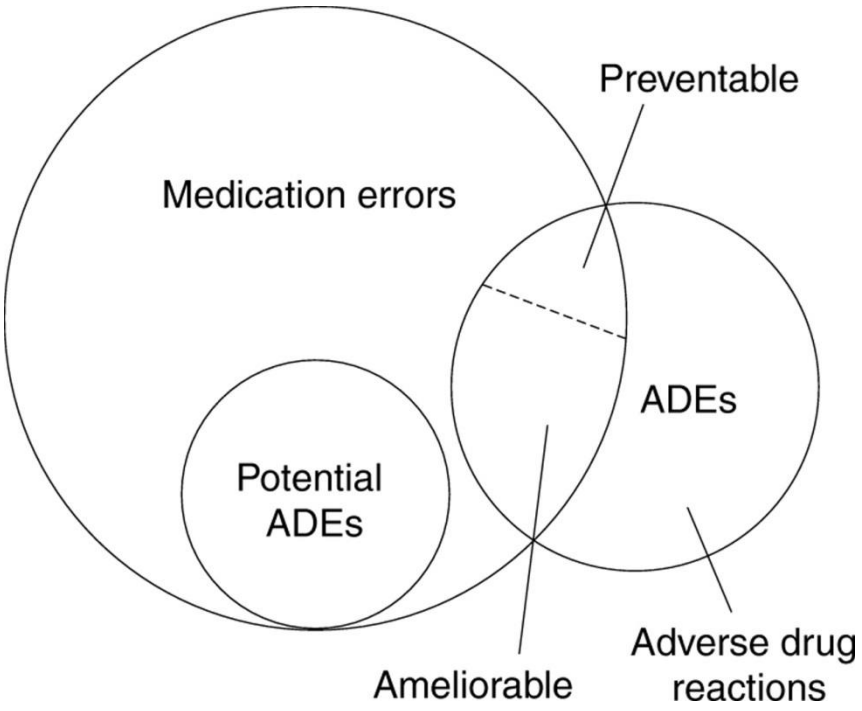

Figure 1.1 Relationship between Adverse Drug Events (ADEs), Potential ADEs, and Medication Errors (adapted from Morimoto et al 2004 [15])

Medication errors further encompass other error categories ranging from prescription error to monitoring and can occur at any stage of the medication use process [13]. However, there is a

lack of consensus regarding the definition of a medication error. For example, a systematic literature review found 26 different terminologies employed for a medication error [17]. The wide variation in the prevalence of medication errors in the literature is partly a reflection of this lack of consensus. For example, Lisby et al [18] applied a more strict definition to error—using harm or risk of harm as cut-off point—and applying this definition reduced the number of medication errors from 34% to 7%. In its broadest sense, medication error is defined by the National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) 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" [19].

In the literature, there are various approaches to classifying medication errors [20]. One of the approaches is to classify based on the types of errors (e.g. wrong medication, dose, frequency, route, and patient). Another approach classifies errors according to whether they occur from mistakes made during the planning of actions (knowledge-based or rule-based mistakes) or errors in carrying out actions (action-based errors, known as "slips", or memory-based errors, known as "lapses"). Errors may also be classified according to their level of severity. And, yet, another most widely used classification consider the stage at which errors are occurred in the medication use process, such as prescribing, dispensing, administration and monitoring [20].

Of particular relevance, another close term employed in association with prescribing errors is a medication discrepancy. There is a difference between the two terms, however. The definition of prescribing error adopted by Dean et al [21] stated that, "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". One component of this definition encompasses unintentional prescribing changes and transcription errors, which might partly define a medication discrepancy. Overall, medication discrepancies—also taken as a measure of medication history errors—are defined as a discrepancy between medication history obtained by a physician and a comprehensive medication history collected by various medication history sources [22]. Nevertheless, apart from discrepancies originated from inappropriately taking medication histories by physicians, discrepancies can also occur from the patient side—for example, as a result of lack of knowledge how to take appropriately prescribed medication [23].

It is also of interest, to make a distinction between intentional and unintentional medication discrepancies. While the latter is certainly categorized as an error, however, some discrepancies could also be deliberate actions following changes in patient's clinical situation (e.g. intentional discontinuation of warfarin following bleeding) [23, 24]. Unlike these categories, however, there are inconsistencies in the way medication discrepancies are classified, and sometimes medication discrepancy is used interchangeably with other medication safety terms, such as prescribing errors [24].

1.3 The Burden of Medication Errors and Adverse Drug Events

1.3.1 International Context

Patient safety has received a significant amount of attention, especially in the last two decades. The 1999 publication "To Err is Human" by the Institute of Medicine [8], shed light on preventable medical errors and on the importance of safe medical care, and since its release, patient safety has become the prominent issue for health care. Later in 2004, the WHO and its partners launched the World Alliance for Patient Safety in response to patient safety issues,

and its goal was to improve patient care worldwide by proposing measures to reduce risks, organizing concepts and definitions on patient safety and suggesting that countries pay greater attention to the theme [25].

Varies studies have investigated the extent of medication errors and adverse drug events. Some prior works [11, 26] in the 1990's have shown that 3.7% of hospitalized patients experienced an adverse event, of which one out of five events were due to medication errors [11, 26]. A systematic review of relatively recent evidence regarding in-hospital adverse events also showed that adverse events during hospital admission affect nearly one out of ten patients, and 15% of the adverse events were medication-related [27]. In either of these findings, ADEs are the second most common cause of patient safety incidents next to operation-related adverse events [11, 27].

Medication errors occur frequently in the hospital environment, but only a few tend to actually cause ADEs [12]. In one inpatient study in the US [12], the frequency of medication errors was 5.3 per 100 medication orders, which is much higher than the ADE rate of 0.25 per 100 orders. Inversely, it is only one-fifth of the medication errors that result in adverse drug events [12].

Not only are medication errors and medication-related adverse events frequent but also are responsible for considerable patient harm [28–30] and undoubtedly costly [31, 32]—to patients, families, and to the society as whole—but, these are often preventable. For example, epidemiological studies in high-income and transitional countries estimated an ADE incidence of 6.5 to 12 per 100 admissions, and nearly 28–48% of these ADES are deemed preventable [28–30, 33]. Again, in 2007, the Institute of Medicine (IOM) estimated that a hospitalized patient in the US experience at least one medication error per day [34], and a recent WHO report showed that medication errors are the cause of at least one death every day, and injure 1.3 million people annually in the USA alone [1], and yet, a quarter of medication-related injuries can be prevented [34]. In another systematic review of medication safety literature in

Australia suggested that at least two medication errors occur for every three patients at the time of admission to hospital, and medication-related problems are the cause of 2–3% of hospital admissions resulted in nearly 230,000 admissions per year, costing the Australian health care system $1.2 billion per annum [35]. Similar rates of adverse drug events have been reported from low-and middle-income countries as those of high-income countries; however, the impact is about twice as much in terms of the number of years of healthy life lost [36], and the global cost associated with medication errors has been estimated at $42 billion USD annually [1]. Preventable ADEs occurred most often at the stage of prescribing (56%) [28], and prescribing errors overall, are the most frequent types of medication errors, occurring in 7% of medication orders, 50% of hospital admissions and 2% of inpatients [37]. Over a quarter of hospital prescribing errors can be attributed to incomplete medication histories at the time of admission [38]. Data have also shown that interfaces of care are particularly high-risk points for medication errors as patients transitioning between episodes of care—for example, more than half of the medication errors occur at transitions of care [39], and nearly one-fifth of the adverse drug events result from errors at interfaces of care [40]. Numerous studies have identified poor communication and failure to reconcile medication history at points of patient transfer as a risk for medication errors when patients move across transition of care [41–44]. For example, a systematic review of 22 studies found that discrepancies between physician-acquired prescription medication histories and comprehensive medication histories at the time of hospital admission are common, occurring in up to 67% of cases [22]. Care transitions are also recognized as vulnerable points for medication-related adverse events because non-intentional changes to medications are common and can result in a huge utilization of health care resources [45–47]. Medication reconciliation as a strategy to prevent such types of incidents is now widely acknowledged and implemented by many hospitals in the developed countries, and to

a lesser extent, in the developing nations. This will be explored in detail in Section 1.6 of this chapter.

1.3.2 African Context

While the issue of patient safety in countries of Africa is not new, there has been a lack of relevant policy and regulations that enforce medication safety monitoring [48], partly because of lack of good data. In most settings, programs to improve patient safety are not in place although the scale of the problem is not different from other reports. Although there is relatively little evidence regarding the burden of MEs and ADEs in this continent, few previous studies have shown that 4.5–8.4% of all hospital admissions are medication related, of which 1.5–6.3 % of patients were admitted as a direct result of ADRs [49, 50]. And, it is only recently that studies in this regard are emerging in Ethiopia. Yet, the burden of this problem is believed to be a public health concern. Two recent ADE studies on the paediatrics have shown an ADE incidence of 7.3–9.1% of all paediatric admissions, and notably, nearly one-third to half are possibly preventable [51, 52].

1.4 Conceptual Approaches to Patient Safety

The 1999 report by the Institute of Medicine (IOM) proposed the application of human factors and systems engineering as methods of closing the quality chasm [8]. According to the Human Factors and Ergonomics Society [53], ‘‘Human factors (or ergonomics) is the scientific discipline concerned with the understanding of the interactions among humans and other elements of a system, and the profession that applies theoretical principles, data and methods to design in order to optimize human well-being and overall system performance”. Carayon et al [54] elaborate many reasons to the lack of measurable improvement in patient safety, including lack of reliable data on patient safety at the national level and organizational level, difficulty in engaging clinicians in patient safety improvement activities and challenges in

redesigning and improving complex health care systems and processes. The authors deduce part of the problem is due to human factors and systems engineering, and suggest that increasing the links between the health sciences and human factors and systems engineering is vital to improve patient safety [54].

The application of human factors engineering in reducing human error and harm to patients is well recognized [55]. This needs, however, an understanding of the nature of human errors and error management approaches. According to Reason [56], for example, suggests two approaches to error management: the person approach and the system approach. Each of these approaches has its model of error causation, and therefore, giving rise to different thoughts about error management. The person approach of human errors focuses on the unsafe acts—errors and procedural errors—arising primarily from mental processes such as inattention, forgetfulness, carelessness, poor motivation, negligence, and recklessness. The person approach focuses on errors of individuals, and this result in practices such as blaming and punishment of the person who committed the error, and because of this anticipated actions, medication errors are not fully reported. On the other hand, the system approach assumes that humans are fallible and are prone to errors, even in the best organizations. Errors are seen as consequences rather than causes, existing in the organizations and organizational processes. The system approach concentrates on the conditions under which individuals work and tries to build defences to avert errors or mitigate their effects.

Although much of the current emphasis in patient safety is of systems factors, considering the personal approach is also important. For example, in a study of prescribing errors using human error theory, Dean et al [57] reported that 57% of errors are due to lapses, whereas 39% are due to mistakes. This implies that patient safety can only be improved if the factors needed to deliver care and those interacting with them should be targeted together.

In today's health care system, patients are experiencing a growing number of transitions of care. Care transitions occur when patients are transferred from one care setting to another, from one department to another within a care setting, or from one care provider to another [39]. This time of transition is considered a high-risk area because of fragment of care or poor communication [41–44], and thus, successful care transitions require safe and effective interactions of people with their environment [54]. The time when patients are transitioning from one setting or provider to another, involves a series of interactions of the patient and the health care provider with a task (e.g. information sharing), other people, tools and technologies, and a physical, social and organizational context (Figure 1.2) (adapted from Carayon et al 2010 [54]).

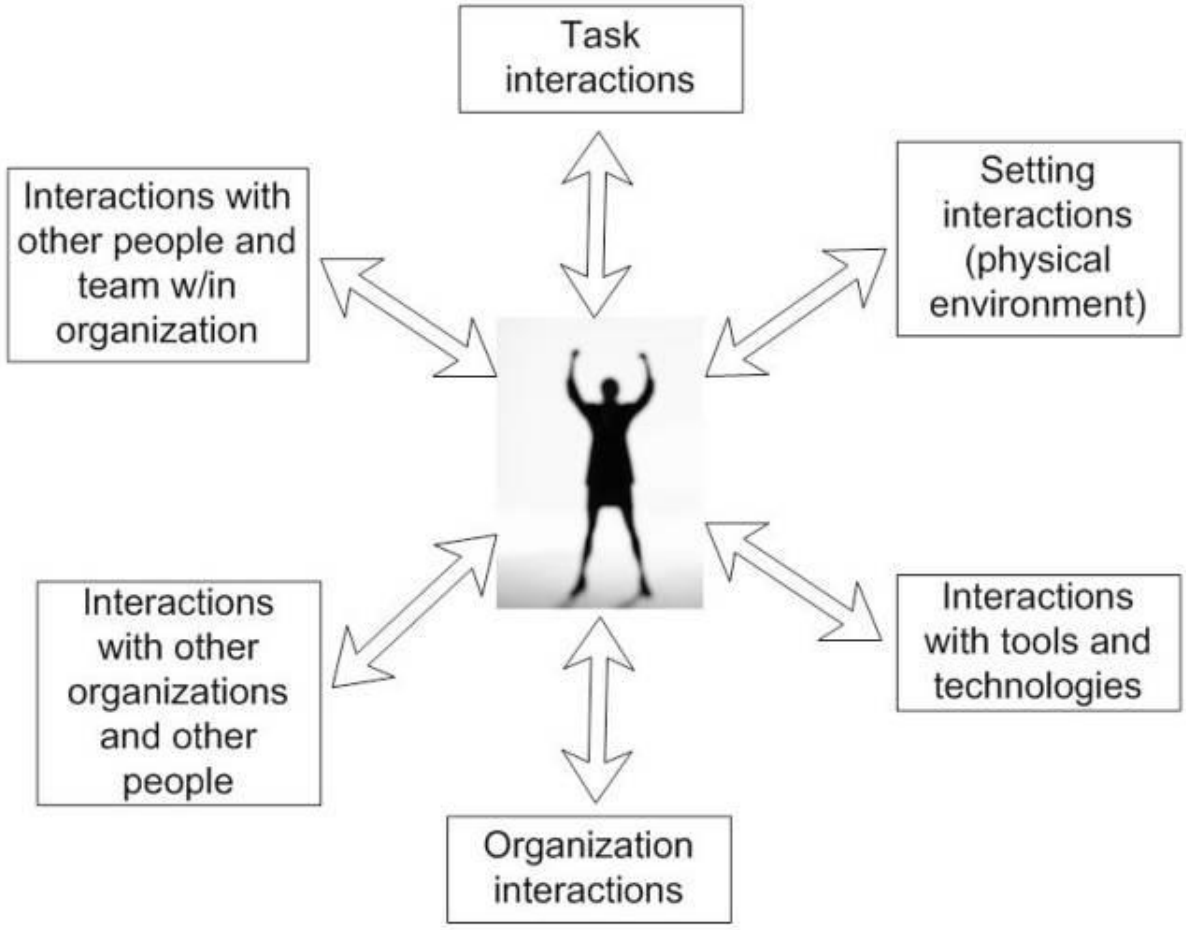

Figure 1.2 Human Factors Model of Interactions (adapted from Carayon et al 2010 [54])

Adherents of the system approach strive for a comprehensive management program aimed at targeting the person, the team, the task, the workplace, and the institution as a whole [56]. Vincent and colleagues [58] proposed a framework for analyzing risk and safety in clinical medicine based on Reason's model of accident causation [56]. This framework identifies seven categories of system factors that can influence clinical practice: institutional context, organizational and management factors, work environment, team factors, individual (staff) factors, task factors, and patient characteristics. This framework has been used by many authors to investigate safety incidents [57, 59, 60].

The other critical factor, aligned with system approach, important for creating high-reliability health care organization is patient safety culture [61]. The Institute of Medicine (IOM) suggested that the biggest challenge to moving toward a safer health care system is changing the patient safety culture from one in which individuals are blamed for errors to one in which errors are treated as opportunities to improve the system and prevent harm [6]. Patient safety culture is defined as "a holistic snapshot of enacted norms, policies, and procedures related to patient safety that guide the behaviours, attitudes, and cognitions of care providers" [62]. There is evidence that links an association between patient safety culture and patient outcomes, including reduced adverse events and mortality [62]. Establishing a culture of safety is an important pre-requisite for patient safety programs [6], and in many of the health care organizations, there is a growing recognition of the importance of establishing a culture of patient safety [63–65].

Patient-centred care has also emerged as a key principle for quality and patient safety [6, 55]. The Institute of Medicine (IOM) in its report, suggested that patients and their families should be informed about uncertainties, risks, and treatment choices [6]. It also stresses that safety and quality should be seen from the perspective of the eyes of patients as well.

In general, ADEs in all health care settings may arise from a combination of patient, provider, and health care system factors, and is a result of both proximate and latent factors (Figure 1.3). While proximate factors included those that involve the patient and/or provider, latent key determinants that may contribute to ADEs are classified as systemic, organizational, or technical factors (adapted from the US, Department of Health and Human Services [66]).

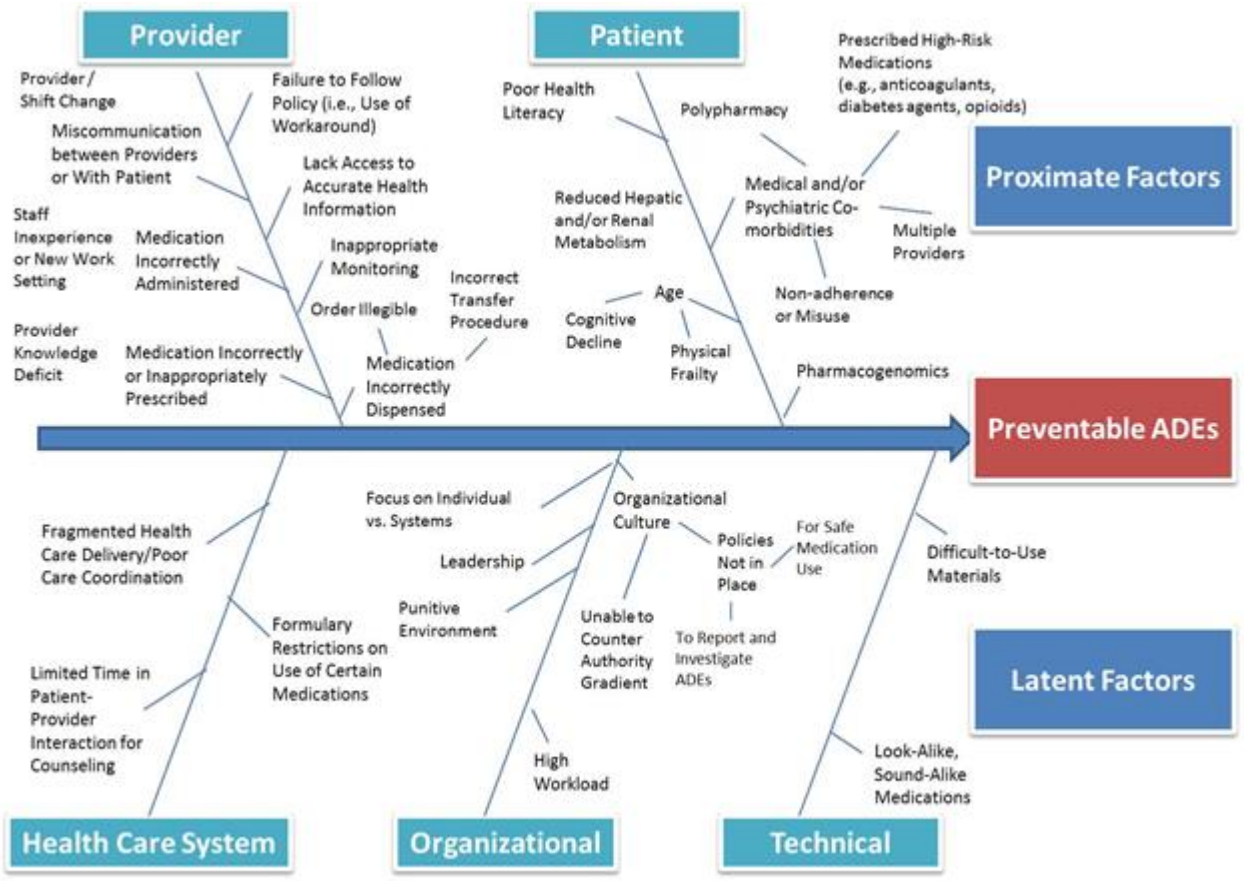

Figure 1.3 Fishbone Diagram – Selected Determinants of Preventable ADEs (adapted from the US, Department of Health and Human Services [66])

1.5 Medication Safety Strategies

While root-cause analysis is an important approach to take preventive measures, it is also vital to explore available evidenced tools in the literature that are widely employed to improve medication safety by many health care organizations. Various medication safety strategies have been recommended for hospital care. For example, prescribing errors may be minimized by the introduction of computerized order entry systems [67, 68], by pharmacist participation in ward rounds [69], and by introducing standardized medication prescription chart [70]. Besides these, another systematic review of strategies employed to mitigate medication errors in an emergency department included medication-error reporting, automated dispensing cabinets, bar-coding systems, medication reconciliation, standardizing medication use processes, and education [71]. Preventing medication errors and ADEs require specific strategies to ensure patient safety at each stage of the medication use process [72]. Each of these stages represents a possible risk-point, and the following table lists the various strategies to combat the risk of medication errors at all steps in the medication use process (Table 1.1) (adapted from the Agency for Health care Research and Quality (AHRQ) [72]).

Table 1.1 Medication Safety Strategies Employed at Each Stage of the Medication Use Process (adapted from the Agency for Health care Research and Quality (AHRQ) [72])

Stage	Safety strategy
Prescribing	• Computerized provider order entry, especially when paired with clinical decision support systems • Medication reconciliation at times of transitions in care • Avoid unnecessary medications by adhering to conservative prescribing principles
Transcribing	• Computerized provider order entry to eliminate handwriting errors
Dispensing	• Clinical pharmacists to oversee medication dispensing process • Use of "tall man" lettering and other strategies to minimize confusion between look-alike, sound-alike medications
Administration	• Adherence to the "Five Rights" of medication administration (Right Medication, Right Dose, Right Time, Right Route, Right Patient) • Barcode medication administration • Minimize interruptions to allow nurses to administer medications safely • Smart infusion pumps for intravenous infusions • Patient education and revised medication labels to improve patient comprehension of administration instructions

Regardless of the strategies implemented, however, the prevention of medication errors rests up on the development of a systems-oriented approach to medication errors, creating a culture of safety, and improving medication error identification and reporting [72].

1.6 Medication Reconciliation as a Medication Safety Strategy

Numerous studies have identified the extent and nature of medication discrepancies between the medications patients were taking prior to admission and their prescribed medication on admission to, and discharge from hospital [22, 41–44]. Medication reconciliation is the safety strategy frequently called for, to prevent unintentional medication discrepancies that occur at care transitions [3]. In 2006, the WHO Collaborating Centre for Patient Safety [4] included medication reconciliation as one of the five standardized patient safety solutions—also known as 'high 5s'—to achieve measurable, significant, and sustainable reductions in challenging patient safety problems. Collaborative countries in the current list are Australia, Canada, France, Germany, the Netherlands, Singapore, Trinidad and Tobago, and the USA and UK. Recently, the WHO [1] also launched a global medication safety initiative to minimize the incidence of preventable medication-related adverse events, and this initiative's main focus is to address the weaknesses in health systems that lead to medication errors and ADEs. It is believed that most medication harms arise from system failures, mainly in the way that care is organized and coordinated, especially when patients going through transitions of care. The majority of these events can be prevented through a formal medication reconciliation process. According to the Institute for Health care Improvement [5], medication reconciliation is defined as:

"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 WHO High 5s medication reconciliation standard operating procedure (SOP) describes the guiding principles for effective implementation of medication reconciliation [4]. The basis for effective medication reconciliation is the development, maintenance, and communication of a

complete and accurate medication list throughout the continuum of care. Gathering the Best Possible Medication History (BPMH) within 24 hours of hospital admission is the first step in the process (Figure 1.4) (adapted from WHO [4]), and once this step is completed, identified discrepancies should be communicated to the prescriber. Creating the BPMH involves using a systematic process for obtaining a medication history, and verifying medication information with one or more sources, as appropriate. The BPMH is more comprehensive than a routine primary medication history taken without all information available. The sources of medication history include:

1. Patient/family medication interview where possible.

2. Other sources of information include:

- Contacting community pharmacists, physicians and/or home care providers
- Inspection of medication vials/patient medication lists
- Government medication database
- Previous patient health records

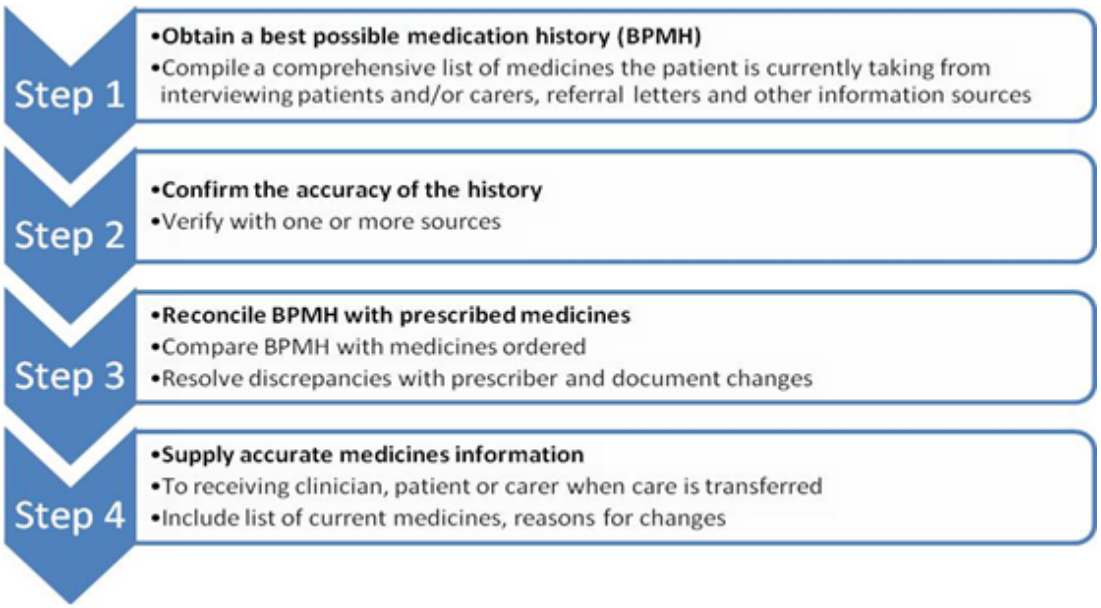

Figure 1.4 The Four Steps in the Medication Reconciliation Process (adapted from WHO [4])

1.6.1 Approaches to Medication Reconciliation

Various approaches have been suggested to improve medication reconciliation. Several types of information technologies have been in use to support the medication reconciliation process. For example, integration of electronic medication reconciliation tools into an internally developed computerized order entry system [73, 74] have been found effective, and such tools have been reviewed [75]. Shared electronic health records have also been proposed to facilitate the medication reconciliation process [76].

Education of prescribers has been suggested to reduce errors in recording of medications at the time of admission to hospital [77], and this approach alongside with other quality improvement methods, such as the introduction of medication documentation templates for electronic prescribing led to a sustained increase in reconciled medications [78]. There are also other studies that used standardized documents, such as the introduction of medication report or reconciliation form [79, 80] and developing a limited list of standardized questions [81] that seemed promising in reducing the incidence of errors.

Patient engagement in the medication reconciliation process is one of the best strategies to prevent medication discrepancies and is now highly recommended [82]. As patients are the primary sources of medication history, patient counselling regarding their medication helps identify clinically meaningful discrepancies and improves the quality of medication history [83], but if this is hindered by limited health literacy, a significantly higher number of medication discrepancies are likely [43].

Many studies have evaluated the impact of pharmacists in medication reconciliation [84, 85], and the role of collaborative models, such as pharmacist-physician, or pharmacist-nurse collaborative medication reconciliation have also been explored as well [45, 46]. The medication reconciliation process is a shared responsibility of health care professionals in

collaboration with patients and families. It requires a team approach including pharmacists, physicians, nurses, pharmacy technicians and other health care providers [4].

1.6.2 Evidence for Effectiveness of Medication Reconciliation

Many observational studies have confirmed that medication errors at care transitions are common, and potentially clinically important. For example, Cornish et al. [42] conducted a prospective study of 151 patients admitted to a general ward in a tertiary care teaching hospital, using at least 4 regular prescription medications, and has found that 54% of the patients had at least one unintended discrepancy between home medications and admission orders. The most common discrepancy (46%) was an omission of a regularly used medication, and that 39% of discrepancies were judged to have the potential to cause moderate to severe harm. In some other selected studies, at least one unintended medication discrepancy has been identified in 16.8–60% of patients [86–94] (Table 1.2).

Table 1.2 Prevalence of Unintentional Medication Discrepancies in Selected Studies

Author, Year	Country, Setting	Study design	Target of intervention	Medications assessed	Patients with at least one unintentional discrepancy
Abu Yassin 2011 [86]	Saudi Arabia, tertiary referral hospital	Prospective	Admission	Prescribed and OTC medications, herbal and other supplements	37%
Allende Bandres 2013 [87]	Spain, tertiary care hospital	Retrospective	Admission, discharge	Prescription medications	16.8%
Bahrani 2014 [88]	Sweden, internal medicine wards	Prospective	Admission	Prescription medications	46%
Coffey 2009 [89]	Canada, tertiary care children's hospital	Prospective	Admission	Prescription and OTC medications	22%
Gleason 2010 [90]	USA, University hospital	Prospective	Admission	Prescription medications	35.9%
Grimes 2008 [91]	Ireland, academic teaching hospital	Prospective	Discharge	Prescription medications	40%
Manias 2009 [92]	Australia, referral hospital	Retrospective	ED	Any medications	34.8%
Vira 2006 [93]	Canada, community hospital	Prospective	Admission and discharge	Prescription medications	60%
Wong 2008 [94]	Canada, tertiary care teaching hospital	Prospective	Discharge	Prescription medications	41.3%

Abbreviation: ED, emergency department

There are a number of hospital-based studies and medication safety initiatives in the USA [73], Spain [74], New Zealand [77], Canada [79], Sweden [80], Belgium [81], the Netherlands [83, 84] and Australia [85] have shown the impact of medication reconciliation in reducing medication errors and adverse drug events. For example, a 2012 systematic review [95] of 26 hospital-based medication reconciliation studies have shown that medication reconciliation intervention has resulted in a reduction in medication discrepancies in 17 of 17 studies,

potential adverse drug events in 5 of 6 studies, and adverse drug events in 2 of 3 studies. However, the impact on post-discharge health care utilization was uncertain. In the contrary, a 2013 systematic review focusing on clinically significant medication discrepancies by Kwan et al [96] noted that most medication discrepancies appeared to have no clinical significance, and the impact of medication reconciliation on reducing clinically significant discrepancies was unclear. On the other hand, both reviews [95, 96] agreed that the actual clinical impact of medication discrepancies after discharge appears to be small, and therefore, medication reconciliation alone does not seem to reduce emergency department visits or readmissions within 30 days. Again, both noted that most successful interventions were those that involve pharmacists in the process.

1.7 Rationale of This Study

The majority of the works on the scale of MEs and the impact of medication reconciliation on the incidence of such errors have been studied in the Western countries. While patient safety is a global public health priority which calls for appropriate actions, the burden of MEs and ADEs is expected to be higher in developing countries [9, 36], including the Africa region, due to resource limitations, such as infrastructure, human resource, and technologies. The African Partnerships for Patient Safety and the guideline for developing national patient safety policy and strategic plan assist African countries in developing comprehensive actions for patient safety, including medication safety, yet, little data are available and research has not been done in many resource-poor settings. It has been suggested that studies should be conducted to measure the extent of inappropriate use of medications, adverse drug events, and medication errors, and each institution should implement national mechanisms to reduce the burden of ADEs and MEs [9]. Particularly, there is a lack of medication reconciliation studies in Africa, and this thesis explores medication reconciliation as a medication safety strategy in Ethiopia.

Although individual medication reconciliation studies conducted elsewhere have been found to be effective in reducing the burden of medication errors and discrepancies, it is unclear which approaches to medication reconciliation are effective, and who shall be responsible for medication reconciliation is still debatable. Previous reviews [95, 96] have shown inconsistent findings regarding the impact of medication reconciliation on the incidence of medication discrepancies, although both agreed that the impact on post-hospital resource utilization was uncertain. Most successful medication reconciliation interventions are due to pharmacist's involvement [95, 96], and yet, the impact on both process and clinical outcomes are largely unknown. Given that, at least three disciplines are involved in the medication reconciliation process—medicine, pharmacy, and nursing—with little agreement on each profession's role and responsibility for the process [97], and thereby, it is unclear who should take overall responsibility for maintaining an accurate medication list. This thesis explores the impact pharmacists could bring as a result of their involvement in the medication reconciliation process. Alternatively, information technology (IT) provides an opportunity to improve medication reconciliation; however, the role of IT and its effectiveness in the reconciliation process is not yet clearly determined. Thus, technology solutions to the process have also been dealt.

The initial inception of this project began from anecdotal experiences in the local hospital setting; that is, in a tertiary care hospital in Ethiopia. Physician colleagues usually recommend pharmacists to take medication history in order to consult patients regarding their medication use because physicians noticed that most patients' understanding of their medication was relatively scanty. Since the time when this was communicated, I and my colleagues (pharmacists) were new to medication reconciliation practice, and we did not have the know-how to conduct this, and there existed a lack of understanding of the importance of medication reconciliation. However, experiences from Australia showed that the role of medication

reconciliation is well acknowledged, and is one of the standards of practice for clinical pharmacy services [98]. For example, I and my colleagues in Australia have assessed the extent of antibiotic documentation in the transition from intensive care unit (ICU) to wards in one metropolitan hospital in Sydney and found that the duration of antibiotics was infrequently documented (Appendix 1). This was another lesson I had taken from this study that led to the conceptualization of medication reconciliation as a medication safety initiative project for the past three years. Besides the antimicrobial stewardship pharmacist, the findings of the Australian study were communicated to intensivists and microbiologists with a suggestion to include a box on the ICU discharge summary which specifically relates to antibiotics and their plan when patients are transferred to wards. In the Australian context, pharmacists are integral to the multidisciplinary team and are providing clinical services for years, including medication reconciliation. However, pharmacist involvement in patient care is a relatively new concept in Ethiopia. Thus, we hypothesized the introduction of medication reconciliation in resource-limited settings might be beneficial, and this thesis aimed to determine the impact of pharmacist conducted medication reconciliation intervention in such settings.

Introducing medication reconciliation is not a sharp end but it should be supported by corresponding changes in attitudes, teamwork, communication, culture, and leadership. According to the WHO High 5s medication reconciliation program [4], the culture of the organization with respect to interdisciplinary collaboration and teamwork significantly influence the effectiveness of the medication reconciliation process, and this has to be explored to look at the changes necessary to improve patient safety. This thesis uses methods from both safety and implementation sciences for successful implementation of the medication reconciliation program. For example, ensuring a culture of safety and organizational support for safety processes are key to patient safety improvement, and using a system approach is vital to identify factors that influence patient safety, but little is known in Ethiopia. Using a theory

to identify the many determinants of the behaviour to be changed (e.g. lack of skill to conduct medication reconciliation) before an implementation of a medication safety program, provides a robust evidence-base for its success [99], which has been rarely explored in similar studies elsewhere.

Overall, this project is a medication safety initiative focusing on medication reconciliation intervention, and the implementation of this initiative is guided by a multi-method approach consisting both qualitative and quantitative methods. This overarching aim can be further broken down into the following objectives:

1. To systematically investigate the current evidence to support the effectiveness of medication reconciliation interventions
2. To assess the African medication safety literature on the extent and nature of medication errors and adverse drug events
3. To assess the views and perceptions of health care professionals about patient safety and patients' experiences of medication-related adverse events in Ethiopian public hospitals
4. To identify the barriers and facilitators to hospital pharmacists' engagement in medication safety activities
5. To investigate the impact of pharmacist-led medication reconciliation interventions on the occurrence of unintentional medication discrepancies before and after implementation

1.8 Thesis Structure

The aims of this thesis were to explore patient safety culture and patients' experiences of medication-related adverse events and to develop, implement and evaluate a theory-informed medication reconciliation intervention, with the aim of minimizing the incidence of unintentional medication discrepancies at hospital admission.

This thesis consists of eleven chapters presented in four parts (Figure 1.5).

Part A (Chapters 1 to 5) provides the technical background and the rationale from which the thesis is built up on, and consecutive literature reviews. Chapters 2 to 4 present systematic reviews and meta-analyses of the effectiveness of pharmacist-led and electronic medication reconciliation interventions, and the fifth chapter is a systematic literature review of the epidemiology of medication errors and adverse drug events in African hospitals.

Part B (Chapter 6) describes the study protocol and research methods used in the remaining studies which sought to address the aforementioned objectives. This chapter elaborates the methodological approaches used in the study, including the behavioural change theory; that is, the theoretical domains framework, which had been employed to identify the barriers and facilitators to medication safety activities, performed by hospital pharmacists, and was used as a foundation for the development of successful medication safety programs, including medication reconciliation.

Part C (Chapters 7 to 10) details the findings of this project. The quantitative results are presented in chapters 7 and 10, whereas the qualitative findings are described in chapters 8 and 9.

Part D (Chapter 11) briefly summarizes the main findings of this study, provides the main conclusions of the research and potential directions for future research.

Figure 1.5 outlines the overall structure of this thesis.

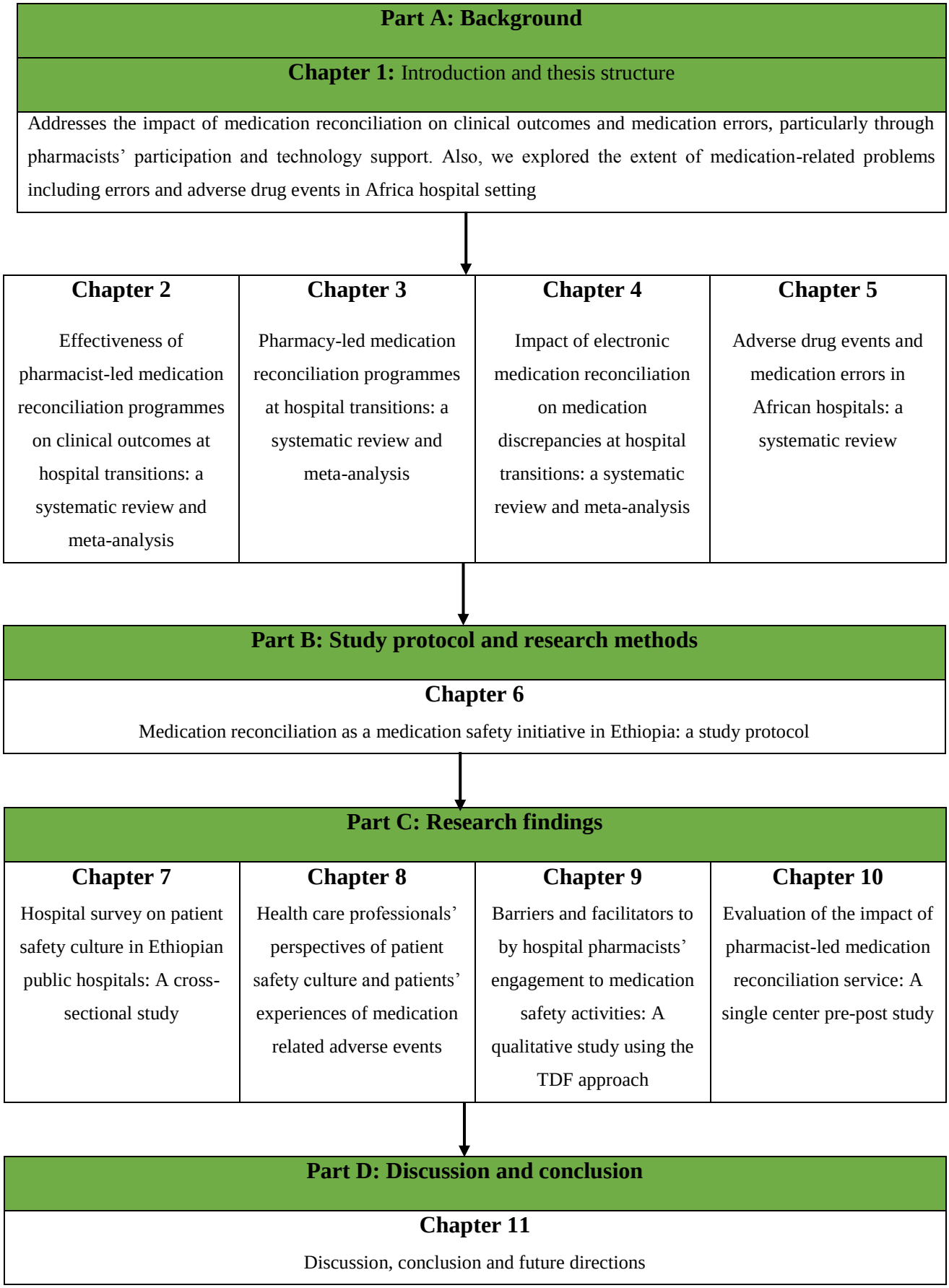

Figure 1.5 Thesis Structure

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Chapter 2

Effectiveness of Pharmacist-led Medication Reconciliation Programmes on Clinical Outcomes at Hospital Transitions: A Systematic Review and Meta-analysis

Mekonnen AB, McLachlan AJ, Brien JE. Effectiveness of pharmacist-led medication reconciliation programmes on clinical outcomes at hospital transitions: a systematic review and meta-analysis. BMJ Open. 2016; 6(2):e010003. doi: 10.1136/bmjopen-2015-010003.

BMJ Open

Effectiveness of pharmacist-led medication reconciliation programmes on clinical outcomes at hospital transitions: a systematic review and meta-analysis

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To cite: Mekonnen AB, McLachlan AJ, Brien JE. Effectiveness of pharmacist-led medication reconciliation programmes on clinical outcomes at hospital transitions: a systematic review and meta-analysis. *BMJ Open* 2016;**6**:e010003. doi:10.1136/bmjopen-2015-010003

► Prepublication history and additional material is available. To view please visit the journal (http://dx.doi.org/10.1136/bmjopen-2015-010003).

Received 17 September 2015
Revised 26 November 2015
Accepted 18 December 2015

For numbered affiliations see end of article.

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ABSTRACT

Objectives: Pharmacists play a role in providing medication reconciliation. However, data on effectiveness on patients' clinical outcomes appear inconclusive. Thus, the aim of this study was to systematically investigate the effect of pharmacist-led medication reconciliation programmes on clinical outcomes at hospital transitions.

Design: Systematic review and meta-analysis.

Methods: We searched PubMed, MEDLINE, EMBASE, IPA, CINHAL and PsycINFO from inception to December 2014. Included studies were all published studies in English that compared the effectiveness of pharmacist-led medication reconciliation interventions to usual care, aimed at improving medication reconciliation programmes. Meta-analysis was carried out using a random effects model, and subgroup analysis was conducted to determine the sources of heterogeneity.

Results: 17 studies involving 21 342 adult patients were included. Eight studies were randomised controlled trials (RCTs). Most studies targeted multiple transitions and compared comprehensive medication reconciliation programmes including telephone follow-up/home visit, patient counselling or both, during the first 30 days of follow-up. The pooled relative risks showed a more substantial reduction of 67%, 28% and 19% in adverse drug event-related hospital revisits (RR 0.33; 95% CI 0.20 to 0.53), emergency department (ED) visits (RR 0.72; 95% CI 0.57 to 0.92) and hospital readmissions (RR 0.81; 95% CI 0.70 to 0.95) in the intervention group than in the usual care group, respectively. The pooled data on mortality (RR 1.05; 95% CI 0.95 to 1.16) and composite readmission and/or ED visit (RR 0.95; 95% CI 0.90 to 1.00) did not differ among the groups. There was significant heterogeneity in the results related to readmissions and ED visits, however. Subgroup analyses based on study design and outcome timing did not show statistically significant results.

Conclusion: Pharmacist-led medication reconciliation programmes are effective at improving post-hospital healthcare utilisation. This review supports the implementation of pharmacist-led medication reconciliation programmes that include some component aimed at improving medication safety.

Strengths and limitations of this study

- This is the first systematic review investigating the effect of pharmacist-led medication reconciliation programmes on clinical outcomes.
- In some of the clinical outcomes evaluated, there is substantial statistical heterogeneity and we could not identify the source of variation among the studies.
- The inclusion of non-controlled studies might affect the quality of evidence as seen by the high risk of bias in these groups of studies.

INTRODUCTION

Medication reconciliation has been recognised as a major intervention tackling the burden of medication discrepancies and subsequent patient harm at care transitions.[1] Unjustifiable medication discrepancies are responsible for more than half of the medication errors occurring at transitions in care, when patients move in and out of hospital or get transferred to the care of other healthcare professionals,[2] and up to one-third could have the potential to cause harm.[3] Incidence of unintentional medication changes is common at care transitions,[3–8] and is one of the reasons for a huge utilisation of healthcare resources.[9–13] Medication reconciliation as a medication safety strategy has been championed by a number of healthcare organisations. It was first adopted in 2005 as a National Patient Safety Goal (NPSG) by the Joint Commission[14] and, later, the WHO and collaborators[15–17] involved themselves in endorsing this strategy across many countries.

Despite these efforts, implementation of a medication reconciliation service is a hospital-wide challenge,[18] and there is no previous clinical evidence as to which member of the healthcare profession(s) or which strategies effectively perform medication reconciliation.[19] A number of medication reconciliation strategies have been utilised for safe patient transitions: use of electronic reconciliation tools,[20–22] standardised forms[23 24] and collaborative models,[25 26] as well as patient engagement[27] and pharmacist-led approaches.[28 29]

The impact of medication reconciliation on clinical outcomes at hospital transitions has been reported, however, two recently published systematic reviews[30 31] have ascertained that the benefit as a patient safety strategy is not clear. Both studies have inconsistent findings on healthcare resource utilisation. Unlike Mueller *et al*,[30] Kwan *et al*[31] did not report significant association between post-hospital healthcare utilisation and medication discrepancies identified through medication reconciliation interventions. Both reviews broadly assessed the effect of medication reconciliation produced by various strategies, including the use of collaborative models. The aim of the present review was, thus, to specifically assess the effectiveness of pharmacist-led medication reconciliation programmes on clinical outcomes during the transition to and from hospital settings.

METHODS

Data sources and searches

The study was conducted utilising Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) group guidelines,[32] including the PRISMA checklist, to ensure inclusion of relevant information. An initial limited search of articles was undertaken and the search strategy was broadened after analysis of the text words contained in the title, abstract and index terms. 'Medication reconciliation', 'medication discrepancies', 'medication errors', 'medication history' and 'pharmac*', were the main Medicine Subject Headings (MeSH) and text word terms in the electronic searches. Then, we carried out a comprehensive search involving all the collections in the databases until December 2014: PubMed/MEDLINE (1946), Ovid/MEDLINE (1946), International Pharmaceutical Abstracts (1970), EMBASE (1966), PsycINFO (1890) and CINHAL (1937) (see online supplementary appendix A). The reference lists of review articles and included studies were manually searched to locate articles that were not identified in the database search. Article search was performed by one reviewer (ABM) with the support of a medical librarian.

Study selection

To be included in the selection, studies were required to present the following: papers that reported medication reconciliation intervention primarily and that provide data on any of these clinical end points (all-cause readmission, emergency department (ED) visits, composite rate of readmission and/or ED visits, mortality, adverse drug event (ADE)-related hospital visit). We adopted the definition of 'medication reconciliation' utilised by the Institute for Healthcare Improvement: 'the process of identifying the most accurate list of a patient's current medicines including the name, dosage, frequency and route—and comparing them to the current list in use, recognising and documenting any discrepancies, thus resulting in a complete list of medications'.[1] Included studies had to be original peer-reviewed research articles that were published in English. The included interventions had to start in the hospital and be performed primarily by a pharmacist, with the aim of improving care transitions to and from a hospital. The intervention had to have been compared with another group that received usual or standard care. 'Usual or standard care' was defined as any care where targeted medication reconciliation was not undertaken as an intervention, or where, if an intervention was conducted, it was not provided by a pharmacist. Along with duplicate references, and other studies that did not satisfy the inclusion criteria and were not medication reconciliation studies, we excluded the following types of studies: other medication reconciliation practices (eg, nurse-led) or practices as part of a multicomponent intervention (eg, medication therapy management), case studies, systematic reviews, qualitative outcomes and non-research articles. Abstracts from conferences and full-texts without raw data available for retrieval were not considered. Therefore, the studies selected for inclusion and exclusion assessment were randomised controlled trials (RCTs), quasi-experimental studies with a control group, and before-and-after studies that evaluated pharmacist-led medication reconciliation programmes at hospital transitions. The titles and abstracts were screened by one author (ABM), and studies identified for full-text review and selected according to inclusion criteria were agreed on by the second (AJM) and third reviewer (JEB).

Data extraction

One review author (ABM) was responsible for data extraction from full-texts, using a modified adopted Cochrane EPOC data collection checklist,[33] including quality assessment of studies. The following information was extracted from each included study: name of first author, year of publication, country and setting where the study was conducted, study design, sample size, target of intervention, patient characteristics, components of intervention, and relevant outcomes and results. If insufficient details were reported, study authors were contacted for further information.

Outcomes and statistical analysis

Our analysis included studies that reported at least one of these end points: healthcare utilisation (readmission, ED visit and composite readmission, and/or ED visit),

mortality and ADE-related hospital visits, compared with usual care in the other arm; and using at least 30 days of follow-up. Studies were eligible for meta-analysis if such end point could be extractable. We analysed data in accordance with the Cochrane handbook.[34] Together with 95% CIs for each outcome, we derived the relative risk and weighted mean differences for dichotomous and continuous variables, respectively.

After we combined data, the analyses were conducted with Cochrane Review Manager (RevMan) V.5.3 software (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014). We performed separate analyses for each outcome measured compared with usual care. We synthesised the results by constructing a forest plot using a random effects model for each of the outcomes. We analysed intention-to-treat data whenever available. The Mantel-Haenszel risk ratio (RR) summary estimate was determined for outcome measures of dichotomous variables and the weighted mean difference was calculated for continuous data variables. To confirm the reliability of the summary estimate, 95% CIs were calculated. Since the analyses included medication reconciliation interventions with multiple components, different designs and follow-up periods, we set a priori that might be associated with some variation in the outcomes between the studies. When there were at least five studies per outcome, subgroup analyses were carried out according to methodological design factors (RCT and non-randomised studies) and outcome timing (duration of follow-up). For studies that reported outcomes at a different duration, the longer follow-up period was taken in the analysis, if there was no difference in the summary estimate. Otherwise, meta-analysis was performed separately for the long-duration and short-duration subgroups. We assessed statistical heterogeneity among studies through calculating τ^2, χ^2 (Q), I^2 and p value. We conducted sensitivity analysis to check the stability of summary estimates to outliers and the change in I^2 when any of the studies were withdrawn from the analysis. We evaluated publication bias by inspection of funnel plot, and Begg-Mazumdar and Egger's test using Comprehensive Meta-analysis, V.3 (Biostat, Englewood, New Jersey, USA). In all analyses, p value <0.05 was considered as statistically significant.

We assessed the risk of bias of individual studies with EPOC risk of bias tool.[33] The main domains considered were random sequence generation, allocation concealment, blinding of outcome assessment, attrition and reporting biases. We also determined whether groups were balanced at baseline in terms of characteristics and outcomes. Included studies were evaluated for each domain and a quality scoring was then calculated for each study. Studies with 'clear data' on each of the domains were given a score of 1, and studies were assigned a point score out of the maximum of 9 (9 domains were included in the risk of bias assessment).

RESULTS

Identification and selection of studies

We identified a total of 2551 citations from searches in the electronic databases and 59 additional records were identified in reference lists of included studies. After removal of duplicate records, title and abstract screening was applied on 1832 publications. After title and abstract review, 1731 publications did not meet the inclusion criteria—the focus for the majority of studies was not related to medication reconciliation interventions. The remaining 101 publications were obtained in full-text and assessed for inclusion. Most full-text articles were excluded either due to reporting of a different outcome of interest (n=34) or because medication reconciliation was not the primary intervention (n=11) (see online supplementary appendix B). After applying all the inclusion criteria, we finally included 17 articles (figure 1).

Characteristics of included studies

Major characteristics of the included studies are presented in table 1. They were randomised controlled trials (n=8, 47%), before-and-after studies (n= 6, 35%) and non-randomised controlled trials (n= 3, 18%). The majority of the studies were conducted in the USA (11 studies),[35–45] and the remainder were in Sweden (3 studies),[46–48] Ireland (2 studies)[49 50] and Australia (1 study).[51] The studies had been conducted between 2002 and 2014. The included studies involved a total of 21 342 adult patients of various ages with sample sizes ranging from 41 to 8959 individuals. No studies in paediatrics were identified. Only three studies were confined to multicentre.[38 49 51] Most studies reported outcomes up to 30 days of follow-up after selection of eligible patients; only six studies[37 46–50] reported longer follow-up of 3-month or more. Interventions were initiated at different care transitions; most were conducted at multiple transitions,[35 37–40 42 44 46–51] and all studies targeting a single transition intervention were carried out at hospital discharge.[36 41 43 45]

Most studies recruited high-risk patients (including elderly patients, patients with multiple medications and patients at risk of medication-related events). Five studies[36 37 39 44 48] focused on a specific patient population, mainly patients with heart failure and chronic obstructive pulmonary disease (COPD). Methodologically, one study[35] stratified patients into two groups: general population and high-risk patients, and another study[37] randomised the population into two levels of intervention: minimal and enhanced.

Some studies compared comprehensive medication reconciliation programmes, for example, multifaceted interventions including telephone follow-up and/or home visit,[44 48 51] and patient counselling,[35 38 41 45] or both telephone/home visit and patient counselling.[37 40 42 43 46 49 50] After medication reconciliation, a few studies[42 46–49] additionally included a formal medication review. Comparator groups in the

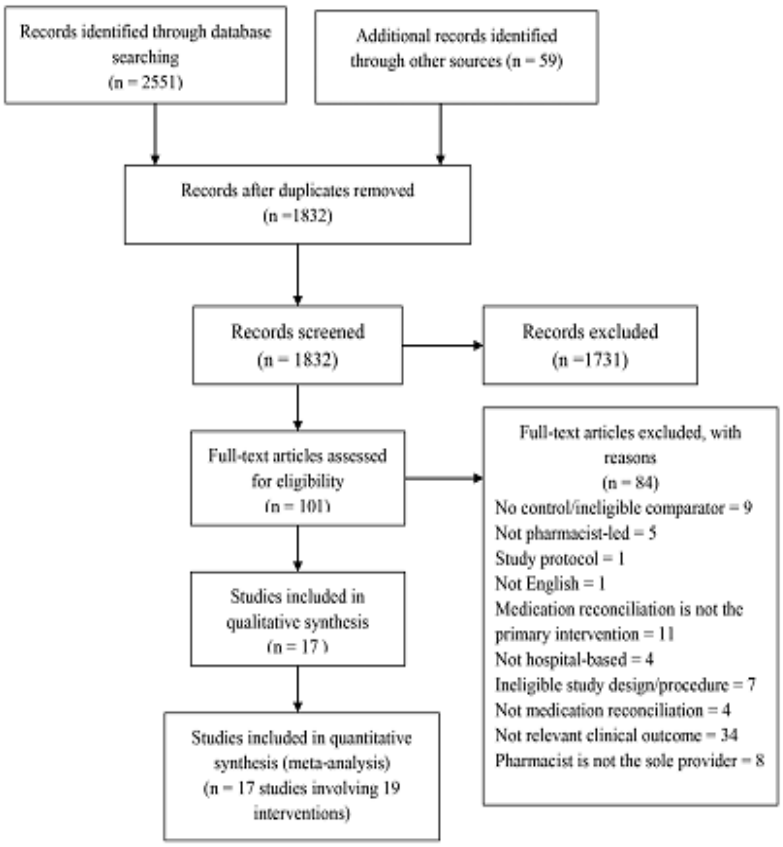

Figure 1 PRISMA flow diagram of the selection of eligible studies.

included studies were varied, and most studies compared medication reconciliation interventions with a usual care group that did not receive pharmacist-led intervention.

Risk of bias assessment

Patients included in the study were similar in baseline characteristics except in five studies,[36 38 39 45 48] which were not clear or different in patient characteristics. However, in only three studies[43 48 51] were baseline clinical outcomes reported or was some form of adjustment analysis performed. Eight out of 17 studies[37 39 40 42 46 49–51] provided enough details on randomisation procedure to be judged as adequate. Among these studies, allocation concealment was fully described in all reports except one.[51] In all but three studies[43 45 50] had care providers and outcome assessors been blinded or objective health outcomes reported. Five studies[37 41 47 48 51] achieved more than 80% complete follow-up. However, only a few studies examined the impact of losses to follow-up or drop-out. High-risk of contamination was suspected in four studies.[35 37 41 47] At least one of our outcomes of interest was selectively reported in four studies.[36 49–51] Overall, on a scale of 9, quality of randomised controlled trials falls within a range of 4–8, whereas for non-randomised controlled trials a lower range of 1–5 score was attained (see online supplementary appendix C).

Effect of interventions

Of the 14 studies that reported data on all-cause readmissions, 13 were eligible for meta-analysis. One study[35] measured this outcome for a high-risk population separately; and another study[37] reported it for two different interventions. Thus, 15 interventions were meta-analysed. Eight studies reported this outcome at 30 days,[35 36 39 41 43–45 51] while three[46 48 49] reported long-term data and two studies[37 38] reported both. Seven studies[35 38 39 41 44 45 49] showed a significant reduction ($p<0.05$) in rehospitalisations although two[39 44] of them had a very small sample size. The pooled RR (n=21 969 patients) across all studies was 0.81 (95% CI 0.70 to 0.95). However, the results of these studies for this end point are substantially heterogeneous (figure 2A). With regard to all-cause emergency department (ED) contacts, seven of eight studies[35 37–39 43 46 48] that measured ED visit as an outcome were pooled. Considering studies that gave two sets of data, nine interventions were meta-analysed. The pooled analysis across all interventions showed some significant difference between the intervention and usual care (RR 0.72; 95% CI 0.57 to 0.92; figure 2B). Evidence showed extreme heterogeneity in this outcome; however, the findings were different when the study by Gardella *et al*[38] was removed; there was no heterogeneity without affecting the significance difference ($p=0.25$; $I^2=22\%$, RR 0.89; 95% CI 0.79 to 0.99).

Table 1 Characteristics of included studies

Author, Year	Country, Setting	Study design	Intervention	Comparator	Target of intervention	Inclusion	Exclusion	Components of intervention	Comparator	Follow-up Period	Relevant outcomes	Main results
Anderegg *et al* 2014[35]	USA, single centre	Before–after	1664	1652	Admission, discharge	Age 18 years or older, discharge from internal medicine, family medicine, cardiology, or orthopaedic surgery medical	Mental illness/ alcohol or drug use; discharge to a rehabilitation unit/ long-term care facility, readmission for chemotherapy/ radiation therapy/ rehabilitation therapy	Admission MedRec, Discharge MedRec, patient education, medication calendar	Control group (admission MedRec as needed)	30 days	Readmission, Readmission and/or ED visit	30-day readmission and/or ED visit (general population): NS; 30-day readmission (high-risk): 12.3% (I) vs 17.8% (U), p=0.042
Bolas *et al* 2004[30]	Ireland, single centre	RCT	81	81	Inpatient stay, discharge, postdischarge	Age 55 years or older, at least 3 regular medications	Transfer to another hospital or nursing home, unable to communicate, mental illness or alcohol-related admission, follow-up was declined	Medication liaison service (comprehensive medication history, discharge letter faxed to GP and community pharmacist, medicines record sheet, discharge counselling, home visit/telephone call)	Standard clinical pharmacy service (not include discharge counselling and liaison service)	3 month	Readmission, hospital stay (following readmission)	Readmission rate: p>0.05; Length of stay: p>0.05
Eisenhower 2014[36]	US, single centre	Before–after	25	60	Discharge	Age 65 years or older, with history of COPD	Left the hospital without medical advice, death within 30 days of discharge	MedRec at discharge, Medication reconciliation form, discharge summary	Usual care (pharmacist was not present during baseline data collection)	30 days	Readmission	Readmission rate: 16% (I) vs 22.2% (U)
Farris *et al* 2014[37]	USA, Single centre	RCT	Minimal=312 Enhanced=311	313	Admission, inpatient stay, discharge	18 years or older, English or Spanish speaker, diagnosis of HPN, hyperlipidaemia, HF, CAD, MI, stroke, TIA, asthma, COPD or receiving oral anticoagulation	Admission to psychiatry, surgery or haematology/ oncology service, could not use a telephone, had life expectancy <6 months, had dementia or cognitive impairment	Admission MedRec, patient education during inpatient stay, discharge counselling, discharge medication list, telephone call, care plan faxed to primary care physician/ community pharmacist	Usual care (admission MedRec, nurse-led discharge counselling and medication list)	90 days	ADEs, readmission, ED visit, readmission and/or ED visit	16% experienced an AE, Healthcare utilisation at 30 days and 90 days: NS

Continued

Table 1 Continued

Author, Year	Country, Setting	Study design	Intervention	Comparator	Target of intervention	Inclusion	Exclusion	Components of intervention	Comparator	Follow-up Period	Relevant outcomes	Main results
Gardella *et al* 2012[38]	US, multicentre	Before–after	1624	7335	Preadmission to post discharge	NA	NA	Preadmission medication list, patient education	Historical control group (preadmission medication list gathered by nurse)	60 days	ADE, ED visits and readmission	30-day readmission: 6% (I) vs 13.1% (U) (OR 2.34, 95% CI 1.87 to 2.94, p<0.001); 60-day readmission: 2.7% (I) vs 7.7% (U) (OR 3.02, 95% CI 2.18 to 4.19, p<0.001)
Gillespie *et al* 2009[46]	Sweden, single centre	RCT	182	186	Admission, inpatient stay and discharge	Age 80 or older	Previous admission during the study period	Admission MedRec, discharge counselling, medication review, faxing discharge summary to primary care physicians, telephone follow-up at 2 months	Usual care (without pharmacist involvement)	12 month	Readmissions, ED visits, mortality	Readmissions: 58.2% (I) vs 59.1% (U) (OR 0.96, 95% CI 0.64 to 1.4); ED visits per patient: 0.35 (I) vs 0.66 (U) (OR 0.53, 95% CI 0.37 to 0.75)
Hawes *et al* 2014[39]	US, single centre	RCT	24	37	Discharge and post discharge	High-risk patients (HF, COPD, hyperglycaemic crisis, stroke ,NSTEM, more than 3 hospitalisations in the past 5 years., 8 or more medications on discharge)	Age <18 years, inability to communicate in English, unable to follow-up (no transportation and no telephone access), transfer to facilities other than primary care, decisional impairment, incarceration	Post discharge medication reconciliation	Usual care (with no pharmacist intervention)	30 days	Readmission, ED visit, readmission and /or ED visit	ED visit: 0 (I) vs 29.7% (U), p=0.004; Readmission: 0 (I) vs 32.4% (U), p=0.002; Composite of hospitalisation or ED visit: 0 (I) vs 40.5% (C), p<0.001
Hellstrom *et al* 2011[47]	Sweden, single centre	Before–after	109	101	Admission, inpatient stay, discharge	Age 65 years or older, at least one regular medication	Staying during the implementation period	LIMM model, admission and discharge MedRec, medication review and monitoring, quality control of discharge MedRec	Standard care (no formal MedRec by clinical pharmacists)	3 month	Readmission and ED visit, ADE-related hospital visit	ED visit and readmission: 45/108 (I) vs 41/100 (U) Mortality, 3 month: 9/108 (I) vs 9/100 (U) ADE-related revisit: 6/108 (I) vs 12/100 (U)
Hellstrom *et al* 2012[48]	Sweden, single centre	Before–after	1216	2758	Admission, inpatient stay	High-risk patients (age ≥65 years with any of HF, RF)	NA	Admission MedRec, structured medication reviews,	Usual care (no clinical pharmacists	6 month	ED visits, hospital	ED visit: 48.8% (I) vs 51.3% (U) (HR 0.95, 95% CI 0.86 to 1.04);

Continued

Mekonnen AB, *et al*. *BMJ Open* 2016;**6**:e010003. doi:10.1136/bmjopen-2015-010003

Table 1 Continued

Author, Year	Country, Setting	Study design	Intervention	Comparator	Target of intervention	Inclusion	Exclusion	Components of intervention	Comparator	Follow-up Period	Relevant outcomes	Main results
								follow-up at least two times a week	working in the wards)		admissions and mortality	All ED visits, hospitalisation or death: 58.9% (I) vs 61.2% (U) (HR 0.96, 95% CI 0.88 to 1.04) Mortality: 18.2% (I) vs 17.3% (U), p=0.55
Koehler *et al* 2009[40]	US, single centre	RCT	20	21	Admission, discharge and post discharge	Age 70 years or older, ≥5 medications, ≥3 chronic comorbid conditions, assisted living, English language, phone contact	Primarily surgical procedure, life expectancy ≤6 months, residence in long-term care facility, refusal to participate, not enrolled within 72 h.	Targeted care bundle, medication reconciliation and education, follow-up call, enhanced discharge form	Usual care (nurse and care coordination staff providing care)	60 days	Readmission and/or ED visits	30 days readmission/ ED visits: 2/20 (I) vs 8/ 21 (U), p= 0.03; 60days readmission/ ED visits: 6/20 (I) vs 9/ 21 (U), p= 0.52
Pal *et al* 2013[41]	US, single centre	NRCT	537	192	Discharge	Age 18 years or older, at least 10 regular medications	NA	Patient counselling, pharmacist medication reconciliation, medication calendar	Usual care (without discharge review by pharmacist)	30 days	Readmission	30 days readmission: 16.8% (I) vs 26.0% (U), p=0.006 ADE prevented: 52.8%
Schnipper *et al* 2006[42]	US, single centre	RCT	92	84	Inpatient stay, discharge, post discharge	Discharge to home, contacted 30 days after discharge, spoke English, cared for primary care physician/internal medicine resident	NA	Discharge medication reconciliation, telephone follow-up, medication review, standard email template, patient counselling	Usual care (medication review by a pharmacist and discharge counselling by a nurse)		ADEs-related hospital visit, readmission and/or ED visit	Preventable ADE: 1% (I) vs 11% (U), p=0.01; ED visit/readmission: 30% (I) vs 30% (U), p>0.99; preventable medication-related healthcare utilisation: 1% (I) vs 8% (U), p= 0.03
Scullin *et al* 2007[43]	Ireland, multicentre	RCT	371	391	Admission, inpatient stay, discharge	Age 65 years or older, at least 4 regular medications, taking antidepressants, previous admission in the past 6 months, taking intravenous antibiotics	Scheduled admissions and admissions from private nursing homes	Integrated medicines management service admission and discharge MedRec, inpatient medication review and counselling, telephone follow-up	Usual care (did not receive integrated medicines management service)	12 month	Length of hospital stay, readmission	LoS reduced by 2 days for intervention vs usual care, p=0.003 Readmissions per patient: 0.8 (I) vs 1 (U)
Stowasser *et al* 2002[51]	Australia, multicentre	RCT	113	127	Admission, discharge	Return to the community following discharge	Outpatients, discharge to hostel or nursing home,	Medication liaison service—medication history confirmation	Usual care (no medication liaison service)	30 days	Mortality, readmission, ED visit	Mortality, 30 days: 2/ 113 (I) vs 3/127 (U): NS

Continued

Table 1 Continued

Author, Year	Country, Setting	Study design	Intervention	Comparator	Target of intervention	Inclusion	Exclusion	Components of intervention	Comparator	Follow-up Period	Relevant outcomes	Main results
							previous enrolment, unable to provide consent and follow-up	with community healthcare professionals (telephone, faxing), 30 days post follow-up				Readmissions: 12/113 (I) vs 17/127 (U) ED visit per patient: 7.54 (I) vs 9.94 (U)
Walker *et al* 2009[43]	US, single centre	NRCT	138	366	Discharge, post discharge	Age 18 years or older, 5 or more regular medications, receiving 1 or more targeted medications, having 2 or more therapy modification, unable to manage their medication, receiving a medication requiring therapeutic drug monitoring	Non-English speaking, stay of 21 days or longer	Patient interviews, follow-up plan, medication counselling, telephone follow-up	Usual care (nurse-led service)	30 days	Readmission, ED visit, readmission and/or ED visit	Readmission, 14 days: 12.6% (I) vs 11.5% (U), p=0.65; Readmission, 30 days: 22.1% (I) vs 18.0% (U), p=0.17; Readmissions and/or ED visits: 27.4% (I) vs 25.7% (U), p= 0.61
Warden *et al* 2014[44]	US, single centre	Before–after	35	115	Admission, inpatient stay, discharge	Age 18–85 years, systolic dysfunction (EF ≤40)	Diastolic dysfunction, valve replacement/left ventricular assist device	Medication reconciliation (admission and discharge), discharge instructions, telephone follow-up	Historical control group (physicians—admission MedRec; nurses-discharge counselling)	30 days	Readmission	All cause readmission, 30-day :17% (I) vs 38% (U) (RR 0.45, 95% CI 0.21 to 0.96, p=0.02), 30 days HF-related readmission: 6%(I) vs 18% (U) (RR 0.31, 95% CI 0.08 to 1.27, p=0.11)
Wilkinson *et al* 2011[45]	US, single centre	NRCT	229	440	Discharge	Age 18 years or older, English speaking, patients with depression, receiving high-risk medications and polypharmacy, poor health literacy, having an absence of social support, prior hospitalisation within the past 6 months	Refusal of pharmacist education, transfer to a skilled nursing facility, or discharge when the pharmacist was not available	Medication history at admission, during hospitalisation and discharge, patient education on discharge	Control group (pharmacists not provide medication counselling at discharge)	30 days	Readmission	Readmission rate: 15.7% (I) vs 21.6% (U) (RR 0.728, 95% CI 0.514 to 1.032, p =0.04)

ADE, adverse drug event; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; D, days; ED, emergency department; EF, ejection fraction; GP, general practitioner; HF, heart failure; HPN, hypertension; I, intervention; IV, intravenous; LIMM, Lund Integrated Medicines Management; LoS, length of stay; MedRec, medication reconciliation; MI, myocardial infarction; NA, not available; NS, non-significant; NSEMI, non-ST segment elevation myocardial infarction; RCT, randomised controlled trials; RF, renal failure; RR, relative risk; TIA, transit ischaemic attack; U, usual care.

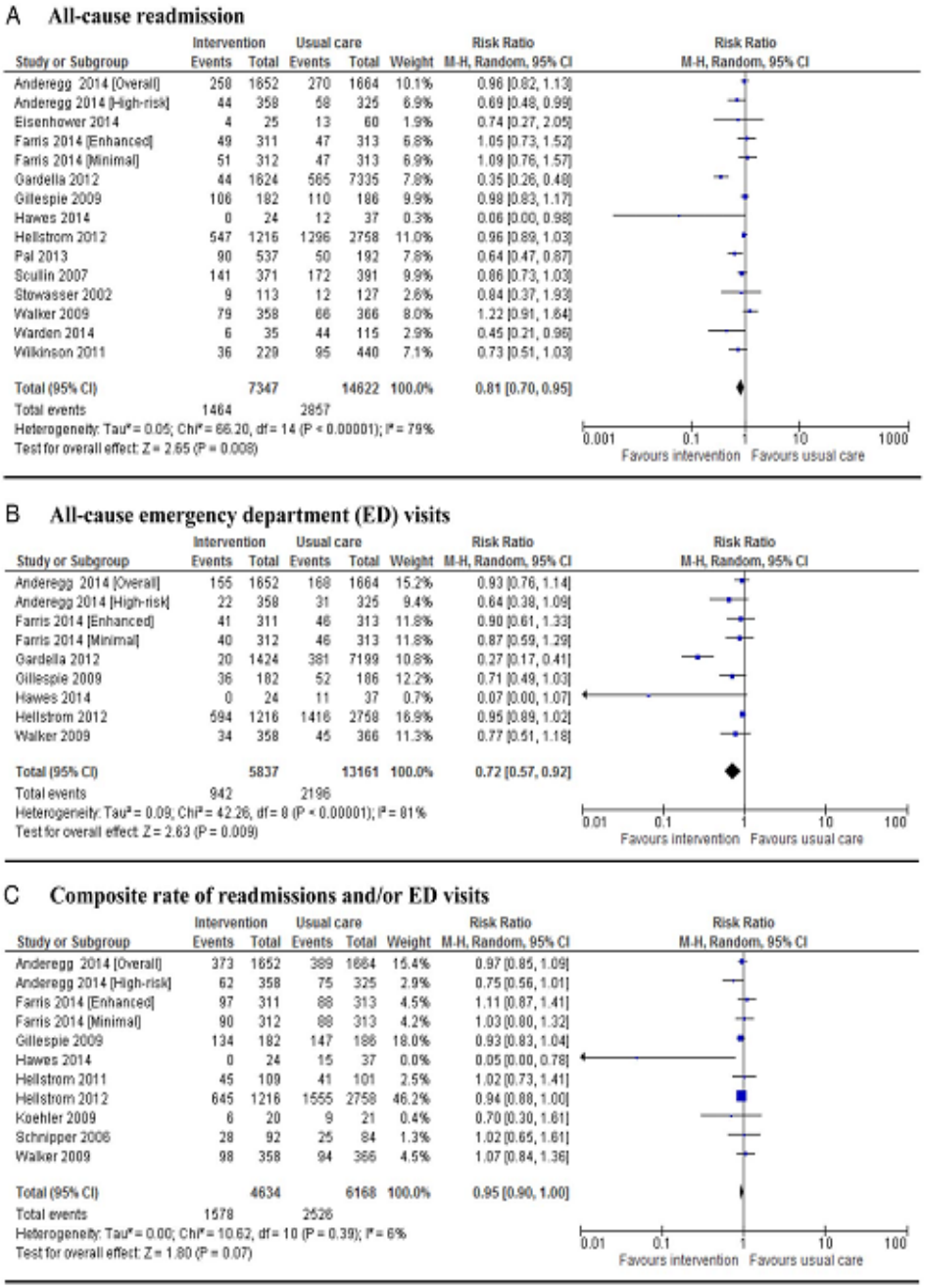

Figure 2 Forest plots of intervention effects on the proportion of patients with all-cause readmission (A), emergency department (ED) visits (B), composite rate of readmissions and/or ED visits (C), adverse drug event-related hospital revisits (D) and mortality (E). Pooled estimates (diamond) calculated by the Mantel-Haenszel random effects model. Horizontal bars and diamond widths represent 95% CIs. Anderegg *et al*[35] stratified patients into two groups: general population and high-risk patients. Farris *et al*[37] randomised the population into different levels of intervention: minimal and enhanced.

Nine studies[35 37 39 40 42 43 46–48] that reported composite all-cause readmission and/or ED visit showed no difference in pooled analysis (RR 0.95; 95% CI 0.90 to 1.00 figure 2C). Only three studies[38 42 47] were meta-analysed for ADE-related hospital revisits. One study[46] did not give data in a suitable form. The pooled result showed a substantial reduction of 67% in hospital revisits (pooled RR 0.33; 95% CI 0.20 to 0.53) when pharmacist-led medication reconciliation programmes were implemented (figure 2D). Seven studies[37 46–51] gave eight separate sets of data for all-cause mortality that had been reported after 30 days to 12 months of follow-up. However, information on mortality from Bolas *et al*[50] and Farris *et al*[37] was not their primary outcome of interest; nevertheless, we included it in our meta-analysis. Overall, there was no significance difference

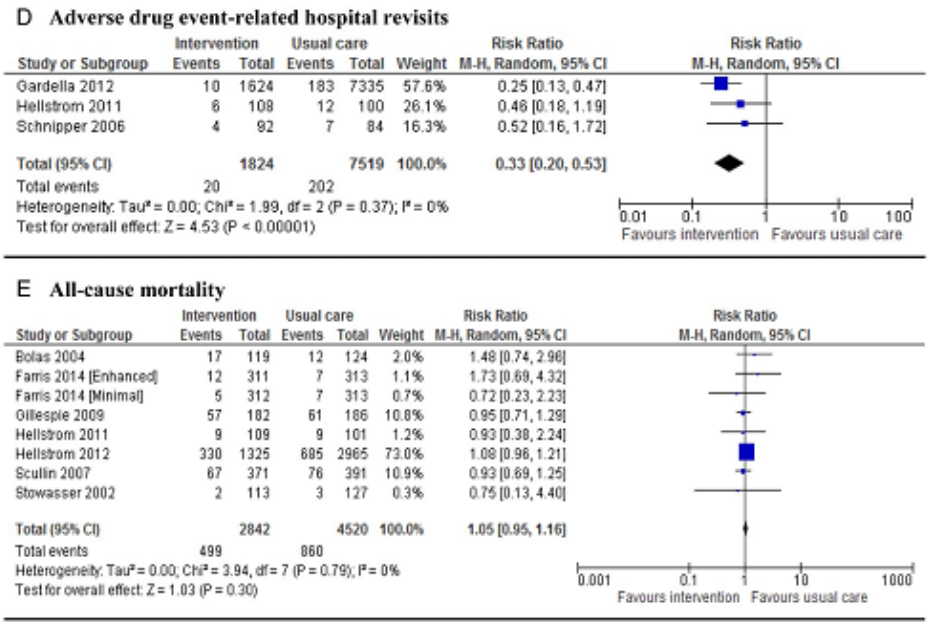

Figure 2 Continued.

between the two groups in terms of all-cause mortality (RR 1.05; 95% CI 0.95 to 1.16) (figure 2E).

Other outcomes

Studies reporting other clinically important outcomes are summarised in table 2. Some studies[46–49] furnished information on the proportion of patients who did not revisit the hospital. The intervention group in the three studies[46 48 49] showed a trend towards an increase in the number of patients who did not revisit the hospital for any causes, and the overall pooled analysis was statistically significant (RR 1.10; 95% CI 1.03 to 1.17). There were no significance differences between the intervention and usual care in terms of other relevant clinical outcomes: length of stay after readmission, readmission per patient, ED visit per patient and proportion of patients with ADEs.

Sensitivity analysis

A one-on-one removal of studies in the meta-analysis did not affect findings in all outcomes except for composite readmission and/or ED visit. A meta-analysis for composite readmission/ED visit showed that only when the study by Faris *et al* (Enhanced)[37] or Hawes *et al*[49] was removed did the result show a significant pooled summary estimate with similar risk ratio (RR 0.95; p=0.02 and 0.03, respectively).

Subgroup analysis

Subgroup analysis comparing studies that reported all-cause readmissions at earlier versus longer follow-up period showed different patterns of effect: the effect of intervention was not statistically significant for longer follow-up subgroups (RR 0.83, 95% CI 0.68 to 1.06, p=0.14), whereas in earlier follow-up subgroups, the

Table 2 Other clinically relevant outcomes

Outcome	Number of studies	Number of patients	RR	CI	WMD	CI
Patients who did not revisit hospital	4	5314	1.10*	(1.03 to 1.17)†		
Hospital stay (after readmission)	2	803			−0.57	(−5.32 to 4.17)‡
Readmission per patient	3	1370			−0.12	(−0.24 to 0.01)‡
ED visit per patient	2	4342			−0.15	(−0.53 to 0.23)‡
Patients with ADE	3	1401	0.94	(0.75 to 1.20)‡		

*RR is >1 when the intervention increased the number of patients who did not revisit the hospital (ie, it showed success).
†p<0.01.
‡p>0.05.
ADE, adverse drug event; ED, emergency department; RR, risk ratio; WMD, weighted mean difference.

effect was significant (RR 0.77, 95% CI 0.60 to 0.98, p=0.03). However, there was no significant difference between these two subgroups. In addition, non-randomised studies showed a significant reduction in all-cause readmission (RR 0.74, 95% CI 0.58 to 0.94, p=0.01) and all-cause ED visit (RR 0.68, 95% CI 0.48 to 0.97, p=0.03), but there was no difference in terms of study design with these outcomes. As opposed to what has been observed in the entire analysis, the composite outcome seemed to have a slight significant reduction in non-randomised studies (RR 0.95, 95% CI 0.90 to 1.00, p=0.04); though there was no difference between the subgroups (see online supplementary appendix D).

Publication bias

We examined the potential for publication bias by constructing a funnel plot and through statistical tests. There was some indication of asymmetry—particularly for all-cause ED visits—in the funnel plot and, therefore, there was some publication bias, as evidenced by the Egger's (p=0.04) and Begg's tests (p=0.01) in this outcome. We did not find any significant evidence of bias in the other outcomes, as shown by Egger's test value of 0.08 for all-cause readmission, 0.57 for composite readmission/ED visit and 0.83 for all-cause mortality; this was further supported by Begg's test p value of 0.13, 0.35 and 0.71, respectively (see online supplementary appendix E).

DISCUSSION

To the best of our knowledge, this is the first meta-analysis to investigate the effectiveness of pharmacist-led medication reconciliation programmes on clinical outcomes at hospital transitions. This review has shown better outcomes in favour of pharmacist-led interventions. We found a substantial reduction in the rate of all-cause readmissions (19%), all-cause ED visits (28%) and ADE-related hospital revisits (67%). However, pooled data on mortality and composite readmission/ED visit favoured neither the intervention nor the usual care. Not only were patients allocated to the intervention group readmitted or not only did they revisit the hospital less frequently, but patients free of any events after hospital discharge also increased (RR 1.10; 95% CI 1.03 to 1.17).

No previous reviews have conclusively and consistently shown effectiveness of medication reconciliation interventions, be it in primary care,[52] long-term settings[53] or hospital transitions.[30 31] Particularly, reviews from hospital-initiated medication reconciliation interventions searched the available literature on medication reconciliation strategies and impact on patient safety, and summarised the evidence that medication reconciliation alone was not strong enough to reduce post discharge hospital utilisation.[30 31] It was not clear to support the effectiveness of such interventions in the hospital setting. However, we believe that the influence of pharmacist's in healthcare utilisation was diluted among those various medication reconciliation strategies and, thus, specifically assessing the effect of pharmacist in medication reconciliation is an important consideration.

Although Thomas *et al*[54] did not find a significant effect in reduction of readmissions due to medication-related problems, our review showed that pharmacists' influence in preventing ADE-related hospital revisits was more impactful than any of the outcomes measured. This might be because medication reconciliation picks patients with discontinued medication more powerfully, where this is the case for studies reporting this outcome.[43 47] Other studies also showed that medication discontinuity is the most common reason for discrepancy-related ADE.[55 56] Although the study by Gillespie *et al*[46] was not included in the meta-analysis of this outcome, it showed a much higher reduction of 80% in medication-related readmissions in the intervention group than in the control group. Readmissions were frequent in earlier follow-up periods. This is as opposed to a review by Kwan *et al*,[31] where harm due to medication discrepancies occurred only some months after discharge. However, for most studies, the duration of follow-up was short; only one-third of interventions followed patients for longer than 30 days. Therefore, it might be difficult to come to a conclusion, as there was no sustained benefit from the intervention, and this was supported by non-significant differences between the subgroups. Moreover, non-randomised studies showed a slight significant reduction in all-cause ED visit and readmission and composite outcome, but there was no difference in terms of study design with these outcomes. Otherwise, pooled estimates showed consistent results in all of these three outcomes, regardless of the study design and duration of follow-up. However, care should be taken in interpreting the results as some of the influence of observational studies on the success of outcome was clear, and their heterogeneity should be taken into consideration.

Some of the studies, as part of their intervention, consisted of intermingled components, and the difficulty in ascertaining the success of pharmacist-led intervention is due only to medication reconciliation. After medication reconciliation, for example, medication review as intervention component was added in some studies. Previous systematic reviews that focused on medication review[57 58] raised a debate as to the impact of medication reviews in general, and pharmacist-led medication reviews in particular. A review by Holland *et al*,[57] where only 8 of the 32 included studies were hospital-based and only 2 of these had extensive medical team involvement at hospital transitions, did not support the evidence for pharmacist-led medication review. On the other hand, one of the issues raised in a Cochrane review[58] was that medication review had varied and wider meaning, and did not stand alone. Prior to medication review, it is medication reconciliation that is practiced routinely at hospital transitions and, thus, considering medication

review without ensuring the most accurate list of a patient's current medications would be theoretical. This would strengthen our anticipation that interventions with medication reconciliation might be as equally effective as those with mixed interventions.

A number of recent studies have investigated medication reconciliation interventions at the level of real practice models or in integrated management of medicines.[47–49] Medication reconciliation interventions are complex interventions targeting fragments of services across the entire spectrum of care transitions, and thus take time and effort, but the outcome of safe patient transition is well worth it. This review further consolidates pharmacist-led medication reconciliation programmes might contribute to quality transitions in combinations of those multifaceted components.

Limitation of the study

There are a number of limitations to this study. First, most studies included high-risk patients, and we did not confirm which patients benefited most from such interventions. Various definitions pertaining to high-risk were employed, including patients with specific disease state, polypharmacy, older age and patients at risk of hospitalisation. Second, interventions target different transitions; we could not take into account this effect in our meta-analysis. For instance, previous prospective studies showed varied results on the rate of medication discrepancies from 30–55% during admission,[59–62] to 35–71% during discharge.[4 63 64] Coleman *et al*[65] showed that patients with medication discrepancies have significantly high rates of readmission. Thus, if this value is extrapolated to clinical outcomes, there might be some variation among studies with respect to these outcomes at the different care transitions. Additionally, few studies were carried out in hospitals where medication reconciliation had already been implemented in some defined areas. Therefore, future studies should evaluate specific areas suited to pharmacist services that would benefit patients the most. Third, most of the studies were single centre evaluations, and there were a few studies with a small number of patients. Considering the success rates within small single centre studies raises an issue about bias. Our included studies were not free of bias and most possessed moderate quality, which leaves the findings open to criticism—for example, Gardella *et al*,[38] in the ADE-related hospital visit, and Hellström *et al*,[48] in the mortality forest plots, accounted for a large proportion of the studied subjects, yet these studies possessed low quality score. Fourth, the lack of homogeneity in the data from this meta-analysis confirms the complexity of medication reconciliation and warrants further investigation. We attempted to investigate the sources of variation between studies, but were unable to explain much of it. We were also unable to assess interactions between medication reconciliation and components of interventions. For example, integrated care models may be particularly effective for improving care for some of the interventions, but not for other types, and a pooled analysis would not identify such interactions. Despite these limitations, our meta-analyses showed that interventions that contain one or more elements of medication reconciliation can improve outcomes at hospital transitions.

We also note that only published studies were included in our work. However, the funnel plot asymmetry and statistical tests suggest that the impact of bias was less likely to have a significant effect on the findings. Only articles published in English were assessed for this review. Potentially, there may have been studies, such as that by Sánchez Ulayar *et al*,[66] published in non-English journals, involving interventions for improving care transitions. In addition, research disseminated through the grey literature, such as conference papers and unpublished reports, was not considered.

CONCLUSION

The results of this meta-analysis indicate that a pharmacist-led medication reconciliation programme at hospital transitions decreases ADE-related hospital revisits, all-cause readmissions and ED visits. However, the effect on mortality and composite all-cause readmission/ED visit is inconclusive based on the current body of evidence, though improvements in the majority of studies were demonstrated. Future research is needed to assess whether improvements in such outcomes can be achieved with this programme and to determine what/which components of the intervention are necessary to improve clinical outcomes. Although our results showed that pharmacist-led medication reconciliation was beneficial at care transitions, we still need further research with robust, large randomised control trials of excellent quality to conform our conclusion. Overall, our findings support the implementation of a pharmacist-led medication reconciliation programme that includes some components aimed at improving medication safety.

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Acknowledgements The authors would like to acknowledge Asres Berhan for his comments on the data analysis and interpretation, and statistical advice on using the meta-analysis software. The authors would also like to acknowledge Lorraine Evison for her invaluable contributions in the electronic database searching and abstract screening.

Contributors ABM was responsible for the study conception and design, under the supervision of JEB. The literature search, abstract screening, study and data extraction were undertaken by ABM with further confirmation by JEB. ABM carried out the initial analysis and drafted the first manuscript. JEB and ABM critically reviewed and revised the manuscript. All the authors have read and approved the final manuscript as submitted.

Funding This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Ethics approval Our study is an investigation of the literature, and does not need ethical approval for retrieving the already available public content.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement No additional data are available.

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Electronic supplementary materials published online for Chapter 2 are supplied as appendices (appendix A, page 269; appendix B, page 272; appendix C, page 282; appendix D, page 283; appendix E, page 287)

Chapter 3

Pharmacy-led Medication Reconciliation Programmes at Hospital Transitions: A Systematic Review and Meta-analysis

Mekonnen AB, McLachlan AJ, Brien JA. Pharmacy-led medication reconciliation programmes at hospital transitions: a systematic review and meta-analysis. J Clin Pharm Ther. 2016; 41(2):128–44. doi: 10.1111/jcpt.12364.

Journal of
Clinical Pharmacy and Therapeutics

Journal of Clinical Pharmacy and Therapeutics, 2016, **41**, 128–144 doi: 10.1111/jcpt.12364

Review Article

Pharmacy-led medication reconciliation programmes at hospital transitions: a systematic review and meta-analysis

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Received 12 August 2015, Accepted 21 January 2016

Keywords: **care transition, hospital, medication discrepancies, medication errors, medication reconciliation, medication review, pharmacy**

SUMMARY

What is known and objective: **Medication reconciliation is recognized as an important tool for the prevention of medication discrepancies and subsequent patient harm at care transitions. However, there is inconclusive evidence as to the impact of medication reconciliation at hospital transitions overall, as well as pharmacy-led medication reconciliation services. This review sought to evaluate the impact of pharmacy-led medication reconciliation interventions on medication discrepancies at hospital transitions and to categorize these interventions as single transition interventions or multiple transitions interventions.**

Methods: **PubMed, MEDLINE, EMBASE, IPA, CINHAL and PsycINFO databases, inclusive from inception to December 2014, were searched. Included studies were published studies in English that compared the effectiveness of pharmacy-led medication reconciliation interventions to usual care and that aimed to assess medication discrepancies at hospital transitions. 'Usual care' was defined as any care where targeted medication reconciliation was not undertaken as an intervention, or if an intervention was conducted, it was not provided by a pharmacist/pharmacy technician.**

Results and discussion: **Nineteen studies which involved a total of 15 525 adult patients were included. Eleven studies were randomized controlled trials. Overall, pharmacy-led medication reconciliation intervention usually revealed a trend towards reduction in medication discrepancies, compared with usual care. Seventeen studies involving 18 medication reconciliation interventions targeting the various transitions (admission, 9; discharge, 4; and multiple transitions, 5) were included in the meta-analysis. Compared with usual care, single medication reconciliation interventions at transitions in care (either admission or discharge) showed a significant reduction of 66% in patients with medication discrepancies (RR 0·34; 95% CI: 0·23–0·50) in favour of the intervention. There was no difference between groups for interventions targeting multiple transitions (RR 0·88; 95% CI: 0·77–1·02). Subgroup analyses confined to RCTs showed that there were no differences for target of transition (admission vs. discharge), type of intervention (multifaceted intervention vs. medication reconciliation) and setting (single centre vs. multicentre), nor pharmacists vs. pharmacy technicians (non-RCTs only). Importantly, medication discrepancies of higher clinical impact were more easily identified through pharmacy-led interventions than with usual care.**

What is new and conclusion: **Pharmacy-led medication reconciliation interventions were found to be an effective strategy to reduce medication discrepancies, and had a greater impact when conducted at either admission or discharge but were less effective during multiple transitions in care. Further studies that are designed to assess the impact of the involvement of pharmacy technicians in medication reconciliation are also needed.**

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WHAT IS KNOWN AND OBJECTIVE

Medication reconciliation has been identified as a major intervention to target and reduce the burden of medication discrepancies and medication errors during transitions in care.[1] Patients are vulnerable when admitted to, and discharged from, hospital, and medication discrepancies have been reported as accounting for over half of the medication errors.[2] Unintended therapeutic changes are common,[3–7] and suboptimal information communication at care transitions can subsequently result in medication errors[8]; of which one-third could have the potential for misadventure and harm.[6] Numerous studies have shown that medication errors impact on unplanned use of health care.[9–11] For example, Coleman *et al.*[12] reported that patients with medication discrepancies have significantly higher rate of readmission compared to those without such discrepancies.

Medication reconciliation as a medication safety strategy has been adopted and championed by a number of patient safety organizations. Medication reconciliation has been defined by the Institute for Healthcare Improvement as 'the process of identifying the most accurate list of a patient's current medicines including the name, dosage, frequency and route – and comparing them to the current list in use, recognising and documenting any discrepancies, thus resulting in a complete list of medications'.[13] Medication reconciliation was first incorporated as a National Patient Safety

Goal (NPSG) in 2005 by the Joint Commission.[14] WHO and collaborators have designed a project for its implementation in a range of countries[15–17] and taken-up into their healthcare policy. However, this programme is not without significant challenges.[18] Recent reviews[19,20] assessed the role of medication reconciliation during hospital transitions, and ascertained that the benefits as a patient safety strategy are not clear. However, these reviews[19,20] confirmed that most successful medication reconciliation interventions were led by or involved pharmacists. Additionally, determining the transition points (admission, during hospitalization, discharge, post-discharge) where the pharmacy staff involvement in medication reconciliation is most beneficial to patients has not been addressed. The aims of this systematic review and meta-analysis were to investigate the available evidence regarding the impact of pharmacy-led medication reconciliation interventions in minimizing medication discrepancies at hospital transitions and to categorize these according to the target of the interventions (single transition interventions, multiple transition interventions).

METHODS

Data sources and searches

This review was conducted according to the PRISMA statement (Preferred Reporting Items for Systematic Reviews and Meta-Analyses).[21] Six electronic databases were assessed for articles relevant to our review from the entire collections as of December 2014: PubMed/MEDLINE (1946), Ovid/MEDLINE (1946), International Pharmaceutical Abstracts (1970), EMBASE (1966), PsycINFO (1890) and CINHAL (1937). Initially, a limited search of the literature was undertaken, and further searching was performed after analysis of keywords contained in the title, abstract and index terms. The following main terms were used as follows: 'medication reconciliation', 'medication discrepancies', 'medication errors', 'medication history' and 'pharmac*' (Appendix S1). Searches were limited to articles published in English and conducted in humans. Bibliographies of included and review articles were manually searched to identify additional studies that were not located in the database search. The first author (ABM) performed the literature search with the support of a medical librarian.

Study selection

Studies were included, regardless of the study design, if they compared pharmacy-led medication reconciliation interventions with usual care and measured medication discrepancies as an outcome of interest. 'Usual care' was defined as any care where targeted medication reconciliation was not undertaken as an intervention, or if an intervention was conducted, it was not provided by a pharmacist. Included studies involved interventions were delivered in the hospital setting and performed primarily by pharmacy personnel, with the aim of reducing medication discrepancies at care transitions to and from hospital. We excluded interventions with medication reconciliation where physicians or nurses assessed medication discrepancies. Studies assessed discrepancies in medical histories, for example – documentation of allergy, were excluded. Medication discrepancies were defined as one or more differences (in dosage, frequency, drug, route of administration), as described by the Institute for Healthcare Improvement (IHI),[13] between the current and previous medication (s) a patient was taking. Duplicate references, conference abstracts and irrelevant studies (case studies, systematic reviews, qualitative outcomes and non-research articles) were excluded. All studies identified for full review and selected according to inclusion criteria were agreed by the second (AM) and third reviewer (JB).

Data extraction and outcomes

One author (ABM) was responsible for data extraction from full texts using an adopted standardized data collection checklist,[22] including quality assessment of randomized studies. Observational studies were evaluated for their quality by applying criteria from the ACROBAT-NRSI statement.[23] Extracted data included the following: name of first author, year of publication, country and setting where the research conducted, study design, total sample size, target of intervention, inclusion and exclusion criteria, components of intervention and relevant outcomes. The primary outcome of interest was medication discrepancies, described in terms of the proportion of patients with medication discrepancies, or as a mean number of discrepancies per patient. The secondary outcome was clinical severity of medication discrepancies. As different scales of severity scoring were utilized in the included studies, quantification of these has not been possible; however, descriptive comments have been included.

Statistical analysis

Meta-analyses of studies were conducted, if the primary outcome was available in a suitable form, according to *Cochrane Handbook for Systematic Reviews of Interventions*.[24] These analyses were conducted with Review Manager (RevMan) version 5.3. (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014). A random-effects model was used to pool data, and results were synthesized by constructing a forest plot. For studies that provided dichotomous data, we derived the Mantel–Haenszel risk ratio, whereas for continuous data, we calculated the mean differences with their associated 95% confidence intervals. Statistical heterogeneity among the studies was explored by observing values, I^2 and P-value. Sensitivity analysis was performed to assess the stability of pooled values when any of the studies was withdrawn from the analysis. Additionally, sensitivity analysis restricting to RCTs was conducted to observe the robustness of the results. Possible sources of heterogeneity were explored through subgroup analysis. Publication bias was evaluated by visual inspection of the funnel plot in this report.

RESULTS

Identification and selection of studies

Electronic database searches yielded 2551 citations. Additionally, a review of reference lists identified 59 articles. On removal of duplicate records, 1832 articles were screened for title and abstract. Of these, 1731 articles did not meet the inclusion criteria. Of the 101 full-text articles obtained, 19 articles met the selection criteria for inclusion in the final analysis (Fig. 1). The reasons for exclusion of studies are described in Appendix S2.

Characteristics of included studies

The included studies involved a total of 15 525 adult patients of various ages with sample sizes ranged from 61 to 8959 individuals. Studies in paediatrics were not identified. The studies had been

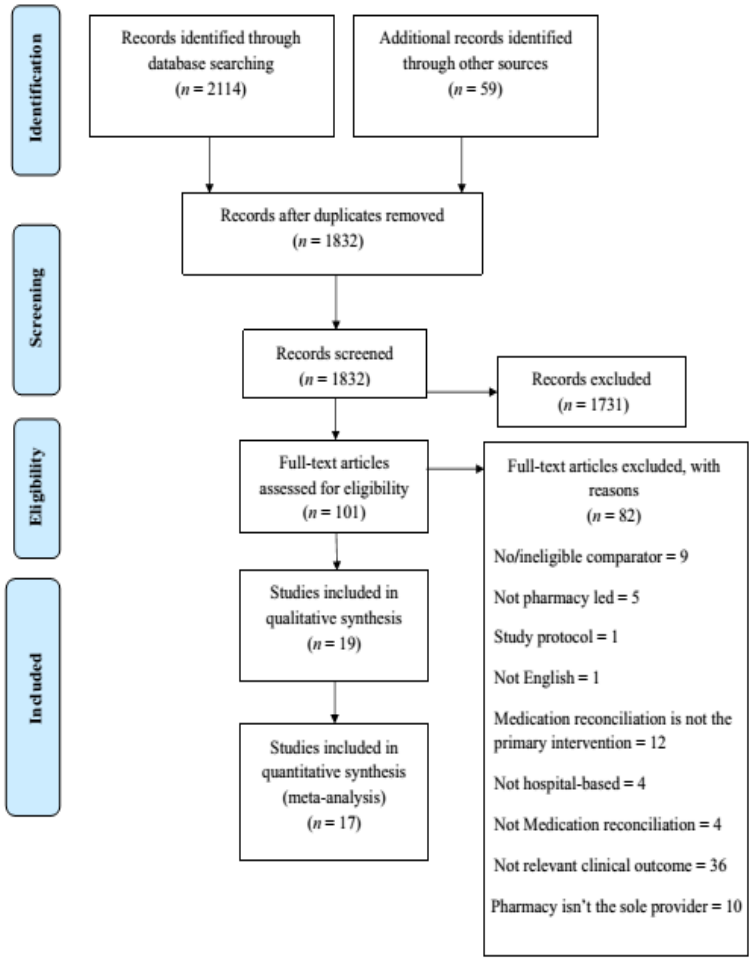

Fig. 1. PRISMA flow diagram of the selection of eligible studies. PRISMA, preferred reporting items for systematic reviews and meta-analyses.

conducted between 2004 and 2014. Eleven studies were randomized controlled trials (RCTs), and eight were non-RCT studies, including five studies that utilized before–after study designs. Seven studies were conducted in USA,[25–31] three in the Netherlands,[32–34] two each in Ireland,[35,36] Canada[37,38] and Australia[39,40] and one each in Sweden,[41] Colombia[42] and France.[43] All but five studies[27,29,34,39,42] were conducted at a single centre. Most studies recruited high-risk patients (including elderly patients, patients with multiple medications and patients at risk of medication-related events). Four studies[26,28,29,32] focused on a specific patient population; most of them, alone or in combination, were patients with heart failure. Some studies compared comprehensive medication reconciliation programmes, for example multifaceted interventions including telephone follow-up/home visit,[26,37,42] patient counselling[38] or both.[29–31,36] Some studies[30,35,41] additionally involved a formal medication review after the medication reconciliation, and one study[39] utilized an electronic medication profile communication between community and hospital pharmacies. Medication reconciliation interventions varied with regard to the target of intervention and initiated at different hospital transitions points, including admission,[27,33,34,37,39,40,42,43] discharge[31,32,38] and multiple transitions.[25,26,28–30,35,36,41] None involved transfer between wards of the hospital. The majority of medication reconciliation interventions were delivered by pharmacists, described as hospital/clinical pharmacists[25,26,28,30,32,35–38,41,43] or pharmacists.[29,31,39–41] In three studies,[27,33,34] pharmacy technicians delivered the medication reconciliation intervention. Overall, there were few details about the number of personnel involved in conducting medication reconciliation services. Twelve studies[24–26,28,31,34–37] assessed both primary and secondary outcomes. Results usually revealed a trend towards reduction in medication discrepancies in the intervention group when compared to usual care (Table 1). Two studies did not contribute data to meta-analysis.[26,36] An assessment of the quality of studies is presented in Appendix S3.

Effect of interventions

Most studies reported medication discrepancies at time of transition but there were a few studies[29,30] that did at 30 days of follow-up. All but two studies[26,36] provided data on outcomes related to the proportion of patients with medication discrepancies. One study[35] reported data for two time points in hospital transitions (admission and discharge) and included these data in the analysis as separate interventions. Of the 19 studies that reported data on medication discrepancies, 17 studies involving 18 medication reconciliation interventions (nine at admission, four at discharge and five at multiple transitions) were included in this meta-analysis. Thirteen of the 18 medication reconciliation interventions, 12 of which were conducted at single transitions, had shown a significant reduction in the proportion of patients with medication

Table 1. Characteristics of included studies

References	Country, Setting	Study design	No. of patients	Target of intervention	Inclusion	Exclusion	Components of intervention	No. and type of pharmacy personnel	Relevant outcomes	Main results
Beckett *et al.*[25]	US, single centre	RCT	81	Admission, inpatient and discharge	Age 75 years or older	Less than 48 h hospital stay, admission to primary service	Patient interview, standard medication reconciliation form	(-) hospital pharmacists	Medication profile appropriateness, clinical severity of medication discrepancies	Medication profile appropriateness: 71% (I) vs. 48% (C), $P = 0.033$; 27·6% of the medication discrepancies may contribute to temporary/ permanent harm
Bergkvist *et al.*[41]	Sweden, single centre	Before–after study	115	Admission and discharge	Age 65 years or older	Terminal stages of disease	Admission medication reconciliation, medication review, systematic medication care plan, discharge summary evaluation	2 hospital pharmacists	Medication errors/ discrepancies	Medication errors per patient: 0·48(I) vs. 1·06(C); patients with at least one medication error: 26·9% (I) vs. 36·3% (C); medications with medication errors (%): 4·8% (I) vs. 12% (C)
Becerra-Camargo *et al.*[42]	Colombia, multicentre	RCT	242	Admission	Age 18 years or older, at least one medication, triage I and II, hospitalized at least for 24 h	Discharge on the same day, not able to answer and communicate, individuals with mental illness	A standardized, comprehensive medication history interview, telephone interviews	(-) research pharmacists/ hospital pharmacists	Medication discrepancy, clinical severity of medication discrepancies	Mean discrepancies per patient: 2·43(I) vs. 4·23(C); at least 1 discrepancy: 60·7% (I) vs. 93·6% (C); 42·7% of the discrepancies were judged to have moderate discomfort whereas 23·9% were classified as severe
Bolas *et al.*[36]	Ireland, single centre	RCT	162	Inpatient, discharge and post-discharge	Age 55 years or older, at least 3 regular medications	Transfer to another hospital or nursing home, unable to communicate, mental illness or alcohol related admission, follow-up was declined	Comprehensive medication history, discharge letter faxed to GP and community pharmacist, medicines record sheet, discharge counselling, home visit/ telephone call	1 hospital pharmacist / clinical pharmacist	Medication-related history interventions, mismatch between discharge prescriptions and home medications, clinical significance of interventions	Medication history problems identified in 80% of patients; on follow-up [at 10–14 days], significant improvement in the correlation between discharge prescription medication and home medication post-discharge in the intervention group with respect to correct drug name ($P < 0.005$) and frequency of dosing ($P < 0.004$) but not for drug dose ($P < 0.07$); 90% of interventions were graded as significant or very significant

(continued)

Table 1 (continued)

References	Country, Setting	Study design	No. of patients	Target of intervention	Inclusion	Exclusion	Components of intervention	No. and type of pharmacy personnel	Relevant outcomes	Main results
Eggink *et al.*[32]	the Netherlands, single centre	RCT	85	Discharge	Age 18 years and older, diagnosis of HF, five or more medications	Transfer to another hospital, nursing home, unable to communicate, mental illness, follow-up declined	Discharge medication reconciliation, verbal and written information, discharge medication list faxed to community pharmacy	1 clinical pharmacist	Medication discrepancy / errors and clinical significance of medication errors	At least 1 discrepancy / prescription error, 39% (I) vs. 68·2% (C) [RR 0·57; 95% CI 0·37–0·88]; medications with discrepancy: 6·1% (I) vs. 14·6% (C); class E or higher (NCC MERP index), 32% (I) vs. 29% (C)
Farley *et al.*[26]	US, Single centre	RCT	592	Admission, discharge and post-discharge	Age 18 years or older, spoke English/Spanish, a diagnosis of cardiovascular disorders, COPD or require anticoagulation	Hearing problems, life expectancy of <6 months, cognitive impairment, psychiatric problems	Minimal intervention includes admission counselling, inpatient and discharge MedRec, discharge medication list; enhanced intervention includes all the above care plus discharge care plan faxed to community physician and pharmacist, follow-up phone call after 3–5 days	4 clinical Pharmacists	Medication discrepancies, clinical severity of medication discrepancies	Discrepancies of higher significance per patient in physician records at 30 days: 0·26(E) vs. 0·49 (M) vs. 0·51(C); $P = 0·013$ Discrepancies of higher significance per patient in physician records at 90 days: 0·44(E) vs. 0·41 (M) vs. 0·50(C); $P = 0·656$
Gardella *et al.*[27]	US, multicentre	Before- after	8959	Admission	–	–	Admission medication reconciliation	16 pharmacist technicians	Accuracy of pre-admission medication lists, severity of medication discrepancies	Pharmacy technicians conformed to the gold standard medication list in 89% of patients compared with 16% of cases compiled by staff nurses at baseline; medication errors classified as having the potential to cause moderate/serious harm decreased from 13·17% to 1·3%

(continued)

Table 1 (continued)

References	Country, Setting	Study design	No. of patients	Target of intervention	Inclusion	Exclusion	Components of intervention	No. and type of pharmacy personnel	Relevant outcomes	Main results
Grimes *et al.*[35]	Ireland, single centre	Before- after study	233	Admission, discharge	Adult medical patients, 3 or more regular medications, admitted to and discharge alive from hospital	Readmission during the study period, staffs admitted as patients	Admission and discharge medication reconciliation, aligned to medical team, medication review, minor and major changes to discharge medication list	2 clinical pharmacists	Medication errors, clinical severity of medication errors	Patients with admission error: 9% (I) vs. 40·5% (C); $P = 0.000$ Patients with discharge medication error: 13·9% (I) vs. 65·3% (C); $P = 0.00$ Patients receiving usual care had a greater likelihood of experiencing a potentially severe discharge error (5·9% vs. 0); moderate harm (53·5% vs. 12%)
Hawes *et al.*[28]	US, single centre	RCT	61	Discharge and post-discharge	High-risk patients [HF, COPD, hyperglycaemic crisis, stroke, NSTEM, more than 3 hospitalizations in the past 5 years, 8 or more medications on discharge]	Age < 18 years, inability to communicate in English, unable to follow-up (no transportation and telephone access),transfer to other facilities other than primary care, decisional impairment, incarceration	Discharge medication reconciliation, care transitions clinic visit 72 h post-discharge [medication history, identifying and resolving medication discrepancies, creating a current medication list, medication counselling on appropriate]	1 clinical pharmacist	Medication discrepancies	Medication discrepancies were identified in 54% of patients; patients with discrepancies at discharge; 50% (I) vs. 56·8% (C), $P = 0.793$; prior to visit, medication discrepancies were resolved in 30% (I) vs. 9.5% (C)

(continued)

Table 1 (continued)

References	Country, Setting	Study design	No. of patients	Target of intervention	Inclusion	Exclusion	Components of intervention	No. and type of pharmacy personnel	Relevant outcomes	Main results
Kripalani *et al.*[29]	US, multicentre	RCT	851	Admission, inpatient, discharge, post-discharge	Hospitalization for ACS or acute decompensated HF	Discharge within 3 h, too ill, not communicate in English/ Spanish, mentally ill, didn't manage medications, not home discharge, lacked telephone, in police custody	Pharmacist assisted medication reconciliation, inpatient counselling, providing low literacy aids, telephone follow-up	11 research pharmacists	[a]Clinically important medication errors, potential ADEs	1 or more clinically important medication errors occurred in 50·8% of patients [50·4% (I) vs. 51·2% (C)] at 30 days post-discharge; 75·3% of the errors were categorized as significant in severity, 22·9% were serious, 1·8% were life threatening Out of all errors, 29·7% errors (also defined as potential ADEs) were attributed to either medication discrepancies or non-adherence. The potential consequences of potential ADEs were rated as significant (n = 289 [68·2%]), serious (n = 130 [30·7%]) or life threatening (n = 5 [1·2%]) Clinical important medication errors per patient: 0·87(I) vs. 0·95(C) [RR 0·929; 95% CI: 0·77–1·10] Potential ADEs per patient: 0·44(I) vs. 0·55(C) [RR 0·8; 95% CI: 0·61–1·04]
Kwan *et al.*[37]	Canada, single centre	RCT	416	Admission	Surgical pre-admission clinic visit before undergoing surgery	Discharge on the same day, not able to answer and communicate, individuals with mental illness	Standardized compressive medication history interview, pre-printed post-operative medication order form, telephone interviews	(-) hospital pharmacist	Medication discrepancies, clinical severity of medication discrepancies	At least 1 medication discrepancy: 20·3% (I) vs. 40·2% (C), P < 0·001); at least 1 medication discrepancy with possible or probable impact: 12·9% (I) vs. 29·9% (C), P < 0·001

(continued)

Table 1 (continued)

References	Country, Setting	Study design	No. of patients	Target of intervention	Inclusion	Exclusion	Components of intervention	No. and type of pharmacy personnel	Relevant outcomes	Main results
Leguelinel-Blache *et al.*[48]	France, single centre	Prospective with observation and intervention	394	Admission	Age 18 years and older, admission at infectious and tropical disease and general medicine	–	Admission medication reconciliation before admission medication order by the physician	2 clinical pharmacists	Medication discrepancies, clinical severity of discrepancies	At least one unintentional medication discrepancies: 2·1% (I) vs. 45·8% (C), $P < 0.005$; 10% had the potential to harm the patient and only 2% were life threatening
Nickerson *et al.*[38]	Canada, single centre	RCT	253	Discharge	Discharge from family practice patient units, not discharged to another hospital, discharged between 8 h and 14 h, at least 1 medication informed consent, community pharmacy agreement, no previous enrolment	Not able to answer, unavailable for follow-up	Pharmacist medication reconciliation, communicated to patient's community pharmacy, discharge counselling, medication compliance chart	1 clinical pharmacist	Frequency and potential clinical impact of drug therapy inconsistencies and omissions	At least 1 drug therapy inconsistency or omission at discharge: 39·6% (I) vs. 56·3% (C) Ninety of the 99 drug therapy inconsistencies or omissions had an intervention ranking of significant or very significant
Schnipper *et al.*[30]	US, single centre	RCT	176	Admission, discharge, post-discharge	Discharge to home, contacted 30 days after discharge, spoke English, cared for primary care physician/ internal medicine resident	–	Discharge medication reconciliation, telephone follow-up after 3 –5 days, medication review, standard email template, discharge counselling	(-) hospital pharmacist	Medication discrepancies	49% had 1 or more unexplained discrepancies at discharge; during telephone follow-up 29% found to have 1 or more unexplained discrepancies; unexplained discrepancies 30 days after discharge: 61% (I) vs. 65% (C)
Tompson *et al.*[39]	Australia, multicentre	RCT	487	Admission	Age 50 years or older, at least 2 chronic condition, at least 3 chronic medications, had to nominate a regular GP and community pharmacy, not living in residential aged care facility	Admission for >24 h, too unwell to provide consent, non-English speaking	Electronic medication profile communication (community pharmacy's 6 month dispensing history), patient interview, review of patient's own medications	1 per hospital trial pharmacists	Medication discrepancies	66% of all patients had at least 1 discrepancy at admission: 67·8% (I) vs. 65% (C), $P = 0.3$; More intervention patients had at least 1 discrepancy resolved in the first 48 h of admission than control patients: 78·1% (I) vs. 36·3% (C), $P < 0.001$

(continued)

Table 1 (continued)

References	Country, Setting	Study design	No. of patients	Target of intervention	Inclusion	Exclusion	Components of intervention	No. and type of pharmacy personnel	Relevant outcomes	Main results
Van den Bemt *et al.*[33]	the Netherlands, single centre	Before-after study	297	Admission	Planning for elective general surgery, screening by anaesthesiologist	Other types of surgical procedures	Collection of community pharmacy medication records, patient interview	(-) pharmacy technicians	Medication discrepancies	At least 1 medication discrepancy: 5·4% (I) vs. 18·6% (C) [RR 0·29;95% CI: 0·12–0·71]
Van den Bemt *et al.*[34]	the Netherlands, multicentre	Before-after study	1543	Admission	Age 65 or older	Individuals without medication	Standard operating procedure [WHO], pharmacist technicians at 12 hospitals, mixed model at 3 hospitals	(-) pharmacy technicians	Medication discrepancies	At least 1 unintentional medication discrepancy (pharmacy-based): 22% (I) vs. 63% (C)[OR, 0·16 (95% CI, 0·12–0·21)]; proportion of medication orders with 1 or more unintentional medication discrepancies: 8% (I) vs. 18% (C)
Vasileff *et al.*[40]	Australia, single centre	NRCT	74	Admission	Age 65 years or older, four or more medications, three or more co-morbidities, at least one previous hospital admission in the last 3 months	Language difficulties, psychiatric and unable to give consent	Pharmacist medication charting	1 research pharmacist	Medication discrepancies, clinical severity of medication discrepancies	At least 1 discrepancy: 3·4% (I) vs. 75·6% (C); significant impact: 52%, very significant impact: 6%
Walker *et al.*[31]	US, single centre	NRCT	504	Discharge	Age 18 years or older, 5 or more regular medications, receiving 1 or more targeted medications, having 2 or more therapy modification, unable to manage their medication, receiving a medication requiring therapeutic drug monitoring	Non-English speaking, stay of 21 days or longer	Patient interviews, follow-up plan, medication counselling, telephone follow-up at 72 h and 30 days	1 research pharmacist	Medication discrepancies	At least 1 discrepancy at discharge: 33·5% (I) vs. 59·6% (C), $P < 0.001$; mean discrepancies per patient: 0·86 (I) vs. 1·28 (C), $P < 0.001$

[a]Composite of ADEs and potential ADEs; patients could contribute more than 1 event and have events of different severity.
ACS, acute coronary syndrome; COPD, chronic obstructive pulmonary disease; (C), control; (–), data not available; GP, general practitioner; HF, heart failure; (I), intervention; MedRec, medication reconciliation; NRCT, non-randomized controlled trial; NSEMI, non-ST segment elevation myocardial infarction; RCT, randomized controlled trials; RR, relative risk.

discrepancies. For the other two studies,[26,36] interventions resulted in mixed effects. According to Farley *et al.*,[26] the mean number of clinically important medication discrepancies per patient in the primary care physician record following the clinical pharmacist's intervention had showed a significant reduction in the intervention group at 30 days (P = 0·013) but not at 90 days (P = 0·656). In a study by Bolas *et al.*,[36] faxing of the discharge prescription allowed a significant improvement in the correlation between discharge medication and home medication in the intervention group with respect to correct drug name and frequency of dosing, but not for drug dose.

For the meta-analysis, the studies were grouped according to the target of intervention; interventions carried out at multiple (two or more transitions) or single transitions (targeting either admission or discharge). Figure 2 shows the forest plot of five studies expressing medication discrepancies dichotomously (proportion of patients with medication discrepancies) at multiple transitions. The pooled result of such studies on this outcome showed no difference in medication discrepancies between the intervention and usual care (RR 0·88; 95% CI: 0·77–1·02, I^2 = 0%). However, meta-analysis of 13 medication reconciliation interventions conducted at a single transition showed a significant reduction of 66% in patients with medication discrepancies (RR 0·34; 95% CI: 0·23–0·50) in favour of the intervention, but this was associated with extreme heterogeneity (I^2 = 96%) (Fig. 3). In the sensitivity meta-analysis of single transition interventions confined to RCTs, there was heterogeneity without affecting the significance difference (RR 0·69; 95% CI: 0·51–0·92, I^2 = 89%) (Fig. 4).

Nine studies reported the number of medication discrepancies per patient as an outcome, but only four[29,31,40,42] were eligible for inclusion in the meta-analysis (three studies target single transitions, one multiple transitions). Studies in this meta-analysis were excluded because of difficulties to extract data[25,26,28,39] or incomplete data to calculate standard deviation.[41] The pooled result for the three single transition medication reconciliation interventions showed a significant difference between the intervention and usual care (mean difference −1·49; 95% CI: −2·80, −0·17) – this was also associated with substantial heterogeneity (I^2 = 91%) (Fig. 5). However, when the Walker *et al.*[31] study was removed, the sensitivity analysis showed no heterogeneity but there was no significance difference (mean difference −2·03; 95% CI: −2·69, −1·38; P = 0·33, I^2 = 0%). Meta-analysis was not conducted for studies targeting multiple transitions; only one study[29] provided adequate data. The mean difference computed for this single study did not find a significant difference between the intervention and usual care groups (mean difference −0·08; 95% CI: −0·25, 0·09).

Subgroup analyses were only conducted for medication reconciliation interventions which measured the proportion of patients with medication discrepancies as outcome at both single and multiple transitions. According to this analysis at a single transition, study design had an effect on this outcome; non-RCTs (RR 0·20; 95% CI: 0·12–0·33) showed a higher reduction in medication discrepancies than RCTs (RR 0·69; 95% CI: 0·51–0·92). In the analysis that included both (RCT and non-RCTs), there was a difference between the intervention and usual care in terms of the type of interventions (medication reconciliation interventions vs. multifaceted interventions). When non-RCTs were removed from the analysis, however, there were not apparent differences for the type of intervention. Also, subgroup analyses confined to RCTs showed that there were no differences for target of transition (admission vs. discharge) and setting (single centre vs. multicentre). The type of pharmacy personnel involved in medication reconciliation did not show any difference between the groups; all RCTs were conducted by pharmacists and were not included in this analysis. Subgroup analyses for multiple transition interventions did not show a different pattern of effect to study design, type of intervention and setting (Table 2). Funnel plots showed no evidence of publication bias for multiple transitions interventions but modest for single transitions (Appendix S4).

Clinical significance of medication discrepancies

The clinical significance of medication discrepancies was reported in two-thirds of the studies. Three studies[32,35,37] compared the percentage of patients with clinically significant discrepancies; two of them[35,37] showed discrepancies of higher impact in the usual care than the intervention. In six studies,[25,36,38,40,42,43] clinically relevant discrepancies (defined as discrepancies with some potential or actual harm) were identified in approximately 28–91% of medication discrepancies. One study[29] reported clinically important medication errors only. Two studies[29,43] assessed life-threatening events in 1·2–2% of medication discrepancies. Methods, classifications and clinical judgement pertaining to this outcome were varied among the studies, however (Table 3). For severity assessment, studies employed different tools; some[27,37,42] adopted a tool developed by Cornish *et al.*[6] and some others[25,32,43] used a medication error index employed by NCC MERP.[44] There

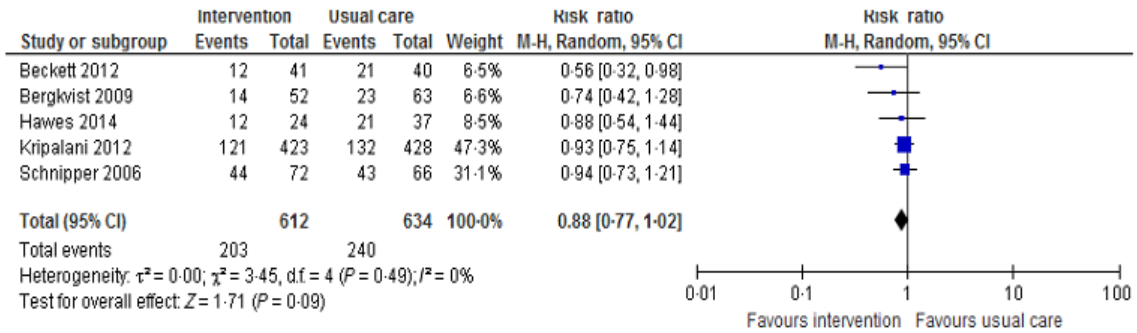

Fig. 2. Meta-analysis of the effectiveness of pharmacy-led medication reconciliation programmes on proportion of patients with medication discrepancies at multiple transitions. Number of patients with medication discrepancies (at least 1) was calculated from the medication profile appropriateness in Beckett *et al.*[25] study.

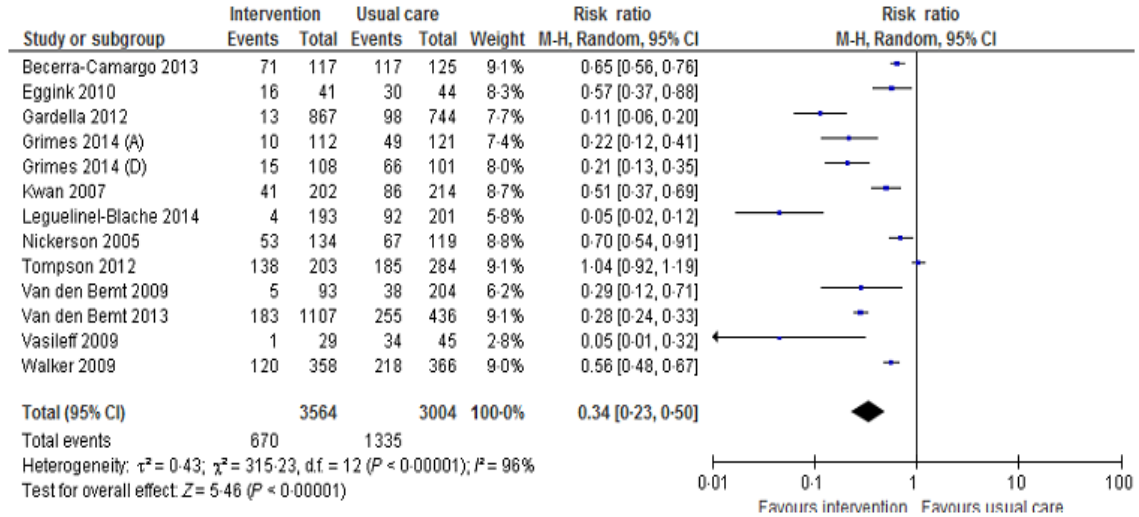

Fig. 3. Meta-analysis of the effectiveness of pharmacy-led medication reconciliation programmes on proportion of patients with medication discrepancies at single transitions. Grimes *et al.*[35] gave separate data for two transitions (admission and discharge), and each was included in the analysis as a separate intervention.

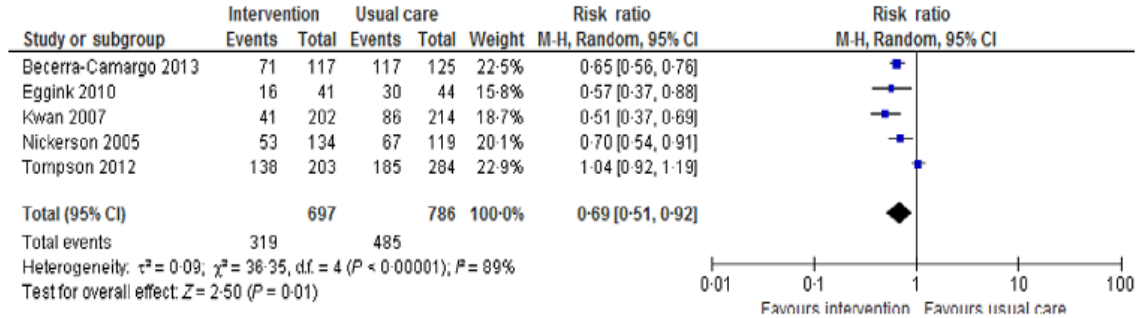

Fig. 4. Meta-analysis of randomized controlled trials measuring the effectiveness of pharmacy-led medication reconciliation programmes on proportion of patients with medication discrepancies at single transitions.

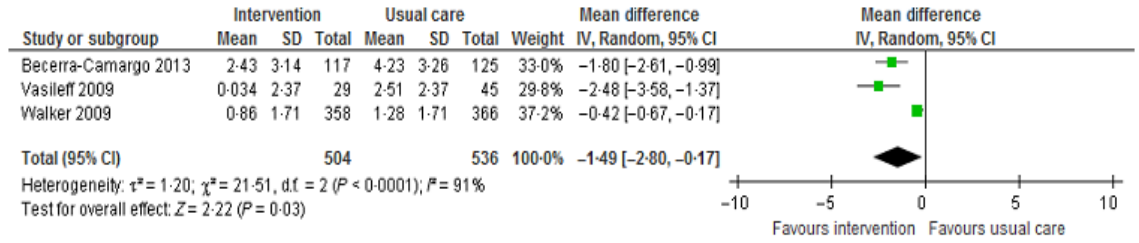

Fig. 5. Meta-analysis of the effectiveness of pharmacy-led medication reconciliation programmes on mean medication discrepancies per patient at single transitions. Mean discrepancies per patient could not be extracted for five studies: Hawes *et al.*,[28] Beckett *et al.*,[25] Farley *et al.*,[26] Tompson *et al.*[39] and Bergkvist *et al.*[41] Standard deviation (SD) of Walker *et al.*[31] was calculated by authors' of this report based on Cochrane's guide.[24]

were also studies which developed a study specific tool.[26,29,40] One study[35] used a visual analogue scale[45] and two other studies[36,38] classified based on earlier tools[46,47] suited for characterizing the impact of pharmacist's interventions. Number and type of evaluators differed among the studies; mostly there were two assessors involving pharmacists.

Table 2. Summary of subgroup analyses

Subgroup analyses[a]	Number of patients	Risk ratio (95% CI)	*P*-value	Subgroup difference, I^2
1. Single transition interventions				
Study design (*n* = 13)				
RCT (*n* = 5)	1483	0·69 (0·51, 0·92)	0·01	94·4%, *P* < 0·0001
NRCT (*n* = 8)[b]	5085	0·20 (0·12, 0·33)	<0·00001	
Type of pharmacy personnel[c]				
Pharmacist (*n* = 5)[d]	1401	0·15 (0·04, 0·52)	0·003	0%, *P* = 0·58
Pharmacy technician (*n* = 3)	3291	0·22 (0·10, 0·48)	0·0001	
Target of transition, combined				
Admission (*n* = 9)	5297	0·27 (0·15, 0·48)	<0·00001	65·7%, *P* = 0·09
Discharge (*n* = 4)	1271	0·49 (0·34, 0·72)	0·0002	
Target of transition, RCT only				
Admission (*n* = 3)	1145	0·71 (0·47, 1·08)	0·11	0%, *P* = 0·78
Discharge (*n* = 2)	338	0·66 (0·53, 0·83)	0·0004	
Type of intervention, combined				
Multifaceted interventions (*n* = 7)[e]	2564	0·52 (0·37, 0·73)	0·0002	86·6%, *P* = 0·006
MedRec only (*n* = 6)	4004	0·19 (0·10, 0·36)	<0·00001	
Type of intervention, RCT only				
Multifaceted interventions (*n* = 4)	1398	0·71 (0·51, 0·98)	0·04	0%, *P* = 0·43
MedRec only (*n* = 1)	85	0·57 (0·37, 0·88)	–	
Type of setting, combined				
Single centre (*n* = 9)	2685	0·32 (0·21, 0·49)	<0·00001	0%, *P* = 0·62
Multicentre (*n* = 4)	3883	0·40 (0·18, 0·86)	0·02	
Type of setting, RCT only				
Single centre (*n* = 3)	754	0·60 (0·49, 0·75)	<0·00001	30·5%, *P* = 0·23
Multicentre (*n* = 2)	729	0·82 (0·52, 1·32)	0·42	
2. Multiple transitions interventions[f]				
Study design (*n* = 5)				
RCT (*n* = 4)	1131	0·89 (0·77, 1·04)	0·14	0%, *P* = 0·51
NRCT (*n* = 1)	115	0·74 (0·42, 1·28)	–	
Type of intervention				
Multifaceted interventions (*n* = 3)	1104	0·91 (0·78, 1·07)	0·26	2·1%, *P* = 0·31
MedRec only (*n* = 2)	142	0·72 (0·46, 1·12)	0·15	
Type of setting				
Single centre (*n* = 4)	395	0·84 (0·68, 1·03)	0·10	0%, *P* = 0·50
Multicentre (*n* = 1)	851	0·93 (0·73, 1·14)	–	

MedRec, medication reconciliation; RCT, randomized controlled trials; Non-RCT, non-randomized controlled trials.
[a]Subgroup analyses based on medication discrepancies per patient as an outcome were not conducted as fewer studies (single transitions, 3 and multiple transitions, 1) reported this outcome.
[b]One study has two separate interventions targeting admissions and discharge independently and counted as two separate cohorts.
[c]Subgroup analysis was performed for non-RCT designs alone; all randomized controlled studies were conducted by pharmacists.
[d]A single data from Grimes *et al.*[35] were taken into account in the analysis, because the same pharmacists were involved in the intervention at both admission and discharge.
[e]Includes other components of intervention such as telephone follow-up/home visit, patient counselling, medication review.
[f]Subgroup analyses confined to RCT were not conducted as there were too few studies; furthermore, there was no difference between the intervention and usual care groups in terms of study design at this transition for this outcome.

DISCUSSION

This systematic review has found that pharmacy-led medication reconciliation programmes have an effect in minimizing medication discrepancies at hospital transitions. Our meta-analysis has shown a substantial reduction of 66% in patients with medication discrepancies favouring the intervention carried out at single transitions (either admission or discharge). But, interventions targeting multiple transitions did not show a difference between the intervention and usual care groups. This finding differed from the Joint Commission's[14] mandate for all healthcare organizations, that is, documenting a complete list of the patient's current medications upon admission and reconciling medications across care transitions (of hospital and post-hospital settings). Hospital-based pharmacy-led medication reconciliation interventions designed at specific transitions, either admission or discharge, might be a sensitive area for picking patients at high risk of medication discrepancies, and thus, medication reconciliation services delimited to these areas might benefit patients the most.

Study design had an effect for the single transition interventions; non-RCT studies reported a greater reduction in medication discrepancies than RCTs did.

Overall, our findings align with previous reviews[19,20] reported that pharmacy-led interventions were more successful, and this review supports pharmacists or pharmacy technicians as main players in delivering medication reconciliation services. In the

Table 3. Clinical significance of medication discrepancies

References	Tool for clinical significance evaluation	Clinical judgment determined by	Classification of severity	Results
Becerra-Camargo *et al.*[42]	Adopted from Cornish *et al.*[6]	Two clinical pharmacists blinded and with consensus	Class 1: unlikely to cause patient discomfort/clinical deterioration Class 2: moderate discomfort/ clinical deterioration Class 3: severe discomfort/ clinical deterioration	42·7% moderate; 33·4% unlikely; 23·9% severe
Eggnik *et al.*[32]	Adopted from NCC MERP[44]	Three pharmacists and a cardiologist with consensus	Class A: no error Class B, C and D: error, but no harm Class E, F, G, H: error and harm Class I: error and death	Class A: 4% (I) vs. 0(C) Class B-D: 64% (I) vs. 71% (C) Class E-H: 32% (I) vs. 29% (C)
Kwan *et al.*[37]	Adopted from Cornish *et al.*[6]	Three pharmacy clinician evaluators blinded and with consensus	Unlikely, possible or probable, based on the potential to cause patient discomfort/clinical deterioration	Unlikely: 25/60(I) vs. 53/157(C) Possible: 23/60(I) vs. 51/157(C) Probable: 12/60(I) vs. 53/157(C) Medication discrepancies with possible or probable patient discomfort and/or clinical deterioration: 58·3% (I) vs. 66·2% (C)
Grimes *et al.*[35]	visual analogue scale (VAS)[45]	Six assessors [hospital and community pharmacists, hospital doctors and GPs]	(0 = no harm, 10 = death); and the scores for each error were further categorized as minor (<3), moderate(3–7) or severe (>7)	No harm (VAS 0): 86·1% (I) vs. 34·1% (C) Minor harm: 1·9% (I) vs. 5·9% Moderate harm: 12% (I) vs. 53·5% (C) Severe harm: 0% (I) vs. 5·9% (C)
Kripalani *et al.*[29]	Their own tool [based on adjudication manual]	2 clinician adjudicators blinded and with consensus	Significant, serious, life threatening	Of 424 medication discrepancies/non-adherence issues, 68·2% were significant, 30·7% serious and 1·2% life threatening Significant (≥1): 22·5% (I) vs. 23·8(C) Serious (≥1): 10·2% (I) vs. 12·1%) Life threatening (≥1): 0·7% (I) vs. 0·5% (C)
Vasileff *et al.*[40]	Their own tool [based on a scale of 5]	multidisciplinary panel[three hospital pharmacists, three doctors, one academic pharmacist and pharmacy researcher]	Severity 0: nil impact Severity 1: minor impact Severity 2: significant impact Severity 3: very significant impact Severity 4: life-saving impact	Of 111 unintentional medication discrepancies, 52% were significant, 40% minor, 6% very significant and 2% did not have impact
Nickerson *et al.*[38]	Adopted from Hatoum *et al.*[46] [6 categories ranking system]	seamless care pharmacist and clinical pharmacist independently	Score 1: adverse significance Score 2: not significant Score 3: somewhat significant Score 4: significant Score 5: very significant Score 6: extremely significant	Of the 99 drug therapy inconsistencies and omissions, 48·5% were significant, 9·1% somewhat significant and 2·4% very significant
Leguelinel-Blache *et al.*[43]	Adopted from NCC MERP[44]	Two clinical pharmacists and one physician	Level 1: no harm [NCC MERP category C] Level 2: monitoring or intervention potentially required to preclude harm [NCC MERP category D] Level 3: potential harm[NCC MERP categories D and above]	Of 226 unintentional medication discrepancies, 48% had no harm, 42% required monitoring/intervention to preclude harm, 10% potential harm and 2% were life threatening

(continued)

Table 3 (continued)

References	Tool for clinical significance evaluation	Clinical judgment determined by	Classification of severity	Results
Beckett *et al.*[25]	Adopted from NCC MERP[44]	pharmacists	Category A: no error Category B-D: error, no harm Category E-H: error, harm Category I: error, death	Of 116 discrepancies, 74·1% were category B and 27·6% were category E
Bolas *et al.*[36]	Adopted from grading system of Eadon 1992[46] [7 scale]	a hospital pharmacist and medical consultant	0 being detrimental to patient health through to 6 which is potentially life saving	Of 225 medication history interventions, 90% were graded as 4 (intervention is significant and results in an improvement in the standard of care) or 5 (intervention is very significant and prevents major organ failure or adverse reaction of similar importance)
Farley *et al.*[26]	Their own tool [3 categories]	Clinical research pharmacists	Low: no risk of harm Moderate: impact outcome and/or possibility of harm High: adversely affect outcome, medications with narrow therapeutic index, medications on Institute for safe medication practices (ISMP) high alert list	Discrepancies per patient in physician records: High level: 0·26(E) vs. 0·49(M) vs. 0·51(C) Mid-level: 2·61(E) vs. 2·45(M) vs. 2·89(C) Low level: 2·31(E) vs. 2·14(M) vs. 2·31 (C)
Gardella *et al.*[27]	Adopted from Cornish *et al.*[6]	hospitalists	Class I: Unlikely to cause harm Class II: potential to cause moderate harm Class III: potential to cause serious harm	Medications with errors with the potential to cause moderate-to-serious harm: 13/867(1·5%) (post-intervention) vs. 98/744(13·1%) (pre-intervention)

E, enhanced; C, control; I, intervention; M, minimal; NCCMRP, National Coordinating Council for Medication Error Reporting and Prevention.

present study, the subgroup analysis has shown no difference between pharmacists and pharmacy technicians as interventionists. This finding is consistent with the Johnston *et al.*[48] study showing that pharmacists and pharmacy technicians were both equally effective in eliciting the best possible medication histories at hospital transitions. In the contrary, a recent prospective cohort study[49] comparing pharmacy technicians with admitting physicians did not show a significant reduction in unintentional medication discrepancies.

The present study has also investigated the clinical impact of medication discrepancies. More clinically relevant medication discrepancies, of which 1·2–2% were life threatening, were identified in this review than the previous, 28–91% vs. 28–49%.[20] Additionally, medication discrepancies were of higher impact in the usual care than the intervention, implying that pharmacy-led interventions had solved discrepancies that might have subsequently caused medication-related events. This further supports our claim that pharmacy-led interventions might be an effective strategy that hospitals should consider to adopt into their quality improvement projects.

There are a number of limitations to this study. Included studies were heterogeneous for interventions, population characteristics and methods for measuring outcomes. There were some variations in definitions and terminologies of medication discrepancies. There were a few studies[29,32,35,36,40,41], where the term medication error and any error in the medication history taking was interchangeably used. One study[38] defined it as drug therapy inconsistency or omission. This variation was also explored in a review by Kostas *et al.*[1] where many studies adopted their own synonym terms reflecting the same idea. The other source of variation was the medication history sources used for medication discrepancy identification. Only a few carried out the best possible medication history comprising all the available sources for medication history. In most of the studies, in the medication history taking process, it was difficult to ascertain the gold standard medication list. The number of medications a patient was taking as initial screening for inclusion was varied among studies and is a possible source of heterogeneity. Also, types of medications involved in discrepancies were also varied; some studies,[40,42,43] for example, considered regular non-prescription and over-the-counter medications. Moreover, rather than splitting the types of medication discrepancies (e.g. omissions, incorrect doses), we tried to focus on the gross definition of medication discrepancy as described by IHI.[13] This would at least minimize the heterogeneity in the reported outcome measure, that is, medication discrepancy. Heterogeneity due to study design effect was evident, however. Additionally, leaving non-RCTs alone, studies were not free of bias and most possessed moderate quality. Tools developed for measuring clinical severity were diverse and it was difficult to compare results across studies because of heterogeneity in methods, classifications and clinical judgment for this outcome. Only published studies in English were included. However, evidence from funnel plot asymmetry suggested that the impact of publication bias was less likely to have a significant effect on the findings. Although having these limitations, our meta-analysis showed that medication reconciliation interventions can improve processes at hospital transitions.

WHAT IS NEW AND CONCLUSION

The results of this systematic review and meta-analysis have shown evidence that pharmacy-led medication reconciliation interventions at hospital transitions, specifically targeting single transitions (either admission or discharge), decrease medication discrepancies compared with usual care. More clinically relevant and discrepancies of higher impact were easily identified through pharmacy-led interventions. Pharmacy-led medication reconciliation interventions, alone or in bundle with other interventions, are a promising strategy for safe patient transition. However, further research is still needed to assess the impact of pharmacy technicians in medication reconciliation interventions and the paradoxes of why multiple transitions interventions are less effective to reduce medication discrepancies.

ACKNOWLEDGEMENTS

We would like to acknowledge Asres Berhan for his statistical advice and Lorraine Evison for helping us in search of articles through electronic databases.

CONFLICT OF INTERESTS

The authors declare that they have no conflict of interests.

SOURCE OF FUNDING

None.

SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Appendix S1. Electronic database searches.

Appendix S2. List of excluded full-text papers and of the reasons for their exclusion.

Appendix S3. Risk of bias assessment.

Appendix S4. Publication assessment.

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Electronic supplementary materials published online for Chapter 3 are supplied as appendices (appendices S1 and S2, page 290; appendix S3, page 300; appendix S4, page 301)

Chapter 4

Impact of Electronic Medication Reconciliation Interventions on Medication Discrepancies at Hospital Transitions: A Systematic Review and Meta-analysis

Mekonnen AB, Abebe T, McLachlan AJ, Brien JE. Impact of electronic medication reconciliation on medication discrepancies at hospital transitions: a systematic review and meta-analysis. BMC Med Inform and Decis Mak. 2016; 16(1):112. doi: 10.1186/s12911-016-0353-9.

Mekonnen et al. BMC Medical Informatics and Decision Making (2016) 16:112
DOI 10.1186/s12911-016-0353-9

BMC Medical Informatics and Decision Making

RESEARCH ARTICLE Open Access

Impact of electronic medication reconciliation interventions on medication discrepancies at hospital transitions: a systematic review and meta-analysis

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Abstract

Background: Medication reconciliation has been identified as an important intervention to minimize the incidence of unintentional medication discrepancies at transitions in care. However, there is a lack of evidence for the impact of information technology on the rate and incidence of medication discrepancies identified during care transitions. This systematic review was thus, aimed to evaluate the impact of electronic medication reconciliation interventions on the occurrence of medication discrepancies at hospital transitions.

Methods: Systematic literature searches were performed in MEDLINE, PubMed, CINHAL, and EMBASE from inception to November, 2015. We included published studies in English that evaluated the effect of information technology on the incidence and rate of medication discrepancies compared with usual care. Cochrane's tools were used for assessment of the quality of included studies. We performed meta-analyses using random-effects models.

Results: Ten studies met our inclusion criteria; of which only one was a randomized controlled trial. Interventions were carried out at various hospital transitions (admission, 5; discharge, 2 and multiple transitions, 3 studies). Meta-analysis showed a significant reduction of 45 % in the proportion of medications with unintentional discrepancies after the use of electronic medication reconciliation (RR 0.55; 95 % CI 0.51 to 0.58). However, there was no significant reduction in either the proportion of patients with medication discrepancies or the mean number of discrepancies per patient. Drug omissions were the most common types of unintended discrepancies, and with an electronic tool a significant but heterogeneously distributed reduction of omission errors over the total number of medications reconciled have been observed (RR 0.20; 95 % CI 0.06 to 0.66). The clinical impact of unintended discrepancies was evaluated in five studies, and there was no potentially fatal error identified and most errors were minor in severity.

Conclusion: Medication reconciliation supported by an electronic tool was able to minimize the incidence of medications with unintended discrepancy, mainly drug omissions. But, this did not consistently reduce other process outcomes, although there was a lack of rigorous design to conform these results.

Keywords: Electronic medication reconciliation, Medication history, Medication safety, Medication errors, Medication discrepancies, Care transition

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Abbreviations: ACROBAT-NRSI, A cochrane risk of bias assessment tool for non-randomized studies of interventions; ADE, Adverse drug event; CI, Confidence interval; CPOE, Computerized physician order entry; EPOC, Effective Practice and Organisation of Care Group; IT, Information technology; IHI, Institute for Healthcare Improvement; MedRec, Medication reconciliation; NCC MERP, National Coordinating Council for Medication Error Reporting and Prevention Scale; PRISMA, Preferred reporting items for systematic reviews and meta-analyses; RCT, Randomized controlled trial; RR, Relative risk; SD, Standard deviation

Background

Medication reconciliation has been recognized as an important approach to improve the quality use of medicines by reducing the burden of medication discrepancies at care transitions [1–4]. Medication discrepancies often occur at transitions in care when patients are admitted to and discharged from a hospital, and are responsible for more than half of the medication errors [5]. Unintentional medication discrepancies are highly prevalent at hospital transitions — for example, two-thirds of inpatients have at least 1 unexplained changes to medication at hospital admission [6], and up to one-third of the medication discrepancies could have a potential for patient harm [7]. Clinically important medication discrepancies could also represent an important cause of adverse drug events (ADEs) [8–10] and healthcare resource utilization [11, 12] during transitions in care.

Medication reconciliation has been adopted and championed by a number of patient safety organizations. Medication reconciliation (MedRec) is defined by the Institute for Healthcare Improvement (IHI) as "the process of identifying the most accurate list of a patient's current medicines including the name, dosage, frequency and route — and comparing them to the current list in use, recognizing and documenting any discrepancies, thus resulting in a complete list of medications" [13]. Depending on the resources available, various approaches to the medication reconciliation intervention are employed internationally, including the use of electronic reconciliation tools [14–16], standardized forms [17, 18], collaborative models [19, 20], and pharmacy-led programs [21, 22]. Particularly, the use of information technology (IT) can increase the accuracy of documentation used for the medication reconciliation, and is now commonly used to facilitate the reconciliation process [23]. One of the main advantages of the electronic medication reconciliation is that the best medication history can be ensured through information sharing [24]. IT-related interventions might reduce medication discrepancies at hospital transitions [25], but there are fewer studies supporting this evidence. Additionally, previous reviews [26, 27] included medication reconciliation interventions carried out by physicians, nurses, pharmacists and electronic medication reconciliation and evaluated both clinical (e.g. hospital readmissions) and process outcomes (e.g. medication discrepancies), but did not specifically assess the impact of electronic medication reconciliation. In the literature, numerous reviews [28–30] examined the impact of electronic prescribing on medication errors and ADEs; however, no reviews have yet examined the impact of IT on medication discrepancies identified through the medication reconciliation process. The purpose of this study was thus, to systematically evaluate the available literature on the effectiveness of electronic medication reconciliation in reducing medication discrepancies during transitions in hospital care.

Methods

Search strategy

This systematic review and meta-analysis was performed according to the PRISMA statement [31], including a checklist to ensure consistent reporting of a systematic review. The search included articles from inception of the databases up to week 3 of November 2015, which were obtained through an extensive search of the following electronic databases: MEDLINE (1946), EMBASE (1966), CINAHL (1937) and PubMed (1946). Some of the key words or Medical Subject Heading (MeSH) terms used in the search were: "medication reconciliation," "medication discrepancies," "medication errors," "medication history," "electronic health records," "patient admission," "patient discharge," "patient transfer," and "hospital". Details on the specific search terms and combinations are provided in the Additional file 1. The literature search also involved manual search of bibliographies of the identified papers. Only studies published in English were included. No restrictions were imposed on year of publication.

Study selection

Two independent reviewers (ABM, TBA) screened abstracts and titles for eligibility. When the reviewers felt that the abstract or title was potentially useful, full copies of the articles were retrieved and considered for eligibility by the reviewers. When discrepancies occurred between reviewers, the final decision was made based on the agreement of these reviewers.

To be included in the selection, studies required to present all of the following: studies which reported data related to the effectiveness of electronic medication

reconciliation intervention, and provided data on medication discrepancies or errors. Medication discrepancies were defined as one or more differences in (dosage, frequency, drug, and route of administration), as described by the IHI [13], between the current and previous medication (s) a patient was taking. We excluded studies with a focus on other types of medication errors (e.g. prescribing errors) that were identified through the non-reconciliation process. The included interventions had to start in the hospital and must be performed primarily by an electronic tool with the aim of minimizing medication discrepancies during transitions in hospital care. Regardless of the study design, the intervention must be compared with another group that received usual or standard care. 'Usual care' was defined as any care in which medication reconciliation was not supported by an electronic tool, or if there was not any previous formal electronic medication reconciliation in place. Only full-text published articles from peer-reviewed journals were eligible for inclusion. Along with duplicate references and studies with a different focus, the following types of studies were excluded: other medication reconciliation practices (e.g. pharmacist-led medication reconciliation programs not supported by technology), case studies, systematic reviews, qualitative outcomes, and non-research articles. Abstracts from conferences and full-texts without raw data available for retrieval were not considered.

Data extraction and quality assessment

Two study authors (ABM, TBA) independently extracted data in a standardized form, including quality assessment of randomized studies [32]. Observational studies were evaluated for their quality by applying criteria from the ACROBAT-NRSI statement including: 1) bias due to confounding, 2) bias in selection of participants into the study, 3) bias in measurement of interventions, 4) bias due to departures from intended interventions, 5) bias due to missing data, 6) bias in measurement of outcomes, and 7) bias in selection of reported results [33]. The response for each criterion was judged based on a scale of low, moderate, serious, critical and no information. Any disagreements between the authors were resolved with mutual consensus. In general, we abstracted the following data: author, year of study, country of origin, study setting and design, number of study participants, target of transition, description of the intervention, length of the study, medications assessed for discrepancy and whether those discrepancies were explicitly described as unintentional changes to medications after clarification was sought from the medical team and/or patient. The primary outcome of interest was the rate and incidence of medication discrepancies, expressed in terms of the proportion of patients with medication discrepancies, or as a mean number of discrepancies per patient, or the proportion of medications/medication orders with discrepancies over the total number of medications reconciled. The secondary outcome was an assessment of the clinical relevance of identified medication discrepancies.

Statistical analysis

Meta-analyses of studies were done according to the *Cochrane Handbook for Systematic Review of Interventions* [34], using the Review Manager (RevMan) Version 5.3. (Copenhagen: The Nordic Cochrane Centre, the Cochrane Collaboration, 2014. (http://tech.cochrane.org/revman/). A random-effects model was employed, and the results were presented in forest plots. For studies providing dichotomous data, the relative risk (RR) with its 95 % confidence interval (CI) was calculated by comparing medication discrepancy rates between the intervention and comparison group. Whereas for continuous data, we calculated the mean differences with their associated 95 % confidence intervals. We assessed statistical heterogeneity by observing τ^2, χ^2 (Q), I^2 and p-value. We attempted to explore the possible sources of heterogeneity through subgroup analysis; however, the inclusion of too few studies in each of the outcomes studied precluded us from carrying out such analyses. Sensitivity analysis was carried out to assess the stability of pooled estimates when any of the studies were withdrawn from the analysis. P-value < 0.05 was considered as statistically significant. Publication bias was not assessed with funnel plots because the number of studies included in the meta-analyses were too few in this report.

Results

Search results

The initial electronic database search resulted in a total of 1672 articles. An additional 5 studies were identified through hand-search of the reference lists of included studies. On removal of duplicate records, 1283 studies were screened for title and abstract. Of these, 1216 studies did not meet the selection criteria. Of the 67 studies obtained in full-text, only 10 studies met the inclusion criteria (Fig. 1). The main reasons for exclusion were either due to reporting of a different outcome of interest ($n = 21$) or medication reconciliation was not supported by information technology ($n = 12$) (Additional file 2).

Characteristics and quality of included studies

Study characteristics

Detail characteristics of the included studies are summarized in Table 1. The included studies were published between 2006 and 2015, and entirely performed

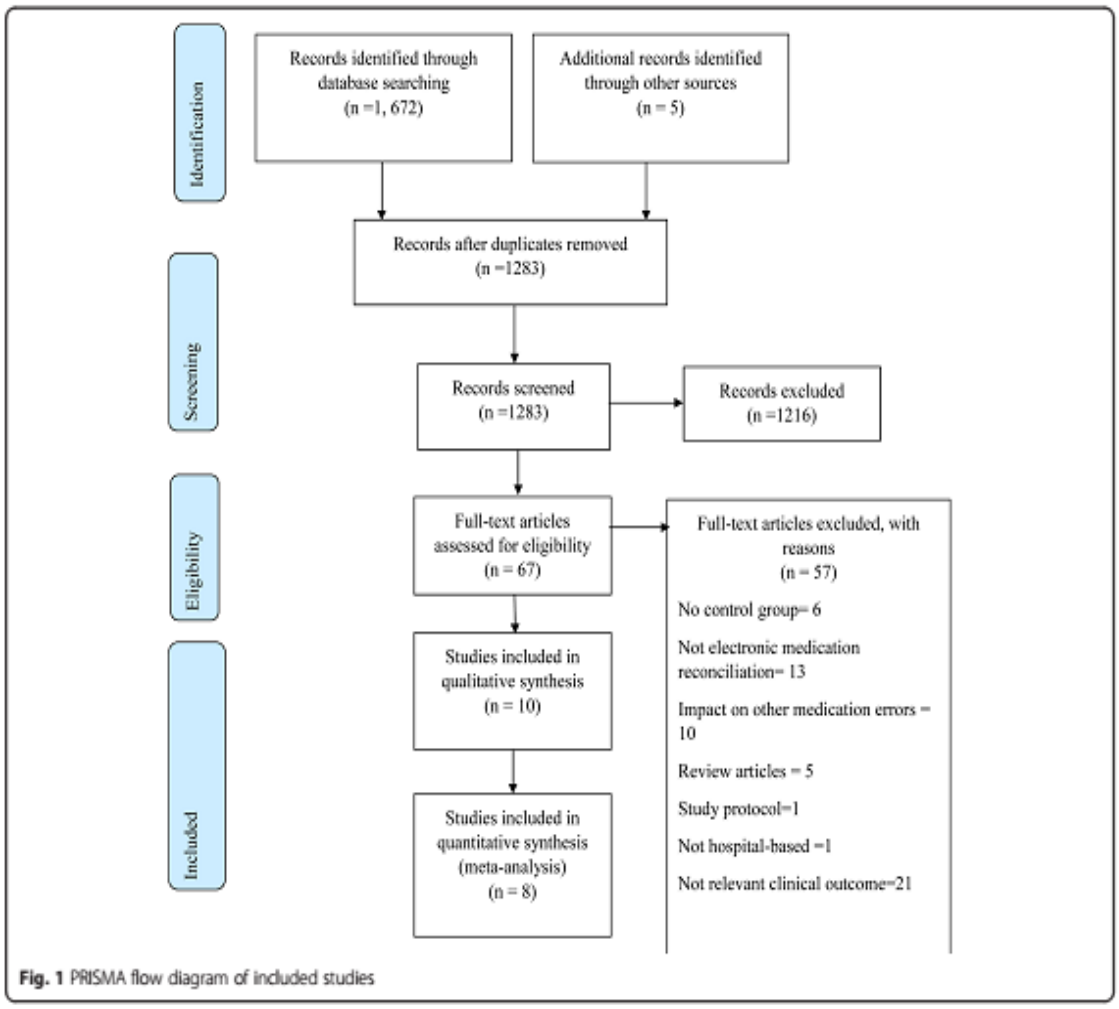

Fig. 1 PRISMA flow diagram of included studies

in the USA [35–41] and Spain [42–44]. Only one study [40] was a randomized controlled trial. The remainder were non-randomized studies, mainly employing a pre-post study design. All except one study [41] were performed in academic centres or tertiary care hospitals. Two studies [37, 40] were conducted at multiple centres. Nine of the 10 included studies involved a total of 21,486 patients of various sample sizes ranging from 100 to 19,476 patients/discharges. The length of study periods ranged from 10 to 70 weeks. The included studies were heterogeneous for interventions, outcomes, target of transitions and methods for measuring outcomes. Electronic medication reconciliation interventions were more variable with regard to the place of transition, and commenced at various points of hospital transition, such as admission [35, 37, 42–44], discharge [36, 41] and multiple transitions [38–40]. Besides the development of an electronic medication reconciliation tool, some studies utilized a multifaceted intervention, including involvement of a computerized reminder alert [35], process re-design (e.g. work-flow) and staff training [40, 44], and integration of an electronic tool with an already existing computerized physician order entry programs [40, 42, 43]. Types of medications explored for medication discrepancy were varied among the studies — for example, other than prescription medications, some studies [35, 38, 39, 44] also considered non-prescription and over-the-counter medications. Exceptionally, there was one study [36] which was specifically focused on antibiotics only. All but one study [38] clearly differentiated unintentional from intentional changes to medications from their report, or explicitly described in their methods as medication discrepancies were unintentional after clarification was sought from the medical team and/or patient. Five studies [37, 38, 42–44] evaluated both the primary and secondary outcomes. However, Schnipper et al. [40] assessed only unintentional medication discrepancies with a potential for patient harm.

Table 1 Characteristics of included studies

Author, Year	Country, Setting	Study design	Participant size	Target of transition	Components of intervention	Length of study	Medications assessed	Verification of discrepancy	Main results
Agrawal 2009 [35]	USA, Tertiary care academic hospital	Pre-post	19,476 patients	Admission	Multidisciplinary admission medication reconciliation, computerized reminder alert	17 ½ months	Prescription and non-prescription medications	Yes	At least 1 unintended discrepancy: 20 % (Pre) vs. 1.4 % (Post) Drug omission was the most common type of discrepancy in both phases
Allison 2015 [36]	USA, Academic tertiary care facility	Pre-post	200 patients	Discharge	Electronic discharge medication reconciliation, staff training	NR	Antibiotics	Yes	At least 1 antibiotic error: 23 % (Pre) vs. 11 % (Post) Percentage of medications with errors: 30 % (Pre) vs. 15 % (Post) Dosage errors were the most common type of medication error in both phases
Boockvar 2010 [37]	USA, Three academic centers	NRCT	469 patients	Nursing home to hospital transfer (admission)	Structured review	NR	Prescription medications	Yes	No difference, with and without EHR, in medication discrepancies (mean difference 0.02; 95 % CI - 0.81 to 0.85) and a high-risk discrepancies (mean difference −0.18; 95 % CI −0.22 to 0.58) per hospitalization episode, and an ADE caused by a medication discrepancy (OR 0.96; 95 % CI 0.18 to 5.01) 46 % of prescribing discrepancies resulted in ADEs were due to drug omissions
Gimeneze-Manzorro 2011 [42]	Spain, Tertiary care hospital	Pre-post	3,781 medications	Admission	Computerized reconciliation tool integrated in a CPOE program	6 months	NR	Yes	Percentage of medications with discrepancies: 7.24 % (Pre) vs. 4.18 % (Post) Drug omission was the most frequent unintended discrepancy in both phases Omission errors: 5.8 % (Pre) vs. 3.4 % (Post)
Gimeneze-Manzorro 2015 [43]	Spain, University general hospital	Pre-post	191 patients	Admission	Nurses gather BPMH via an electronic reconciliation tool, use of CPOE	6 months	Prescription medications	Yes	At least 1 unintended discrepancy: 40.2 % (Pre) vs. 38.1 % (Post) Medications with unintended discrepancies: 10.6 % (Pre) vs. 6.6 % (Post)

Table 1 Characteristics of included studies *(Continued)*

									Of all unintended discrepancies, 144 (86.2 %) were due to drug omissions Omission errors: 9.2 % (Pre) vs. 5.6 % (Post)
Kramer 2007 [38]	USA, General medical unit	Pre-post	283 patients	Admission, discharge	Pharmacists and nurses collaborated to electronically complete admission and discharge medication reconciliation, discharge medication counselling	13 months	Prescription, non-prescription and herbal supplements	No	Post-implementation, patients took significantly more prescription and nonprescription medications.
Murphy 2009 [39]	USA, Academic medical center	Pre-post	SU, 149 discharges; MU, 134 discharges	Admission, discharge	Multidisciplinary MedRec using an electronic tool	2 ½ months	Prescription and non-prescription medications	Yes	Percentage of medications with unintended discrepancies: 90 % (Pre) vs. 47 % (Post) [SU]; 57 % (Pre) vs. 33 % (Post) [MU] On the surgical unit, omitted home medications (reduced from 21 % of orders to 0 %), omitted inpatient medications (from 8 to 1 %) and in the medical unit, omitted home and inpatient medications were both reduced from 11 to 0 %.
Schnipper 2009 [40]	USA, Two academic hospitals	RCT	322 patients	Admission, discharge	IT designed MedRec integrated into the CPOE system, interdisciplinary medication reconciliation intervention comprising novel IT and process re-design, supportive roles (e.g. training)	NR	NR	Yes	Mean number of medication discrepancies with a potential for harm per patient: 1.44 (C) vs. 1.05 (I) [RR 0.72 (0.52–0.99)]
Poole 2006 [41]	USA, Community hospital	Pre-post	100 patients	Discharge	Formation of a medication list from pre-existing electronic sources and reconciliation of discharge medications with this list	6 months	prescription medications	Yes	Statistically significant improvement with intervention vs. control in at least 1 outcome in this category; i.e., drug frequency, dose and therapeutic duplication Resolution of discrepancies in frequency increased by 65 % Resolution of discrepancies in dosages improved by 60 % Resolution of therapeutic duplication was addressed in 58 % of cases

Table 1 Characteristics of included studies *(Continued)*

Zoni 2012 [44]	Spain, University general hospital	Pre-post	162 patients	Admission	IT-designed MedRec, clinical sessions and training	12 months	Regular medications, OTC and homeopathic products	Yes	Percentage of medications with unintended discrepancies:3.5 % (Pre) vs. 1.8 % (Post) At least 1 unintended discrepancy: 23.7 % (Pre) vs. 14.6 % (Post) Drug omission was the most common unintended discrepancy Omission error: 2.6 % (Post) vs. 2 % (Pre)

ADE adverse drug event, *BPMH* best possible medication history, *CPOE* computerized physician order entry, *C* control, *EHR* electronic health record, *I* intervention, *IT* information technology, *MedRec* medication reconciliation, *MU* medical unit, *NR* not reported, *OR* odds ratio, *OTC* over-the-counter, *Pre* pre-implementation, *Post* post-implementation, *RCT* randomized controlled trial, *RR* relative risk, *SU* surgical unit

Table 2 Summary of risk of bias assessment for non-randomised studies according to A Cochrane Risk of Bias Assessment Tool for Non-randomized Studies of Interventions (ACROBAT-NRSI) [33]

References	Bias due to confounding	Bias in selection of participants into the study	Bias in measurement of interventions	Bias due to departures from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result	Overall bias
Agrawal 2009 [35]	Serious	Low	Low	No information	No information	Serious	Low	Serious
Allison 2015 [36]	Low	Low	Moderate	No information	Low	Moderate	Moderate	Moderate
Boockvar 2010 [37]	Low	Moderate	Low	Moderate	No information	Moderate	Low	Moderate
Gimeneze- Manzorro 2011 [42]	Serious	No information	Low	No information	No information	Moderate	Low	Serious
Gimeneze- Manzorro 2015 [43]	Moderate	Low	Serious	No information	Moderate	Moderate	Low	Moderate
Kramer 2007 [38]	Serious	Low	Low	Moderate	No information	Serious	Serious	Serious
Murphy 2009 [39]	No information	No information	Moderate	Moderate	No information	Moderate	Moderate	Moderate
Poole 2006 [41]	No information	Moderate	Low	Low	No information	Serious	Moderate	Serious
Zoni 2012 [44]	Low	Low	Moderate	No information	Low	Moderate	Low	Moderate

Note: Risk of bias judgment was based on a scale of low, moderate, serious, critical and no information

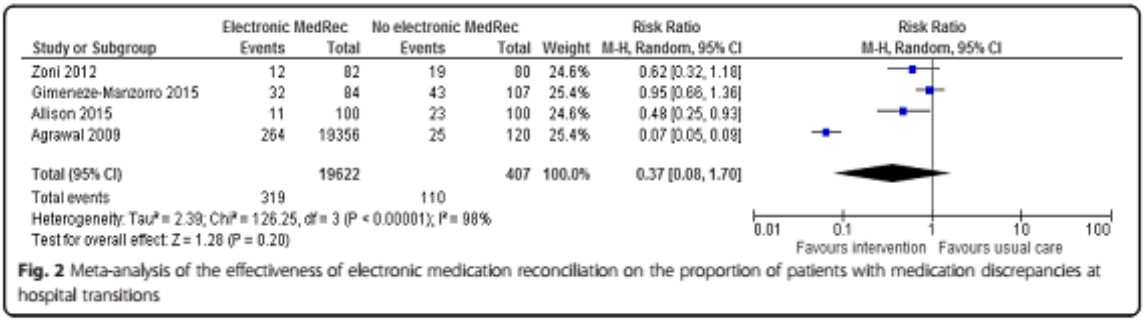

Fig. 2 Meta-analysis of the effectiveness of electronic medication reconciliation on the proportion of patients with medication discrepancies at hospital transitions

Quality of studies

The quality assessments of included studies were performed separately for randomized and non-randomized studies. Schnipper et al. [40] was the only randomized study assessed for its quality using the EPOC [32] risk of bias assessment tool. Except that the medication discrepancies were not assessed blindly, this study [40] was found to have a low risk of bias in terms of randomization, allocation concealment, baseline outcomes and characteristics, attrition, contamination and selection biases. The quality of non-randomized studies is described in Table 2. Using the ACROBAT-NSRI assessment tool, the overall bias among the studies were classified as moderate in five studies [36, 37, 39, 43, 44], whereas the remaining studies were judged to have a serious risk of bias.

Effectiveness of electronic MedRec interventions

Of the 10 studies that reported data on medication discrepancies, 8 studies targeting various transitions (admission, 5 studies; discharge, 1 study and multiple transitions, 2 studies) were included in the meta-analyses. Two studies [38, 41] did not contribute data in a suitable form for the meta-analysis. In one of these studies, [38] the aim was to evaluate the efficiency of an electronic tool in facilitating the reconciliation process, and did not specifically give data regarding the effectiveness of the intervention. A pharmacist-nurse initiated admission and discharge medication reconciliation by Kramer et al. [38] showed an improvement in medication history completeness after implementation of an electronic tool; that is, patients in the post-implementation group took significantly more prescription and non-prescription medications, and the total number of medications significantly exceeded the number taken by the pre-implementation group. Poole et al. [41] was the other study not included in the meta-analysis due to the outcomes evaluated. Poole et al. [41] demonstrated an effective computerization of the medication reconciliation process, and found an improvement in the safety of patients by minimizing medication discrepancies in frequency, dose and therapeutic duplication at the time of discharge — resolution of discrepancies increased by 65, 60 and 58 %, respectively.

Meta-analyses were performed in-terms of the proportion of patients with medication discrepancies, or as mean number of medication discrepancies per patient or incidence of medications with discrepancies over the total number of medications. Also, the most common type (s) of discrepancies were elaborated and synthesized quantitatively.

Proportion of patients with medication discrepancies

Only four studies [35, 36, 43, 44] reported the proportion of patients with at least one medication discrepancy.

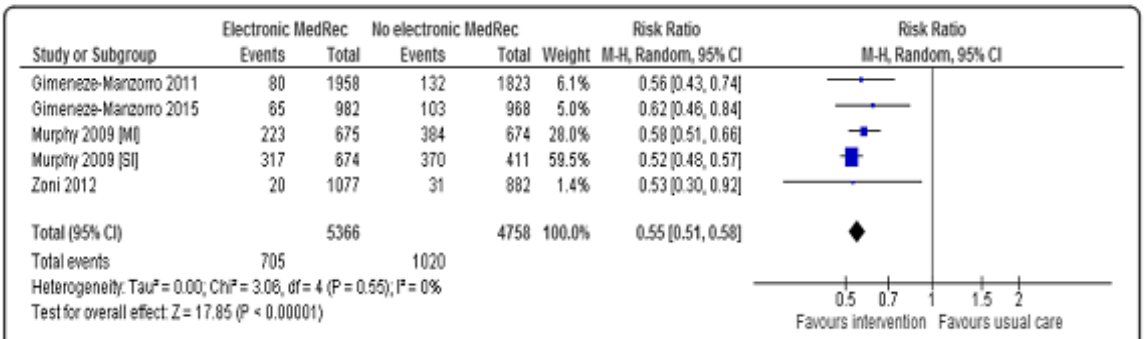

Fig. 3 Meta-analysis of the effectiveness of electronic medication reconciliation on the incidence of medications with unintentional discrepancies over the total number of medications reconciled at hospital transitions

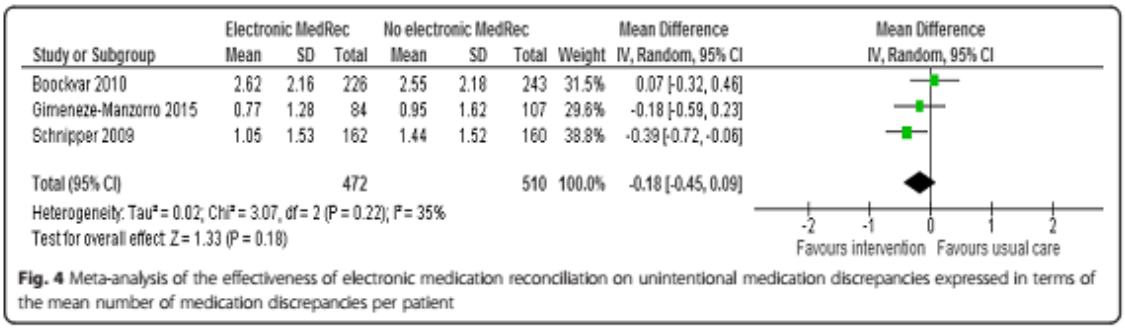

Fig. 4 Meta-analysis of the effectiveness of electronic medication reconciliation on unintentional medication discrepancies expressed in terms of the mean number of medication discrepancies per patient

Figure 2 shows the forest plot of 4 studies expressing medication discrepancies dichotomously (proportion of patients with medication discrepancies). The pooled result of such studies on this outcome showed no difference in medication discrepancies between the intervention and usual care (RR 0.37; 95 % CI 0.08 to 1.70; $p = 0.2$), and this was associated with substantial heterogeneity ($I^2 = 98$ %). However, when Agrawal et al. [35] study was removed, the sensitivity analysis showed modest heterogeneity without affecting the significance difference (RR 0.70; 95 % CI 0.46 to 1.09; $p = 0.12$, $I^2 = 48$ %).

Proportion of medications with unintended discrepancy

Four studies [39, 42–44] were able to report the incidence of unintended discrepancies over the total number of medications reconciled. One study [39] reported data for two different hospital units (surgical and medical unit) and included these data in the analysis as separate interventions. Meta-analysis of data from the five electronic medication reconciliation interventions conducted at various transitions showed a significant reduction of the incidence of medications with discrepancies in favour of the intervention (RR 0.55; 95 % CI 0.51 to 0.58; $p < 0.00001$, $I^2 = 0$ %) (Fig. 3).

Mean medication discrepancies per patient

Only three studies [37, 40, 43] reported the mean number of medication discrepancies per patient as an outcome. The pooled result for these three medication reconciliation interventions did not show a significant difference between the intervention and usual care groups (mean difference −0.18; 95 % CI −0.45 to 0.09; $p = 0.18$, $I^2 = 35$ %) (Fig. 4).

Type (s) of medication discrepancies

Seven studies [34–36, 38, 41–43] reported the most common type (s) of medication discrepancies. Except in one study [36], the most common type of medication discrepancy identified by the majority of the studies was omission error. Four studies involving five interventions gave data in terms of the percentage of omission errors over the total number of medications reconciled, and were included in the meta-analysis. Here, Murphy et al. [39] reported data for two different hospital units; i.e., surgical and medical unit, and included in the analysis as two cohorts of interventions. Two studies [35, 36] in this meta-analysis were excluded because of an absence of a common denominator in the calculation of the pooled estimate. Meta-analysis of the five interventions expressing the proportion of omission errors over the total number of medications showed a significant reduction of 80 % in favour of the intervention (RR 0.20; 95 % CI 0.06 to 0.66; $p = 0.008$, $I^2 = 96$ %) (Fig. 5). On sensitivity analysis, this effect is greatly influenced by Murphy 2009 [SI] study [39]; removal of this intervention showed a non-significant and heterogeneously distributed reduction in omission errors (RR 0.43; 95 % CI 0.17 to 1.04; $p = 0.06$, $I^2 = 91$ %).

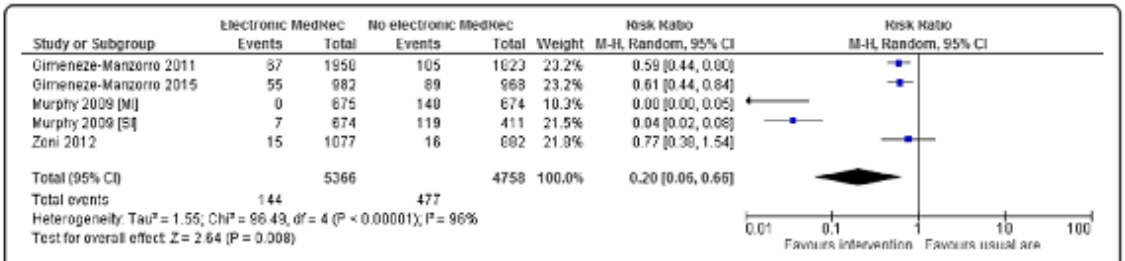

Fig. 5 Meta-analysis of the effectiveness of electronic medication reconciliation on the percentage of omission errors over the total number of medications reconciled

Clinical significance of medication discrepancies

The clinical impact of medication discrepancies was reported in five studies [37, 38, 42–44]. One study [40] reported medication discrepancies with a potential for harm only. Most of the studies described that the majority of the unintended discrepancies did not cause any harm to the patient, and were grade C in severity according to the National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) classification [45]; that is, the error reached the patient but caused no harm. Two studies reported [37, 46] actual patient harm requiring intervention or prolonged hospitalization in 7 to 55 % of medication discrepancies. One study [42] compared the incidence of severe medication errors before and after implementation of an electronic tool, and found that there was a significant reduction in severity of medication discrepancies post-implementation (5.3 % vs. 2.4 %, $p < 0.0001$). Schnipper et al. [40] showed fewer medication discrepancies with the potential to cause serious harm, such as re-hospitalization in the intervention than the usual care group, 0.27 vs. 0.34 per patient, respectively. For severity assessment, four of the five studies adopted a medication error index employed by the NCC MERP [45], and evaluators in these studies were pharmacists and medical coordinators/physicians (Table 3).

Discussion

Main findings

This systematic review on electronic medication reconciliation interventions did not identify a consistent impact in minimizing the occurrence of unintentional medication discrepancies during transitions in hospital care. Specifically, pooled estimates showed a 63 % reduction in patients with medication discrepancies; however, this was not statistically significant, nor was the mean number of medication discrepancies per patient. But, the intervention had significantly reduced the percentage of medications with unintended discrepancy and drug omissions over the total number of medications reconciled. However, it should be noted that the findings were derived from a subset of studies that reported each outcome of interest. Drug omissions were the most common types of unintended discrepancies identified through an electronic tool. The clinical importance of unintended discrepancies was evaluated in five studies. There was no potentially fatal error identified, and most errors were minor in severity.

Comparison with previous research

To the best of our knowledge, this is the first systematic review and meta-analysis that focused on the impact of electronic medication reconciliation on the rate and incidence of unintentional medication discrepancies at transitions in hospital care. Previous reviews [26, 27]

Table 3 Clinical significance of unintentional medication discrepancies

Author, year	Tool for clinical significance evaluation	Clinical judgment determined by	Results
Boockvar 2010 [37]	NCC MERP [45]	Discussion between 2 physicians or 1 physician and 1 pharmacist	46 % of prescribing discrepancies causing ADEs were asymptomatic, 52 % were associated with symptoms and 3 % caused a prolonged or an additional hospital stay.
			No prescribing discrepancies caused permanent disability or death.
Gimeneze-Manzorro 2015 [43]	NCC MERP [45]	Consensus between the pharmacist and the medical coordinator	Grade C, 79.2 %
			Grade D, 13.6 %
			Grade E, 7.1 %
Gimeneze-Manzorro 2011 [42]	NCC MERP [45]	Pharmacist discuss with medical coordinators	Most errors were grade C in severity in both phases.
			Severe errors: Pre-implementation, 96/1,823 (5.3 %); Post-implementation, 48/1,958 (2.4 %)
Kramer 2007 [38]	Nickerson et al. 2005 [48]	NR	Pre-implementation: 3 MEs (2 category B errors, 1 category C error)
			Post-implementation: 4 MEs (3 category B errors, 1 category C error)
Zoni 2012 [44]	NCC MERP [45]	Consensus between the pharmacist and the medical coordinator	Most of the unintended discrepancies would cause no harm to the patient.
			In the pre-implementation, there were 2 patients where either patient monitoring would be required or the patient would suffer temporary damage.

MEs medication errors, *NCC MERP* National Coordinating Council for Medication Error Reporting and Prevention, *NR* not reported

evaluating the importance of medication reconciliation overall had not consistently reported the effectiveness of medication reconciliation interventions. However, latest reviews regarding medication reconciliation interventions carried out through pharmacist assessment have shown an impact on some of the clinical (e.g. all-cause readmission) and process outcomes (e.g. medication discrepancies) [46, 47]. For instance, our previous study [47] showed a substantial reduction of 66 % in patients with medication discrepancies favouring pharmacy-led interventions carried out at single transitions (either admission or discharge). However, the present study showed a non-significant reduction in either of the outcomes studied; that is, the proportion of patients with medication discrepancies, or mean number of medication discrepancies per patient. Unlike the previous review [47], the present study did not differentiate effects due to place of transition, and in that study, multiple transitions interventions were less effective in reducing medication discrepancies. In the current study, there were some studies with multiple transitions included in the meta-analyses. This might have brought differences in effect and significance.

In the present study, drug omissions were the most frequent errors and this is consistent with other published works [6, 7]. It is not surprising to observe dosage errors as the commonest errors identified in a study by Alison et al. [36]; the type of medications studied for discrepancy were antibiotics, and this group of medications are mainly indicated for acute treatment of infections. As Zoni et al. [44] allude to, there exists a relationship between chronic medicines use and the occurrence of unintended discrepancy, mainly drug omissions.

This study identified only a few of the unintended discrepancies having clinical impact on patient care. However, data from previous studies [27, 46] reported more clinically important discrepancies in 28 to 91 % of medication discrepancies. This variation might be because these reviews [27, 46] largely involved multifaceted interventions, including people and technology.

Implications for practice and policy

While with information technology it is possible to share medication information and facilitate medical consultation between healthcare professionals, it has also resulted in reduction of medication errors and ADEs [28–30]. Most importantly, computerized physician order entry (CPOE) programs complemented with a medication reconciliation service might be an important approach in preventing the various types of medication errors occurred in a hospital setting. While a CPOE system would be able to fill the lack of prescriber's knowledge, it would not able to detect unintentional omission of medications the patient was taking at home during transitions in hospital care [35]. It was thus, a CPOE program paired with a medication reconciliation service might be able to bridge the gaps in continuity of patient care, and further ensures a comprehensive medication history of patients. However, careful integration of the tool is very important for successful implementation of computerized medication reconciliation services. For example, Schnipper et al. [40] has depicted differences in the extent of integration of the medication reconciliation tool into a computerized provider entry applications between hospitals, and this has brought huge differences in effect. In general, effective medication reconciliation likely requires a multifaceted approach involving people, process, technology and that technology interventions alone may not consistently reduce errors.

Strengths and limitations of the study

The main strength of this study was the exploration of the effectiveness of an electronic tool on unintentional medication discrepancies with broader inclusion criteria across a range of hospital transitions, not limited to specific transition (s). We did not select studies based on patient population (paediatric, adult) and study design. We imposed no limit on the year of publication, and we searched an extensive articles of the international literature. However, this study is not without limitations. The main limitation is that there were fewer published studies of sufficient scientific quality that adequately addressed the effects of electronic medication reconciliation on unintentional medication discrepancies. There was also heterogeneity among studies for interventions, outcomes, target of transition, study duration and methods for measuring outcomes. The number and types of medications evaluated for medication discrepancy varied among the studies. Also, the heterogeneity of the intervention needs to be considered — for example, some interventions were integrated into in an already existing computerized physician order entry programs and there were some sort of workflow redesign and staff teaching. The number and type of team who initiated an electronic interventions for medication reconciliation, and the person (s) who routinely assessed medication discrepancies were also varied. In the meta-analysis of patients with at least one discrepancy, one study of low scientific quality [35] had a great number of patients and un-proportionate sample in the intervention group and, as a result, contributed to a large extent to the pooled result and heterogeneity. The pooled estimate in this outcome did not significantly reduce the incidence of medication discrepancies and the confidence intervals crossed the line of the usual care group and were rather wide. We included only published studies in English, and the number of included studies were not enough to assess publication bias that might be arisen from language restriction and non-inclusion of non-published data.

Implications for future study

There is a lack of high-quality studies with rigorous designs that investigate the impact of electronic medication reconciliation on medication discrepancies. Additionally, it is important that future studies should assess the clinical impact of medication discrepancies for complete evaluation of the interventions. A clear separation of intentional from unintentional medication discrepancies, and further verification of the identified discrepancies from the responsible practitioner and/or team should be noted in their report. Overall, future research should be involved at more rigorous evaluations of the interventions and evaluation of commercially available electronic medication reconciliation tools, aimed at minimizing unintentional medication discrepancies at transitions in hospital care. Studies in the paediatrics population were not identified, and studies in this regard are also urgently needed.

Conclusion

Medication reconciliation supported by information technology was found to be an important tool for minimizing the percentage of medications with unintentional discrepancies over the total number of medications reconciled. Of particular note, omission errors were reduced in a great extent after the use of an electronic tool. But, implementation of an electronic medication reconciliation did not favour the intervention in other process outcomes; that is, patients with at least one medication discrepancy and mean number of medication discrepancies per patient. However, limitations in the available literature such as lack of well-designed studies precluded us from concluding that no effect exists. Careful integration of electronic interventions with other medication reconciliation components (i.e., supportive roles and processes) to improve outcomes of interest would be more appropriate.

Additional files

Additional file 1: Search strategy employed in the electronic databases search (DOCX 16 kb)

Additional file 2: The main reasons for exclusion of full-text articles (DOCX 19 kb)

Acknowledgements

We would like to acknowledge Lorraine Evison, academic liaison librarian, for helping us in the search of articles through electronic databases.

Funding

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Availability of data and materials

All relevant data are within the paper and its supporting information files.

Authors' contributions

ABM was responsible for the study conception and design under the supervision of JEB. ABM and TBA undertook literature searching, abstract and title screening and data extraction. ABM carried out the initial analysis, and drafted the first manuscript. JEB and AJM critically reviewed and revised the manuscript. All the authors have read and approved the final manuscript as submitted.

Competing interests

The authors declare that they have no competing interests.

Consent for publication

Not applicable.

Ethics approval and consent to participate

Our study is an investigation of the literature, and does not need ethical approval for retrieving the already available public content.

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Received: 17 March 2016 Accepted: 18 August 2016
Published online: 22 August 2016

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Electronic supplementary materials published online for Chapter 4 are supplied as appendices (additional file 1, page 302; additional file 2, page 306)

Chapter 5

Adverse Drug Events and Medication Errors in African Hospitals: A Systematic Review

Alemayehu B. Mekonnen, Tariq M. Alhawassi, Andrew J. McLachlan, Jo-anne E. Brien. Adverse Drug Events and Medication Errors in African Hospitals: A Systematic Review. Drugs - Real World Outcomes (2017). DOI: 10.1007/s40801-017-0125-6

Drugs - Real World Outcomes
DOI 10.1007/s40801-017-0125-6

SYSTEMATIC REVIEW

Adverse Drug Events and Medication Errors in African Hospitals: A Systematic Review

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Abstract

Background Medication errors and adverse drug events are universal problems contributing to patient harm but the magnitude of these problems in Africa remains unclear.

Objective The objective of this study was to systematically investigate the literature on the extent of medication errors and adverse drug events, and the factors contributing to medication errors in African hospitals.

Methods We searched PubMed, MEDLINE, EMBASE, Web of Science and Global Health databases from inception to 31 August, 2017 and hand searched the reference lists of included studies. Original research studies of any design published in English that investigated adverse drug events and/or medication errors in any patient population in the hospital setting in Africa were included. Descriptive statistics including median and interquartile range were presented.

Results Fifty-one studies were included; of these, 33 focused on medication errors, 15 on adverse drug events, and three studies focused on medication errors and adverse drug events. These studies were conducted in nine (of the 54) African countries. In any patient population, the median (interquartile range) percentage of patients reported to have experienced any suspected adverse drug event at hospital admission was 8.4% (4.5–20.1%), while adverse drug events causing admission were reported in 2.8% (0.7–6.4%) of patients but it was reported that a median of 43.5% (20.0–47.0%) of the adverse drug events were deemed preventable. Similarly, the median mortality rate attributed to adverse drug events was reported to be 0.1% (interquartile range 0.0–0.3%). The most commonly reported types of medication errors were prescribing errors, occurring in a median of 57.4% (interquartile range 22.8–72.8%) of all prescriptions and a median of 15.5% (interquartile range 7.5–50.6%) of the prescriptions evaluated had dosing problems. Major contributing factors for medication errors reported in these studies were individual practitioner factors (e.g. fatigue and inadequate knowledge/training) and environmental factors, such as workplace distraction and high workload.

Conclusion Medication errors in the African healthcare setting are relatively common, and the impact of adverse drug events is substantial but many are preventable. This review supports the design and implementation of preventative strategies targeting the most likely contributing factors.

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s40801-017-0125-6) contains supplementary material, which is available to authorized users.

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Published online: 14 November 2017

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Key Points

This is the first literature review of African-based studies that focuses on medication errors and adverse drug events.

There have been limited reports on medication safety in African countries in the past, but this is rapidly increasing.

Of all patients admitted to hospital, a median of 2.8% of adverse drug events resulted in hospital admission in the general population, ranging to as high as 5.5% in the adult population.

Regardless of the medication use process, dosing problems were the most commonly reported type of error.

1 Introduction

Quality patient care is a priority in all healthcare systems; however, patient safety can be compromised leading to potential medical harms [1]. Patient safety has been a growing priority led by pioneer US studies: the Harvard Medical Practice Study [2, 3] and the Institute of Medicine Report [4]. In USA, it has been reported that 3.7% of all hospitalised patients experienced an adverse event [2], and preventable adverse drug events (ADEs) alone resulted in 7000 deaths annually [4]. Despite developments in healthcare, these incidents continue to pose a significant problem globally [5, 6] and remain a concern for consumers, many practitioners and patient safety advocates.

Patient safety is a human rights issue and a subject matter increasingly researched in many developed countries [7]. However, in the absence of comprehensive healthcare coverage in the developing countries of Africa, assuring patient safety remains a considerable challenge when countries strive to provide quality patient care. According to the United Nations [8], Africa consists of 54 fully recognised member states with a current population of approximately 1 billion, and more than 40% of the population in the sub-Saharan Africa is in extreme poverty [9]. The average health expenditure per person in sub-Saharan Africa countries is below US$100 per annum compared with US$6110 in Australia and US$9146 in USA [10]. Healthcare systems in Africa face severe health threats in the context of scarce resources and underdeveloped healthcare infrastructure, and the spectrum of patient safety problems in this continent is unique in that most countries lack integrated automated health systems to support patient care [11].

Patient injuries attributed to medication misadventures, including medication errors (MEs) and ADEs, are among the most common incidents in hospitals [2] and have important clinical, economic and social consequences. For example, a review of Australian [12] medication safety literature in 2003 showed that 2–4% of all hospital admissions are thought to be medication related. An updated review in 2009 [13] consistently reported a similar burden of medication-related morbidity costing the Australian healthcare system US$660 million annually. However, given the distinct nature of the morbidity profile and drug utilisation pattern, and the level of awareness and patient safety culture, the burden of medication-related problems cannot be extrapolated for areas of poverty in Africa [11].

While there have been many previous reviews of the literature related to the burden of MEs and ADEs in the hospital setting [14–23], most of these reviews have included few or no African studies. There has been no systematic review that broadly assessed the burden of MEs and ADEs in African hospitals. Therefore, the aims of this study were to review the available African-based literature with a focus on: (1) the epidemiology of ADE-related mortality and morbidity; (2) the causality, severity and preventability of ADEs; (3) the magnitude and types of MEs, and their clinical significance, and (4) the main factors reported to contribute to MEs in these studies.

2 Methods

2.1 Definitions

This study adopted the definition of 'medication error' approved by the National Coordinating Council for Medication Error Reporting and Prevention [24]: "a medication error is any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient or consumer". Medication errors can occur at any stage of the medication use process, including product labelling, packaging and monitoring. However, this study specifically targets errors occurred at the ordering, transcribing, dispensing and administration stages, and during medication history taking. Various definitions pertaining to each of the ME types are well documented in the international literature [15, 17, 20, 21]. We, thus, solely classified studies based on the stage of the medication use process in which an error occurred. The definition of ADE employed in this study was "any injury resulting from medical

interventions related to a drug," and included both adverse drug reactions (ADRs), in which harm occurs as a result of the intrinsic nature of a medication, as well as complications from MEs [25]. The World Health Organization (WHO) definition of ADR is "a response to a drug which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis or therapy" [26]. An injury that is the result of ME is classified as a preventable ADE whereas a non-preventable ADE (also known as an ADR) is an injury other than an error, for example, the occurrence of anaphylactic reactions in a patient with no known previous history of a drug allergy [25]. Another closely related terminology used in pharmacovigilance and epidemiology studies is an adverse event. It generally refers to an unintended injury occurring during medical management, but which does not necessarily have a causal relation to the drug, such as delayed or improper diagnosis [1, 2].

2.2 Data Sources and Searches

This study used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines in reporting the results [27]. A systematic literature search was conducted using five electronic databases from inception to 31 August, 2017: PubMed (1946), MEDLINE (1946), EMBASE (1966), Web of Science (1864) and Global Health (1910). We categorised the search terms into three key concepts and combined them using the AND Boolean operator [Appendix S1 of the Electronic Supplementary Material (ESM)]. No year of publication was imposed on the search strategy but was limited to the English language. In some databases, a database-specific limitation was employed as in the Web of Science where article searching was limited to the health sciences field, and abstract availability was considered in the EMBASE and PubMed databases. Additionally, articles were identified by hand searching the bibliographies of included studies, and contact with local medication safety experts was made to identify other relevant published articles. One reviewer (ABM) with the support of a medical librarian carried out the literature search.

2.3 Study Selection

The lead author (ABM) screened the titles and abstracts of retrieved studies and evaluated against the inclusion and exclusion criteria. Selected abstracts then underwent full-text screening. The full texts of studies that were potentially eligible were evaluated by the same primary reviewer, and then the final inclusion was agreed on by two of the authors (AJM, JEB).

2.3.1 Inclusion Criteria

We included peer-reviewed original published articles, irrespective of the study design, that investigated the frequency and nature of MEs and/or ADEs. We did not set any limitations on how ME types had been defined in the original research studies. Similarly, the types of events included were overlooked as far as the working definition remained the same, such events range from ADRs to ADEs. Studies that addressed adverse events were included only if injuries due to medications were reported, and data related to these were extracted. The primary outcome of interest was the frequency of MEs (expressed in terms of the number of prescriptions/medication orders/observations with MEs of any type) and/or the proportion of patients who experienced an ADE as a cause for admission or occurred during hospitalisation. Secondary outcomes of interest included an assessment of the nature of ADEs (e.g. fatality and preventability) and MEs (e.g. clinical significance). As we sought to evaluate the African medication safety literature broadly, we also included studies that assessed healthcare professionals' experiences, possible causes of MEs as reported by the original studies. We placed no restriction on the target population, but studies should be carried out in an African hospital setting.

2.3.2 Exclusion Criteria

Studies that investigated failures in optimising drug therapy (e.g. drug dosage adjustment in patients with renal failure), pharmaceutical issues (e.g. counterfeit or sub-standard medicines), events caused by single drugs or drug classes (e.g. co-trimoxazole, Antiretrovirals) or disease condition (e.g. human immunodeficiency virus/acquired immunodeficiency syndrome, diabetes mellitus), and studies that aimed to assess knowledge and attitude to ADR reporting were excluded. In addition, studies evaluating non-adherence to medication or self-harm (intentional toxicity) were excluded. Conference abstracts, case studies, commentaries and reviews were not considered in this review.

2.4 Quality Assessment

While there are limited approaches for appraising observational studies of ADEs, we assessed such studies for their quality. One review author (ABM) assessed all ADE studies for their methodological quality based on the ten criteria used by Smyth et al. [28]. The main domains considered were study design, methods for identifying ADEs, methods used to establish the causal relationship between drug and effect, and tools for assessing the preventability and severity of ADEs. The quality of ME

studies was evaluated and reviewed according to the 13 criteria adopted from the previous two studies [20, 29]. Criteria were graded as yes, no, unclear or not reported.

2.5 Data Extraction and Statistical Analysis

Data abstraction was performed using a standardised data collection tool, which included study characteristics (publication details, African country, hospital setting, study design, sample size and duration of the study, target population), identification of ADEs and/or MEs (definition, method of data collection, information relating to assessment of causality, severity and preventability) and major findings (the frequency and clinical impact of MEs of any type, prevalence data on ADEs causing admission and occurring in the hospital, including clinical severity and preventability). In studies presenting adverse event data, only data for events due to medications (e.g. drug-related complications and therapeutic errors) were extracted. The most common factors contributing to MEs as reported by the included studies were also extracted.

Adverse drug event studies were reported according to the patient population (paediatric, all ages or adult), and the types of MEs were stratified into sub-categories (prescribing, administration, mixed). We used the term ADE consistently; however, some of the studies provided ADR data. The included studies were heterogeneous, and a meta-analysis was not conducted. However, it was possible to analyse the frequency of ADEs and MEs through calculation of the median occurrence rates and interquartile ranges (IQRs) across studies. For ease of median (IQR) calculation and comparison across the studies, data extracted from the included studies had been converted into a common denominator.

3 Results

3.1 Search Results

The literature search identified a total of 1316 citations, which included 38 articles identified by hand searching articles (Fig. 1). After removing duplicate citations, title and abstract screening were applied on 1112 articles; of which, 136 were selected for full-text review. Fifty-one articles were finally identified for inclusion in the study (Fig. 1). The most common reasons for excluding articles after the full-text review were ADE prevalence data from specific diseases and/or drugs or classes of drugs, and studies that assessed knowledge and attitude of healthcare professionals for ADR reporting (Appendix S2 of the ESM). Of the 51 studies, 15 reported on ADEs [30–44], 33 reported on MEs (of any type) [45–77], and three studies reported on ADEs and MEs [78–80]. The 51 studies were from nine (of the 54) African countries: Nigeria (16), South Africa (11), Ethiopia (9), Egypt (6), Morocco (3), Ghana and Uganda (each 2), and Sudan and Tunisia (each 1) (Fig. 2).

3.2 Characteristics of Adverse Drug Event Studies

Of the 18 included studies investigating ADEs, six were conducted in South Africa and were published between 1979 and 2017. Eleven of the 18 studies were prospective studies, and one was mixed (retrospective and prospective), whereas the remainder were retrospective or cross-sectional studies. A total number of 16,080 patients (excluding mutual patients from Mouton et al. [40] study) were evaluated for ADEs in these studies, mostly in the adult patient population. Four studies [33, 41, 42, 79] clearly reported ADE data for paediatric patients. Female patients comprised 52.2% of the population (8097/16,080). Studies varied in their duration from 5 days to 3 years, and most studies [30, 32, 36, 38–40, 44] were exclusively conducted in the general medical wards (Table 1).

3.2.1 Quality Assessment of Adverse Drug Event Studies

Using the assessment criteria adopted from Smyth et al. [28], the quality of ADE studies was evaluated. Four studies [33, 34, 40, 42] met all the ten criteria (Appendix S3 of the ESM). All included ADE studies clearly defined their study design. A variety of methods were used to detect ADEs. The most common method was medical record review [30, 33–40, 44, 79, 80]. Ten studies [33, 34, 36, 39, 40, 42, 44, 78–80] used a multifaceted approach for identification of ADEs: a medical record review in combination with other methods, such as voluntary reports, participation in clinical rounds, patient/carrier interview and prescription/laboratory data review. The reported assessment of ADEs with respect to causality, severity and preventability varied among the studies. Causality assessment was described in 15 studies, mostly using the WHO definition [85, 88] (four studies). Severity was measured in 13 studies, mostly using the WHO criteria [82] (three studies) and the same number of studies assessed preventability, predominantly using the Schumock and Thornton method [83] (eight studies) (Table 1). All but three studies [30, 32, 36] provided information about the person responsible for the investigation of the initial ADE detection. Usually a team of physicians, nurses and pharmacists was involved. Verification of the identified ADEs was addressed in eight studies [33–35, 37–41]. The WHO definition [26, 89] of ADRs had been adopted in the majority of studies [31, 34, 38, 41, 42, 44], but two studies [30, 36] did not

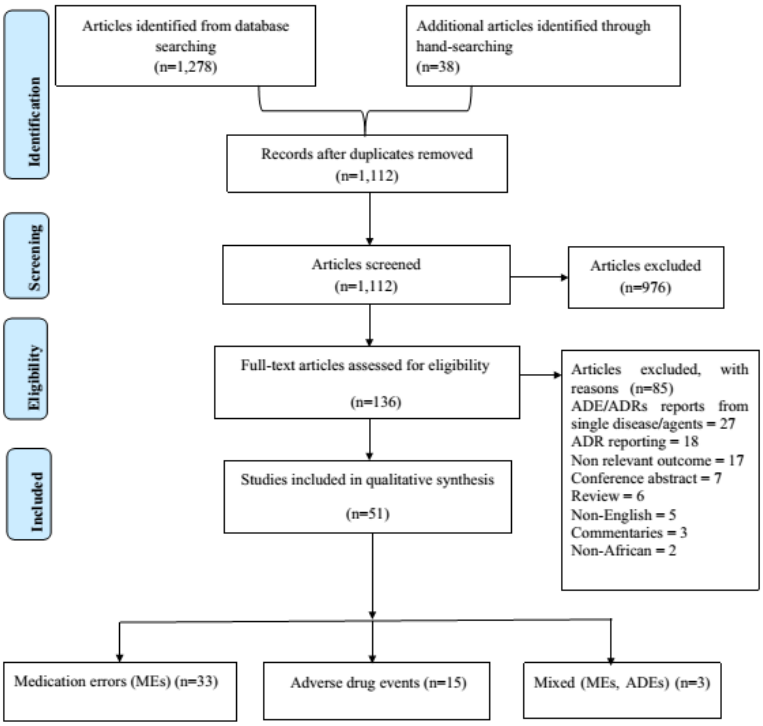

Fig. 1 Preferred reporting items for systematic reviews and meta-analyses flow diagram of the selection of eligible studies. *ADR* adverse drug reaction

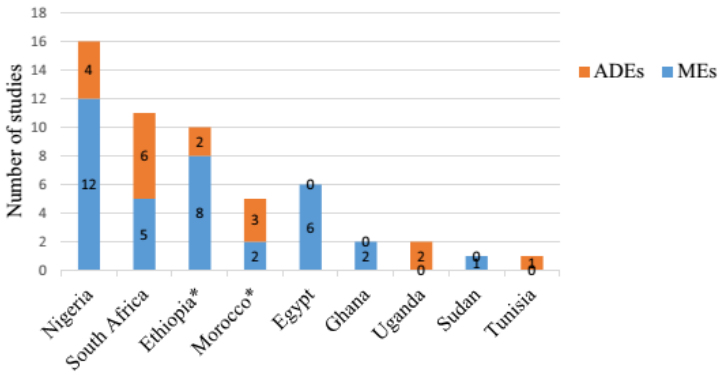

Fig. 2 Graph showing origin of included studies. * one study from Ethiopia and two studies from Morocco gave data for both adverse drug events (ADEs) and medication errors (MEs), and counted as independent studies in this figure

explicitly state the description of an incident (Appendix S4 of the ESM).

3.2.2 *Frequency and Nature of Adverse Drug Events*

3.2.2.1 Adverse Drug Events Causing Hospital Admissions A total of 11 studies [30–33, 36, 38, 40–44] involving 12,903 patients reported the number of patients for which an ADE was the primary reason for hospitalisation. Of these studies, three targeted the paediatric population only [33, 41, 42]. In any patient population, the percentage of patients who were admitted as a direct cause of ADEs and not another condition, varied from 0.4% [41] to 14.3% [43]. The overall median ADE prevalence showed that 2.8% (IQR: 0.7–6.4%) of patients were admitted in African hospitals as a result of ADEs (Table 2).

Table 1 Characteristics of adverse drug event (ADE) studies carried out in African hospitals

Author, year	Country	Setting	Study design	Sample size (patients), duration	Characteristics of the population	Method of detection	Assessment of ADEs		
							Causality	Severity	Preventability
Aderemi-Williams, 2015 [30]	Nigeria	Medical ward	Retrospective chart review	624, NR	Adult Male: 57.4%	Medical record review	NR	NR	NR
Benkirane, 2009 [31]	Morocco	Medical, surgical, ICUs and EDs	Retrospective cross-sectional	1390, 5 days	Adult and paediatric Male: 60%	Solicited information from clinicians	Begaud 1985 [81]	WHO [82]	Schumock 1992 [83]
Benkirane, 2009 [78]	Morocco	ICU	Prospective cohort	696, 3 months	Adult and paediatric Male: 54.6%	Daily physician rounds, monitoring for medication ordering and transcribing, solicited reports from health professionals	Begaud 1985 [81]	WHO [82]	Consensus agreement
Cooke, 1985 [32]	South Africa	Medical ward	Prospective observational	300, NR	Age ≥10 years Male: 50%	NR	Trunet 1980 [84]	NR	NR
Eshetie, 2015 [33]	Ethiopia	Paediatric ward	Prospective observational	600, 2 months	Paediatric Male: 61.8%	Chart review, ward round, patient/caregiver interview, voluntary staff report	WHO-UMC [85]	NCC MERP [24]	Schumock 1992 [83]
Dedefo, 2016 [79]	Ethiopia	Paediatric ward	Prospective observational	233, 1 month	Paediatric Male: 63.9%	Chart review, ward round, patient/caregiver interview, voluntary report	Naranjo [86]	NCC MERP [24]	Consensus agreement
Jennane, 2011 [80][a]	Morocco	ICU	Prospective cohort	63, 6 weeks	Adult Male: 59%	Clinical round, voluntary and verbal report, chart review, assessing prescriptions and transcriptions	NR	WHO [82]	NR
Kiguba, 2017 [34]	Uganda	Medical and gynaecological wards	Prospective cohort	762, 5 months	Adult Female: 70%	Clinical examination, medical record review, patient/caregiver/ward staff interviews	Naranjo [86]	DAIDS AE Grading Table [87]	Schumock 1992 [83]
Letaief, 2010 [35][b]	Tunisia	Clinical departments	Retrospective cohort	620, NR	General population Female: 53.4%	Medical record review	Wilson 1995 [88]	Wilson 1995 [88]	Wilson 1995 [88]
Mabadeje, 1979 [36]	Nigeria	Medical wards	Prospective cohort	360, 4 months	General population Male: 54%	Medication history interview, review of the nurses' records and hand-over notes	NR	NR	NR
Matsaseng, 2005 [37]	South Africa	Gynaecology ward	Retrospective chart review	793, 9 months	NR, all female	Medical record review	Leappe 1991 [3]	Brennan 1991 [2]	Leappe 1991 [3]
Mehta, 2008 [38]	South Africa	Medical wards	Prospective observational	665, 3 months	Adults Female: 51%	Medical record review	WHO [89]	Temple 2004 [90]	Schumock 1992 [83]
Mouton, 2015 [39]	South Africa	Medical wards	Cross-sectional survey	1904, 30 days	Adult Female: 56%	Medical record review, medication history, review of prescriptions and laboratory data	WHO-UMC [85]	NA	Schumock 1992 [83]

Table 1 continued

Author, year	Country	Setting	Study design	Sample size (patients), duration	Characteristics of the population	Method of detection	Assessment of ADEs		
							Causality	Severity	Preventability
Mouton, 2016 [40][c]	South Africa	Medical wards	Cross-sectional survey	1904, 30 days	Adult Female: 56%	Medical record review, medication history and review of laboratory data	WHO-UMC [85]	Temple 2004 [89]	Schumock 1992 [83]
Oshikoya, 2007 [41]	Nigeria	Paediatric ward	Retrospective prospective	3821, 3 years	Paediatric Male: 58%	Medical and nursing record review, prescription chart review	Jones 1982 [91]	Martínez-Mir 1996 [92]	Done, but not clear
Oshikoya, 2011 [42]	Nigeria	Paediatric ward	Prospective observational	2004, 18 months	Paediatric Male: 61%	Medical and nursing records review, review of prescription charts, attending clinical rounds, reports from healthcare professionals	Jones 1982 [91]	Schirm 2004 [93]	Schumock 1992 [83]
Tipping, 2006 [43]	South Africa	Emergency unit	Prospective cross-sectional	517, 4 months	Elderly Female: 59%	Primary physician and/or principal investigator assessment	Nebeker 2004 [94]	NR	NR
Tumwikirize, 2011 [44]	Uganda	Medical wards	Longitudinal observational	728, 6 months	Age > 13 years Female: 56%	History and physical examination, medical record review	Naranjo [86]	Dorman 2000 [95]	Schumock 1992 [83]

AE adverse event, DAIDS Division of AIDS, *ED* emergency department, *ICU* intensive care unit, *IQR* interquartile range, *NCCMERP* National Coordinating Council for Medication Error Reporting and Prevention, *NA* not applied, *NR* not reported, *WHO* World Health Organization, *WHO-UMC* World Health Organization-Uppsala Monitoring Centre

[a] Non-preventable ADEs [also called adverse drug reactions] were not collected

[b] Letaife [35] did not provide separate data for ADEs

[c] Mouton [40] used the same groups of patients as with Mouton [39], with a different outcome of interest

Table 2 Frequency, seriousness and preventability of adverse drug events (ADEs) in African hospitals

Author, year	Prevalence of ADE-related admission (%)[b]	Incidence of ADEs during hospitalisation (%)[b]	Prevalence of any suspected ADE (%)[b]	Proportion of serious ADEs (%)[c]	ADE-related fatality (%)[b]	Preventability (%)[c]
Aderemi-Williams, 2015 [30]	6.4	4.3				
Benkirane, 2009 [31]	1.4	4.2		47.5	0.1	13.2
Benkirane, 2009 [78]		11.5		51.8	0.3	30.0
Cooke, 1985 [32]	4.6					
Eshetie, 2015 [33]	0.7[a]	7.7[a]		9.0	0.2	33.0
Dedefo, 2016 [79]		7.3		5.9	0.0	47.0
Jennane, 2011 [80]		12.7		87.5	3.2	
Kigbua, 2017 [34]		25.0		31.0	0.0	55.0
Letaief, 2010 [35]		2.7[a]		NS	NS	NS
Mabadeje, 1979 [36]	2.8	13.1				
Matsaseng, 2005 [37]		9.8[a]		NS	NS	NS
Mehta, 2008 [38]	6.3	6.3	8.4	50.4[a]	0.3[a]	46.0
Mouton, 2015 [39]					2.9	43.5
Mouton, 2016 [40]	8.5[a]			23.5	[d]	45.0
Oshikoya, 2007 [41]	0.4	0.7		SG	0.1	97.7
Oshikoya, 2011 [42]	0.6	1.1		SG	0.1	20.0
Tipping, 2006 [43]	14.3[a]		20.1			
Tumwikirize, 2011 [44]	1.5	49.5	4.5	0.0	0.0	4.1
Median (IQR)	2.8 (0.7–6.4)	7.5 (4.3–16.1)	8.4 (4.5–20.1)	23.5 (9.0–50.0)	0.1 (0.0–0.3)	43.5 (20.0–47.0)

IQR interquartile range, *NS* no specific data available, *SG* only severity grading reported

[a] Not provided directly in the study, interpreted from other presented data

[b] The total number of patients was used as a denominator in the respective studies

[c] The total number of reported ADEs was used as a denominator in the respective studies

[d] Mortality data from the Mouton et al. study [40] were already used in the calculation of the mortality rate by their previous study [39] and are not presented here

After the exclusion of studies that reported data on the paediatric population only, the median prevalence estimate was found to be 5.5% (IQR: 1.8–8.0%).

3.2.2.2 Any Suspected Adverse Drug Events at Hospital Admission Three studies [38, 43, 44] estimated the percentage of patients experiencing any ADEs, which may or may not be the cause for hospitalisation, at the time of hospital admission. Of the total 1900 patients evaluated for any suspected ADEs at hospital admission, at least one ADE was identified in 192 patients, and the overall median prevalence of any suspected ADEs in these studies was 8.4% (IQR: 4.5–20.1%) (Table 2).

3.2.2.3 Adverse Drug Events during Hospitalisation No separate ADE data were reported in one study [35]; the aim was not primarily an assessment of ADEs. Fourteen studies [30, 31, 33–38, 41, 42, 44, 78–80] reported the occurrence of ADEs during hospitalisation. The percentage of patients who developed at least one ADE during a hospital stay ranged from 0.7% [41] to 49.5% [44], with an overall median incidence of 7.5% (IQR: 3.8–12.8%) (Table 2). After the exclusion of studies carried out solely on the paediatric population, the median percentage for this outcome was reported to be 10.7% (IQR: 4.3–16.1%).

3.2.3 Severity and Seriousness of Adverse Drug Events

Thirteen studies [31, 33–35, 37, 38, 40–42, 44, 78–80] assessed the seriousness and/or severity of an ADE; however, data for two studies [35, 37] were not available as ADE-specific data were not provided. Assessment of clinical severity varied among the included studies, and one study [34] clearly made a distinction between severity and seriousness measurement, and two studies [41, 42] reported the severity of ADEs only. Many studies (9/13) reported the seriousness of ADEs, but this was also assessed variably, and thus, for ease of analysis, we broadly classified serious ADEs (like Symth et al. [28] did) as those that caused either death or were life threatening, resulted in

permanent disability or hospital admission or prolonged hospitalisation. Of the 9 studies, one study [44] did not report serious events during admission and/or hospitalisation, and the remainder included serious ADEs of various rates: 5.9% [79] to 87.5% [80] of all ADEs. The median proportion of serious ADEs reported by all the nine studies was 31.0% (IQR: 7.5–51.1%) of all ADEs (Table 2). The median occurrence of serious ADEs, when paediatric-only studies were excluded, was found to be 47.5% (IQR: 23.5–51.8%).

Only one study from South Africa [39] entirely focused on mortality associated with ADRs, investigating the proportion of deaths attributed to ADRs in medical in-patients at four hospitals through a review of medical notes, medication exposure (during the previous 30 days) and laboratory data. This study estimated that ADEs contributed to the death of 2.9% of hospital admissions, and 16% of all hospital deaths were attributed to ADEs [39]. In the remainder of studies, the mortality rate associated with ADEs was reported as a secondary outcome of interest. In general, no fatal ADEs were reported in three studies [34, 44, 79], and nine studies [31, 33, 38–42, 78, 80] reported fatal ADEs in 68 of 12,866 patients included in the analysis. In the general population, the median mortality rate attributed to ADEs was estimated to be 0.1% (IQR: 0.0–0.3%) (Table 2). However, when the paediatric data were excluded, deaths associated with ADEs was reported in a median of 0.3% (IQR: 0.0–2.9%) of all patients.

3.2.4 Preventability of Adverse Drug Events

Thirteen studies [31, 33–35, 37–42, 44, 78, 79] performed a preventability assessment for ADEs describing a variable preventability of 4% [44] to 97.7% [41] of all events. However, data for Letaief et al. [35] and Matsaseng and Moodley [37] were not available as ADE-specific data could not be extracted, but showed a preventability of 60 and 55%, respectively, in the overall incidence of adverse events. The median percentage of preventable ADEs reported by all the remaining 11 studies was 43.5% (IQR: 20.0–47.0%) of all ADEs (Table 2).

3.3 Characteristics of Medication Error Studies

Of all the 36 ME studies (including those evaluated both MEs and ADEs), ten studies did not specify the type of MEs; 14 studies evaluated medication administration errors and 12 studies assessed prescribing errors. No studies were identified that specifically reported transcribing errors, dispensing errors and medication history errors. Most studies (12/36) were conducted in Nigeria and 8 studies [55, 60, 62, 67–69, 74, 78] were conducted in a multicentre setting. Five studies [50, 52, 56, 65, 79] were solely conducted in a paediatric ward and one study [73] in an obstetric ward. Two pre-post studies were identified [49, 50], and the remaining were either observational studies (prospective or retrospective) or quantitative/qualitative surveys. Of these, eight questionnaire-based studies and two mixed-method studies were identified (six administration errors, three prescribing errors, one mixed error) to evaluate MEs reported by various healthcare professionals (Table 3).

3.3.1 Quality Assessment of Medication Error Studies

After the application of the quality assessment criteria against ME studies, criteria appropriate for any ME study, no study met all the 13 criteria. One study (each) fulfilled 12 and ten criteria, 2 studies met 9 criteria and 8 studies met eight criteria. The remaining studies met seven or fewer criteria (Appendix S3 of the ESM). The type of MEs was not specified in ten studies, and various definitions for ME were used in the included studies (Appendix S4 of the ESM). Eleven studies did not describe adequate details of MEs, and studies differed in methods for identifying MEs. The majority of the studies employed a prescription review (to identify prescribing errors) and observations (for assessing medication administration errors) but one study [61] did not explicitly report the method of error detection (Table 3).

3.3.2 Frequency and Nature of Medication Errors

3.3.2.1 Medication Errors (Mixed) All but one study [74] that assessed MEs of any type were able to report details of the error rate. However, these data were difficult to summarise as error rates were presented in different ways. For example, MEs were reported in 75% [79] to 97% of patients [76], 10–54.8% of medication orders [72, 80], 4.2% of prescriptions [73] and 2.9% of medication doses [75]. Additionally, the incidence of MEs were reported in 7.5–7.8 per 100 admissions [78, 80], 7.7–9.7 per 1000 patient-days [78, 80] and 40.5 per 100 person-years [71]. Six studies [73, 75, 77–80] explicitly described the stage at which errors were occurred in the medication use process. Most errors were identified during prescribing, median (IQR): 41.3% (26.8–58.3%) [73, 75, 77–80] followed by the administration stage, median (IQR): 20.6% (12.5–41.6%) [73, 75, 77–80] and then the monitoring stage, median (range) 16.7% (8.4–25.0%) [77, 79].

3.3.2.2 Prescribing Errors Studies that addressed prescribing errors reported a median error rate of 57.4% (IQR: 22.8–72.8%) of all prescriptions [45, 51, 52, 54] and 40.0% (IQR: 8.8–49.5%) of medication orders [46, 49, 53, 54, 56] (Fig. 3).

Table 3 Characteristics of medication error (ME) studies carried out in African hospitals

Author, year	Country	Setting	Study design	Sample (e.g. no. of patients or prescriptions/ charts), duration	Characteristics of sample	Method of data collection	Clinical significance assessment (yes/no, tool)	Results
Prescribing errors								
Agalu, 2011 [45]	Ethiopia	ICU, tertiary hospital	Cross-sectional	69 patients (398 prescriptions), 67 days	General population Female: 55.6%	Prescription review	NR	52.5% of prescriptions contain at least 1 error
Ajemigbitse, 2013 [46]	Nigeria	Medical and paediatric specialties, tertiary hospital	Retrospective	400 patients (6819 medication orders), 1 year	General population Female: 76.5%	Review of medication records	Yes, Dornan 2009 [96]	40.9% of medication orders have errors
Ajemigbitse, 2013 [47]	Nigeria	Medical, paediatric and private wing wards	Prospective qualitative (mixed)	37 doctors, 6 months	NR	Prescription review and interview of prescribers	NR	90 errors are committed by 37 doctors
Ajemigbitse, 2014 [48]	Nigeria	Tertiary hospital	Questionnaire	30 doctors, 3 months	NR	Structured questionnaire	NR	One quarter of respondents failed to check prescriptions with a reference source and drug interactions
Ajemigbitse, 2016 [49]	Nigeria	Medical and paediatric wards	Pre-post	Baseline (control): 2065 medication orders, 6 months	NR	Prescription review	NR	Baseline prescribing error rate, 270/2065 (13.08%)
Alagha, 2011 [50]	Egypt	Paediatric ward, university hospital	Pre-post	Pre: 139 patients (1417 medication orders) Post: 101 patients (1096 medication orders), 10 months	Paediatric population	Educational sessions, provision of drug use assists, designing a medication order chart, physician feedback	Yes, own tool	78% of orders have least 1 error
Arulogun, 2011 [51]	Nigeria	Four units (medical out-patient, general out-patient, wards, accident and emergency)	Cross-sectional (mixed)	1866 prescriptions, NR	NR	Prescription review, observation and in-depth interview	NR	Prescription error rate, 76.3%
Oshikoya, 2007 [52]	Nigeria	Paediatric outpatient department, university teaching hospital	Retrospective	1944 prescriptions, 5 months	NR	Prescriptions review	NR	Prescription error rate, 62.2%

Table 3 continued

Author, year	Country	Setting	Study design	Sample (e.g. no. of patients or prescriptions/ charts), duration	Characteristics of sample	Method of data collection	Clinical significance assessment (yes/no, tool)	Results
Sada, 2015 [53]	Ethiopia	ICU of a specialised hospital	Retrospective	220 charts (882 prescription episodes), 1 year	Age >12 years Male: 54.5%	Chart review	Yes, Bates 1995 [25]	Prevalence of 40 errors per 100 orders (359 MEs)
Yinusa, 2004 [54]	Nigeria	Orthopaedic hospital	Retrospective	5823 prescriptions/ 13,833 items, 3 months	NR	Prescription review	Yes, Neville 1989 [97]	749 prescriptions (12.9%) contained errors; 4.5% of the prescription items have at least 1 error
Yousif, 2011 [55]	Sudan	Multicentre (public and private hospitals and pharmacies)	Cross-sectional	2000 prescriptions, 9 months	NR	Prescription review	Yes, Neville 1989 [97]	Only 1 prescription was considered ideal with no error; 12.2% of the prescriptions contained potentially serious errors
Zeleke, 2014 [56]	Ethiopia	Paediatric ward, referral hospital	Cross-sectional	136 admissions (384 medication orders), 1 month	Paediatric population Male: 61.8%	Prescription review	NR	Prescribing error rate, 58.07%; 34.70 prescribing errors in 100 patient-days
Medication administration errors								
Acheampong, 2016 [57]	Ghana	Adult ED, tertiary care hospital	Cross-sectional observational	338 patients (1332 medication administration observations), 4 months	Adult population Female: 55.9%	Direct observations of medication administration, medication order review	Yes, Chua [98]	27.2% of all observations have MAEs but 22.8% when wrong time error is excluded
Agalu, 2012 [58]	Ethiopia	ICU, specialised teaching hospital	Prospective cross-sectional	54 patients (1200 medication administration observations), 6 weeks	General population Female: 55.6%	Direct observation and review of medication charts	NR	51.8% of all observations have MAEs
al Tehewy, 2016 [59]	Egypt	Medical wards	Descriptive observational	237 patients (2400 medication administration observations), 3 months	Adult population Male: 60.8%	Direct observation	Yes, NCC MERP [24]	85% of the observations had at least 1 error
Amponsah, 2016 [60]	Ghana	Anaesthetic practice (national study)	Questionnaire	164 physician assistants, NR	Physician assistants Male: 62.2%	Self-reporting survey	Yes, self-report	65.5% of respondents had experienced MEs

Table 3 continued

Author, year	Country	Setting	Study design	Sample (e.g. no. of patients or prescriptions/ charts), duration	Characteristics of sample	Method of data collection	Clinical significance assessment (yes/no, tool)	Results
Amucheazi, 2009 [61]	Nigeria	University teaching hospital	Retrospective	895 elective procedures, NR	NR	NR	NR	5 patients (0.55%) were affected by MAEs
Blignaut, 2017 [62]	South Africa	Medical and surgical wards, eight public hospitals	Cross-sectional observation	315 patients (1847 medication administration observations), 7 months	NR	Direct observation, double checking	NR	296 errors were identified (94% of patients)
Gordon, 2004 [63]	South Africa	Department of Anaesthesia, University of Cape Town	Questionnaire	65 anaesthetists, NR	NR	Self-reporting survey	Yes, self-report	93.5% of respondents admitted to having administered a wrong drug or the right drug into the wrong site
Gordon, 2006 [64]	South Africa	University of Cape Town	Questionnaire	133 anaesthetists, NR	NR	Self-reporting survey	Yes, self-report	94% admitted to having inadvertently administered a wrong drug; 303 wrong drug administrations
Feleke, 2010 [65]	Ethiopia	Paediatric ward, specialised teaching hospital	Prospective	52 patients (218 observations), 2 weeks	Paediatric population	Medication administration observations	NR	Of all observations, 89.9 % of MAEs were identified
Feleke, 2015 [66]	Ethiopia	Inpatient departments of a referral hospital	Prospective	263 patients (360 administration interventions), 2 weeks	Adult Female: 53.6%	Questionnaire-based interviews, observations	NR	The incidence of MAEs was 56.4%; 260 (98.8 %) of patients encountered at least 1 type of MAE
Labuschagne, 2011 [67]	South Africa	31 public hospitals	Questionnaire	84 doctors, NR	NR	Questionnaire	Yes, self-report	39.3% of participants committed at least 1 event of erroneous drug administration
Llewellyn, 2009 [68]	South Africa	3 tertiary care hospitals	Prospective	30, 412 anaesthetics, 6 months	NR	Anaesthetics form	Yes, self-report	Incidence of MAEs and near-misses, 1:274; the actual error made was 1 in 460 anesthetics
Nwasor, 2014 [69]	Nigeria	6 secondary and tertiary hospitals	Questionnaire	43 anaesthetists, NR	NR	Questionnaire	Yes, self-report	56% of the respondents admitted to ever having a ME
Oshikoya, 2013 [70]	Nigeria	Paediatric wards, public hospitals	Questionnaire	50 nurses, NR	Paediatric nurses Female: 100%	Questionnaire	NR	64% committed at least 1 ME

Table 3 continued

Author, year	Country	Setting	Study design	Sample (e.g. no. of patients or prescriptions/ charts), duration	Characteristics of sample	Method of data collection	Clinical significance assessment (yes/no, tool)	Results
MEs (mixed)								
Agu, 2014 [71]	Nigeria	Outpatient pharmacy, 14 secondary public hospitals	Prospective cohort	6882 patients, 3 years	General population Female: 67%	Active screening programme using pharmaceutical care daily worksheet	NR	Incidence rate of MEs, 40.5 per 100 person-years
Negash, 2013 [72]	Ethiopia	Adult ED, specialised teaching hospital	Prospective cross-sectional	742 patient charts, 2 weeks	Adult population Male: 59%	Patient chart review, direct patient/career interview	NR	Of 2968 medication orders, 54.8% have at least 1 error (prescribing and administration)
Kandil, 2012 [73]	Egypt	Obstetric ED, university hospital	Prospective	10,000 women (47,192 prescriptions), 9 months	Adult, Female: 100%	Chart review, review of nurses' notes	NR	4.18% of prescriptions have errors of any type
Ogunleye, 2016 [74]	Nigeria	Tertiary hospitals	Questionnaire	2386 healthcare professionals, 6 months	Doctors, pharmacists, nurses Female: 60.7%	Questionnaire	NR	47% self-reported at least 1 ME (of any type)
Sabry, 2014 [75]	Egypt	8 general wards and 3 critical units, private general hospital	Prospective	277,661 prescribed doses, 7 months	NR	Medication review, communicate with other healthcare professions and document interventions	NR	2.8% of doses have problems; prescribing errors, 37%; administration errors, 20%; medication overdose, 15%
Sabry, 2009 [76]	Egypt	Surgical, medical and mixed ICUs, teaching hospital	Prospective	220 patients, 1 year	Adult, Male: 66.8%	Observation for any medication related problems/errors	NR	619 medication problems detected in 213 patients (only 3% were free of problems)
Shehata, 2016 [77]	Egypt	Tertiary care teaching hospitals	Prospective	1200 reports, 6 months	General population Male: 44%	Incident reporting	Yes, NCC MERP [24]	Prescribing errors, 54%; monitoring, 25%; administration, 16%; dispensing, 3%; transcribing, 2%
Benkirane, 2009 [78]	Morocco	7 ICU wards, academic and military hospitals	Prospective cohort	696 patients, 3 months	Adult and paediatric, Male: 54.6%	Daily physician rounds, monitoring for medication ordering and transcribing, solicited reports from health professionals	Yes, NCC MERP [24]	Incidence rates per 100 admissions, 7.5; overall ME incidence rate was 7.7 per 1000 patient-days; prescribing stage, 71.1%; administration stage, 21.2%; transcribing stage, 5.7%

Table 3 continued

Author, year	Country	Setting	Study design	Sample (e.g. no. of patients or prescriptions/ charts), duration	Characteristics of sample	Method of data collection	Clinical significance assessment (yes/no, tool)	Results
Dedefo, 2016 [79]	Ethiopia	Paediatric ward	Prospective observational	233 patients, 1 month	Paediatric Male: 63.9%	Chart review, ward round, patient/caregiver interview, voluntary report	Yes, NCC MERP [24]	75.1 % of patients experienced at least 1 error; the incidence of MEs: 46 MEs per 100 orders, 220 MEs per 100 admissions, 51.4 MEs per 100 patient-days. Ordering stage, 45.8%; administration, 34.9%; monitoring; 8.4%; dispensing 4.1%
Jennane, 2011 [80]	Morocco	ICU, university hospital	Prospective	63 patients (4942 orders), 6 weeks	Adult, Male: 59%	Clinical round, voluntary and verbal report, chart review, assessing prescriptions and transcriptions	Yes, WHO [82]	The incidence of MEs: ten MEs per 100 orders, 780 MEs per 100 admissions, 967 MEs per 1000 patient-days; transcribing stage, 60%; ordering stage, 35%

ED emergency department, *ICU* intensive care unit, *MAE* medication administration error, *NCCMERP* National Coordinating Council for Medication Error Reporting and Prevention, *NR* not reported, *WHO* World Health Organization

Fig. 3 Graph showing the extent of the prescribing error rate in African hospitals. Light bars indicate total medication orders used as denominators for error calculation. Solid bars indicate total prescriptions used as denominators for error calculation

3.3.2.3 Medication Administration Errors Eight studies [57–59, 61, 62, 65, 66, 68] calculated medication administration error rate. A study by Amucheazi and Ajuzieogu [61] analysed only a single component of the medication administration procedure in an anaesthetic department, with incorrect drug administration reported in 0.5% of elective surgical procedures. A study by Llewellyn et al. [68] has reported an administration error incidence of one in 274 anesthetics administered. These events were further consolidated from self-reports [60, 63, 64, 67, 69] showing that 39–94% of doctors/anaesthetists/physician assistants reported at least one medication administration error in their career. Other than anaesthetic administration errors, one questionnaire-based study [70] of a paediatric nurse's experience of medication administration errors reported that 64% of nurses described at least one error over the course of their career. Overall, at least one medication administration error has been reported in a median of 56.4% (IQR: 39.5–87.5%) of all medication administration observations [57–59, 65, 66].

3.3.3 Types of Medication Errors

The most common type of errors reported in the reviewed studies was greatly influenced by the methodological approach, and there were also various classifications of error types depending on the medication use process. In general, all but five studies [47, 55, 61, 64, 67] included some details regarding the most common types of errors in their report. Of these, 29 of the 31 studies identified the type of MEs reported commonly and was a prescription and/or an administration for an incorrect dose. Other commonly reported errors included wrong drug combination and/or selection (21/31), wrong route of administration (17/31), omission errors (15/31) and wrong frequency and/or duration (11/31) (Table 4).

Table 4 Types of common medication errors (MEs) reported in the African hospital setting

Author, year	Types of MEs													
	Wrong drug/ selection[a]	Wrong frequency/duration	Omission errors	Wrong dose[b]	Wrong dosage form	Wrong route	Wrong time	Wrong administration technique	Wrong rate of administration	Wrong concentration/ dilution	Wrong instruction	Unauthorised order	Abbreviation and ineligible writing	Incompleteness of prescription	Others[c]
Prescribing errors															
Agalu, 2011 [45]	√	√	√	√		√							√		
Ajemigbitse, 2016 [49]				√		√							√	√	
Ajemigbitse, 2013 [46]	√		√	√	√	√							√	√	√
Ajemigbitse, 2014 [48]	√			√	√							√	√	√	
Alagha, 2011 [50]	√	√		√					√	√	√			√	
Arulogun, 2011 [51]			√	√								√		√	√
Oshikoya, 2007 [52]				√											
Sada, 2015 [53]	√	√		√									√	√	
Yinusa, 2004 [54]				√	√									√	√
Zeleke, 2014 [56]	√	√		√	√									√	
Medication administration errors															
Acheampong, 2016 [57]	√		√	√	√		√	√				√			
Agalu, 2012 [58]			√	√		√	√		√			√			
al Tehewy, 2016 [59]	√			√		√	√	√							√
Amponsah, 2016 [60]	√			√		√				√					
Blignaut, 2017 [62]	√		√	√		√	√								√
Gordon, 2004 [63]	√					√									
Feleke, 2010 [65]			√	√			√	√				√			
Feleke, 2015 [66]			√	√		√	√	√				√			√
Llewellyn, 2009 [68]	√		√	√		√									

Table 4 continued

Author, year	Types of MEs														
	Wrong drug/ selection[a]	Wrong frequency/duration	Omission errors	Wrong dose[b]	Wrong dosage form	Wrong route	Wrong time	Wrong administration technique	Wrong rate of administration	Wrong concentration/ dilution	Wrong instruction	Unauthorised order	Abbreviation and ineligible writing	Incompleteness of prescription	Others[c]
Nwasor, 2014 [69]															√
Oshikoya, 2013 [70]	√	√		√		√	√								
MEs (mixed)															
Agu, 2014 [71]	√	√		√										√	√
Benkirane, 2009 [78]	√	√	√	√	√		√	√	√						√
Dedefo, 2016 [79]	√	√	√	√	√	√	√								√
Negash, 2013 [72]	√	√	√	√	√	√									√
Jennane, 2011 [80]		√	√	√		√									√
Kandil, 2012 [73]			√	√		√	√		√			√			√
Ogunleye, 2016 [74]	√			√		√								√	√
Sabry, 2014 [75]	√			√											√
Sabry, 2009 [76]	√			√											√
Shehata, 2016 [77]	√	√	√	√	√	√	√		√						√

√ indicates inclusion of specific error types in the respective studies

[a] Includes inappropriate drug/regimen, duplicate therapy, unnecessary medication, drug–drug interactions and contraindicated drug

[b] Both under-dose and over-dose are categorised under wrong dose

[c] Includes wrong drug name [46]; irrational use of drugs [51]; guidelines not followed, wrong pack size [54]; wrong documentation and patient [59]; wrong patient [62]; documentation errors [66, 74]; labelling errors [69]; need drugs for untreated medical problems and ineligible client for taking medication [71]; illegible handwriting [72]; prescription errors [73]; prescription and administration errors, adverse drug reactions, wrong interpretability of culture's sensitivity, need drugs for an untreated condition and therapeutic failure [75]; monitoring error, antibiotic misuse, stopping necessary medications [76]; monitoring error, wrong patient, contraindications, therapeutic duplication [77]; wrong preparation and mixing [78]; wrong patient, non-adherence, monitoring error [79]; lack of patient monitoring [80]

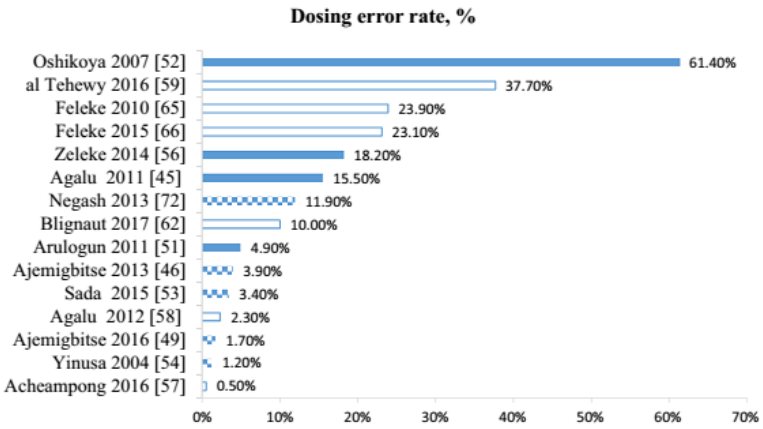

Fig. 4 Graph illustrating the percentage of prescriptions or medication orders or medication administrations with dosing errors in African hospitals. Light bars indicate the study used the total number of medication orders as a denominator to calculate dosing errors. Solid bars indicate the total number of prescriptions and white bars indicate the total number of medication administrations as denominators for dosing errors

Specifically, error rates among the studies were greatly affected by the definitions pertaining to MEs (of any type). In studies with a broader error definition, including the completeness of a prescription (e.g. dosage form, age of a patient, legalisation of the prescription), a higher error of this type was reported in the respective studies. Negash et al. [72], for example, have shown that there were no medication orders described on the dosage form on the prescription. Similarly, other studies [47, 51, 54, 56] also reported the provision of incomplete prescribing information (incomplete description of prescription items, omission of duration, legality of prescription) in 52–86% of all prescriptions. This review revealed that MEs of any type associated with dosing problems have been shown in a median of 14.2% (IQR: 7.8–21.7%) of all errors. Specifically, a median of 15.5% (IQR: 7.5–50.6%) of the prescriptions and 3.4% (IQR: 1.5–7.9%) of the medication orders, and 16.6% (IQR: 1.9–27.4%) of the medication administration observations were reported to contain dosing errors (Fig. 4).

3.3.4 Clinical Significance of Medication Errors

Most of the studies did not investigate the clinical impact of the reported MEs. Excluding those studies that measured consequences of MEs through self-reports, 11 studies addressed the impact of MEs [46, 50, 53–55, 57, 59, 77–80]. However, these studies varied in terms of measuring tools for the clinical significance of errors. Of all the MEs collated, only four fatal errors from three studies [57, 78, 80] were reported, and in six studies [46, 53, 54, 57, 78, 80], the median percentage of clinically serious MEs (defined as errors with a potential to cause death, and were life threatening or resulted in permanent disability or prolonged hospitalisation [28]) were identified in 5.1% (IQR: 1.7–29.2%) of MEs. Data from self-reports [63, 67–69] also showed that most of the errors committed by healthcare professionals were trivial and would not have resulted in deaths.

3.4 Factors Contributing to Medication Errors

Investigating the factors that contributed to MEs was the focus of 15 studies [47, 48, 55, 57, 60, 63, 64, 67, 69, 70, 74, 75, 77–79]. Only one qualitative study [47] using human error theory uncovered the causes of prescribing errors committed by junior medical doctors in an in-patient setting. In contrast, 9 of the 15 studies [48, 55, 60, 63, 64, 67, 69, 70, 74] employed self-report data to assess the possible causes of MEs as a whole, causation data from four studies [57, 75, 77, 78] were based on individual errors, and it was not clear how these data were collected in one study [79]. The factors most commonly cited as contributory to MEs were individual factors (e.g. fatigue and inadequate knowledge/training), working environment (e.g. distraction and high workload) and task (e.g. look-alike names and labelling deficits) (Table 5).

4 Discussion

4.1 Main Findings

This is the first systematic review of the burden and nature of MEs and ADEs in African hospitals. This study was able to identify 51 studies in nine African countries; of these, 18 assessed ADEs. In any patient population, the median prevalence of any suspected ADE on hospital admission (that could likely or unlikely lead to admission/hospitalisation) was 8.4% while a median of 2.8% of patients were

Table 5 Factors reported to be contributing to medication errors

Contributing factors	Author, year														
	Ajemigbitse, 2014 [48]	Ajemigbitse, 2013 [47]	Amponsah, 2016 [60]	Benikrane 2009 [78]	Dedefo, 2016 [79]	Gordon, 2004 [63]	Gordon, 2006 [64]	Labuschagne, 2011 [67]	Llewellyn, 2009 [75]	Nwasor, 2004 [69]	Oshikoya, 2013 [70]	Yousif, 2011 [55]	Shehata, 2016 [77]	Acheampong, 2016 [57]	Ogunleye, 2016 [74]
Individual															
Fatigue	√	√	√	√		√	√	√		√				√	√
Confusion	√	√													
Memory lapses				√										√	
Rushing	√														
Inadequate monitoring/ reporting				√											
Inadequate knowledge/training		√		√	√						√		√	√	√
Rule violation				√											
Inappropriate administration technique				√											
Low morale	√	√													
Work environment															
High workload	√	√									√	√		√	√
Distraction	√	√	√				√	√			√				
Busyness	√														
Lack of resources (e.g. equipment)				√							√		√	√	
Time of the day	√														
Team															
Communication deficits		√	√												√
No senior support	√														
Task															
Lack of documentation															√
Labelling deficits						√	√	√	√	√					
Transcription error				√											
Unclear prescriptions/ illegible writing					√						√		√	√	
Multi-tasking	√														
Unfamiliar patient	√										√				

Table 5 continued

Contributing factors	Author, year	Ajemigbitse, 2014 [48]	Ajemigbitse, 2013 [47]	Amponsah, 2016 [60]	Benikrane 2009 [78]	Dedefo, 2016 [79]	Gordon, 2004 [63]	Gordon, 2006 [64]	Labuschagne, 2011 [67]	Llewellyn, 2009 [75]	Nwasor, 2004 [69]	Oshikoya, 2013 [70]	Yousif, 2011 [55]	Shehata, 2016 [77]	Acheampong, 2016 [57]	Ogunleye, 2016 [74]
Look-alike drug names/labelling				√			√				√	√		√		
Syringe swap								√	√							
Misidentification of drugs/ampoules								√	√	√						
Careless checking/ not checking						√						√				

√ indicates inclusion of specific contributing factors in the respective studies

admitted as a direct cause of ADEs. Adverse-drug event-related fatalities were relatively uncommon but the rate varied across the studies considerably, and it was reported that close to 44% of the ADEs were deemed preventable. It was reported that the rate of MEs was high, and most commonly occurred at the stage of prescribing. Dosing errors have been frequently reported; however, many of the errors were clinically insignificant. A range of factors contributing to MEs has been described in African hospitals including fatigue, lack of knowledge and training, high workload and workplace distraction.

4.2 Comparison with Existing Literature

There is a lack of high-quality studies with rigorous designs that investigate medication safety in African hospitals. In fact, the study of MEs can be considered a relatively new area of research as studies have only emerged since 2004 [63], although research on outcomes from ADEs dates back to the 1970s [36].

Although there was a wider variation in the definition, method of detection and assessment, this review has shown that African hospitals reported a higher rate of MEs than similar reviews conducted on data mainly from developed countries [15–17] but was consistent with other reviews from the Middle East [20, 21] and Southeast Asia [29]. In the present study, the majority of the studies evaluated medication administration errors; however, the prescribing stage is the stage at which the highest error rate occurred in African hospitals. Other reviews have also demonstrated that prescribing errors were the most common MEs to occur in the hospital setting [17, 20]. However, a review of the extent of MEs in Iran reported that medication administration errors were the most commonly reported types of errors [21]. This difference may be owing to the high number of studies that evaluated medication administration errors in that review (83% of the studies). A previous systematic review [20] from Middle Eastern countries reported an incidence of prescribing errors in 7.1–90.5% of prescriptions, which is comparable to the present study examining African hospitals. However, a review [17] of studies from USA or the UK (72% of the studies) reported a lower rate of prescribing errors (2–14%). Similarly, the rate of administration errors in this study is comparable to that from Middle Eastern countries (9.4–80%) [20, 21] and Southeast Asia (15.2–88.6%) [29] but higher than that reported from developed countries (8.6–28.3%) [15].

In the present study of medication administration errors, the surgical/anaesthetic department has shown a different pattern in terms of the frequency and nature of incidents reported. Only a single component of the medication

administration procedure; that is, wrong medication administration with an emphasis on anesthetic medications only were reported, and much of the concern was because of a syringe swap or syringe/drug misidentification of anaesthetics. A lower incidence of MEs in anaesthesia was reported, and this may be expected and consistent with other studies [99, 100], as this may be considered a relatively safe environment, but still over two thirds of doctors/anaesthetists/physician assistants reported making at least one error during their career.

Regardless of the medication use process, dosing problems were the most commonly reported types of errors, which is supported by previous reviews [20, 21]. This study has identified most errors were clinically insignificant. In the extreme, there were also medication-related fatalities not reported in previous reviews [15, 20, 21] or reports from developed countries [101, 102]. However, the prevalence of ADE-related admission aligns with data from the international literature [12, 13, 22, 23]. For example, a systematic review of European studies [23] has identified individual studies with the highest fatal ADRs in 0.49% of all patients admitted because of ADRs, which is lower than that reported in our review (2.9%). Unlike the pattern in developed countries, a larger proportion of ADE-related deaths in Africa is mostly the result of medications used in the treatment of human immunodeficiency virus and tuberculosis [38, 39], also reflecting the high burden of these diseases in the African hospital setting.

Many systematic reviews have estimated the proportion of patient admissions attributable to ADEs to range between 2 and 5.3% [12, 13, 22, 23, 28]. Our median ADE estimate for ADEs that occurred during hospitalisation is close (only when the paediatric studies were excluded) to an estimate from another systematic review of ADRs in the elderly, which has reported an ADR prevalence of 11.5% [103]. Our finding that many of the ADEs were deemed preventable is in line with a systematic review by Hakkarainen et al. [104], which estimated that 52 and 45% of the ADEs are preventable in the adult outpatient and inpatient settings, respectively. This highlighted the importance of designing appropriate prevention strategies for the best possible reduction in medication-related harms.

4.3 Strengths and Limitations

The main strength of this study was the exploration of the medication safety literature with broader inclusion criteria (consisting of ADEs and MEs) across a range of hospital settings in Africa. No limit on the year of publication was applied, and also an extensive search of articles was done. For example, our study identified studies that were not included in previous systematic reviews, such as in the Leendertse et al. study [105], which includes only one African study. Furthermore, our search strategy was able to identify many relevant studies not previously located.

However, the strengths of the results and evidence base presented in this review depend on the strength of data collected from the individual study. For instance, validity and reliability of ADE detection were infrequently reported, and the majority of studies relied on an initial single screening phase without further verification from an independent review. Studies often lacked a valid assessment tool to help establish causality between medication misadventures/harms and the offending agent, and the same for preventability and severity. There were also heterogeneities among the included studies with regard to the methods used to detect ADEs and their definition, which may be one of the reasons for a wide range of individual estimates. Over half of the studies did not provide a working definition of a ME nor described components of a ME. Additionally, different definitions of a ME were used among the studies, and there was variability in the typology of MEs, for example, some studies excluded dosage form errors, illegibility and legalisation of the prescription. There was also a wide variation in the methods of data collection, and inconsistencies in ME assessment and reporting, leading to difficulties in estimating the rate of MEs.

We did not perform a thematic analysis for causes of errors in this study. This was because there was heterogeneity in the way studies reported these data, and mainly the data were extracted from questionnaire-based studies. There was only one study that used a human error theory for explaining error causes, and for ease of simplicity, we summarised error causes as individual, work environment, team and task factors. Furthermore, the quality of these studies was judged grossly and not on an outcome basis. Another potential limitation of this study is the restriction of the search to published literature and English language. Limiting the search to the English language might contribute to our few included studies; notably, publications from French-speaking countries might delimit the number of articles included in the present study. Apart from language, the African content is characterised by a diverse geographical area and thus, caution should be taken in the interpretation of our findings. It should also be noted that the scanning of titles and abstracts of the search results was performed by a single researcher. However, our review was comprehensive and because there has been no published review addressing these issues in Africa, this review sheds light on the extent of MEs and their associated harms in the African hospital setting.

4.4 Implications for Future Research

This review highlights that African hospitals share much of the challenges in the medication safety literature observed across the globe. A challenge in reviewing these studies is that, there is no universally accepted method for either causality assessment of ADEs [106] or estimation of its preventability [107], nor a denominator for error rate reporting [108] and a tool for severity measurement [109]. However, when designing patient safety programmes specifically targeting MEs and their misadventure, it is essential that future studies should assess the causality, preventability and clinical consequences associated with them. More importantly, the effectiveness of medication safety programmes designed to reduce errors requires these tools for complete evaluation. Unfortunately, in our review, only two pre-post studies were retrieved that aimed to decrease the frequency of prescribing errors.

In countries with better resources, medication safety programmes are well integrated with the healthcare system [110, 111]. In developing countries like many in Africa, however, healthcare coverage is prioritised to medication safety, and the medication use system is not evidence based [33]. However, the medical community believes in the need to implement strategies to protect patients from medication harms. This warrants interventional programmes to be tested despite the resource limitations. Of the various strategies, adoption of electronic prescribing [110] and greater targeted involvement of pharmacists [111–113] in care teams are documented internationally. Currently, there is also an influx of information technology in the African healthcare system [114], and an extension of a pharmacist's role in patient care [115], which could lead to a momentous change in medication safety programme implementation. Furthermore, individual factors, such as knowledge deficits, were described as a major contributing factor for medication incidents; thus, educational sessions may be essential as a preventive strategy and should be evaluated in future studies. No studies that specifically assessed transcribing errors, dispensing errors and documentation errors in African hospitals were retrieved.

5 Conclusion

This review has found that there have been limited reports on medication safety in African countries in the past, but this is increasing over time. There is, however, a lack of high-quality studies with rigorous designs that investigate the frequency and nature of MEs and ADEs. Based on the current literature, ADEs are an important cause of morbidity in African hospitals, both on admission and during hospitalisation, but many are deemed preventable. Medication errors are common and mostly occur at the prescribing stage. Dosing errors are frequently reported, but many of the reported errors are clinically trivial. There is a paucity of information on other types of errors, such as dispensing, transcribing and documentation errors. Designing preventive strategies to target the most likely contributing factors is of paramount importance.

Acknowledgements Alemayehu B. Mekonnen gratefully acknowledges funding to support his PhD training provided by The University of Sydney International Students' Scholarship. The authors acknowledge the support provided by King Saud University, Vice Deanship of Research Chairs.

Compliance with Ethical Standards

Funding This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Conflict of interest Alemayehu B. Mekonnen, Tariq M. Alhawassi, Andrew J. McLachlan, and Jo-anne E. Brien have no conflicts of interest directly relevant to the content of this article.

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Electronic supplementary materials published online for Chapter 5 are supplied as appendices (appendix S1, page 314; appendix S2, page 315; appendix S3, page 327; appendix S4, page 333)

PART B: STUDY PROTOCOL and RESEARCH METHODS

Chapter 6

Medication Reconciliation as a Medication Safety Initiative: A Study Protocol

Mekonnen AB, McLachlan AJ, Brien JE, Mekonnen D, Abay Z. Medication reconciliation as a medication safety initiative in Ethiopia: a study protocol. BMJ Open. 2016; 6(11): e012322 doi: 10.1136/bmjopen-2016-012322

BMJ Open

Medication reconciliation as a medication safety initiative in Ethiopia: a study protocol

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To cite: Mekonnen AB, McLachlan AJ, Brien JE, *et al*. Medication reconciliation as a medication safety initiative in Ethiopia: a study protocol. *BMJ Open* 2016;**6**:e012322. doi:10.1136/bmjopen-2016-012322

► Prepublication history and additional material is available. To view please visit the journal (http://dx.doi.org/10.1136/bmjopen-2016-012322).

Received 17 April 2016
Revised 16 August 2016
Accepted 25 October 2016

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ABSTRACT

Introduction: Medication related adverse events are common, particularly during transitions of care, and have a significant impact on patient outcomes and healthcare costs. Medication reconciliation (MedRec) is an important initiative to achieve the Quality Use of Medicines, and has been adopted as a standard practice in many developed countries. However, the impact of this strategy is rarely described in Ethiopia. The aims of this study are to explore patient safety culture, and to develop, implement and evaluate a theory informed MedRec intervention, with the aim of minimising the incidence of medication errors during hospital admission.

Methods and analyses: The study will be conducted in a resource limited setting. There are three phases to this project. The first phase is a mixed methods study of healthcare professionals' perspectives of patient safety culture and patients' experiences of medication related adverse events. In this phase, the Hospital Survey on Patient Safety Culture will be used along with semi-structured indepth interviews to investigate patient safety culture and experiences of medication related adverse events. The second phase will use a semi-structured interview guide, designed according to the 12 domains of the Theoretical Domains Framework, to explore the barriers and facilitators to medication safety activities delivered by hospital pharmacists. The third phase will be a single centre, before and after study, that will evaluate the impact of pharmacist conducted admission MedRec in an emergency department (ED). The main outcome measure is the incidence and potential clinical severity of medication errors. We will then analyse the differences in the incidence and severity of medication errors before and after initiation of an ED pharmacy service.

Strengths and limitations of this study

- This is the first study in Ethiopia that will assess the impact of a pharmacist led medication reconciliation service.
- This study is novel in that it uses a behavioural change theory for implementation of medication safety programmes.
- Multi-method exploration of patient safety issues will add substantial strength to our study.
- The sampling technique in both the interviews and survey may carry a risk of bias.

INTRODUCTION

Patient safety initiatives

Quality patient care is a priority issue in all healthcare sectors; however, clinical errors are known to compromise patient safety.[1] Patient safety incidents gained attention after the works of pioneer US studies: the Harvard Medical Practice Study[2 3] and the Institute of Medicine Report.[4] In the USA, it has been reported that 3.7% of all hospitalised patients experienced an adverse event,[2] and medication errors alone resulted in 7000 deaths annually.[4] Medication errors constitute the most common preventable cause of patient safety issues, and has been studied extensively in developed countries.[2–6] Despite current advancements in healthcare, these incidents continue to pose a significant problem globally,[7] and are the concern of many hospitalists and patient safety activists.

Medication safety in African hospitals

Patient injuries attributed to medication related adverse events are among the most common incidents in hospitals,[2] and have important economic and humanistic consequences. Furthermore, given the morbidity profile and the high burden of malaria, HIV/AIDS and tuberculosis in Africa, along with the level of awareness and patient safety culture, the extent of medication related adverse events in African hospitals is thought to be higher than elsewhere in the world.[8] For example, studies have shown that 1.5–6.5% of hospital admissions are attributed to adverse drug events (ADEs),[9 10] and 2.5–47% of inpatients encountered an ADE during their hospital stay.[9 11] One-fifth to more than a half of the reported ADEs were severe events,[10 12–14] of

which ADE related fatalities were reported in 0.07–2.9% of patient admissions to hospital.[12 15 16] However, up to half of the ADEs were due to medication errors and were preventable.[10] The most reported types of medication errors in African healthcare settings were prescribing errors, occurring in 13–76% of all prescriptions.[17–20] Yet the extent of medication errors and ADEs have not been fully evaluated in African settings,[8] and medication safety programmes designed to prevent them could represent the first step in improving patient safety.

Medication reconciliation as a medication safety strategy

More than half of the medication errors occurred at care transitions, when patients were admitted to, or discharged from, a hospital or transferred to the care of other healthcare professionals.[21] Medication reconciliation (MedRec) as a tool for the prevention of these errors and consequent patient harm has been advocated internationally.[22 23] MedRec has been defined by the Institute for Healthcare Improvement as "the process of identifying the most accurate list of a patient's current medicines, including the name, dosage, frequency and route—and comparing them to the current list in use, recognising and documenting any discrepancies, thus resulting in a complete list of medications".[22]

Under the leadership of the WHO, patient safety programmes, including MedRec, have been implemented across a range of countries[23–26] and taken up as healthcare policy. For example, MedRec has been recognised as a priority patient safety solution by the Australian Commission on Safety and Quality in Healthcare.[26] Prior to MedRec being routinely practised in Australia, there was 1 omitted medicine from the medication chart for every 2 people at hospital admission.[27] Also, previous studies showed that 60–80% of patients had a discrepancy in their medication history.[28 29]

Studies examining medication errors have been undertaken in many countries, including developing nations,[30 31] in a range of settings, such as emergency units,[32–38] critical/intensive care units,[39] and paediatric[40–42] and geriatric units.[43–48] There is evidence that MedRec decreases the frequency of medication errors[49 50] and drug related readmissions.[51 52]

MedRec with various approaches has been employed to improve medication safety, including, but not limited to, technology assisted tools,[53–55] use of standardised forms,[34 56] collaborative models,[33 57] as well as patient engagement[58] and pharmacist led approaches.[59 60] Previous studies have shown benefits from involving pharmacists in MedRec.[59 60] However, the impact of MedRec overall, as well as pharmacist led MedRec practice, has not yet been described in sub-Saharan Africa.

Patient safety culture in the Ethiopian context

Despite a lack of research, patient safety in Ethiopia is believed to be a serious concern. A previous local study[61] in paediatrics ward showed an incidence of 9.2 ADEs per 100 admissions, of which one-third were deemed preventable. As healthcare managers strive to improve the quality of patient care, there is a growing recognition of the importance of establishing a culture of patient safety. Developing a patient safety culture was one of the recommendations made by the Institute of Medicine[4] to assist hospitals in improving patient safety. According to the Agency of Healthcare Research and Quality (AHRQ),[62] patient safety culture is described as an understanding of the values, beliefs and norms about what is important in an organisation and what attitudes and behaviours related to patient safety are supported, rewarded and expected. Thus it is important for healthcare organisations to assess their patient safety culture to gain a clear understanding of the patient safety aspects requiring urgent attention, identify the strengths and weaknesses of their safety culture,[63] and assist hospitals in identifying their existing patient safety problems.[64] Studies on patient safety culture, mostly set in developed countries,[63–66] have been published. However, there are no data about the current state of the patient safety culture in Ethiopian hospitals. Furthermore, no studies have specifically investigated implementation of MedRec services from a behavioural theory perspective, involving both barriers and facilitators of a wide range of behavioural determinants in the implementation of evidence based practice.

This project is a medication safety initiative focusing on MedRec at care transitions in Ethiopian public hospitals, and implementation of this service is guided by a multi-method approach consisting of three different but inter-related studies to inform our study objectives. Specifically, the aims of this study are: to explore healthcare professionals' views of patient safety issues, medical error, and event reporting and patients' experiences of medication related adverse events; to use a theoretical framework to help identify the barriers and facilitators to medication safety activities delivered by hospital pharmacists; and to evaluate a pharmacist led MedRec practice in one of the teaching hospitals in Ethiopia.

METHODS AND ANALYSES

Study setting and period

This is a multi-phased study that is being conducted in public hospitals in the Amhara region of Ethiopia. The Amhara region is one of nine regions of Ethiopia located in the northern part of the country. This region has an estimated total population of approximately 18 million, with the majority (87.4%) being rural inhabitants. This region has 17 public hospitals, 520 health centres and 2941 health posts.[67]

There are three phases to this research project. Phases 1 and 2 are being conducted in 10 selected public hospitals in the Amhara region, including 4 teaching or referral hospitals (Gondar University, Felege Hiwot, Debre Markos and Debre Tabor) and 6 district hospitals

(Metema, Debark, Chagni, Finoteselam, Woldiya and Enat). Phase 3 will be carried out in one teaching hospital (Gondar University Hospital (GUH)). The study started in February 2016 and will end in July 2017.

Phase 1: a study of healthcare professionals' perspectives of patient safety culture and patients' experiences of medication related adverse events

This is a mixed methods study consisting of a survey and qualitative research. The survey measures dimensional scores of the patient safety culture. Using a scale to quantify the scores for patient safety is, however, not explanatory.[68] In addition, a shared decision between the patient and healthcare professional is central for a sustainable patient safety culture. Therefore, a survey supported by an indepth interview is well acknowledged as a meaningful assessment of patient safety culture through the eyes of healthcare professionals and patients.[68]

Questionnaire study

The survey aims to evaluate the patient safety culture of public hospitals in the Amhara region. The study focus is on public hospitals only as most of the population in the region use public hospitals. The study adopted the Hospital Survey on Patient Safety Culture (HSOPSC) developed by AHRQ.[69] HSOPSC has been widely used in assessing patient safety culture and has also been validated in non-US countries.[64 65] The survey consists of 42 items that measure 12 patient safety culture composites: communication openness, feedback and communication about errors, frequency of events reported, handovers and transitions, management support for patient safety, non-punitive response to error, organisational learning and continuous improvement, overall perceptions of patient safety, staffing, supervisor/manager expectations and actions promoting safety, and teamwork across and within units. Background characteristics of participants include questions related to job category, type of hospital (teaching/referral, district), years of working experience overall and in the current working area, work setting and working hours per week. The questionnaire is in English, as English is the main language of communication in Ethiopian hospitals. This questionnaire, together with the participant information statement, was distributed to conveniently selected healthcare professionals by the research team and required about 10–15 min to complete. These participants were recruited from the 10 hospitals in the Amhara region, and included physicians, nurses, pharmacists and paramedics (eg, technicians). The sample size was estimated to be 480, by considering 95% CI, a 5% margin of error and 25% contingency for a non-response rate, and assuming that patient safety culture score was rated as excellent in 50% of respondents.

The response to each item in the questionnaire was assessed using a 5 point Likert scale, where 1 is 'strongly disagree' and 5 is 'strongly agree'. The patient safety grade (measured on a scale of excellent, very good, acceptable, poor and failing) and number of events reported were the other two outcome variables of interest. Currently, we are entering the collected data into SPSS v21, and data will be analysed when data entry is accomplished. The HSOPSC included both positively and negatively worded items. For easier interpretation of the results, AHRQ[69] and other studies[63–66] recommend the use of 'average positive' for calculating each item scores—that is, the percentage of positive responses for each item will be calculated, and negatively worded items will be reversed when computing per cent positive response. We will define areas of strength as items for which 75% of respondents answer positively and areas requiring improvement as those scoring <50%.[62] Additionally, univariate and multivariate analyses will be conducted to examine statistical associations between independent characteristics and patient safety grade and number of events reported. The mean scores for each of the HSOPSC subscales are taken as dependent variables, and these will be tested against the independent variables, such as job characteristics (profession and qualification), department and type of hospital (teaching/referral, district), work experience (career length, experience in the current unit/hospital) and workload (working hours).

Indepth interview

The qualitative part of the phase 1 investigation aims to assess patient safety strategies employed by those hospitals through indepth interviews with different stakeholders (healthcare professionals and patients) working in 10 hospitals in the Amhara region. The contact details of participants (healthcare professionals) were retrieved from the human resource office or related office of the respective hospitals. We are using purposeful sampling to identify the initial sample and then the remaining data collection is being aided by snowball sampling. We will invite healthcare professionals who are involved in the care of patients by letter or email, as appropriate. Patients who are in hospital at the time of data collection and were taking regular medications before admission will be invited for interview by a healthcare professional who is already a participant in this study. Next, we will contact patients for further invitation into the study. We will employ semi-structured interviews informed by the interview guide (see online supplementary additional file 1) for the collection of data. All interview guides have been translated from the English versions to the local language (Amharic) by two non-official translators who are native speakers and working in the healthcare industry, and validated by two of the research group (ABM, DM). Interview tools have been translated to foster faster communication and expression of ideas.

Before the interview, we will inform respondents about the aim of the interview, and those who consent will be given further details on the nature of the study to

ensure that interviewees understand what is required of them. We will conduct face to face interviews at a time and place to suit the participants, and the interviews are expected to last approximately 30–60 min. We will forward both open and close ended questions to interviewees to describe their experiences of medication safety issues and strategies employed to prevent medication related adverse events. We will encourage participants to reflect on their own experiences of medication related adverse events, and we will ask them to think about an example of a known medication related adverse event when answering questions.

The interviewer will use prompts when necessary to encourage further elaboration. We will give 50 Ethiopian birr to participants in appreciation of their time. All interviews will be conducted by an English/Amharic speaking investigator (ABM). We will collect data from each of the two participant groups until a point of saturation is reached. We will record all interviews using audiotape with informed consent of participants. After data collection is completed, the principal investigator will carry out verbatim Amharic transcriptions of all interviews, which will then be translated into English, assigned a unique identifier and imported into a computer programme (Nvivo V10) for qualitative data analysis. Thematic analysis will then be carried out, and emerging topics will be identified as themes and sub-themes.

Phase 2: barriers and facilitators to medication safety activities delivered by hospital pharmacists

This is a qualitative study using focus group discussions (FGD) with hospital pharmacists working in selected public hospitals in the region to gather data on the barriers and facilitators to medication safety activities. We will employ FGDs in this phase because the interactive nature of focus groups is specifically important when group norms and cultural values of particular groups are of interest, and to explore the degree of consensus on a given topic,[70] including implementation of an intervention to promote medication safety. Many factors can affect the adaptability of an evidence based intervention, and the success of implementation efforts depends on a careful assessment of barriers to, and facilitators of, the behaviour to be changed.[71] A theory based identification of such factors provides a theoretically robust evidence base to inform implementation of an intervention.[71] The underpinning theoretical model used in this study is the Theoretical Domains Framework (TDF).

Theoretical Domains Framework

Increasing the uptake of evidence into clinical practice and improving patient outcomes needs behaviour change. The TDF from health psychology provides the basis for such an approach, ensuring that a wide range of possible theoretical explanations for the behaviours can be considered. Built from 33 behavioural theories, the TDF was developed to make theories more accessible for implementation researchers.[72] According to Michie *et al*,[72] the TDF has 12 domains to explain behaviour change: (1) knowledge, (2) skills, (3) social/professional role and identity, (4) beliefs about capabilities, (5) beliefs about consequences, (6) motivation and goals, (7) memory, attention and decision processes, (8) environmental context and resources, (9) social influences, (10) emotion regulation, (11) behavioural regulation and (12) nature of the behaviour. The TDF has been extensively used to identify barriers to change in clinical practice to develop interventions.[73 74] To justify implementation of pharmacist led MedRec, it will be critical to understand the perceived barriers and facilitators underlying the individual pharmacist's role in medication safety. Thus this study uses the TDF to develop a theory informed intervention aimed at improving medication safety of patients at hospital transitions.

Focus group discussions

In this study, FGDs will be guided by questions designed based on the TDF (table 1). For each of the 12 domains that could act as facilitators or barriers to current medication safety practices and a successful MedRec implementation, the authors developed several interview questions. The number of interview questions ranged between 2 and 5 for each of the 12 domains, for a total of 43 questions to cover a wide range of constructs assigned to each domain. The questions were initially drafted by one researcher (ABM) and then refined by health service researchers (AJM, JEB) and discussed by the research team to check for clinical relevance. The discussion questions will be pilot tested with at least two hospital pharmacists to assess clarity and focus, and revised accordingly.

The sample population will be all hospital pharmacists in the 10 public hospitals across the region. Pharmacists will be selected using a purposive sampling strategy augmented with snowball sampling. Participants will be recruited either by letter or email invitation. Participants willing to be interviewed by sending an email or by returning a signed consent form will be contacted. The principal investigator (ABM), who is experienced in qualitative study, will conduct and facilitate the FGD using the translated version (Amharic) of the topic guide. Pharmacists will be encouraged to talk about internal beliefs and attitudes that may hinder them from providing clinical pharmacy services, including medication safety roles. All discussion sessions will be audiotaped and recorded. Two of the researchers (ABM, ZA) will read all of the FGD Amharic transcripts, and will be translated into English. Transcripts will then be coded based on the 12 domains of the TDF, and thematic analysis of pharmacists' statements into the relevant theoretical domains will be performed.[75] Briefly, the analysis will involve identifying contextualised brief statements related to the barriers and facilitators to medication safety activities, categorising statements

Table 1 Interview guide questions for focus groups according to Michie's theoretical domains[72]

Domains	Interview questions
Knowledge	Are there any hospital guidelines for pharmacists to deliver clinical pharmacy services?
	What do you think the level of evidence is for these guidelines?
	What do you know about medication reconciliation and review?
	What do you think is the level of evidence for medication reconciliation and review?
	Can you describe pharmacists' roles in medication safety activities?
Skills	Do you know how to deliver clinical pharmacy services?
	Do you know how to deliver medication reconciliation and review services?
	Is identification of medication related problems difficult for you?
	Have you attended in-service training to deliver clinical pharmacy services?
Social/professional role	Is doing medication reconciliation and review compatible with your professional role?
	Who is responsible for these services at your hospital?
	Do you think hospital guidelines supports your professional roles as a pharmaceutical care practitioners?
Beliefs about capabilities	How easy or difficult do you find performing clinical pharmacy activities?
	What problems have you encountered?
	How capable are you in performing medication reconciliation and review?
	How confident are you that you can do these services despite difficulties?
	How comfortable do you feel to undertake these services?
Beliefs about consequences	What are the likely positive/negative outcomes of reporting/communicating medication related problems?
	What are the costs of delivering medication reconciliation and review, and what are the costs of the consequences of these services?
	Are you concerned if these services are not provided at your hospital?
	Do the benefits of doing these services outweigh the costs?
	Does the evidence suggests that doing these services are beneficial?
Motivation and goals	How motivated are you to deliver medication reconciliation and review?
	Are there incentives to provide these services?
	Do you have any other hospital activity that hinders these services?
Memory, attention and decision processes	Will you consider providing medication reconciliation and review services? If so, how frequently would you undertake this activity?
	How much priority have you given to these services?
Environmental context and resources	To what extent do physical factors or resources facilitate or hinder delivering medication reconciliation/review?
	Are there competing tasks and time constraints?
	Are the necessary resources available to undertake these services?
	Do these services have advantages compared with the standard care?
	Do government and local authorities provide sufficient support for these services?
Social influences	Are clinical pharmacy services in the hospital well acknowledged by other healthcare professionals?
	Do hospital managers acknowledge your role?
	Is there any obstruction to these activities in your hospital?
	Have you observed others providing these clinical services?
Emotion	What things worry you the most in providing medication reconciliation/review services?
	To what extent do emotional factors facilitate or hinder these services?
Behavioural regulation	Have you received feedback from other healthcare professionals regarding these services?
	What intimal steps are needed to deliver these services?
Nature of the behaviours	What do you currently do?
	How long are the changes going to take?
	Are there any systems in place for sustainable long term changes?

into TDF domains and mapping the underlying theoretical constructs within domains. Both inductive and deductive approaches will be used so as not to miss any themes. To assess agreement between two researchers, all extracted themes and sub-themes will be reviewed in a meeting, and disagreements will be solved through consensus.

Phase 3: evaluation of the impact of a pharmacist led MedRec service. Single site before and after study

This phase of the project is the main objective of this study, and the aim is to investigate the impact of a pharmacist led MedRec service on the rate and incidence of unintentional medication discrepancies in an emergency ward of the GUH, Ethiopia. GUH is located

in Gondar town in the Amhara regional state. It is the primary hospital in the northwest region of Ethiopia. GUH provides specialised health services through its medical and other clinical and diagnostic departments for a catchment population of approximately 5 million people.

The sample size calculation is based on the prevalence of medication errors in previous local studies, which was identified as 52–58% of all prescriptions.[17 76] Assuming a reduction in medication errors from 55% to 45%, 80% power, 5% significance level (two sided), we required 127 patients, 51 for the baseline and 76 for the intervention. Hospital discharge statistics showed that this sample size would be achievable in 3 months. A baseline assessment of medication discrepancies will thus be conducted for 1 month during hospital admission. Medication discrepancies are defined as one or more differences in dosage, frequency, drug or route of administration, as described by the Institute for Healthcare Improvement,[22] between the current and previous medication (s) a patient was taking. A pharmacist led MedRec intervention will then be carried out prospectively for 2 months. Inclusion criteria will be patients >18 years of age, hospitalised for at least 24 hours and taking at least two home/regular medications on admission.

The standard practice in the current department involves physicians taking the patient's medication history using patient provided information; however, hospital pharmacists do not participate in medication history taking and prescription review in the emergency department. The intervention will involve use of the best possible medication history (BPMH),[77] which is based on a structured interview with the patient about medication use and retrieving other sources of medication history, including discharge and referral letters, the patient's own medicines and carrier interview. One pharmacy staff member will be trained in the techinques of how to get the BPMH by a research pharmacist (ABM). MedRec will be conducted after patients are informed of the study and give written consent. Medication use will be documented within 24 hours of patient admission through a data collection tool prepared for the purpose of this study (see online supplementary additional file 2). The pharmacist will then compare the BPMH with the admission prescription order of the patient issued by the physician in charge.

All identified discrepancies will be brought to the attention of the physician at admission and verification of these discrepancies will be made—that is, intentional versus unintentional changes to medications. Intentional medication discrepancies are medication changes due to new clinical status of the patient, and are clinically justifiable but not documented in the patient's medical record. Thus only unintentional medication discrepancies (also called as medication errors) will be reported. The main outcome measure is the incidence of medication errors and the potential clinical severity of such errors. The potential clinical severity of medication errors will be judged by a consensus between a clinical pharmacist and a physician using a tool developed by Cornish *et al*.[78] Descriptive statistics will be used to characterise the types of medication errors and the χ^2 test will be used to analyse differences in the incidence and severity of medication errors between the baseline and intervention groups. Statistical significance is set at $p<0.05$.

Ethics and dissemination

The study protocol was approved by the University of Sydney Human Research Ethics Committee (project No: 2015/818) and the institutional review board of the University of Gondar, Ethiopia (O/V/P/RCS/05/624/2016). The data from this study will be disseminated to researchers, clinicians and health planners in peer reviewed health journals and conference publications. One or more meetings will be held locally to give feedback to participants and contributors to the study.

DISCUSSION

Patient safety in general, and medication safety in particular, has become a matter of growing interest and increasing priority for hospital managers. A safety culture is a necessary prerequisite for the improvement of patient safety. However, it is unclear how healthcare professionals and patients in Ethiopia perceive patient safety. This study will describe the views of healthcare professionals in hospitals about patient safety culture and patients' experiences of medication related adverse events, and use a behavioural change theory to implement a MedRec service. MedRec is a complex intervention conducted across a range of hospital transitions, and will therefore apply the TDF to a behaviour that is complex—for example, involving multiple procedures and conducted by various healthcare professionals.

This study has several strengths. This is the first study in Ethiopia that will assess the impact of a pharmacist led MedRec service, and is also novel in that it uses a theory informed implementation of this new practice as a medication safety strategy. The use of multi-method for the exploration of patient safety culture and practice will add substantial strength to our study. Use of behavioural theory that is commonly used in implementation studies will allow us to identify and select potentially relevant domains to target behaviour in detail. This study will contribute to the knowledge base by providing more evidence to confirm the importance of MedRec in improving the Quality Use of Medicines when patients are admitted to hospital. The challenge of designing quality improvement projects in resource limited settings is workload among the staff. We hope the data from this study will help develop evidence based medication safety interventions to strengthen the capacity and performance of hospital pharmacists in settings where resources are scarce. This study is not without limitations. The

sampling technique in the qualitative study may carry a risk of bias by recruiting participants who may have similar opinions and experiences. To minimise this, participants will be requested to nominate other participants who have different experiences and practice in medication safety. Moreover, we will use an iterative process for data collection and analysis for the qualitative studies in phases 1 and 2 until we are sure that there are no new ideas emerging.

Acknowledgements This project was conducted as a partial fulfilment for a PhD in pharmacy (health services and patient safety theme) for ABM. He is supported by the University of Sydney International Students' Scholarship.

Contributors ABM, AJM and JEB contributed to the conception and design of the study. ABM drafted the first protocol. JEB and ABM refined the study protocol with contributions from all co-authors (AJM, DM and ZA). All authors read and approved the final manuscript.

Competing interests None declared.

Ethics approval The study protocol was approved by the University of Sydney Human Research Ethics Committee (project No: 2015/818) and the institutional review board of the University of Gondar, Ethiopia (O/V/P/RCS/05/624/2016).

Provenance and peer review Not commissioned; externally peer reviewed.

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Electronic supplementary materials published online for chapter 6 are supplied as appendices (additional file 1, page 373; additional file 2, page 398)

PART C: RESEARCH FINDINGS

Chapter 7

Hospital Survey on Patient Safety Culture in Ethiopian Public Hospitals

Mekonnen AB, McLachlan AJ, Brien JE, Mekonnen D, Abay Z. Hospital survey on patient safety culture in Ethiopian public hospitals: a cross sectional study. Safety in Health 2017; 3:11. DOI: 10.1186/s40886-017-0062-9

Mekonnen *et al. Safety in Health* (2017) 3:11
DOI 10.1186/s40886-017-0062-9

Safety in Health

RESEARCH ARTICLE Open Access

Hospital survey on patient safety culture in Ethiopian public hospitals: a cross-sectional study

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Abstract

Background: Internationally, patient safety is increasingly seen as a priority area, and improving patient safety highly depends on achieving a culture that supports and encourages health care staffs to report their errors or near misses without fear of punishment. In Ethiopia, however, patient safety culture is a relatively new focus, and little is known regarding the current status of patient safety culture in public hospitals. The purpose of the current study was thus, aimed to assess the views and perceptions of health care professionals about patient safety culture in public hospitals in Ethiopia.

Methods: A cross-sectional study, utilizing the 'Hospital Survey on Patient Safety Culture (HSOPSC)' questionnaire was carried out in 2016 in the Amhara region. A self-administered questionnaire was distributed to the 480 health care staffs, including physicians, nurses, pharmacists, and other clinical and non-clinical staffs. Data were summarized as percentages, means, and standard deviations. ANOVA and chi-square tests were employed to examine statistical differences between health care worker's characteristics and patient safety predictors. We also computed internal consistency coefficients, correlation analysis, and exploratory factor analysis.

Results: A total of 410 questionnaires were returned (response rate, 85.4%). The overall patient safety score (46%) and most of the scores related to dimensions were lower than the benchmark scores. The positive response rate of two dimensions ('Teamwork within units' and 'Organizational learning–continuous improvement') received the highest score (each 72%), and the lowest score was attributed to 'Staffing' (26%). Approximately, two thirds of staffs reported at least one event in the past 1 year. Nurses reported better in the overall patient safety score compared with other health care professionals ($P = 0.03$). The internal consistency of the total survey was fairly satisfied (Cronbach's $\alpha = 0.77$).

Conclusions: There is a severe deficit of patient safety culture in Ethiopian public hospitals. Creating a positive patient safety culture by implementing actions that support all dimensions of safety culture is inevitable. Further research is needed to confirm the applicability of the translated version of the HSOPSC in the Ethiopian hospital settings.

Keywords: Patient safety, Patient safety culture, Hospital, Error reporting, Adverse event, Ethiopia

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Background

Adverse events due to medical care remain a significant source of morbidity and mortality across the globe [1, 2] and have been identified as a matter of increasing priority for hospital managers and policy makers. However, much of the evidence base comes from developed countries as there is a paucity of published literature on patient safety in low- and middle-income countries [3]. Yet the magnitude of harm resulting from unsafe patient care is known to be large in these countries than in the developed nations [2, 4]. Until recently, patient safety in Africa has been absent from national policies but now has undergone renaissance through the WHO African Partnerships for Patient Safety (APPS) and increasingly seen as a basic right within the context of universal health coverage [5].

Despite a lack of research, patient safety in Ethiopia is believed to be a serious concern. A previous local study in the paediatrics ward has shown an incidence of 9.2 adverse drug events per 100 hospital admissions, of which one third could be preventable [6]. As health care managers strive to improve the quality of patient care, there is a growing recognition of the importance of establishing a culture of safety in Ethiopia [7]. Developing a patient safety culture was one of the recommendations made by the Institute of Medicine [8] to assist hospitals in improving patient safety. According to the Agency for Healthcare Research and Quality (AHRQ) [9], patient safety culture is described as an understanding of the values, beliefs, and norms about what is important in an organization and what attitudes and behaviours related to patient safety are supported, rewarded, and expected. It is, thus, important for health care organizations to assess their patient safety culture to obtain a clear understanding of the patient safety aspects requiring urgent attention, identify the strengths and weaknesses of their safety culture [10], and assist hospitals to identify their existing patient safety problems [11]. Studies on patient safety culture, mostly come from developed countries [10–13], have been published. In Ethiopia, however, patient safety culture is a relatively new focus, and little is known regarding the current status of patient safety culture in public hospitals. This study is part of a large project designed to implement patient safety programs [14], and it was included with the hypothesis that measuring patient safety culture is a priority step for a successful implementation of patient safety programs. Specifically, the current study was performed to assess the views and perceptions of health care professionals about patient safety culture in public hospitals in Ethiopia.

Methods

Study design, setting, and population

This is a cross-sectional study conducted over a 3-month period (February–April 2016) in the Amhara region. Amhara region is one of the nine regions of Ethiopia located in the northern parts of the country. This region has an estimated total population of approximately 18 million people, and the majority (87.4%) of the population are rural inhabitants. This region has 17 public hospitals, 520 health centers, and 2941 health posts [15]. Health care professionals were recruited from ten hospitals of the region and involved physicians, nurses, pharmacists, and other clinical and non-clinical staffs (e.g. technicians). The *sample size* was estimated to be 480, and convenient sampling was used to select the participants. The methodology of this study was described elsewhere [14].

Survey instrument

This study adopted the 'Hospital Survey on Patient Safety Culture' (HSOPSC) developed by the Agency for Healthcare Research and Quality (AHRQ) [16], as a safety culture assessment instrument. The original HSOPSC has been validated in the USA hospital setting [17] and has also been widely employed to assess perceptions of hospital staff about patient safety issues, medical error, and event reporting in the non-US countries [11, 12]. The instrument consists 42 items that measure 12 patient safety culture composites: 'Communication openness' (3 items), 'Feedback and communication about errors' (3 items), 'Frequency of events reported' (3 items), 'Handoffs and transitions' (4 items), 'Management support for patient safety' (3 items), 'Non-punitive response to error' (3 items), 'Organizational learning–continuous improvement' (3 items), 'Overall perceptions of patient safety' (4 items), 'Staffing' (4 items), 'Supervisor/manager expectations and actions promoting safety' (4 items), and 'Teamwork across and within units' (4 items each). In our study, however, there was one item that was not applicable to fit the Ethiopian context. A statement about 'Staffing' which reflects the use of agency/temporary staff for patient care was not included in this questionnaire. It is unlikely to employ an agent or a temporary staff in public hospitals in Ethiopia.

The response to each item in the questionnaire was assessed using a 5-point Likert scale of agreement (from 1: 'Strongly disagree' to 5: 'Strongly agree') or frequency (from 1: 'Never' to 5: 'Always'). There were also two single-item outcome variables: the overall patient safety grade (measured on a scale of 'Excellent', 'Very good', 'Acceptable', 'Poor', and 'Failing') and the number of events reported in the past 12 months.

Background variables of participants included questions related to job category, type of hospital (teaching/referral, district), work experience (overall and in the current working area), work setting, and working hours per week.

The questionnaire is kept in English, as English is the main language of communication in Ethiopian hospitals. This paper-based questionnaire together with the participant information statement was distributed to the selected

hospitals and participants by a person recruited for this purpose and required about 10–15 min to complete. Health care staffs who worked in their respective hospital for at least 6 months prior to the administration of the questionnaire were included in the study.

Data analysis

We entered the collected data and analysed using SPSS Version 21. Descriptive statistics were used to summarize the demographic data and scores of patient safety culture dimensions/items and safety outcomes (patient safety grade, the number of events reported). The HSOPSC included both positively and negatively worded items. For easier interpretation of the results, the AHRQ [16] and other studies [10–13] recommend the use of 'average positive' for calculating each item scores. Percent positive is the percentage of positive responses (e.g. Agree, Strongly agree) to positively worded items (e.g. 'People support one another in this unit') or negative responses (e.g. Disagree, Strongly disagree) to negatively worded items (e.g. 'We have safety problems in this unit'). That is, for positively worded items, responses 4 and 5 corresponded to positive answers whereas this meant responses 2 and 1, respectively, for the negatively worded items. Composite-level scores were computed by summation of the items within the composite scales and dividing by the number of items with non-missing values. We defined areas of strengths as items for which 75% of the respondents answered positively, whereas areas requiring improvement as those scored below 50% [9].

Cross tables were constructed, and chi-square test was used to examine the statistical difference between health care workers' characteristics—such as the type of hospital they are working, profession, and work experience—and patient safety grade and the number of events reported. We also used ANOVA to examine differences in patient safety culture composites across these characteristics.

We used Cronbach's alpha (α) to evaluate the reliability of the questionnaire. Reliability greater than or equal to 0.7 (indicating that the items measure the same concept) has been taken as an acceptable level of internal consistency [18]. The construct validity was examined using Pearson's correlation coefficient between two scale scores. P value < 0.05 was considered as statistically significant. Bartlett's test of sphericity was used to determine the sufficiency of inter-item correlations. The sampling adequacy was determined using the Kaiser-Meyer-Olkin (KMO) measure. Exploratory factor analysis was performed using principal component analysis with varimax rotation.

Results

Characteristics of respondents

A total of 480 questionnaires were distributed; of which, 410 were returned, giving a response rate of 85.4%. Many of the respondents were nurses (39.3%) and were employed in the medical unit (22.9%). The majority of respondents reported work experience of less than 1 year both in their current hospital and unit. Most had work duties of 40–59 h per week (54.8%). More than half of the respondents were from teaching/referral hospitals, and 95% reported their work involves direct patient care (Table 1).

Patient safety culture dimensions

In this study, the percentage of positive responses for the 12 patient safety culture dimensions ranged from 26 to 72%, and the mean positive responses for all dimensions were 46%. The lowest positive response rate of dimension was 'Staffing' (26%), while the highest positive response rate of dimensions was 'Organizational learning–continuous improvement' and 'Teamwork within units' (each 72%). In the remainder of dimensions, except for 'Teamwork across units' (57%), all composite scores were less than 50%.

Comparison of safety culture dimensions

When comparing the mean composite scores against the international benchmark, our study has found only one comparable average positive score; that is, 'Organizational learning–continuous improvement' with the score obtained from 680 hospitals in the USA [19]. There was also one comparable mean score related to 'Teamwork across units' with the data from 68 Lebanese hospitals [20] but better score in the 'Non-punitive response to error'. The rest composites had less average positive scores than the USA and the Lebanese data (Fig. 1).

Patient safety culture items

In the present study, the positive response rate for each of the items ranged from 22 to 85%. The highest positive response rate of the items was 'We are actively doing things to improve patient safety' (85%), while the lowest positive response rate of the item was 'Staff in this unit work longer hours than is best for patient care' (37%). Altogether, there were 24 items (of 41 safety culture items) with less than 50% of the average positive score (Table 2).

Safety culture outcomes

In this study, the percentage of health care staff who rated the level of patient safety grade as 'Very good' or 'Excellent' was 37.6% which was lower than the USA (76%) and the Lebanese score (73.4%) (Fig. 2). On the contrary, two thirds of the Ethiopian staffs reported at least one event over the past 12 months whereas only 45% in the USA and 41% in the Lebanon did (Fig. 3). There were significant differences in the responses to patient safety grade and the number of events reported between this study and the benchmark countries (all $P < 0.0001$).

Table 1 Socio-demographic and professional characteristics of respondents

Characteristics	*N* (%)
Working unit	
Medical unit	94 (22.9)
Surgery	31 (7.6)
Gyn/Obs	53 (12.9)
Paediatrics	40 (9.8)
Pharmacy	71 (17.3)
Laboratory	28 (6.8)
Others[a]	93 (22.7)
Staff position	
Nurses	161 (39.3)
Physicians	82 (20.0)
Pharmacists	71 (17.3)
Technicians	35 (8.5)
Others[b]	61 (14.9)
Years in hospital	
< 1 year	235 (57.3)
1–5 years	139 (33.9)
6–10 years	25 (6.1)
11–15 years	7 (1.7)
16–20 years	1 (0.3)
≥ 20 years	3 (0.7)
Years in current department	
< 1 year	236 (57.6)
1–5 years	146 (35.6)
6–10 years	21 (5.1)
11–15 years	4 (1.0)
16–20 years	2 (0.5)
≥ 20 years	1 (0.2)
Work experience	
< 1	168 (41.0)
1–5 years	190 (46.3)
6–10 years	37 (9.0)
11–15 years	5 (1.2)
16–20 years	4 (1.0)
≥ 20 years	6 (1.5)
Working hours per week[c]	
< 20 h	10 (2.5)
20–39 h	66 (16.2)
40–59 h	223 (54.8)
60–79 h	63 (15.5)
80–99 h	23 (5.6)
≥ 100 h	22 (5.4)
Type of hospital	
District	184 (44.9)
Teaching or referral	226 (55.1)
Contact with patients	
Yes	388 (95.0)
No	22 (5.0)

[a]Includes orthopaedics, general ward, outpatient department, drug information center, dental clinic, and eye clinic
[b]Includes druggist, anaesthetist, health officer, reproductive health specialist, emergency surgeon, dental surgeon, optometrist, anaesthetic nurse, and clinical ophthalmic assistance
[c]Three missing values

Demographic characteristics that influence safety culture dimensions, patient safety grade, and number of events reported

Comparison of scores for the dimensions of patient safety culture revealed better results for district hospitals compared with those of teaching/referral hospitals in terms of 'Communication openness' (P = 0.01), 'Organizational learning–continuous improvement', and 'Teamwork across units' (P = 0.02). Overall, the nurse's perception of patient safety culture was higher (P = 0.03), and specifically, higher scores for the dimensions 'Organizational learning–continuous improvement' (P = 0.004) and 'Management support for patient safety' (P = 0.000) were reported from nurses than other health care staffs. Higher scores were observed in those staffs with less work experience for the dimension 'Organizational learning–continuous improvement' (Additional file 1). Additionally, cross table results showed that nurse staffs were more likely to report an 'excellent/very good' patient safety grade (P = 0.001), while health care staffs from other category were more likely report at least one event in the past 12 months than the other counterparts (P = 0.006) (Table 3).

Reliability and validity

Reliability analysis of the 41 items showed satisfactory internal consistency, i.e. Cronbach's α = 0.77, and ranged from 0.16 to 0.75 for the dimensions (Table 2). The dimension 'Staffing' had the lowest Cronbach's α value whereas 'Frequency of events reported' had the highest coefficient. Despite having no effect on the overall survey reliability, exclusion of the item 'Hospital management seems interested in patient safety only after an adverse event happens' would result in the 'Management support for patient safety' dimension reliability increasing from 0.48 to 0.70.

Table 4 shows the inter-correlations of the 12 dimensions and correlations between the total patient safety score and each dimension. 'Organizational learning–continuous improvement' is the dimension which was

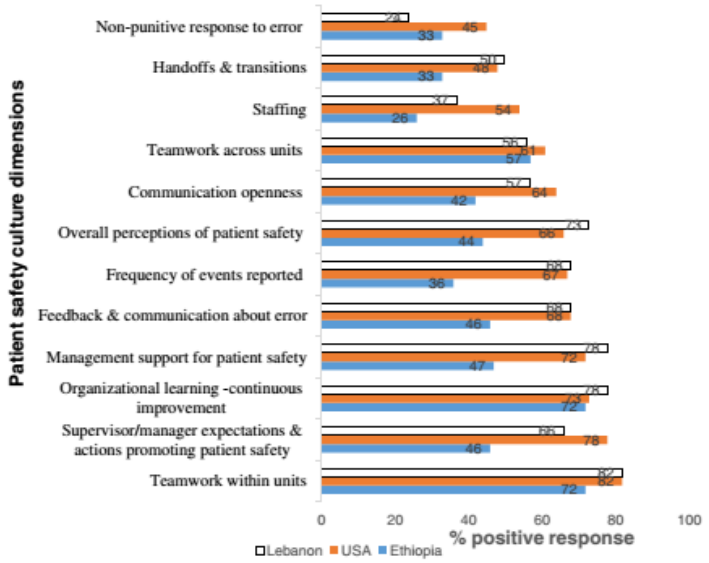

Fig. 1 Comparison of mean patient safety culture composite scores of Ethiopian public hospitals and benchmark scores [19, 20]. The composite-level percentage of positive responses was calculated using the following formula: [number of positive responses to the items in the composite/total number of responses to the items (positive, neutral, and negative) in the composite (excluding missing responses)] × 100

most correlated with 'Team work within units' (r = 0.58) but also the least correlated with 'Handoffs and transitions' (r = 0.01). The highest correlation was observed between 'Feedback and communication about errors' and the overall scale (r = 0.68). Ten of the 12 dimensions were significantly correlated with the total scale.

Barlett's test of sphericity for the questionnaire demonstrated sufficient inter-item correlations (χ^2 = 3805; df = 820, P = 0.000), and the KMO measure of sampling adequacy was satisfactory 0.858. Exploratory factor analysis extracted 11 factors which explained 59.3% of the variance. Four items (A7, A8, A10, A13) from the original questionnaire were dropped based on factor loadings for each item (all loadings > 0.40). The distribution of the items among dimensions was found to be different from that in the AHRQ model; except the dimensions 'Supervisor/manager expectations and actions promoting safety' (items B1 to B4) and 'Frequency of events reported' (items D1 to D3), the remaining items were clustered into several two or three dimensions not fitting to the factor structure of HSPOSC (Additional file 2).

Discussion

Assessing and promoting a culture of safety is recognized as a prerequisite step towards improving patient safety [21]. Culture assessment tools, such as the HSOPSC, provide an avenue for understanding the existing patient safety issues and increasingly utilized to gauge the changes in culture over time [19, 22]. The present study investigated the current status of patient safety culture in Ethiopian public hospitals using the HSOPSC instrument. The results of this study revealed that the overall positive response rate for all dimensions of the HSOPSC survey was not satisfactorily enough, akin to the findings from another local study [23]. Wami et al. [23] assessed the patient safety culture in Jimma Zone (Oromia region) and have found that the overall mean score for the positive perception of patient safety culture dimension was 46.7%. However, our study scored lower results when compared with the findings from other low- and middle-income countries (e.g. China (65%) [18], Lebanon (61.5%) [20], Saudi Arabia (61%) [24], Palestine (54%) [25], Taiwan (64%) [26]), and developed countries (e.g. the USA (65%) [19] and the Netherlands (52.2%) [13]). Of all the patient safety culture composites, there was none that fits the criteria for areas of strength. This also showed a severe deficit of patient safety culture in the studied hospitals. This is not a surprising fact given the tremendous work and emphasize on universal health care coverage, and interest in quality is only a recent move. Despite significant improvements in health care services, issues related to quality and safety have been inconsistently integrated into the Ethiopian health care system but, recently, the government ratified strategies for improving quality nationwide in the next 5 years (2016–2020) [27].

This study has identified many areas that need improvement. For example, the dimensions that received the highest positive response but yet needs some improvement were 'Teamwork within units' and 'Organizational learning–continuous improvement'. These dimensions were

Table 2 Percent average positive response for an item-level and composite

Composites and items	% positive[a]	Mean (SD)
Teamwork within units (Cronbach's $\alpha = 0.71$)	72	3.66 (0.75)
A1. People support one another in this unit	83	3.89 (0.93)
A3. When a lot of work needs to be done quickly, we work together as a team to get the work done	74	3.74 (0.99)
A4. In this unit, people treat each other with respect	75	3.75 (1.01)
A10.When one area in this unit gets really busy, others help out	56	3.27 (1.20)
Supervisor/manager expectations and actions promoting patient safety (Cronbach's $\alpha = 0.48$)	46	3.11 (0.48)
B1. My supervisor/manager says a good word when he/she sees a job done according to established patient safety procedures	62	3.44 (1.13)
B2. My supervisor/manager seriously considers staff suggestions for improving patient safety	61	3.39 (1.11)
B3. Whenever pressure builds up, my supervisor/manager wants us to work faster, even if it means taking shortcuts (R)[b]	28	2.77 (1.05)
B4. My supervisor/manager overlooks patient safety problems that happen over and over (*R*)	33	2.82 (1.15)
Organizational learning–continuous improvement (Cronbach's $\alpha = 0.54$)	72	3.74 (0.74)
A6. We are actively doing things to improve patient safety	85	4.02 (0.97)
A8. Mistakes have led to positive changes here	63	3.49 (1.04)
A12. After we make changes to improve patient safety, we evaluate their effectiveness	69	3.69 (1.04)
Management support for patient safety (Cronbach's $\alpha = 0.48$)	47	3.08 (0.88)
F1. Hospital management provides a work climate that promotes patient safety	51	3.09 (1.30)
F8. The actions of hospital management show that patient safety is a top priority	52	3.28 (1.27)
F9. Hospital management seems interested in patient safety only after an adverse event happens (R)	37	2.89 (1.12)
Feedback and communication about error (Cronbach's $\alpha = 0.71$)	46	3.31 (0.91)
C1. We are given feedback about changes put into place based on event reports	31	3.02 (1.05)
C3. We are informed about errors that happen in this unit	50	3.38 (1.20)
C5. In this unit, we discuss ways to prevent errors from happening again	57	3.55 (1.15)
Frequency of events reported (Cronbach's $\alpha = 0.75$)	36	3.00 (0.99)
D1. When a mistake is made, but is caught and corrected before affecting the patient, how often is this reported?	39	3.14 (1.21)
D2. When a mistake is made, but has no potential to harm the patient, how often is this reported?	30	2.84 (1.14)
D3. When a mistake is made that could harm the patient, but does not, how often is this reported?	38	3.02 (1.29)
Overall perceptions of patient safety (Cronbach's $\alpha = 0.22$)	44	3.02 (0.55)
A9. It is just by chance that more serious mistakes do not happen around here (R)	35	2.84 (1.15)
A14. Patient safety is never sacrificed to get more work done	41	2.94 (1.18)
A16. We have patient safety problems in this unit (R)	36	2.83 (1.22)
A17. Our procedures and systems are good at preventing errors from happening	64	3.50 (1.10)
Communication openness (Cronbach's $\alpha = 0.37$)	42	3.12 (0.85)
C2. Staff will freely speak up if they see something that may negatively affect patient care	43	3.17 (1.21)
C4. Staff feel free to question the decisions or actions of those with more authority	35	2.92 (1.27)
C6. Staff are afraid to ask questions when something does not seem right (R)	47	3.27 (1.34)
Teamwork across units (Cronbach's $\alpha = 0.51$)	57	3.36 (0.71)
F2. Hospital units do not coordinate well with each other (R)	54	3.25 (1.21)
F4. There is good cooperation among hospital units that need to work together	58	3.39 (1.21)
F6. It is often unpleasant to work with staff from other hospital units (R)	51	3.30 (1.07)
F10. Hospital units work well together to provide the best care for patients	66	3.53 (1.08)
Staffing (Cronbach's $\alpha = 0.16$)	26	2.49 (0.73)
A2. We have enough staff to handle the workload	32	2.49(1.30)
A5. Staff in this unit work longer hours than is best for patient care (R)	22	2.39 (1.15)

Table 2 Percent average positive response for an item-level and composite *(Continued)*

A13. We work in 'crisis mode' trying to do too much, too quickly (R)	24	2.60 (1.10)
Handoffs and transitions (Cronbach's $\alpha = 0.60$)	33	2.84 (0.76)
F3. Things 'fall between the cracks' when transferring patients from one unit to another (R)	30	2.82 (1.05)
F5. Important patient care information is often lost during shift changes (R)	37	2.89 (1.18)
F7. Problems often occur in the exchange of information across hospital units (R)	35	2.92 (1.06)
F11. Shift changes are problematic for patients in this hospital (R)	32	2.73 (1.21)
Non-punitive response to error (Cronbach's $\alpha = 0.44$)	33	2.91 (0.77)
A7. Staff feel like their mistakes are held against them (R)	26	2.76 (1.04)
A11. When an event is reported, it feels like the person is being written up, not the problem (R)	37	3.05 (1.06)
A15. Staff worry that mistakes they make are kept in their personnel file (R)	36	2.94 (1.17)
Overall (Cronbach's $\alpha = 0.77$)	46	3.15 (0.35)

[a]Mean percentage of positive responses calculated according to AHRQ instructions for every respondent
[b]Negatively worded items that were reverse coded (R)

also the highest rated in other studies but were areas of strength in hospitals across many countries, including Chinese [18], Lebanese [20], Taiwanese [26], and Saudi hospitals [24]. On the other hand, the dimension that had the lowest score was 'Staffing', reflecting that health care providers feel that staff allocation was not enough to handle the patient safety-related workload. A study conducted in the region [28] elaborated inadequate staffing levels as one of the reasons why patient safety is hard to achieve in countries, such as Ethiopia. Similar results were also observed in studies conducted in China [18], Lebanon [20], and Taiwan [26] but received a higher rating in the USA [19] and the Netherlands [26]. These disparities might be aroused as a result of the higher number of health care force in the developed countries. For instance, the Ethiopian health workforce is only 0.7 per 1000 population, lower than the WHO recommendation of 2.3 health workers per 1000 population [29]. However, it should be noted that staffing is part of the solution to patient safety issues but not the sole driver of change, as we can see the results from developed nations [19, 26] have not (yet) achieved the arbitrarily set value of 75% average positive score for all the dimensions.

It is also interesting to observe that the dimensions 'Handoffs and transitions' and 'Non-punitive response to error'—regardless of hospital type, profession, and work experience—were identified as major safety problems in this study. Health care staffs from the Middle-East, such as Palestine, Lebanon, and Saudi Arabia, were more negative about a non-punitive response to errors, whereas the American and Dutch health care staffs were more worried about information exchange when patients were handed over to the next provider and/or transferred to another unit. Although problems with handoffs and care transitions in the developed world might be due to the complexity of health care, ours was largely correlated and

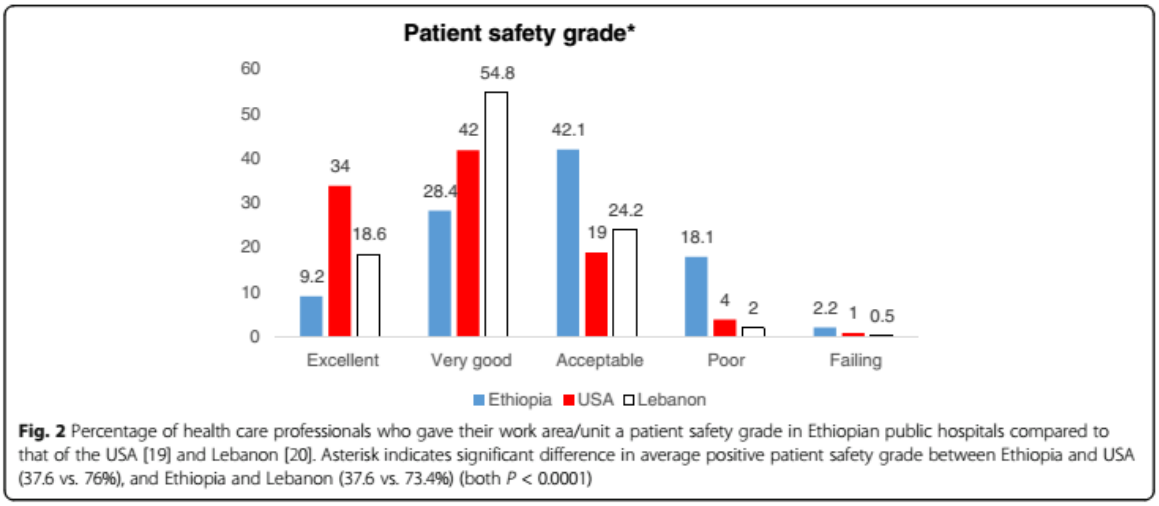

Fig. 2 Percentage of health care professionals who gave their work area/unit a patient safety grade in Ethiopian public hospitals compared to that of the USA [19] and Lebanon [20]. Asterisk indicates significant difference in average positive patient safety grade between Ethiopia and USA (37.6 vs. 76%), and Ethiopia and Lebanon (37.6 vs. 73.4%) (both $P < 0.0001$)

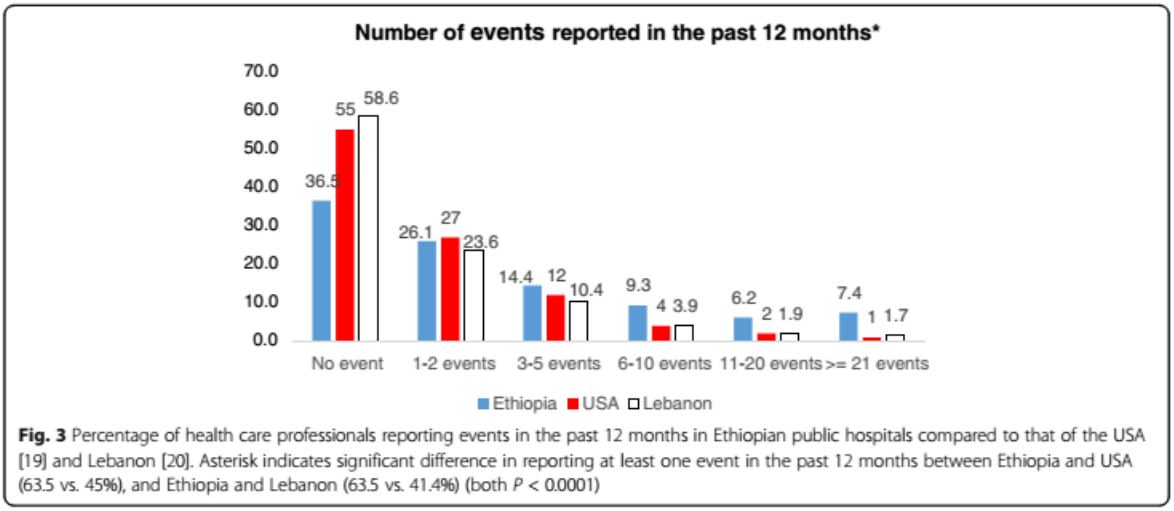

Fig. 3 Percentage of health care professionals reporting events in the past 12 months in Ethiopian public hospitals compared to that of the USA [19] and Lebanon [20]. Asterisk indicates significant difference in reporting at least one event in the past 12 months between Ethiopia and USA (63.5 vs. 45%), and Ethiopia and Lebanon (63.5 vs. 41.4%) (both $P < 0.0001$)

severely affected by the lack of teamwork across units, punitive response to error, and managerial inaction for promoting patient safety. The Institute of Medicine [8] has identified the challenges health care organizations move towards a safer health system; that is, moving from a culture of blame to one in which errors are treated not as personal failures but as opportunities to improve the system and prevent harm. This cultural transformation in the context of Ethiopia is not due to the willingness of staffs only but needs a strong leadership that enables staffs safety conscious, committed to learn from their mistakes and prevents errors from happening again.

Although the punitive approach to error reporting was commonly reflected in the Ethiopian health care staffs—as was the Arab world—this study uniquely identified better results in event reporting. That is two thirds of health care staffs reported at least one event in the past 1 year, when compared with the study reported in Lebanon (41%), Palestine (47%), Saudi Arabia (57%), and even in the USA (45%). However, the overall patient safety grade remained lower compared with that in the Lebanon (73.4%), Palestine (63.5%), Saudi Arabia (60%), and the USA (76%). Although previous studies [30, 31] have shown that there is an association between culture and safe care practices (e.g. event reporting), this study did not show such relationship. This might be because Ethiopian staffs—particularly, other health workers not classified as nurses, physicians or pharmacists—were very enthusiastic towards event reporting, but the level of cohesiveness across the teams and professional boundaries might impact

Table 3 Distribution of two outcome variables across staff position, type of hospital, and work experience

Characteristics	*Patient safety grade, *N* (%)			*Number of events reported, N (%)		
	Excellent/very good	Poor/failing/acceptable	*P* value	No events	At least one event	*P* value
Staff position						
Nurses	69(47.6%	76(52.4%)	**0.001**	47(32%)	100(68%)	**0.006**
Physicians	18(24.3%)	56(75.7%)		38(53.5%)	33(46.5%)	
Pharmacists	14 (24.1%)	44(75.9%)		22(37.9%)	36(62.1%)	
Others	34(41.5%)	48(58.5%)		22(28.6%)	55(71.4%)	
Type of hospital						
District	65(38.9%)	102 (61.1%)	0.63	57(34.5%)	108(65.5%)	0.47
Teaching/referral	70 (36.5%)	122 (63.5%)		72(38.3%)	116(61.7%)	
Work experience						
< 1 year	58 (40%)	87(60%)	0.68	59(40.7%)	86(59.3%)	0.25
1–5 year	60 (35.3%)	110 (64.7%)		57(35.4%)	104(64.6%)	
> 5 year	17 (38.6%)	27 (61.4%)		13(27.7%)	34(72.3%)	

Bold value indicates statistical significance

*Association between patient safety grade and number of events reported, $P = 0.75$

Table 4 Correlations with the total score and inter-correlation of the 12 dimensions

Dimensions	1	2	3	4	5	6	7	8	9	10	11	12	Total
1. Teamwork within units	1												0.57**
2. Supervisor/manager expectations and actions promoting patient safety	0.13*	1											0.38**
3. Organizational learning–continuous improvement	0.58**	0.11*	1										0.52**
4. Management support for patient safety	0.29**	0.15**	0.31**	1									0.59**
5. Feedback and communication about error	0.43**	0.13*	0.44**	0.31**	1								0.68**
6. Frequency of events reported	0.26**	0.10*	0.28**	0.30**	0.53**	1							0.57**
7. Overall perceptions of patient safety	0.08	0.05	0.05	0.08	0.12*	0.05	1						0.32**
8. Communication openness	0.31**	0.12*	0.25**	0.33**	0.52**	0.34**	0.13*	1					0.63**
9. Teamwork across units	0.35**	0.18**	0.34**	0.48**	0.34**	0.24**	0.13**	0.32**	1				0.66**
10. Staffing	−0.15**	0.08	−0.30**	0.005	−0.10**	−0.07	0.07	0.03	−0.03	1			0.09
11. Handoffs and transitions	−0.04	0.17**	−0.01	0.08	0.06	0.10*	0.09	0.16**	0.24**	0.06	1		0.40**
12. Non-punitive response to error	−0.22**	0.11*	−0.25**	−0.10*	−0.11*	−0.15**	0.08	−0.11*	−0.03	0.15**	0.20**	1	0.06

*Correlation is significant at *P* value less than 0.05
**Correlation is significant at *P* value less than 0.01

information exchange which could possibly jeopardize patient safety. Aveling et al. [28] were also described this challenge in two Eastern-African countries.

The present study has identified variations in the perception of patient safety culture across hospital types and staff positions. The results showed that nurses were found to have a positive effect on many patient safety culture predictors. As Nie et al. [18] allude to, nurses spend more time with patients and have the opportunity to deal with patient safety issues. Therefore, a higher score for nurses in safety culture is expected, and a similar finding was also reported by El-Jardali et al. [32]. The scores of district hospitals were also higher than those of teaching/referral hospitals in few of the dimensions.

This study has many limitations that need to be acknowledged. First, the assessment was given in English. Although English is the medium of instruction in the Ethiopian medical and health colleges and is the main language of communication in hospitals, staffs might not felt comfortable in responding—this might also impact the understandability of the instrument. One might think the questionnaire being in English, might affect the responses in some of the items in this study, but a recent study from Ethiopia assessing the patient safety culture assessed through native language has yet reported the same overall average positive patient safety culture score [23]. Secondly, although the internal consistency of the survey was fairly enough, the reliability analysis of individual constructs identified many factors with lower than adequate levels of reliability (alpha < 0.7). This could be partly caused by the factor structure of the HSOPSC model for these items might not fit the data well [26] but also indicate the instability of aspects measured by the instrument, which is linked to professionals' perception of safety at a given time and this, in turn, is extremely subject to change [33]. Designing an optimal model becomes more apparent. Unlike other studies focused on tool development, this study was not designed for optimization of HSOPSC measurement model; however, we conducted a model modification effort to examine if a reduced model can yield more similar factor structure to that of the original HSOPSC. But this model did not show an apparently better factor structure similar to that of the HSPOS. It is, thus, the performance of an Amharic language safety culture measuring tool should be evaluated in future studies. Finally, the HSPOC as a patient safety measure might not explicitly evaluate safety issues that would arise as a result of resource limitations, such as infrastructure. There is evidence that poor infrastructure, an absence of adequate equipment and supplies, profoundly affects health care staffs to provide safe patient care [28]. This needs caution in the interpretation of findings—as the lower score values in the patient safety culture might not reflective of cultural scores per se.

Conclusion

There is a severe deficit of patient safety culture in Ethiopian public hospitals. The overall patient safety score and most of the scores related to dimensions were lower than the benchmark score. Although the punitive approach to error reporting was commonly reflected, yet two thirds of staffs reported at least one event in the past 1 year. Creating a positive patient safety culture by implementing

actions that support all dimensions of safety culture is inevitable. The internal consistency of the total survey was fairly satisfied. However, the reliability analysis of individual constructs showed many factors less than an adequate level of Cronbach's alpha. Further research is needed to confirm the applicability of the translated version of the HSOPSC in the Ethiopian hospital settings.

Additional files

Additional file 1: Comparison of mean composite scores across type of hospital, staff position, and work experience. (DOCX 15 kb)

Additional file 2: Factor loadings in each item. (DOCX 16 kb)

Abbreviations

AHRQ: Agency for Healthcare Research and Quality; APPS: African Partnership for Patient Safety; HREC: Human Research Ethics Committee; HSOPSC: Hospital Survey on Patient Safety Culture; KMO: Kaiser-Meyer-Olkin

Acknowledgements

Alemayehu B. Mekonnen gratefully acknowledges the funding to support his PhD training provided by The University of Sydney International Students' Scholarship.

Funding

The study did not receive any external funding.

Availability of data and materials

The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

All authors conceptualized the study. ABM, AJM, JEB, DM, and ZA have all made significant contributions to the scientific content of this manuscript. ABM carried out data collection and analysis. ABM carried out the initial analysis and drafted the first manuscript. AJM, JEB, DM, and ZA critically reviewed and revised the manuscript. All the authors have read and approved the final manuscript.

Ethics approval and consent to participate

The study was approved by the University of Sydney Human Research Ethics Committee (HREC)—Project Number: 2015/818—and the Institutional Review Board of the University of Gondar, Ethiopia (O/V/P/RCS/05/624/2016).

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

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Received: 21 July 2017 Accepted: 31 August 2017
Published online: 13 September 2017

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Electronic supplementary materials published online for chapter 7 are supplied as appendices (additional file 1, page 340; additional file 2, page 341)

Chapter 8

Health care Professionals' Perspectives of Patient Safety and Patients' Experiences of Medication-related Adverse Events

Mekonnen AB, McLachlan AJ, Brien JE, Mekonnen D, Abay Z. Healthcare professionals' perspectives of patient safety and patients' experiences of medication-related adverse events: a qualitative study from Ethiopia. (Submitted to BMC Health Services journal)

8.1 Abstract

Background: Patient safety has received international attention over the last two decades; however, there are limited reports from Africa. This study aimed to explore health care professionals' perspectives on patient safety and patients' experiences of medication-related adverse events in public hospitals in the Amhara region, in Ethiopia.

Methods: A Hospital Survey on Patient Safety Culture (HSOPSC) questionnaire was administered to the 480 health care professionals (HCPs) working in ten public hospitals in Ethiopia. This included free-text comments about patient safety, incident and error reporting systems. Semi-structured in-depth interviews with HCPs were conducted. Patients were also approached to be interviewed about their experiences of perceived medication-related adverse events. Data were analysed using content analysis.

Results: Of the 410 questionnaires received, 132 health care professionals included free-text comments, and a total of 27 semi-structured in-depth interviews were undertaken (including 19 patients, and eight HCPs). Many HCPs revealed that patient safety incidents were common, and most were medication related. HCPs identified 26 factors that influenced patient safety, and the data were further merged, resulting in six main themes being identified: 'work environment factors', 'organizational and managerial factors', 'individual HCPs factors', 'task factors', 'team factors', and 'patient factors'. The greatest barriers to optimal patient safety reported were workforce and material deficiencies, physical environment (e.g. poor infrastructure) and lack of managerial support for patient safety. Most patients experienced at least one perceived medication-related adverse event. Patient's experiences of medication-related adverse events did not seem to affect patient's satisfaction for health services.

Conclusion: This study showed that patient safety incidents were perceived to be common, and many factors were identified as barriers to patient safety. Patients expressed a range of experiences related to their medication.

8.2 Introduction

Patient safety is increasingly recognized internationally as a priority for improving the quality of patient care [1]. Adverse events in hospitals affect nearly one in ten patients, and some of these events are preventable [2]. Medication-related adverse events are the most frequent types of adverse events [2] and are associated with prolonged hospital stay, increased economic burden and an almost twofold increase in the risk of mortality [3]. Although there is a limited data on patient safety literature in the developing countries [4], harm resulting from unsafe patient care is thought to be higher in these nations than in developed countries [5]. In Africa, this is increasingly viewed as a basic right under the umbrella of universal health care coverage and access [6].

Until recently, most patient safety efforts have been focused on the detection and analysis of adverse events. Efforts should also be made to enhance a culture of safety among health care professionals to create an approach to prevent adverse events and to create a safe environment, where problems can be discussed without fear of retribution [1]. Comprehensive patient safety systems, including both a culture of safety and organizational supports for safety processes, are key to patient safety improvement. Health care professionals, managers, and patients are encouraged to be vigilant in identifying potential or actual errors, taking appropriate measures to prevent harm, and disclosing appropriate information on errors that do occur to facilitate learning and the redesign of care processes [7]. Patient safety culture is described, according to the Agency for Health care Research and Quality (AHRQ) [8], as an understanding of the values, beliefs, and norms about what is important in an organization and what attitudes and behaviours related to patient safety are supported, rewarded, and expected.

It has become apparent that health care organizations need to gain a clear understanding of patient safety aspects requiring urgent attention and identify the strengths and weaknesses in delivering safe patient care [9].

Although patient safety and error reduction are the shared responsibility of all health care professionals, clinicians rely on patients as a source of evidence for their safety, and patients' engagement in safety initiatives is crucial in achieving higher levels of patient safety [10, 11]. Yet, patients may not commonly be involved in reporting adverse events, including medication-related events [12]. Examining health care professionals' perspective of patient safety culture and factors influencing patient safety is an initial step, and a shared decision between the patient and the health care professional is central to sustainable patient safety culture [13]. There is a growing recognition of the importance of establishing a culture of safety in health care. Two studies [14, 15] have reported patient safety issues in Ethiopia. While research using quantitative methods is necessary to identify and quantitate relevant issues, a qualitative methods approach is needed to explore perspectives of health care professionals and patients on patient safety and medication-related adverse events.

8.3 Methods

8.3.1 Study Setting and Participants

The study was conducted in the Amhara region of Ethiopia. It is one of the nine regions of Ethiopia located in the northern part of the country, with an estimated total population of approximately 18 million. This region has 17 public hospitals, 520 health centers, and 2941 health posts (—also called as satellite health stations) [16]. The Ethiopian health care system is challenged by poor health care financing, and it is highly dependent on out-of-pocket health expenditure. Out-of-pocket health expenditure (% of private expenditure on health) was 80% as of 2011 [17]. Mainly, the population receives health services from public health institutions. This study was conducted in 10 conveniently selected public hospitals in the Amhara region (four teaching/referral hospitals and six district hospitals). Study participants were recruited from these hospitals and included physicians, nurses, pharmacists, other health care

professionals (e.g. technicians) and patients. The study was conducted between February and August 2016.

8.3.2 Data Collection

This qualitative study was performed as part of a larger project, designed to implement patient safety programs in a resource limited-setting [18]. The present study [18] aimed at assessing health care professionals' perspectives on patient safety, and patients' experiences of medication-related adverse events through a mixed-methods study comprising a survey and in-depth interviews. For the survey, we adopted the 'Hospital Survey on Patient Safety Culture' (HSOPSC) questionnaire developed by the Agency for Health care Research and Quality (AHRQ) [19] (Appendix 4.2). This questionnaire consists 42 Likert-scale items that measure 12 patient safety culture composites, and a section for two outcome variables: overall patient safety grade and the number of events reported. This survey includes a collection of socio-demographic characteristics, and a free-text field for health care professionals to provide comments on patient safety, error or incident reporting.

Purposive and snowball techniques were utilized to identify potential study participants. Invitations to participate were sent via letter or email to health care professionals that had worked in their hospital for at least 6 months. Patients (aged > 18 years) who were in-hospital at the time of data collection and were taking at least two regular medications were also invited for interview by a healthcare professional who had been a participant in this study. A semi-structured interview guide was used (Appendix 5.6). All interview guides were translated from English versions to the local language (Amharic) by two translators who are native speakers and working in the health care industry and validated by two of the research team (ABM, DM). Informed consent was obtained and we conducted face-to-face interviews at a time and place to suit the participants. We encouraged patients to reflect their own experiences of medication-related adverse events and asked them to describe an example of a known medication-related

adverse event they encountered during their hospital visits. We used prompts when necessary to encourage further elaboration, and all interviews were conducted by an English/ Amharic speaking investigator (ABM). We collected data with each of the two participant groups until a point of saturation was reached. The interviews lasted between 20 to 60 minutes for HCPs and 15 to 35 minutes for patients. We recorded all interviews using audio-tape with the informed consent of participants.

8.3.3 Data Analysis

The principal investigator carried out verbatim Amharic transcriptions of all interviews, which were then translated into English, and assigned a unique identifier. Texts were analysed using a qualitative content analysis as described by Hsieh and Shannon [20]. The current study incorporates qualitative data from both text-comments and interview data, and qualitative content analysis is best suited for this study as it creates an opportunity for quantification of data [21].

The first step involved reading of transcripts for overall understanding, and then transcripts were coded using conventional content analysis techniques [21]. That is, we highlighted the exact words from the text that appeared to capture key words and concepts. We approached the text many times, and through the process, labels for codes that reflected the key thought emerged. Inter-related or similar codes were then merged into different categories. An integrated approach to the coding structure was employed [22], and thus, categories were developed inductively and deductively. The categories were also developed taking into consideration the main factors affecting patient's safety proposed by Vincent et al.'s [23] multilevel framework (i.e. institutional, organizational and management, work environment, task, team, staff, and patient factors). Descriptive statistics were used to summarize the demographic data.

8.3.4 Ethical Consideration

The study was approved by The University of Sydney Human Research Ethics Committee (HREC) - Project No. 2015/818, and the Institutional Review Board of the University of Gondar, Ethiopia (O/V/P/RCS/05/624/2016).

8.4 Results

Of the 410 questionnaires received, 132 health care professionals included free-text comments related to patient safety, error and incidence reporting. The comments presented here were collected from the diverse range of professionals, including nurses, physicians, pharmacists and paramedics (e.g. technicians, administrative staffs) across various hospital working units (Table 8.1). Additionally, 22 patients and 16 HCPs were invited for an interview; of these, a total of 27 semi-structured in-depth interviews were undertaken (19 patients, and 8 HCPs) (Figure 8.1). The mean age was 46 (range, 19–79 years) for patients and 30 (range, 26–36 years) for health care professionals.

Table 8.1 Participant Characteristics

Characteristics	Number of respondents	Percentage of respondents (n=132)
Working unit		
Medical unit	31	24%
Surgery	13	10%
Gyn/Obs	14	11%
Paediatrics	12	9%
Pharmacy	17	13%
Laboratory	14	11%
Others*	29	22%
Staff position		
Nurses	52	39%
Physicians	20	15%
Pharmacists	21	16%
Technicians	17	13%
Others**	22	17%
Years in hospital		
< 1	82	62%
1 – 5	47	35.5%
6 – 10	1	1%
11 – 15	2	1.5%
16 – 20	0	0%
≥ 20	0	0%
Years in current department		
< 1	80	61%
1 – 5	47	35.5%
6 – 10	3	2%
11 – 15	2	1.5%
16 – 20	0	0%
≥ 20	0	0%
Work experience		
< 1	51	38.5%
1 – 5	65	49%
6 – 10	12	9%
11 – 15	1	1%
16 – 20	2	1.5%
≥ 20	1	1%
Working hours per week		
< 20	2	1.5%
20-39	22	16.5%
40-59	78	59%
60-79	16	12%
80-99	7	5%
≥ 100	7	5%
Type of hospital		
District	62	47%
Teaching or referral	70	53%

* Includes departments such as radiology, anaesthesia, orthopaedics, general ward, outpatient department, dental clinic, eye clinic; **Includes druggist, anaesthetist, health officer, reproductive health specialist, emergency surgeon, dental surgeon, optometrist, anaesthetic nurse, clinical ophthalmic assistance

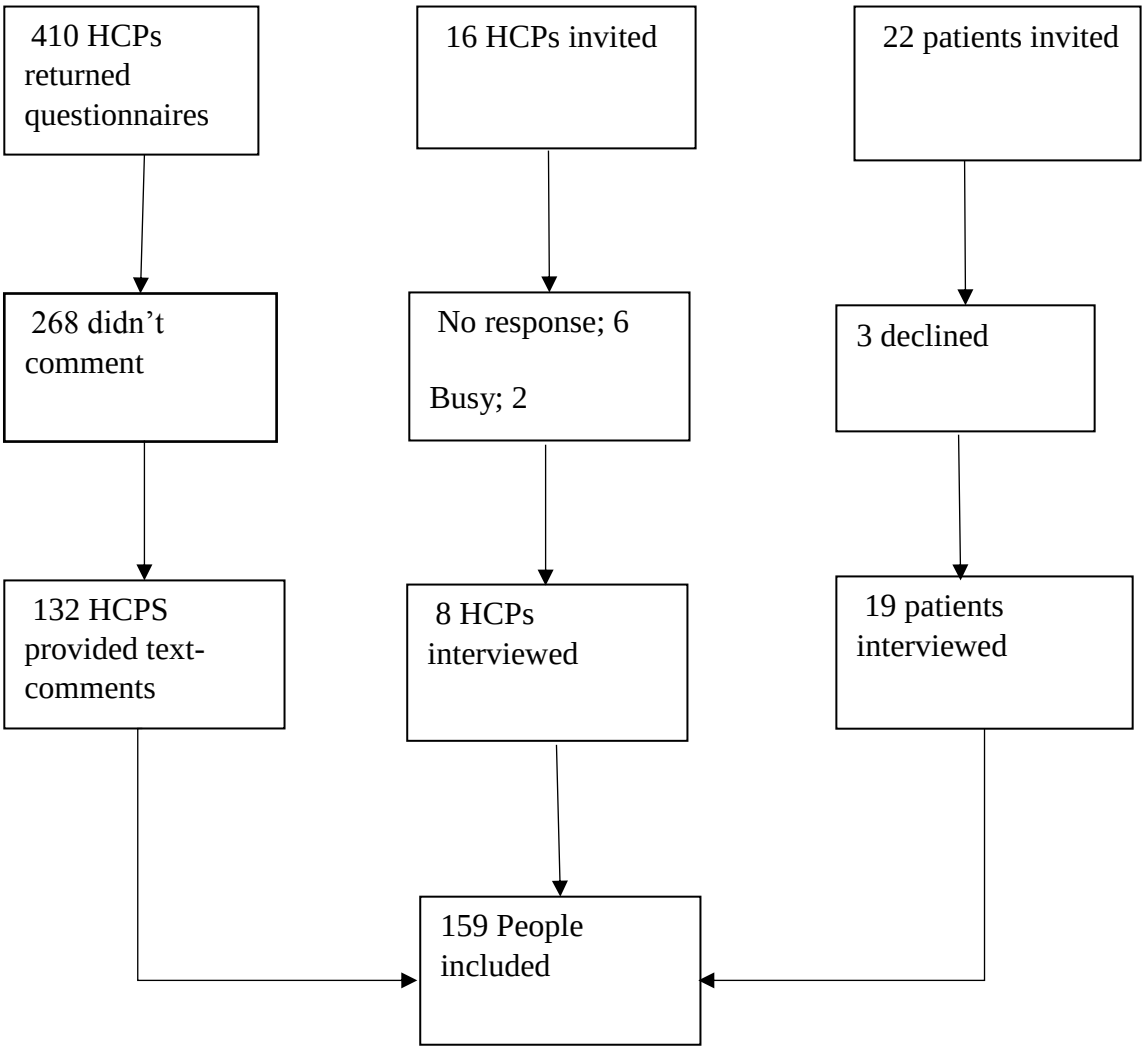

Figure 8.1 Flow Chart of Included Participants

Health care professionals' perspectives on patient safety

1. Barriers and facilitators to patient safety

We identified 26 factors that influenced patient safety, and this was further merged, resulting in six main themes classified as 'work environment factors', 'organizational and managerial factors', 'individual HCPs factors', 'task factors', 'team factors', and 'patient factors'. Seven of the 26 factors functioned as both barriers and facilitators, eighteen factors were perceived only as barriers, and only one as a facilitator. Table 8.2 presents a summary of the factors influencing patient safety, as perceived by the HCPs.

Table 8.2 Factors Affecting Patient Safety, as Perceived by Health care Professionals

Categories	Codes	*Number of respondents	Patient safety barriers	Patient safety facilitators
Work environment factors	Workforce deficiencies and workload	35	√	
	Material deficiencies	34	√	
	Physical environment	22	√	√
	Shift patterns	4	√	
Organizational and management factors	Safety focus	25	√	√
	Leadership incapability	9	√	
	Political commitment	8	√	
	Financial constraints	13	√	
	Blame culture	8	√	
Individual HCP factors	Lack of adequate knowledge, attitude, skills	19	√	
	Staff commitment and satisfaction	14	√	√
	Professional accountability	5	√	√
Task factors	Incident reporting	14	√	√
	Delay in getting health services	7	√	
	Infection prevention procedures	7	√	√
	Lack of safety protocols	3	√	
	Trend prescribing	2	√	
	Poor documentation	2	√	
	Lack of patient counselling	1	√	
	Lack of follow-up	1	√	
Team factors	Communication	14	√	√
	Poor teamwork	13	√	
	Lack of supervision	1	√	
Patient factors	Economic constraints	4	√	
	Patient involvement	3		√
	Patient illiteracy	2	√	

***** The total number of respondents (from text and interview data) who mentioned the respective factors that are perceived to affect patient safety.

Work environment

The majority of HCPs concerned about the lack of enough health care professional, whom able to sacrifice himself/herself for patient safety. And, the associated workload, that could also be due to the high patient flow, obliged HCPs to engage with routine things, and ended them restless. These imply the perceptions of high pressure imposed on them, which could result in a lack of time for involving oneself into the patient safety practice, as this is also a time taking process. Participants suggested that the health care system should have adequate numbers of well-trained health care workers to provide safe quality care.

"Patient safety is something we have to think about it. With the staffs we have and the spaces available for patient admissions greatly impacted the safety of patients. I think this is a general comment that should be forwarded to the hospital director or CEO" [Nurse, Gondar university hospital].

"It is unthinkable to achieve the best patient safety possible without having enough staffs" [Anaesthetist, Debre Markos hospital].

In relation to material context, the problem was so vast that the participants expressed deficiencies in terms of supplies (e.g. gown, mask, pillow, personal protective materials, and mattress), adequate and functional equipment (e.g. CT scan, ultrasound, X-ray), and availability of medications, such as antibiotics. Participants also suggested that hospitals should have functional equipment and a constant supply of medications in order to enable provision of the right treatment at the right time. Also, the unavailability of these services meant that the patient should have to look for services out of the hospital, which is usually expensive in the studied areas.

"The other important medication related problem is related to availability. Most of the time ceftazidime and antivenom are not available in the hospital pharmacy. So, there is an inappropriate excessive cost incurred on the patient as they bought it from community

pharmacies. You can imagine a cost for antivenom is 900 birr in the hospital whereas it is 1200 birr outside. Surprisingly enough, these medications are not available in this hospital" [Nurse, Gondar university hospital].

Various aspects of the physical environment posed threats to patient safety. There was a strong belief among health care professionals that patient safety is about having a safe physical environment, including safe infrastructure and cleanliness that create a safe environment for patients. A safe environment was characterized as involving well-designed buildings with adequate space (e.g. rooms for various services such as patient admissions and waiting area, wards, rest rooms, and offices), consistent supply of water and electricity, and furniture (e.g. tables, bed). It was also characterized as one which promoted patients' physical safety by maintaining cleanliness.

"The issue of patient safety is a question for this hospital. Patients are lying on the corridor everywhere. I don't think patients get rid of their disease because of their medication only, it also because of other additional psychological treatments" [Nurse, Gondar university hospital].

Very few people also described as shift changes and schedules were very problematic in delivering safe patient care. Unlike the previous two shift system, this was particularly an issue after an 8 hour shift endorsed by the Regional Health Bureau; their fear was mostly emanated from the provision of incomplete information for the person who going to take over the activity.

"…8 hour shift is difficult to hand over the full information from the off going person to the ongoing person" [Nurse, Metema hospital].

Organizational and managerial factors

Whereas many HCPs expressed mixed views on the managerial support for patient safety initiatives, all described patient safety was something that should be prioritized and involved strong leadership. There was, however, a huge gap between what the interviewees agreed and

what the administrative staff/leaders were doing. The participants described managers barely involved, and there was a lack of commitment to promote patient safety. Their focus was mainly on service expansion than working towards improving patient safety, according to HCPs. Managers devoted themselves for political acceptance and gave emphasis on unrelated matters to patient safety, such as political mobilization of the staffs. And yet, some explained their position as a manager was due to their ties with some senior politically affiliated individual, and not merit based.

"Most hospital managers focused whether the customer gets the service or not rather than really questioning the customer's safety is maintained or not, and nobody follows whether the patient is getting complete care or not" [Pharmacist, Metema hospital].

"Many autocrats are there and are freely paid… no one can freely say about them because their relatives may be put on higher/senior management position" [Pharmacist, Debark hospital].

At the organizational level, financial constraints were mentioned by many HCPs as an important factor to the challenge in achieving improved patient safety. The data ascertained that these financial problems can extend up to the non-existence of duty programs, and lack of incentives and additional benefits for the staffs. They said that these could greatly impact the service delivery, and of course, the satisfaction of staffs.

"….the hospital partially supports us but we need additional support schemes to strengthen our effort. We are doing this service because of our initiative without any additional payment" [Pharmacist, Metema hospital].

Blame culture was one of the factors influencing patient safety, as perceived by the HCPs. There was a strong convergence in views that HCPs were not reporting events due to fear of negative repercussions, such as punishment and conflicts at the workplace. Fear of punishment was particularly mentioned as a key reason for not reporting patient safety incidents. Openness

about incidents, and learned from mistakes were hardly undertaken, and most incidents were withheld, with the fear that HCPs who had honestly reported their mistakes were usually blamed and/or demoted from their position.

"It is game to think about patient safety, all personnel does activities by fearing punishment from their supervisor, seniors" [Physician, Gondar university hospital].

"Most workers do not report errors or events because they fear that they will be responsible and questioned" [Pharmacist, Felege Hiowt referral hospital].

Individual HCPs factors

Many HCPs ascertained that there was a severe deficit of knowledge and skills that are important for ambitious patient safety initiatives, and few HCPs also believed negative attitude towards incident reporting posed a problem on patient's safety. Yet, there were few HCPs that had questioned the quality of professionals, and this was being declined from time to time. And thus, training is important to equip the HCPs with the necessary knowledge and skill, and sensitization regarding patient safety awareness is part and parcel of the solution. Less experienced HCPs, for example, during medication administration might result in compromised patient safety and coach them to prevent untoward occurrences were rarely done.

"I think we need some kind of sensitization to all of the staffs. Besides, whenever there is an update on guidelines, it is important to arrange training for the whole staff" [Pharmacist, Metema hospital].

"For example, if you made the physician to change something he might complain why the nurse is doing as such" [Nurse, Gondar university hospital].

Participants also noted mixed feelings regarding staffs commitment to quality patient care and professional accountability. While most cited that the problems were arose as a result of lack of staffs' interest, various comments were forwarded; to mention a few, running for personal benefit, inattentiveness for the patient, and dissatisfaction with the work they were doing. Many

added that without the staff being satisfied in the workplace, it was tough to think about quality patient care, which in turn, affects the satisfaction of patients. There was also unfairness in patients' treatment, such as taking care of a patient with close social contact but ignoring the voiceless. According to participants, there were also very few keen professionals devoted themselves for patient safety, even in areas where they are not paid for.

"The majority runs to have personal benefit and to look like mistake free than for questioning/asking/doing for better patient safety directly or indirectly. But few did it" [Physician, Gondar university hospital].

"Specifically, in the emergency related to triage, emergency is not for an emergency patient rather being for those having social contact….Only those having a big family and serious people are getting the attention for the service, the calm ones are ignored" [Lab technician, Felege Hiwot referral hospital].

Task factors

The majority of the HCPs agreed that patient safety incidents/ errors occurred in their workplace, and aware that these were poorly reported. For example, there was no system to record and report incidents and there was a view that, because of this, incidents that occurred were continually undetected and under-reported. Although there was no robust system for incidence reporting including forms and documents, yet, there were few participants expressed their view that incidences were rarely occurred, and even when they occurred, they were not reported fearing their bad consequences. In the contrary, very few participants pointed out that there were staffs engaged in reporting incidents/errors although this was also declining recently.

"We don't have a culture of reporting when problems occur in a hospital. We are usually holding it. As you know the fate of reporting, we don't have a culture of exposing wrong doings" [Nurse, Gondar university hospital].

"No mistakes so far have been reported to me. There is no such type of system. Even if mistakes occurred they tend to be held among the health care professionals than being reported" [Nurse, Gondar university hospital].

Another issue participants rose in relation to task factors were the delay in getting health services and procedures related to infection prevention. There were times when patients were waiting for a long period of time (more than a week) to get health services, and at times, lab results lost, and for services, such as receiving comments for radiology examination, it might take up to a day or more. Participants argued that infection prevention was not done appropriately, for example, cross contamination was a possibility, and patient transfer of specimens without personal protective equipment was a reality. There were fewer participants, however, that their hospital had been endorsing proper infection prevention techniques, and the incidence of hospital acquired infections was on the verge of declining.

"There is a delay of lab results because of the shortage of laboratory technicians, miscommunications between porters and interns, lab results are repeatedly lost and the patient doesn't get the service timely" [Lab technician, Felege Hiwot referral hospital].

Other task-related factors that negatively affect the safety of patients listed were the absence of protocols and guidelines for patient safety, trend prescribing, poor documentation, and the lack of follow up and patient counselling.

"Surprisingly enough, the major problems arising are as a result of catching up things as a trend and thinking that is appropriate to do that way. But, when we tried to dig out the situation, as there was no any scientific evidence for this or there were already changed evidences, rules or procedures" [Pharmacist, Metema hospital].

Team factors

Data analysis revealed that communication with colleagues in the workplace could affect patient safety, positively or negatively. For example, many believed that patient care is a shared

responsibility among the HCPs, and important patient information should thus, be communicated. This also paves a way for free discussions regarding patient safety issues, and prevents future incidences that might be occurred, and promotes a culture of continuous improvement. Participants also believed that HCPs and patients needed to have good interpersonal relationships, communication, and cooperation to improve patient safety processes and practices. However, many argued that activities were poorly communicated and coordinated, teamwork was not prioritized, lack of respect prevailed, and supervision regarding patient safety issues was rarely done.

"There are many obstacles for patient safety, these are: the top managers do not communicate well with the health care providers to promote patient safety" [Anaesthetist, Debre Tabor hospital].

"Most importantly, teamwork is an important thing but usually ignored" [Nurse, Gondar university hospital].

Patient factors

The interview data also ascertained patients as factors to the barriers and facilitators to their own safety. While financial constraints and illiteracy likely to hinder patient's safety, patient involvement in their care was described as a facilitator to their own safety.

"What I thought regarding the barriers to medication safety issues is the interaction between the pharmacist and the patient. For example, the way you communicate with the patient matters. The way they understand might be different from you, and you might think them as they understand it. So asking their feedback is very important part of the channel. So receiving any feedback from the patient is very important for medication safety" [Pharmacist 2, Debre Markos hospital].

2. Common incidents and strategies to improve patient safety

Beyond the barriers and facilitators to patient safety improvement discussed above, common incidents/errors were reported, and suggestions were provided for further enhancing safety. Most incidents were medication-related and ranged from minor prescription errors to fatal events, such as an overdose of anaesthetics. Apart from medication availability and issues related to patient adherence, common incidences as reported by the participants included dispensing errors (e.g. atropine was dispensed in place of morphine), wrong diagnosis and mismatch between diagnosis and prescribed medication, administering the wrong drugs to the wrong patient (e.g. arisen as result of exchange in patient's name), giving the wrong dose (e.g. injecting the wrong dosage and overload of IV fluids), taking a medication for which patients are allergic to and/or experiencing serious side effects that need treatment change but were actually made to continue, unnecessary and duplication of therapy, the patient is in need of a medication but not actually order to take, product defect and drug interactions, and problems in writing the prescription including the dose.

One of the main research questions driving this study was to identify the strategies required to enhance patient safety practices, and this was more explored in the in-depth interview. Participants identified a range of changes in practices, processes, structures, and systems that they believed would help improve patient safety in the Ethiopian health care system. Some of the suggestions given were:

- Involving clinical pharmacists in the multidisciplinary teams
- Preparing safety protocols, checklists, and guidelines for process evaluation, and implementing hospital reform and nursing standards
- Providing adequate trained human power
- Improvement of work-place environment (including infrastructure and materials)
- Instituting leadership for patient safety

- Creating positive attitude and awareness of HCPs and hospital managers for patient safety
- Promoting collaboration, teamwork and all stakeholders involvement for patient safety, including the patient
- Allocating a person/team responsible for patient safety evaluation
- Providing adequate patient education

Patients' experiences of medication-related adverse events

At the time of the interview, patients had been taking medications for their illness for at least 6 months and for a maximum of 10 years. Most patients' primary diagnoses were hypertension, diabetes mellitus, and heart failure, and the number of medications they had been taking was 2 to 4. Patients revealed various perceived experiences to their medication; and of these, 14 patients had encountered at least one medication-related adverse event. These adverse events ranged from minor/moderate discomfort, such as heartburn, headache, and dizziness to severe events (e.g. unconsciousness).

"Sometime ago, I was engaged in a heavy duty and unknowingly, I was found unconscious. I understood later that it hadn't been injected in such occasions. I was in the middle of death and life! After that, I extremely take caution in the usage of my medications" [Patient 10, Male, 79].

"Even worse I don't feel good when taking my medicines, it burns my heart" [Patient 11, Male, 52].

"The problem currently is feeling a sense of heart burn, but the medication I was taking before didn't do that" [Patient 6, Female, 35].

The majority of patients received medication counselling regarding their adverse impact, and had fairly adequate knowledge about their medications and knew why they were taking them. However, patients were naive to medication errors or mistakes committed as a result of HCPs

during their recent hospital visit. Medication changes were common, and participants believed that any changes in their medication brought both negative and positive consequences. For example, few participants were very concerned about their medication and questioned whether it had added any aggravating effect on their problem.

"I told my doctors to stop the medication in case I am getting better but they advised me to continue it" [Patient 4, Female, 50].

"…I was told to drop off all the medications I was taking before…they advised me as the medicine I was taking before is not useful for me…they order to take only one medicine…as to my thinking this is my problem…if the medicine is not a benefit for me from the beginning, I thought it is not good for my health" [Patient 1, Male, 36].

Most patients were satisfied with their health services, although those not happy with the services were patients perceiving private hospitals were better in maintaining their safety. Patient's experiences of medication-related adverse events did not seem to affect patient's satisfaction for health services, however. Patients had described various perspectives to improve their safety, and many of the problems raised were related to high patient flow, affordability issues, medication availability, and delay in getting health services.

8.5 Discussion

Although unsafe patient care is thought to be higher in the developing nations, less is known about patient safety [5]. Investigation of patient safety issues in Ethiopian health care is sparsely done and is an area of research that is relatively new. It is only recently that the government ratified a five year (2016–2020) strategy for improving quality patient care in the nation [24]. The present study provides a wider perspective on patient safety as viewed by both HCPs and patients in public hospitals of Amhara region of Ethiopia.

As part of the HSOPSC study, we explored HCPs perspectives of patient safety using thematic analysis of data that emerged from comments received from the self-administered questionnaire, and from an in-depth interview of HCPs. Comments received from HCPs about patient safety, including error and incident reporting, and data analysed from an in-depth interview of HCPs revealed a significant amount of information about their perceptions of patient safety, and the barriers and facilitators that influenced the provision of safe patient care. We identified that many HCPs were well aware of patient safety incidents and/or errors but rarely reported due to many factors. Six factors that fall at many different levels within the health care, ranging from individual health care staffs' factors and patient involvement to organizational context were identified.

The findings of this study indicated that the greatest barriers for achieving an optimal patient safety were workforce and material deficiencies, physical environment (e.g. poor infrastructure) and lack of managerial support for patient safety. Most of these factors were consistent with the findings reported in previous studies in Ethiopia [14, 15]; however, some of the findings such as task factors, and patient factors were scarcely or not reported at all in these local studies. Our previous survey showed that, of all the patient safety culture composites, staffing received the least score complementing our finding that understaffing is a very serious issue that leads to a compromised patient safety. The greatest challenge—lack of human resource is not unique to this study, but other similar findings were also observed in resource-limited settings, including China [25], Lebanon [26] and Taiwan [27] but received a higher rating in the developed nations, such as the USA [28]. There are studies showing that heavy nursing workload [29], and lower pharmacy staffing levels [30] adversely affect patient safety. Besides nurse staffing levels, Aiken et al [29] also showed that poor nurse work environments—a work environment lacking adequate resources, communication, and leadership commitment—have a significant effect on patient mortality.

Unlike other more developed nations, one of the difficulties and challenges faced by Ethiopian health care system is the lack of infrastructure (e.g. rooms for patient admissions), poor sanitation, and material deficiencies (e.g. supplies, adequate and functional equipment, and medications) for achieving an optimal patient safety outcome. Parts of the problem for all of these are interrelated with inadequate government funding and clinical leadership. The seriousness of these problems are vast, and in one or the other way, resulting in poor patient care, and the problem extends from delaying in getting health services to avoidable patient harm. Aveling et al [15] also emphasized in their findings that the scale and impact of material deprivation along with the weakness of clinical governance and accountability differentiates the findings from high-income countries. Additionally, a lack of management support and organizational safety culture were identified by participants in this study as a barrier to patient safety in Ethiopian public hospitals. According to the participants, many managers were incompetent and not safety conscious, and their primary aim was health service expansion. There were yet, managers who devoted their time for the mere purpose of political promotion and most appointees were based on political affiliation than clinical leadership. Among the participants, there was a strong held belief that without having the appropriate person at the right place, it would be tough to achieve what hospitals are striving to do, and it is senseless to talk about other problems arisen as result of lack of effective clinical governance. While improving patient safety requires adequate resources (e.g. human and material) but these are not adequate on their own; also requires managerial support and change in culture and structure of governance [31, 32].

The findings of this study also highlighted individual staff factor considerations, most notably, a lack of knowledge, skills, and attitude pertaining to patient safety, otherwise necessary for the delivery of safe patient care. The lack of patient safety competencies identified by participants encompassed a lack of knowledge and skills pertinent to correctly prescribing

medications, administration of injections, and monitoring patients. Although participants noted there were few keen staffs committed to sacrifice for patient safety, many did not have interest, and usually not happy with what they were doing. Participants, on the other hand, revealed that those who adhered to their professional responsibility were the ones who took initiatives for improving patient safety. Various task factors were related to patient safety problems, such as the absence of incident reporting, not following infection prevention procedures, delay in delivering health services, and the lack of safety protocols, patient counselling and follow-up. Participants mentioned that poor communication and teamwork, lack of cooperation, respect and supervision, together with the lack of an incident reporting system undermine the development of a culture of safety in Ethiopian public hospitals. Previous studies [14, 15] also showed that inter-professional communication is weak, and this is mostly due to hierarchical differences, and patient safety is greatly influenced by the norms and values of professional thought and status. These findings also correspond with the findings of studies conducted in Sweden [33, 34]. The presence of professional hierarchies reflects that HCPs feel uncomfortable, and encounter difficulties to raise their concerns with other colleagues [33]. An organizational culture that promotes reporting and encourages non-punitive response to error and improved communication are reported as important factors to improve patient safety culture [34]. However, the participants in our study described that incident reporting was infrequently done, when so do, it was usually not documented.

The HCPs believed that patient involvement in patient's own safety influenced patient safety positively. However, economic constraints and insufficient health literacy negatively impacted their safety. These findings were also supported by individual patient interviews. Although little is known, there is currently an international move towards patient engagement in their care [35]. Yet, this depends on the level of health literacy [36], and findings in our study affirm that there were patients who poorly understood their medication and disease, and sometimes

they intended to stop their chronic medication. Some patients associated this intention with their perceived experiences of medication-related adverse events, and in the contrary, patient's experiences of medication-related adverse events did not seem to affect their satisfaction with health services. This might come from the way patients think about their safety; that is, patients might associate the medication-related event with the effectiveness of therapy. They might also think medication-related adverse events are inevitable occurrences following medication taking, and associate their satisfaction with the delivery of other health services (e.g. timeliness, affordability, availability). We did not explore the causes of patient's perceived medication-related adverse events, but in few patients there seemed a lack of understanding of their medication, and at times, medication changes were problematic.

In the present study, many strategies to promote patient safety have been suggested. The multifactorial nature of patient safety barriers and facilitators suggests that patient safety solutions are as diverse as their problem [37], and could be directed at various levels, such as the health care professional, teams, patients, work environment, and organizations. Although many of the barriers for patient safety in this study were emanated from lack of resources, such as human and material, our initiative will not address the broad underlying causes of patient safety problems (e.g. inadequate resources), but rather target specific levels, including teamwork, communication and process design to prevent medication errors from actually reaching the patient [18].

One of the strengths of this study is, in the previous study (Chapter 7), we depicted that the lower scores achieved in the studied areas might not be the direct reflections of the 'cultural' components but might also be related to resource limitations not addressed in the HSOPSC, such as lack of equipment and infrastructure. The HSOPSC as a patient safety measure might not exhaustively explore safety issues. However, this study explored patient safety issues from the perspectives of both HCPs and patients. Yet, this study has a number of limitations. Text-

comments were limited in scope as they were collected from a larger hospital-based survey (HSOPSC). However, given the anonymous nature of data collected, health care professionals were able to provide frank and honest information about patient-safety issues not previously discussed, such as political value.

8.6 Conclusion

The findings of this study showed that patient safety incidents were common, and many factors were identified as challenges to achieve an optimal patient safety in Ethiopian public hospitals. Particularly, the greatest barriers to achieve an optimal patient safety were workforce and material deficits, the physical environment (e.g. poor infrastructure) and lack of managerial support for patient safety. Most patients experienced at least one perceived medication-related adverse event. Most patients were satisfied with their health services, although some patients perceived private hospitals were better at maintaining their safety. Patient's experiences of medication-related adverse events did not seem to affect patient's satisfaction for health services.

8.7 References

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Supplementary materials for chapter 8 are supplied as appendices (appendix 4.2, page 353; appendix 5.6, page 373)

Chapter 9

Barriers and Facilitators to Hospital Pharmacists' Engagement in Medication Safety Activities: A Qualitative Study Using the Theoretical Domains Framework

Mekonnen AB, McLachlan AJ, Brien JE, Mekonnen D, Abay Z. Healthcare professionals' perspectives of patient safety and patients' experiences of medication-related adverse events: a qualitative study from Ethiopia (Revision submitted to Journal of Pharmaceutical Policy and Practice)

9.1 Abstract

Background: Hospital pharmacists play a central role in medication safety activities. However, in Ethiopia, this role has been launched recently and little is known about the current status of this extended services. Using the Theoretical Domains Framework (TDF), we aimed to identify the barriers and facilitators to hospital pharmacists' engagement in medication safety activities across various public hospitals in the Amhara region of Ethiopia.

Methods: Eight focus group discussions, using an interview guide that was drawn upon the TDF, were conducted with 44 hospital pharmacists to explore their beliefs regarding their involvement in clinical services. Group discussions were audio-recorded, transcribed verbatim, and analysed using directed content analysis based on the TDF. Relevant domains were identified by applying relevance criteria to each of the domains in the TDF.

Results: Content analysis revealed six domains that influence hospital pharmacists' engagement in medication safety activities. These domains included 'Knowledge', 'Skills', 'Environmental context and resources', 'Motivations and goals', 'Social influences' and 'Social/professional role'. Most hospital pharmacists believed knowledge gap was an issue, as was the lack of training and supportive skills although some expressed as they were competent enough for their skills in identifying medication related problems. Most participants were very much enthusiastic for their extended roles, and were positive towards the future of the profession; however, competing priorities along with the lack of remuneration and awareness (of other health care professionals) regarding the profession's role were barriers to service delivery. There were also a number of resource constraints, such as staffing, infrastructure and government funding, and acceptance rate of pharmacist's recommendation that were likely to influence the clinical practice of pharmacists.

Conclusion: Using the TDF**,** this study identified a wide range of barriers and facilitators to hospital pharmacists' engagement in medication safety activities in resource-limited settings. There existed considerable interrelationships between domains that were perceived to influence hospital pharmacists' behaviours, and this might assist in designing behaviour change interventions that will target common behavioural domains.

9.2 Introduction

Medications are the most common health care interventions used to improve the health outcome of patients when used safely and appropriately. However, they are also the major source of patient safety incidents [1]. The issue of medication safety has received increased attention since the publication of *To Err is Human: Building a Safer Health System* [1] in the USA, and is now a concern of many other countries [2–4]. In developing countries such as Africa, patient harm from adverse events is thought to be higher than elsewhere the world [5, 6]. Also, medication errors and adverse drug events in Ethiopia are believed to be significant public health problems [7–11], and studies in this regard are increasingly been published.

Many studies have identified various strategies to improve medication safety in the hospital environment, including but not limited to, computerized physician order entry with or without clinical decision support [12–14], barcode technology [15], educational sessions [16], and pharmacist involvement [17–19]. Specifically, the role of the hospital pharmacist has been rapidly evolving beyond the traditional roles of medication dispensing and distribution to expanded clinical services [20], and their role in improving medication safety is well acknowledged. The hospital pharmacist plays a prominent role in cutting adverse drug events, and medication errors [20], and medication safety activities, such as drug use evaluation, admission medication histories, adverse drug reaction management, and participation in medical rounds are believed to be associated with reduced mortality rates [21]. Also, our

previous systematic reviews confirmed the positive impact of pharmacists, particularly when pharmacists are engaged in medication reconciliation at care transitions [22, 23]. Unlike the developed countries, pharmacists' involvement in direct patient care is a recent journey in Ethiopia [24]. Major changes in the curricula have been made after a 5-year Bachelor of Pharmacy (BPharm) with a 1-year clerkship program has been launched in 2009. To date, standards and guidelines have been endorsed nationally—for example, the *Ethiopian Hospital Reform Implementation Guidelines* that require pharmacists to deliver direct patient care services, and this is taken as a minimum regulatory standard in the health facilities by the Ethiopian Standards Authority and the Ethiopian Food, Medicine and Health Care Administration and Control Authority (FMHACA) [25]. However, little is known about the current status of the implementation of these extended services, as well as the barriers and facilitators experienced by hospital pharmacists in delivering patient care services in Ethiopian public health facilities. The present study was part of a larger project aimed at implementing pharmacist-led medication safety programs (i.e. medication reconciliation) [26], and the implementation of this service was guided by a theoretical framework to help identify the barriers and facilitators to hospital pharmacists' engagement in medication safety activities in selected public hospitals in the Amhara region, Ethiopia.

9.3 Method

9.3.1 Study Setting and Participants

The study was conducted in eight public hospitals, all located in the Amhara region in the north western part of Ethiopia. This region is inhabited by approximately 18 million people and comprised of 17 public hospitals, 520 health centers and 2,941 health posts [27]. The Ethiopian health care system is challenged by poor health care financing, and close to 80% of the health expenditure is dependent on out-of-pocket expense [28], and the population mainly receives health services from public health institutions.

Pharmacists were recruited from 4 teaching/referral and 4 district hospitals, and there were a total of 252 pharmacy staffs (pharmacists, 140; pharmacy technicians, 112) working in the studied hospitals at the time of data collection. Of the 140 hospital pharmacists, only 61 were involved in direct patient care or clinical pharmacy services and were eligible to be included in this study; that is, these pharmacists were either clinical pharmacists or graduate pharmacists of the new patient-oriented curriculum or pharmacists with an in-service training on clinical pharmacy services. The study was conducted between February and August 2016.

9.3.2 Study Design

This is a qualitative study using focus group discussions (FGD). FGDs were employed in this study because the interactive nature of focus groups is specifically important when group norms and cultural values of particular groups are of interest, and to explore the degree of consensus on a given topic [29], including implementation of an intervention to improve medication safety. Many factors can affect the adaptability of an evidence based intervention, and the success of implementation efforts depends on a careful assessment of barriers to, and facilitators of, the behaviour to be changed [30]. A theory based identification of such factors provides a theoretically robust evidence base to inform implementation of an intervention [30]. The underpinning theoretical model used in this study is the Theoretical Domains Framework (TDF).

Increasing the uptake of evidence into clinical practice and improving patient outcomes needs behaviour change. The TDF from health psychology provides the basis for such an approach, ensuring that a wide range of possible theoretical explanations for the behaviours can be considered. Built from 33 behavioural theories, the TDF was developed to make theories more accessible for implementation researchers [31]. According to Michie et al [31], the TDF has 12 domains to explain behaviour change: (1) ‘Knowledge’, (2) ‘Skills’, (3) ‘Social/ professional role and identity’, (4) ‘Beliefs about capabilities’, (5) ‘Beliefs about consequences’, (6)

'Motivation and goals', (7) 'Memory, attention and decision processes', (8) 'Environmental context and resources', (9) 'Social influences', (10) 'Emotion regulation', (11) 'Behavioural regulation' and (12) 'Nature of the behaviour'. The TDF has been extensively applied across a range of clinical behaviours such as prescribing, adverse drug event reporting, and transfusion behaviours [32–35].

9.3.3 Data Collection

In this study, FGDs were guided by questions designed based on the TDF (Appendix 5.6). For each of the 12 domains that could act as facilitators or barriers to current medication safety practices, the authors developed several interview questions. The number of interview questions ranged between 2 and 5 for each of the 12 domains, for a total of 43 questions to cover a wide range of beliefs assigned to each domain. The questions were initially drafted by one researcher (ABM) and then refined by health service researchers (AJM, JEB) and discussed by the research team to check for clinical relevance. Interview guides were translated from English versions to the local language (Amharic) by two translators who are native speakers and working in the health care industry and validated by two of the research group (ABM, DM).

Initially, pharmacists were selected using a purposive sampling strategy, and this was further facilitated with snowball sampling. Selection of participants also considered variations in health service structure (teaching/referral and district) to capture a wide range of beliefs in the clinical practice of pharmacists. Opportunistically, we also interviewed a mix of hospital pharmacists who were attending an in-service training from various public hospitals in the region. Participants were recruited by letter invitation, and those willing to participate were contacted after a signed consent form had been submitted. The principal investigator (ABM) conducted and led the FGDs using the translated version (Amharic) of the topic guide. Prompts

were used when necessary and pharmacists were encouraged to talk about their internal beliefs and attitudes that may hinder them from providing clinical pharmacy services, including medication safety roles. The discussions approximately lasted between 60 to 90 minutes, and data were collected until a point of saturation was reached. All discussion sessions were audiotaped and recorded.

9.3.4 Data Analysis

An Amharic/English speaking investigator (ABM) carried out verbatim Amharic transcriptions of all interviews and then translated into English. A coding guide was prepared based on previously published definitions [31, 36] and utilized for the purpose of consistent reporting (Appendix 8). Using the 12 domains of the TDF as a coding framework, directed content analysis of texts into the theoretical domains was performed [37]. Briefly, the analysis involved identifying contextualized brief statements related to the barriers and facilitators to medication safety activities, categorizing statements into TDF domains and mapping the underlying theoretical constructs within domains. The theoretical domains that were judged to be relevant were identified by considering the frequencies of the beliefs reported, the presence of conflicting beliefs, and evidence of strong beliefs that may influence the behaviour under investigation [34]. In establishing domain relevance, all of these factors were considered concurrently. Conventional content analysis was also conducted, and both analyses approaches were employed so as not to miss any themes [35].

9.3.5 Ethical Consideration

The study protocol was approved by the University of Sydney Human Research Ethics Committee (project No: 2015/818) and the institutional review board of the University of Gondar, Ethiopia (O/V/P/RCS/05/624/2016). All participants gave written informed consent, and each group was assigned a unique identifier, and anonymity was maintained at all times during the research process.

9.4 Results

Forty-four hospital pharmacists took part in eight focus groups, comprising four to nine participants per group (Table 9.1). Participants represented from eight hospitals, the majority of whom were males (n= 39). The mean clinical experience and age of the participants were 2.4 and 25.8 years, respectively (Table 9.1).

Table 9.1 Number and Characteristics of Participants in Each of the Eight Focus Groups

Focus groups	Number of participants	Age, mean	Male, n	Experience (years), mean
DMH–FG1	5	24.6	5	2
DMH–FG2	5	24.8	4	1.8
FHRH–FG1	5	26.8	5	2.8
FHRH–FG2	5	27.2	4	3
GUH	6	26.5	5	2.4
DTH	9	26	7	2.6
FH	4	25.5	4	2
Mixed hospitals*	5	24.8	5	2.8
Total	44	25.8	39	2.4

*****Hospital pharmacists from Metema, Woldiya, Gondar University, and Enat hospitals were involved.

Abbreviations: DMH, Debre Markos hospital; DTH, Debre Tabor hospital; FHRH, Felege Hiwot referral hospital; FH, Finoteselam hospital; FG, focus group; GUH, Gondar university hospital

Barriers and facilitators

Conventional content analysis across all focus groups did not reveal different themes, and thus, we present our findings according to our primary data analysis plan. Using the directed content analysis, barriers and facilitators perceived by hospital pharmacists as being more relevant to the delivery of medication safety activities were categorized within six of the TDF domains.

These domains included 'Knowledge', 'Skills', 'Environmental context and resources', 'Motivation and goals', 'Social influences', and 'Social/professional role'.

Knowledge and skills

In most of the discussions, participants did not distinguish between knowledge and skill domains—for example, participants mentioned the lack of knowledge and skills altogether as barriers to their activities, and thus, in this study, they are presented together.

Participants expressed mixed views regarding the level of knowledge and skill necessary for complete delivery of clinical services and most believed there was a lack of awareness for those pharmacists' extended roles. To the extreme, awareness issues from the pharmacy side were severe and its implication in the service delivery process was highly significant. Because these were not usually supported with further training, most participants held a strong firm in that pharmacists who lacked the know-how about clinical services had greatly impacted the service delivery and believed they should be targets for future interventions .

"…those [pharmacists] who have knowledge about the service, and know what the service is about, support the service we are doing. Whereas those who pass most of their time at dispensing and not have enough knowledge and awareness about clinical pharmacy are not considering as we are working" [*Referral hospital, Focus group#2*].

Trainings were arranged occasionally; however, most were not suitable to the interest of strengthening clinical pharmacy services. "*Even the trainings are more focused on system strengthening like APTS* [Auditable Pharmaceutical Transactions and Services] *and they are so much science oriented. They are not clinical based"* [*Referral hospital, Focus group#3*].

It was mentioned that, initially, there were some kinds of in-service trainings organized for clinical pharmacists to equip them with communication skills and pharmaceutical care. But, this had been stopped for a while.

"The training that was prepared for the generic pharmacists to equip them clinical knowledge was already stopped" [*Referral hospital, Focus group#4*].

Participants also raised issues such as the lack of an evidence and guidelines that showed how much their input affects the clinical practice, and this was further supported by the lack of consistent service although hospital pharmacists were confident enough in their skills in identifying medication-related problems. For instance, medication review was done with a limited scope, and there were no organized ways to perform medication reconciliation. . During ward visit, hospital pharmacists took medication history, and used it for pharmaceutical care decisions; however, this was done inconsistently and the evidence-base was not clear to many.

"…the history is important for our decision, and we are working on medication reconciliation and review although it is not uniform… This is what we are currently doing, but I am not quite how strong the evidence for this, probably we will going to evaluate in the process" [*Referral hospital, Focus group#3*].

Environmental context and resources

Initially, this domain was found to be less relevant from the perspective of behavioural change theory. But, later we understood that this domain had significant interactions with hospital pharmacists' viewpoints expressed in the other domains considered as relevant in this study, such as motivation and goals, social influences and social/professional role. Overall, environmental constraints were highly referred by hospital pharmacists as being a major barrier to the delivery of medication safety activities. In this part of the domain, there was none who mentioned enabling factors regarding resource issues and all shared a common reflection on the consequences of environmental constraints on their role. Ranges of resource constraints were raised as barriers. Unlike other clinicians, for example, there had not been any room available for practicing pharmacists nearby to the wards they were working.

"We are going far from the place where we are, but other HCPs follows patients at their own site" [*District hospital, Focus group#6*].

In contrast to dispensing role, hospital pharmacists perceived clinical services add substantial time commitments and associated with many hardships.

"Even we are busy of reading at home, it is not different from an academic life" [*Teaching hospital, Focus group#5*].

"Pharmacists don't want to face hardships" [*District hospital, Focus group# 1*].

The majority of participants also stressed that the lack of human resource was the challenge for delivering clinical services. In the studied hospitals, staff attrition was common and most participants believed this had been increased recently. Unlike teaching and referral hospitals, district hospitals also faced a severe shortage of other resources, such as reference books, guidelines, and computers with internet access.

Participants reported that ward-based hospital pharmacy services were limited in scope and delivered inconsistently. For example, these services were not done over the weakened, and duty programs were stopped for a while, and participants believed this had imposed work burden when getting back to work on Monday. Participants also felt that, if many of their concerns had been solved, they believed this may boost their energy and perceived how much the concerned bodies were ready to accept hospital pharmacists' extended roles. However, most pharmacists hesitated whether this had been met, given the lack of government funding and support for these services. Although part of the problem was explained by budget deficits nationally, participants cited that at least the government can play a major role in the technical support of these extended services. Additionally, clinical services were rarely and irregularly documented though there were institutional variations. In most of the studied hospitals, pharmacy own documents prepared for the purpose of recording clinical activities were not

part of the medical record, or if it had been in place, pharmacist's documentation was done infrequently.

"...we do believe there is a severe problem of clinical pharmacy documentation. There is no body who support us in this regard" [*Referral hospital, Focus group#3*].

Motivation and goals

A range of conflicting views regarding hospital pharmacists' motivation and goals were collected. For example, most participants believed that what they were doing was a mere initiative from their side and not a cascaded role that was approved and endorsed by the government. "*Now, most of us are doing this work because we are interested in this"* [*District hospital, Focus group#6*]. However, creating something out of nothing was challenging, and lacked remuneration, and a concern among the majority of hospital pharmacists. Some participants stated that patients were highly benefited from the clinical services hospital pharmacists were giving although they themselves did not have any extra benefit for these additional clinical services.

"From the perspective of staff, I am feeling like a person giving free service" [*Referral hospital, Focus group#1*].

Hospital pharmacists urged concerned bodies in support of these services through a remuneration scheme, and they believed this would likely bring major changes in the clinical practice of pharmacists.

"...as you most satisfied with these [staff benefits], *you will going to do more interventions, and these can bring a good outcome"* [*Referral hospital, Focus group#4*].

Although participants strongly believed that there should have been a complete provision of clinical services, these were not done because hospital pharmacists would like to prefer a less challenging job or else, as a result of human resource shortages, they had been placed for other hospital services such as dispensing roles.

"As any human, they [hospital pharmacists] *might inclined towards a less challenging job" Referral hospital, Focus group#4*].

Participants also believed that, as a result of the cancellation of weakened and duty programs which were practiced before, staffs thought that this was the least incentive they were thinking of, and this had affected their moral negatively.

"It is not fair to cancel the Saturday and Sunday services. Before, we did weekend services, and even there was duty program and we did CP service and those things at least moralize us" [*Referral hospital, Focus group#1*].

Many participants emphasized why hospital pharmacists lacked the inspiration for delivering clinical services, whereas they mentioned that the curriculum is very much patient oriented unlike the previous courses, yet there were few hospital pharmacists struggled into the duty of dispensing with the mere reason of collecting an additional benefit from the extra hours, but this was not arranged for clinical services. And because of this, most pharmacists preferred dispensing to clinical services.

"We suffered so much when we studied CP [clinical pharmacy] *and the work is challenging, but we are treated as previous pharmacists who studied a little bit advanced courses. There are many challenges with us. There are many differences in the curriculum, but there are things you will lose. For example, the region allows duty only for dispensing, and for this reason, at least to collect 500 or 600 birr for the duty program we are doing it rather than the clinical service. We don't dislike the job but it is because of this reasons and not attitude problem that most of us prefer dispensing"* [*Referral hospital, Focus group#2*].

Surprisingly enough, there were also enthusiastic hospital pharmacists who did not see things from resource or financial gains perspective but devoted themselves for the growth of the profession. For these groups of participants, human resource was not a challenge if they were given the support from health managers, and which in turn, greatly impacted the staff's

motivation and commitment. If given the support from the management, participants considered this as their major driving force for their motivation.

"Nowadays, there is also support from the management and this has been increased from time to time, and this is a motivating factor by itself" [*Mixed hospitals, Focus group#8*].

"So, the changes I have seen at the management is like incentives for us" [*Mixed hospitals, Focus group#8*].

Social influences

Although hospital pharmacists were very much enthusiastic for new roles, these were in fact, influenced by the lack of acceptance of their role to other members of the health care team and lack of managerial support in implementing clinical pharmacy services. From the perspective of managerial support, managers overlooked clinical services but more focused on dispensing roles, and that was attributed majorly to lack of staff to take over the dispensing role. There were also participants expressed their views that managers acknowledged the importance of clinical pharmacy services and highly appreciated it but because of the staff shortage matters, those pharmacists who were working in the hospital wards were assigned to the dispensing rooms. This was more aggravated when more staffs had increasingly left their job whenever they got other better opportunities. In addition, controversies over interest also mentioned as a reason for not continually deliver this service, particularly between managers from the department and the hospital.

"He [the hospital manager*] is ambitious to develop the service more. However, when you come to the department of clinical pharmacy, there is a problem in the way pharmacists are looking at the service. Even, you can see that some pharmacists are not attending our morning session"* [*Referral hospital, Focus group#3*]. On the other hand, HCPs who were supportive and ready to accept pharmacists' input did have some know-how about clinical pharmacy or had been

exposed to some form of sensitization workshops. This was also expressed to some extent in pharmacists themselves.

"Even other health care professionals are accepting our roles except those who don't have the know-how. And even this is because the necessary sensitization was not given to them" [*Referral hospital, Focus group#3*].The level of acceptance was different from institution to institution. Various mentions were given for this. First, in institutions where the numbers of specialists were fewer, the input from pharmacists was taken as crucial and thus, the rate of pharmacist's acceptance was better. However, in hospitals where there were highly experienced seniors, it was a challenge for pharmacists to recommend interventions. And, pharmacists recommended interventions were better taken up by those colleagues having the same level of seniority. However, there were also pharmacists commenting seniors had the best connections with them than others, and their input was better entertained although most seniors were not that much aware of cognitive services delivered by hospital pharmacists. In addition, those HCPs who believed in team and collaborative works were the most likely candidates for promoting clinical pharmacy services.

"We know that pharmacists working in Debre Markos and Felege Hiwot are doing better, and have better acceptance. Because their level is almost equal" [*Teaching hospital, Focus group#5*].

"With seniors, there is no problem to accept your recommendation. Actually, the main prescribing authority rests on them. The main problem with other staffs below seniors is they need an approval from seniors. As compared to interns, the GPs accept you better" [*Referral hospital, Focus group#3*].Participants mentioned that clinical pharmacy services were included as one of the hospital standards and had been getting the support from government policy side, and thus, no health care staff opposed the existences of these services. Notably, government's commitment to enact on behalf of the hospital pharmacist's impact in the health care system

has been found more influential than ever, and the likelihood of accepting pharmacists extended roles to other staffs is possibly geared by the government's pressure.

"...So, everything rests on the government's commitment. Our acceptance also depends on the government's work. If the government is committed, for example, to order every health care professional to review our recommendation, like nurses, are checking the progress notes of physicians, physicians should also review the progress notes of clinical pharmacists, and give their decision as accepted or rejected. The biggest responsibility is to the government for other staffs to consume pharmacist's input" [*Referral hospital, Focus group#2*].

Social/professional role

Regarding medication safety activities delivered by hospital pharmacists, it was mentioned that professional compatibility was not a concern but what matters was the lack of understanding of the profession's mission in the eye of other health care cadres. There was a considerable variation in the clinical practice of pharmacists among institutions—for example, there were institutions that praise the role of hospital pharmacists and yet, there were who had seen them as fault finders. One pharmacist commented:

"During identifying DTPs [drug therapy problems] *and any other problems related to medications, they are considering like we are pointing the one who is responsible for the care of the patient"* [*Mixed hospitals, Focus group#8*].

Whatever it is, however, the major facilitating factor for this was, role recognition by other staff members.

"Those who understand the health benefit of clinical pharmacy services, for example, some physicians are trying to call hospital pharmacists for ward round participation, and give the recognition for clinical pharmacists as we are needed during ward round" [*Mixed hospitals, Focus group#8*].

"There are times when the physicians don't start round unless the clinical pharmacist is available" [*District hospital, Focus group#6*].

It was mentioned that the hospital standards currently ratified by the government well advocated the integration of pharmacists in care teams. However, few pharmacists believed a lack of differentiation between technical and clinical services and role duties for pharmacists from the government itself.

"The government didn't see the distinction between technicians, pharmacists, and clinical pharmacists" [*District hospital, Focus group#7*].

Although there existed some level of recognition from various sides, yet there had been a lack of awareness regarding the role of hospital pharmacists in medication safety activities at the level of health bureau, regional or federal level.

"…there are staffs who are not aware of the role of clinical pharmacists. There are staffs who ask us what we are doing in the ward, on the other hand, there are who eagerly want us, and even among these, there do have various perceptions of the profession" [*Referral hospital, Focus group#2*].

With regard to social/professional role, there have been numerous unfinished assignments that due attention, according to the participants. Awareness campaigns should be devised, and a well-designed job description should have been in place. Because of the lack of job description best suited for clinical activities, participants felt that there seemed an overlap of activities and also, other HCPs perceived as if their role was taken. Few participants commented how other staffs, specifically physicians were looking at them; they stressed that their therapy recommendation was not usually entertained by the physicians, and the physicians hesitate to accept their extended role.

Regardless of financial gains and acceptance, most hospital pharmacists were positive towards the future of the profession.

"We are taking the challenges as challenges, and we are thinking the future might be brighter. We don't know what will happen and in that sense, we are trying our best" [*District hospital, Focus group#6]*.

"...we are working for the benefit of the profession, not for us, we are paying our life, and we are wishing only the best future" [*District hospital, Focus group#6*].

"...we are working expecting the future might be bright" [*District hospital, Focus group#6*].

9.5 Discussion

To the best of our knowledge, this was the first study to apply the TDF to categorize the barriers and facilitators to hospital pharmacists' engagement in medication safety activities. The present study identified a wide range of factors that may influence the uptake of medication safety interventions delivered by hospital pharmacists. Overwhelmingly, hospital pharmacists identified more barriers than facilitators in delivering clinical services. Derived from the TDF, the factors identified in this study were clustered into six domains: 'Knowledge', 'Skills', 'Environmental context and resources', 'Motivations and goals', 'Social influences' and 'Social/professional role'. In comparison with other studies using the TDF framework, the domains 'Knowledge', 'Skills', 'Environmental context and resources', 'Social influences' were identified as vital areas which could be targeted in the implementation of medication safety programs [32, 33, 35], although other issues such as, 'Motivation and goals' [32, 33] and 'Social/professional roles' [32] were also equally important. Outside the TDF, some of our findings were consistent with a previous study exploring the factors affecting the implementation of clinical pharmacy performance indicators, including medication reconciliation [38]. Minard et al [38] reported that the challenges surrounding hospital pharmacists' implementation of these indicators comprised of documentation challenges, work burden, environmental constraints and competing priorities. Using a theory-based approach,

the present study uncovers additional relevant barriers—for example, the lack of knowledge and skills necessary for the execution of clinical services and poor acceptance of pharmacists' recommendation. On the other hand, environmental constraints identified in the current study were prominent, and there was none which was mentioned as facilitator in the context of resource issues. Most importantly, although all participants frequently and consistently reported the 'Environmental context and resources' domain without variation in their views, it was found that there existed some important interlinks with the domains judged to be relevant. For example, as a consequence of human resource deficits, managers reinforced hospital pharmacists to take over the dispensing role ('Motivation and goals'), and because of the absence of duty and weekend programs, hospital pharmacists perceived this as a lack of government funding and support, which in turn, was a result of the lack of recognition and acceptance of these extended roles ('Social/professional role'). Duncan et al [32] explained the interactive nature across the TDF domains and highlighted the importance of considering theoretical links between domains as far as interrelationships between domains exist.

Unlike the environmental constraints, the barriers and facilitators that were reported by hospital pharmacists showed inter-institutional and -individual variations in the remainder of domains. While the analysis of the interview data indicated major differences in individual thoughts related to hospital pharmacists' knowledge, skills, and social/professional role as well as their motivation and goals, inter-institutional variation mainly appeared in the social influence domain. Particularly, hospital pharmacists working in district hospitals clearly indicated their interventions were better entertained and accepted by other health care members, and there was an increasing demand for these services—for example, expressed in the number of telephone inquiries and consultations received in these hospitals. Previous studies demonstrating pharmacist provided therapy recommendation in care teams have reported positive clinical and economic outcomes, and these have been associated with high acceptance rates [39–41]. For

instance, when pharmacists participate in ward rounds, they could able to cut two-third of preventable ADEs with acceptance rate as high as 99% [40]. Another recent study [42] has also shown a high acceptance rate of pharmacist-provided services associated with medication reconciliation as compared with other clinical services, such as those related to medication indication, efficacy, and therapeutic drug monitoring. Given the positive impact of pharmacist-led medication reconciliation services [22, 23], and the evidence that these services have shown better acceptance [42], it is our opinion that pharmacists' clinical services in the studied hospitals, mainly those above the district level, might be well utilized if they could able to implement medication reconciliation services.

Apart from the challenges encountered with regard to knowledge and skill deficits (e.g. lack of supportive skills such as blood pressure measurement, and knowledge about rare diseases/diagnosis)—participants associated this with the challenges in the currently designed curricula, hospital pharmacist's roles in medication safety were poorly understood in the medical community. Particularly, product-oriented pharmacists' awareness, and the lack thereof, was predominantly affected the extended roles implemented by ward-based pharmacists. This finding is consistent with a study that has shown pharmacists' self-perception as barriers to their extended roles [43]. Outside pharmacists, participants highlighted that other HCPs recognition of pharmacist's roles in medication safety activities was limited; however, a recent local study reported that a large proportion of HCPs had a positive attitude towards clinical pharmacy services but the extent of the available service was below their expectation [44]. The present study has also identified that, in the eyes of health managers, dispensing was thought to be a core business and thus, hospital pharmacists were reinforced for other competing priorities. There were no remuneration schemes or incentives arranged for pharmacist's cognitive services. As a result, many pharmacists preferred dispensing to clinical services. A previous national study has also shown that close to two-thirds of pharmacists

delivering clinical pharmacy services are dissatisfied with their job, and this is mainly due to unattractive incentive packages [25].

All participants expressed a desire for further trainings and certifications to target their knowledge and skills gaps; this was also a motivating factor for delivering these services. To target other domains (e.g. 'Social/professional role', 'Social influence'), awareness creation campaigns targeting the whole medical community (including the management, other pharmacists, and HCPs) may facilitate the uptake of pharmacist's cognitive services. In addition, government recognition and supervision of hospital pharmacists' clinical services have been cited as a main driving factor, and participants perceived these services should not have been confined to few settings and national endorsement of these services have been found to be necessary. Bilal et al [45] have also confirmed that Ethiopian graduate pharmacists are very much enthusiastic to promote clinical pharmacy service but the challenge is the minimal effort made at the level of institutions.

This study has several strengths and limitations. Applying the TDF approach, we have for the first time identified a range of barriers, as well as facilitators in relation to hospital pharmacists' engagement in medication safety activities. As we employed focus group discussions for data collection, the data generated was possibly rich [46], and also, the interview guide was structured across the TDF domains that could able to elicit as many factors as possible, although this renders prioritization of domains for intervention development difficult [47]. However, we adopted the relevance criteria utilized by previous studies for prioritizing relevant domains of potential interventional targets [32, 34]. One important challenge in relation to coding statements into the theoretical domains was the existence of overlaps between domains. In this instance, it might be difficult to determine the origin of barrier and facilitator and prioritize interventions [48]. Fortunately, in the current study, the domains that have been found

with some interrelationships were included in the priority list of behaviours for possible intervention.

In contrast to other studies which also judged beliefs about capabilities [49], beliefs about consequences [33, 49], memory/attention and decision processes [32, 35, 49] as relevant domains for a successful medication safety intervention, these domains in our study were described infrequently ('Memory/attention and decision processes') and varied little ('Beliefs about capabilities'), and participants were confident enough in the positive impact of clinical pharmacy services ('Beliefs about consequences'). Although participants consistently reported challenges to the service delivery but in their accounts, we understood that was meant barriers encountered in the whole process and not attributed to their incapability in carrying out medication review and reconciliation, for example. Additionally, an important point worth discussing is regarding the targeted behaviour (i.e. medication safety activities delivered by hospital pharmacists) that we would like to intervene have certain unique features as compared to other studies. While other studies focused on some specifically targeted behaviours (e.g. prescribing behaviour [32, 35], prescribing and dispensing behaviour [35] and ADE reporting [33]), our study included a range of bundled interventions, also termed as clinical pharmacy services. A core sets of eight clinical pharmacy performance indicators have been established [38], including admission and discharge medication reconciliation. However, the issue of medication reconciliation was new to the local setting, and we intended to ask our interviewees from the broader perspective rather than as an isolated element, and interview questions had been designed, accordingly. Hospital pharmacists expressed their beliefs from the broader array of these services, and beliefs for each of the afro mentioned domains should have been thus, viewed from that angle.

Another study's limitation was that it involved a homogeneous group of participants; that is, only pharmacists who taught in the newly designed patient-oriented curricula were included. It

did not take the thoughts from the perspective of product-oriented pharmacists. However, pharmacists were sampled from eight hospitals of varies level (district, general and tertiary), and this mix could possibly enhance transferability of findings to other settings.

9.6 Conclusion

This is the first study to investigate the potential barriers and facilitators to implementing evidence-based medication safety activities delivered by hospital pharmacists using the TDF, and is an initial step necessary for informing theory-based interventions to target these barriers. The current study sheds light on hospital pharmacists' perceptions of their clinical services, including medication reconciliation, in settings where resources are limited. The majority of the participants were very much enthusiastic for their extended roles and were positive towards the future of the profession; however, there were a number of factors likely to influence their behavior in the clinical practice of pharmacists. The multifaceted behavioural interventions surrounding hospital pharmacist's engagement in medication safety activities were predominantly related to six theoretical domains: 'Knowledge', 'Skills', 'Environmental context and resources', 'Motivations and goals', 'Social influences' and 'Social/professional role'. There existed considerable interrelationships between domains that were perceived to influence hospital pharmacists' behaviours, and this might assist in designing behaviour change interventions that will target common behavioural domains.

9.7 References

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Supplementary materials for chapter 9 are supplied as appendices (appendix 4.2, page 353; appendix 8, page 404)

Chapter 10

Evaluation of the Impact of Pharmacist-led Medication Reconciliation Intervention: Single Center Pre-Post Study

Mekonnen AB, McLachlan AJ, Brien JE, Mekonnen D, Abay Z. Evaluation of the impact of pharmacist-led medication reconciliation intervention: A single center pre-post study from Ethiopia (Submitted to International Journal of Clinical Pharmacy)

10.1 Abstract

Background: The role of pharmacists in medication reconciliation is highly acknowledged in the majority of developed nations. However, the impact of this strategy in resource limited countries, such as Ethiopia is not explored. The aim of this study was thus, to investigate the impact of pharmacist-led medication reconciliation interventions on the incidence of unintentional medication discrepancies before and after the implementation of this service.

Method: A single center, prospective, pre-post study was conducted in an emergency ward of a tertiary care university hospital, and included adult patients (aged over 18 years) that had been hospitalized for at least 24 hours and were taking at least 2 home medications on admission. The intervention involved the assignment of a pharmacist to the emergency care team so as to take the best possible medication history and reconcile this list with the current medications in use. The main outcome measures were the incidence and potential clinical severity of unintentional medication discrepancies.

Results: A total of 123 patients were included (pre-intervention, 49; post-intervention, 74). The proportion of patients with at least one unintended discrepancy was reduced from 59% to 10.5% after the intervention ($p < 0.0001$). The percentage of medications with unintended discrepancies was lower in the post-intervention phase than in the pre-intervention phase (3.5% vs. 42 %, respectively; $p < 0.0001$). The percentage of patients with potentially severe clinical impact medication discrepancies reduced significantly after the intervention ($p=0.001$). Most importantly, the likelihood of occurrence of unintentional medication discrepancies was approximately 17 times more often in the absence of pharmacist intervention (OR 16.45, 95% CI 5.22, 51.85).

Conclusion: This study has found that pharmacist-led medication reconciliation intervention was impactful, and was able to minimize the incidence of unintentional medication

discrepancies significantly. Implementation of this strategy is feasible, and pharmacists might be key resource personnel for the safe use of medications during care transitions.

10.2 Introduction

Medication errors are the leading cause of hospital morbidity, and more than half of the medication errors occur at transitions of care, when patients move in and out of a hospital or transferred to the care of other health care provider [1]. Numerous studies identified suboptimal documentation communication at points of patient transfer as a risk for medication errors, and unintentional prescribing changes—also called as medication discrepancies—are common during transitions in care [2–7] and are the concerns for patient safety because of their potential to cause harm. A systematic review of the incidence of medication history errors revealed that 19% to 75% of discrepancies between home medications and admission medications were errors [8], and up to 39% of the unintentional medication discrepancies could have moderate to severe potential for patient harm [9]. Clinically significant medication discrepancies could also represent an important contributor to adverse drug events (ADEs) and health care resource utilization [7, 9–13]—for example, Coleman et al [13] reported that patients with medication discrepancies experienced a significantly higher rate of re-hospitalization at 30 days compared with patients without such discrepancies.

Medication reconciliation is recognized as an important approach to improve the Quality Use of Medicines by tackling the burden of medication discrepancies. Medication reconciliation as a National Patient Safety Goal (NPSG) was first endorsed in 2005 by The Joint Commission [14]. Since the last decade, this strategy is being effectively implemented across care transitions in many other settings and endorsed among various patient safety organizations [15–17].

There is growing evidence that medication reconciliation decreases the frequency of unintentional medication discrepancies [18, 19] and adverse drug event-related readmissions

[10–12]. Medication reconciliation supported by an electronic tool, as well as pharmacist-led approaches have been found effective in reducing unintended discrepancy [20, 21]. Most importantly, medication reconciliation programs conducted at single transition (either admission or discharge) showed a significant reduction of 66% in patients with medication discrepancies in favour of pharmacist-led intervention [21]. This intervention has also shown a substantial reduction in the rate of all-cause readmissions, all-cause ED visits, and adverse drug event-related hospital revisits although the impact of such programs on mortality and composite outcomes was inconclusive [22].

Medication reconciliation is well acknowledged in many of the developed countries; however, the impact of this strategy overall, as well as pharmacist-led medication reconciliation initiatives, has not yet been described in sub-Saharan Africa. In the present study, we evaluated the impact of pharmacist-led medication reconciliation at the emergency ward of a university hospital on the occurrence of unintentional medication discrepancies before and after the implementation of this service. We also assessed the potential clinical severity of medication discrepancies and compared the differences between pre- and post-intervention groups.

10.3 Methods

10.3.1 Study Setting, Design, and Population

The study was carried out in an emergency ward of Gondar University Hospital (GUH), which is a tertiary and public hospital in Gondar town in the Amhara regional state. It is the primer hospital in the northwest region of Ethiopia. GUH provides specialized health services through its medical and other clinical and diagnostic departments for a catchment population of approximately 5 million people.

This study was part of a larger project aimed at implementing pharmacist-led medication reconciliation programs, and the study protocol for the whole project has been published elsewhere [23]. The current study was a single center, prospective, pre-post study with no

equivalent control group conducted between February and August 2016. Patients in both periods were enrolled in the same ward. This study lasted a total of 6 months. .

Eligible patients were adults (aged over 18 years) taking at least two home/regular medications on admission, and patients had to stay for at least 24 hrs to be eligible for inclusion in our study. In other words, patients who transferred to other wards or discharged from ED within 24 hrs were not included in our study. Patients were provided both verbal and written information, and were requested for their willingness to participate in the study, and were included only after written informed consent was obtained. Patients were conveniently enrolled on weekdays, and recruitment targets were pre-determined using the predefined calculation; that is, the sample size was estimated using the prevalence of medication errors in the previous local studies, which was identified as 52% to 58% of all prescriptions [24, 25]. Assuming a 45% relative reduction in medication errors, 80% power, 5% significance level (two-sided), we required a total of 127 patients, 51 for the baseline and 76 for the intervention (http://medcal.org). Hospital discharge statistics showed that this sample size would be achievable over the study period.

10.3.2 Data Collection

For the purpose of this study, medication discrepancies were defined as one or more differences in (dosage, frequency, drug, route of administration), as described by the Institute for Health care Improvement (IHI) [26], between the current and previous medication (s) a patient was taking, whereas medication reconciliation had been adopted as "the process of identifying the most accurate list of a patient's current medicines, including the name, dosage, frequency, and route—and comparing them to the current list in use, recognizing and documenting any discrepancies, thus resulting in a complete list of medications" [26].

During the study period, the standard practice in the current ward involved physicians in taking patient's medication history using patient provided information; however, hospital pharmacists

did not participate in the medication history taking and prescription review at the emergency ward. During the implementation phase, however, hospital pharmacists were assigned and involved in taking the best possible medication history (BPMH) [17], which was based on a structured interview with the patient about medication use and retrieving other sources of medication history, including discharge and referral letters, patient's own medicines and carrier interview. At the time of data collection, five hospital pharmacists, on a weekly rotation basis (one per week), were engaged in delivering medication reconciliation service at the emergency ward. In this study, a baseline assessment of medication discrepancies had been conducted for one month during admission at the emergency ward. It should be noted that before the intervention commences, findings from the baseline assessment were communicated to the ward team and there were a series of sessions in creating awareness about the impact of medication reconciliation overall, as well as the role of pharmacists in the process. A pharmacist-led medication reconciliation intervention had been then carried out prospectively for two months.

For the purpose of data collection, one pharmacy staff member who was not involved in the intervention had been trained in the techniques of how to get the BPMH by a research pharmacist (ABM). Medication reconciliation was conducted after patients were informed of the study and gave written consent. Medication use had been documented through a data collection tool prepared for the purpose of this study (Appendix 6.5). Irrespective of the phase, a single pharmacist using the same procedure collected medication discrepancies within 24 hrs of the patient's admission; the difference between the two phases of the study lied on the timing in taking the BPMH and the assignment of hospital pharmacists to deliver medication reconciliation service. During the standard care process, the pharmacist (data collector) performed the BPMH after the physician's admission prescription order whereas, in the implementation phase, hospital pharmacists were fully integrated to the admission process and

conducted medication reconciliation before the physician's prescription order. In the implementation phase of this study, the pharmacist (data collector) compared the BPMH (of his own) with the physician's admission prescription order that had also been considered by hospital pharmacists. In both stages of the study, all identified discrepancies had been brought to the attention of the physician in charge at admission and verification of these discrepancies was made; that is, intentional vs unintentional changes to medications. Intentional medication discrepancies were medication changes due to new patient's clinical status, and were clinically justifiable but not documented in the patient's medical record. Thus, only unintentional medication discrepancies (also called as medication errors) had been reported. The main outcome measure was the incidence of unintentional medication discrepancies along with their potential clinical severity. The potential clinical severity of medication discrepancies was judged by a consensus between a clinical pharmacist and a physician using a tool developed by Cornish et al [5]. According to this tool, discrepancies were classified as mild—unlikely to cause patient discomfort/clinical deterioration, moderate—moderate discomfort/clinical deterioration, and severe—severe discomfort/clinical deterioration.

10.3.3 Data Analysis

Data were entered into Excel 2013 and analysed using SPSS version 20 (IBM Corp., Armonk, NY). Descriptive statistics were used to report patient demographics and clinical characteristics. Categorical variables were compared for pre-and post-intervention groups using chi-square or Fisher's exact test and continuous variables were compared using Student's t test. Univariate and multivariate logistic regression analysis was used to investigate predictors of at least 1 medication discrepancy. Statistical significance was set at $p < 0.05$.

10.3.4 Ethical Consideration

Ethical approval was obtained from the University of Sydney Human Research Ethics Committee (HREC)—Project Number: 2015/818, and the Institutional Review Board of the University of Gondar, Ethiopia (O/V/P/RCS/05/624/2016).

10.4 Results

Patient characteristics

During the two phases of the study, 123 patients were enrolled in the study, 49 patients were included in the pre-intervention study, and 74 patients in the post-intervention. There were no significant differences in patient characteristics between the groups, except for a higher mean number of current medications in the post-intervention group (4.26 vs 3.55, respectively; P = 0.04) (Table 10.1). A total of 489 medications were reconciled, 174 drugs in pre-phase and 315 in the post-intervention, and in both phases of the study, the most prescribed classes of medications were anti-infectives (36%), cardiovascular (34%), gastrointestinal (10%), central nervous system (6%) and endocrine and metabolic (5%).

Table 10.1 Patients' Demographic and Clinical Characteristics

Characteristic		Both phases (n=123)	Pre-intervention (n=49)	Post-intervention (n= 74)	P-value
Age, mean (±SD)		45.0 (17.7)	48.6 (18.6)	42.7(16.9)	0.07
Age >= 65 years, n (%)		24 (19.5)	12 (24.5%)	12 (16.2%)	0.26
Sex	Male (%)	63 (51.2)	23 (46.9)	40 (54.1)	0.44
	Female (%)	60 (48.8)	26 (53.1)	34 (45.9)	
Primary diagnosis, n (%)	Infectious diseases	55(44.7)	24 (49)	31 (41.9)	0.189
	Cardiovascular system	30 (24.4)	14 (28.6)	16 (21.6)	
	Endocrine and metabolic disorders	11 (8.9)	4 (8.2)	7 (9.5)	
	Gastrointestinal	9 (7.3)	1 (2)	8 (10.8)	
	Central nervous system	6 (4.9)	2 (4.1)	4 (5.4)	
	Respiratory	4 (3.3)	3 (6.1)	1 (1.4)	
	Miscellaneous	8 (6.5)	1 (2)	7 (9.5)	
Co-morbidities, mean (±SD)		1.1 (0.8)	1.2 (0.8)	1.1 (0.9)	0.79
Preadmission medications, mean (±SD)		2.8 (1.2)	3.1 (1.3)	2.7 (1.0)	0.10
Current medications, mean (±SD)		4.0 (1.8)	3.6 (2.1)	4.3 (1.61)	0.04

Abbreviation: SD, Standard deviation

Main outcome measures

In both periods, a total number of 84 unintentional medication discrepancies had been identified; 73 discrepancies pre-intervention and 11 unintended discrepancies post-intervention. The percentage of medications with unintended discrepancies decreased from

42% (73/174) to 3.5% (11/315) after the intervention ($p < 0.0001$). The proportion of patients with at least 1 unintended medication discrepancy was 59% (29/49) in the pre-intervention phase, compared to 10.5% (8/76) in the post-intervention phase ($p < 0.0001$) (Table 3). Among these 37 patients, 12 patients each had 1 and 2 discrepancies, 9 patients had 3 discrepancies, 2 patients had 4 discrepancies, and 1 patient each had 6 and 7 discrepancies. The overall discrepancy rate was 0.68 per patient (SD 1.28); it was 1.49 (SD 1.66) in the pre-phase and 0.15 (SD 0.46) in the post-intervention phase ($p < 0.0001$) (Table 10.2).

Table 10.2 Comparison of Medication Discrepancies between the Pre-and Post-intervention Group

Outcome	Both phases	Pre-intervention	Post-intervention	P-value
Medications with unintentional discrepancies, n (%)	84 (17)	73 (42)	11 (3.5)	<0.0001
Patients with at least 1 discrepancy, n (%)	37 (30)	29 (59)	8 (10.5)	<0.0001
Patients with at least 1 intentional discrepancy, n (%)	116 (94)	44 (90)	72 (97.5)	0.11
Unintentional discrepancies per patient, mean (±SD)	0.68 (1.28)	1.49 (1.66)	0.15 (0.46)	<0.0001
Intentional discrepancies per patient, mean (±SD)	3.07 (2.06)	2.57 (1.87)	3.41 (2.12)	0.027

Abbreviation: SD, Standard deviation

Among the 84 unintentional medication discrepancies identified from the 489 medications surveyed, the most frequent medication error was ‘omission’ (56%), as shown in Figure 10.1.

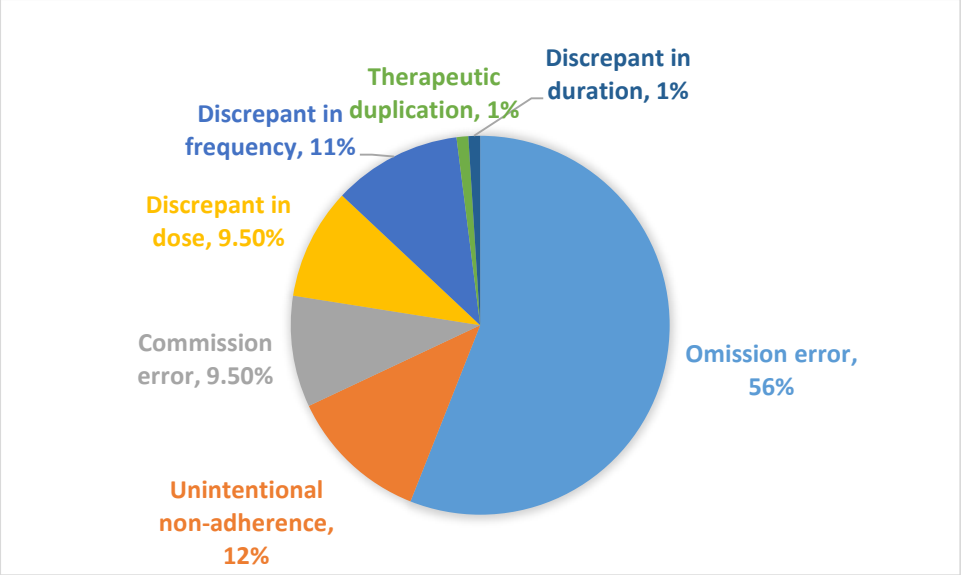

Figure 10.1 Types of Unintentional Medication Discrepancies

The most common medication classes involved with unintentional discrepancy were those which acted on the cardiovascular system, followed by infectious diseases, central nervous system and endocrine and metabolic disorders. However, adjustment for prescription frequency showed that vitamins and minerals accounted for another common medication class, but this estimation was derived from fewer prescriptions (Table 10.3).

Table 10.3 Medication Class with Unintended Discrepancies

Medication class	Medications with UD, n (%)	Medications with UD adjusted for prescription frequency
Anti-infectives	22 (26.2)	22/177 (12.4)
Cardiovascular	41 (48.8)	41/166 (24.7)
Gastrointestinal	4 (4.8)	4/50 (8.0)
Central nervous system	6 (7.1)	6/29 (20.7)
Endocrine and metabolic disorders	6 (7.1)	6/25 (24.0)
Blood and blood products	1 (1.2)	1/17 (5.9)
Vitamins and minerals	2 (2.4)	2/7 (28.6)
Respiratory	2 (2.4)	2/16 (12.5)

Abbreviation: UD, Unintentional discrepancy

The physician/pharmacist team assessed the potential severity of unintentional discrepancies, and found that 5 (7%) of 74 patients in the intervention phase had at least 1 unintentional medication discrepancy with the potential to cause severe clinical deterioration, compared with 14 (29%) of 49 patients in the pre-intervention group ($p = 0.001$). There was a moderate level of agreement among evaluators in judging the potential clinical impact of medication discrepancies (Cohen's kappa, $K= 0.447$; $p < 0.0001$). Among the 84 unintentional medication discrepancies identified in both phases of the study, most discrepancies (61%) were evaluated as potentially causing severe patient discomfort or clinical deterioration whereas 21% of the discrepancies were deemed unlikely to cause harm or clinical deterioration, and the remaining 18% were judged to have the potential to cause moderate discomfort or clinical deterioration. Table 10.4 shows examples of potential clinical severity rating for unintentional medication discrepancies.

Table 10.4 Examples of Unintentional Medication Discrepancies with their Potential Clinical Severity; rated according to Cornish et al tool [5]

Examples of unintentional discrepancy	Type of discrepancy	Potential clinical severity
Scenario 1. A patient's home medications were ART and co-trimoxazole prophylaxis therapy (CPT). During hospital admission, the physician was well aware of the ART but not CPT use by the patient and was not documented in the patient chart.	Omission error	Mild
Scenario 2. A 27 years old female patient admitted with a diagnosis of CNS toxoplasmosis secondary to retroviral infection (RVI), had been prescribed omeprazole at some private clinic for ulcer related complaints and was already taken it for the past 14 days. During admission, she did not have any ulcer related complaints but omeprazole was continued without any indication.	Unnecessary drug therapy	
Scenario 3. A known hypertensive patient on enalapril 2.5 mg po/day, hydrochlorothiazide 12.5 mg po/day, aspirin 81 mg po/day, simvastatin 20 mg po/day was admitted at ED. The patient brought only simvastatin, other medications were not at the patient's hand. The intern informs the patient to continue the medications but the patient was taking only three of the medications. The patient was not taking hydrochlorothiazide and the intern was not aware of this.	Omission error	Moderate
Scenario 4. A patient with 5 home medications [simvastatin, nifedipine, enalapril, aspirin, and hydrochlorothiazide] had detected an unintentional reduction of enalapril dose from 10 mg po/day to 5 mg po/day at hospital admission. Simvastatin 20 mg BID was also changed to simvastatin 20 mg po/day unintentionally.	Discrepancy in dose	

Scenario 5. Before hospital admission, the prescribed digoxin dose was 0.125 mg daily but on comprehensive medication history taking, a patient was found to take 0.125 mg BID of digoxin.	Discrepancy in dose	
Scenario 6. A patient was taking KCl 1 tablet but what actually on the chart was 2 tablets three times daily. Looking at the patient's K level, it was too low; i.e., 2.4 meq/l, part of the problem might be the patient was taking 1 tab of KCl while instructed to take 2 tab.	Discrepancy in dose	Severe
Scenario 7. A patient had been visiting two medical centers, in one of the centers, she was advised to take 40 mg po BID frusemide but no improvement. Later, she visited another center and ordered to take 40 mg po of frusemide twice daily. Although in the referral letter it was noted as she was taking 40 mg po furosemide, on comprehensive medication history, this patient was taking frusemide 80 mg po BID, the patient was assuming as if she was taking two different products from these two different institutions.	Discrepancy in dose	
Scenario 8. A 50 year old female patient with heart failure was taking furosemide and spironolactone as her regular medicines, and admitted for pneumonia. But during admission, the physician was not aware of these medications although the medication (spironolactone) was at the patient's hand and Lasix was at home. The physician only treats the patient's current diagnosis.	Omission error	
Scenario 9. A patient was taking 6 regular medications. But after hospital admission, it was found that atorvastatin was missed somewhere in the management. In addition, on comprehensive medication history, this patient was taking 5 mg po of warfarin whereas the order was 2.5 mg po of warfarin and because of this, the patient's warfarin was run out a couple of weeks ago before his current admission.	Omission error, unintentional non-adherence	

Scenario 10. Frusemide 20 mg po BID was written in the home medicines list but on the current medicines list, it was written down as furosemide 20 mg po daily. In addition, this patient was ordered to take ciprofloxacin 500 mg po TID but on comprehensive medication history, it was found that the patient was taking 1 tablet per day of ciprofloxacin (500 mg only).	Discrepancy in frequency	
Scenario 11. A patient was previously ordered to take furosemide 20 mg po TID, spironolactone 25 mg po per day, erythromycin 500 mg po BID and hydrochlorothiazide 12.5 mg po per day. But on detail medication history, the patient's hydrochlorothiazide was unintentionally discontinued. Also, a reassessment of the patient's medication, this patient was taking erythromycin 250 mg po BID instead of 500 mg po BID, and spironolactone 50 mg po per day instead of 25 mg po per day.	Omission error, discrepancy in dose	

Abbreviation: ART, Antiretroviral; BID, *bis in die* (two times a day); CNS, Central Nervous System; CPT, Co-trimoxazole prophylaxis therapy; ED, Emergency department; mg, Milligram; PO, Per oral; tab., Tablet; TID, *ter in die* (three times a day).

In the univariate analysis of patients who experienced unintended discrepancies revealed significant differences in patients with more than 2 preadmission medications compared to patients with 2 medications (62% vs 38%, respectively, p = 0.03). However, there was no significant association with other variables of interest such as age, gender, the number of comorbidities and current medications and major diagnosis. In multivariate analysis, the number of preadmission medications was also the only variable that had a significant independent relationship with having unintentional medication discrepancy (OR 3.05, 95% CI 1.12–8.29; p = 0.029). The effect of the intervention remained statistically significant (p < 0001) after adjustment for all other predictor variables, and the likelihood of occurrence of unintentional medication discrepancies was approximately 17 times more often if there was no pharmacist intervention (OR 16.45, 95% CI 5.22–51.85).

10.5 Discussion

Recently, there has been a trend shift in hospital pharmacy services—from dispensing roles to that of ward-based clinical activities—and thus, Ethiopian pharmacists have been increasingly engaged in direct patient care roles, such as ward round, medication review and participate in morning sessions [27]. However, many challenges surrounding pharmacists' involvement in medication safety activities had been found, and this was mainly due to human resource deficiencies as well as the lack of training opportunities and government funding [Chapter 9]. National efforts had been undergone to assess the implementation status of clinical pharmacy services, and it was found that these services had received wider recognition although limited in scope and the practice lacked uniformity across hospitals [27]. For example, medication reconciliation was not formally practiced, and the impact of this strategy when performed by pharmacists was not dealt.

The current study was a medication safety initiative, and to our knowledge, it was the first study investigating the impact of pharmacist-led medication reconciliation programs in resource-limited settings. Although many patient safety organizations across the globe endorsed medication reconciliation as a safety strategy [15–17], the impact of this program was not tested in sub-Saharan Africa, including Ethiopia. The findings of this study suggested that pharmacists assigned to an ED played a significant role in improving medication safety, and it was found that pharmacist-led medication reconciliation within 24 hours of adult admission significantly decreased the incidence of patients with at least one unintentional medication discrepancy; an absolute reduction of 48.5%. This finding is similar to previous studies [28–30] conducted at ED that have shown an absolute reduction of 33% to 72% in patients with unintentional medication discrepancies. The impact pharmacists might bring in minimizing medication discrepancies was an area of interest—and this, could possibly strengthen the present findings—and our previous meta-analysis of 13 medication reconciliation interventions conducted at a single transition (either admission or discharge) has shown a substantial reduction of 66% in patients with medication discrepancies (RR 0.34; 95% CI: 0.23–0.50) in favour of pharmacist-led medication reconciliation interventions [21]. In another review of electronic medication reconciliation interventions [20], unlike the present study, medication reconciliation supported by an electronic tool did not consistently reduce the proportion of patients with medication discrepancies. In contrast, this tool was able to show a significant reduction of 45 % in the proportion of medications with unintentional discrepancies (RR 0.55; 95 % CI 0.51–0.58). In the latter measure, the current study also showed a significant reduction of the percentage of medications with unintended discrepancies from 42% to 3.5% after the intervention ($p < 0.0001$). Notably, in either of these measures, the international goal of the WHO; that is, a 75% relative reduction in medication discrepancies [28], was achieved through

pharmacist involvement in medication history taking at ED; it was 82% using patients as a unit of analysis and 95% using medications as a unit of analysis (data not shown).

In the present study, unintentional medication discrepancies at hospital admission were common, occurring in 59% of patients during the pre-intervention assessment. This proportion is comparable with previous studies that have shown one or more medication discrepancies in 54–75.6% of patients at hospital admission [5, 28, 29], but there are also higher unintentional discrepancy occurrences from reports in other studies [2, 30]. Various definitions pertaining to medication discrepancies, and differences in the method of data collection might explain the variations between studies. In a systematic review of 95 studies by Almanasreh et al. [31] have shown that more than two-thirds of the studies did not utilize a BPMH, and the authors of that study urged the need to clearly define and classify medication discrepancies for ease of comparisons between studies. As an illustration, a systematic review of 22 medication history error studies; of which, only 5 were able to distinguish between unintentional discrepancies and intentional therapeutic changes, at least one medication history error had been found in 10–67% of patients, overall. However, it was 27–54% of patients who were in fact experienced at least one medication history error when the findings are delimited to these 5 studies [8]. This review [8] had been conducted a decade ago, and yet a higher discrepancies rates have been reported since then [2, 28–30]. This might be as a result of an emerging complex care needs, and an increasing incidence of chronic diseases that put individuals with many health care needs and medications. Zoni et al. [18] have identified, for example, the relationship between chronic medication use and the occurrence of unintended discrepancy, and our study was also substantiated our explanation derived from the multivariate analysis. That is, there existed a significant independent relationship between the number of preadmission medications and unintentional medication discrepancy. Previous studies [2, 32] have also confirmed the

associations between unintentional medication discrepancies and the number of medications at admission.

The most common medication discrepancy identified in this study was the complete omission of a preadmission medication a patient was taking before admission, and this was also the most common discrepancy reported in some previous studies [2, 5, 29, 30, 32]. Apart from medication omission, unintentional non-adherence to medications was highly prevalent in this study and this finding has been rarely described in other medication reconciliation studies conducted at hospital admission. Given the lower literacy level identified as a barrier to patient safety in our previous study [Chapter 8], this finding is not surprising. Because this type of discrepancy is emanated from the patient itself unlike other types of discrepancies originated from inappropriately taking medication histories by health care professionals—for example, the patient's medication is correctly prescribed as digoxin 0.125 mg daily but what the patient was actually taking was 0.125 mg twice per day. An instrument, Medication Discrepancy Tool [33], developed for identification and characterization of medication discrepancies was also intended to assess the patient's role in managing his/her medication regimen across care transitions. Previous studies that used this tool, for example, Coleman et al [13] have reported unintentional nonadherence as one of the most frequently identified medication discrepancies during the transition from hospital to home.

The medication class most commonly associated with unintended discrepancies was that acting on the cardiovascular system, which is similar to other publications [3, 5, 18, 32], but this was also among the most frequently prescribed medication group, and thus, after making adjustment for the frequency of prescriptions this study identified other higher risk medication classes; that is, vitamins and minerals. Accordingly, Pippins et al [3] and Zoni et al [18] have also identified other classes of medications, such as gout medications and medications used for the treatment of dermatological and ophthalmologic disorders, respectively.

Evaluating the potential clinical impact of unintentional discrepancies identified in this study, it was judged that 61% of the discrepancies have had the potential to cause severe patient discomfort or clinical deterioration. Although clinical measures, such as hospital readmission were not collected in this study, we believed that patients with medication discrepancies—particularly, those with the potential to cause severe clinical deterioration—might encounter a higher rate of hospital readmission. Coleman et al [13] have shown that 14.3% of patients with medication discrepancies were readmitted at 30 days compared with only 6% of patients who did not have any discrepancies ($p = 0.04$). The present study also demonstrated the pharmacist's impact in reducing severe discrepancies, which is in line with our previous review [22] that has identified more clinically important medication discrepancies in the usual care than pharmacy-led medication reconciliation interventions, implying that the intervention might have resolved discrepancies before reaching to the patient.

Irrespective of the potential severity of medication discrepancies, however, the occurrence of unintentional discrepancies was approximately 17 times more often if there was no pharmacist intervention. Pharmacists are uniquely trained in therapeutics, including medication history taking [34], and thereby, pharmacist-acquired medication history is complete and comprehensive than that obtained by other health professionals [35, 36]. Pharmacists could potentially play a central role in ensuring accurate and complete medication histories, and in this study there had been better documentation of medications as observed from a higher number of documentation regarding intentional changes to treatment in the intervention, compared to the pre-intervention phase ($p = 0.027$).

This study has an important clinical implication in public hospitals in Ethiopia where medication history taking was purely assigned to physicians or physician interns. Pharmacists could be important resources aiding busy physicians in availing complete medication histories important for therapeutic decision at the time of hospital admission. However, having an impact

does not mean that this process is easily going given the matters that are dealt in Chapter 9. There are various behavioural determinants, such as knowledge, skill, competing priorities and willingness of pharmacists in medication history taking that should be targeted for successful implementation. Medication reconciliation was initially introduced as one of the Joint Commission's National Patient Safety Goal in 2005 [14], and later endorsed globally, and much has been improved since its inception as a strategy to reduce and resolve discrepancies. However, there has been a number of hospital wide challenges before success stories have been told from various countries, including the Netherlands, Australia, and France [37]; and this will not be an exception for Ethiopian hospitals.

This study had several limitations. We did not follow patients with unintentional discrepancies whether these had been resolved subsequently or not, although prescribers agreed that the identified discrepancies were unintentional. It was also difficult to take complete medication history from some patients who had a low level of health literacy, and the problem was even worse when additional sources of medication history were not available. Because of the nature of study design, we could not attribute the impact was due to the intervention only; there was no concurrent control group and the study was done as part of a quality initiative. For example, during the intervention phase, we created awareness of the staff involved in emergency care about the importance of medication reconciliation, and coincidently, there had been some process redesign (e.g. changes in patient flow pattern) that could possibly change physicians' usual practices.

10.6 Conclusion

This is the first study investigating the impact of pharmacist-led medication reconciliation initiative in Africa and has found that pharmacist intervention was able to reduce the incidence of unintentional medication discrepancies significantly. Unintentional medication

discrepancies were common at hospital admission, mainly medication omissions and most were classified as potentially impactful. Implementing this strategy in the Ethiopian setting is feasible, and pharmacists may be regarded as an important resource personnel for the safe use of medications during care transitions.

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Supplementary material for chapter 10 is supplied as appendix (appendix 6.5, page 398)

PART D: DISCUSSION and CONCLUSION

Chapter 11

Discussion, Conclusion and Future Directions

11.1 Overview

Given the global burden of medication errors and the resulting adverse outcomes, a number of medication safety programs have been in use internationally for improving medication-related outcomes. Medication reconciliation is one such program, which has been recognized as an important approach to the Quality Use of Medicines. This strategy has been adopted as a standard practice in many developed countries. However, the impact of this strategy overall, as well as pharmacist-led medication reconciliation programs are inconclusive. Before the implementation of this program in settings where this has not been in place, one of the queries posed by the researchers of this study was to synthesize the evidence supporting the impact of medication reconciliation as a medication safety strategy. Whilst medication-related harms also represent one of the patient safety issues that concern the developing nations, including Ethiopia, there are not many research publications in medication safety, nor evidence-based interventions aimed to tackle the burden of medication errors and subsequent patient harm.

Although pharmacists' involvement in clinical services is a relatively new practice in the Ethiopian health care system, we hypothesized that the introduction of pharmacist-led medication reconciliation initiatives may be beneficial, and we aimed to determine whether this strategy is feasible in such settings. The work presented in this thesis has shown the journey towards the implementation of this strategy in resource-limited settings and informed by a sequence of four separate but inter-related studies; the first three were preparatory works, and the last provided evidence for effectiveness. It is our opinion that a program's success is measured by its effectiveness, as well as its sustainability. The latter was fuelled by the preparatory works in guiding the intervention. Broadly, this thesis uses methods from both safety and implementation sciences for successful implementation of the medication reconciliation program. System approaches to patient safety, such as patient safety culture has been explored, and patients' experiences of medication-related adverse events have been

discussed followed by an implementation of a theory informed medication reconciliation intervention during hospital admission. This thesis was thus, utilized a multi-method exploration of patient safety issues to develop, implement and evaluate a medication safety program designed to reduce the burden of unintentional medication discrepancies at transitions in care. An overview of how each discrete component of the project forms a cohesive whole is graphically illustrated in Figure 11.1 below.

The findings of the above phases of research were presented in the preceding chapters of this thesis, and specifically, this chapter is a summary of discussions and conclusions driven from the findings presented in Chapters 2 to 10. The strengths and limitations of the studies included in this thesis are also discussed. Finally, this chapter concludes with the implications for future medication safety research directions.

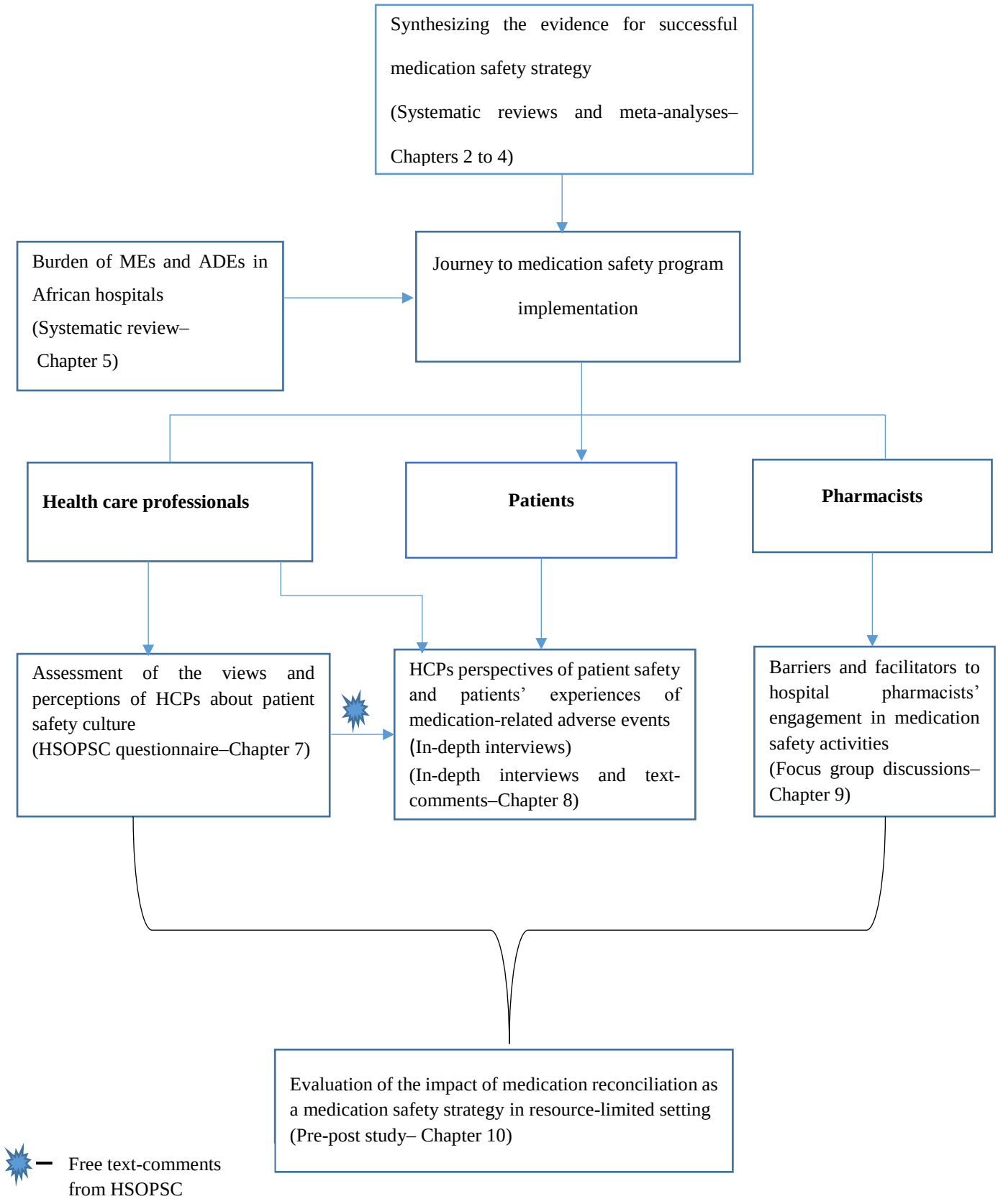

Figure 11.1 Overview of the Journey to Implementation of Medication Reconciliation as a Medication Safety Strategy

11.2 Discussion of Main Findings

11.2.1 Pharmacy-led Approach to Medication Reconciliation

Previous two systematic reviews of hospital-initiated medication reconciliation interventions have shown inconsistent findings regarding the impact of medication reconciliation in either improving clinical outcomes or reducing medication discrepancies [1, 2]. As a result, it was uncertain to support the effectiveness of medication reconciliation interventions. But, both agreed that most successful medication reconciliation interventions are due to pharmacist's involvement; however, the impact on both process and clinical outcomes is largely unknown. Having taken this into consideration, we hypothesized that the impact of pharmacists in clinical and process outcomes were diluted amidst the various medication reconciliation approaches, such as collaborative models and technology supported interventions, and therefore, a pertinent step in the journey to medication safety program implementation would be to evaluate the effectiveness of pharmacy-led medication reconciliation programs as a stand-alone consideration. Systematic reviews and meta-analyses of the effectiveness of pharmacy-led medication reconciliation interventions were then conducted, and the findings have demonstrated a significant impact from involving pharmacists in the medication reconciliation. Most importantly, as detailed in Chapter 2, the intervention helps to cut adverse drug event-related hospital revisits, subsequent emergency department hospital visits and hospital readmissions. However, there is no evidence that such interventions have an impact on mortality and composite all-cause readmission and ED visits. Similarly, pharmacy-led medication reconciliation interventions were also led to a significant decline in the prevalence of unintentional medication discrepancies when conducted at either admission or discharge.

While much has been said regarding the uncertainties in the impact medication reconciliation could have, as well as the lack of clear roles and responsibilities in conducting this service among the health care professionals, the above two reviews of ours have demonstrated a clear

role for pharmacists in the medication reconciliation process. The issue of who shall be responsible for medication reconciliation was debatable, and this has been seen in a survey of health care providers' perceptions of their roles and responsibilities in conducting medication reconciliation in the Arabian Gulf [3] and has found a lack of agreement among clinicians about their role in the process. On their perception of their role in the process, physicians and pharmacists considered their professions as the main providers while nurses considered physicians followed by themselves as the main players with limited roles for pharmacists [3]. This has also been observed in the USA [4], showing that most implementation efforts involve physicians and nurses, with little roles for pharmacists, and thus, pharmacists are underutilized in the medication reconciliation process. Many argue this to the fact that, unlike pharmacists, the aforementioned professions are available all the time in the wards, and pharmacy staffing is an issue [3]. A recent national survey conducted in the USA to assess pharmacist roles in medication reconciliation has shown that pharmacists do not routinely or consistently provide medication reconciliation, and there exists insufficient recognition of the value of pharmacists' roles by medical and nursing staff [5]. In fact, a number of health care organizations stated this process as a shared responsibility of health care providers in collaboration with patients/clients and families, and pharmacists are given the coordination role for the whole process [6, 7]. The American Society of Health-System Pharmacists (ASHP) position statement also describes that pharmacists, because of their distinct knowledge, skills, and abilities, are uniquely qualified to lead interdisciplinary efforts to establish and maintain an effective medication reconciliation process in hospitals and across health systems [8]. This clearly shows a discrepancy between what most organizations have recommended with what actually is the practice. It should be noted that, however, pharmacy staffing may be an issue and scope of pharmacy practice might vary from country to country. For example, clinical pharmacy practice is well established in

Australia, and medication reconciliation in hospitals is almost exclusively performed by pharmacists [9].

Furthermore, evidence from effectiveness evaluation of pharmacist-led medication reconciliation intervention has shown that this approach has been found as a very sensitive strategy in preventing ADE-related hospital revisits, and we believed that this intervention is powerful in picking patients with discontinued medications. Medication discontinuity—also called as omission of medications—is the most common identified medication discrepancy [10], and is also the common reason for discrepancy-related ADEs [11]. It is interesting to note that, while previous reviews of pharmacist-led medication reviews did not show a significant reduction in unplanned hospital readmissions [12, 13], the systematic review presented in Chapter 2 support the evidence that pharmacist-led medication reconciliation is an effective strategy, and strengthen our claim that considering medication review without ensuring the most accurate list of a patient's current medication would be theoretical.

The quest for evidence had not been stopped there, but it extended to searching other patient safety solutions, including other health care providers' initiated interventions. The literature on physician- or nurse-led medication reconciliation interventions was scanty, and thus, as a viable option, we synthesized the evidence for electronic tools in supporting the medication reconciliation process.

11.2.2 Information Technology Approach to Medication Reconciliation

In Chapters 2 and 3, we have discussed the impact of pharmacy-led medication reconciliation interventions on clinical and process outcomes, respectively. In these days of high techs; however, the use of information technology (IT) in facilitating information communication overall, and in supporting accuracy in medication documentation are highly demanding. For instance, IT supported documentation communication ensures comprehensive medication history of patients through information sharing, and is now commonly employed to facilitate

the medication reconciliation process [14]. In Chapter 4, we addressed the impact of an electronic tool on the incidence of medication discrepancies identified through the medication reconciliation process, the findings of which yielded a significantly lower proportion of medications with an unintended discrepancy, mainly drug omissions. But, there was no significant reduction in either the proportion of patients with medication discrepancies or the mean number of discrepancies per patient. The clinical impact of electronic interventions is also less clear. There was a lack of rigorous designs to ascertain these findings, however. Overall, effective medication reconciliation likely requires a multifaceted approach involving people, process, technology and that technology intervention alone may not consistently reduce errors.

One of the lessons learned from this systematic review, as detailed in Chapter 4, is the approach to pair computerized physician order entry programs (CPOE) with a medication reconciliation service in reducing medication errors. The existence of CPOE would not be able to detect unintentional omission of medications the patient is taking at home but would able to fill the gaps in prescriber's knowledge [15]. Therefore, a CPOE program complemented with a medication reconciliation service may be able to bridge the gaps in continuity of patient care, and further ensures a comprehensive medication history of patients, and is a viable option for those hospitals which have an existed CPOE program. However, this also needs careful integration of the tool for successful implementation of computerized medication reconciliation services.

Regardless of whether IT-based approaches were clearly superior to a pharmacist (or human) led approach, the fact that these interventions are less likely to be implemented in low resource-settings led to the selection of feasible interventions. Thus, it becomes clear that and taking the available resource into consideration, the pharmacy-led approach has been selected for the journey towards implementation of medication reconciliation service in the Ethiopian hospital

settings. As highlighted in Chapter 1, local and international experiences are the grounds for this initiative, and the impact of medication reconciliation had not been tested in Africa, including Ethiopia. As the main motive of this thesis is to implement this new service in different hospitals in resource-limited settings in Africa, it is imperative to explore the extent of medication-related problems, including errors and adverse drug events in the African hospital setting

11.2.3 The Burden of MEs and ADEs in African Hospitals

While the burden of MEs and ADEs is largely unknown in the African health care setting, our systematic review of the African medication safety literature has shown that prescribing errors are the most commonly reported types of medication errors, and 4.2% of adult admissions are thought to be medication-related. Yet, most are preventable. This paves a way to design and implement preventive measures to target the burden of MEs and ADEs, one of which is the medication reconciliation intervention. This review, as highlighted in chapter 5, has also reported a severe lack of interventional studies in the area of medication safety.

However, implementation of medication reconciliation as a medication safety strategy is not a final outcome but it should be supported by corresponding changes in attitudes, teamwork, communication, culture, and leadership. According to the WHO High 5s medication reconciliation program [16], the culture of the organization with respect to interdisciplinary collaboration and teamwork significantly influence the effectiveness of the medication reconciliation process, and we believe this has to be explored to look at the changes necessary to improve patient safety. Ensuring a culture of safety and organizational supports for safety processes are key to patient safety improvement, and using a system approach is vital to identify factors that influence patient safety. In the following sections, we will discuss how health care professionals' perceived patient safety and will identify the existing patient safety problems in the Ethiopian public hospitals using both qualitative and quantitative methods. We also

believed that the overall picture of patient safety is not complete without addressing patients' experiences of medication-related adverse events from the perspective of patients themselves.

11.2.4 Health care Professionals' Perspective of Patient Safety and Patients' Experiences of Medication Related Adverse Events

Policies with regard to patient safety issues have been inconsistently integrated into the Ethiopian health care system, and it is only recently that the government of Ethiopia ratified a five year (2016–2020) strategic plan for improving the quality of patient care [17]. Given the wider commitment taken by the government for health care coverage and access, most patient safety efforts have been limited in scope and practice. As a result, investigation of patient safety issues in the Ethiopian health care is an area of research that is relatively new.

In Chapters 7 and 8, we explored patient safety issues from both the perspective of health care professionals and patients sides. Overall, health care professionals' perspective of patient safety culture was not satisfactorily enough, as measured by the HSOPSC instrument. The dimensions 'Teamwork within units' and 'organizational learning–continuous improvement' received the highest positive score, while 'staffing' scored the lowest. Interestingly, the dimensions 'handoffs and care transitions' and 'punitive response to error' were the other safety problems identified in this study. Particularly, problems with handoffs and care transitions were largely correlated and severely affected by a lack of teamwork across units, punitive response to error reporting and managerial inaction for promoting patient safety. These findings have also been uncovered during the in-depth interviews, as highlighted in Chapter 8. The interview data ascertained that incident reporting was infrequently done, when do so, it was usually not documented. Poor communication and teamwork, lack of cooperation, respect and supervision, together with the lack of an incident reporting system undermine the development of a culture of safety in the Ethiopian public hospitals. Previous local studies [18, 19] also reported that inter-professional communication is weak—mostly due to hierarchical differences—and

patient safety is greatly influenced by the norms and values of professional thought and status. The presence of professional hierarchies reflects that HCPs feel uncomfortable, and encounter difficulties to raise their concerns with other colleagues [20]. An organizational culture that promotes reporting and encourages non-punitive response to error and improved communication are reported as important factors to improve patient safety culture [21].

According to the Institute of Medicine [22], one of the challenges health care organizations encountered for the movement towards safer health system is a culture of blame. In other words, errors should not be treated as personal failures but as opportunities for improvement. This cultural transformation in Ethiopia may need more work and needs a strong leadership that enables staffs to be safety conscious, committed to learn from their mistakes and prevents errors from happening again. However, according to health care professionals, lack of managerial support had been identified as a barrier to patient safety. Participants also mentioned that most managers devoted their time for the mere purpose of political promotion and that most appointees were based on political affiliation than clinical leadership. There was a strong held belief among the participants that without having the appropriate person at the right position, it would be unlikely to achieve what hospitals are striving to do, and it does not make sense to talk about other problems due to the lack of effective clinical governance.

Furthermore, the interview data revealed other findings that the HSOPSC as a patient safety measure could not evaluate patient safety issues that have arisen as a result of resource limitations. Unlike developed countries, for example, the challenges faced by the Ethiopian health care system identified the lack of infrastructure (e.g. lack of rooms for patient admissions), poor sanitation, and material deficiencies (e.g. supplies, medications, and laboratory equipment) for achieving desired patient safety outcomes. While patient safety improvement requires adequate resources (e.g. human and material), these are not adequate on

their own; it also requires managerial support and change in culture and structure of governance [23, 24].

The interview data also revealed other important findings that the HSOPSC and other local studies [18, 19] did not or scarcely reported. . For instance, participants identified a lack of patient safety competencies, such as adequate knowledge and skills pertinent to correctly prescribe medications, administer medications and monitor patients. Task factors related to patient safety problems, such as the absence of incident reporting, delay in delivering health services, and the lack of safety protocols were cited as barriers to patient safety improvement. Although the HCPs believed that patient involvement in their own safety positively influenced patient safety, economic constraints and health illiteracy negatively impacted patient safety. These have also been mentioned from the individual patient interviews. Patients expressed a range of experiences related to their medication, and sometimes patients intended to stop their chronic medication because of this. Although patients encountered a number of medication-related adverse events, they were satisfied with the treatment they were taking. The possible explanation for this is that the way patients were thinking about their own safety. Patients might associated this with an effectiveness of therapy, or might perceived medication-related adverse events are inevitable occurrences following medication taking, and mostly they associated their satisfaction with the delivery of health services, such as timeliness, affordability and service availability.

Many strategies to promote patient safety have been suggested from the HCPs, as detailed in Chapter 8. Given the multifactorial nature of patient safety barriers, however, patient safety solutions are as diverse as their problem [25] and could be directed at various levels, such as the health care professional, patients, task factors, work environment, and organizations. Many of the barriers for patient safety in this study emanated from the lack of resources (e.g. human and material), but our medication safety initiative did not address the broad underlying causes

of patient safety problems (e.g. inadequate resources), but rather target specific levels, including teamwork, patients, communication (e.g. at care transitions) and process design to prevent medication errors from actually reaching the patient. As previously mentioned, our initiative was a journey towards implementation of a pharmacist-led medication reconciliation service in settings where this service had been limited or not available at all. Thus, exploration of the barriers and facilitators that might influence hospital pharmacist's engagement in medication safety activities may help service providers or planners to target successful delivery of quality patient care.

11.2.5 Barriers and Facilitators to Hospital Pharmacists' Engagement in Medication Safety Activities

Unlike the developed countries, pharmacists' involvement in clinical services is at the early stage in Ethiopia [26]. As a result, little is known regarding the current status of Ethiopian pharmacist's extended services, such as medication review and reconciliation, as well as the barriers and facilitators to hospital pharmacists' engagement in medication safety activities.

As highlighted in Chapter 9, we employed implementation science concepts for the success of our journey. It has been suggested that many factors can influence uptake of evidence-based interventions, and the success of implementation journey is highly dependent on a careful assessment of barriers to, and facilitators of, the behaviour to be changed, and identification of such factors provide a theoretically robust evidence base to inform implementation of an intervention [27]. Using the Theoretical Domains Framework (TDF), we identified a wide range of factors that may influence the uptake of medication safety interventions delivered by hospital pharmacists. The majority of hospital pharmacists were very much enthusiastic for their extended roles and were positive towards the future of the profession; however, there were a number of factors likely to influence their clinical practice. These factors were clustered into

six predominant domains: ‘Knowledge’, ‘Skills’, ‘Environmental context and resources’, ‘Motivation and goals’, ‘Social influences’, and ‘Social/professional role’.

Environmental constraints (e.g. lack of government funding and human resource) were consistently identified as prominent barriers, and there was none which was identified as a facilitator in the context of resource issues. There have also been some links with other domains judged to be relevant, such as motivation and goals and social/professional role.

Unlike the environmental constraints, in the remainder of domains, a diverse range of views had been reflected from hospital pharmacists. For example, dispensing was thought to be a core business for the majority of health managers, and thus, hospital pharmacists were reinforced for other competing priorities. There was no remuneration schemes or incentives arranged for these cognitive services delivered by hospital pharmacists, and because of this, most pharmacists preferred dispensing to clinical services. A recent national study has also shown that two-thirds of hospital pharmacists are dissatisfied with their job, and this is mainly due to unattractive incentive packages [28]. There were yet enthusiastic hospital pharmacists who devoted themselves for the mere growth of the profession, and for these groups of pharmacists, the main concern was the lack of managerial and government support and the lack of role recognition by other members of the health care team.

While major differences in individual thoughts related to hospital pharmacists’ knowledge, skills, and social/professional role as well as motivation and goals existed, inter-institutional variation mainly appeared in the social influence domain. For example, hospital pharmacists working in district hospitals clearly indicated that their recommendations were better entertained and accepted by other health care professionals, and there was also an increasing demand for clinical pharmacy services. Particularly, those HCPs who believed in team and collaborative works were the most likely candidates for promoting clinical pharmacy services. Previous studies have demonstrated pharmacist provided therapy recommendation in care

teams resulted in positive clinical and economic outcomes, and these have been associated with high acceptance rates [29, 30]. A study by Anderegg et al [31] has shown that a high acceptance rate of pharmacist-provided services is associated with medication reconciliation as compared with other clinical services, such as those related to medication indication, efficacy, and therapeutic drug monitoring. Given the positive impact of pharmacist-led medication reconciliation programs, as outlined in Chapters 2 and 3, and the evidence that these services have shown better acceptance [31], it is our opinion that pharmacists' clinical services in the studied hospitals, mainly those above the district level, may be well utilized if they could able to implement medication reconciliation services.

11.2.6 Pharmacist-led medication reconciliation intervention – Pre-post study

This part of the thesis has been described in Chapter 10, and it was a single center investigation of the impact of pharmacist-led medication reconciliation intervention on the incidence of unintentional medication discrepancies before and after the implementation of this service. Many health care organizations endorsed medication reconciliation as a medication safety strategy [32–34], but the impact of this program was not tested in Africa. Our intervention suggested that pharmacists assigned to an emergency department played a significant role in improving medication safety, and had found that admission medication reconciliation significantly minimized the proportion of patients with at least one unintentional medication discrepancy. As described in Chapter 3, this finding is consistent with the meta-analysis of 13 medication reconciliation interventions conduct at either admission or discharge. In contrast, medication reconciliation intervention supported by an electronic tool (Chapter 4) did not consistently reduce the proportion of patients with medication discrepancies. Most importantly, our intervention achieved the international goal of the WHO [35]; that is, a 75% relative reduction in medication discrepancies was achieved through pharmacist involvement in medication history taking at ED.

The most common medication discrepancy identified was the complete omission of a pre-admission medication a patient was taking before admission, and this was also the most commonly reported discrepancy in a previous study [10]. Although it has been rarely reported in other medication reconciliation studies, unintentional non-adherence to medications was highly prevalent in our study, as highlighted in Chapter 10. This finding may be attributed to the lower patient health literacy level, as identified in Chapter 8—as one of the barriers to patient safety improvement in Ethiopian public hospitals. This is expected because this type of discrepancy is emanated from the patient itself unlike other types of discrepancies originated from inappropriately taking medication histories by health care professionals. An instrument, Medication Discrepancy Tool [36], developed for identification and characterisation of medication discrepancies was also intended to assess the patient's role in managing his/her medication regimen across care transitions. Previous studies that used this tool, for example, Coleman et al [37] have reported unintentional nonadherence as one of the most frequently identified medication discrepancies during the transition from hospital to home.

It is also of interest to note that, most of the discrepancies identified were judged to have had the potential to cause severe patient discomfort or clinical deterioration. We did not collect hospital readmission as an outcome measure, but we believed that patients with medication discrepancies—particularly, those with the potential to cause severe clinical deterioration—may encounter a higher rate of hospital readmission. Coleman et al [37] have shown that 14.3% of patients with medication discrepancies were readmitted at 30 days compared with only 6% of patients who did not have any discrepancies ($P = 0.04$). However, our intervention did not show a difference between the pre- and post-intervention groups in terms of the potential clinical impact of unintentional medication discrepancies. In the contrary, our systematic review (Chapter 3) identified more clinically important medication discrepancies in the usual

care than pharmacy-led medication reconciliation interventions, implying that the intervention might have resolved discrepancies before reaching to the patient.

Overall, our intervention has an important clinical implication in the Ethiopian health system where medication history taking are purely assigned to physicians or physician interns. Notably, pharmacists may be an important resource personnel aiding busy physicians in availing complete medication histories important for therapeutic decision at the time of hospital admission. Given the barriers that could possibly impact pharmacist's role in medication safety activities, as detailed in Chapter 9, having an impact does not mean that this intervention is easily implemented. There are various behavioural determinants, such as knowledge, skill, competing priorities and willingness of pharmacists in medication history taking that should be targeted for successful implementation. Leave alone the Ethiopian health system, implementation of medication reconciliation in the developed world had faced the same challenges before success stories had been told from various countries, including the Netherlands, Australia, and France [38], and this will not be an exception for the Ethiopian hospitals.

11.3 Strengths and Limitations

This thesis presents a serious of steps in the journey to medication safety program implementation. It encompasses systematic reviews to find an evidence-base for a successful medication safety program, and the use of a number of research methods to address the research aims and objectives. This thesis is unique in many aspects, one of which is the use of a multi-method approach for the exploration of patient safety issues, and novel in that it used a behavioural change theory for a successful implementation of medication safety programs. However, it has a number of methodological issues that should be taken into considerations. The strengths and limitations of this thesis have been discussed in detail in the previous

chapters, consequently, this section will summarize those judged to be the most notable, and those which have the broadest relevance to the whole thesis.

We had conducted a series of systematic reviews pertaining to medication safety (Chapters 2 to 5). This had been done purposefully given the limited evidence-base available to date pertaining to interventions to improve medication safety. Systematic reviews provide data for rational decision making [39], and can support policy making [40], as well as able to inform if the research question of interest has already been answered before a new study begins [41]. It was thus, instrumental to evaluate the available literature to help select an effective medication safety program that would be a promising strategy for implementation. Basically, systematic reviews and meta-analyses, are important tools for evidence-based medicine [42], and that was the primary reason for using these approaches. Meta-analysis, subset of a systematic review, is a statistical procedure that integrates the results of several independent studies and plays a central role in evidence-based medicine. In the hierarchy of clinical evidence—for example, meta-analyses are in the top [42]. However, the evidence-base from the meta-analyses depend strongly on the quality of the studies identified to estimate the pooled effect. Typically, but not necessarily, randomized controlled studies are frequently employed in deriving conclusions from meta-analytic procedures. An empirical evidence showed that non-randomized studies tended to show larger treatment effects [42]. In Chapters 2 to 4, we included studies from randomized, non-randomized and observational studies to evaluate the effectiveness of interventions, and this is an inherent limitation to the review conclusions.

Given the limited synthesis and review of the literature regarding medication safety, a systematic review detailing medication errors and adverse drug events in African hospitals had been done to have a broad understanding of the burden of medication-related problems, and to search any available medication safety programs in place. In opting to identify and evaluate the broader African medication safety literature, we did not focus on a specific research question, nor delimited to the Ethiopian setting. It should also be noted that limiting the search

to the English language may contribute for lesser included studies; notably, some publications from francophone countries were evident.

In Chapters 7 and 8, health care professionals' perspective of patient safety and patients' experiences of medication-related adverse events had been addressed. For the better understanding of these research questions, we utilized mixed methodological approaches involving both quantitative and qualitative methods. A combination of both methodological approaches is to provide the most comprehensive results, and it is believed that pharmacy practice research can benefit from a study that uses both quantitative and qualitative data to develop a strong evidence-base to support pharmacy-led services [43], including medication reconciliation. In Chapter 7, we adopted an HSOPSC questionnaire to assess the views and perceptions of health care professionals about patient safety culture. In this chapter, calculating patient safety culture scores were appropriate to identify existing patient safety problems. The questionnaire for this study was kept in English, and this might impact the understandability of the instrument. In fact, English is the medium of instruction and language of communication in the Ethiopian health care system. Since the HSOPSC survey explores patient safety issues from the perspective of systems approach, it did not attest other safety issues from the perspective of personal approach (e.g. health care professionals, patients), and did not explicitly evaluate safety issues that would arise as a result of resource limitations (e.g. inadequate equipment, unavailability of medications). Although the focus of the thesis was on medication safety, we broadly utilized the patient safety culture questionnaire internationally used for general patient safety assessment and thus, lacks specificity to medications. But, it is our opinion that HSOPSC evaluate safety issues from the perspective of systems approach, and this would not be different for medication safety culture as well. Still, we believed that medication safety is a core subset of the many patient safety issues, and the use of HSOPSC as a tool can elaborate many of the medication safety culture issues in it.

The semi-structured interviews, utilized in Chapter 8, were thus essential for eliciting deeper views from both HCPs and patients regarding patient safety issues. Text comments (from the HSOPSC survey) had been collated and merged to strengthen the findings of the in-depth interview. The qualitative results presented in Chapter 8, yielded both similar and unique findings—for example, understaffing and work burden was cited as one of the factors affecting patient safety in both of the research methods whereas safety issues from the perspective of other resource limitations (e.g. poor infrastructure, material deprivation) were reported in the qualitative findings. The inclusion of text-comments was also able to provide unique data that had not been discussed in the interview data—for example, managerial incapability and political affiliation as barriers to patient safety had been mentioned in the text-comments. The sampling technique may carry a risk of bias in both the interviews and survey, however, this thesis explored safety issues from the wider perspective (including patients) and the use of mixed-method gave a complete picture for the whole patient safety issues.

In Chapter 9, our focus was narrowed to pharmacists only, and focus group discussions were employed to facilitate data gathering. FGDs as a tool permits richness and flexibility in the collection of data and is an effective method in supplying information about how people think, feel, or act regarding a specific topic [44]. Together with other methods, it can be used for preliminary research, or to prepare specific subjects in a large project. However, one of the limitations in this chapter of the thesis was that homogeneous groups of participants were involved in the FGDs. We did not take the thoughts from the perspective of product-oriented pharmacists; at the time of data collection, these pharmacists were engaged only in dispensing activities. In fact, it is highly recommended to involve homogeneous groups in order to capitalize on people's shared experiences [45].

The strengths in the focus group discussions were the use of the theoretical framework to guide the discussions but also aided to identify many factors that can affect the adaptability of an

evidence-based intervention. When designing questions according to the theoretical framework, however, we incorporated a wide range of questions exploring a core set of clinical pharmacy services. But, it should be noted that admission and discharge medication reconciliation is one of the core clinical activities delivered by hospital pharmacists although the issue of medication reconciliation was new to the local situation.

Overall, although the use of various qualitative methods helped to fill the gaps inherent to the individual data collection tools, data analysis was done by one researcher that may still carry some risk of bias.

In Chapter 10, we evaluated the impact of pharmacist-led medication reconciliation interventions on the incidence of unintentional medication discrepancies and had found that implementing this strategy is feasible and pharmacists may be regarded as an important resource personnel for the safe use of medications during care transitions. However, having an impact might not be necessary meant that the intervention will be successfully and sustainably practiced. One of the innovative solutions to this was the exploration of behavioural determinants that were likely influenced medication safety activities delivered by hospital pharmacists, as highlighted in Chapter 9. This implies that behavioural determinants should be targeted before success is evident. However, we did not target each of the factors, but of course, our intention was to prepare hospital pharmacists for new roles. For example, competing priorities and the lack of reimbursement for clinical services had been described as barriers to hospital pharmacists' medication safety activities, and such issues need wider attention. On the other hand, in the implementation process, there was a room for equipping hospital pharmacists' with the knowledge and skill important for delivering medication reconciliation.

We proposed to initiate interventions both at hospital admission and discharge. But, due to resource limitation, we limited the implementation to hospital admission only. Although the time between pre-intervention and post-intervention assessment was short, there had been

important changes to patient flow structure during the implementation phase. Before and during implementation, serious of discussions regarding the importance of pharmacist's involvement in medication history taking with the staffs engaged in emergency care had been taken. Thus, our findings should be interpreted with caution. .

11.4 Conclusion

Overall, this thesis was a medication safety initiative focusing on medication reconciliation intervention, and the implementation of this initiative was guided by a multi-method approach consisting both qualitative and quantitative methods. It was thus, to the best of our knowledge, for the first time that this study has investigated the impact of pharmacist-led medication reconciliation in the African hospital setting, and the journey to implementation was informed by a serious of systematic reviews, alongside with a theoretically robust evidence-based exploration of the barriers to implementation. This journey was also supported by the identification of safety processes, such as assessing the culture of safety from the perspective of HCPs, and exploration of patients' experiences of medication-related events.

The results of systematic reviews and meta-analyses have shown an evidence that medication reconciliation interventions carried out through pharmacist assessment at hospital transitions were found to be an effective strategy for improving clinical outcomes (e.g. ADE-related hospital visits, all-cause readmissions, and ED visits), as well as process outcomes, such as the occurrence of unintentional medication discrepancies. More clinically relevant and discrepancies of higher impact were easily identified through pharmacy-led medication reconciliation programs. Literature exploring medication reconciliation supported by an

electronic tool has also been collated and has found that electronic tools did not consistently reduce process outcomes.

Patient safety culture in the studied hospitals has been found lower than the benchmark studies. Importantly, understaffing followed by problems during handoffs and care transitions and punitive response to error were identified as major safety problems. Particularly, hand offs and care transitions were largely affected by the lack of teamwork across units, punitive response to error reporting and managerial inaction for promoting patient safety. In addition to system factors presumed to affect patient safety, other factors such as individual HPCs, patient, and task factors have been identified as challenges to achieve an optimal patient safety in Ethiopian public hospitals. Resource limitations (e.g. material deficiencies, poor infrastructure) have been indicated as the greatest barriers for patient safety, and these have been scarcely or not reported at all in other similar studies elsewhere. Patients expressed a range of perceived experiences related to their medication, and a number of strategies required to improve patient safety practices have been suggested. Changes in practice, processes, structure, and systems were believed to help improve patient safety in the Ethiopian health care system. For example, engaging pharmacists in the multidisciplinary team have been one of the suggestions to improve medication safety.

The results of this thesis have demonstrated that hospital pharmacists were very much enthusiastic for their extended roles and were positive towards the future of the profession; however, there were many factors that likely influenced their behaviour in the clinical practice. Theory-based identification of behavioural determinants affecting hospital pharmacists' engagement in medication safety activities were predominantly related to 'Knowledge',

'Skills', 'Environmental constraints', 'Motivation and goals', 'Social influences', and 'Social/professional role'.

Whilst unintentional medication discrepancies were highly prevalent at the time of hospital admission, this study also found that pharmacist-led medication reconciliation was able to minimize the occurrence of discrepancies significantly. Thus, implementation of medication reconciliation as a medication safety strategy is feasible, and pharmacists may be regarded as key resource personnel for the safe use of medications at the time of hospital admission. However, the sustainability of this service utilization is highly dependent on other behavioural determinants, such as knowledge and skill, competing priorities, and reimbursement for clinical services.

11.5 Future Directions

The research presented in this thesis represents a significant body of work to the journey to the implementation of medication reconciliation programs. This is a preliminary step for assessing the feasibility of medication reconciliation service in a resource-limited setting, and there are yet many avenues for future research in medication safety and in the broader area of patient safety. Research opportunities are as diverse as the areas covered in this thesis, and the target of subjects for improvement and future research may include patients, HCPs, pharmacists and health care managers.

Given the negative patient safety culture revealed in this thesis, awareness creation campaigns targeting HCPs and health care managers in order to be safety conscious, and to further initiate development of quality improvement projects are demanding. Patient safety culture as a whole, can be taken as a quality improvement agenda in each of the hospitals studied, as well as each specific dimensions (e.g. handoffs and care transitions) are in fact, need to be addressed. Culture influences health care professional's motivation to engage in safety behaviours, and

creating a safer health care system needs cultural transformation [46]. Leadership in the health care shapes the culture, this, in turn, shapes the information flow and processing which has an important effect on patient safety. Better up take of innovations, such as patient safety highly depend on leaders that favour cooperation, creativity, and safety [47]. The findings of this thesis demonstrated that leadership incapability existed, and leadership positions were mostly not merit based. Besides awareness creation campaigns, leadership skill development schemes might be necessary for health care managers, and patient safety from the perspective of health care managers should be explored in future studies.

Although efforts to evaluate patient safety culture over time is an important aspect of ensuring safety—this might not be sufficient alone—but, it should also be supported through the introduction of patient safety teaching into the curricula for all medical and health science students. This could be achieved, for example, by the Multi-professional Patient Safety Curriculum Guide developed by the WHO [48]. This guide is mainly used for implementing patient safety education in universities/schools worldwide and targets education in the fields of dentistry, medicine, midwifery, nursing and pharmacy, and other related health-care professions. The guide enables HCPs to facilitate the incorporation of patient safety principles into their practice, in a wide range of educational and cultural settings [48]. Patient safety teaching should also be corroborated by an increase in awareness, skills, and knowledge in medical ethics among the clinicians.

A number of other suggestions to improve patient safety in the Ethiopian health care system have been forwarded, and these included changes in practices, processes, structures, and systems. None of these have been evaluated in the Ethiopian health care system and could be a subject of research for future studies.

Although the internal consistency of the whole survey that we employed for measurement of patient safety culture (HSOPSC) was fairly satisfied, the reliability analysis of individual

constructs showed many factors less than adquate level of Cronbach's alpha. Unlike other studies focused on tool development, this study was not designed for optimization of HSOPSC measurement model. Thus, further research is needed to confirm the applicability of the translated version of the HSOPSC, preferably Amharic in the Ethiopian hospital settings.

This thesis covered some patient-related factors which influenced patient safety. Patients' understanding of their medication was also not adequate. The second common unintentional medication discrepancy identified in this thesis was unintentional non-adherence (Chapter 10), the most likely culprit for this may be related to lack of adequate knowledge about their medication. However, comprehensive assessment of the factors affecting patients' engagement in patient safety had not been done. Patients can play an important role in improving patient safety by becoming actively involved in their health care, and patient involvement in safety is an emerging field of interest [49]. Therefore, future studies targeting factors affecting patient involvement in patient safety, as a stand-alone consideration, is of interest. The impact of patient counselling on patients' knowledge about their medication should also be sought in the future.

With respect to hospital pharmacists' activities in medication safety, awareness creation campaigns targeting the whole medical community (including the management, and other HCPs) could help facilitate the uptake of hospital pharmacist's cognitive services into clinical practice. And, yet there is a room for further studies that could also examine these extended services in the eyes of patients and other health care providers. Most importantly, product-oriented pharmacists' perspective of this new role could be explored. The findings of this thesis also highlighted clear gaps in hospital pharmacists' gaps in knowledge and skills necessary for delivering clinical services. While a national in-service training for practicing hospital pharmacists is a key first step to equip pharmacists with the necessary knowledge and skills needed to solve clinical challenges successfully, but the ultimate solution rests up on revisions in the undergraduate pharmacy curriculum that includes pharmacist's role in medication reconciliation.

The findings within this thesis have also identified further areas associated with pharmacist-led medication reconciliation programs which should be prioritized for research. Given the extended role of pharmacists in the Ethiopian health care system, medication reconciliation service, undoubtedly, represents an additional role that can be assumed by hospital pharmacists. As we illustrated in the limitation, however, it was difficult to attribute the impact was due to pharmacist involvement only. Thus, further interventional studies with rigorous study designs, possibly a randomized control trial could be used to confirm our results. Further research is also warranted to understand the impact of this intervention on some of the clinical outcomes of interest (e.g. adverse drug event-related hospital visits, all-cause ED visit). It would be intersting as well for future studies to explore the economic value of pharmacist-led medication reconciliation where financial constraints are common.

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APPENDICES

Appendix 1. Letter Correspondence

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Official Journal of the Society of Hospital Pharmacists of Australia
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LETTERS TO THE EDITOR

DOCUMENTING ANTIBIOTIC USE IN TRANSITION FROM INTENSIVE CARE UNIT TO WARDS

To the Editor,

Antibiotics are among the most prescribed medicines; however, nearly half of the prescribed antibiotics are not used appropriately.[1] Antimicrobial stewardship has been shown to reduce inappropriate antibiotic use by 22–36%,[2] and specifically, the impact is significant in intensive care units (ICUs).[3] Stewardship of antimicrobial use in hospitals is a current priority,[4] and documentation across transitions of care is a key aspect of patient safety.[5] Previous work has shown that documentation is an issue. It has shown that most ICU-restricted antimicrobials were prescribed according to national guidelines, but only one-third of patients on restricted antimicrobials had documented 'approval' in the medical notes. Authors concluded that 'better documentation on treatment plans … is needed during transition from ICU to the wards'.[5] In anecdotal experience there may be little documentation or communication regarding the indication for an antibiotic and the planned duration of treatment across transitions of care.

A retrospective audit of antibiotic documentation during ICU transfer was conducted at St Vincent's Hospital, Sydney, during 1–31 May 2014. Approval for the study was obtained from St Vincent's Hospital Human Research Ethics Committee. It identified a cohort of patients transferred from the ICU to general hospital wards while on antibiotic treatment. All documentation in the medical notes and electronic medicines management system regarding the antibiotic prescription, including the indication, proposed duration of treatment and plan for review monitoring and follow-up were reviewed.

The number of patient transfers on antibiotics was 59; in three of these the antibiotic was for long-term prophylaxis and were excluded from further analysis. The mean ICU length of stay was 2.9 ± 2.4 (range: 1–15) days. In this study cohort, a total of 72 antibiotics were prescribed with ceftriaxone (14/72) being the most common.

In 44 of 56 patient transfers, there was documentation in the medical record about antibiotic therapy, of which five transfers were general comments (e.g. 'continue antibiotics', 'intravenous antibiotics' and 'hold off antibiotics'). The proportion of transfers with documentation that specified intended antibiotic duration in the ICU medical notes was 13 of 44 (30%), with 9 of the 13 receiving antibiotics on the ward consistent with documented intended duration of antibiotic treatment. The actual antibiotic duration median was 2 days (range: 2–9 days), and only one course continued for 7 days or more (1/9, 11%). In 31 of the 44 transfers, no antibiotic duration was documented. The actual antibiotic duration median was 3 days (range: 1–16 days); in eight courses of antibiotics they continued for 7 days or more (8/31, 25%). Indication was documented in 36 of 56 patient transfers. The plan for ongoing monitoring of the patient with respect to antibiotic therapy was documented in 20 of the transfers, most of which were related to infection symptom resolution (e.g. 'continuation of antibiotics until fevers settle' and 'request for infectious disease specialist consultation').

In conclusion, this study has found that documentation of antibiotic duration during transfer from ICU to the wards was done infrequently. Lack of documentation may contribute to longer antibiotic treatment. This study informs future larger studies on documentation and communication related to antibiotic therapy and the need for antimicrobial stewardship, particularly across transitions of care.

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Journal of Pharmacy Practice and Research (2016) **46**, 91–93
doi: 10.1002/jppr.1155

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USES OF NON-PRESCRIPTION IBUPROFEN BY CONSUMERS FROM COMMUNITY PHARMACIES IN SOUTH AUSTRALIA

To the Editor,

A recent study of over-the-counter (OTC) analgesic use by urban Aboriginal patients in South Australia has highlighted the potential for serious health risks that could result from limited knowledge about safe use of analgesics, their side effects and contraindications.[1] Another study also found that many consumers were using ibuprofen despite having contraindications, warnings, precautions or potential drug interactions.[2] We report here the findings of a study addressing the use of non-prescription ibuprofen by consumers from four community pharmacies in South Australia.

Consumers visiting one of the four randomly selected pharmacies during the 3-month study period were asked to complete a self-administered, anonymous survey. The researcher approached the consumers, explained the study, and asked whether they had used non-prescription ibuprofen. Those who responded yes were asked to complete the survey in the pharmacy. Consumers' consent to participate was deemed to be indicated by the return of the completed survey. Those who were younger than 18 years or could not speak fluent English were excluded. The completed questionnaires were folded and placed in a closed box by the participants. The survey was designed to obtain information on the age and gender of the consumers, understanding of the consumers about the safe use of ibuprofen (including what conditions ibuprofen is used for), frequency of ibuprofen use, and whether the consumers talked to a health professional (e.g. doctor or pharmacist) about their use of OTC ibuprofen.

Of the 93 consumers completing the survey, most were female (n= 75, 80.6%), and most were aged less than 65 years. The majority of consumers (95%) provided a single answer when they were asked what conditions is ibuprofen used for, and 5% reported that they did not know the answer. Sixty-two consumers (67%) indicated that ibuprofen is used for pain, such as headache, migraines, joint problems, period pain, muscular pain and dental pain, 23 (25%) reported that ibuprofen is used for inflammation and 3 (3.2%) indicated that ibuprofen is used for fever.

Sixty-one (66%) consumers reported they did not talk to their doctor or a pharmacist about their use of OTC ibuprofen, and 77 (83%) had used OTC ibuprofen for at least 6–12 months. Sixty consumers (71%) reported they had used OTC ibuprofen for longer than a year, 11 (12%) had used ibuprofen for more than 6 months and 16 (17%) had used the drug for less than 6 months. However, most consumers (86%) used ibuprofen only when needed and less than once per week, 12% used ibuprofen once per week and 2.1% used ibuprofen every day. Twenty-nine consumers (31%) were also currently taking prescription medicines for conditions where ibuprofen may be contraindicated, or where interactions with ibuprofen may occur. Potentially interacting medicines included angiotensin converting enzyme-inhibitors and selective serotonin reuptake inhibitors. These findings suggest the need to improve consumers' understanding on their use of OTC medicines, reinforcing the important roles of pharmacists in promoting safer use of non-prescription ibuprofen.

Appendix 2. Electronic Supplementary Materials Published Online

A2.1 Electronic Supplementary Materials Published Online for Chapter 2

A. Online supplementary appendix A: Electronic database searches

Medline, IPA and PsychINFO

#	Searches	Results
1	((medic$ or drug$) adj2 discrepanc$).mp.	524
2	((medic$ or drug$) adj2 reconciliation$).mp.	1,193
3	((medic$ or drug$) adj2 histor$).mp.	75,175
4	((medic$ or drug$) adj2 list$).mp.	5, 023
5	(((medic$ adj2 chart$) or (medic$ adj2 record$)) adj2 assessment).mp.	125
6	((medic$ or drug$ or prescription$ or (medic$ adj2 chart$) or (medic$ adj2 record$)) adj2 review$).mp.	35,859
7	((medic$ or drug$) adj2 congruence$).mp.	20
8	((medic$ or drug$) adj2 management).mp.	37,424
9	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8	151,309
10	patient admission.mp. or Patient Admission/	20,054
11	patient discharge.mp. or Patient Discharge/	21,100
12	patient transfer.mp. or Patient Transfer/	6,658
13	Hospitalization/ or hospital transfer.mp.	81,536
14	"Continuity of Patient Care"/ or care transition.mp.	15,531
15	inpatients.mp. or Inpatients/	58,575

16	seamless care.mp.	154
17	continuum of care.mp.	3,103
18	"Delivery of Health Care, Integrated"/ or integrated health care.mp.	10,066
19	10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18	199,032
20	pharmac*.mp.	905,186
21	9 and 19 and 20	1,144
22	limit 21 to (abstracts and english language and humans)	1009

CINHAL

#	Searches	Results
S18	S14 AND S15 AND S16 Limiters-Peer Reviewed; English Language; Abstract Available	267
S17	S14 AND S15 AND S16	396
S16	S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13	306,305
S15	S1 OR S2 OR S3 OR S4 OR S5 OR S6	9,033
S14	"Pharmac*"	101,387
S13	(MH "Continuity of Patient Care+") OR "continu*"	187,044
S12	"seamless care"	104
S11	(MH "Inpatients")	55,914
S10	"emergency medic*"	29,880
S9	"transition of care"	143
S8	(MH "Transfer, Discharge")	3058
S7	(MH "Patient Admission") OR (MH "Hospitalization+") OR (MH "Patient Discharge+")	56,917
S6	"medication discrepancies"	45
S5	"medication discrepancy"	10
S4	"drug history"	122
S3	(MH "Medication Errors+")	8,626

S2	(MH "Medication History")	60
S1	(MH "Medication Reconciliation")	472

Embase

#	Searches	Results
24	#1.20 AND #1.21 AND #1.22 AND #1.23 [english]/lim AND [humans]/lim AND [abstracts]/lim	335
23	#1.15 OR #1.16 OR #1.17 OR #1.18 OR #1.19	375,805
22	#1.5 OR #1.6 OR #1.7 OR #1.8 OR #1.9 OR #1.10 OR #1.11 OR #1.12 OR #1.13 OR #1.14	454,467
21	#1.1 OR #1.2 OR #1.3 OR #1.4	4,019
20	pharmac*	3,875,936
19	'hospitalized patients'/exp OR 'hospitalized patients'	74,696
18	'inpatients'/exp OR 'inpatients'	108,750
17	'patient transfer'/exp OR 'patient transfer'	40,927
16	'patient discharge'/exp OR 'patient discharge'	96,003
15	'patient admission'/exp OR 'patient admission'	137,129
14	'medication'/exp OR medication AND record	179,120
13	'medication'/exp OR medication AND record AND systems	4,687
12	'medication'/exp OR medication AND record AND assessment	14,853
11	'medication'/exp OR medication AND record AND ('review'/exp OR review)	44,320
10	'medication'/exp OR medication AND chart AND ('review'/exp OR review)	9,372
9	medic* OR drug* AND list*	52,323
8	'medication'/exp OR medication AND ('history'/exp OR history)	91,985
7	'drug'/exp OR drug AND ('history'/exp OR history)	213,214
6	'drug'/exp OR drug AND ('history'/exp OR history) AND taking	9,182
5	'medication'/exp OR medication AND ('history'/exp OR history) AND taking	5389
4	'medication'/exp OR medication AND reconciliation AND errors	443
3	'medication'/exp OR medication AND ('history'/exp OR history) AND errors	570
2	'medication'/exp OR medication AND discrepancies	2464
1	'medication'/exp OR medication AND reconciliation	1453

PubMed

((((((medication reconciliation) OR medication discrepancies) OR medication history) OR ((medication AND (chart OR record) AND assessment)))) AND (((continuity of care) OR seamless care) OR ((hospital* OR inpatient* OR interface* OR discharge* OR admission*)))) AND pharmac***** [640]

B. Online supplementary appendix B: List of excluded full text papers and of the reasons for their exclusion

No control group/ ineligible comparator

Boso ribelles et al (2011). "Evaluation of a plan for cardiology medication reconciliation on admission, and patient information at discharge, in a teaching hospital." EJHP Practice 17(1)

Anderegg, S. V., et al. (2013). "Acceptance of recommendations by inpatient pharmacy case managers: unintended consequences of hospitalist and specialist care." Pharmacotherapy: The Journal of Human Pharmacology & Drug Therapy **33**(1): 11-21.

Cornu, P., et al. (2012). "Effect of medication reconciliation at hospital admission on medication discrepancies during hospitalization and at discharge for geriatric patients." Annals of Pharmacotherapy **46**(4): 484-494.

Hellstrom, L. M., et al. (2012). "Errors in medication history at hospital admission: prevalence and predicting factors." BMC Clin Pharmacol **12**: 9.

Lessard, S., et al. (2006). "Medication discrepancies affecting senior patients at hospital admission." Am J Health Syst Pharm **63**(8): 740-743.

Mergenhagen, K. A., et al. (2012). "Pharmacist- versus physician-initiated admission medication reconciliation: impact on adverse drug events." American Journal of Geriatric Pharmacotherapy **10**(4): 242-250.

Midlov, P., et al. (2012). "The effect of medication reconciliation in elderly patients at hospital discharge." International Journal of Clinical Pharmacy **34**(1): 113-119.

Quennery, S., et al. (2011). "Added value of pharmacist-acquired drug histories in an orthopaedic ward." Acta Clinica Belgica **66**(3): 196-199.

Reeder, T. A. and A. Mutnick (2008). "Pharmacist- versus physician-obtained medication histories." American Journal of Health-System Pharmacy **65**(9): 857-860.

Not Pharmacist-led medication reconciliation

Lalonde, L., et al. (2008). "Effectiveness of a medication discharge plan for transitions of care from hospital to outpatient settings." American Journal of Health-System Pharmacy **65**(15): 1451-1457.

Midlov, P., et al. (2008). "Medication report reduces number of medication errors when elderly patients discharged from hospital." Pharmacy World & Science 30(1): 92-98.

Schnipper, J. L., et al. (2009). "Effect of an electronic Medication reconciliation application and process redesign on potential adverse drug events a cluster-randomized trial." Archives of Internal Medicine **169**(8): 771-780.

Showalter, J. W., et al. (2011). "Effect of standardized electronic discharge instructions on post-discharge hospital utilization." J Gen Intern Med **26**(7): 718-723.

Zoni, A. C., et al. (2012). "The impact of medication reconciliation program at admission in an internal medicine department." European Journal of Internal Medicine **23**(8): 696-700.

Study protocol

Salanitro, A. H., et al. (2013). "Rationale and design of the Multicenter Medication Reconciliation Quality Improvement Study (MARQUIS)." BMC Health Serv Res **13**: 230.

Not English

Sanchez Ulayar, A., et al. (2012). "Pharmaceutical intervention upon hospital discharge to strengthen understanding and adherence to pharmacological treatment." Farm Hosp **36**(3): 118-123.

Medication reconciliation is not the primary intervention

Nester TM et al (2002).” Effectiveness of a pharmacist acquired medication history in promoting patient safety”. Am J Health-Syst Pharm 59:2221-25.

Lisby M et al (2010). “The effect of systematic medication review in elderly patients admitted to an acute ward of Internal Medicine”. Basic & Clinical Pharmacology & Toxicology 106: 422–427.

Edwards, S. J., et al. (2014). "Outcomes assessment of a pharmacist-directed seamless care program in an ambulatory oncology clinic." Journal of Pharmacy Practice **27**(1): 46-52.

Fera T, Anderson C, Kanel KT, Ramusivich DL. Role of a care transition pharmacist in a primary care resource center. Am J Health Syst Pharm. 2014; 71(18):1585-90.

Hutchison LJ, Mayzell GG, Bailey SC, Broyles JE. Impact of a discharge medication therapy management program in an extended care hospital. Consult Pharm 2014; 29(1):33-8.

Marotti, S. B., et al. (2011). "A randomised controlled trial of pharmacist medication histories and supplementary prescribing on medication errors in postoperative medications." Anaesthesia and Intensive Care **39**(6): 1064-1070.

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Sarangarm, P., et al. (2013). "Impact of pharmacist discharge medication therapy counselling and disease state education: Pharmacist Assisting at Routine Medical Discharge (project PhARMD)." American Journal of Medical Quality **28**(4): 292-300.

Spinewine, A., et al. (2007). "Effect of a collaborative approach on the quality of prescribing for geriatric inpatients: a randomized, controlled trial." J Am Geriatr Soc **55**(5): 658-665.

Szkiladz, A., et al. (2013). "Impact of pharmacy student and resident-led discharge counselling on heart failure patients." Journal of Pharmacy Practice **26**(6): 574-579.

Taber, D. J., et al. (2013). "Improved patient safety and outcomes with a comprehensive interdisciplinary improvement initiative in kidney transplant recipients." Am J Med Qual **28**(2): 103-112.

Not hospital based

Stewart S et al (1998). "Effects of a home-based intervention among patients with congestive heart failure discharged from acute hospital care". Arch Intern Med 158:1067-1072.

Boockvar, K. S., et al. (2006). "Medication reconciliation for reducing drug-discrepancy adverse events." American Journal of Geriatric Pharmacotherapy **4**(3): 236-243.

Kilcup, M., et al. (2013). "Postdischarge pharmacist medication reconciliation: impact on readmission rates and financial savings." J Am Pharm Assoc (2003) **53**(1): 78-84.

Stewart, A. L. and K. J. Lynch (2014). "Medication discrepancies despite pharmacist-led medication reconciliation: the challenges of maintaining an accurate medication list in primary care." Pharm Pract (Granada) **12**(1): 360.

Ineligible study design/procedure

Carter, M. K., et al. (2006). "Pharmacist-acquired medication histories in a university hospital emergency department." American Journal of Health-System Pharmacy **63**(24): 2500-2503.

Karapinar-Carkit, F., et al. (2009). "Effect of medication reconciliation with and without patient counselling on the number of pharmaceutical interventions among patients discharged from the hospital." Annals of Pharmacotherapy **43**(6): 1001-1010.

Musgrave, C. R., et al. (2013). "Improving transplant patient safety through pharmacist discharge medication reconciliation." American Journal of Transplantation **13**(3): 796-801.

Mudge AM, Shakhovskoy R, Karrasch A. Quality of transitions in older medical patients with frequent readmissions: opportunities for improvement. Eur J Intern Med. 2013;24(8):779-83.

Sen S, Siemianowski L, Murphy M, McAllister SC. Implementation of a pharmacy technician-centered medication reconciliation program at an urban teaching medical center. Am J Health Syst Pharm. 2014;71(1):51-6.

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Not medication reconciliation intervention

Eijsbroek, H., et al. (2013). "Medication issues experienced by patients and carers after discharge from the intensive care unit." J Crit Care **28**(1): 46-50.

Hohmann, C., et al. (2013). "Adherence to hospital discharge medication in patients with ischemic stroke: a prospective, interventional 2-phase study." Stroke **44**(2): 522-524.

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Romero, C. M., et al. (2013). "Effects of the implementation of a preventive interventions program on the reduction of medication errors in critically ill adult patients." Journal of Critical Care **28**(4): 451-460.

Not relevant clinical outcome

Smith L et al (1997). “An investigation of hospital generated pharmaceutical care when patients are discharged home from hospital". Br J Clin Pharmacol 1997; 44: 163–165.

Michels R et al (2003). "Programme using pharmacy technicians to obtain medication histories.” American Journal of Health-System Pharmacy 60: 1982-86.

Alassaad, A., et al. (2013). "Prescription and transcription errors in multidose-dispensed medications on discharge from hospital: an observational and interventional study." J Eval Clin Pract **19**(1): 185-191.

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Becerra-Camargo, J., et al. (2013). "A multicentre, double-blind, randomised, controlled, parallel-group study of the effectiveness of a pharmacist-acquired medication history in an emergency department." BMC Health Services Research 13: 337.

Beckett, R. D., et al. (2012). "Effectiveness and feasibility of pharmacist-led admission medication reconciliation for geriatric patients." Journal of Pharmacy Practice 25(2): 136-141.

Benson, J. M. and G. Snow (2012). "Impact of medication reconciliation on medication error rates in community hospital cardiac care units." Hospital Pharmacy **47**(12): 927-932.

Bergkvist, A., et al. (2009). "Improved quality in the hospital discharge summary reduces medication errors - LIMM: Landskrona Integrated Medicines Management." European Journal of Clinical Pharmacology **65(**10): 1037-1046.

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Buckley MS, Harinstein LM, Clark KB, Smithburger PL, Eckhardt DJ, Alexander E, et al. Impact of a clinical pharmacy admission medication reconciliation program on medication errors in "high-risk" patients. The Annals of pharmacotherapy. 2013; 47(12):1599-610.

Chan, E. W., et al. (2010). "An intervention to encourage ambulance paramedics to bring patients' own medications to the ED: impact on medications brought in and prescribing errors." Emerg Med Australas **22**(2): 151-158.

Conklin, J. R., et al. (2014). "Care Transitions Service: A pharmacy-driven program for medication reconciliation through the continuum of care." American Journal of Health-System Pharmacy: 802-810.

Eggink, R. N., et al. (2010). "The effect of a clinical pharmacist discharge service on medication discrepancies in patients with heart failure." Pharmacy World & Science 32(6): 759-766.

Farley, T. M., et al. (2014). "Effect of clinical pharmacist intervention on medication discrepancies following hospital discharge." International Journal of Clinical Pharmacy 36(2): 430-437.

Fertleman, M., et al. (2005). "Improving medication management for patients: The effect of a pharmacist on post-admission ward rounds." Quality and Safety in Health Care 14(3): 207-211.

Grant, R. W., et al. (2003). "Improving Adherence and Reducing Medication Discrepancies in Patients with Diabetes." Ann Pharmacother **37**(7): 962-969.

Grimes, T. C., et al. (2014). "Collaborative pharmaceutical care in an Irish hospital: Uncontrolled before-after study." BMJ Quality and Safety 23(7): 574-583.

Hale, A. R., et al. (2013). "Perioperative medication management: expanding the role of the preadmission clinic pharmacist in a single center, randomised controlled trial of collaborative prescribing." BMJ Open **3**(7).

Hayes, B. D., et al. (2007). "Pharmacist-conducted medication reconciliation in an emergency department." American Journal of Health-System Pharmacy **64**(16): 1720-1723.

Hick, H. L., et al. (2001). "The impact of the pharmacist on an elective general surgery pre-admission clinic." Pharmacy World & Science **23**(2): 65-69.

Ho, P. M., et al. (2014). "Multifaceted intervention to improve medication adherence and secondary prevention measures after acute coronary syndrome hospital discharge: a randomized clinical trial." JAMA Intern Med **174**(2): 186-193.

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Nickerson, A., et al. (2005). "Drug-therapy problems, inconsistencies and omissions identified during a medication reconciliation and seamless care service." Health care Quarterly 8 Spec No: 65-72.

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Magalhães GF, Santos GB, Rosa MB, Noblat Ld A. Medication Reconciliation in Patients Hospitalized in a Cardiology Unit. PLoS ONE 2014; 9(12): e115491. doi: 10.1371/journal.pone.0115491.

Mortimer, C., et al. (2011). "The impact of an aged care pharmacist in a department of emergency medicine." J Eval Clin Pract **17**(3): 478-485.

Peyton, L., et al. (2010). "Evaluation of medication reconciliation in an ambulatory setting before and after pharmacist intervention." J Am Pharm Assoc (2003) **50**(4): 490-495.

Rahman, M. H., et al. (2005). "An evaluation of pharmacist-written hospital discharge prescriptions on general surgical wards." International Journal of Pharmacy Practice **13**(3): 179-185.

Tompson, A. J., et al. (2012). "Utilizing community pharmacy dispensing records to disclose errors in hospital admission drug charts." International Journal of Clinical Pharmacology & Therapeutics **50**(9): 639-646.

Van den Bemt, P. M., et al. (2009). "Medication reconciliation performed by pharmacy technicians at the time of preoperative screening." Ann Pharmacother 43(5): 868-874.

Van den Bemt, P. M., et al. (2013). "Effect of medication reconciliation on unintentional medication discrepancies in acute hospital admissions of elderly adults: a multicenter study." J Am Geriatr Soc 61(8): 1262-1268.

Vasileff, H. M., et al. (2009). "The effect on medication errors of pharmacists charting medication in an emergency department." Pharmacy World & Science 31(3): 373-379.

Leguelinel-Blache G, Arnaud F, Bouvet S, Dubois F, Castelli C,Roux-Marson C, Ray V, Sottoe A, Kinowski J. Impact of admission medication reconciliation performed by clinical pharmacists on medication safety. Eur J Intern Med 2014; 25(9):808-14.

Pharmacist is not the sole provider

Poole DL et al (2006). "Medication reconciliation: a necessity in promoting a safe hospital discharge." Journal for Health care Quality **28**(3):12-19.

Coffey M et al (2009). "Implementation of admission medication reconciliation at two academic Health Sciences centers: challenges and success factors." Health care Quarterly 12 Special Issue 2009

Dedhia, P., et al. (2009). "A quality improvement intervention to facilitate the transition of older adults from three hospitals back to their homes." Journal of the American Geriatrics Society **57**(9): 1540-1546.

Duggan, C., et al. (1998). "Reducing adverse prescribing discrepancies following hospital discharge." International Journal of Pharmacy Practice **6**(Jun): 77-82.

Henneman, E. A., et al. (2014). "An evaluation of a collaborative, safety focused, nurse-pharmacist intervention for improving the accuracy of the medication history." J Patient Saf **10** (2): 88-94.

Jack, B. W., et al. (2009). "A reengineered hospital discharge program to decrease rehospitalisation: a randomized trial." Annals of Internal Medicine **150**(3): 178-187.

Nassaralla, C. L., et al. (2007). "Implementation of a medication reconciliation process in an ambulatory internal medicine clinic." Qual Saf Health Care **16**(2): 90-94.

Setter, S. M., et al. (2009). "Effectiveness of a pharmacist-nurse intervention on resolving medication discrepancies for patients transitioning from hospital to home health care." American Journal of Health-System Pharmacy **66**(22): 2027-2031.

C. Online supplementary appendix C: Summary of risk of bias assessment*

Study reference	Randomization	Allocation concealment	Similarity of baseline characteristics	Similarity of baseline outcomes	Incomplete outcome data	Assessors blind to outcome	Absence of contamination	Selective outcome reporting	Free of other biases	Total†
Anderegg 2014	-	+	+	?	?	+	-	-	+	4
Bolas 2004	+	+	+	?	-	-	?	-	+	4
Eisenhower 2014	-	-	?	?	-	+	+	-	-	2
Farris 2014	+	+	+	?	+	+	-	+	+	7
Gardella 2012	-	-	?	?	?	+	+	+	-	3
Gillespie 2009	+	+	?	?	?	+	+	+	+	6
Hawes 2014	+	+	?	?	?	+	+	+	+	6
Hellstrom 2011	-	-	+	?	+	+	-	+	-	4
Hellstrom 2012	-	-	+	?	+	+	+	+	-	5
Koehler 2009	+	+	+	?	?	+	+	+	-	6
Pal 2013	-	-	+	?	+	+	-	+	-	4
Schnipper 2006	+	+	+	?	?	+	+	+	+	7
Scullin 2007	+	+	+	?	?	+	?	+	+	6
Stowasser 2002	+	?	+	+	+	+	+	-	+	8
Walker 2009	-	-	+	?	-	?	+	+	+	4
Warden 2014	-	-	+	?	?	+	+	+	+	5
Wilkinson 2011	-	-	?	?	?	-	?	+	-	1

Key: +, clear; -, not done;?, unclear.

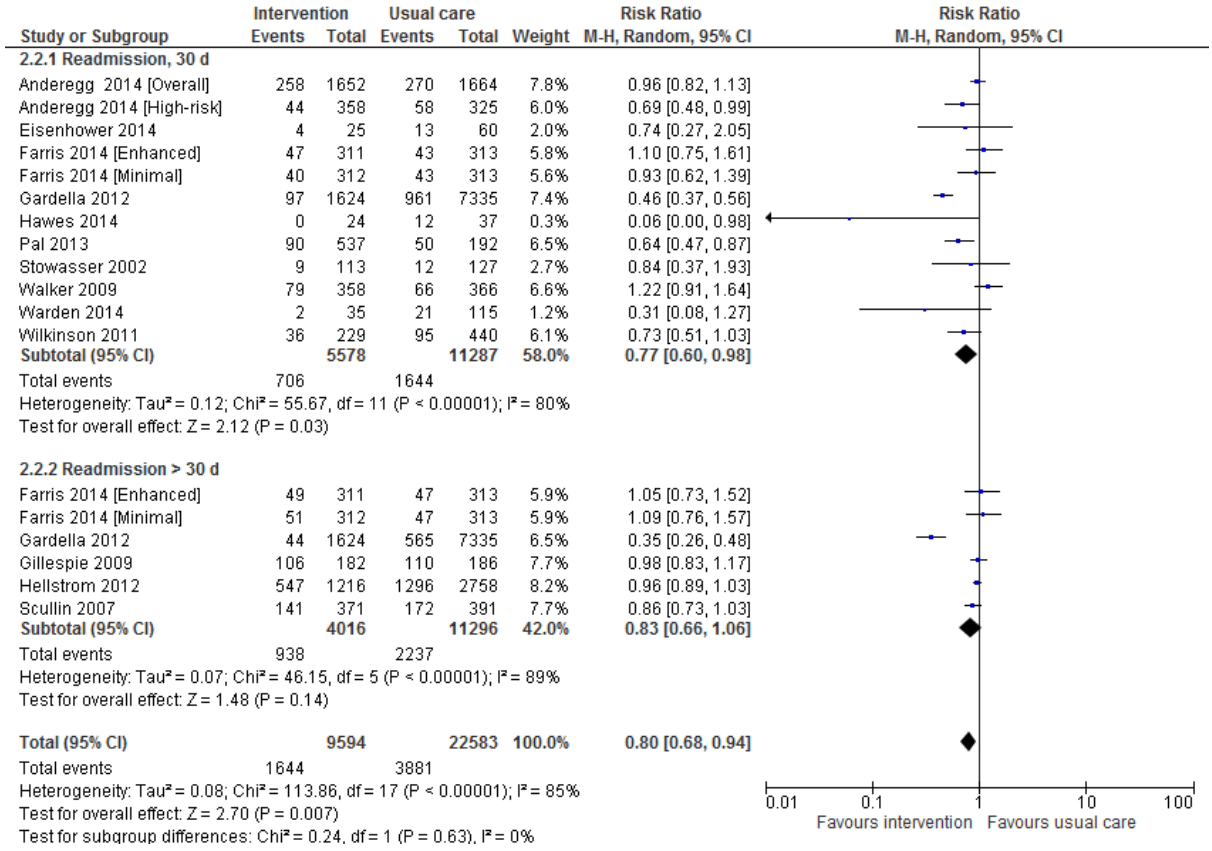
*EPOC risk of bias assessment; modified for non-controlled studies.

†Studies with a 'clear data' on each of the domains were given a score of 1.

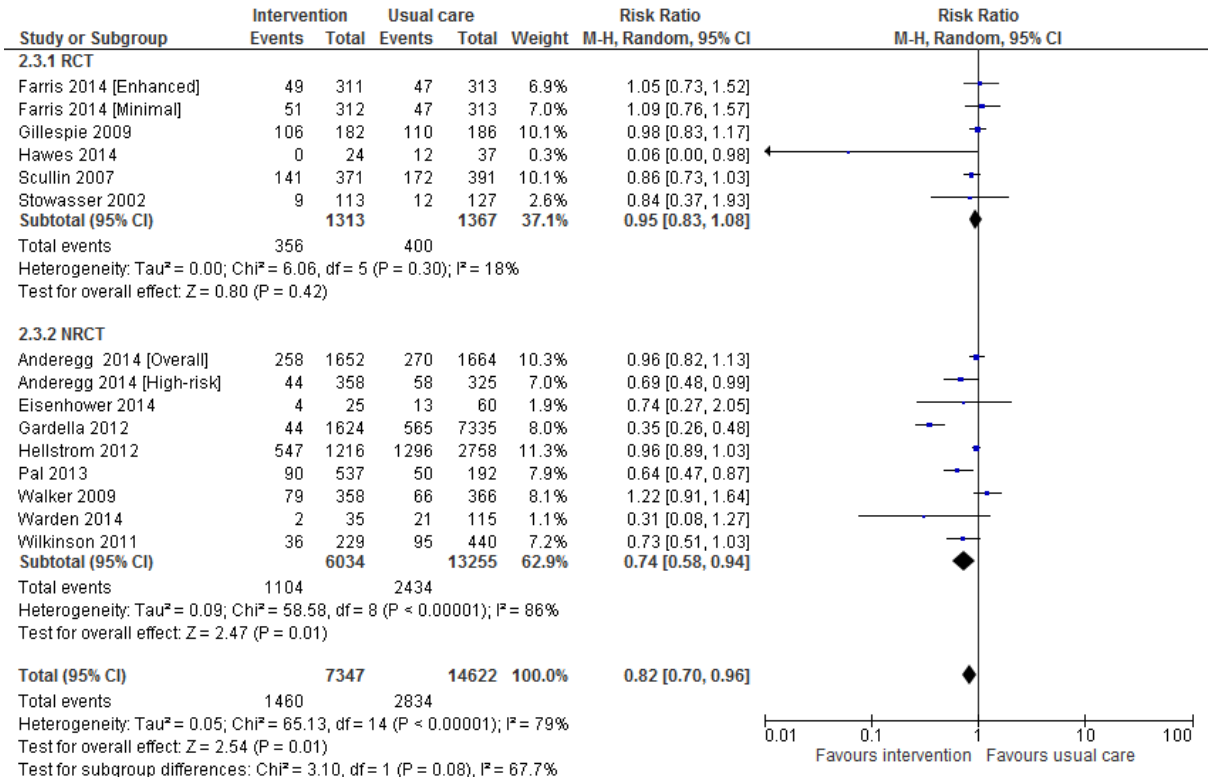
D. Online supplementary appendix D: Subgroup analysis

All-cause readmission

Subgroup analysis based on outcome timing

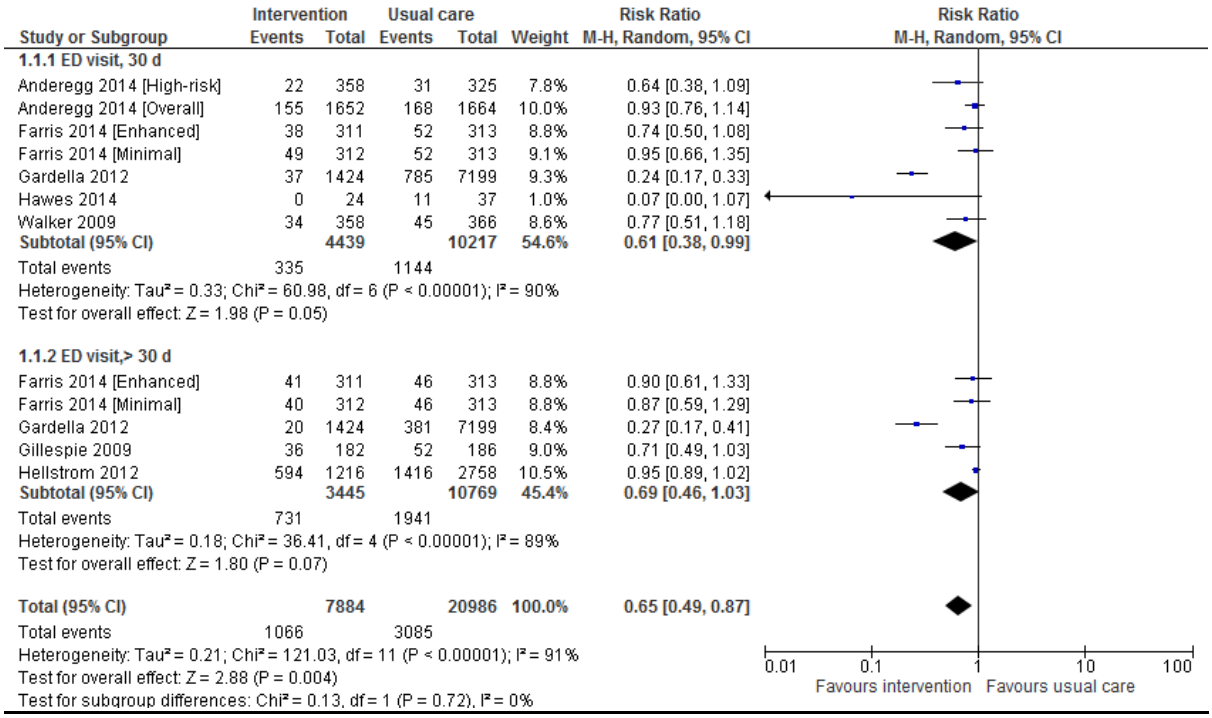


Subgroup analysis based on study design

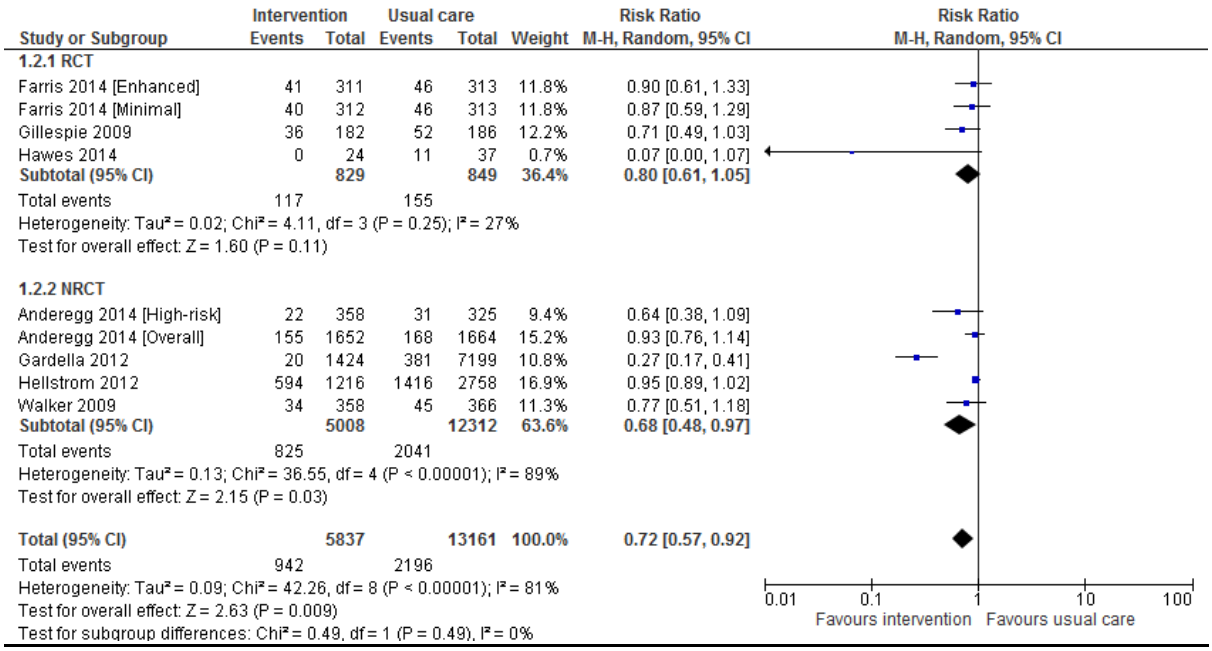


All-cause ED visits

Subgroup analysis based on outcome timing

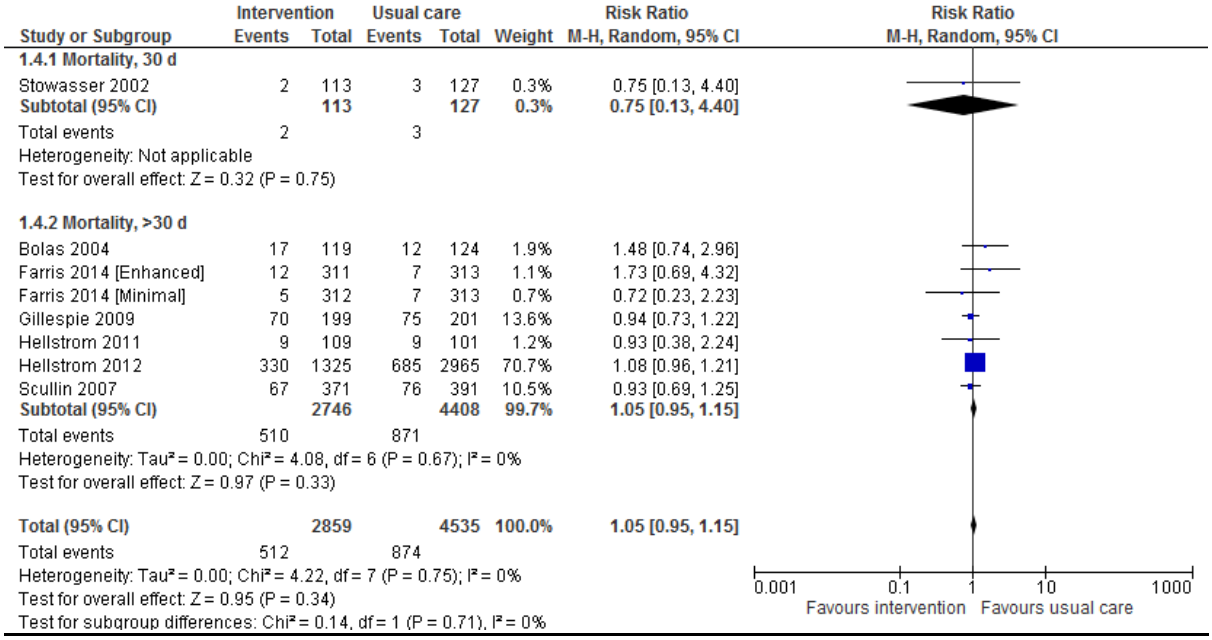


Subgroup analysis based on study design

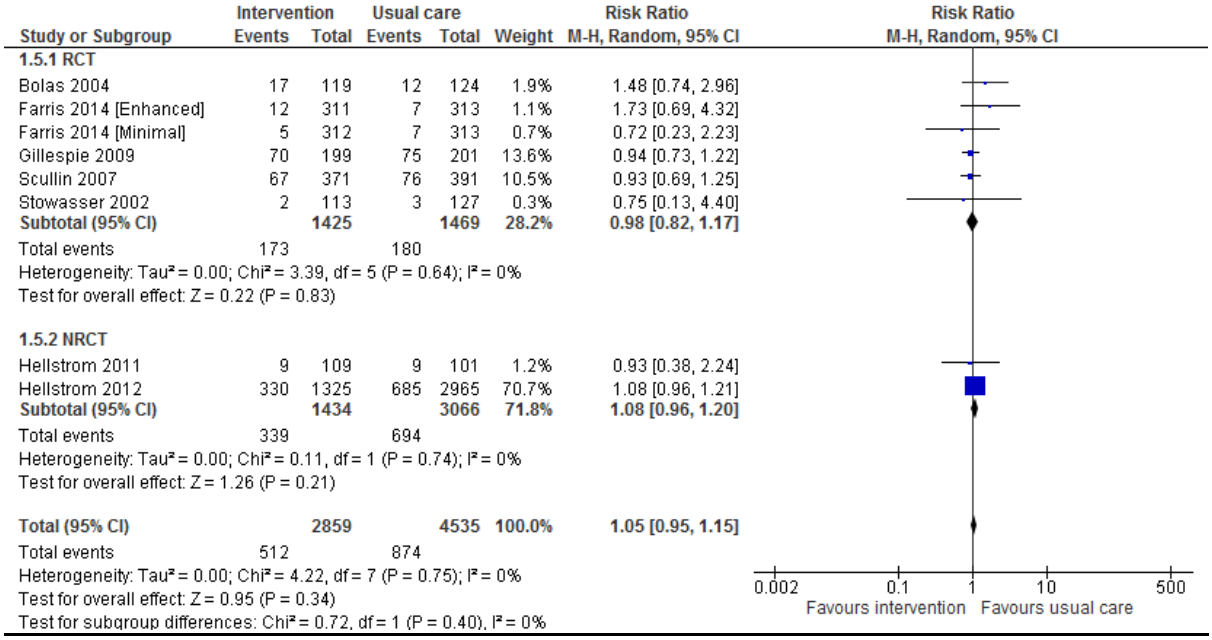


All-cause mortality

Subgroup analysis based on outcome timing

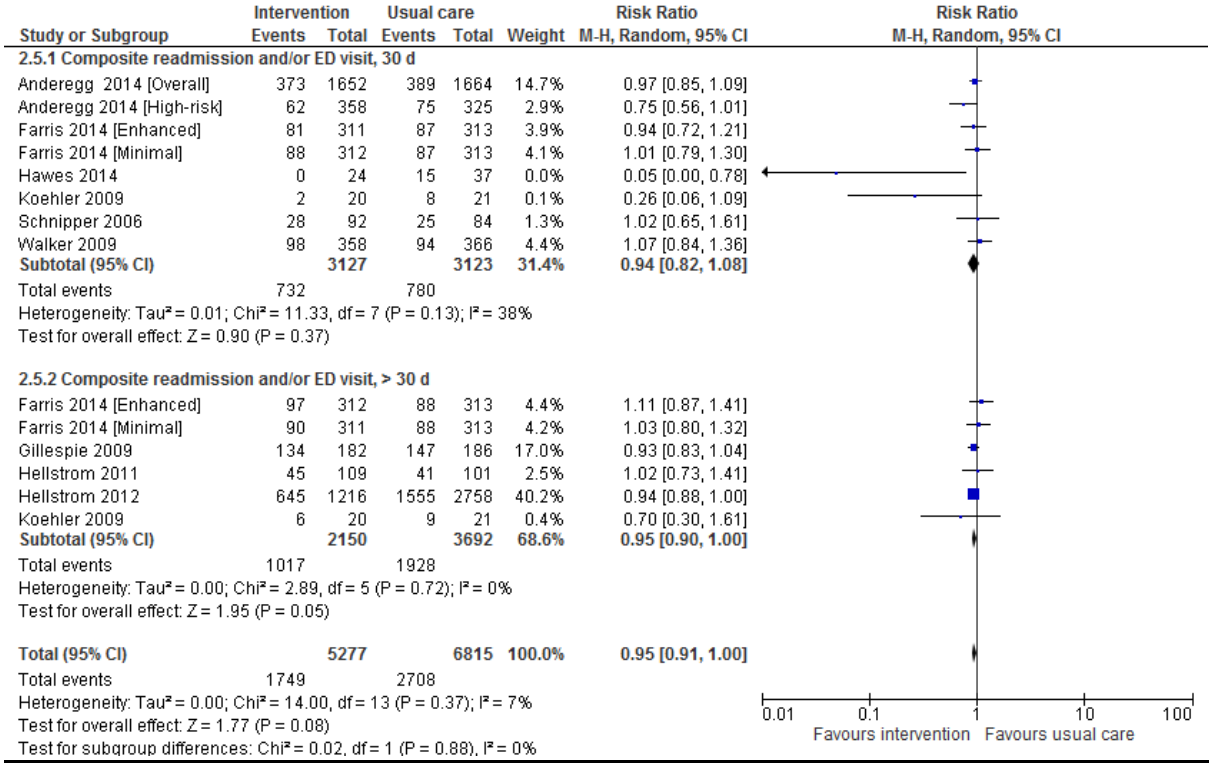


Subgroup analysis based on study design

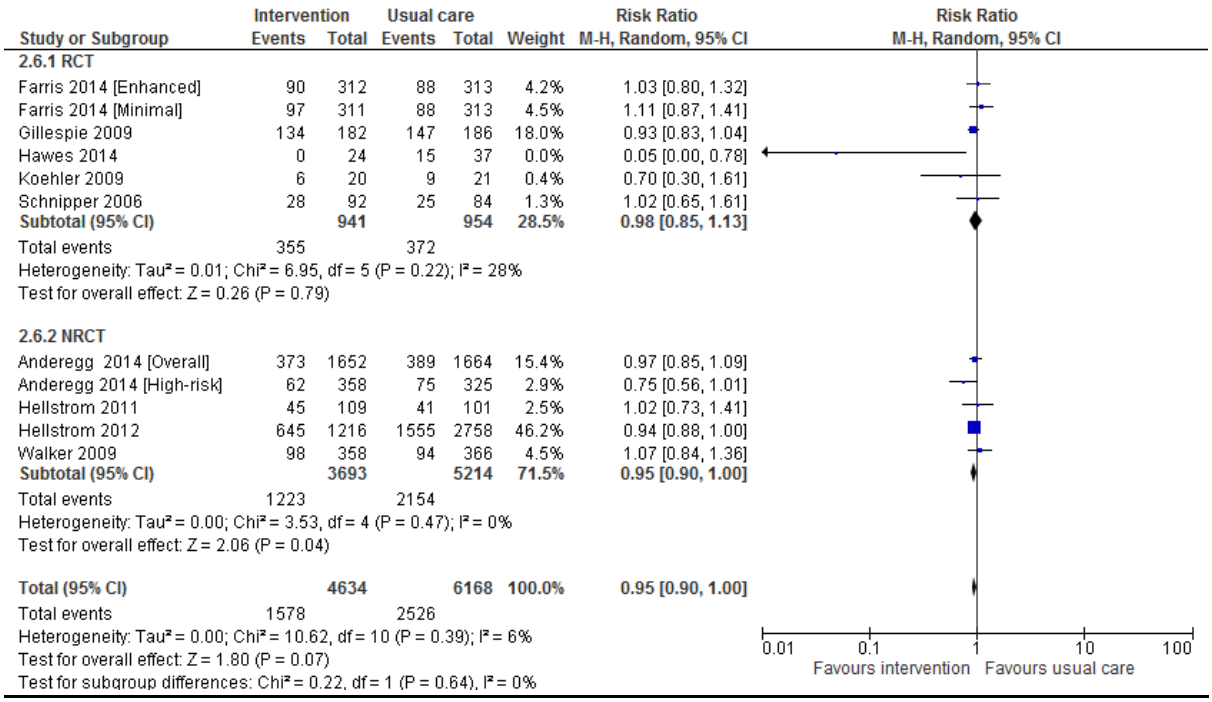


Composite readmission and/or ED visit

Subgroup analysis based on outcome timing

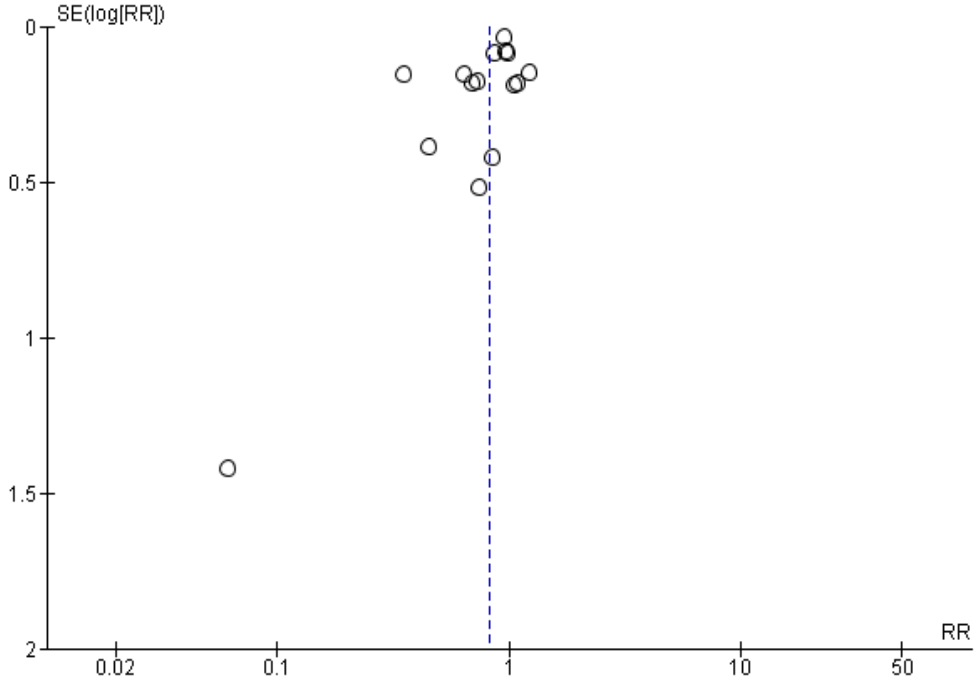


Subgroup analysis based on study design

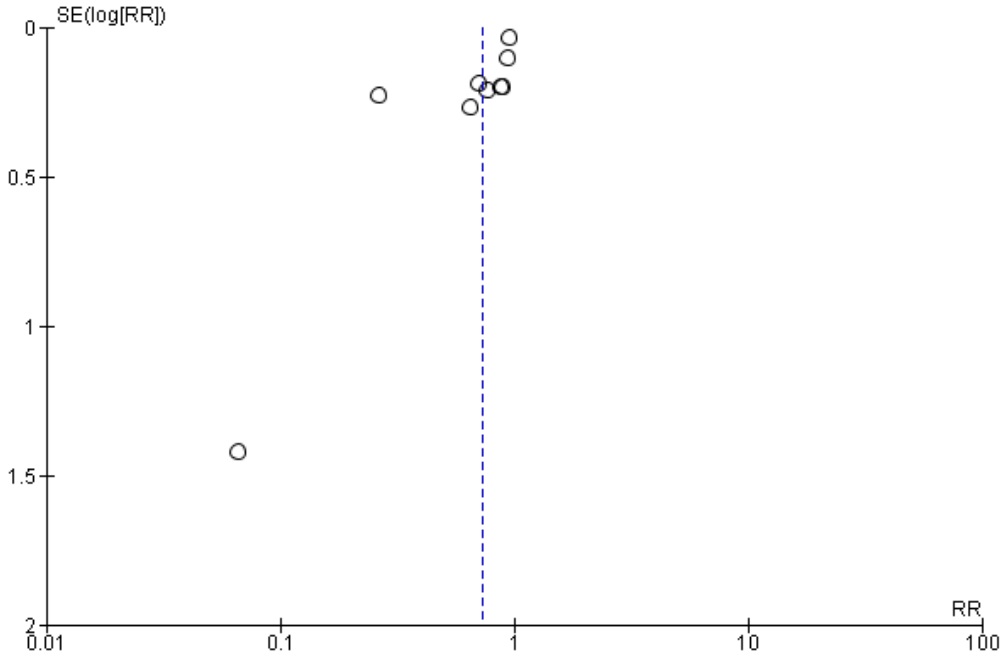


E. Online supplementary appendix E: Funnel plots

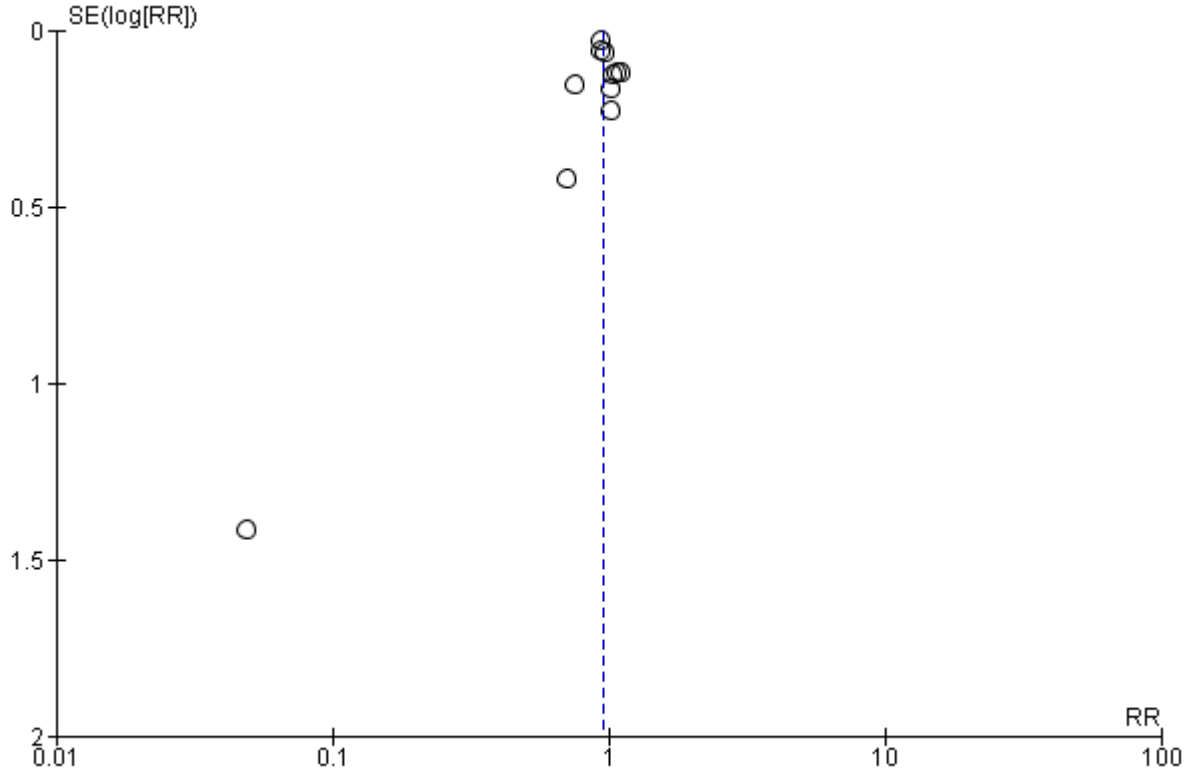
a. All-cause readmission Egger's test, p= 0.08; Begg's test, p=0.13



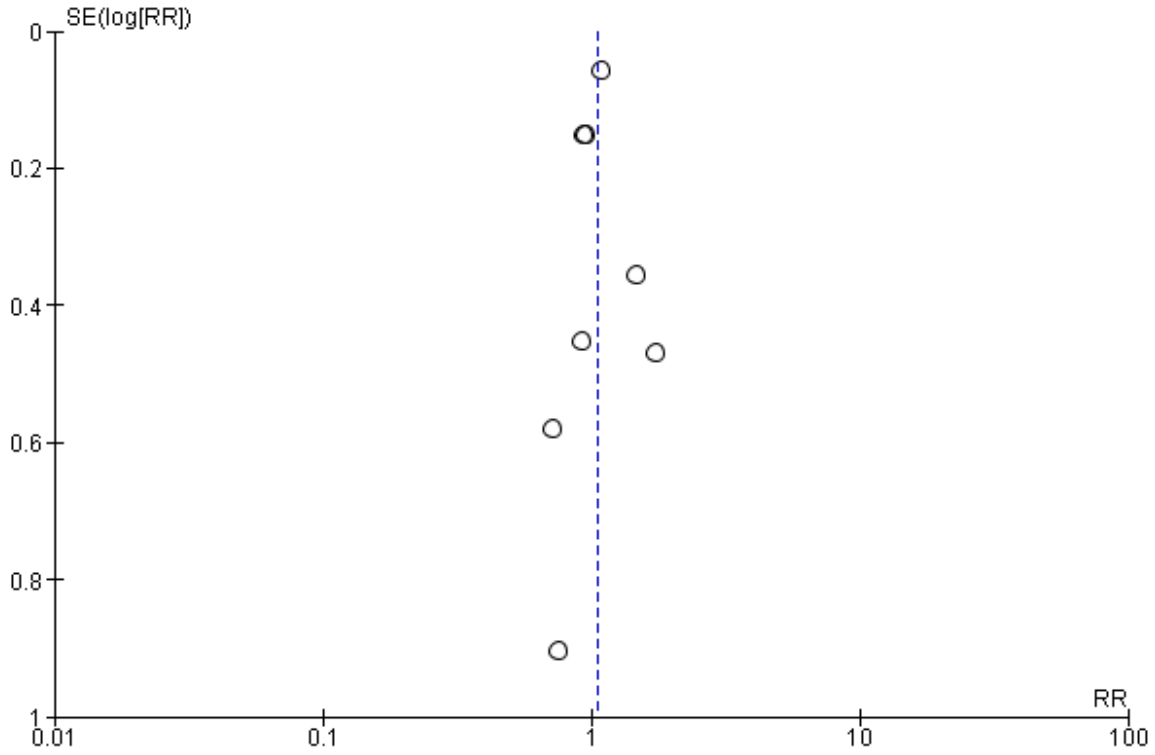
b. All-cause ED visit Egger's test, p= 0.04; Begg's test, p=0.01



c. Composite readmission and/or ED visit Egger's test, p= 0.57; Begg's test, p=0.35



d. All-cause mortality Egger's test p=0.83; Begg's test p=0.71



Funnel plots for the four outcomes for patients at hospital transitions. a) all-cause readmission b) all-cause ED visit c) composite readmission and/or ED visit d) all-cause mortality. The vertical line in the graphs corresponds to the pooled relative risk across studies.

A2.2 Electronic Supplementary Materials Published Online for Chapter 3

A. Appendix S1: Electronic database searches

- *The same search strategy used in A2.1 – A was employed for this systematic review*.

B. Appendix S2: List of excluded full-text papers and of the reasons for their exclusion

No/ineligible comparator

Boso ribelles et al (2011). "Evaluation of a plan for cardiology medication reconciliation on admission, and patient information at discharge, in a teaching hospital." EJHP Practice 17(1)

Anderegg, S. V., et al. (2013). "Acceptance of recommendations by inpatient pharmacy case managers: unintended consequences of hospitalist and specialist care." Pharmacotherapy: The Journal of Human Pharmacology & Drug Therapy **33**(1): 11-21.

Carter, M. K., et al. (2006). "Pharmacist-acquired medication histories in a university hospital emergency department." American Journal of Health-System Pharmacy **63**(24): 2500-2503.

Cornu, P., et al. (2012). "Effect of medication reconciliation at hospital admission on medication discrepancies during hospitalization and at discharge for geriatric patients." Annals of Pharmacotherapy **46**(4): 484-494.

Hellstrom, L. M., et al. (2012). "Errors in medication history at hospital admission: prevalence and predicting factors." BMC Clin Pharmacol **12**: 9.

Lessard, S., et al. (2006). "Medication discrepancies affecting senior patients at hospital admission." Am J Health Syst Pharm **63**(8): 740-743.

Midlov, P., et al. (2012). "The effect of medication reconciliation in elderly patients at hospital discharge." International Journal of Clinical Pharmacy **34**(1): 113-119.

Quennery, S., et al. (2011). "Added value of pharmacist-acquired drug histories in an orthopaedic ward." Acta Clinica Belgica **66**(3): 196-199.

Reeder, T. A. and A. Mutnick (2008). "Pharmacist- versus physician-obtained medication histories." American Journal of Health-System Pharmacy **65**(9): 857-860.

Not pharmacy-led medication reconciliation

Lalonde, L., et al. (2008). "Effectiveness of a medication discharge plan for transitions of care from hospital to outpatient settings." American Journal of Health-System Pharmacy **65**(15): 1451-1457.

Midlov, P., et al 2008. "Medication report reduces number of medication errors when elderly patients are discharged from hospital." Pharmacy World & Science 30(1): 92-98.

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Pharmacy is not the sole provider

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C. Appendix S3: Risk of bias assessment

RCT: EPOC summary of risk of bias assessment

Study reference	Randomization	Allocation concealment	Similarity of baseline characteristics	Similarity of baseline outcomes	Incomplete outcome data	Assessors blind to outcome	Absence of contamination	Selective outcome reporting	Free of other biases	Total
Becerra-Camargo 2013	+	+	+	+	+	+	+	+	+	9
Beckett 2012	+	?	+	?	+	-	-	+	+	5
Bolas 2004	+	+	+	?	-	-	-	-	+	4
Eggink 2010	+	-	+	?	+	?	?	+	+	5
Farley 2014	+	?	+	?	-	+	+	+	-	5
Hawes 2014	+	+	?	?	?	+	+	+	+	6
Kripalani 2012	+	+	?	+	+	+	+	+	-	7
Kwan 2007	+	+	+	?	+	+	+	+	-	7
Nickerson 2005	+	+	-	?	+	?	+	+	+	6
Schnipper 2006	+	+	+	?	+	+	+	+	+	8
Tompson 2012	+	-	+	?	+	-	+	+	+	6

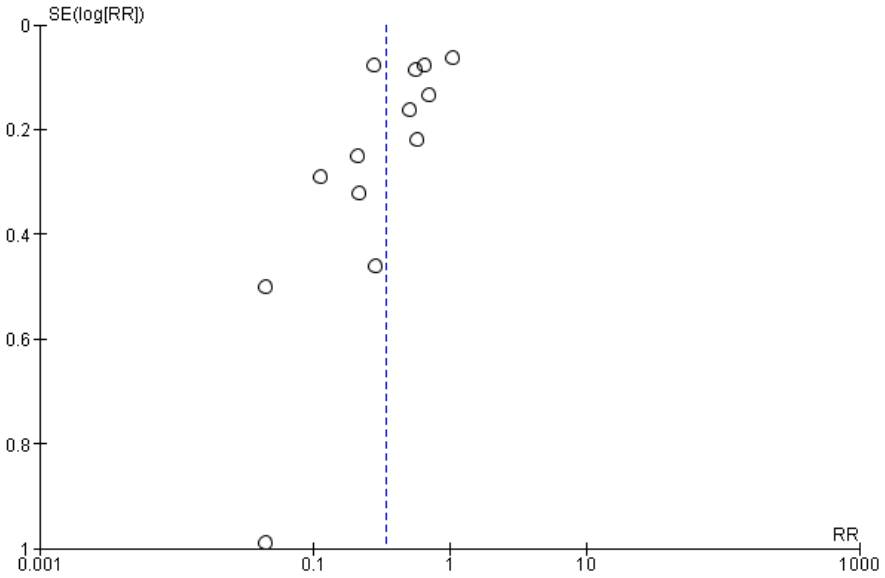
NRCT: A Cochrane Risk of Bias Assessment Tool: for Non-randomized studies of Interventions (ACROBAT-NRSI) summary of risk of bias assessment

References	Bias due to confounding	Bias in selection of participants into the study	Bias in measurement of interventions	Bias due to departures from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result	Overall bias
Bergkvist 2009	Moderate	Low	Low	Serious	Moderate	Low	Low	Moderate
Gardella 2012	Serious	No information	Serious	No information	No information	Critical	Moderate	Serious
Grimes 2014	Moderate	Low	Low	No information	Serious	Low	Low	Moderate
Leguelinel-Blache 2014	Serious	Moderate	Moderate	Serious	No information	Low	Low	Serious
Van den Bemt 2009	Moderate	Low	Low	Moderate	No information	Serious	Low	Moderate
Van den Bemt 2013	Moderate	Low	Low	Low	No information	Moderate	Low	Moderate
Vasileff 2009	Moderate	Low	Moderate	No information	No information	Serious	Low	Moderate
Walker 2009	Low	Low	Moderate	Low	Low	Low	Low	Low

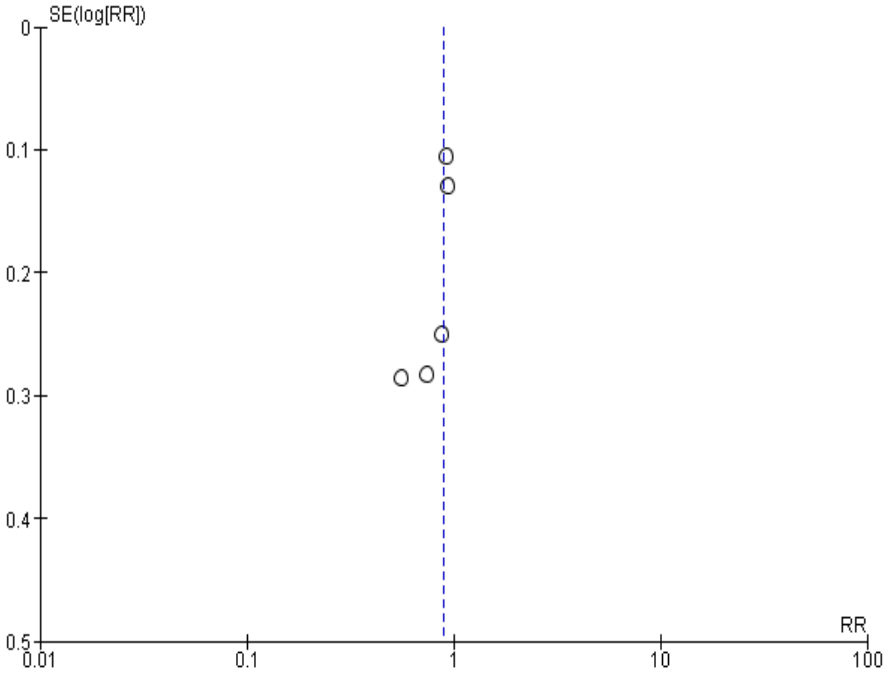
Note: risk of bias judgment was based on a scale of low, moderate , serious, critical and no information

D. Appendix S4: Publication bias assessment

a. Single transitions



b. Multiple transitions



Funnel plots for patients with medication discrepancies at hospital transitions. a) Single transition interventions b) multiple transitions interventions. The vertical line in the graphs corresponds to the pooled relative risk across studies.

A2.3 Electronic Supplementary Materials Published Online for Chapter 4

A. Additional file 1: Search strategy employed in the electronic databases search

MEDLINE

Database: Ovid MEDLINE(R) <1946 to November Week 3 2015>

1 Medication Errors/ or Medical History Taking/ or medication discrepancies.mp. or Medication Reconciliation/ (28739)

2 ((medic$ or drug$ or prescription$ or (medic$ adj2 chart$) or (medic$ adj2 record$)) adj2 review$).mp. (26100)

3 ((medic$ or drug$) adj2 histor$).mp. (67680)

4 (((medic$ adj2 chart$) or (medic$ adj2 record$)) adj2 assessment).mp. (87)

5 ((medic$ or drug$) adj2 list$).mp. (2789)

6 exp "Continuity of Patient Care"/ or electronic medication reconciliation.mp. (41625)

7 electronic health records.mp. or exp Medical Records Systems, Computerized/ or exp Electronic Health Records/ or exp Hospital Information Systems/ (46859)

8 patient admission.mp. or Patient Admission/ (20332)

9 patient discharge.mp. or Patient Discharge/ (22203)

10 inpatients.mp. or Inpatients/ (36275)

11 Patient Transfer/ or hospital transfer.mp. or Hospitalization/ (86171)

12 1 or 2 or 3 or 4 or 5 or 6 (253,018)

13 8 or 9 or 10 or 11 (152106)

14 7 and 12 and 13 (816)

15 limit 14 to (english language and humans) (688)

PubMed

(((((("medication errors"[MeSH Terms] OR ("medication"[All Fields] AND "errors"[All Fields]) OR "medication errors"[All Fields]) OR (("pharmaceutical preparations"[MeSH

Terms] OR ("pharmaceutical"[All Fields] AND "preparations"[All Fields]) OR "pharmaceutical preparations"[All Fields] OR "medication"[All Fields]) AND discrepancies[All Fields])) OR ("medication reconciliation"[MeSH Terms] OR ("medication"[All Fields] AND "reconciliation"[All Fields]) OR "medication reconciliation"[All Fields])) OR (("pharmaceutical preparations"[MeSH Terms] OR ("pharmaceutical"[All Fields] AND "preparations"[All Fields]) OR "pharmaceutical preparations"[All Fields] OR "medication"[All Fields]) AND ("safety"[MeSH Terms] OR "safety"[All Fields]))) OR ("patient safety"[MeSH Terms] OR ("patient"[All Fields] AND "safety"[All Fields]) OR "patient safety"[All Fields])) OR (("pharmaceutical preparations"[MeSH Terms] OR ("pharmaceutical"[All Fields] AND "preparations"[All Fields]) OR "pharmaceutical preparations"[All Fields] OR "medication"[All Fields]) AND ("history"[Subheading] OR "history"[All Fields] OR "history"[MeSH Terms]))) AND ((((("electronic health records"[MeSH Terms] OR ("electronic"[All Fields] AND "health"[All Fields] AND "records"[All Fields]) OR "electronic health records"[All Fields] OR ("electronic"[All Fields] AND "medical"[All Fields] AND "record"[All Fields]) OR "electronic medical record"[All Fields]) OR ("electronic health records"[MeSH Terms] OR ("electronic"[All Fields] AND "health"[All Fields] AND "records"[All Fields]) OR "electronic health records"[All Fields])) OR ("electronic prescribing"[MeSH Terms] OR ("electronic"[All Fields] AND "prescribing"[All Fields]) OR "electronic prescribing"[All Fields])) OR ("medication systems"[MeSH Terms] OR ("medication"[All Fields] AND "systems"[All Fields]) OR "medication systems"[All Fields]))) AND ((((("patient admission"[MeSH Terms] OR ("patient"[All Fields] AND "admission"[All Fields]) OR "patient admission"[All Fields]) OR ("patient discharge"[MeSH Terms] OR ("patient"[All Fields] AND "discharge"[All Fields]) OR "patient discharge"[All Fields])) OR ("patient transfer"[MeSH Terms] OR ("patient"[All Fields] AND "transfer"[All Fields]) OR "patient transfer"[All Fields])) OR

(("hospitals"[MeSH Terms] OR "hospitals"[All Fields] OR "hospital"[All Fields]) AND transition[All Fields])) AND (hasabstract[text] AND "humans"[MeSH Terms] AND English[lang]) [484]

EMBASE

Id.	Query	Results
#19.	(('medication errors'/exp OR 'medication errors') OR (medication AND discrepancies) OR 'medication reconciliation' OR (medication AND history) OR (adverse AND events) OR 'patient safety') AND ('electronic health records' OR 'electronic medical records' OR 'electronic prescribing' OR (medication AND record AND systems)) AND ('patient admission' OR 'patient discharge' OR 'patient transfer' OR (hospital AND transition)) AND [english]/lim AND [humans]/lim	65
#18.	(('medication errors'/exp OR 'medication errors') OR (medication AND discrepancies) OR 'medication reconciliation' OR (medication AND history) OR (adverse AND events) OR 'patient safety') AND ('electronic health records' OR 'electronic medical records' OR 'electronic prescribing' OR (medication AND record AND systems)) AND ('patient admission' OR 'patient discharge' OR 'patient transfer' OR (hospital AND transition))	76
#17.	'patient admission' OR 'patient discharge' OR	39,746

'patient transfer' OR (hospital AND transition)	
#16. 'electronic health records' OR 'electronic medical records' OR 'electronic prescribing' OR (medication AND record AND systems)	16,447
#15. ('medication errors'/exp OR 'medication errors') OR (medication AND discrepancies) OR 'medication reconciliation' OR (medication AND history) OR (adverse AND events) OR 'patient safety'	301,291
#14. hospital AND transition	36,177
#13. 'patient transfer'	953
#12. 'patient discharge'	1,682
#11. 'patient admission'	1,070
#10. medication AND record AND systems	2,806
#9. 'electronic prescribing'	1,915
#8. 'electronic medical records'	7,990
#7. 'electronic health records'	4,373
#6. 'patient safety'	80,714
#5. adverse AND events	192,591
#4. medication AND history	23,266
#3. 'medication reconciliation'	1,554
#2. medication AND discrepancies	1,206
#1. 'medication errors'/exp OR 'medication errors'	15,174

CINHAL

#	Searches	Results
S16	S12 AND S13 AND S14 Limiters-Peer Reviewed; English Language; Abstract Available	435

S15	S12 OR S13 OR S14	674
S14	S9 OR S10 OR S11	72,625
S13	S7 OR S8	61,923
S12	S1 OR S2 OR S3 OR S4 OR S5 OR S6	75,743
S11	(MH "Patient Admission") OR "patient admission" OR (MH "Readmission")	13,316
S10	(MH "Transfer, Discharge") OR "patient transfer"	3,522
S9	(MH "Inpatients") OR "hospital transition"	58,707
S8	(MH "Electronic Order Entry") OR "electronic prescribing"	1,750
S7	(MH "Computerized Patient Record") OR "electronic health records" OR (MH "Medical Records+")	60,556
S6	(MH "Patient Safety+") OR "patient safety"	60,966
S5	(MH "Adverse Health Care Event+") OR (MH "Adverse Drug Event+") OR "adverse event"	34,393
S4	(MH "Medication History") OR "medication history" OR (MH "Patient History Taking+")	12,227
S3	(MH "Medication Reconciliation") OR "medication reconciliation"	768
S2	"medication discrepancies"	55
S1	(MH "Medication Errors+") OR "medication errors" OR (MH "Treatment Errors+")	14,370

B. Additional file 2: The main reasons for exclusion of full-text articles

Excluded studies with reasons

Electronic prescribing tool on the impact of other medication errors

1. Abramson, E. L., et al. (2011). "Transitioning between electronic health records: Effects on ambulatory prescribing safety." Journal of General Internal Medicine 26(8): 868-874.
2. Abramson, E. L., et al. (2013). "A long-term follow-up evaluation of electronic health record prescribing safety." Journal of the American Medical Informatics Association 20(E1): e52-e58.
3. Agostini, J. V., et al. (2007). "Use of a computer-based reminder to improve sedative-hypnotic prescribing in older hospitalized patients." Journal of the American Geriatrics Society 55(1): 43-48.

4. Armada, E. R., et al. (2014). "Computerized physician order entry in the cardiac intensive care unit: Effects on prescription errors and workflow conditions." Journal of Critical Care 29(2): 188-193 186p.
5. Barron, W. M., et al. (2006). "Information technology. Implementing computerized provider order entry with an existing clinical information system." Joint Commission Journal on Quality & Patient Safety 32(9): 506-516 511p.
6. Callen, J., et al. (2010). "Accuracy of medication documentation in hospital discharge summaries: A retrospective analysis of medication transcription errors in manual and electronic discharge summaries." International Journal of Medical Informatics 79(1): 58-64.
7. Shawahna, R., et al. (2011). "Electronic prescribing reduces prescribing error in public hospitals." Journal of Clinical Nursing 20(21/22): 3233-3245 3213p.
8. Turchin, A., et al. (2011). "Unexpected effects of unintended consequences: EMR prescription discrepancies and hemorrhage in patients on warfarin." AMIA ... Annual Symposium Proceedings/AMIA Symposium 2011: 1412-1417.
9. Upperman, J. S., et al. (2005). "The impact of hospitalwide computerized physician order entry on medical errors in a pediatric hospital." J Pediatr Surg 40(1): 57-59.
10. Weant, K. A., et al. (2007). "Medication-error reporting and pharmacy resident experience during implementation of computerized prescriber order entry." Am J Health Syst Pharm 64(5): 526-530.

No control group

1. Agrawal, A., et al. (2007). "Evaluation of an electronic medication reconciliation system in inpatient setting in an acute care hospital." Studies in Health Technology & Informatics 129(Pt 2): 1027-1031.

2. Arora, V., et al. (2007). "Medication discrepancies in resident sign-outs and their potential to harm." Journal of General Internal Medicine 22(12): 1751-1755.
3. Lee, J. Y., et al. (2010). "Medication reconciliation during internal hospital transfer and impact of computerized prescriber order entry." Annals of Pharmacotherapy 44(12): 1887-1895.
4. Palchuk, M. B., et al. (2010). "An unintended consequence of electronic prescriptions: prevalence and impact of internal discrepancies." J Am Med Inform Assoc 17(4): 472-476.
5. Sinvani, L., et al. (2012). "Medication reconciliation in transition of care: Broken telephone or patient safety goal?" Journal of the American Geriatrics Society 60: S216.
6. Walke, L. M., et al. (2012). "Identification of medication discrepancies in discharge paperwork among patients in the co-operate geriatrics/surgery co management program." Journal of the American Geriatrics Society 60: S230.

Not electronic medication reconciliation

1. Bala, M., et al. (2011). "Medicines reconciliation on discharge: Implementation of a new model of working on the cardiology unit at the Leeds Teaching Hospitals NHS Trust." Clinical Pharmacist 3(4): S8.
2. Beckett, R. D., et al. (2012). "Effectiveness and feasibility of pharmacist-led admission medication reconciliation for geriatric patients." J Pharm Pract 25(2): 136-141.
3. Bergkvist, A., et al. (2009). "Improved quality in the hospital discharge summary reduces medication errors--LIMM: Landskrona Integrated Medicines Management." European Journal of Clinical Pharmacology 65(10): 1037-1046.

4. Becerra-Camargo, J., et al. (2013). "A multicentre, double-blind, randomised, controlled, parallel-group study of the effectiveness of a pharmacist-acquired medication history in an emergency department." BMC Health Serv Res 13: 337.
5. Grimes, T. C., et al. (2014). "Collaborative pharmaceutical care in an Irish hospital: uncontrolled before-after study." BMJ Qual Saf 23(7): 574-583.
6. Lee, Y. Y., et al. (2013). "Pharmacist-conducted medication reconciliation at hospital admission using information technology in Taiwan." Int J Med Inform 82(6): 522-527.
7. Lindquist, L. A., et al. (2013). "Primary care physician communication at hospital discharge reduces medication discrepancies." J Hosp Med 8(12): 672-677.
8. Lingaratnam, S., et al. (2013). "A controlled before and after study to evaluate a patient and health professional partnership model towards effective medication reconciliation." J Oncol Pharm Pract 19(1): 48-56.
9. Lu, Y., et al. (2013). "Quality improvement through implementation of discharge order reconciliation." Am J Health Syst Pharm 70(9): 815-820.
10. Schwarz, M. and R. Wyskiel (2006). "Medication reconciliation: developing and implementing a program." Critical Care Nursing Clinics of North America 18(4): 503-507.
11. Tompson, A. J., et al. (2012). "Utilizing community pharmacy dispensing records to disclose errors in hospital admission drug charts." International Journal of Clinical Pharmacology & Therapeutics 50(9): 639-646.
12. Andreoli, L., et al. (2014). "Medication reconciliation: a prospective study in an internal medicine unit." Drugs Aging 31(5): 387-393.
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Different outcome of interest

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2. Bourne, R. S. and C. L. Choo (2012). "Pharmacist proactive medication recommendations using electronic documentation in a UK general critical care unit." Int J Clin Pharm 34(2): 351-357.
3. Cooley, T. W., et al. (2012). "Implementation of computerized prescriber order entry in four academic medical centers." Am J Health Syst Pharm 69(24): 2166-2173.
4. Ghibelli, S., et al. (2013). "Prevention of Inappropriate Prescribing in Hospitalized Older Patients Using a Computerized Prescription Support System (INTERcheck)." Drugs & Aging 30(10): 821-828 828p.
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Review

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2. Motamedi, S. M., et al. (2011). "The efficacy of computer-enabled discharge communication interventions: a systematic review." BMJ Quality & Safety 20(5): 403-415
3. Niazkhani, Z., et al. (2009). "The impact of computerized provider order entry systems on inpatient clinical workflow: a literature review." Journal of the American Medical Informatics Association 16(4): 539-549 511p.
4. Reckmann, M. H., et al. (2009). "Does computerized provider order entry reduce prescribing errors for hospital inpatients? A systematic review." Journal of the American Medical Informatics Association 16(5): 613-623 611p

5. van Rosse, F., et al. (2009). "The effect of computerized physician order entry on medication prescription errors and clinical outcome in pediatric and intensive care: a systematic review." Pediatrics 123(4): 1184-1190 1187p.

Study protocol

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Not hospital-based

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A2.4 Electronic Supplementary Materials Published Online for Chapter 5

A. Appendix 1: Medline search strategy

1st concept - terms related to medication errors and adverse drug events
1. medication errors.mp.
2. exp Medication Errors/
3. exp Medication Systems, Hospital/
4. exp "Drug-Related Side Effects and Adverse Reactions"/
5. medication safety.mp.
6. prescribing errors.mp.
7. exp Pharmacy Service, Hospital/
8. exp Drug Prescriptions/
9. dispensing errors.mp.
10. transcribing errors.mp.
11. exp Nursing Staff, Hospital/ or administration errors.mp.
12. medication history.mp.
13. exp Medical History Taking/
14. medication errors.ti.
15. prescribing errors.ti.
16. dispensing errors.ti.
17. administration errors.ti.
18. adverse drug reactions.ti.
19. adverse drug events.ti.
2nd concept - terms describing hospital setting
20. exp Hospitals/
21. exp Hospitalization/
22. hospitalization.mp.
23. exp Patient Admission/
24. admission.mp.
25. exp Patient Discharge/
26. discharge.mp.

3rd concept - describing African regions
27. exp Africa, Western/
28. exp Africa, Northern/
29. exp South Africa/
30. exp Africa, Southern/
31. exp Africa, Eastern/
32. exp Africa, Central/
33. exp "Africa South of the Sahara"/
34. Africa.mp.

The search terms used in each key concept were combined using the OR Boolean operator, and then all the 3 key concepts were connected using the 'AND' operator. Broadly, this searching strategy was similar between databases.

B. S2 Appendix: Excluded articles with reasons

ADE/ADRs reports from single disease/agents

1. Abah IO, Akanbi M, Abah ME, Finangwai AI, Dady CW, Falang KD, et al. Incidence and predictors of adverse drug events in an African cohort of HIV-infected adults treated with efavirenz. Germs. 2015; 5(3):83-91.
2. Abdissa SG, Fekade D, Feleke Y, Seboxa T, Diro E. Adverse drug reactions associated with antiretroviral treatment among adult Ethiopian patients in a tertiary hospital. Ethiop Med J. 2012; 50(2):107–13.
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H1N1 Mass immunization in Ghana: a prospective study. Drug Saf. 2013; 36(4):259–66.

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8. Bwire R, Kawuma HJ. Hospital-based epidemiological study of reactions, Buluba Hospital, 1985-89. Leprosy Review. 1993;64(4):325-9.
9. Elkhabbazi H, Benkirane R, Khadmaoui A, Sefiani H, Quyou A, Hami H, et al. Cutaneous adverse drug reactions in Morocco: A prospective study. Drug Saf. 2014; 37 (10):888.
10. Kajungu DK, Erhart A, Talisuna AO, Bassat Q, Karema C, Nabasumba C, et al. Paediatric pharmacovigilance: use of pharmacovigilance data mining algorithms for signal detection in a safety dataset of a paediatric clinical study conducted in seven African countries. PloS one. 2014;9(5):e96388.
11. Khaled A, Kharfi M, Ben Hamida M, El Fekih N, El Aidli S, Zeglaoui F, et al. Cutaneous adverse drug reactions in children. A series of 90 cases. La Tunisie medicale. 2012; 90(1):45-50.
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13. Korhonen C, Peterson K, Bruder C, Jung P. Self-reported adverse events associated with antimalarial chemoprophylaxis in peace corps volunteers. American Journal of Preventive Medicine. 2007; 33(3):194-9.
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16. Luyckx VA, Steenkamp V, Rubel JR, Stewart MJ. Adverse effects associated with the use of South African traditional folk remedies. Cent Afr J Med. 2004; 50(5–6):46–51.
17. Masenyetse LJ, Manda SO, Mwambi HG. An assessment of adverse drug reactions among HIV positive patients receiving antiretroviral treatment in South Africa. AIDS Research and Therapy. 2015;12:6.
18. Namme Luma H, Doualla MS, Choukem SP, Temfack E, Ashuntantang G, Achu Joko H, et al. Adverse drug reactions of Highly Active Antiretroviral Therapy (HAART) in HIV infected patients at the General Hospital, Douala, Cameroon: a cross sectional study. Pan Afr Med J. 2012; 12:87.
19. Njuguna C, Stewart A, Mouton JP, Blockman M, Maartens G, Swart A, et al. Adverse Drug Reactions Reported to a National HIV & Tuberculosis Health Care Worker Hotline in South Africa: Description and Prospective Follow-Up of Reports. Drug safety. 2016; 39(2):159-169.
20. Paul IM, Reynolds KM, Kauffman RE, Banner W, Bond GR, Palmer RB, et al. Adverse events associated with pediatric exposures to dextromethorphan. Clinical toxicology (Philadelphia, Pa). 2017; 55(1):25-32.

21. Peter JG, Lehloenya R, Dlamini S, Risma K, White KD, Konvinse KC, et al. Severe delayed cutaneous and systemic reactions to drugs: A global perspective on the science and art of current practice. J Allergy Clin Immunol Pract. 2017; 5(3):547-63.
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23. Salami TA, Asalu AF, Samuel SO. Prevalence of cutaneous drug eruptions in adult Nigerians with HIV/AIDS. Nigerian Postgraduate Medical Journal. 2010; 17(2):160-3.
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Studies assessing ADR reporting (KAP studies)

1. Alraie NA, Saad AA, Sabry NA, Farid SF. Adverse drug reactions reporting: a questionnaire-based study on Egyptian pharmacists' attitudes following an awareness workshop. J Eval Clin Pract. 2016;22(3):349-55.

2. Bello SO, Umar MT. Knowledge and attitudes of physicians relating to reporting of adverse drug reactions in Sokoto, north-western Nigeria. Ann Afr Med. 2011;10(1):13-8.
3. Cliff-Eribo KO, Choonara I, Dodoo A, Darko DM, Sammons H. Adverse drug reactions in Ghanaian children: review of reports from 2000 to 2012 in VigiBase. Expert opinion on drug safety. 2015;14(12):1827-33.
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6. Gurmesa LT, Dedefo MG. Factors affecting adverse drug reaction reporting of healthcare professionals and their knowledge, attitude, and practice towards ADR reporting in Nekemte town, West Ethiopia. Biomed Res Int. 2016;2016:5728462.
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8. Katusiime B, Semakula D, Lubinga SJ. Adverse drug reaction reporting among health care workers at Mulago National Referral and Teaching hospital in Uganda. Afr Health Sci. 2015;15(4):1308-17.
9. Khoza S, Madungwe I, Nyambayo P, Mthethwa J, Chikuni O. Adverse drug reactions reporting at a referral hospital in Zimbabwe. Cent Afr J Med. 2004;50(11–12):104–7.

10. Kiguba R, Karamagi C, Waako P, Ndagije HB, Bird SM. Recognition and reporting of suspected adverse drug reactions by surveyed health care professionals in Uganda: key determinants. BMJ Open. 2014; 4(11). e005869.
11. Kiguba R, Karamagi C, Waako P, Ndagije HB, Bird SM. Rare, serious and comprehensively described suspected adverse drug reactions reported by surveyed health care professionals in Uganda. Ann Glob Health. 2015; 81(1): 77.
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15. Okezie EO, Fawole OI. Adverse drug reactions reporting by physicians in Ibadan, Nigeria. Pharmacoepidemiology Drug Saf. 2008;17(5):517–22.
16. Okonkwo PO, Egere JU, Ogbuokiri JE. Adverse drug reactions in a developing country: problems encountered in a surveillance programme in a Nigerian hospital. Cent Afr J Med. 1980;26(11):239–42.
17. Ruud KW, Srinivas SC, Toverud E-L. Addressing gaps in pharmacovigilance practices in the antiretroviral therapy program in the Eastern Cape Province, South Africa. Res Social Adm Pharm. 2010;6(4):345–53.

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Non-relevant outcome

1. Anyika EN, Alade TB. Evaluation of pharmacists' participation in post-admission ward rounds in a tertiary hospital in South-West Nigeria. Nig Q J Hosp Med. 2009;19(3):151–4.
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3. King RC, Fomundam HN. Remodeling pharmaceutical care in Sub-Saharan Africa (SSA) amidst human resources challenges and the HIV/AIDS pandemic. Int J Health Plann Manage. 2010;25(1):30–48.
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9. Sabry NA, Farid SF. The role of clinical pharmacists as perceived by Egyptian physicians. The International journal of pharmacy practice. 2014;22(5):354-9.
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14. Thinyane KH, Cooper VLJ. Causes of hospital admission among patients receiving highly active antiretroviral therapy. Res J Med Sci. 2013;7(5):130–3.
15. Yusuff K, Awotunde M. The frequency of drug history documentation in an institutionalized tertiary care setting in Nigeria. Journal of Pharmacy & Pharmaceutical Sciences. 2005;8(2):141-6.

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Non-English

1. Amor M, Bensghir M, Belkhadir Z, Ghannam A, Azendour H, Drissi Kamili N, et al. [Medication errors in anesthesia: a Moroccan university hospitals survey]. Annales francaises d'anesthesie et de reanimation. 2012;31(11):863-9.
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Non-African setup

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Review

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C. S3 Appendix: Methodological quality assessment

1. Methodological quality assessment for ADE studies

	Aderemi-Williams 2015 [30]	Benkirane 2009 [31]	Benkirane 2009 [78]	Cooke 1985 [32]	Dedefo 2016 [79]	Eshetie 2015 [33]	Jennane 2011 [80]	Kiguba 2017 [34]	Letaief 2010 [35]	Mabadeje 1979 [35]
Study design										
Was the study design clear (prospective, retrospective, combined)?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Methods for identifying ADEs										
Were the methods used to identify ADEs described in sufficient detail?	N	Y	Y	N	Y	Y	Y	Y	N	Y
Were data collection methods (case-record review, medication chart review and laboratory data) clearly described?	Y	Y	Y	NR	Y	Y	Y	Y	Y	Y
Were the individuals (physicians, pharmacists, nurses) who identifies ADEs clearly described?	N	Y	Y	NR	N	Y	Y	Y	Y	N
Methods for determining the causality										
Was the process of establishing the casual relationship described in detail?	N	Y	N	Unclear	N	Y	N	Y	Y	NR
Were standard methods (validated tool) used in the assessment?	N	N	Y	Y	N	Y	N	Y	Y	NR
Methods for determining preventability										
Was the assessment process of establishing preventability described in detail?	NR	N	N	NR	Y	Y	N	Y	N	NR
Were standard methods (validated tool) used in the assessment?		Y	N	NR	Y	Y	N	Y	Y	NR
Methods for determining severity										
Was the assessment process of establishing predictability described in detail?	NR	N	Y	NR	Y	Y	Y	Y	N	NR
Were standard methods (validated tool) used in the assessment?	NR	Y	Y	NR	Y	Y	Y	Y	Y	NR
Total	2	7	7	2	7	10	6	10	7	3

Abbreviation: Y, yes; N, no; NR, not reported

Methodological quality assessment for ADE studies (Cont'd)

	Matsaseng et al 2005 [37]	Mehta 2008 [38]	Mouton 2015 [39]	Mouton 2016 [40]	Oshikoya 2011 [42]	Tipping 2006 [43]	Tumwikirize 2011 [44]	Oshikoya 2007 [41]
Study design								
Was the study design clear (prospective, retrospective, combined)?	Y	Y	Y	Y	Y	Y	Y	Y
Methods for identifying ADEs								
Were the methods used to identify ADEs described in sufficient detail?	N	N	Y	Y	Y	N	Y	Y
Were data collection methods (case-record review, medication chart review and laboratory data) clearly described?	Y	Y	Y	Y	Y	N	Y	Y
Were the individuals (physicians, pharmacists, nurses) who identifies ADEs clearly described?	Y	Y	Y	Y	Y	Y	Y	Y
Methods for determining the causality								
Was the process of establishing the casual relationship described in detail?	Y	Y	Y	Y	Y	N	N	Y
Were standard methods (validated tool) used in the assessment?	Y	Y	Y	Y	Y	Y	Y	Y
Methods for determining preventability								
Was the assessment process of establishing preventability described in detail?	NR	Y	Y	Y	Y	NR	N	N
Were standard methods (validated tool) used in the assessment?	Y	Y	Y	Y	Y	NR	Y	N
Methods for determining severity								
Was the assessment process of establishing predictability described in detail?	NR	Y	N	Y	Y	NR	N	NR
Were standard methods (validated tool) used in the assessment?	Y	Y	N	Y	Y	NR	Y	NR
total	7	9	8	10	10	3	7	6

Abbreviation: Y, yes; N, no; NR, not reported

2. Methodological quality assessment: MEs

	Agalu 2011 [45]	Agalu 2012 [58]	Ajemigbitse 2016 [49]	Ajemigbitse 2013 [46]	Ajemigbitse 2013 [47]	Ajemigbitse 2014 [48]	Alagha 2011 [50]	Arulogun 2011 [51]	Oshikoya 2007 [52]	Sada 2015 [53]	Yinusa 2004 [54]
Aims/objectives of the study clearly stated.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Definition of what constitutes a medication error.	Y	N	N	Y	N	Y	Y	Y	Unclear	Y	N
Error categories specified.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Error categories defined.	Y	N	N	Y	N	Y	Y	N	N	Y	N
Presence of a clearly defined denominator.	Y	Y	Y	Y	N	N	Y	Y	Unclear	N	Unclear
Data collection method described clearly.	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	N
Setting in which study conducted described.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Sampling and calculation of sample size described.	N	N	N	Y	N	N	N	Y	N	Y	N
Reliability measures	N	N	N	N	N	N	N	N	N	N	N
Measures in place to ensure that results are valid.	N	N	Y	N	N	N	N	N	N	N	N
Limitations of study listed.	Y	Y	Y	Y	Y	N	Y	N	N	Y	N
Mention of any assumptions made.	N	N	N	N	N	N	N	N	N	N	N
Ethical approval.	Y	Y	Y	Y	Y	Y	N	N	N	Y	N
Total	9	7	7	10	6	7	8	7	4	9	3

Abbreviation: Y, yes; N, no;

Methodological quality assessment: MEs (Cont'd)

	Yousif 2011 [55]	Zeleke 2014 [56]	Amucheazi 2009 [61]	Gordon 2004 [63]	Gordon 2006 [64]	Feleke 2010 [65]	Feleke 2015 [66]	Labuschagne 2011 [67]	Llewellyn 2009 [68]	Agu 2014 [71]	al Tehewy 2016 [59]
Aims/objectives of the study clearly stated.	Y	Y	N	Y	Y	Y	N	Y	Y	Y	Y
Definition of what constitutes a medication error.	N	Y	N	N	N	Y	Y	N	Y	Y	Y
Error categories specified.	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y
Error categories defined.	N	Y	N	N	N	Y	Y	N	N	N	N
Presence of a clearly defined denominator.	Y	N	Y	Unclear	Unclear	Y	N	Unclear	Y	Y	Y
Data collection method described clearly.	Y	Y	N	N	N	Y	N	Y	Y	Y	Y
Setting in which study conducted described.	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y
Sampling and calculation of sample size described.	N	N	N	N	N	N	Y	N	N	N	N
Reliability measures	N	N	N	N	N	N	Y	N	N	N	Y
Measures in place to ensure that results are valid.	N	N	N	N	N	N	N	N	N	Y	N
Limitations of study listed.	N	Y	N	N	Y	N	Y	N	N	Y	N
Mention of any assumptions made.	N	N	N	N	N	N	N	N	N	N	N
Ethical approval.	N	Y	N	N	Y	N	Y	Y	Y	Y	Y
Total	5	8	2	3	5	7	8	5	7	8	8

Abbreviation: Y, yes; N, no

Methodological quality assessment: MEs (Cont'd)

	Benkirane 2009 [78]	Dedefo 2016 [79]	Negash 2013 [72]	Jennane 2011 [80]	Kandil 2012 [73]	Sabry 2014 [75]	Sabry 2009 [76]	Nwasor 2014 [69]	Oshikoya 2013 [70]	Shehata 2016 [77]
Aims/objectives of the study clearly stated.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Definition of what constitutes a medication error.	Y	Y	Y	Y	N	N	N	N	Y	N
Error categories specified.	N	Y	N	N	N	N	N	Y	Y	Y
Error categories defined.	N	Y	Y	N	Y	Y	N	N	N	N
Presence of a clearly defined denominator.	Y	Y	Unclear	Y	N	Y	N	Unclear	N	Y
Data collection method described clearly.	Y	Y	N	Y	N	Y	N	N	Y	Y
Setting in which study conducted described.	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Sampling and calculation of sample size described.	N	N	N	N	N	N	N	N	N	N
Reliability measures	Y	Y	N	Y	N	N	N	N	N	N
Measures in place to ensure that results are valid.	Y	N	N	N	N	N	Y	N	Y	N
Limitations of study listed.	Y	Y	N	N	N	Y	Y	N	Y	Y
Mention of any assumptions made.	N	N	N	N	N	N	N	N	N	N
Ethical approval.	N	Y	Y	Y	N	Y	N	N	Y	Y
Total	8	7	5	7	3	7	4	3	8	7

Abbreviation: Y, yes; N, no

Methodological quality assessment: MEs (Cont'd)

	Acheampong 2016 [57]	Amponsah 2016 [60]	Blignaut 2017 [62]	Ogunleye 2016 [74]	
Aims/objectives of the study clearly stated.	Y	N	Y	Y	
Definition of what constitutes a medication error.	Y	N	N	Y	
Error categories specified.	Y	N	Y	Y	
Error categories defined.	Y	N	N	N	
Presence of a clearly defined denominator.	Y	N	N	Y	
Data collection method described clearly.	Y	Y	Y	Y	
Setting in which study conducted described.	Y	N	Y	Y	
Sampling and calculation of sample size described.	N	N	Unclear	N	
Reliability measures	Y	N	Y	N	
Measures in place to ensure that results are valid.	Y	N	Y	N	
Limitations of study listed.	Y	N	Y	N	
Mention of any assumptions made.	Y	N	N	N	
Ethical approval.	Y	Y	Y	Y	
Total	12	2	8	7	

Abbreviation: Y, yes; N, no

D. S4 Appendix: Definition and assessment of ADEs and MEs

1. Definition and assessment of ADEs

Author, year	Definition and/or description of the incident	A person/ team responsible for identification	Further verification of ADEs	Person responsible for causality, severity and preventability assessment
Adverse drug events				
Aderemi-Williams 2015 [30]	NR	NR	NR	NR
Benkirane 2009 [31]	An injury resulting from medical interventions related to a drug (WHO definition)[26]	Medical residents	NR	Causality, 2 experienced investigators Severity, NR Preventability, NR
Benkirane 2009 [78]	Bates et al 1995 [25] ADE definition (ADRs and complications from MEs)	Pharmacists investigators		Two reviewers of the pharmacovigilance centre staffs evaluated causality and severity Preventability: NR
Cooke 1985 [32]	Any undesired or unintended effect of drugs	NR	NR	NR
Eshetie 2015 [33]	Any incident resulting in injury from any stage of the medication use process (ordering, transcribing, dispensing, administrating and monitoring)	Multidisciplinary	Pediatrics team	Causality: clinical pharmacist Severity and preventability: two senior pediatric residents
Dedefo 2016 [79]	An ADE refers to all ADRs, including allergic or idiosyncratic reactions, as well as MEs that result in harm to a patient	Pharmacist researcher	NR	Severity and preventability: one pediatrician and one clinical pharmacist
Jennane 2011 [80]	Any injury resulting from medical interventions related to a drug	A pharmacist and a physician	NR	Causality, NR Severity: Physician reviewers rated the severity of ADEs

				Preventability, NR
Kiguba 2017 [34]	WHO definition of ADR [85]	A medical doctor, pharmacist and degree nurse	Study physicians (gynecologist/obstetrician, internist) and research pharmacist (senior clinical pharmacist)	Consensus agreement on ADR causality, prevent- ability, severity and seriousness was reached in a commit- tee headed by the ward-based study physician and senior clinical pharmacist
Letaief 2010 [35]	Injury related to medical management in contrast to complications of the disease	Medical student	2 expert physicians	NR
Mabadeje 1979 [36]	NR	NR	NR	NR
Matsaseng 2005 [37]	An injury that was caused by medical management (rather than the underlying disease)	Researcher	Supervising specialist	NR
Mehta 2008 [38]	WHO definition of ADR [89]	Clinical pharmacology team	Clinical pharmacist, 4 clinical pharmacology registrars and a hospital pharmacist	2 clinical pharmacology consultants assess cases for causality, severity and preventability
Mouton 2015 [39]	ADR according to the definition of Aronson and Ferner[a]	Clinical pharmacologist	Clinical pharmacologist, clinical pharmacist, at least 1 physician/internist	A multidisciplinary review panel assessed ADRs for causality and preventability
Mouton 2016 [40]	ADR according to the definition of Aronson and Ferner[a]	One medical doctor and 2 pharmacists	Multidisciplinary panel discussion	A multidisciplinary case review panel assessed ADRs for causality, preventability, and severity
Oshikoya 2007 [41]	WHO definition of ADR [26]	Clinical pharmacologist, pediatrician, pharmacist	Pharmacists, pharmacologist, pediatric dermatologist	NR

Oshikoya 2011 [42]	WHO definition of ADR [26]	A pediatric clinical pharmacologist, pediatricians, 2 hospital pharmacists	NR	The pediatric clinical pharmacologist and one of the two pharmacists assess the suspected ADRs for causality, severity and preventability independently
Tipping 2006 [43]	ADEs, as defined by the South African Medicines Formulary	Primary physician and/or the principal investigator	NR	NR
Tumwikirize 2011[44]	WHO definition of ADR [89]	A physician and a pharmacist	NR	NR

NR, Not reported

[a]Aronson JK, Ferner RE. Clarification of terminology in drug safety. Drug Saf 2005; 28:851-70.

2. Definition and assessment of MEs

Author, year	Definition and/or description of the incident	Person/team assessing the clinical significance
Prescribing errors		
Agalu 2011 [45]	Prescribing error implies deviation of medication prescribing from standard practices excluding dosage form errors, illegible hand writing, and failure to authenticate the prescription with signature and/or date	NR
Ajemigbitse 2016 [49]	NR	NR
Ajemigbitse 2013 [46]	Any deviation from a complete, accurate and legible prescription, as it pertains to errors on the prescription and not the prescribing decision or dispensed medicines	3 clinical pharmacists
Ajemigbitse 2014 [48]	NR	NR
Ajemigbitse 2013 [47]	A prescribing decision or prescription writing process that results in an unintentional, significant reduction in the probability of treatment being timely and effective or increases the risk of harm when compared with generally accepted practice	NR
Alagha 2011 [50]	An error that occurs at the stage of prescribing excluding date of order and signature of the prescriber	A clinical pharmacist and a consultant pediatrician
Arulogun 2011 [51]	Prescriptions were evaluated for legality (name of patient, date, prescription number, signature) and for other types of error such as dose, duration, illegible writing	NR
Oshikoya 2007 [52]	NR	NR
Sada 2015 [53]	Prescribing error: deviation of medication prescribing from standard practices (as indicated in standard	The principal investigator and 1 internist

	treatment guidelines, textbooks, and software) excluding, indication without drug, dosage form errors, illegible hand writing, and failure to authenticate the prescription with signature and/or date.	
Yinusa 2004 [54]	All prescription items which did not conform to the criteria for prescription writing as stated in the British National formulary	NR
Yousif 2011 [55]	Neville et al [97] definition of prescribing errors	NR
Zeleke 2014 [56]	Deviation of medication prescribing from standard practices and includes inappropriate (incorrect) drug selection, wrong dose, wrong frequency, wrong route and wrong dosage form	NR
Medication administration errors		
Acheampong 2016 [57]	An administration error is said to be occurred when what was administered is different from what had been prescribed.	2 clinical pharmacists
Agalu 2012 [58]	Deviation from the conventional method of administration of a particular drug as ordered by the prescribing physician	NR
al Tehewy 2016 [59]	A deviation from a prescriber's valid prescription or the hospital's policy in relation to drug administration, including failure to correctly document the administration of a medication.	NR
Amponsah 2016 [60]	NR	Self-report
Amucheazi 2009 [61]	NR	NR
Blignaut 2017 [62]	NR	NR
Gordon 2004 [63]	Wrong drug administrations or the right drug into the wrong site	Self-report
Gordon 2006 [64]	Wrong drug administrations	Self-report

Feleke 2010 [65]	A medication error that occurs while administering a medication to a patient including unauthorized use of medicines	NR
Feleke 2015 [66]	Medication administration error: A medication error (time, dose, missed drug, unauthorized, route, technique, and documentation errors) that occurs while the time of administering IV, IM, SC, and PO medication to the patient by the nurse	NR
Labuschagne 2011 [67]	NR	Self-report
Llewellyn 2009 [68]	NR	Self-report
Nwasor 2014 [69]	NR	Self-report
Oshikoya 2013 [70]	Wrong medicine dose measurement, administration of wrong medicines, wrong patient, wrong route of administration, wrong timing and speed of administration, and omission of medications	NR
Medication errors (Mixed)		
Agu 2014 [71]	NR	NR
Dedefo 2016 [79]	NR	NR
Benkirane 2009 [78]	Adopted from NCCMERP [24]	2 reviewers of the pharmacovigilance center
Negash 2013 [72]	Adopted from ASHP[b]	NR
Jennane 2011[80]	Adopted from NCCMERP [24]	2 physician evaluators
Kandil 2012 [73]	Administration error: a medication error that occurred while administering a medication to a patient including unauthorized error, Prescription error: a failure in the prescription writing process that resulted in a wrong instruction	NR
Ogunleye 2016 [74]	Any error in prescribing, dispensing, or administration of drugs, irrespective of whether such errors lead to adverse consequences or not	NR
Sabry 2014 [75]	Prescribing errors, adopted from Anderson 2003;	NR

	Administration errors, any deviation from the physician's medication order as written on the patient's chart including timing problems, missing doses as observed from the administration sheet and after confirming with the nurse, an extra dose as observed from the quantities of unit doses remaining in the patient's tray, or wrong infusion flow rate	
Sabry 2009 [76]	Any problems connected with medications prescribed to the enrolled patients	NR
Shehata 2016 [77]	Adopted from NCCMERP [24]	NR

NR, not reported

[b] ASHP guidelines on preventing medication errors in hospitals. Am J Hosp Pharm 1993; 50:305-14.

A2.5 Electronic Supplementary Materials Published Online for Chapter 7

A. Additional file 1. Comparison of mean composite scores across type of hospital, staff position and work experience

Composites	**Type of hospital,** Mean (SD)			**Staff position,** Mean (SD)					**Work experience,** Mean (SD)			
	District	Teaching /referral	P value	Nurse	Physician	Pharmacist	Others	P Value	< 1 year	1-5 year	> 5 year	P value
Teamwork within units	3.71(0.68)	3.62(0.79)	0.18	3.73(0.68)	3.65(0.71)	3.54(0.78)	3.64(0.85)	0.35	3.67(0.69)	3.71(0.76)	3.44(0.82)	0.07
Supervisor/manager expectations and actions promoting patient safety	3.08(0.46)	3.13(0.50)	0.35	3.14(0.48)	3.12(0.52)	3.03(0.44)	3.11(0.47)	0.47	3.13(0.47)	3.08(0.50)	3.14(0.48)	0.55
Organizational learning–continuous improvement	3.82(0.70)	3.66(0.75)	**0.02**	3.86(0.68)	3.57(0.74)	3.57(0.74)	3.78(0.78)	**0.004**	3.78(0.71)	3.76(0.75)	3.49(0.73)	**0.04**
Management support for patient safety	3.12(0.87)	3.06(0.88)	0.47	3.22(0.76)	2.72(0.96)	3.14(0.89)	3.13(0.90)	**0.000**	3.06(0.93)	3.13(0.82)	3.00(0.90)	0.53
Feedback and communication about error	3.41(0.88)	3.24(0.92)	0.06	3.39(0.89)	3.20(0.97)	3.26(0.89)	3.33(0.89)	0.44	3.23(0.89)	3.34(0.93)	3.45(0.87)	0.27
Frequency of events reported	3.05(0.99)	2.95(0.99)	0.33	3.00(0.96)	2.90(1.04)	2.90(0.90)	3.15(1.03)	0.30	3.00(1.02)	3.04(0.95)	2.84(1.02)	0.44
Overall perception of patient safety	3.01(0.49)	3.03(0.58)	0.67	2.96(0.55)	3.05(0.49)	3.01 (0.59)	3.09(0.53)	0.32	3.03(0.54)	2.99(0.54)	3.09(0.58)	0.50
Communication openness	3.24(0.82)	3.02(0.86)	**0.01**	3.24(0.82)	3.01(0.97)	2.98(0.74)	3.12(0.84)	0.11	3.11(0.87)	3.14(0.84)	3.03(0.84)	0.69
Teamwork across units	3.45(0.70)	3.29(0.72)	**0.02**	3.45(0.71)	3.16(0.76)	3.29(0.69)	3.43(0.66)	0.14	3.32(0.70)	3.39(0.73)	3.40(0.70)	0.59
Staffing	2.42(0.76)	2.54(0.70)	0.11	2.54(0.71)	2.52(0.78)	2.56(0.70)	2.32(0.71)	0.09	2.42(0.71)	2.51(0.73)	2.59(0.75)	0.28
Handoffs and transitions	2.88(0.77)	2.81(0.76)	0.40	2.86(0.76)	2.76(0.75)	2.89(0.74)	2.85(0.80)	0.73	2.92(0.74)	2.78(0.78)	2.85(0.76)	0.22
Non-punitive response to error	2.89(0.79)	2.94(0.76)	0.52	2.83(0.75)	2.90(0.74)	2.99(0.80)	3.02(0.81)	0.20	2.95(0.77)	2.86(0.79)	3.01(0.72)	0.28
Overall score	3.19(0.32)	3.12(0.39)	0.08	3.20(0.35)	3.07(0.42)	3.10(0.35)	3.18(0.31)	**0.03**	3.16(0.38)	3.15(0.34)	3.12(0.37)	0.82

B. Additional file 2. Factor loadings in each item

Items	1	2	3	4	5	6	7	8	9	10	11
A4. In this unit, people treat each other with respect	0.75										
A6. We are actively doing things to improve patient safety	0.70										
A1. People support one another in this unit	0.66										
A3.When a lot of work needs to be done quickly, we work together as a team to get the work done	0.65										
A12. After we make changes to improve patient safety, we evaluate their effectiveness	0.50										
A17. Our procedures and systems are good at preventing errors from happening	0.44										
F8. The actions of hospital management show that patient safety is a top priority		0.75									
F1. Hospital management provides a work climate that promotes patient safety		0.70									
F10. Hospital units work well together to provide the best care for patients		0.67									
F4. There is good cooperation among hospital units that need to work together		0.60									
C2. Staff will freely speak up if they see something that may negatively affect patient care			0.72								
C5. In this unit, we discuss ways to prevent errors from happening again			0.64								
C3. We are informed about errors that happen in this unit			0.62								
C1. We are given feedback about changes put into place based on event reports			0.62								
C4. Staff feel free to question the decisions or actions of those with more authority			0.54								

B2.My supervisor/manager seriously considers staff suggestions for improving patient safety	0.72			
B1.My supervisor/manager says a good word when he/she sees a job done according to established patient safety procedures	0.72			
B4. My supervisor/manager overlooks patient safety problems that happen over and over	-0.65			
B3.Whenever pressure builds up, my supervisor/manager wants us to work faster, even if it means taking shortcuts	-0.58			
F5. Important patient care information is often lost during shift changes		0.70		
F7. Problems often occur in the exchange of information across hospital units		0.66		
F9. Hospital management seems interested in patient safety only after an adverse event happens		0.62		
F11. Shift changes are problematic for patients in this hospital		0.60		
F6. It is often unpleasant to work with staff from other hospital units		0.49		
D2. When a mistake is made, but has no potential to harm the patient, how often is this reported?			0.79	
D3. When a mistake is made that could harm the patient, but does not, how often is this reported?			0.74	
D1. When a mistake is made, but is caught and corrected before affecting the patient, how often is this reported?			0.70	
A11. When an event is reported, it feels like the person is being written up, not the problem				0.73
A9. It is just by chance that more serious mistakes don’t happen around here				0.55

A15. Staff worry that mistakes they make are kept in their personnel file		0.46				
F3. Things "fall between the cracks" when transferring patients from one unit to another			0.64			
F2. Hospital units do not coordinate well with each other			0.59			
A2. We have enough staff to handle the workload				0.72		
A14. Patient safety is never sacrificed to get more work done					0.67	
A16. We have patient safety problems in this unit					0.50	
C6. Staff are afraid to ask questions when something does not seem right						0.65
A5. Staff in this unit work longer hours than is best for patient care	-0.43					0.55

Appendix 3. Ethical Approvals

A3.1 Ethics Approval - The University of Sydney

THE UNIVERSITY OF SYDNEY

Research Integrity
Human Research Ethics Committee

Wednesday, 2 December 2015

Prof Jo-anne Brien
Pharmacy; Faculty of Pharmacy
Email: jo-anne.brien@sydney.edu.au

Dear Jo-anne

I am pleased to inform you that the University of Sydney Human Research Ethics Committee (HREC) has approved your project entitled "**Medication reconciliation as a medication safety initiative in a resource limiting settings: the case of Ethiopia"**.

Details of the approval are as follows:

Project No.: **2015/818**

Approval Date: **28 November 2015**

First Annual Report Due: **28 November 2016**

Authorised Personnel: **Brien Jo-anne; McLachlan Andrew; Mekonnen Alemayehu;**

Documents Approved:

Date	Type	Document
13/11/2015	Participant Info Statement	PIS - Qualitative Study Version 2
13/11/2015	Questionnaires/Surveys	Hospital Survey on Patient Safety Version 2
13/11/2015	Participant Info Statement	PIS - Hospital Survey Version 2
13/11/2015	Participant Consent Form	PCF - Qualitative Study Version 2
13/11/2015	Participant Info Statement	PIS - Prospective Audit Version 1
13/11/2015	Participant Consent Form	PCF - Prospective Audit Version 1
13/11/2015	Other Instruments/Tools	Prospective Audit Tool Version 2
13/11/2015	Study Protocol	Protocol Version 2
25/11/2015	Interview Questions	Interview Guide Questions Version 2.0
25/11/2015	Recruitment Letter/Email	Letter for Participant Invitation

HREC approval is valid for four (4) years from the approval date stated in this letter and is granted pending the following conditions being met:

Special Condition/s of Approval

- Approve on condition that all local approvals are sought and copies of those approvals are retained on file as part of your study records. You do not need to provide a copy to the Ethics Office.

Research Integrity
Research Portfolio
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NSW 2006 Australia

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ABN 15 211 513 464
CRICOS 00026A

- It will be a condition of approval that independently certified translations of the public documents should be submitted in IRMA via a "Compliance with Special Conditions of Approval" form prior to being distributed for the study. The translations must be certified by a person who is a native speaker or highly competent in the specific language. A statutory declaration to this effect would be appropriate if not completed by an official translator. A statutory declaration form can be found here: (http://www.ag.gov.au/STATDEC).
  In the declaration the translators need to indicate that the translated documents are a true and accurate representation of the English language versions submitted to the HREC, include a list of the documents translated (with version number) and provide details of the translator's fluency in the language.

Condition/s of Approval

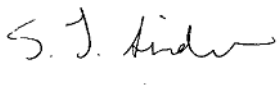
- Continuing compliance with the National Statement on Ethical Conduct in Research Involving Humans.
- Provision of an annual report on this research to the Human Research Ethics Committee from the approval date and at the completion of the study. Failure to submit reports will result in withdrawal of ethics approval for the project.
- All serious and unexpected adverse events should be reported to the HREC within 72 hours.
- All unforeseen events that might affect continued ethical acceptability of the project should be reported to the HREC as soon as possible.
- Any changes to the project including changes to research personnel must be approved by the HREC before the research project can proceed.
- Note that for student research projects, a copy of this letter must be included in the candidate's thesis.

Chief Investigator / Supervisor's responsibilities:

1. You must retain copies of all signed Consent Forms (if applicable) and provide these to the HREC on request.
2. It is your responsibility to provide a copy of this letter to any internal/external granting agencies if requested.

Please do not hesitate to contact Research Integrity (Human Ethics) should you require further information or clarification.

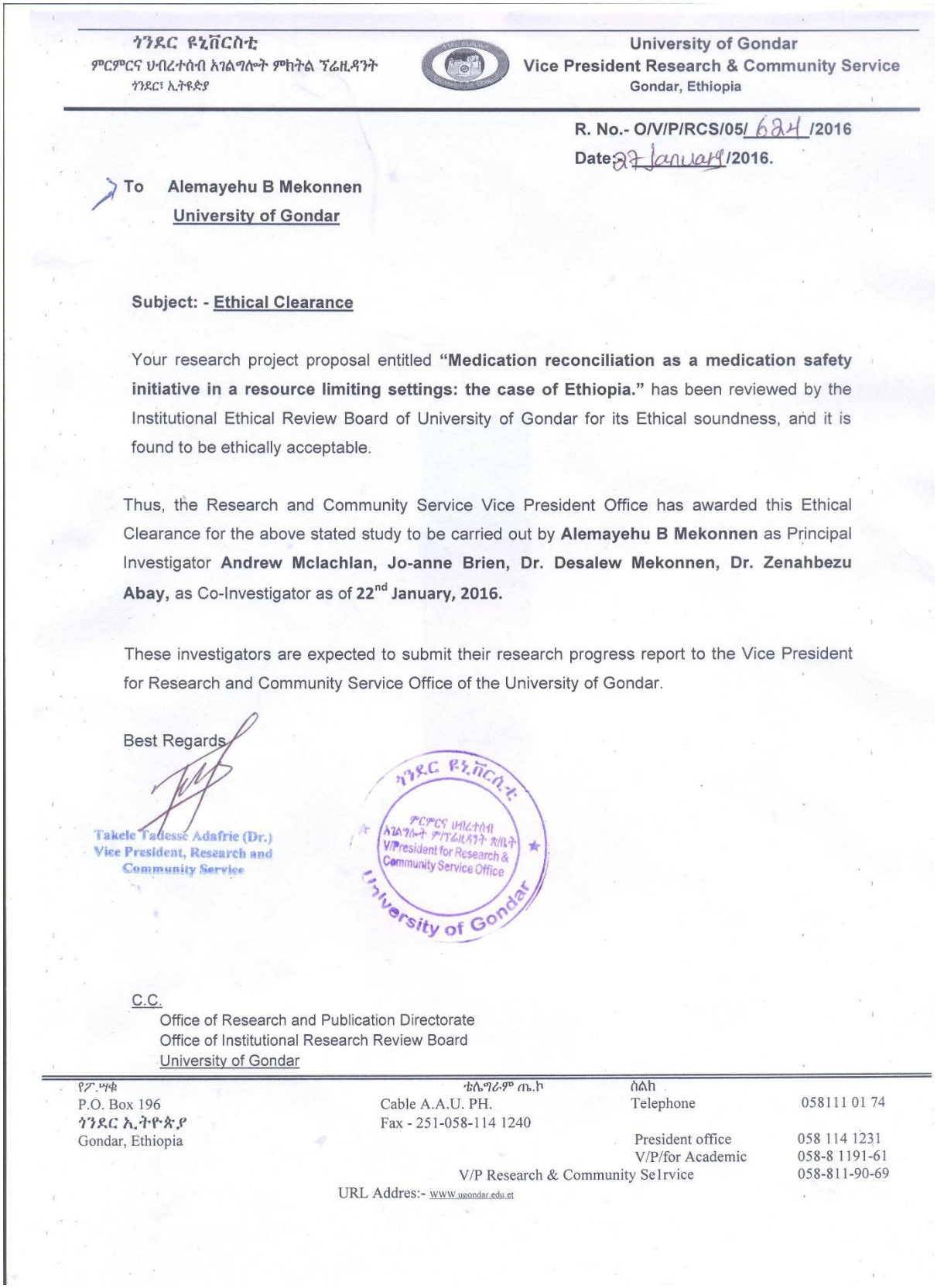
Yours sincerely



Dr Stephen Assinder
Chair
Human Research Ethics Committee

This HREC is constituted and operates in accordance with the National Health and Medical Research Council's (NHMRC) National Statement on Ethical Conduct in Human Research (2007), NHMRC and Universities Australia Australian Code for the Responsible Conduct of Research (2007) and the CPMP/ICH Note for Guidance on Good Clinical Practice.

A3.2 Ethics Approval – The University of Gondar, Ethiopia



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University of Gondar
Vice President Research & Community Service
Gondar, Ethiopia

R. No.- O/V/P/RCS/05/ 624 /2016
Date: 27 January /2016.

To Alemayehu B Mekonnen
University of Gondar

Subject: - Ethical Clearance

Your research project proposal entitled **"Medication reconciliation as a medication safety initiative in a resource limiting settings: the case of Ethiopia."** has been reviewed by the Institutional Ethical Review Board of University of Gondar for its Ethical soundness, and it is found to be ethically acceptable.

Thus, the Research and Community Service Vice President Office has awarded this Ethical Clearance for the above stated study to be carried out by **Alemayehu B Mekonnen** as Principal Investigator **Andrew Mclachlan, Jo-anne Brien, Dr. Desalew Mekonnen, Dr. Zenahbezu Abay,** as Co-Investigator as of **22nd January, 2016.**

These investigators are expected to submit their research progress report to the Vice President for Research and Community Service Office of the University of Gondar.

Best Regards,

Takele Tadesse Adafrie (Dr.)
Vice President, Research and Community Service

ጎንደር ዩኒቨርሲቲ ምርምርና ህብረተሰብ አገልግሎት ምክትል ፕሬዚዳንት ጽ/ቤት Vice President for Research & Community Service Office University of Gondar

C.C.
Office of Research and Publication Directorate
Office of Institutional Research Review Board
University of Gondar

ፖ.ሣቁ P.O. Box 196 ጎንደር ኢትዮጵያ Gondar, Ethiopia
ቴሌግራም ጠ.ኮ Cable A.A.U. PH. Fax - 251-058-114 1240
ስልክ Telephone 058111 01 74
President office 058 114 1231
V/P/for Academic 058-8 1191-61
V/P Research & Community Se1rvice 058-811-90-69
URL Addres:- WWW.ugondar.edu.et

A3.3 Statutory Declarations

STATUTORY DECLARATION 1

I, Wubante Demilew working as a lecturer at Bahir Dar Health Science College in the department of pharmacy make the following declaration.

- I translated the English versions of Interview Guide Questions Version 2 and Patient Information Statement (PIS) and Consent Forms (PCF) Versions 2 into the local language (Amharic) for the qualitative study of of healthcare professionals' and patients' perspectives in medication safety for the project number 2015/818.
- Amharic is my mother tongue and I have a previous experience of translating documents for research purpose in the healthcare industry

I declared that the translated documents are a true and accurate representation of the English language versions submitted to the Sydney HREC.

Declared at University of Gondar, School of Pharmacy head office on 12 of November 2015.

Before me,

Alemayehu Berhane,

PhD student at University of Sydney and former lecturer at School of Pharmacy, University of Gondar

STATUTORY DECLARATION 2

I, Ousman Abubker working as a clinical pharmacist and lecturer of pharmacotherapy at the University of Gondar in the department of clinical pharmacy make the following declaration.

- I translated the English versions of Patient Information Statement (PIS) and Consent Forms (PCF) Versions 2 into the local language (Amharic) for the study of a medication reconciliation service in an Internal Medicine ward of Gondar University Hospital for the project number 2015/818.
- Amharic is my mother tongue and I have experience in working with patients

I declared that the translated documents are a true and accurate representation of the English language versions submitted to the Sydney HREC.

Declared at University of Gondar, School of Pharmacy head office on 12 of November 2015.

Before me,

Alemayehu Berhane,

PhD student at University of Sydney and former lecturer at School of Pharmacy, University of Gondar

Appendix 4. Survey Instruments

A4.1Participant Information Statement – Hospital Survey

ABN 15 211 513 464

Jo-anne Brien BPharm BS (Pharm), PharmD, FRPharmS
Professor of Clinical Pharmacy (St. Vincent's Hospital)

Room S343
Building A15 (Faculty of Pharmacy)
The University of Sydney
NSW 2006 AUSTRALIA
Telephone: +61 2 9351 2363
Facsimile: +61 29351 4391
Email: joanne.brien@sydney.edu.au
Web: http://www.sydney.edu.au/

Hospital Survey on Patient Safety

PARTICIPANT INFORMATION STATEMENT

Dear research participants,

You are invited to take part in a research study about your perceptions of patient safety culture occurred in a hospital. You have been invited to participate in this study because you are involved in patient care.

What is the study about?

Patient safety is a global public health issue. But, patient safety is usually compromised due to medication– related incidents. Studies have shown that 1.5% - 6.5% of admissions in African hospitals are thought to be medication related; however, up to half of these are preventable.

To decrease the burden of such incidents, different patient safety strategies are employed and implemented internationally. However, there is lack of literature in this matter in Ethiopia. This study aims to explore healthcare professionals' opinions of patient safety culture in

selected Ethiopian public hospitals and this inform other subsequent quality improvement programs.

Who is running the study?

The study is being conducted by Alemayehu B Mekonnen and will form the basis for the degree of Doctor of Philosophy at the University of Sydney under the supervision of Professor Jo-anne Brien and Professor Andrew McLachlan (Faculty of Pharmacy, University of Sydney) and Dr. Desalew Mekonnen and Dr. Zenahbezu Abay (Department of Internal Medicine, University of Gondar)

What does the study involve?

If you agree to participate in this study, you will be requested to complete the anonymous questionnaire and return it to the researchers. The questionnaire has 42 items divided into 9 sections. The questionnaire takes approximately 10 to 15 minutes to complete. The confidentiality of your personal details will be maintained at all times. Any publications arising from this study will not include information identifying individual participants.

Can I withdraw from the study?

Being in this study is completely voluntary and you are not obliged to complete the questionnaire. Submitting a completed questionnaire is an indication of your consent to participate in the study. You can withdraw any time prior to submitting your completed questionnaire. However, once you have submitted your questionnaire, your responses cannot be withdrawn.

Will the study benefit me?

You may not personally get any benefits directly from participating in the study and also there is no any risk or harm that this research will bring to you. However, we recognize the time and effort required by staff to complete the questionnaire. While we cannot reimburse to all

participants rather we invite you to enter a prize draw after completion of the questionnaire in consideration of your time. There will be three lottery draws. The 1st prize winner will receive 1000 ETB, the 2nd prize winner 600 ETB and the 3rd winner a 400 ETB. Entry in the lottery draw is optional. For your chance to win one of the prizes, please fill in your details on the prize draw ticket (sticker) and return to the researchers. It should be noticed that there is no identifiable information noted on the questionnaire.

Researchers contact information

If you have any questions or would like to know more about this study, please feel free to contact the chief investigator, Professor Jo-anne Brien on Telephone (+61 2 9351 2363) or at joanne.brien@sydney.edu.au (Email) Or the onsite project researcher, Dr. Zenahbezu Abay on Telephone (+ 251920 24 81 30) or at Email (abayzenah@yahoo.com)

Alternatively the student researcher, Mr Alemayehu B Mekonnen, may be contacted on Telephone (+251973937980) or at email: aber5592@uni.sydney.edu.au

What if I have a complaint or any concerns about the study?

Research involving humans in Australia is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this study have been approved by the HREC of the University of Sydney (Protocol number: 2015/818). As part of this process, we have agreed to carry out the study according to the *National Statement on Ethical Conduct in Human Research (2007).* This statement has been developed to protect people who agree to take part in research studies.

If you are concerned about the way this study is being conducted or you wish to make a complaint to someone independent from the study, please contact the university using the details outlined below. Please quote the study title and protocol number.

Hospital survey on patient safety

Version 2.0 January 22, 2016

The Manager, Ethics Administration, University of Sydney:

- **Telephone:** +61 2 8627 8176
- **Email:** ro.humanethics@sydney.edu.au
- **Fax:** +61 2 8627 8177 (Facsimile)

Or for local complaints contact:

Nebiyu Mesfin, Director of the Institutional Review Board of the University of Gondar

- **Telephone**: +251926042997
- **Email**: hakimulig@gmail.com

Hospital survey on patient safety

Version 2.0 January 22, 2016

A4.2 Questionnaire

Hospital Survey on Patient Safety

Instructions

This survey asks for your opinions about patient safety issues, medical error, and event reporting in your hospital and will take about 10 to 15 minutes to complete.

If you do not wish to answer a question, or if a question does not apply to you, you may leave your answer blank.

- *An **"event"** is defined as any type of error, mistake, incident, accident, or deviation, regardless of whether or not it results in patient harm.*
- ***"Patient safety"** is defined as the avoidance and prevention of patient injuries or adverse events resulting from the processes of health care delivery.*

SECTION A: Your Work Area/Unit

In this survey, think of your "unit" as the work area, department, or clinical area of the hospital where you spend *most* of your work time or provide *most* of your clinical services.

What is your primary work area or unit in this hospital? Select ONE answer.

☐ Internal Medicine	☐ Psychiatry/mental health	☐ Other, please specify:
☐ Surgery	☐ Rehabilitation	
☐ Obstetrics	☐ Pharmacy	
☐ Pediatrics	☐ Laboratory	
☐ Emergency department	☐ Radiology	
☐ Intensive care unit	☐ Anesthesiology	

SECTION A: Your Work Area/Unit (continued)

Please indicate your agreement or disagreement with the following statements about your work area/unit.

	Strongly Disagree ▼	Disagree ▼	Neither ▼	Agree ▼	Strongly Agree ▼
1. People support one another in this unit	☐1	☐2	☐3	☐4	☐5
2. We have enough staff to handle the workload	☐1	☐2	☐3	☐4	☐5
3. When a lot of work needs to be done quickly, we work together as a team to get the work done	☐1	☐2	☐3	☐4	☐5
4. In this unit, people treat each other with respect	☐1	☐2	☐3	☐4	☐5
5. Staff in this unit work longer hours than is best for patient care	☐1	☐2	☐3	☐4	☐5
6. We are actively doing things to improve patient safety	☐1	☐2	☐3	☐4	☐5
7. Staff feel like their mistakes are held against them	☐1	☐2	☐3	☐4	☐5
8. Mistakes have led to positive changes here	☐1	☐2	☐3	☐4	☐5
9. It is just by chance that more serious mistakes don't happen around here	☐1	☐2	☐3	☐4	☐5
10. When one area in this unit gets really busy, others help out	☐1	☐2	☐3	☐4	☐5
11. When an event is reported, it feels like the person is being written up, not the problem	☐1	☐2	☐3	☐4	☐5
12. After we make changes to improve patient safety, we evaluate their effectiveness	☐1	☐2	☐3	☐4	☐5
13. We work in "crisis mode" trying to do too much, too quickly	☐1	☐2	☐3	☐4	☐5
14. Patient safety is never sacrificed to get more work done	☐1	☐2	☐3	☐4	☐5
15. Staff worry that mistakes they make are kept in their personnel file	☐1	☐2	☐3	☐4	☐5
16. We have patient safety problems in this unit	☐1	☐2	☐3	☐4	☐5
17. Our procedures and systems are good at preventing errors from happening	☐1	☐2	☐3	☐4	☐5

Hospital Survey on Patient Safety
Version 2.0 January 22, 2016

SECTION B: Your Supervisor/Manager

Please indicate your agreement or disagreement with the following statements about your immediate supervisor/manager or person to whom you directly report.

	Strongly Disagree ▼	Disagree ▼	Neither ▼	Agree ▼	Strongly Agree ▼
1. My supervisor/manager says a good word when he/she sees a job done according to established patient safety procedures	☐1	☐2	☐3	☐4	☐5
2. My supervisor/manager seriously considers staff suggestions for improving patient safety	☐1	☐2	☐3	☐4	☐5
3. Whenever pressure builds up, my supervisor/manager wants us to work faster, even if it means taking shortcuts	☐1	☐2	☐3	☐4	☐5
4. My supervisor/manager overlooks patient safety problems that happen over and over	☐1	☐2	☐3	☐4	☐5

SECTION C: Communications

How often do the following things happen in your work area/unit?

Think about your hospital work area/unit…	Never ▼	Rarely ▼	Some-times ▼	Most of the time ▼	Always ▼
1. We are given feedback about changes put into place based on event reports	☐1	☐2	☐3	☐4	☐5
2. Staff will freely speak up if they see something that may negatively affect patient care	☐1	☐2	☐3	☐4	☐5
3. We are informed about errors that happen in this unit	☐1	☐2	☐3	☐4	☐5
4. Staff feel free to question the decisions or actions of those with more authority	☐1	☐2	☐3	☐4	☐5
5. In this unit, we discuss ways to prevent errors from happening again	☐1	☐2	☐3	☐4	☐5
6. Staff are afraid to ask questions when something does not seem right	☐1	☐2	☐3	☐4	☐5

Hospital Survey on Patient Safety
Version 2.0 January 22, 2016

SECTION D: Frequency of Events Reported

In your hospital work area/unit, when the following mistakes happen, *how often are they reported?*

Think about your hospital work area/unit…	Never ▼	Rarely ▼	Some-times ▼	Most of the time ▼	Always ▼
1. When a mistake is made, but is *caught and corrected before affecting the patient*, how often is this reported?	☐1	☐2	☐3	☐4	☐5
2. When a mistake is made, but has *no potential to harm the patient*, how often is this reported?	☐1	☐2	☐3	☐4	☐5
3. When a mistake is made that *could harm the patient*, but does not, how often is this reported?	☐1	☐2	☐3	☐4	☐5

SECTION E: Patient Safety Grade

Please give your work area/unit in this hospital an overall grade on patient safety.

A	B	C	D	E
☐	☐	☐	☐	☐
Excellent	Very Good	Acceptable	Poor	Failing

SECTION F: Your Hospital

Please indicate your agreement or disagreement with the following statements about your hospital.

Think about your hospital work area/unit…	Strongly Disagree ▼	Disagree ▼	Neither ▼	Agree ▼	Strongly Agree ▼
1. Hospital management provides a work climate that promotes patient safety	☐1	☐2	☐3	☐4	☐5
2. Hospital units do not coordinate well with each other	☐1	☐2	☐3	☐4	☐5
3. Things "fall between the cracks" when transferring patients from one unit to another	☐1	☐2	☐3	☐4	☐5
4. There is good cooperation among hospital units that need to work together	☐1	☐2	☐3	☐4	☐5
5. Important patient care information is often lost during shift changes	☐1	☐2	☐3	☐4	☐5
6. It is often unpleasant to work with staff from other hospital units	☐1	☐2	☐3	☐4	☐5
7. Problems often occur in the exchange of information across hospital units	☐1	☐2	☐3	☐4	☐5
8. The actions of hospital management show that patient safety is a top priority	☐1	☐2	☐3	☐4	☐5
9. Hospital management seems interested in patient safety only after an adverse event happens	☐1	☐2	☐3	☐4	☐5
10. Hospital units work well together to provide the best care for patients	☐1	☐2	☐3	☐4	☐5
11. Shift changes are problematic for patients in this hospital	☐1	☐2	☐3	☐4	☐5

Hospital Survey on Patient Safety
Version 2.0 January 22, 2016

SECTION G: Number of Events Reported

In the past 12 months, how many event reports have you filled out and submitted?

a. No event reports
b. 1 to 2 event reports
c. 3 to 5 event reports
d. 6 to 10 event reports
e. 11 to 20 event reports
f. 21 event reports or more

SECTION H: Background Information

This information will help in the analysis of the survey results.

1. **How long have you worked in this hospital?**

a. Less than 1 year
b. 1 to 5 years
c. 6 to 10 years
d. 11 to 15 years
e. 16 to 20 years
f. 21 years or more

2. **How long have you worked in your current hospital work area/unit?**

a. Less than 1 year
b. 1 to 5 years
c. 6 to 10 years
d. 11 to 15 years
e. 16 to 20 years
f. 21 years or more

3. **Typically, how many hours per week do you work in this hospital?**

a. Less than 20 hours per week
b. 20 to 39 hours per week
c. 40 to 59 hours per week
d. 60 to 79 hours per week
e. 80 to 99 hours per week
f. 100 hours per week or more

4. **What is your staff position in this hospital? Select ONE answer that best describes your staff position.**

a. Nurse
b. Attending/Staff Physician
c Resident Physician/Physician in Training
d. Pharmacist
e. Intern
f. Technician (e.g. Lab, Radiology)
g. Administration/Management
h. other, specify _____

5. In your staff position, do you typically have direct interaction or contact with patients?

a. YES, I typically have direct interaction or contact with patients.

b. NO, I typically do NOT have direct interaction or contact with patients.

6. How long have you worked in your current specialty or profession?

a. Less than 1 year

b. 1 to 5 years

c. 6 to 10 years

d. 11 to 15 years

e. 16 to 20 years

f. 21 years or more

SECTION I: Your Comments

Please feel free to write any comments about patient safety, error, or event reporting in your hospital.

THANK YOU FOR COMPLETING THIS SURVEY.

Hospital Survey on Patient Safety
Version 2.0 January 22, 2016

Appendix 5. Qualitative Study Documents

A5.1 Letter of Invitation

ABN 15 211 513 464

Jo-anne Brien BPharm BS (Pharm), PharmD, FRPharmS
Professor of Clinical Pharmacy (St. Vincent's Hospital)

Room S343
Building A15 (Faculty of Pharmacy)
The University of Sydney
NSW 2006 AUSTRALIA
Telephone: +61 2 9351 2363
Facsimile: +61 29351 4391
Email: joanne.brien@sydney.edu.au
Web: http://www.sydney.edu.au/

Prof (Dr.) (Mr.) (Mrs.) (Ms.) _____

Subject: Participation in a study

We would like invite you to participate in a study entitled "A qualitative study of healthcare professionals' and patients' perspectives in medication safety". This study aims to explore healthcare professionals' perspectives and patients' experiences of medication safety problems, as well as the barriers and facilitators for medication safety activities involving pharmacists in selected public hospitals in the Amhara region of Ethiopia. You have been invited to participate in this study because you are involved in patient care or you are receiving hospital services. Research participants include both healthcare professionals and patients.

In this study, we would like to conduct an interview with healthcare professionals to discuss medication safety issues in hospitals, and we would like to interview patients about their experiences of medication-related problems during their hospital stay.

This study will be conducted by Alemayehu B Mekonnen, in Ethiopia, and this study is part of his studies for a University of Sydney Doctor of Philosophy (PhD) degree. His research

supervisors at the University of Sydney are Professors Jo-anne Brien and Andrew McLachlan. Colleagues in Ethiopia are Drs Desalew Mekonnen and Zenahbezu Abay.

If you are willing to participate, please contact Alemayehu B Mekonnen on Telephone (+2519737980) or at Email: aber5592@uni.sydney.edu.au

Regards,

Alemayehu B Mekonnen

Pharmacist and PhD candidate

on behalf of the Research Team

A5.2 Participant Information Statement – English Version

ABN 15 211 513 464

Jo-anne Brien BPharm BS (Pharm), PharmD, FRPharmS
Professor of Clinical Pharmacy (St. Vincent's Hospital)

Room S343
Building A15 (Faculty of Pharmacy)
The University of Sydney
NSW 2006 AUSTRALIA
Telephone: +61 2 9351 2363
Facsimile: +61 29351 4391
Email: joanne.brien@sydney.edu.au
Web: http://www.sydney.edu.au/

"A qualitative study of healthcare professionals' and patients' perspectives in medication safety"

PARTICIPANT INFORMATION STATEMENT

Dear research participants,

You are invited to take part in a research study about your perceptions of medication safety problems occurred in a hospital. You have been invited to participate in this study because you are involved in patient care or you are getting hospital services. Participation in this research study is voluntary. So it's up to you whether you wish to take part or not.

By giving your consent to take part in this study you are telling us that you:

- ✓ Understand what you have read
- ✓ Agree to take part in the research study as outlined below

What is the study about?

Patient safety is a global public health issue. But, patient safety is usually compromised due to medication– related incidents. Studies have shown that 1.5% - 6.5% of admissions in African hospitals are thought to be medication related; however, up to half of these are preventable.

To decrease the burden of such incidents, different medication safety strategies are employed internationally. However, there is none which tasted in the Ethiopian hospital setup.

This study aims to explore healthcare professionals' and patient's perspectives of medication safety problems and the barriers and facilitators of medication safety activities done by pharmacists in selected Ethiopian public hospitals.

Who is running the study?

The study is being conducted by Alemayehu B Mekonnen and will form the basis for the degree of Doctor of Philosophy at the University of Sydney under the supervision of Professor Jo-anne Brien and Professor Andrew McLachlan (Faculty of Pharmacy, University of Sydney) and Dr. Desalew Mekonnen and Dr. Zenahbezu Abay (Department of Internal Medicine, University of Gondar)

What does the study involve?

Only in-patients and healthcare professionals involved in the care of patients are invited for interview and hospital pharmacists for focus group discussions. If you agree to participate in this study, you will be requested to sign for your consent and arrange an appropriate schedule and place for interview or discussions. The interview or discussion takes approximately 30 - 60 minutes during in hospital or your working hours. Interviews are conducted by a single student researcher (Alemayehu B Mekonnen) through audio recording and your personal information will be maintained through use of unique codes. The confidentiality of your personal details will be maintained at all times. Any publications arising from this study will not include information identifying individual participants.

Can I withdraw from the study?

Being in this study is completely voluntary and you do not have to take part. Your decision whether to participate will not affect your current or future relationship with the researchers at

the University of Sydney or the University of Gondar or anyone else at respective hospital staffs.

You are free to stop the interview at any time. Unless you say that you want us to keep them, any recordings will be erased and the information you have provided will not be included in the study results. You may also refuse to answer any questions that you do not wish to answer during the interview. If you take part in a focus group, you are free to stop participating at any stage or to refuse to answer any of the questions. However, it will not be possible to withdraw your individual comments from our records once the group has started, as it is a group discussion.

Will the study benefit me?

As reimbursement you will receive 50 ETB for your time.

Will I be told the results of the study?

You have a right to receive feedback about the overall results of this study. You can tell us that you wish to receive feedback by ticking the relevant box on the consent form. This feedback will be in the form of a one page lay summary. You will receive this feedback after the study is finished.

Researchers contact information

If you have any questions or would like to know more about this study, please feel free to contact the chief investigator, professor Jo-anne Brien on Telephone (+61 2 9351 2363) or at joanne.brien@sydney.edu.au (Email) Or the onsite project researcher, Dr. Zenahbezu Abay on Telephone (+ 251920 24 81 30) or at Email (abayzenah@yahoo.com)

Alternatively the student researcher, Mr Alemayehu B Mekonnen, may be contacted on Telephone (+251973937980) or at email: aber5592@uni.sydney.edu.au

What if I have a complaint or any concerns about the study?

Research involving humans in Australia is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this study have been approved by the HREC of the University of Sydney (Protocol number: 2015/818). As part of this process, we have agreed to carry out the study according to the *National Statement on Ethical Conduct in Human Research (2007)*. This statement has been developed to protect people who agree to take part in research studies.

If you are concerned about the way this study is being conducted or you wish to make a complaint to someone independent from the study, please contact the university using the details outlined below. Please quote the study title and protocol number.

The Manager, Ethics Administration, University of Sydney:

- **Telephone:** +61 2 8627 8176
- **Email:** ro.humanethics@sydney.edu.au
- **Fax:** +61 2 8627 8177 (Facsimile)

Or for local complaints contact:

Nebiyu Mesfin, Director of the Institutional Review Board of the University of Gondar

- **Telephone**: +251926042997
- **Email**: hakimulig@gmail.com

A5.3 Participant Information Statement – Amharic Version

ABN 15 211 513 464

Jo-anne Brien BPharm BS (Pharm), PharmD, FRPharmS
Professor of Clinical Pharmacy (St. Vincent's Hospital)

Room S343
Building A15 (Faculty of Pharmacy)
The University of Sydney
NSW 2006 AUSTRALIA
Telephone: +61 2 9351 2363
Facsimile: +61 29351 4391
Email: joanne.brien@sydney.edu.au
Web: http://www.sydney.edu.au/

የመድሃኒት ህክምና ተግዳሮቶች በተመለከተ የጤና ባለሙያዎችና የታካሚዎች ምልከታ

<u>ለተሳታፊው መረጃ</u>

ለተከበራችሁ የምርምር ተሳታፊዎች:

በሆስፒታል ውስጥ ስለሚከሰት የመድሃኒት ህክምና ተግዳሮቶች በሚመለከት ያላችሁን አስተያየት፣ ምልከታ እንድትሰጡበት ይህ ምርምር ጋብዟችኃል። የተጋበዛችሁበትም ምክንያት ታካሚውን ስለምታገለግሉ ወይም ህክምና እያገኛችሁ ስለሆነ ነው። በዚህ ምርምር ተሳትፎ ለማድረግ በጎ ፍቃደኝነትን ይጠይቃል። ስለዚህ መሳተፍ ያለመሳተፍ የእርስዎ ምርጫ ነው።

በዚህ ጥናት ፍቃደኝነትዎን በማሳወቅ፣ የሚከተሉትን እንደገለፁልን፦

- ያነበቡትን እንደተረዱና
- ከዚህ በታች እንደተገለፀው በጥናቱ ተሳታፊ ለመሆን እንደተስማሙ

ጥናቱ ስለምድን ነው?

የህሙማን ደህንነት መጠበቅ ቅድሚያ የሚሰጠው የማህበራዊ ጤና ጉዳዮች አንዱ ነው። ነገር ግን የህሙማን ደህንነት ብዙ ጊዜ ከመድሃኒት ጋር በተያያዙ ችግሮች ይጓደላል። በአፍሪቃ ውስጥ የተደረጉ የተለያዩ ጥናቶች እንደሚያመለክቱት ከሆነ ከ ፲.5% - 6.5% የሚሆኑት ህመሙን ወደ ሆስፒታል ለመግባታቸው ምክንያት ከመድሃኒት ጋ የተገናኘ ነው ፤ ነገር ግን ግማሽ ያህሉን አስቀድሞ መከላከል ይቻላል።

በአለም አቀፍ ደረጃ ይህንን ጫና ለመቀነስ የተለያዩ የመድሃኒት ደህንነትን ለማስጠበቅ የሚያገለግሉ እስትራቴጅዎች አሉ። ነገር ግን ምንም አይነት ሙከራ ኢትዮጵያ ውስጥ አልተካሄደም።

የዚህ ጥናት ዋና ዓላማም የመድሃኒት ህክምና ተግዳሮቶች በተመለከተ የጤና ባለሙያዎችና የታካሚዎች ምልከታ በአንድ የኢትዮጵያ ዩንቨርስቲ ሆስፒታል ውስጥ ዳሰሳ ማድረግ ነው።

ጥናቱን የሚያካሂደው ማን ነው?

ጥናቱ የሚከናወነው በአቶ አለማየሁ ብርሃኔ በኩል ሲሆን ይህም ለእሱ ፒኤችዲ ማሟያ ከሲዲኒ ዩንቨርስቲ በ ፕ/ር ጆ ኣን ብራይን እና በ ፕ/ር አንድሪው ማክላችላን (ከ ፋርማሲ ት/ት ክፍል፤ ሲዲኒ ዩንቨርስቲ) እና ዶ/ር ደሳለው መኮነን እንዲሁም ዶ/ር ዝናህብዙ አባይ (ከውስጥ ደዌ ት/ት ክፍል: ጎንደር ዩንቨርስቲ) መሪነት ነው።

ጥናቱ የሚያካትታቸው ነገሮች ምንድን ናቸው?

ህሙማንና የጤና ባለሙያዎች ብቻ ለቃለ መጠየቁ ይጋበዛሉ።በዚህ ጥናት ለመሳተፍ ፍቃደኛ ከሆኑ፤ለፍቅደኝነትዎ ፊርማዎን ያስቀምጣሉ: ለቃለ መጠየቅ የሚመቸወትን ጊዜ እና ቦታ ያመቻቻሉ። ቃለ መጠየቁ የሚደረገው በስራ ሰዓት ወይም ሆስፒታል ውስጥ ሲሆን በአማካኝ ከ 30 - 60 ደቂቃ ይወስዳል። ቃለ መጥየቁ የሚከናወነው በመቅረፀ ድምፅ በአቶ አለማየሁ ብርሃኔ ሲሆን ማንነትዎም አይገለጥም። ማናቸውም የሚሰጡት መረጃ ሚስጥራዊነቱ የተጠበቀ ነው። ከዚህ ምርምር የሚወጡ ፅሁፎች የማናቸውንም የምርምር ተሳታፊዎች የማንነት መረጃ አያወጣም።

ከጥናቱ መውጣት ይቻላል?

ጥናቱ ሙሉ በሙሉ በፍቃደኝነት የተመሰረተ ነው፤ መሳተፍም ግዴታ አይደለም።ተሳትፎ ለማድረግ በመወሰንህ (ሽ) ከጎንደር ዩነቨርስቲ ሰራተኞች ወይም ይህን ጥናት ከሚያደርግ ሰው ጋር ያለህን (ሽን)የነበረ ወይም ወደ ፊት የሚኖረውን ግንኙት የሚጎዳ አይሆንም።

በማንኛውም ሰዓት ቃለ መጠየቁን የሙተው መብት አለህ (ሽ)። የሰጡን መረጃ እንድንጠቀምበት እስካልፈቀዱልን ድረስ ማንኛውም መረጃወች ይደመሰሳሉ ወይም የጥናቱ አካል አይሆኑም።

መመለስ የማይፈልጉትን ጥያቄ አለመመለስ ይችላሉ።

ጥናቱ ሊጠቅመኝ ይችላል?

በጥናቱ ተሳትፎ ስላደረጉ 50 ብር ይከፈልዎታል።

የጥናቱ ውጤት ይነገረኛል?

ስለጥናቱ ውጤት የማወቅ መብት አለዎት።ፍላጎትዎን ከፍቃደኝነት መጠየቂያ ፎርም ላይ ጭረት በማድረግ ማሳወቅ ይቻላል።.ይህም በ 1 ገፅ ማጠቃለያ ይገለፃል። ይህ የሚሆነው ግን ጥናቱ ከተጠናቀቀ በኋላ ነው።

ጥናቱን የሚያካሂዱትን ማግኘት ከፈለጋቹሁ

ማነኛውም ስለጥናቱ ማወቅም ሆነ ጥያቄ መጠየቅ ከፈለጋቹሁ፣ እባክዎትን ፕ/ር ጆ ኣን ብራይን በስልክ ቁ. +61 2 9351 2363 ወይም በ ኢሜይል አድራሻ joanne.brien@sydney.edu.au ፤ ዶ/ ር ዝናህ ብዙ አባይን በስልክ ቁ + 251920 24 81 30 ወይም በ ኢሜይል አድራሻ abayzenah@yahoo.com

ወይም አቶ አለማየሁ ብርሃኔን በስልክ ቁ +251973937980 ወይም በ ኢሜይል አድራሻ aber5592@uni.sydney.edu.au ማግኘት ይቻላል።

አቤቱታ ወይም ቅሬታ ቢኖረኝስ?

አውስትራሊያ ውስጥ በሰው ላይ የሚከናወን ምርምር ሂውማን ሪሰርች ኢቲክስ ኮሚቴ (HREC) በሚባል የገለልተኛ ሰወች ስብስብ ይታያል። ይህ ጥናት በሲዲኒ ዩንቨርስቲ HREC ፀድቋል (ፕሮቶኮል ቁጥር፡ 2015/818) ።

በዚህ ሂደት መሰረት ጥናቱ በብሔራዊ የስነ ምግባር ደንብ (2007) መሰረት እንድምንሰራው ተስማምተናል።. ይህ ደንብ የወጣው በምርምር ስራዎች የሚሳተፉ ሰዎችን ለመጠበቅ ነው።

የጥናቱ አካሂድ ላይ አቤቱታ ካለብዎት ወይም ቅሬታዎን ለሌላ አካል ማሳወቅ ከፈለጉ እባክዎ ን ዩንቨርስቲውን ታች በተገለፀው አድራሻ ያመልክቱ። የጥናቱን ርዕስና ፕሮቶኮል ቁጥር ያጣቅሱ።

- **ስልክ ቁ:** +61 2 8627 8176
- **ኢሜይል:** ro.humanethics@sydney.edu.au
- **ፋክስ:** +61 2 8627 8177

ወይም በአካባቢዎ አቤቱታዎን ለማቅረብ:

ኑብዩ መስፍን: የጎንደር ዩንቨርስቲ ኢንስቲቱሽናል ሪቪው ቦርድ ዳይሬክተር

- **ስልክ ቁ**: +251926042997
- **ኢሜይል:** hakimulig@gmail.com

A5.4 Consent Form – English Version

ABN 15 211 513 464

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Web: http://www.sydney.edu.au/

"A qualitative study of healthcare professionals' and patients' perspectives in medication safety"

PARTICIPANT CONSENT FORM

I,..... [PRINT NAME], agree to take part in this research study.

In giving my consent I state that:

- ✓ I understand the purpose of the study, what I will be asked to do, and any risks/benefits involved.
- ✓ I have read the Participant Information Statement and have been able to discuss my involvement in the study with the researchers if I wished to do so.
- ✓ The researchers have answered any questions that I had about the study and I am happy with the answers.
- ✓ I understand that being in this study is completely voluntary and I do not have to take part. My decision whether to be in the study will not affect my relationship with the

researchers or anyone else at the University of Sydney and University of Gondar now or in the future.

- ✓ I understand that I can withdraw from the study at any time.
- ✓ During interview about medication safety problems, I understand that I may stop the interview at any time if I do not wish to continue, and that unless I indicate otherwise any recordings will then be erased and the information provided will not be included in the study. I also understand that I may refuse to answer any questions I don't wish to answer.
- ✓ During discussions about the barriers and facilitators to medication safety activities done by pharmacists, I understand that I may leave the focus group at any time if I do not wish to continue. I also understand that it will not be possible to withdraw my comments once the group has started as it is a group discussion.
- ✓ I understand that personal information about me that is collected over the course of this project will be stored securely and will only be used for purposes that I have agreed to. I understand that information about me will only be told to others with my permission, except as required by law.
- ✓ I understand that the results of this study may be published, but these publications will not contain my name or any identifiable information about me unless I consent to being identified
- ✓ I consent to:

Audio-recording YES □ NO □

A qualitative study of healthcare professionals' and patients' perspectives in medication safety

Version 2.0 January 22, 2016

Would you like to receive feedback about the overall results of this study?

YES ☐ **NO** ☐

If you answered **YES**, please indicate your preferred form of feedback and address:

☐ Postal: _____

☐ Email: _____

.....

Signature

.....

PRINT name

.....

Date

A qualitative study of healthcare professionals' and patients' perspectives in medication safety

Version 2.0 January 22, 2016

A5.5 Consent Form – Amharic Version

ABN 15 211 513 464

Jo-anne Brien BPharm BS (Pharm), PharmD, FRPharmS
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The University of Sydney
NSW 2006 AUSTRALIA
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Web: http://www.sydney.edu.au/

የመድሃኒት ህክምና ተግዳሮቶች በተመለከተ የጤና ባለሙያዎችና የታካሚዎች ምልከታ

<u>የተሳታፊዎች ፍቃደኝነት ማሳወቂያ ፎርም</u>

እኔ _____ (ስም) በዚህ ጥናት ለመሳተፍ ተስማምቻለሁ።

ስለማማም፥

- የጥናቱን ዓላማ ተረድቸዋለሁ፤ ምን መጠየቅ እንዳለብኝም አውቃለሁ።
- ስለተሳታፊው የተገለፀውን አንብቢያለሁ፣እናም በጥናቱ ለመሳተፍ ከፈለግሁኝ ከተመራማሪዎች ጋር እወያያለሁ።
- ተመራማሪው ለሚጠይቀኝ ማንኛውም ጥያቄ ለመመለስ ደስተኛ ነኝ።
- ጥናቱ ሙሉ በሙሉ በፍቃደኝነት የተመሰረተ ነው፤ መሳተፍም ግዴታ አይደለም።ተሳትፎ ለማድረግ በመወሰንህ(ሽ) ከንንደር ዩኒቨርስቲ ሰራተኞች ወይም ይህን ጥናት ከሚያደርግ ሰው ጋ ያለህን (ሽን)የነበረ ወይም ወደ ፊት የሚኖረውን ግንኙት የሚነዳ አይሆንም።
- በማንኛውም ሰዓት ከጥናቱ መውጣት እንደምችል ተረድቻለሁ።
- በማንኛውም ሰዓት ቃለ መጠየቁን የመተው መብት አለኝ። የምሰጠው መረጃ እንዲጠቀሙበት እስካልፈቀድኩኝ ድረስ ማንኛውም መረጃወች ይደመሰሳሉ ወይም የጥናቱ አካል አይሆኑም። መመለስ የማልፈልገውን ጥያቄ አለመመለስ እችላለሁ።

- በዚህ ፕሮጀክት የሚሰበሰበው ግለሰባዊ መረጃ በጥብቅ እንደሚጠበቅ ተረድቻለሁ፣ለዚህ ዓላማም ብቻ እንደሚያገለግልም ተረድቻለሁ።
- ስለ እኔ መረጃ ለሌሎች ለማሳወቅ የእኔን ፍቃደኝነት እንደሚጠይቁ ተረድቻለሁ።
- ይህ ጥናት ህትመት ላይ እንደሚውል እረዳለሁ፣ ነገር ግን ማናቸውም ህትመት ያለ እኔ ፍቃድ የእኔን ስም መጥቀስ አይችልም።
- ለመቅረፀ ድምፅ ፍቃደኛ ነዎት

አዎ □ አይደለም □

ስለጥናቱ ውጤት ማወቅ ይፈልጋሉ?

አዎ □ አይደለም □

መልስዎ አዎ ከሆነ እባክዎን እንዴት እንደምናሳውቀዎ ይግለፁልን

□ በፖስታ _____

□ በኢሜይል _____

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A5.6 Interview Guide Questions – English Version

Interview guide questions for healthcare workers

1. What is your role and how long have you been doing this?
2. Who are the colleagues you work most closely with (physicians, nurses, pharmacists, others)
3. How do you describe your working relationship with physicians/ nurses/ pharmacists/others?
4. To what extent is patient safety is a priority for your hospital? If so, is there any evidence for this?
5. What do you think the main priorities for your hospital in terms of improving patient safety? And what changes would like to see?
6. In your opinion what are the important medication safety problems encountered in your hospital? What kinds of medication related issues worry you the most?
7. What sorts of mistakes/things going wrong occur most commonly?
8. What are the major errors causing medication problems in your practice site?
9. What do you think are the causes of these problems? And how can these be prevented?
10. What does medication safety to you mean?
11. How does medication safety relate to your work? Are you involved in medication safety activities?
12. What are the strengths of the hospital in terms of improving medication safety?
13. Are there any medication safety initiatives in place that you are aware of? If so, how much successful is it/ are these?
14. What are the challenges in improving medication safety in your hospital?
15. How do you think about the safety of patients at your practice site?
16. What are the measures have you taken to ensure the safety of patients?
17. Could you please tell us how you personally involved in patient safety management

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A) When you make mistakes, do you report these? Why?

B) How do you respond when/ if you find others doing things 'wrongly'?

C) How do you discuss adverse drug events with patients?

D) Could you share any medication incident examples you are aware of that have occurred in your practice site.

18. What kind of patient safety strategy do you want to be implemented in your hospital?

19. How do you think the hospital can do better in patient safety?

20. What are the roles for other healthcare professionals in patient safety?

Interview guide for patients

Thank you for participating in this survey.

1. What types of services did you receive during your recent visit to the hospital?

    A. Are you satisfied with the services? Why? (Or Why not?)

    B. Did you attend other health organizations (other than this hospital) for the same health problems? When and Why?

2. Why did you choose this particular hospital?

    A. What do you think about the quality of services provided by the hospital?

    B. Who referred you to this hospital?

3. Did you have any concerns about your safety when you visited the hospital?

    A. What were your concerns?

    B. What were you aware of?

    C. What have you done to make sure you are safe?

    D. What do you think you can do better to ensure your safety?

    E. What do you think the hospital can do (or do better) to ensure your safety?

As you know, medicines sometimes cause harm to patients, even without an error being made by a health care professional.

4. Did your doctor, nurse or pharmacist discuss with you the potential adverse impact of your medicines?

    A. Have you experienced this before?

    B. Was it easy to understand?

    C. Did you have to make a decision about taking your medicines? How did you make that decision?

5. Have you experienced or noticed any mistakes/medication errors in your recent visit to the hospital?

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A. Who do you think should be responsible for the problems?

B. Do you think the problems preventable? If yes, why and how? If not, why?

C. How did the hospital respond to the problems?

D. Are you satisfied with the way the hospital handle these problems? Why?

6. What measures are you most satisfied in relation to patient safety?

A. What was done?

B. Who did it? How?

C. Why are you satisfied?

7. Have you been consulted about how to improve quality use of medicines?

A) What suggestions did you make?

B) Did you think they were considered by the hospital?

8. How do you think the hospital can do better in patient safety?

Interview guide for hospital pharmacists

Theoretical domains and their corresponding interview questions

Domains	Interview questions
Knowledge	Are there any hospital guidelines for pharmacists to deliver clinical pharmacy services? What do you think the level of evidence is for these guidelines? What do you know about medication reconciliation and review? Can you decribe pharmacists' roles in medication safety activities?
Skills	Do you know how to deliver clinical pharmacy services? Do you know how to deliver medication reconcilaition and review servies? Is identification of medication related problems difficult for you? Have you atteneded in-serivce training to deliver clinical pharmacy services?
Social/professional role	Is doing medication reconicilation and review compatible with your professional role? Who is responsible for these services at your hospital? Do you think hospital guidelines supports your professional roles as a pharmaceutical care practitioners?
Beliefs about capabilties	How easy or difficult do you find performing clinical pharmacy activities ? What problems have you encountered? How capable are you in performing medication reconciliation and review?

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	How confident are you that you can do these services despite difficulties? How comfortable do you feel to undertake these services?
Beliefs about consequences	What are the likely positive/negative outcomes of reporting/communicating medication related problems? What are the costs of delivering medication reconciliation and review and what are the costs of the consequences of these services? Are you concerned if these services are not provided at your hospital? Do benefits of doing these services outweigh the costs? Does the evidence suggests that doing these services are beneficial?
Motivation and goals	How motivated are you to deliver medication reconciliation and review? Are there incentives to provide these services? Do you have any other hospital activity that hinders these services?
Memory, attention and decision processes	Will you consider providing medication reconciliation and review services? If so, how frequently would you undertake this activity? How much priority have you given to these services?
Enviromental context and resources	To what extent do physical factors or resources facilitate or hinder to deliver medication reconicilation/review? Are there competing tasks and time constraints? Are the necessary resources available to undertake these services?

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	Do these services have advantages compared with the standard care? Do government and local authorties provide sufficient support for these services?
Social influences	Are clinical pharmacy services in the hospital well acknowledged by other healthcare professionals? Do hospital managers acknowledge your role? Is there any obstruction to these activities in your hospital? Have you observed others doing providing these clinical services?
Emotion	What things worry you the most in providing medication reconcilation/review services? To what extent do emotional factors facilitate or hinder these serivces?
Behavioural regulation	Have you received feeedback from other healthcare professionals regarding these services? What initial steps are needed to deliver these services?
Nature of the behaviours	What do you currently do? How long will changes going to take? Are there any systems in place for sustainable long term changes?

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A5.7 Interview Guide Questions – Amharic Version

ለጤና ባለሙያዎች የቀረበ ቃለ-መጠየቅ

1. ስራህ (ሽ) ምንድን ነው?ለምን ያህል ጊዜስ ቅይተሃል?
2. ብዙ ጊዜ ከማን ጋር በቅርርብ ትሰራለህ (ሽ)? (ከሐኪም/ነርስ/ፋርማሲስት/ከሌሎች)
3. ከሐኪም/ነርስ/ፋርማሲስት/ከሌሎች ጋር ያለህ (ሽ) የስራ ግንኙነት እንዴት ታየዋለህ (ሽ)?
4. በምትሰራበት ሆስፒታል የህሙማን ደህንነት ምን ያህል ቅድሚያ ይሰጠዋል? ለዚህ ማስረጃ ይኖራል?
5. የህሙማንን ድህንነት ከመጠበቅ አኳያ ሆስፒታልዎ ቅድሚያ የሚሰጣቸው ምን ይመስሉሃል (ሻል)? ምን ዓይነት ለውጦችስ ማየት ይፈልጋሉ?
6. በአንተ (ቺ) ዓመለካከት በእናንተ ሆስፒታል ያሉ ከመድሃኒት ጋር ተያይዞ የሚከሰቱ ችግሮች ዋና ዋናወቹ ምንድን ናቸው? ከመድሃኒት ጋር በተያያዘ በጣም የሚያስጨንቅህ ምንድን ነው?
7. ብዙ ጊዜ ምን ዓይነት ስህተቶች ይከሰታሉ? በምትሰራበት/በምትሰሪበት ቦታ በብዛት የሚከሰቱ የመድሃኒት አጠቃቀም ችግር ምንድን ናቸው?
8. የነዚህ ችግር መነሻ ምን ሊሆን ይችላል ብለህ ትገምታለህ (ሽ)? እንዴት መከላከል ይቻላል?
9. ላንተ (ች) የመድሃኒት ደህንነት ምንድን ነው?
10. እንዴትስ ከስራህ (ሽ) ጋ ይገናኛል?
11. የመድሃኒት ደህንነትን ከማሻሻል አኳያ የሆስፒታሉ ጠንካራ ጎን ምንድን ነው?
12. ይህንን ለመተግበር የነበሩ እንቅስቃሴዎች ነበሩ ወይ? ምን ያህልስ ውጤታማ ናቸው?
13. የመድሃኒት ደህንነትን ለማሻሻል የሚገጥሙ መሰናክሎች ምንድን ናቸው?
14. በምትሰራበት ቦታ ያለውን የህሙማን ደህንነት እንዴት ታየዋልህ (ሽ)?
15. የህሙማንን ደህንነት ለማረጋገጥ የምትጠቀምበት መመዘኛዎች ምንድን ናቸው?
16. በግልዎ ያደረጉትን እርምጃ ሊነግሩን ይችላሉ?
    ሀ. ስህተት ስትፈጥር (ሪ) ሪፖርት ታደርጋለህ (ሽ)?ለምን?
    ለ. ሌሎች ስህተት ሲሰሩ ብታገኝ ምን ታደርጋለህ (ሽ)?
    ሐ. ከመድሃኒት ጋር ተያይዘው ለሚከሰቱ ችግሮች ከህሙማን ጋር እንዴት ትወያያላቹህ?
    መ. በሚሰሩበት ቦታ ከመድሃኒት ጋ ተያይዞ የተከሰተ ችግር ካለ ቢያካፍሉን
17. ምን ዓይነት የህሙማን ደህንነት ማረጋገጫ እስትራቴጅ ተግባራዊ ቢሆን ትመርጣለህ?

የመድሃኒት ህክምና ተግዳሮቶች በተመለከተ የጤና ባለሙያዎችና የታካሚዎች ምልከታ

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18. ሆስፒታሉ ቢሰራበት ብለህ (ሽ) የምታስበው (የምታስቢው)? የሌሎች ጤና ባለሙያዎች ሚናስ?

<u>ለህሙማን የቀረበ ቃለ-መጠየቅ</u>

1. ወደ ሆስፒታል መጥተው ምን ዓይነት አገልግሎት አገኙ?

ሀ. ለምንስ ዓላማ ነበር?

ለ. በአገልግሎቱ ደስተኛ ነህ (ሺ)?

ሐ. ከሌሎች የጤና ተቋማት አገልግሎቱን አግኝተሀል? መቼ እና ለምን?

2. ሆስፒታሉን ለምን መረጥከው?

ሀ. ሆስፒታሉ ውስጥ ስለሚሰጠው የአገልግሎት ጥራት ምን ታስባለህ (ሽ)?

ለ. እንዴት አወቅህ (ሺ)?

ሐ. ማን ላከህ (ሽ)?

3. መድሃኒቶች አንዳንዴ ህሙማንን ሊጎዱ ይችላሉ ፤ነገር ግን ይህ ችግር በጤና ባለሙያዎች የተፈጠረ ላይሆን ይችላል ።ወደዚህ ሆስፒታል ሲመጡ ያጋጠምዎ እክል አለ?

ሀ. ያሳሰበህ (ሽ) ነገርስ ምንድን ነው?

ለ. እንዴት አወቀህ (ሽ)?

ሐ. ይህ እንዳይገጥምህስ ምን አደረግህ?

መ. የተሻለ ለማድረግስ ምን አሰብህ (ሽ)?

ሠ. ሆስፒታሉስ ምን ማድረግ አለበት ትላለህ(ሽ)?

4. የምትወስዳቸው መድሃኒቶች ሊያስከትሉ የሚችሉትን ጉዳት ከዶ/ር፤ ነርስ ወይም ፋርማሲስት በምን መልኩ ትወያያላቹህ?

ሀ. ከዚህ በፊት ኢጋጥሞህ ያውቃል?

ለ. እና ተገንዝበኸዋል?

ሐ. የመጨረሻ ውሳኔህ (ሽ) እንዴት አደረግህ(ሽ)?

5. በቅርቡ ወደ ሆስፒታል በሄድህበት (በሄድሽበት) ወቅት ያጋጠሙህ (ሽ) ወይም ያየሀችው(ያየሻቸው) ያላግባብ የሆኑ አሰራሮች/ስህተቶች/ የመድሃኒት አጠቃቀም ችግር አሉ?

ሀ. ለዚህ ችግር መፈጠር ተጠያቂው ማን ሊሆን ይችላል?

ለ. ችግሩን መከላከል ይቻላል ብለህ ታስባለህ? አዎ ካልህ (ሽ) ለምን እና እንዴት? ካልሆነስ ለምን?

ሐ. ሆስፒታሉ ችግሮችን እንዴት ይፈታቸዋል?

መ. ሆስፒታሉ ችግሮችን የሚፈታበት ሁኔታ ያስደስትዎታል?ለምን?

6. የህመማንን ድህንነት ከማስጠበቅ አኳያ ከተወሰዱ እርምጃዎች ያስገረመህ ምንድን ነው?

ሀ. ምን ነበር?

ለ. ማን አደረገው? እንዴት?

7. ጥራት ያለው የመድሃኒት አጠቃቀም እንዲኖርህ (ሽ) ተነግረዎታል?

ሀ. ምን አይነት ምክር ተመክረዋል?

ለ. ሆስፒታሉ እነዚህን ነገሮች አጽዕኖት ሰጥቷቸዋል ብለው ያስባሉ?

8. ሆስፒታሉ ቢሰራበት ብለህ (ሽ) የምታስበው (የምታስቢው)?

ለሆስፒታል ፋርማሲስቶች የቀረበ ቃለ-መጠየቅ

Domains	ቃለ-መጠየቅ
Knowledge	ሆስፒታሉ ክሊኒካል ፋርማሲ ሰርቪስ እንዲሰሩ ደንግጓል ወይ? ድንጋጌው ምን ይላል? ምን አይነት ማረጋገጫስ አለ? ስለ መድሃኒት ሪኮንስሌሽንና ሪቪው ምን ያውቃሉ? የመድሃኒት ሪኮንስሌሽንና ሪቪው ከማድረግ አኳያ የፋርማሲስትን ስራ ያውቃሉ? ለምን እንደሚሰሩስ ያውቃሉ?
Skills	ክሊኒካል ፋርማሲ ሰርቪስ እንዴት እንደሚሰራ ያውቃሉ? የመድሃኒት ሪኮንስሌሽንና ሪቪውስ እንዴት እንደሚሰራ ያውቃሉ? ከመድሃኒት ጋር ተያይዞ የሚከሰቱ ችግሮችን መለየት ይከብደዎታል? ክሊኒካል ፋርማሲ ሰርቪስ ለመስጠት ሰልጥነዋል?
Social/professional role	መድሃኒት ሪኮንስሌሽንና ሪቪው መስራት ሙያው ይፈቅዳል? ይህን አገልግሎት የሚሰጠው በዋናነት ማን ነው? የሆስፒታሉ ደንብ የመድሃኒት ደህንነትን ማስጠበቅ እንደሙያዊ ስራ አድርጎ ይወስደዋል ወይ?
Beliefs about capabilties	የክሊኒካል ፋርማሲ ሰርቪስ መስራት ምን ያህል ከባድ ወይም ቀላል ነው? ምን አይነት ችግርስ ኣጋጠመዎት? መድሃኒት ሪኮንስሌሽንና ሪቪው መስራት ምን ያህል ይችላሉ? ችግሮችም ቢኖሩ እነዚህን አገልግሎቶች ለመስጠት ምን ያህል እርግጠኛ ነዎት? እነዚህን አገልግሎቶች ሲሰጡ ምን ያህል ምቾት ይሰጠዎታል?
Beliefs about consequences	ከመድሃኒት ጋር ተያይዞ የሚከሰቱ ችግሮችን ሪፖርት ማድረግ ምን አይነት አዎንታዊም ይሁን አሉታዊ ተፅዕኖ አለው? መድሃኒት ሪኮንስሌሽንና ሪቪው መስጠት ምን ያህል ያስከፍላል? የእነዚህ አገልግሎቶች ውጤትስ ምን ያህል ያወጣል? እነዚህ አገልግሎቶች ሆስፒታል ውስጥ ባይኖሩስ?

	የእነዚህ አገልግሎቶች ጥቅም ከወጫቸው ያመዝናል? እነዚህን አገልግሎቶች መስጠት ጥሩ ነው የሚል ማስረጃስ አለ?
Motivation and goals	መድሃኒት ሪኮንስሌሽንና ሪቪው ለመስጠት ምን ያህል ዝግጁ ነዎት? እነዚህን አገልግሎቶች ለመስጠት የተለየ የሆነ ማበረታቻ አለ? እነዚህን እንዳትሰራ የሚያደርግ ሌላ የሆስፒታል ስራ አለዎት ወይ?
Memory, attention and decision processes	መድሃኒት ሪኮንስሌሽንና ሪቪው ለመስጠት አስበው ያውቃሉ? ከሆነስ ምን ያህል? ለእነዚህ አገልግሎቶችስ ምን ያህል ዋጋ ይሰጣሉ?
Enviromental context and resources	ፊዚካል ፋክተርስ ወይም ሪሶርስስ እነዚህን አገልግሎቶች ለመስጠት ምን ያህል ያፋጥናሉ ወይም ይጎትታሉ? ሌላ ስራ እንዲሁም የጊዜ መጣበብ አለ ወይ? እነዚህን አገልግሎቶች ለመስጠት አስፈላጊው ሪሶርስስ አሉ? እነዚህ አገልግሎቶች በፊት ሲሰራበት ከነበረው የተለየ ጥቅም ይኖራቸዋል? እነዚህ አገልግሎቶች እንዲሰጡ መንግስትና የበላይ አካላት ድጋፍ ያደርጋሉ ወይ?
Social influences	የክሊኒካል ፋርማሲ ሰርቪስን ሌሎች የጤና ባለሙያዎች ተቀብለው ታል? የሆስፒታል ኃላፊዎችስ? ሆስፒታል ውስጥ ስራዎን የሚያደናቅፍ አለ? ይህን ስራ ሌሎች ሲሰሩ አይተው ያውቃሉ?
Emotion	መድሃኒት ሪኮንስሌሽን/ሪቪው ለመስጠት ያስጨንቀኛል የሚሉት ምንድን ነው? ምን ያህል ስሜታዊ ባህሪዎ ይህን ሰርቪስ ያፋጥነዋል ወይም ይጎትተዋል ይላሉ?
Behavioural regulation	ስለእነዚህ አገልግሎቶች ከሌሎች የጤና ባለሙያዎች አስተያየት ተቀብለው ያውቃሉ? እነዚህን አገልግሎቶች ለመስጠት ምን አይነት ቅድመ ሁኔታዎች ያስፈልጋሉ ይላሉ?
Nature of the behaviours	አሁን ምን እየሰሩ ነው? ለውጥ ለማየት ምን ያህል ጊዜ ይፈጃል? ቀጣይነት ያለው ለውጥ ለማየት የሚያስችል ሲስተም አለ ወይ?

Appendix 6. Prospective Study Documents

A6.1 Participant Information Statement – English Version

ABN 15 211 513 464

Jo-anne Brien BPharm BS (Pharm), PharmD, FRPharmS
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NSW 2006 AUSTRALIA
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Web: http://www.sydney.edu.au/

"A pilot study of a medication reconciliation service in an Internal Medicine ward of Gondar University Hospital"

PARTICIPANT INFORMATION STATEMENT

What is this study about?

You are invited to take part in a research study about your medication use before and after your admission to a hospital and the aim of this project is to pilot test a medication reconciliation service in Gondar University Hospital (GUH), Ethiopia.

You have been invited to participate in this study because you are currently admitted to an internal medicine ward of Gondar University Hospital. This Participant Information Statement tells you about the research study. Knowing what is involved will help you decide if you want to take part in the research. Please read this sheet carefully and ask questions about anything that you don't understand or want to know more about.

Participation in this research study is voluntary.

By giving your consent to take part in this study you are telling us that you:

- ✓ Understand what you have read.
- ✓ Agree to take part in the research study as outlined below.
- ✓ Agree to the use of your personal information as described.

Who is running the study?

The study is being conducted by Alemayehu B Mekonnen and will form the basis for the degree of Doctor of Philosophy at the University of Sydney under the supervision of Professor Jo-anne Brien and Professor Andrew McLachlan (Faculty of Pharmacy, University of Sydney) and Dr. Desalew Mekonnen and Dr. Zenahbezu Abay (Department of Internal Medicine, University of Gondar)

What will the study involve for me?

In this study, you will be asked to access your medical records for medication use during your hospital stay. From the medical record, information including your age, sex, diagnosis, co-morbidities, medication use (during admission and discharge), and any documented concerns in the medication use process will be collected. The confidentiality of your personal details will be maintained at all times. Any publications arising from this study will not include information identifying individual participants.

Who can take part in the study?

The inclusion criteria will be that patients with age of over 18 years, had been hospitalized for at least 24 hours and taking at least two home/regular medications on admission.

Can I withdraw from the study?

Being in this study is completely voluntary and you do not have to take part. Your decision whether to participate will not affect your current or future relationship with the researchers or anyone else at the University of Sydney/ Gondar University Hospital staffs.

If you decide to take part in the study and then change your mind later, you are free to withdraw at any time. You can do this by notifying the researcher, and the information we have collected will no longer be included in the study results.

If you decide to withdraw from the study, we will not collect any more information from you. Please let us know at the time when you withdraw what you would like us to do with the information we have collected about you up to that point. If you wish your information will be removed from our study records and will not be included in the study results, up to the point that we have analysed and published the results.

Are there any risks or costs associated with being in the study?

Aside from giving up your time, we do not expect that there will be any risks or costs associated with taking part in this study.

Will the study benefit me?

You may receive non-financial direct benefits from the medication reconciliation service that would be tested – for example, prevention of medication related events and/or counselling on appropriate use of medications.

What will happen to information about me that is collected during the study?

By providing your consent, you are agreeing to us collecting personal information about you for the purposes of this research study. Your information will only be used for the purposes outlined in this Participant Information Statement, unless you consent otherwise.

Your information will be stored securely and your identity/information will be kept strictly confidential, except as required by law. Study findings may be published, but you will not be individually identifiable in these publications.

Will I be told the results of the study?

You have a right to receive feedback about the results of this study. You can tell us that you wish to receive feedback by ticking the relevant box on the consent form. This feedback will

be delivered to a nominated physician immediately after the identification of any medication-related problem.

Researchers contact information

If you have any questions or would like to know more about this study, please feel free to contact the chief investigator, Professor Jo-anne Brien on Telephone (+61 2 9351 2363) or at joanne.brien@sydney.edu.au (Email) Or the onsite project researcher, Dr. Zenahbezu Abay on Telephone (+ 251920 24 81 30) or at Email (abayzenah@yahoo.com)

Alternatively the student researcher, Mr Alemayehu B Mekonnen, may be contacted on Telephone (+251973937980) or at email: aber5592@uni.sydney.edu.au

What if I have a complaint or any concerns about the study?

Research involving humans in Australia is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this study have been approved by the HREC of the University of Sydney (Protocol number: 2015/818). As part of this process, we have agreed to carry out the study according to the *National Statement on Ethical Conduct in Human Research (2007).* This statement has been developed to protect people who agree to take part in research studies.

If you are concerned about the way this study is being conducted or you wish to make a complaint to someone independent from the study, please contact the university using the details outlined below. Please quote the study title and protocol number.

The Manager, Ethics Administration, University of Sydney:

- **Telephone:** +61 2 8627 8176
- **Email:** ro.humanethics@sydney.edu.au
- **Fax:** +61 2 8627 8177 (Facsimile)

Or for local complaints contact:

Nebiyu Mesfin, Director of the Institutional Review Board of the University of Gondar

- **Telephone**: +251926042997
- **Email**: hakimulig@gmail.com

A6.2 Participant Information Statement – Amharic Version

ABN 15 211 513 464

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Web: http://www.sydney.edu.au/

"የመድሃኒት ሪኮንስሌሽን አገልግሎት ለመተግበር የሚደረግ የመኪራ ጥናት በጎንደር ዩኒቨርስቲ ሆስፒታል በውስጥ ደዌ ት/ት ክፍል"

<u>ለተሳታፊው መረጃ</u>

ጥናቱ ስለምድን ነው?

ሆስፒታል ከመግባትዎ በፊትና ከገቡ በኃላ ያለውን የመድሃኒት አጠቃቀም ለመዳሰስ ይህ ጥናት ጋብዟችኋል፤ የምርምር አላማውም የመድሃኒት ሪኮንስሌሽን አገልግሎት በጎንደር ዩኒቨርስቲ ሆስፒታል ፣ኢትዮጵያ የመኪራ ጥናት ለማድረግ ነው።

የተጋበዙበትም ምክንያት በጎንደር ዩኒቨርስቲ ሆስፒታል በውስጥ ደዌ ት/ት ክፍል ተኝተው እየታከሙ ስለሆነ ነው።

ይህ የተሳታፊ መረጃ ስለዚህ ጥናት ያትታል።ጥናቱ የሚያካትታቸውን ነገሮች ማወቅ የጥናቱ ዓካል ለመሆን ያለወትን ፍላጎት ለመወሰን ያስችላል። ስለዚህ እባክ ዎን በጥንቃቄ ያንብቡና ያልተረዱትን ወይም የበለጠ ማወቅ የሚፈልጉትን ይጠይቁ።

ጥናቱ በፈቃደኝነት ላይ የተመሰረተ ነው።

በዚህ ጥናት ፍቃደኝነትዎን በማሳወቅ፤ የሚከተሉትን እንደገለፁልን፡-

- ✓ ያነበቡትን እንደተረዱና
- ✓ ከዚህ በታች እንደተገለፀው በጥናቱ ተሳታፊ ለመሆን እንደተስማሙ
- ✓ እንደተገለጠው ግላዊ መረጃ እንደንጠቀም ስለመፍቀድዎ

ጥናቱን የሚያካሂደው ማን ነው?

ጥናቱ የሚከናወነው በአቶ አለማየሁ ብርሃኔ በኩል ሲሆን ይህም ለእሱ ፒኤችዲ ማሚያ ከሲዲኒ ዩንቨርስቲ በ ፐ/ር ጆ አን ብራይን እና በ ፐ/ር አንድሪው ማክላችላን (ከ ፋርማሲ ት/ት ክፍል፤ ሲዲኒ ዩንቨርስቲ) እና ዶ/ር ደሳለው መኮነን እንዲሁም ዶ/ር ዝናህብዙ አባይ (ከውስጥ ደዌ ት/ት ክፍል: ጎንደር ዩንቨርስቲ) መሪነት ነው።

ጥናቱ ከእርስዎ የሚፈልገው?

በዚህ ጥናት የእርስዎን የመድሃኒት አጠቃቀም በተመለከተ መረጃ ለማግኘት የህክምና ማህደርዎን እንጠቀምበት ዘንድ ይጠየቃሉ። ከህክምና ማህደርዎም እድሜዎን፣ፆታዎን፣ በሽታዎን፣ተጓዳኝ በሽታዎንና እየተጠቀሙ ያለውን መድሃኒት (ሲገቡና ሲወጡ) እንዲሁም በመድሃኒት አጠቃቀም ወቅት ያጋጠሙ ማናቸውም እክሎች ይሰበሰባሉ።ማናቸውም የሚሰጡት መረጃ ሚስጥራዊነቱ የተጠበቀ ነው። ከዚህ ምርምር የሚወጡ ፅሁፎች የማናቸውንም የምርምር ተሳታፊዎች የማንነት መረጃ አያወጣም።

በጥናቱ የሚሳተፉት እነማን ናቸው?

ዕድሚያቸው ከ 18 ዓመት እና ከዚያ በላይ፣ ቢያንስ ለ 24 ሰዓት ተኝተው የሚታከሙና ወደ ሆስፒታል ሲመጡ ቢያንስ 2 መድሃኒት እየወሰዱ የነበሩ ታካሚዎችን ይመለከታል።

ከጥናቱ መውጣት ይቻላል?

ጥናቱ ሙሉ በሙሉ በፍቃደኝነት የተመሰረተ ነው፤ መሳተፍም ግዴታ አይደለም።ተሳትፎ ለማድረግ በመወሰንህ (ሽ) ይህን ጥናት ከሚያደርጉ የጎንደር/የሲዲኒ ዩኒቨርስቲ ሰራተኞች ወይም ሌሎች ሆስፒታል ሰራተኞች ጋር ያለህን (ሽን) የነበረ ወይም ወደ ፊት የሚኖረውን ግንኙት የሚጎዳ አይሆንም።

በጥናቱ ለመሳተፍ አስበው፣ በኋላ ግን ሃሳብዎን ከቀየሩ በማናቸውም ጊዜ ከጥናት እራስዎን ማግለል ይቻላል፣የተሰበሰበ መረጃ ካለም የጥናቱ አካል አይሆንም።

ከጥናቱ እራስዎን ማግለል ካሰቡ ምንም አይነት ተጨማሪ መረጃ ከእርስዎ አንወስድም። እባክዎን ጥናቱ እስኪቋረጥ ድረስ የተሰበሰበው መረጃ ምን እንድናደርገው እንደፈለጉ ያሳውቁን።

ስለእርስዎ ያለን መረጃ ካለን የጥናት መረጃ ማህደር እንዲወጡ ከፈለጉ፣የጥናቱ ውጤት አካልም ዓይሆኑም፣ እስከህትመትም አይደርሱም።

በጥናቱ መሳተፌ ማናቸውም ዓይነት ጉዳት ወይም ወጪዎች ይኖሩብኛል?

A pilot study of a medication reconciliation service in an Internal Medicine ward of Gondar University Hospital
Version 1.0 January 22, 2016

ጊዜዎን ከመሻማት በስተቀር በዚህ ጥናት መሳተፍ ምንም አይነት ጉዳት ወይም ወጭዎች ይኖርብዎታል ብለን አንጠብቅም።.

ጥናቱ ሊጠቅመኝ ይችላል?

ከመድሃኒት ሪኮንስሊሽን አገልግሎት በገንዘብ የማይመነዘር ጥቅም ሊያገኙ ይችላሉ። ለምሳሌ፦ ከመድሃኒት ተያያዥነት ያላቸው እክሎችን መከላከል እና/ ወይም ስለመድሃኒት አጠቃቀም የምክር አገልግሎት መስጠት

ስለእኔ የተሰበሰበው መረጃ ምን ይሆናል?

ለዚህ ጥናት ዓላማ ሲባል ፍቃድኝነትዎን በመስጠት መረጃ እንድንሰበስብ ተስማምተዋል። መረጃዎ በዚህ በተሳታፊው መረጃ አንቀፅ እንደተገለፀው ለዚህ ዓላማ ብቻ ይውላል፣ ከፍቃድዎ ውጭ የሚሆን ምንም ነገር የለም።

መረጃዎ በጥንቃቄ ታሽጎ ይቀመጣል፣ ሚስጥርዎ በጥብቅ የተጠበቀ ነው። ጥናቱ ሊታተም ይችላል ነገር ግን ማናቸውም ህትመት ስምዎን አይጠቅስም።

የጥናቱ ውጤት ይነገረኛል?

ስለጥናቱ ውጤት የማወቅ መብት አለዎት።ፍላጎትዎን ከፍቃደኝነት መጠየቂያ ፎርም ላይ ጭረት በማድረግ ማሳወቅ ይቻላል።. ከመድሃኒት ጋር ተያያዥ ያላቸው ችግሮች ከተገኙ የሚያገለግልዎት የጤና ባለሙያ እንዲያውቅ ይደረጋል።

ጥናቱን የሚያካሂዱትን ማግኘት ከፈለጋቹሁ

ማነኛውም ስለጥናቱ ማወቅም ሆነ ጥያቄ መጠየቅ ከፈለጋቹሁ፣ እባክዎትን ፕ/ር ጆ ኣን ብራይን በስልክ ቁ. +61 2 9351 2363 ወይም በ ኢሜይል አድራሻ joanne.brien@sydney.edu.au ፣ ዶ/ ር ዝናህ ብዙ አባይን በስልክ ቁ + 251920 24 81 30 ወይም በ ኢሜይል አድራሻ abayzenah@yahoo.com

ወይም አቶ አለማየሁ ብርሃኔን በስልክ ቁ +251973937980 ወይም በ ኢሜይል አድራሻ aber5592@uni.sydney.edu.au ማግኘት ይቻላል።

አቤቱታ ወይም ቅሬታ ቢኖረኝስ?

አውስትራሊያ ውስጥ በሰው ላይ የሚከናወን ምርምር ሂውማን ሪሰርች ኢቲክስ ኮሚቴ (HREC) በሚባል የገለልተኛ ሰወች ስብስብ ይታያል። ይህ ጥናት በሲዲኒ ዩንቨርስቲ HREC ፀድቋል (ፕሮቶኮል ቁጥር፡ 2015/818) ።

በዚህ ሂደት መሰረት ጥናቱ በብሔራዊ የስነ ምግባር ደንብ (2007) መሰረት እንድምንሰራው ተስማምተናል።. ይህ ደንብ የወጣው በምርምር ስራዎች የሚሳተፉ ሰዎችን ለመጠበቅ ነው።

A pilot study of a medication reconciliation service in an Internal Medicine ward of Gondar University Hospital
Version 1.0 January 22, 2016

የጥናቱ አካሂድ ላይ አቤቱታ ካለብዎት ወይም ቅሬታዎን ለሌላ አካል ማሳወቅ ከፈለጉ እባክዎ ን ዩንቨርስቲውን ታች

በተገለፀው አድራሻ ያመልክቱ። የጥናቱን ርዕስና ፕሮቶኮል ቁጥር ያጣቅሱ።

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- **ኢሜይል:** ro.humanethics@sydney.edu.au
- **ፋክስ:** +61 2 8627 8177

ወይም በአካባቢዎ አቤቱታዎን ለማቅረብ:

ኑብዩ መስፍን: የጎንደር ዩንቨርስቲ ኢንስቲቱሽናል ሪቪው ቦርድ ዳይሬክተር

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A6.3 Consent Form – English Version

ABN 15 211 513 464

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"A pilot study of medication reconciliation service in an Internal Medicine ward of Gondar University Hospital"

PARTICIPANT CONSENT FORM

I,..... [PRINT NAME], agree to take part in this research study.

In giving my consent I state that:

- ✓ I understand the purpose of the study, what I will be asked to do, and any risks/benefits involved.
- ✓ I have read the Participant Information Statement and have been able to discuss my involvement in the study with the researchers if I wished to do so.
- ✓ The researchers have answered any questions that I had about the study and I am happy with the answers.
- ✓ I understand that being in this study is completely voluntary and I do not have to take part. My decision whether to be in the study will not affect my relationship with the

researchers or anyone else at the University of Sydney and University of Gondar now or in the future.

- ✓ I understand that I can withdraw from the study at any time.
- ✓ I understand that personal information about me that is collected over the course of this project will be stored securely and will only be used for purposes that I have agreed to. I understand that information about me will only be told to others with my permission, except as required by law.
- ✓ I understand that the results of this study may be published, but these publications will not contain my name or any identifiable information about me.

Would you like to receive feedback about the results of this study?

YES ☐ NO ☐

If you answered **YES**, please indicate your preferred form of feedback and address:

☐ Postal: _____

☐ Email: _____

.....

Signature

.....

PRINT name

.....

Date

A6.4 Consent form – Amharic Version

ABN 15 211 513 464

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"የመድሃኒት ሪኮንሲሌሽን አገልግሎት ለመተግበር የሚደረግ የሙከራ ጥናት በጎንደር ዩኒቨርስቲ ሆስፒታል በውስጥ ደዌ ት/ት ክፍል"

<u>የተሳታፊዎች ፍቃደኝነት ማሳወቂያ ፎርም</u>

እኔ _____ (ስም) በዚህ ጥናት ለመሳተፍ ተስማምቻለሁ።

ስለማማም፥

- የጥናቱን ዓላማ ተረድቸዋለሁ፤ ምን መጠየቅ እንዳለብኝም አውቃለሁ።
- ስለተሳታፊው የተገለፀውን አንብቢያለሁ፤እናም በጥናቱ ለመሳተፍ ከፈለግሁኝ ከተመራማሪዎች ጋር እወያያለሁ።
- ተመራማሪው ለሚጠይቀኝ ማንኛውም ጥያቄ ለመመለስ ደስተኛ ነኝ።
- ጥናቱ ሙሉ በሙሉ በፍቃደኝነት የተመሰረተ ነው፤ መሳተፍም ግዴታ አይደለም።ተሳትፎ ለማድረግ በመወሰንህ(ሽ) ከጎንደር ዩኒቨርስቲ ሰራተኞች ወይም ይህን ጥናት ከሚያደርግ ሰው ጋ ያለህን (ሽን)የነበረ ወይም ወደ ፊት የሚኖረውን ግንኙት የሚጎዳ አይሆንም።
- በማንኛውም ሰዓት ከጥናቱ መውጣት እንደምችል ተረድቻለሁ።
- በማንኛውም ሰዓት ቃለ መጠየቁን የመተው መብት አለኝ። የምሰጠው መረጃ እንዲጠቀሙበት እስካልፈቀድኩኝ ድረስ ማንኛውም መረጃወች ይደመሰሳሉ ወይም የጥናቱ አካል አይሆኑም። መመለስ የማልፈልገውን ጥያቄ አለመመለስ እችላለሁ።

- በዚህ ፕሮጀክት የሚሰበሰበው ግለሰባዊ መረጃ በጥብቅ እንደሚጠበቅ ተረድቻለሁ፣ለዚህ ዓላማም ብቻ እንደሚያገለግልም ተረድቻለሁ።
- ስለ እኔ መረጃ ለሌሎች ለማሳወቅ የእኔን ፍቃደኝነት እንደሚጠይቁ ተረድቻለሁ።
- ይህ ጥናት ህትመት ላይ እንደሚውል እረዳለሁ፣ ነገር ግን ማናቸውም ህትመት የእኔን ስም መጥቀስ አይችልም።

ስለጥናቱ ውጤት ማወቅ ይፈልጋሉ?

አዎ ☐ አይደለም ☐

መልስዎ አዎ ከሆነ እባክዎን እንዴት እንደምናሳውቀዎ ይግለፁልን

☐ በፖስታ _____

☐ በኢሜይል _____

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A6.5 Data Collection Tool

Data collection tool

1. **Socio-demographic, diagnosis and medication therapy data abstraction form**

Patient initials: _____Card. No.:_____ Bed No._____

Patient age: _____ Sex: M _____ F _____

Date of admission: _____ Date of discharge: _____

Current working Diagnosis: _____

Other co-morbidities: _____

_____

Medication history form

Allergy history: _____

No. of medications on admission _____

Previous/Home medications (Includes prescriptions, OTC medications, herbal/dietary supplements)

Ser. No	Previous/Home medications	Dose	Route	Frequency	duration	Treatment continued (Yes/No)

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Current medications

Ser. No	Drug name	Dose , Route, Frequency, duration	Date started	Date stopped	Remarks

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Discharge medications

Ser. No	Drug name	Dose, Route, Frequency, duration	Remarks

N.B. For PRN medication, please include the dose, time and date given

If there is any patient concerns in the medication use process (eg. Significant drug-drug interactions, any medication related problems), specify

_____

_____

Final Diagnosis (Discharge summary):

NB: For this patient, fill the following up on discharge:

1. Total number of medications the patient took
2. Total number of medication doses s/he took during stay
3. If there is any discrepancies in treatment identified at any time in this patient, please use the medication discrepancy collection form.

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2. Medication discrepancies collection form

I. Patient information:

Age : _____

Sex: Male_____ Female ____

Diagnosis: _____

II. Occurrence of medication discrepancies

A) What type (s) of discprenacy (cies) is it?

1) Intentional medication discrepancies

a) Yes

b) No

2) Unintentional medication discrepancies

a) Yes

b) No

B) If it is unintentional medication discrepancy, please describe the error, including description and consequences if any

C) Is this error occurred at admission, or discharge?

III. What type (s) of medication error (s) is occurred in this patient? (tick all that apply)

a) Omitted drug

b) Discrepant in frequency

c) Discrepant in dose

d) Discrepant in route

e) Commission error

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f) Different drug from the same therapeutic class without clinical explanation

g) Others, specify _____

Clinical severity assessment

Categorizing the clinical seveirty of unintentional medication discrepancies (Adapted from Cornish et al 2005)

a) Class 1=Unlikely to cause patient discomfort/clinical deterioration

b) Class 2= moderate discomfort/clinical deterioration

c) Class 3= severe discomfort/clinical deterioration

Appendix 7. Safety Protocol

Safety protocol

We planned to conduct a research in a low resource setting taking Ethiopia as a case. It is a medication safety initiative aimed at implementing a new pharmacy service. The protocol listed under with is an assessment of possible risks to the safety of Mr Alemayehu B Mekonnen. Although Mr Mekonnen is originally from Ethiopia where the research will be conducted, we tried to list down the possible risks and mitigating measures to manage those risks as below:

- The researcher understands that this form of research carries with it a set of unique challenges and issues. The following undertakings have been devised to minimise the risks involved while not placing undue constraints on the conduct of the research.
- Previous experience in working or researching in the area to be visited.
- Familiarity with, or expertise in, the local language
- The researcher's local contact person is: Dr. Zenahbezu Abay (Telephone:+ 251920 24 81 30 or Email:abayzenah@yahoo.com)
- The researcher has a high level of knowledge of the geographic, social, political, cultural, ethnic and religious contexts of the region. This includes familiarity with accepted gender norms within the research context, and an understanding of the limitations these may place on the research
- The researcher has confirmed that there are currently no travel warnings from the Department of Foreign Affairs and Trade for Ethiopia
- The researcher undertakes to follow the University of Sydney guidelines on Fieldwork Safety Standards
- This safety protocol has been agreed and accepted by the researcher and the co-researcher named in the protocol

Professor Jo-anne Brien

Alemayehu B Mekonnen

Appendix 8. Coding Guide: Description of 12 Theoretical Domains from TDF

Domain label	Description of domain content
Knowledge	Knowledge of the field (i.e. whether there is adequate evidence) and individuals' knowledge of the evidence or of a guideline.
Skills	Covers the possibility that new skills would be required by the staff who are required to implement a new procedure.
Social/professional role and identity	The clinical thinking and norms of a particular profession.
Beliefs about capabilities	How confident clinicians are that they could change their practice effectively
Beliefs about consequences	Often regarded as core to clinical reasoning, this domain covers the perceived benefits and harms of a clinical action. In some contexts it can also include consequences for the clinician such as workload, pay, career progression, or for the hospital or health service.
Motivation and goals	The relative priority that is given to one clinical issue, compared with other demands.
Memory, attention and decision processes	The level of attention that is needed to perform the key clinical action (i.e. is forgetting likely to be a problem) and the processes by which clinical decisions are made by individuals and teams.
Environmental context and resources	Includes the physical (including financial) issues that may limit change, including staffing levels and time as well as equipment or space.

Social influences	The influence of other individuals or groups on clinical practice, for example, patients, patients' families, pressure groups.
Emotion	Includes issues such as work stress, patient anxiety and other emotional factors that may help or hinder the uptake of new approaches to care.
Behavioural regulation	Includes the 'how' of changing clinical practice: what are the practical strategies that would facilitate or hinder uptake of a new practice.
Nature of the behaviours	Some new practices are very similar to current practice and so are easier to implement than new practices that require a dramatic change in ways of working.

Source: Cuthbertson et al 2013.