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*PhD Title: The role of pharmacists in the management of
chronic disease and prevention of adverse drug reactions*

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I am aware of university regulations governing plagiarism and I declare that this document is all my own work except where I have stated otherwise.

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Dedications

I would like to dedicate this PhD thesis to my wife and my two lovely children. I would also like to dedicate this thesis to my parents for their support and encouragement.

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List of abbreviations

ADR	Adverse drug reaction
BMJ	British Medical Journal
CI	Confidence interval
COPD	Chronic Obstructive Pulmonary Disease
CPCF	Community pharmacy contractual framework
CRD	Centre for reviews and dissemination
CSM	Committee on the Safety of Medicines
CVD	Cardiovascular disease
DBP	Diastolic blood pressure
DRP	Drug related problem
ED	Emergency Department
HSE	Health survey for England
LDL	Low density lipoprotein
MHRA	Medicines and Healthcare Products Regulatory Agency
MI	Myocardial infarction
MUR	Medicine use review
NICE	National Institute for Health and Care Excellence
NMS	New medicines service
NSAIDs	Non-Steroidal Anti-inflammatory drugs
OTC	Over the counter
PSNC	Pharmaceutical Services Negotiating Committee
RCT	Randomised controlled trial
REV MAN	Review manager (software for meta-analysis)

RPS	Royal Pharmaceutical Society
SBP	Systolic blood pressure
SD	Standard deviation
SJS	Stevens-Johnson syndrome
TEN	Toxic epidermal necrolysis
UHCW	University Hospital Coventry and Warwickshire
WHO	World Health Organisation

Abstract

Community pharmacists are increasingly expected to improve disease management both by aiming to improve the effective use of medicines and by reducing the occurrence and severity of preventable adverse drug reactions (ADRs). The current PhD research began by assessing the challenges to the medicines reconciliation from patients' perspectives. A questionnaire-based audit identified two important risk factors for reporting ADRs: being unaware of why medicines were prescribed and not recalling prior warnings about possible ADRs. These findings led to the evaluation of pharmacists' engagement with patients within pharmacy services such as the New Medicine Service (NMS).

A questionnaire-based service evaluation of the NMS provided support for this service as an opportunity to improve identification and management of ADRs. This evaluation also highlighted the poor contribution of pharmacists towards reporting of ADRs. The findings led to the evaluation of ADR reporting by community pharmacists. This audit-based study identified lack of time and uncertainty about the seriousness of ADRs as the main barriers towards spontaneous reporting. The reporting of ADRs linked to high blood pressure medicines in this study indicated the need to assess the role of community pharmacists in the management of high blood pressure. A systematic review and meta-analysis suggested that pharmacist-led interventions made a significant impact on the management of systolic and diastolic blood pressure.

Learning from two audits, a service evaluation and a systematic review led to the development of a randomised controlled trial that assessed the impact of written pharmacist-led education on patients with high blood pressure. Interventions by pharmacists working in community pharmacies were associated with improvements in the control of hypertension, however, the mean difference in blood pressure between the intervention and control group was not statistically significant. Compared to participants in the control group, there was a significant improvement in the knowledge about hypertension and its treatment in the intervention group. The participants in this study gave a positive response about the involvement of pharmacists in the management of long-term medical conditions such as hypertension.

The UK government wants to see a central role for pharmacists in patient care. The evidence presented in this research suggests that pharmacists have the potential to play a bigger role in patient care. Patients also recognize this potential and appear to be willing to seek pharmacists' advice on health-related issues. Pharmacists would need to identify their specific learning needs to help them deliver a more patient-centred care. They would also require the support and recognition from other stakeholders in particular the GPs.

Executive summary

The primary focus of this thesis is to determine whether studying patients' knowledge about their medicines and pharmacists' systems for interacting with patients may lead to identifying ways in which pharmacists can improve their role in patient care. This thesis assessed patients' knowledge about their medicines and evaluated the engagement of community pharmacists with patients about their medicines. It also reflected on the level and understanding of pharmacists about ADRs and used a systematic review and meta-analysis to report the efforts of pharmacists in the management of chronic disease. Finally, it used a randomised controlled trial (RCT) to illustrate the potential of pharmacists in the management of hypertension.

Chapter 1: This chapter serves as a background to the thesis. It considers the importance of ADRs, the role of medicines reconciliation in reducing the severity of ADRs and challenges to the effective implementation of medicines reconciliation. This chapter also explores the possible association of patients' knowledge about their medications with the incidence of ADRs and the role of the NMS in improving medication use in patients. Furthermore, it discusses the contribution of pharmacists in the reporting of ADRs. Finally, this chapter uses hypertension as a test of concept to illustrate the potential for pharmacists' involvement in chronic disease management.

Chapter 2: This chapter outlines the overall research question and the aims and objectives of this research.

Chapter 3: This chapter assesses the challenges to medicines reconciliation in the Emergency Department (ED) and investigates the relationship between patients' knowledge about their

medicines and self-reported ADRs. A two phased questionnaire-based audit was conducted in the ED of a large teaching hospital in the Midlands (UK) from February to March, 2012. Patients were asked to provide names and reasons for their treatment(s) including over the counter products and to record any experience of ADRs. 341 patients were assessed over a period of 20 days. Information from 25% of the study group on their medications was either unavailable or limited. Twenty-two patients were not taking medications and 59 were not well enough to participate. Two important risk factors for reporting ADRs were identified: being unaware of why medicines were prescribed (odds ratio 3.9, 95% Confidence Interval CI 1.5 to 8.7, $p = 0.001$) and not recalling prior warnings about possible ADRs (odds ratio 12.2, 95% CI 4.7 to 30.6, $p < 0.001$). This study highlights the importance of obtaining accurate information from high risk patients about their medications and the challenges involved in capturing this vital information. However, in the absence of an independent verification of the information provided by patients through an adapted questionnaire, the findings of this study should be interpreted with caution. Majority of the patients included in this study did not recall prior advice given to them by the pharmacists on potential ADRs. These findings led to evaluate the engagement of pharmacists with patients within the current pharmacy services such as the NMS.

Chapter 4: This chapter evaluates the impact of the NMS on medication use in patients starting a new medication for a long-term medical condition. A questionnaire-based service evaluation was conducted in community pharmacies located in the West Midlands area for three months from July to September, 2012. 20 community pharmacists based in 14 pharmacies returned 295 questionnaires from which completely anonymised data of 285 patients was included in the study (160 female and 125 male). On the first NMS assessment, 82 patients reported drug-related problems including adverse effects and incorrect use of

medications. Of the 82 patients, 58 patients received advice from pharmacists. At the NMS follow up stage, 39 (67%) of the 58 patients who received advice from pharmacists reported resolution of their drug-related problems while only four (17%) of the 24 patients who did not receive pharmacists' advice reported resolution of their problems (odds ratio 10.2, 95% CI 3.0 - 34.2 $p < 0.001$). A total of 51 patients reported suspected ADRs with their medicines in this study. However, pharmacists who participated in this study did not report any of the suspected ADRs to the Medicines and Healthcare Products Regulatory Agency (MHRA). The poor contribution of pharmacists towards ADR reporting led to the evaluation of ADR reporting by pharmacists.

Chapter 5: This chapter aims to evaluate the reporting of ADRs by community pharmacists. A questionnaire based audit was conducted in the UK from April to September 2012. A total of 139 questionnaires were returned (78 females and 61 males). Two important factors for reporting an ADR were identified: being confident of which reactions to report (odds ratio 1.8, 95% CI 1.1 to 3.0 $p = 0.011$ Fisher's exact test) and being confident of how to report (odds ratio 4.3, 95% CI 2.5 to 7.5 $p < 0.0001$). Lack of time and uncertainty about the seriousness of an ADR were among the barriers to spontaneous reporting. However, the use of an adapted questionnaire indicates that the findings of this study should be viewed with caution. Pharmacists reported a number of ADRs suspected with anti-hypertensive medications. The association of ADRs with anti-hypertensive medications led to the assessment of the impact of pharmacist-led interventions on blood pressure control.

Chapter 6: This chapter presents a systematic review and meta-analysis of RCTs that assessed the impact of community pharmacist-led interventions on blood pressure control in patients with hypertension. Eight electronic databases were searched up to 30th November 2013, with

no start date (Web of Science, Embase, The Cochrane Library, Medline Ovid, Biomed Central, Biosis, Citation Index, CINAHL, PsycINFO). Search terms included "community pharmacy", "hypertension", OR "blood pressure", "randomised controlled trial" and "intervention". All studies included were RCTs involving patients with hypertension, with or without cardiovascular-related co-morbidities, with difference in blood pressure as an outcome. Data collected included study design, baseline characteristics of study populations, types of interventions, and outcomes. The Cochrane tool was used to assess risk of bias. From 340 articles identified on initial searching, 16 RCTs (3032 patients) were included. Pharmacist-led interventions included patient education on hypertension, management of prescribing and safety problems associated with medication, and advice on lifestyle. These interventions were associated with significant reductions in systolic (11 studies [2240 patients]; -6.1 mm Hg [95% CI, -3.8 to -8.4]; $p < 0.00001$) and diastolic blood pressure (11 studies [2246 patients]; -2.5 mm Hg [95% CI, -1.5 to -3.4; $p < 0.00001$). These interventions could be useful for improving clinical management of hypertension. However, this review could not determine the particular pharmacist intervention responsible for improvements in blood pressure control. The findings of this review led to the assessment of the impact of a specific pharmacist intervention on the management of blood pressure control.

Chapter 7: This chapter aims to determine whether structured education provided to patients verbally and in writing by community pharmacists about blood pressure and its treatment will a) be better retained by patients and b) be associated with improved blood pressure control. A RCT was conducted in four community pharmacies in the West Midlands area. The study had two groups (an active or intervention group where participants received verbal NMS intervention as well as written information on blood pressure and its treatment; and a control group where participants received verbal NMS intervention only). Participants in both groups

were required to attend four visits in total over a period of six months (at week 0, 2, 4 and 26). They were required to complete a questionnaire during all four visits. Blood pressure of all participants was also recorded during all four visits. In addition, a participant satisfaction survey was conducted at the six-month follow up. One-way ANOVA (repeated measures) was used to calculate the mean difference in systolic and diastolic blood pressure (in mm Hg) from baseline across all study visits. Cross tabulation was used to analyse the responses to hypertension knowledge questions.

A total of 66 participants were recruited between January 2014 and June 2014. There was an overall mean reduction in systolic blood pressure from baseline in both intervention group $F(3, 24) = 3.17, p = 0.04$ and control group $F(3, 30) = 3.4, p = 0.02$. However, there was no statistically significant difference between the two groups in treatment effect $F(1, 54) = 0.17, p = 0.91$. There was an overall mean reduction in diastolic blood pressure from baseline during the study in both intervention group $F(3, 24) = 3.17, p = 0.02$ and control group $F(3, 30) = 3.9, p = 0.01$. As observed for systolic blood pressure, there was no difference between the two study groups in treatment effect $F(1, 54) = 0.36, p = 0.78$. However, compared to participants in the control group, there was a significant improvement in the knowledge about hypertension and its treatment in the intervention participants. The participants of this study gave a positive response about the involvement of pharmacists in the management of long-term medical conditions such as hypertension.

Chapter 8: This final chapter summarises all the key findings of this research and discusses their implications for practice and for future research. On reflection, this thesis has only partly achieved its overall aim. The findings of this support the vision of the government that wants to see a central role for pharmacists in patient care. However, this research recognises the

challenges in the complex transition in pharmacists' role from dispensing to a clinically oriented role. Pharmacists would need to engage more effectively with the patients about their medicines and their adverse effects. The NMS provides pharmacists with the opportunity to engage with patients about their chronic medicines. However, deviations from service specifications of the NMS by pharmacists, such as the under-reporting of suspected ADRs, may reflect the organisational pressure on pharmacists to deliver a certain number of NMS consultations. Organisations should provide adequate resources to pharmacists to improve the quality of these services and to allow pharmacists to promptly report suspected ADRs.

The findings of this research highlight the important potential of pharmacists in the management of long-term medical conditions such as hypertension. However, any such extension in the activities of pharmacists would very much rely on the support from other stakeholders in particular the GPs. Future research should aim to explore collaborative partnerships between GPs and pharmacists and assess the impact of their combined efforts on patient healthcare outcome. Future research is also needed to assess the impact of pharmacist-led interventions on the management of other prevalent medical conditions in the UK including diabetes, obesity and ischemic heart disease.

Chapter One

1 Introduction

This chapter serves as a background to all five objectives of the thesis. It attempts to address the first objective by discussing the challenges to effective medicines reconciliation and by considering the possible association between patients' knowledge about their medicines and their incidence of ADRs. It addresses the second objective by considering the role of the NMS in improving medication use in patients. It then discusses the contribution of pharmacists to the reporting of ADRs to address the third objective of the thesis. Finally, this chapter uses hypertension to address the fourth and fifth objective by discussing the potential of pharmacists in the management of long-term medical conditions.

“Pharmacists should move from behind the counter and start serving the public by providing care instead of pills only”.

(Van Mil, Schulz & Tromp, 2004 p.309).

This quote by Van Mil, Schulz and Tromp (2004, p.309) reflects my own practice as a community pharmacist in the UK that has led me to question whether pharmacists' expertise and skills have been fully utilized in improving the medication use by patients. As of January 2010, there were 15.4 million people in England with at least one long-term medical condition (around 30% of the population); and it is estimated that by 2025 this number will rise to 18 million (Department of Health, 2010). The Department of Health (2010) defines a long-term

condition or a chronic condition as “a condition that cannot be at present, be cured but is controlled by medication and/or other treatment/therapies”.

Around 1.8 million people visit pharmacies every day in the UK (Pharmaceutical Services Negotiating Committee [PSNC], 2014). Community pharmacies in the UK are located in high streets, in the neighbourhood centres, in supermarkets and in the heart of the most deprived communities. Many of these pharmacies are open for extended hours when other health care centres are not available (PSNC, 2014). According to the National Health Service (NHS) Business Services Authority figures, there were 11,495 community pharmacies in England on 31st March 2013 and there were 22 pharmacies per 100,000 population in England (Health and Social Care Information Centre, 2013). Convenient access is one of the strengths of community pharmacy and according to Department of Health figures, 99% of the population can get to a pharmacy within 20 minutes by car and 96% by walking or by public transport (Department of Health, 2008).

One of the key roles of a pharmacist includes the distribution of medicines, an integral part of the management of long-term medical conditions; yet 30 to 50% of medicines prescribed for long-term conditions are not taken as intended (World Health Organisation [WHO], 2003). A recent study that assessed adherence to medications for hypertension in 208 hypertensive patients suggested that 25% of the patients were totally or partially non-adherent to anti-hypertensive medications (Tomaszewski, White, Patel, Masca, Damani, Hepworth et al., 2014). Hypertension or high blood pressure is a chronic disease that is defined as the presence of consistently higher blood pressure readings of 140 over 90, or higher (National Clinical Guideline Centre, 2011). Hypertension is a major risk factor for future cardiovascular diseases

such as heart attack or stroke, chronic kidney disease (CKD), cognitive decline and premature death (National Clinical Guideline Centre, 2011).

Better adherence to anti-hypertensive medication reduces the risk of cardiovascular disease (Corrao, Parodi, Nicotra, Zambon, Merlino, Cesana et al., 2011). This large population-based prospective study with 24,000 patients reported that patients who adhered to their treatment for hypertension without discontinuation had a 37% reduced risk of cardiovascular outcomes compared to patients who experienced at least one episode of discontinuation (Corrao et al., 2011).

The incidence of ADRs with anti-hypertensive medications may contribute to poor adherence to blood pressure treatment (Curb, Borhani, Blaszkowski, Zimbaldi, Fotiu, & Williams, 1985). According to this five-year study in the United States that involved over 5000 patients, 9.3% of the study patients discontinued their treatment due to definite or probable ADRs and an additional 23.4% of patients stopped their medications due to possible ADRs (Curb et al., 1985). Another multi-centre study with over 28,000 participants in Italy reported that diuretics and calcium channel blockers (both anti-hypertensive medications) were among the drugs that were most commonly responsible for ADRs (Onder, Pedone, Landi, Cesari, Della Vedova et al., 2002). An ADR is defined by the MHRA as an unwanted or harmful reaction experienced following the administration of a drug or a combination of drugs under normal conditions of use and which is expected to be related to the drug (MHRA, 2014). For example, it could be the extension of the pharmacological effect of a drug such as severe reduction of blood pressure by an anti-hypertensive drug, or an unexpected reaction from the drug from its usual dose, such as anaphylactic shock from penicillin administration (MHRA, 2014).

Due to the significance of adherence to anti-hypertensive medications in preventing cardiovascular diseases (Corrao et al., 2011) and the association of better adherence with adequate blood pressure control (Elliott, 2008), I will use hypertension as a test of concept in my research.

The introduction of this thesis has three sections. Section one, will a) explain the importance of ADRs, b) risk factors associated with ADRs, c) explain medicines reconciliation and barriers to medicines reconciliation and d) explore links between patient knowledge about medicines and the incidence of ADRs. Section two, will a) consider the roles for pharmacists, b) explain the community pharmacy contract, c) define and explain the NMS and d) discuss the reporting of ADRs by pharmacists. Section three, will a) explain the significance of hypertension, b) evaluate the role of pharmacists in the management of hypertension, c) consider public views on the involvement of pharmacists in chronic-disease management and d) discuss the importance of providing written education to patients on their medications.

1.1 Adverse drug reactions (ADRs) and their importance

ADRs are a significant cause of hospital admissions (Pirmohamed, James, Meakin, Green, Scott, Walley et al., 2004). This six-month long prospective analysis of nearly 19,000 hospital admissions in the UK reported that ADRs were responsible for 6.5% of hospital admissions (Pirmohamed et al., 2004). The study reported that around two-thirds of serious ADRs were preventable and predictable from their known pharmacology and interactions with other drugs (Pirmohamed et al., 2004). However it must be recognised that the assignment of a hospital admission as being related to an ADR in this study was made on a clinical judgment that could have been variable among individuals.

More recently, a cross-sectional Swedish study that assessed the prevalence of ADRs in 4,403 hospital admissions reported that over 4% urgent hospital admissions were due to ADRs (Pedros, Quintana, Rebolledo, Porta, Vallano & Arnau, 2014). This study suggested that ADRs were dose-related and predictable in more than 90% of cases (Pedros et al., 2014). However, this study was conducted in a single hospital which may limit the generalisation of the findings.

ADRs are not only associated with morbidity and mortality but also impose a significant burden on the healthcare services (Pirmohamed et al., 2004). For example in the UK, Pirmohamed et al. (2004) projected the annual cost of ADR related hospital admissions to the NHS to be 466 million pounds. In Germany, a prospective observational study involving 2262 patients was undertaken to analyse the direct costs of adverse drug events contributing to the ED admissions over a two year period (Meier, Maas, Sonst, Patapovas, Muller, Plank-Kiegele et al., 2014). The study reported that the mean costs related to the diagnosis of adverse drug events were 2743 Euros which when extrapolated at the national scale would amount to 2.245 billion Euros (Meier et al., 2014). Similarly, evidence from a systematic review that included 51 studies involving both adult and paediatric patients estimated the overall cost of ADR related-hospital admissions to be 2,401 dollars per patient (Khan, 2013). However, caution is needed in interpreting the findings of this systematic review as no formal quality assessment of the included studies was undertaken.

1.1.1 Risk factors associated with ADRs

Various risk factors have been associated with ADRs. Pedros et al. (2014) reported that the risk of urgent ADR-related hospital admission increases by 60% in patients ≥ 65 years. The association of advanced age with ADRs has also been reported in a systematic review that

included 25 prospective observational studies with 106,586 patients (Kongkaew, Noyce & Ashcroft, 2008). This systematic review reported that the hospital admission rate related to ADRs was 10.7% in the elderly as compared to 6.3% in adults and 4.1% in children (Kongkaew et al., 2008).

The association of advanced age with ADRs might be explained by the multiple medications (polypharmacy) prescribed to the elderly population (Pedros et al., 2014). Pedros et al. (2014) reported that the risk of ADR-related hospital admission increased by 5-fold in patients taking more than three medicines and by 9-fold in those taking more than 10 medicines. The association of polypharmacy with ADR-related hospital admissions has also been reported in a prospective study in Greece (Alexopoulou, Dourakis, Mantzoukis, Pitsariotis, Kandyli, Deutsch et al., 2008). This single centre study assessed 548 hospital admissions over a six months period and reported that patients taking four or more medicines had a significantly higher probability of having an ADR-related hospital admission ($p = 0.011$) (Alexopoulou et al., 2008).

Female gender is another risk factor that is potentially associated with the incidence of ADRs. For example, a prospective multi-centre study involving 2,371 patients reported that females had a 1.5 times higher risk of experiencing an ADR compared to males (odds ratio 1.5, CI 1.31 to 1.94; $p < 0.0001$) (Zopf, Rabe, Neubert, Gabmann, Rascher, Hahn et al., 2008).

This part of the section highlights that ADRs are not only associated with morbidity and mortality but also impose a significant burden on the healthcare services. Furthermore, various risk factors for ADRs have been identified in this section. These include advanced age, female gender and polypharmacy. These findings have led to an important question: how

to reduce polypharmacy? The next part of this section considers the importance of medicines reconciliation in reducing polypharmacy.

1.1.2 What is medication reconciliation?

Medication reconciliation is the process of obtaining an up to date and accurate list of medications taken by a patient e.g. prior to hospital admission when deciding on the medicines to be prescribed at hospital (Institute for Healthcare Improvement, 2014). The process of medicines reconciliation should account for any changes or discrepancies in patients' medications and must ensure that these changes have been effectively communicated to the patients or carers (Institute for Healthcare Improvement, 2014).

Evidence from a prospective controlled study involving 210 elderly patients in Sweden suggested that medication reconciliation helped to reduce both the number of inappropriate drugs taken by patients and unscheduled drug related visits to hospital (Hellstrom, Bondesson, Hoglund, Midlov, Holmdahl, Rickhag et al., 2011). All healthcare organisations in the UK that admit adult in-patients have been instructed to put in place policies for medicines reconciliation on hospital admission (National Institute for Health and Care Excellence [NICE] & National Patient Safety Agency [NPSA], 2007). However, obtaining an accurate list of medications from every in-patient may be challenging due to many factors. One of the factor is that patients may be taking medications that they may have obtained themselves, for example over the counter (OTC) medicines, herbal medicines or vitamins (NICE & NPSA, 2007). As presented in Figure 1.1 (personal development), patients may have multiple health care contacts including GP, hospital, psychiatry, HIV clinics and multiple sources of medicines that include pharmacy, online sources, supermarkets, herbal shops and friends.

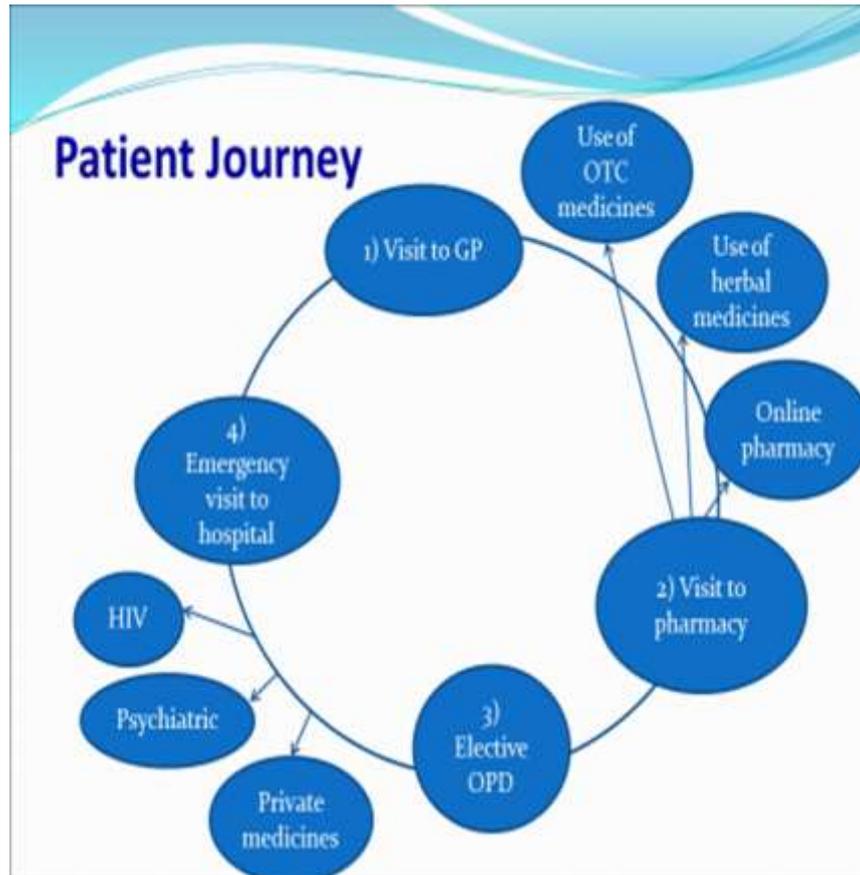


Figure 1-1 Potential patient journey across multiple health care contacts

Medicines reconciliation can be even more challenging in busy settings such as the ED of a hospital where staff members may fail to obtain an accurate and up to date medication history due to lack of time (Institute of Medicine, 2006). This is evident from the findings of a prospective observational study that involved 98 patients who were admitted to a hospital in the United States (Caglar, Henneman, Blank, Smithline & Henneman, 2011). The study by Caglar et al. (2011) reported that 56% of the ED medication lists of these patients had an omission, 80% had a dosing or frequency error and 87% of the lists had at least one error.

This part of the section underscores the importance of medicines reconciliation in reducing the number of inappropriate medicines taken by patients. It recognises that the process of

medicines reconciliation is challenging due to many factors including lack of time by hospital staff and multiple health care contacts available to patients. Evidence suggests that patients' lack of knowledge about their medicines could also be a barrier to the implementation of medication reconciliation (Clay, Halasyamani, Stucky, Greenwald & Williams, 2008). Chapter 3 of this thesis explores the challenges to medication reconciliation by conducting an audit in the ED of a hospital. The next part of this section explores whether patients' knowledge about their medicines has any association with the incidence of ADRs.

1.1.3 Links between patient knowledge and the incidence of ADRs

A previously published questionnaire-based survey was conducted in Liverpool to determine if public perceptions about medicine safety, awareness of medicines' side effects and reporting behaviours were related to their experiences of suspected side effects (Krska, Jones, McKinney & Wilson, 2011). The survey involved face to face interviews with 436 participants who were 18 years or older (Krska et al., 2011). The results of this study suggested that 198 participants (45%) had experienced an ADR, however only 33 (7.6%) of the study participants claimed to have a good knowledge about side effects (Krska et al., 2011). This study did not suggest any association of the knowledge about medications by patients and their experience of ADRs (Krska et al., 2011).

The implication of lack of knowledge about medicines in the incidence of ADRs has been reported in a retrospective qualitative study (Butt, Cox, Lewis & Ferner, 2011). This study used detailed semi-structured interviews with 14 adult survivors of Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) admitted to two teaching hospitals in the UK (Butt et al., 2011). Both SJS and TEN are caused by medicines and are serious life-threatening ADRs (Butt et al., 2011). The study reported that all 14 participants were aware

that SJS and TEN were caused by their medications. However, none of the participants recalled any prior warnings of the development of adverse effects such as SJS or TEN with their medications (Butt et al., 2011).

A study by Butt et al. (2011) highlights the importance of communicating the benefits and risks of medications to patients. In the UK, community pharmacists are encouraged to play an active role in services aimed at improving medication use by patients. The next section considers the roles of pharmacists in the UK including the scope of various services offered under the community pharmacy contract.

1.2 Roles of pharmacists

There are over 70,000 registered pharmacists, pharmacy technicians and pharmacy premises in England, Scotland and Wales (General Pharmaceutical Council, 2013). Dispensing of prescriptions is one of the major activities of community pharmacists and there has been an increase in their dispensing workload in the recent years (Hassell, Seston, Schafheutle, Wagner & Eden, 2011). The number of prescription items dispensed by community pharmacies in England in 2012-13 was 914.3 million compared to 82.6 million items dispensed by GPs and 6.9 million by appliance contractors (Health and Social Care Information Centre UK, 2013).

Besides dispensing prescriptions, pharmacists provide a wide range of public health services, including smoking cessation, NHS health checks, sexual health (e.g. contraception and Chlamydia screening), and weight management (Royal Pharmaceutical Society [RPS], 2014). Pharmacists are also undertaking NHS Health Checks, for example, for vascular disease,

men's health, blood pressure, blood glucose monitoring and Body Mass Index (BMI) assessment (Department of Health, 2008).

1.2.1 The community pharmacy contract

In 2005, a new NHS Community Pharmacy Contractual Framework (CPCF) was introduced in the UK (Department of Health, 2005a). Although dispensing of prescriptions remained the mainstay of the contract together with supply of appliances and disposal of waste, new clinical services were introduced in the CPCF. Under the new CPCF, pharmacy services were placed into three categories: essential services, locally commissioned services and advanced services to incorporate the basic pharmacy services as well as the extended roles of the pharmacists (Department of Health, 2005a; Noyce, 2007). A description of these services is given below.

1.2.1.1 Essential Services

Under the CPCF, the essential services are: dispensing, public health, repeat dispensing, signposting, supply of appliances, support for self-care, disposal of unwanted medicines and clinical governance (PSNC, 2014). These eight services are the traditional pharmacy services that represent the core pharmacy contract and failure to provide these services constitutes a breach of CPCF.

1.2.1.2 Locally Commissioned Services

Locally commissioned community pharmacy services can be contracted via various routes and by different commissioners, including Local Authorities, Clinical Commissioning Groups and NHS England's area teams (PSNC, 2014).

1.2.1.3 Advanced Services

The current four advanced services offered within the CPCF are: Medicine Use Reviews (MURs), NMS, Appliance Use Reviews and Stoma Appliance Customisation (PSNC, 2014). Community pharmacies can choose to provide any of these services as long as they meet the requirements set out in the Secretary of State Directions (PSNC, 2014).

MUR and NMS are the two most dominant advanced services offered by pharmacists. MUR was the first advanced service introduced in the new CPCF. A MUR is a consultation offered by the pharmacist to the patients about their medicines. It allows pharmacists to explain the medication use to patients about all their medications including both prescribed from the doctor as well the non-prescribed such as the OTC medications. In October 2011, three national target groups for MURs were introduced. The three national target groups introduced were: patients taking high risk medications including NSAIDs, anticoagulants, antiplatelets and diuretics, patients recently discharged from the hospital with changes in their medicines and, patients taking medications for respiratory diseases such as asthma and Chronic Obstructive Pulmonary Disease (COPD). The NMS is the fourth advanced service that was introduced in the NHS CPCF on 1st October 2011.

The Department of Health (2010) has projected an increasing number of patients with long-term conditions in the UK. Furthermore, adherence to medicines by patients with long-term conditions is poor (World Health Organisation, 2003; Tomaszewski et al., 2014). The next part of this section explains the background behind the development of NMS and the potential role of this service in the management of long-term medical conditions.

1.2.2 The New Medicines Service (NMS) for chronic conditions

A pivotal study published in the British Medical Journal (BMJ) reported that approximately 30% of newly diagnosed hypertensive patients stop taking their blood pressure medication by six months and 50% stop by 12 months (Vrijens, Vincze, Kristanto, Urquhart & Burnier, 2008). The blue line in Figure 1.2 represents the decrease in compliance to blood pressure medications by the percentage of patients who were still taking their blood pressure medications following the commencement of their treatment (Vrijens et al., 2008). As shown in Figure 1.2, around 50% of the patients had discontinued their blood pressure medications by 12 months. Similar rates of persistence with prescribed blood pressure medications were reported in another study that assessed 82,824 patients (Morgan & Yan, 2004). Only 51% of these newly-treated hypertensive patients obtained their hypertension prescriptions for at least one full year (Morgan & Yan, 2004).

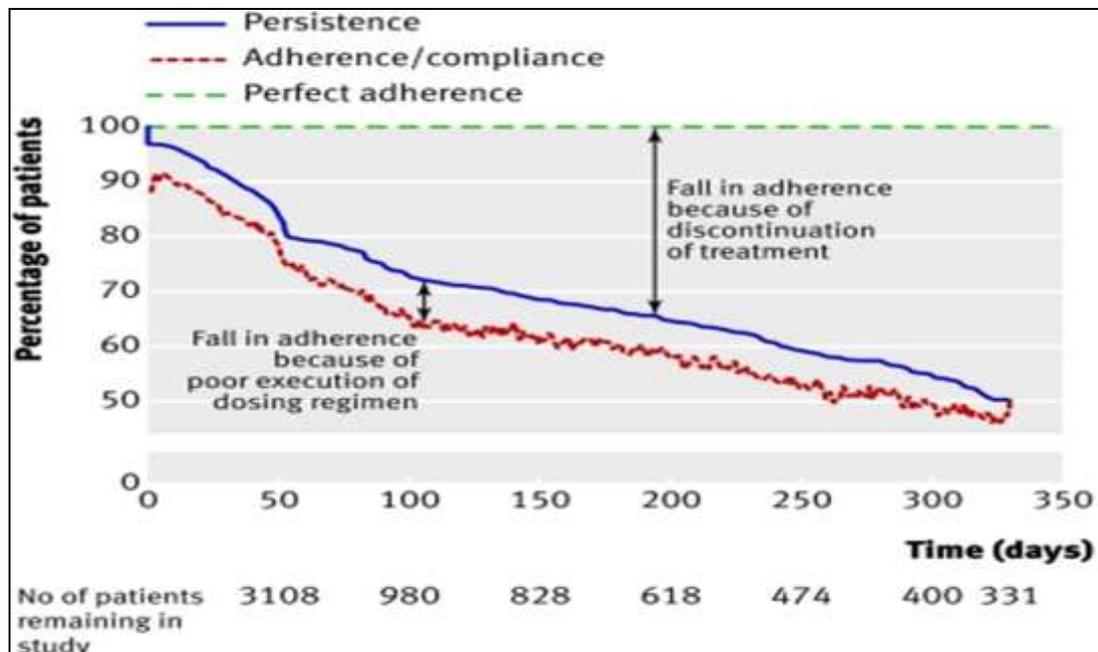


Figure 1-2 Time course of adherence/compliance parameters (execution, persistence).

Permission to use this figure was obtained from both the author (Vrijens et al., 2008) and the publisher (BMJ).

Poor medication adherence does not only contribute to morbidity and death (Osterberg & Blaschke, 2005) but is also associated with a significant financial impact on the health services through medicines waste. For example, a study evaluating the scale, costs and causes of medicine waste in England reported that the cost of medicine waste is estimated to be around £250 – £300 million per year in England. This figure equates to around £1 in every £25 spent on NHS medicines (Trueman, Taylor, Lowson, Bligh, Meszaros, Wright et al., 2010). The likelihood of poor medication adherence by patients seems to be greater with their new medications as opposed to the existing ones (Barber, Parsons, Clifford, Darracott & Horne, 2004). According to this longitudinal survey of 258 patients, around one third of the patients did not take their new medication as prescribed (Barber et al., 2004). However, this study used patients' self-reports of adherence that may not reflect the true incidence of non-adherence (Barber et al., 2004).

A RCT involving 500 patients was conducted in the UK (Clifford, Barber, Elliott, Hartley & Horne, 2006). The study assessed the impact of a telephone-advisory service provided by the pharmacist (Clifford et al., 2006). At the 4-week follow-up, patients who received the advisory service from pharmacists experienced fewer medication problems than the patients in the control group (23% vs. 34%, $p = 0.021$). Similarly, non-adherence to medications was lower in the intervention group compared to control group (9% vs. 16%, $p = 0.032$) (Clifford et al., 2006). The finding of this study led to the introduction of the NMS in the community pharmacy contract.

The NMS is a free NHS service, offered through the pharmacy, to help patients understand their condition and get the most out of their new medicine. The NMS can be provided to

patients who have been newly prescribed a medication in any of four long-term therapeutic areas or treatment options: asthma and COPD, type 2 diabetes, antiplatelet/anticoagulant therapy and hypertension. The service is designed to help patients to find out more about the new medicine they are taking and to help them sort out any problems identified with their new medicine (PSNC, 2013). Eligible patients receive the NMS service in two stages: an intervention stage within two weeks of starting the new medication conducted in the pharmacy or over the telephone, and a follow-up stage three weeks later (PSNC, 2013).

The uptake of NMS by community pharmacies has been successful (PSNC, 2014). There were 11,495 community pharmacies in England on 31st March, 2013 (Health and Social Care Information Centre UK, 2013). Of the 11,495 pharmacies, more than 90% of the pharmacies in England have provided NMS to their patients (PSNC, 2014). The NMS was initially commissioned until March 2013, which was later extended to September 2013, then to December 2013 and subsequently extended to March 2014. Now it has been extended until 31st March 2015 subject to an evaluation commissioned by the Department of Health, UK (PSNC, 2014). This evaluation work was a RCT and was carried out by the Nottingham University on behalf of the Department of Health, UK (Elliott, Boyd, Waring, Barber, Mehta, Chuter et al., 2014). This trial involved 504 patients and reported that NMS had improved medicine adherence in patients by 10% (Elliott et al., 2014). However, this study did not explain the reasons or factors which contributed to the improvement in medication adherence. Chapter 4 extends the previous assessment of the NMS on medication adherence by defining the reports of concerns about medication safety, efficacy and use, and the resolution both of adverse effects of drugs and patient problems with use of their medications.

This part of the section explains the background behind the development of NMS and the potential role of this service in the management of long-term medical conditions. The NMS also provides an opportunity for community pharmacists to report suspected ADRs through the national Yellow Card Scheme (MHRA, 2014). Spontaneous reporting of suspected ADRs is fundamental in the post-marketing surveillance of medicines and helps in ensuring medicine safety (MHRA, 2014). The next part of this section evaluates the level of ADR reporting by community pharmacists.

1.2.3 Reporting of ADRs by community pharmacists

The thalidomide tragedy in 1961 led to the establishment of Committee on the Safety of Drugs (CSD) in the UK (RPS, 2011). CSD was a voluntary scheme that worked in close collaboration with the pharmaceutical industry to ensure an early detection of ADRs. One of the actions of CSD was the setting up of a voluntary scheme known as the Yellow Card Scheme (RPS, 2011). The responsibility of monitoring ADRs was later taken over by the Committee on Safety of Medicines (CSM) that introduced a new version of the Yellow Card Scheme. It was this scheme that identified the eye damage caused by the anti-hypertensive medication known as practolol (RPS, 2011). In 1975 a "black triangle" symbol was introduced to monitor the safety of new medicines for at least two years after marketing (RPS, 2011). The Yellow Card Scheme was originally confined to doctors. In 1997, this scheme was extended to hospital pharmacists and in 1999, all community pharmacists in the UK were permitted to report ADRs (RPS, 2011).

An estimated 1.8 million people visit pharmacies every day in the UK (PSNC, 2014). However, despite this frequent interaction with the public, the number of ADR reports submitted by community pharmacists remains low (Jadeja & McCreedy, 2012). According to

Jadeja and McCreedy (2012), 370 ADR reports are submitted annually by community pharmacists that accounts for 3 to 4% of all direct health professional reporting in the UK. A questionnaire-based survey of 30 community pharmacists was conducted to assess the knowledge and attitudes towards ADR reporting by pharmacists (Green, Mottram, Raval, Proudlove & Randall, 1999). This study reported that although 28 (93%) of pharmacists were aware of the Yellow Card Scheme, only one had submitted an ADR report (Green et al., 1999). Pharmacists who took part in this study cited lack of time and lack of information as some of the reasons for not reporting ADRs (Green et al., 1999). Further high quality studies are required to update the current evidence base on the reporting of ADRs by community pharmacists. Chapter 5 of this thesis evaluates the level of ADR reporting by community pharmacists in the UK.

This section presents the scope of various pharmacy services offered by community pharmacists in the UK. This section also highlights the potential of pharmacist-led NMS in improving the medication use by patients with long-term medical conditions. The next section specifically focuses on hypertension and the role of community pharmacists in improving the management of this disease.

1.3 Hypertension and its significance

1.3.1 What is hypertension?

Hypertension or high blood pressure is defined as the presence of consistently higher blood pressure readings of 140 over 90 mm Hg, or higher (National Clinical Guideline Centre, 2011).

1.3.1.1 Implications of hypertension in cardiovascular events

Hypertension or high blood pressure is a major risk factor for future cardiovascular diseases such as heart attack or stroke, chronic kidney disease, cognitive decline and premature death (National Clinical Guideline Centre, 2011). An increase in systolic blood pressure by every 2 mm Hg rise has been associated with an increased risk of ischaemic heart disease mortality by 7% and an increase in the risk of mortality related to stroke by 10% (NICE, 2011). A meta-analysis involving one million adults in USA reported that every 1 mm Hg reduction in systolic blood pressure could prevent about 10,000 deaths related to coronary heart disease in the US each year (Lewington, Clarke, Qizilbash, Peto, Collins & Collaboration, 2002). Another study suggested that a sustained 2 mm Hg reduction in diastolic blood pressure would be expected to result in a 6% reduction in the risk of coronary heart disease and 15% decrease in stroke (Cook, Cohen, Hebert, Taylor & Hennekens, 1995).

1.3.1.2 Prevalence of hypertension

Despite the presence of sufficient evidence that has demonstrated the impact of adequate blood pressure control on cardiovascular mortality, hypertension continues to be poorly controlled in the community and remains a serious challenge. For example in the United States, the prevalence of hypertension among U.S. adults aged ≥ 18 years is approximately 31% and increases with age to approximately 70% among persons aged ≥ 65 years (Yoon, Gillespie, George & Wall, 2012). High blood pressure is also common in England. Based on the definition of high blood pressure (with the persistent reading of 140 mmHg or higher systolic and a reading of 90 mmHg or above diastolic), 31.5% of men and 29.0% of women in England are hypertensive (Health and Social Care Information Centre, 2012).

There has been an improvement in the management of high blood pressure in the UK over the last ten years (Figure 1.3). Between 2003 and 2010 in England, the percentage of adult population with controlled hypertension increased from 5.4% to 10.3% in men and from 6.0% to 10.9% in women (Health and Social Care Information Centre, 2012). Between 2003 and 2010, the proportion of adults in the population with untreated hypertension fell from 20.1% to 14.7% among men and from 15.8% to 10.3% among women (Health and Social Care Information Centre, 2012). On the other hand, the percentage of hypertensive adults with uncontrolled hypertension and taking blood pressure medications has not changed much since 2003, and remain at 6–8% in both men and women (Health and Social Care Information Centre, 2012).

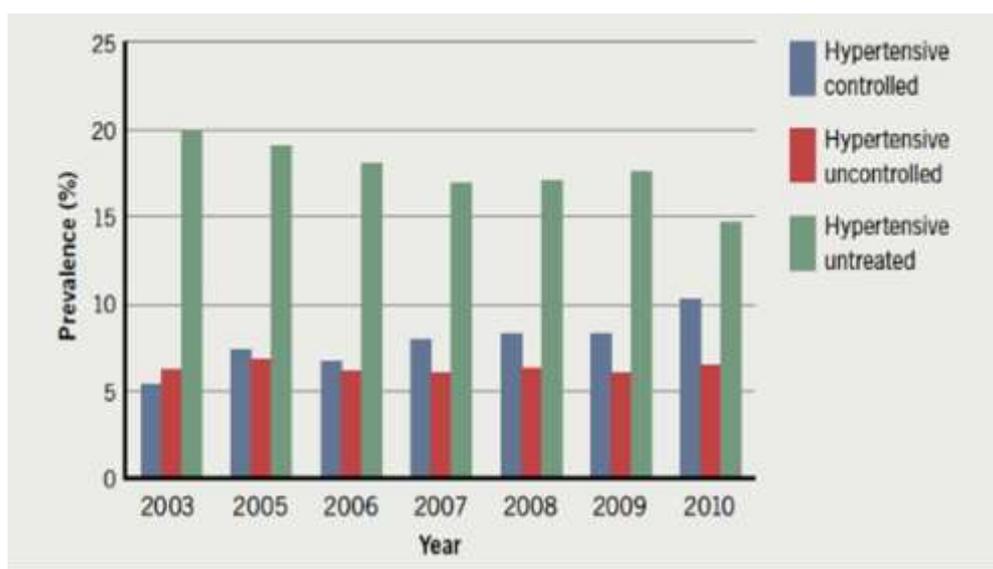


Figure 1-3 Prevalence of controlled and uncontrolled hypertension in UK (re-used with the permission of the Health and Social Care Information Centre).

1.3.1.3 Lifestyle changes that can help to reduce blood pressure

A meta-analysis of RCTs with nearly 3000 patients reported that a reduction in salt intake by 100 mmol/day (6 g of salt) would be expected to reduce systolic blood pressure by 7.1 mm Hg and reduce diastolic blood pressure by 3.9 mm Hg in hypertensive patients (He &

MacGregor, 2002). The WHO (2012) recommends that salt intake for adults should be less than 2000 milligrams of sodium, or 5 g of salt per day. A high alcohol intake is another risk factor for high blood pressure (Briasoulis, Agarwal & Messerli, 2012). Evidence from this meta-analysis of prospective studies with nearly 34,000 males and 20,000 females reported that an alcohol consumption of 31 to 40 grams per day in males was associated with an increased risk of hypertension (Relative Risk 1.77; 95% CI 1.39 to 2.26; $p < 0.01$) (Briasoulis et al., 2012). This study also reported an increased risk of hypertension in females who had a heavy consumption of alcohol (Briasoulis et al., 2012). Engagement in regular physical activity also helps to reduce blood pressure as an increase in BMI accounts for higher blood pressure (NICE, 2011).

This part of the section discusses the prevalence of hypertension and the serious implications of this disease in future cardiovascular events. The next part of this section highlights the contribution of pharmacists in the management of high blood pressure.

1.3.2 Can pharmacists play a role in the management of hypertension?

A systematic review and meta-analysis of 28 studies was conducted to determine if patient outcomes including systolic and diastolic blood pressure were sensitive to pharmacists' interventions (Machado, Bajcar, Guzzo & Einarson, 2007). The review by Machado et al. (2007) reported that pharmacists-led interventions including medication management and provision of education to patients on hypertension significantly reduced systolic blood pressure in the intervention group by 10.7 mm Hg ($p = 0.002$) as compared to a reduction of 3.2 mm Hg in the control group ($p = 0.36$). The beneficial impact of pharmacist-led interventions on adherence to anti-hypertensive medications, systolic and diastolic blood pressure has also been reported in another systematic review and meta-analysis (Morgado,

Morgado, Mendes, Pereira & Castelo-Branco, 2011). This review included 15 studies with 3280 hypertensive patients and reported reduction in both systolic ($p < 0.001$) and diastolic blood pressure ($p = 0.002$) (Morgado et al., 2011). However, it should be acknowledged that the literature search in this review was conducted only in those databases that were freely available to the reviewers of this review.

Evidence from a systematic review and meta-analysis that involved data from 30 RCTs (11,765 patients) reported that pharmacist-led care either alone or in collaboration with other health care professionals including doctors and nurses was associated with a reduction in systolic and diastolic blood pressure by 8.1 mm Hg and 3.8 mm Hg respectively (Santschi, Chiolero, Burnand, Colosimo, Paradis et al., 2011a). However the possibility of publication bias and considerable heterogeneity among the included studies should be borne in mind when interpreting the findings of this review. More recently, a systematic review and meta-analysis of RCTs was conducted to assess the impact of pharmacists' interventions on blood pressure control (Santschi, Chiolero, Colosimo, Platt, Taffe, Burnier et al., 2014). The review included 39 RCTs that contained a data of 14,224 patients (Santschi et al., 2014). Compared with usual care, pharmacist-led interventions were associated with a greater reduction in systolic blood pressure (-7.6 mm Hg) and diastolic blood pressure (-3.9 mm Hg). However, the inclusion of complex and multi-faceted pharmacists' interventions in this review did not allow the reviewers to identify which particular pharmacist intervention was responsible for improvement in blood pressure control. Chapter 6 extends the previous assessment of the impact of community pharmacist interventions on blood pressure control by conducting a systematic review and meta-analysis of pharmacist interventions in community pharmacies only.

This section highlighted the potential contributions of community pharmacists in the management of hypertension. It is however, important to understand what the public thinks about the involvement of pharmacists in the management of long-term conditions.

1.3.3 Public views about the involvement of pharmacists in chronic-disease management

The public opinion about the role of community pharmacists in the UK is diverse. For example, the perception of pharmacists as advisors on health care was not shared by the public in a study conducted in community pharmacies in the UK and was found to be at odds with the expectations of the public (Hassell, Noyce, Rogers, Harris, & Wilkinson, 1998). Similar findings were also reported in a cross-sectional study conducted at 13 general practices in the UK (Hammond, Clatworthy & Horne, 2004). This study involved nearly 4000 patients and was aimed to explore the prevalence of patients' visits to the General Practitioners (GPs) (Hammond et al., 2004). GPs classified 260 (7%) of the patient visits as unnecessary and believed that these visits could have been managed by a community pharmacist (Hammond et al, 2004). Of the 260 patients whom GPs believed could have been managed by a community pharmacist, majority of these patients (59%) did not agree with the GPs' opinion and believed that visiting the pharmacist would not have been appropriate for their problem (Hammond et al., 2004).

The recently concluded evaluation work of the NMS involving 500 participants in the UK has reported a positive evaluation from the participants about NMS (Elliott et al., 2014).

Participants of this study considered NMS as an opportunity to discuss issues related to their new medicines as well to explore other health-related issues (Elliott et al., 2014). However, it needs to be acknowledged that only 19 participants were interviewed in this study to obtain

their views about NMS. Furthermore, it was not clear from the study what proportion of these participants gave a positive evaluation of NMS (Elliott et al., 2014).

Patients require access to information about their medications to enable them to improve their understanding of the risks and benefits of their treatment (Van Geffen, Kruijtbosch, Egberts, Heerdink & Hulten, 2009; Feifer, Greenberg, Rosenberg-Brandl & Franzblau-Isaac, 2010; Lamberts, Bouvy & Hulten, 2010). The next section discusses the advantages of providing written information to patients about their medications.

1.3.4 Provision of written education to patients on their medications

An observational study was conducted in the United States to assess the quality of information provided by physicians to their patients when prescribing new medications (Tarn, Heritage, Paterniti, Hays, Kravitz & Wenger, 2006). This study reported that only one third of the discussions focussed on explanation of adverse effects of medications and only half of the patients received directions on medication use from their physicians (Tarn et al., 2006).

Research suggests that provision of written medical advice to patients about a disease and its treatment is better retained by patients than verbal information (Victoria, 1981). Written information is also associated with improved patient satisfaction and knowledge (Gibbs, Waters & George, 1989). However, caution is needed in the delivery of written information to patients as any misleading information on the potential adverse effects of medications can have a negative impact on medication compliance (Buchter, Fechtelpeter, Knelangen, Ehrlich & Waltering, 2014). One example of such adverse effect on medication compliance by patients was witnessed in 1995 in the UK, when the overly exaggerated risk of blood clots with the third generation oral contraceptives led to many unwanted pregnancies (Furedi,

1999). Chapter 7 assesses the impact of pharmacist-led written education on improving patients' knowledge about blood pressure and its treatment. This study aims to determine if provision of written education to patients will be associated with an improvement in their blood pressure control.

Summary of chapter

In summary, this chapter has presented very limited evidence that highlights the challenges to effective medicines reconciliation and suggests an association between lack of patient's knowledge about their medications and the incidence of ADRs. It has also provided limited evidence that demonstrates the potential of the NMS in improving medication use to patients. It has to some extent highlighted the understanding of community pharmacists about ADRs and the barriers to ADR reporting. It has also provided evidence to illustrate the potential of pharmacists in the management of hypertension. However, this chapter has not provided any evidence to demonstrate the impact of pharmacist-led written education on improving patients' knowledge about blood pressure and their blood pressure control.

1.4 Rationale for the whole study

Evidence suggests that 30 to 50% of medicines prescribed for long-term medical conditions are not taken as intended (WHO, 2003). One of the many possible reasons of non-adherence to medicines by patients include the incidence of ADRs (Curb et al., 1985). Poor adherence to medicines by patients should not be seen as the patient's problem. It represents an important limitation in the delivery of healthcare on part of healthcare professionals including pharmacists (NICE CG76, 2009). Improving medicines adherence requires an exploration of patients' perspectives of medicines and the reasons why they may not want or are unable to use them (NICE CG76, 2009). Therefore, there is a need to gain an insight into patients' medications and their experience of ADRs.

The White paper titled "A vision for pharmacy in the new NHS" outlines the government's vision for community pharmacy (Department of Health, 2003). It calls for using pharmacy strengths towards the delivery of a safer, effective and more patient-centred care (Department of Health, 2003). It requires community pharmacists to broaden their current contributions towards patient care and expects them to assume greater responsibility than they currently do (Department of Health, 2003).

It is therefore important to evaluate the current schemes of pharmacists' engagement with patients such as the NMS as well as to reflect on the understanding of pharmacists about ADRs. It is also important to assess the potential of pharmacists in the management of long-term medical conditions such as high blood pressure. Findings of these initial studies may then help in developing a new pharmacist supported method for a more effective and safer use of medicines by patients.

Chapter Two

2 Research question

This chapter outlines the overall research question and the overall aims and objectives of this research.

The main purpose of this thesis is to determine whether studying patients' knowledge about their medicines and pharmacists' systems for interacting with patients may lead to identifying ways in which pharmacists can improve their role in patient care.

2.1 Aims

- 1) To explore challenges to ADR prevention from the perspectives of pharmacists and patients.
- 2) To assess the impact of pharmacist interventions in the management of chronic disease such as hypertension.
- 3) To use results from this initial work to explore ways in which pharmacist involvement could help in ensuring safe and effective use of medications by patients.

2.2 Objectives

- 1) To explore the challenges of medicines reconciliation in patients attending the ED and to gain an insight into their medications and their experience of ADRs.
- 2) To analyse within the NMS currently offered by pharmacists: the spectrum of medicines considered, points for action identified and outcomes within 30 days of these interventions.

- 3) To evaluate the current understanding of community pharmacists about ADRs, level of ADR reporting and barriers to ADR reporting.
- 4) To conduct a systematic review and meta-analysis of the impact of pharmacist interventions on blood pressure control.
- 5) Using the NMS as basis, conduct a feasibility study of a new pharmacist supported method for more effective use of medicines by patients with hypertension.

Chapter Three

3 Barriers to medication reconciliation in patients with acute medical problems: a questionnaire based assessment of patient insight into their medications and self-reported prevalence of ADRs

This chapter aims to address the first objective of the thesis by exploring the challenges to effective medicines reconciliation in patients attending the ED and by gaining an insight into their medications and their experience of ADRs.

3.1 Abstract

This chapter assessed the challenges to medicines reconciliation in the ED and investigated the relationship between patients' knowledge about their medicines and self-reported ADRs. A two phased questionnaire-based audit was conducted in the ED of a large teaching hospital in the UK from February to March, 2012. Patients were asked to provide names and reasons for their treatment(s) including over the counter products and to record any self-reported experience of ADRs. 341 patients were assessed over a period of 20 days. Information from 25% of the study group on their medications was either unavailable or limited. Twenty-two patients were not taking medications and 59 were not well enough to participate. Two important risk factors for reporting ADRs were identified: being unaware of why medicines were prescribed (odds ratio 3.9, 95% Confidence Interval CI 1.5 to 8.7, $p = 0.001$) and not recalling prior warnings about possible ADRs (odds ratio 12.2, 95% CI 4.7 to 30.6, $p < 0.001$). This study highlights the importance of obtaining accurate information from high risk patients about their medications and the challenges involved in capturing this vital

information. A high prevalence of recalled ADRs was identified, with increased self-reported ADR risk inversely linked to patient knowledge of their medications.

3.2 Background

ADRs impose a major clinical and cost burden on acute hospital services (Meier et al., 2014; Pirmohammed et al., 2004). There is a major interest in whether better medication reconciliation may help to reduce ADR severity and avoid the most serious preventable reactions (Karapinar-Carkit, Borgsteede, Zoer, Siegert, Van Tulder, Egberts et al., 2010). Medication reconciliation requires an up to date and accurate list of medications taken by a patient (Institute for Healthcare Improvement, 2014). The process should account for any changes or discrepancies in patients' medications and must ensure that these changes have been effectively communicated to the patients or carers (Institute for Healthcare Improvement, 2014). Evidence suggests that medication reconciliation can reduce the unscheduled drug related visits to hospital (Hellstrom et al., 2011).

The process of medication reconciliation can be challenging in a high risk area such as the ED of a hospital where patients are acutely unwell, and where decisions on medications are particularly important. Further, in such busy settings, staff members may fail to obtain an accurate and up to date medication history due to lack of time and can end up producing an inaccurate medication list (Institute of Medicine, 2006). This is evident from the findings of a previous study which showed that ED medications lists are not accurate (Caglar et al., 2011). Patients' lack of knowledge of their medications may also act as a barrier in implementing the process of medicines reconciliation (Institute of Medicine, 2006; Barnsteiner, 2008) which in turn could increase the incidence of ADRs and compromise medication safety. There is limited evidence to suggest a relationship between lack of patient's knowledge about their

medications and the incidence of ADRs (Butt et al., 2011). Furthermore, there is a need to explore the factors that may influence the implementation of the medication reconciliation process in a high risk area. This study therefore aimed to explore the challenges of medicines reconciliation in a high risk population such as patients attending the ED and to gain an insight into their medications and their experience of ADRs.

3.3 Methods

A questionnaire-based audit (see Appendix A for project proposal form) was conducted in the ED of a large teaching hospital in the Midlands in February and March 2012. The audit was approved by the audit committee (Appendix B). The first phase of the audit was conducted between 8.00 am and 4.00 pm for a period of 10 weekdays only. On the availability of more staffing resources, a second phase of the audit was conducted for another 10 days including both weekdays and weekends throughout the 24 hour period.

3.3.1 Study development

A questionnaire was developed (see Appendix C) using feedback from the members of the audit team that included two medical consultants, a pharmacy student and a medical student. The format and style of some questions was adapted from those in the Yellow Card reporting form for health care professionals (MHRA, 2014). The questionnaire was adapted to include specific questions to assess the knowledge of patients about their medications and awareness about their adverse effects. A separate interview schedule was developed to help the members of the audit team in shaping their conversation with the study participants. The questionnaire comprised of 12 questions and was estimated to take approximately five minutes to complete. All patients were questioned on indications for their medicines, awareness of potential adverse effects, OTC and herbal use, history of ADRs and lifestyle. Patients were allowed to seek the assistance of a relative, friend or carer to assist them in completing it. For some

questions, patients were encouraged to provide as many answers as relevant to them. For other questions, patients were required to tick one box only. The length and the layout of the questionnaire were carefully considered to get maximum response rate. The questionnaire had two sides of A4 and avoided ambiguous and multi-part questions.

3.3.1.1 Ethical approval

As it was a clinical audit, the research and development office of the hospital advised that ethical approval was not necessary (see Appendix D for clarification on ethical approval). Prior consent was obtained from the patients before data collection. Patients who agreed to participate were briefed on the aims and objectives of the study by a member of the audit team. All information collected from the patients was kept strictly confidential. The procedures for handling, processing, storage and destruction of the data complied with the Data Protection Act 1998. Only members of the audit team had access to the completed questionnaires.

3.3.2 Study participants

The audit included patients aged 16 or over, male or female, currently on treatment with one or more medications including OTC medications and who were attending the ED of UHCW with an acute medical presentation. Patients were included in the study based on their ability and willingness to participate. Patients were eligible to take part if they were either taking prescribed or OTC medications at the time of the study or had taken these medications in the last three months. Recruitment of patients in the audit was limited to patients who could read and write English. This was done to avoid the possibility of interpreter bias. Patients were not included if they were under 16 years of age, pregnant or too unwell to participate.

3.3.3 Study procedure

3.3.3.1 Questionnaire administration and data collection

The questionnaire was piloted on a small number of patients attending the ED of the hospital. Patients completed the questionnaire in two steps. In the first step, patients were asked to complete the questionnaire themselves. It was followed by a brief interview by a member of the audit team to ensure questions were completed. Members of the audit team approached the patients after they had been booked in by the triage nurses and were waiting to be seen by the doctors/nurses.

3.3.3.2 Statistical analysis

Statistical analysis was performed with SPSS (IBM version 22). Summary descriptive statistics were generated from the questionnaire data using SPSS. Summary data are presented in tables and figures, as appropriate. Results are presented as odds ratios and 95% confidence intervals, where appropriate. Statistical analysis was performed with Fisher's exact test to explore the association between patients' knowledge about their medicines and incidence of self-reported ADRs. A p-value < 0.05 was considered to be statistically significant. A step-wise multivariable linear regression analysis was conducted to explore the influence of various explanatory or independent variables including age, gender, BMI, ethnicity, medical conditions, number of medicines used by patients, smoking, intake of alcohol, spinach, broccoli, asparagus, grapefruit juice, awareness of reasons of medication use and prior warnings about ADRs, with the incidence of ADRs recalled by patients as the dependent variable. Advice was obtained by a statistician (Dr Nick Parsons) prior to conducting the regression analysis.

3.4 Results

A total of 341 patients were assessed during the audit. 256 (75%) of patients were included (age range was 17 to 96, 122 were male). The 85 exclusions (25%) of study population were: 59 patients who were not well enough to participate, 22 patients who were not taking any medications, two agitated patients under guard and two who were severely deaf and had left reading glasses at home. The number of current medicines, including OTC use, ranged from 1–12. Information obtained was limited in five patients; one by tiredness, one due to mild dementia and three due to language problems. Although family members were present to interpret, they were only aware of or able to obtain partial information about their relatives' medicines.

All patients were questioned on indications for their medications and awareness of potential adverse effects. A total of 52 (20%) of the patients did not know the reason for taking their medications and 116 (45%) patients were not aware of adverse effects of their medications. When warnings were recalled, these were said to be from the GP or a package insert. Only eight patients recollected specific advice from a community pharmacist. 103 (40%) patients reported using OTC medications, mainly paracetamol and NSAIDs. In one patient, no tablets had been renewed in the previous four months. 79 ADRs were recorded in 62 (24%) patients with 17 patients suffering from multiple ADRs. In three patients, an ADR was the cause of their current acute medical presentation. Reported ADRs included rash, dizziness, wheeze, constipation, GI bleeding/ulceration and severe myalgia (ciprofloxacin) as summarised in Table 3.1.

Table 3-1 Examples of some of the ADRs self-reported by patients

Age (Yrs)	Gender (M/F)	No. of Medicines used	No. of ADRs	Drugs Involved	Prior Warning about Side Effect
43	F	4	1	Trastuzumab	Yes
85	F	5	2	Amlodipine, Doxycycline	No
85	F	5	1	Co-codamol	No
64	M	12	2	Penicillin, Aspirin	No
29	M	1	1	Codeine	Yes
85	M	6	2	Aspirin, Bisoprolol	No
63	M	1	1	Warfarin	No
28	F	5	1	Tramadol	Yes
72	F	2	1	Simvastatin	No
19	F	2	1	Erythromycin	No
56	M	1	1	Aspirin	No

Antibiotics (chiefly penicillin) were responsible for 15 ADRs, followed by ten due to opioid analgesics (codeine or tramadol) and nine caused by NSAIDs. Other classes of medications contributing to ADRs were statins, anti-coagulants, calcium channel blockers, diuretics and anti-psychotic medications. Two important risk factors for reporting ADRs were identified: being unaware of why medicines were prescribed (odds ratio 3.9, 95% Confidence Interval CI 1.5 to 8.7, $p = 0.001$) and not recalling prior warnings about possible ADRs (odds ratio 12.2, 95% CI 4.7 to 30.6, $p < 0.001$).

3.4.1 Multiple linear regression analysis

The analysis was restricted to 198 patients who were taking prescribed medications. Only awareness of the reasons of medication use had a weak but statistically significant linear association with the incidence of self-reported ADRs (R^2 0.025, $p = 0.002$). None of the other variables showed any significant association with ADRs recalled by patients.

3.4.2 Confounding and its control

Although this study suggested possible association between the incidence of ADRs and the lack of knowledge about medicines by patients; such association could have been explained by confounding. Confounding is commonly referred to the mixing of effects (Rothman, 2004) and observational studies such as this study are more susceptible to the effects of confounding (Hennekens & Buring, 1987). Potential confounders in this study that were not considered during data analysis and may have led to bias in the results included the use of herbal medicines by patients, types of smoking, types of alcohol and the number of units consumed per week, reason of medical presentation to the hospital, allergies and family medical history. These confounding factors along with any other unknown confounders are better controlled by using an RCT to establish causality.

3.5 Discussion

This chapter identified a high prevalence of recalled ADRs and suggested that lack of knowledge about medications and their adverse effects was associated with increased incidence of self-reported ADRs. Information from a number of patients was either unavailable or limited that indicates the challenges in capturing information about medicines from high risk patients and suggests major scope to improve systems for medication reconciliation.

Previous work reported that medication lists produced in the ED are not accurate (Caglar et al., 2011). This is the first audit based study that explored the barriers to medication reconciliation in patients attending the ED with acute medical problems. During the audit, information from 25% of the study group on their medicines was either unavailable or limited. Although family members were present to interpret, they were only aware of or able to obtain partial information about their relatives' medications. Incomplete medication histories at the time of admission have been reported to be responsible for at least 27% of prescribing errors (Brown, 2012).

This study reported that only 32 (17%) patients brought a list of their medications to the hospital. This finding is consistent with the findings of a previous study conducted in the United States (Vilke, Marino, Iskander & Chan, 2000). This survey reported that only 17% of the study patients brought a list of their medications to the ED (Vilke et al., 2000). Patients are not known to be accurate historians of their medication history (Rodehaver & Fearing, 2005) and may not have the desired literacy to maintain or communicate a list of their current medicines (Kutner, Greenberg & Jin, 2006). Research indicates that the most common error that occurs while taking medication history is the omission of a regularly used medication (Chan, Taylor, Marriott & Barger, 2009; Cornish, Knowles, Marchesano, Tam, Shadowitz, Juurlink et al., 2005; McLeod, Lum & Mitchell, 2008). Patients must be encouraged to bring their medications including OTCs to every healthcare counter (Jacobson, 2002). The use of a limited simple questions list has been reported to significantly reduce drug omissions by almost 50% and can be a simple tool to improve medication reconciliation in the ED (De Winter, Vanbrabant, Spriet, Desruelles, Indevuyt, Knockaert et al., 2011).

40% of the study population reported using OTC medicines this audit. These findings are in parallel with the findings of a previous study that involved over 3,000 participants in the United States (Qato, Alexander, Conti, Johnson, Schumm & Lindau, 2008). This study reported that 42% of the study participants used at least one OTC medication (Qato et al., 2008). GP prescription lists do not provide information on what may potentially be important unrecognised OTC use of these drugs. Such unrecognised use of OTC NSAIDs may trigger or exacerbate medical conditions such as GI ulcers; intrinsic asthma; heart failure; blood pressure control and renal impairment.

A high prevalence of self-recalled ADRs was reported by patients in this audit. Similar findings have also been reported in a questionnaire-based public survey in Liverpool (Krska et al., 2011). This survey reported that (45.4%) of the surveyed participants recalled an experience of ADR from a prescription medication, an OTC medication or both (Krska et al., 2011). Antibiotics (chiefly penicillin) were responsible for 15 ADRs reported by patients, followed by ten due to opioid analgesics (codeine or tramadol) and nine caused by NSAIDs. The suspected association of these medications with ADRs has also been reported in a study carried out by a working group associated with Danish Medicines Agency's network (Danish Health and Medicines Authority, 2011).

Nearly half (45%) of the study population in this audit did not recall any prior warnings about potential ADRs. This finding seems to correlate with the results of a survey by the Picker Institute (Richards & Coulter, 2007). According to this survey, only 58% of primary care patients who were prescribed new medicines in 2006 were given enough information about the potential ADRs from medications (Richards & Coulter, 2007). Research indicates that female patients have a 1.5 fold greater risk of developing an ADR than male patients (Zopf et

al., 2008). The increased tendency of females to develop ADRs was also confirmed in this study where 35 out of 62 patients who recalled the experience of an ADR were females. Polypharmacy was another risk factor associated with the incidence of ADRs in this study. More than half (56%) of the study participants who recalled an experience of ADR were using three or more medications.

Although it is believed that medication reviews and patient counselling provided by pharmacists can help to improve identification of ADRs (Schnipper, Kirwin, Cotugno, Wahlstrom, Brown, Tarvin et al., 2006), this role of pharmacists was not reflected in the findings of this study. In this audit, only eight patients recalled any prior advice given to them by the pharmacists on potential ADRs. These findings highlight a major challenge for pharmacists and suggest that despite frequent interaction of pharmacists with patients, patients seem to lack knowledge about their medications. More research is needed to establish how health professionals and pharmacists in particular can ensure that education of patients about their medicines is more effective, and whether this will reduce the incidence and severity of avoidable ADRs.

This study has several limitations. Although this study suggested possible association between the incidence of ADRs and the lack of knowledge about medicines by patients; such association could have been explained by confounding. Any known or unknown confounders are better controlled by using an RCT to establish causality. Another limitation of the study was the lack of an independent verification of the information provided by patients on their medications and history of ADRs. Thus a patient could have listed their medications incorrectly or could have stated incorrectly that they knew the reason of taking their medications. As the audit team did not verify the responses against patients' hospital or GP

records, the actual number of patients not knowing about their medications could be higher or vice versa. However, it could be argued that it was an audit based study and was not an investigational study. Patients were assessed on their willingness and ability to participate in the study. In other words, the sample population was a convenience sample of patients.

Summary of chapter

This chapter has demonstrated the challenges in capturing information from high risk patients about their medications. It has also suggested the possible association of the lack of knowledge about medications and their adverse effects with increased incidence of self-reported ADRs. Majority of the patients did not recall prior advice given to them by the pharmacists on potential ADRs. However, in the absence of an independent verification of the information provided by patients through an adapted questionnaire, the findings of this study should be interpreted with caution. This chapter has therefore partially addressed the first objective of the thesis.

3.6 Conclusion

This study highlights challenges in obtaining information from high risk patients. Patients' lack of knowledge about their medicines is one of the barriers in implementing the process of medicines reconciliation and a contributing factor in the incidence of self-reported ADRs. However, in the absence of an independent verification of the information provided by patients through an adapted questionnaire, the findings of this study should be interpreted with caution. Future research is needed to establish how health care professionals and pharmacists in particular can ensure that education of patients about their medicines is more effective, and whether this will reduce the incidence and severity of avoidable ADRs.

The next chapter evaluates the engagement of pharmacists with patients within the current pharmacy services such as the NMS.

Chapter Four

4 A questionnaire-based service evaluation of the community pharmacist NMS for patients starting a new treatment for a long-term medical condition

This chapter aims to address the second objective of the thesis. It aims to do so by analysing the spectrum of medicines considered in the NMS, points for actions identified and outcomes within 30 days of these interventions.

4.1 Abstract

This chapter evaluated the impact of the NMS on medication use in patients starting a new medication for a long-term medical condition in the UK. A questionnaire-based service evaluation was conducted in community pharmacies located in the West Midlands area for three months from July to September, 2012. Twenty community pharmacists based in 14 pharmacies returned 295 questionnaires from which completely anonymised data of 285 patients was included in the study (160 female and 125 male). On first NMS assessment, 82 patients reported drug-related problems including adverse effects and incorrect use of medications. Of the 82 patients, 58 patients received advice from pharmacists. At the NMS follow up stage 39 (67%) of the 58 patients who received advice from pharmacist reported resolution of their drug-related problems while only four (17%) of the 24 patients who did not have pharmacist advice reported resolution of their problems (odds ratio 10.2, 95% CI 3.0 - 34.2 $p = 0.0001$). This evaluation provides support for the NMS as an opportunity to improve detection of ADRs and resolution of incorrect use of medicines by patients. Further research is needed to address the policy implications of the NMS, including analyses of the clinical and

cost-effectiveness of this service, and the sustainability of this form of pharmacist intervention in the long-term in clinical practice.

4.2 Background

Research suggests that approximately 50% of patients with long-term medical conditions do not take their medications as prescribed (Vrijens et al., 2008; WHO, 2003). Poor adherence to medication by patients is not only associated with increased morbidity and death (Osterberg & Blaschke, 2005), but is also associated with a significant financial impact on the health services through medicines waste. For example, a study evaluating the scale, costs and causes of medicine waste in England reported that the cost of medicine waste is estimated to be around £250 – £300 million per year in England (Trueman et al., 2010).

In the UK, community pharmacists are encouraged to play an active role in clinical services aimed at improving patient adherence with their medications. The NMS is based on actions and advice arising from subjective assessment of patients who have been newly prescribed a medication for a long-term condition, combined with follow up to address any concerns or issues patients may have once they have started using the new medicine. Issues identified within the NMS may include ineffective use of medications and detection of ADRs that may affect compliance to medications.

Proof of concept research (Barber et al., 2004; Clifford et al., 2006) was used in the development of this new service, showing how interventions by a pharmacist can help to improve patient adherence to their medications. Patients who used a pilot telephone-based pharmacist service experienced fewer medication problems and made less use of other NHS services, reducing both costs of healthcare and GP time (Clifford et al., 2006). The NMS can be provided to patients who have been newly prescribed a medication in any of four long-term therapeutic areas or treatment options: asthma and COPD, type 2 diabetes,

antiplatelet/anticoagulant therapy and hypertension (PSNC, 2013). The new medication could have been prescribed for a newly diagnosed condition or an existing long-term medical condition.

Eligible patients receive the NMS in two stages: an intervention stage within two weeks of starting the new medication, conducted in the pharmacy or over the telephone, and a follow-up stage three weeks later (PSNC, 2013). A recently conducted evaluation work carried out on behalf of the Department of Health, UK has concluded that the implementation of the NMS has been very successful in the UK and over 90% of community pharmacies have now offered this service (Elliott et al., 2014). This study demonstrated that NMS had significantly improved medicine adherence in patients by 10% (Elliott et al., 2014). However, this study did not explain the reasons or factors which contributed to the improvement in medication adherence. The aim of this study was to extend the previous assessment of the NMS on medication adherence by defining the reports of concerns about medication safety, efficacy and use, and the resolution both of adverse effects of drugs and patient problems with use of their medications.

4.3 Methods

A questionnaire-based service evaluation of the NMS was conducted in community pharmacies located in the West Midlands area, UK for a period of three months (July-Sep, 2012).

4.3.1 Objectives

1) To conduct an anonymised service evaluation of NMS offered by community pharmacists.

- 2) To access qualitative and quantitative data within NMS looking at patterns of use and case studies.
- 3) To describe the spectrum of medicines which have been the subject of patient interviews by the pharmacists, points for actions identified by pharmacists and initial reminders by the pharmacists to the outcomes of these interventions.
- 4) To use this initial work in defining key areas where the NMS has been most successful, both in terms of specifics, medicines and actions which have been needed and helpful.

4.3.2 Study development

A questionnaire approach was used in this study. A 12-item questionnaire (see Appendix E) was adopted from the validated set of worksheets produced by the PSNC, 2013 for pharmacists to apply the NMS in practice. This questionnaire was piloted on a group of four community pharmacists and was also presented at two Local Pharmaceutical Committees (LPC) in the West Midlands area. These LPCs represent pharmacists from various retail backgrounds including large multiples, small multiples, supermarkets and independent pharmacy contractors. The LPC members provided their feedback and suggestions on the length and layout of the questionnaire.

4.3.2.1 Primary outcomes

Reports of concerns about medication safety, efficacy and use, and their resolution.

4.3.2.2 Secondary outcomes

Pharmacovigilance measured through reported number of yellow cards submitted to the MHRA.

4.3.2.3 Ethical approval

Based on the University of Warwick research code of practice, this project fell within the category of service evaluation and therefore ethics approval was not required (see Appendix F). No personal data from patients or pharmacists was collected. All collected data was kept strictly confidential. The procedures for handling, processing, storage and destruction of the data complied with the Data Protection Act 1998.

4.3.3 Study participants

Data provided by community pharmacists involved patients eligible for the NMS (male or female) who had received their first prescription for a medication to treat medical conditions including asthma and COPD, type 2 diabetes, high blood pressure, and conditions for which anti-platelet treatment was indicated.

4.3.4 Study procedure

4.3.4.1 Questionnaire distribution and data collection

A total of 120 community pharmacists were invited to take part in the study. Invitations were sent through the Dudley LPC who supported and endorsed this study. Pharmacists were required to complete the questionnaire using one anonymised example of a complete NMS data set per month for each of the four medical conditions where possible. Thus each pharmacist was requested to complete 12 questionnaires in total during the three month monitoring period.

4.3.4.2 Interventions

Interventions considered in this study were those expected to be received by patients within NMS from community pharmacists as per service specifications produced by the PSNC,

(2013). These interventions included both drug/medicine related and non-medicine/drug related interventions. The drug related interventions included an assessment of patient adherence to the new medication, identification of any problems the patient may be having with their new medication(s) and exploration of possible solutions to reported problems. The non-medicine/drug related interventions included lifestyle changes such as advice offered by pharmacists on healthy eating, advice on weight management, smoking, alcohol consumption, physical activity and advice on sexual health. These interventions were conducted either by telephone or in pharmacy consultation rooms and were delivered at two stages: intervention stage 7 to 14 days of patient recruitment and follow-up stage (14 to 21) days after the first intervention stage (PSNC, 2013).

4.3.4.3 Statistical analysis

Statistical analysis was performed using IBM SPSS (version 22). Summary descriptive statistics were generated from the questionnaire data using SPSS. Summary data are presented in tables and figures as appropriate. Statistical analysis was performed with Fisher's exact test to analyse the categorical data. A P value < 0.05 was considered to be statistically significant.

4.4 Results

A total of 20 community pharmacists based in 14 pharmacies returned the completed questionnaires. The questionnaires had anonymous data of 295 patients recruited by these pharmacists in three months from 1st July 2012 to 1st September 2012. Ten questionnaires were excluded from this study due to missing data. Of the 285 patients included in the study, 160 (56%) patients were female and 125 (44%) were male.

4.4.1 Medications and conditions

A total of 285 medications were recorded on the returned questionnaires. Hypertension was the most common condition among the four medical conditions considered in the study with 145 (51%) patients receiving a new anti-hypertensive medication.

Hypertension was followed by asthma or COPD with 88 (31%) patients receiving a new medication, while diabetes and antiplatelets/anticoagulants accounted for 37 (13%) and 15 (5%) of patients respectively. Figure 4.1 describes the four medical conditions which were part of NMS interventions delivered by participating pharmacists.

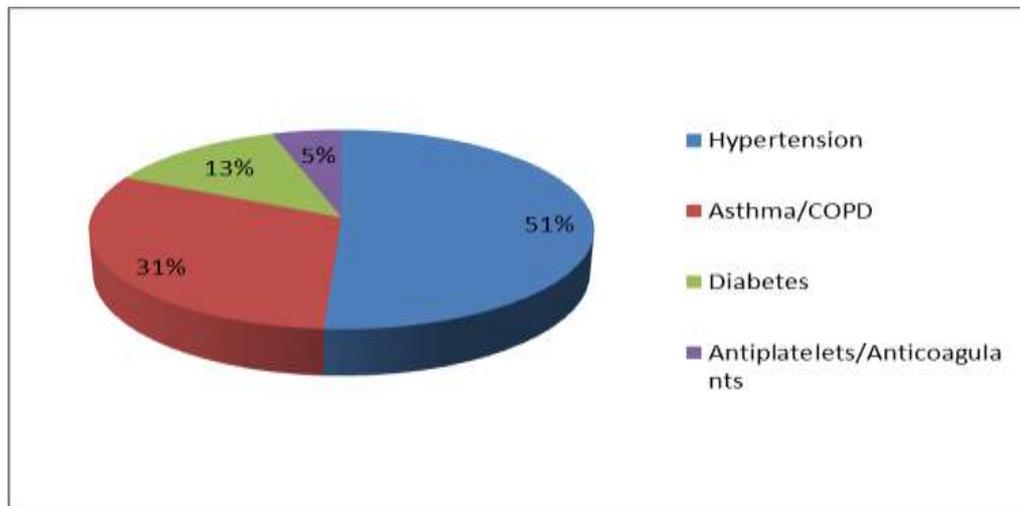


Figure 4-1 Proportion of the four medical conditions used in NMS interventions.

Among the 145 anti-hypertensive medications prescribed, calcium channel blockers (mainly amlodipine) and ace-inhibitors (mainly ramipril) were the two main classes of medications used in the interventions. Short acting β_2 -adrenergic receptor agonists (mainly salbutamol) dominated the agents used for asthma or COPD treatment, while biguanides (metformin) was the most common medicine prescribed for diabetic patients. Aspirin and warfarin were the

two main medicines used as antiplatelets and anticoagulants respectively. Table 4.1 describes a list of medicine classes on which NMS interventions were delivered.

Table 4-1 List of medication classes used in NMS interventions

Class of medication	Medical condition	No. of medications
Ace inhibitors	Hypertension	40
Calcium Channel blockers	Hypertension	45
Angiotensin receptor blockers	Hypertension	20
Beta blockers	Hypertension	15
Diuretics	Hypertension	15
Alpha blockers	Hypertension	7
Renin inhibitors	Hypertension	1
centrally acting drugs	Hypertension	2
Short acting β 2-adrenergic receptor agonist	Asthma or COPD	36
Long acting β 2-adrenergic receptor agonist	Asthma or COPD	13
Corticosteroid + Long acting β 2-adrenergic receptor agonist	Asthma or COPD	19
Corticosteroid	Asthma or COPD	17
Leukotriene receptor antagonist	Asthma or COPD	3
Biguanide	Diabetes	20
Sulfonylurea	Diabetes	7

Alpha glucosidase inhibitor	Diabetes	1
GLP-1 receptor agonists	Diabetes	1
DPP-4 inhibitors	Diabetes	3
Insulin Analog	Diabetes	4
Biguanide+DPP-4 inhibitors	Diabetes	1
Antiplatelet	Antiplatelets/Anticoagulants	9
Anticoagulant	Antiplatelets/Anticoagulants	6

4.4.2 Quantitative description of interventions

A total of 285 NMS interventions were delivered by the participating pharmacists in the three month study period. 279 of these interventions were conducted over the telephone while remaining six were conducted at the pharmacy premises (pharmacy consultation rooms). 243 of the interventions were recorded as complete interventions with patients receiving advice at both initial and follow up stages. 42 (15%) of patients did not complete the follow-up stage of the NMS. The reasons for non-completion included 28 patients not contactable, eight patients had their medication stopped by the prescriber, five patients referred to the prescriber and one patient admitted to hospital.

Pharmacists recorded 269 patients as adherent (self-reported by patients) to their medicines, while 16 patients were found to be non-adherent at the intervention stage. The reasons for non-adherence included one patient getting concerned after reading the leaflet, one patient been admitted to hospital and 14 patients been advised by their GP to stop taking their medicine. The adherence rate to anti-diabetic medications and anti-platelets/anticoagulants was found to be highest among the four medical conditions considered in the NMS (100 and

97 %) while rate of adherence to anti-hypertensive medications and asthma or COPD medications was recorded to be 94% each.

4.4.3 Description of ADRs recorded by pharmacists

51 (18%) of the 285 patients reported ADRs with their newly prescribed medications. The incidence of ADRs was reported to be highest for anti-diabetic medications and anti-hypertensive medications (25% each) while medications used for asthma or COPD and antiplatelet/anticoagulants had the lowest incidence of reported ADRs (7% each). Common ADRs reported by patients included dry cough, swollen ankles, headaches, and dizziness. Twenty-two patients who reported ADRs with their new medications were referred to their GP by the pharmacists. There is a specific requirement on the NMS worksheets to record suspected ADR through yellow card reporting (PSNC, 2013). No yellow cards were reported as submitted to the MHRA.

4.4.4 Description of medication efficacy issues recorded by pharmacists

A total of four patients reported lack of efficacy with their prescribed medications. These included three patients taking anti-hypertensive medications (one patient taking alpha-blocker and two patients taking beta-blockers) and one patient taking medication for asthma (β 2-adrenergic receptor agonist).

4.4.5 Description of incorrect use of medications by patients

27 (10%) of patients included in the study were not using their new medications correctly when assessed by pharmacists at the intervention stage. In 17 of these patients, the incorrect use of medication was related to asthma or COPD. In eight patients, there were concerns about the use of anti-hypertensive medications (seven were missing doses and one was taking

medication at the wrong time). One patient was not taking his anti-diabetic medication as prescribed and the remaining patient was not taking her anti-platelet medication as prescribed.

4.4.6 Description of healthy lifestyle advice given by pharmacists

65 (23%) patients were reported to receive advice on healthy lifestyle from pharmacists. The most common lifestyle advice given to patients was related to diet and nutrition (Figure 4.2).

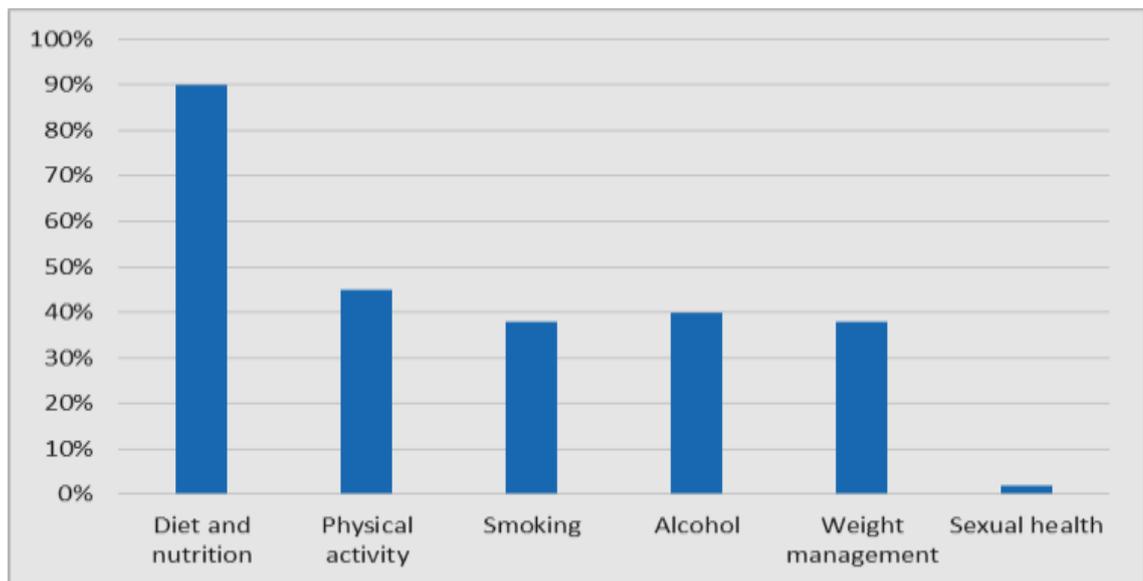


Figure 4-2 Proportion of lifestyle advice given to 65 patients by pharmacists.

4.4.7 Effectiveness of pharmacists' interventions

A total of 82 patients reported drug-related problems including adverse effects, lack of medication efficacy and incorrect use of their medications at the intervention stage. 58 of the 82 patients were reported to have received advice from pharmacists while 24 patients did not receive advice from the pharmacists. Thirty-nine (67%) of the 58 patients who received pharmacist advice reported resolution of their drug-related problems at the follow-up stage (16 due to ADRs and 26 due to the incorrect use of medications) while 19 patients did not report resolution of their problems at the follow up stage. Of the 24 patients who did not receive advice from pharmacists, only four (17%) of patients reported resolution of their

problems at follow up stage (three problems due to ADRs and one related to incorrect use of medicines) while the remaining 20 patients did not report any resolution of their problems. The odds ratio in favour of reported resolution of problems with pharmacist advice vs. no recorded advice was 10.2 (95% CI 3.0 to 34.2; $p < 0.0001$, Fisher's Exact test).

4.4.8 Examples of advice provided by pharmacists

Pharmacists recorded various types of advice given to patients within NMS. Some of the examples of advice provided by pharmacists were:

Advice 1 (Ramipril 5mg): Patient did not take her medication as she felt ok and also read the leaflet and got concerned about the side effects. Patient was assured that it was safe to take her medication.

Advice 2 (Ramipril 2.5mg): Patient was explained first dose hypotensive effect. Patient was advised to take the first dose at night.

Advice 3(Diltiazem mr 90mg): Patient experienced palpitations, was referred back to GP and the doctor stopped the medication.

Advice 4 (Moxonidine 200mcg): Patient did not like taking tablet. Was reassured it was safe to use.

Advice 5 (Salbutamol): Informed patient to use the salbutamol inhaler when needed but is not expected to use salbutamol frequently due to clenil (beclometasone).

Advice 6 (Warfarin): Patient was explained what INR means and was also advised to carry warfarin passport.

4.4.9 Confounding and its control

Although this study demonstrated the contribution of NMS in detecting ADRs and incorrect use of medicines by patients; these findings could have been explained by confounding.

Potential confounders in this study that were not measured during the study included the BMI, ethnicity, medical conditions, number of medicines used by patients, smoking, intake of alcohol, allergies and family medical history. These confounding factors along with any other unknown confounders are better controlled by using an RCT to establish causality.

4.5 Discussion

Long-term medical conditions are imposing an increasing burden on health care systems. In England alone, around 15 million people are estimated to have a long-term condition (LTC) requiring medication and other therapies (Department of Health, 2010). The findings of this chapter demonstrate the important contributions of community pharmacists within the NMS including both detecting a high rate of ADRs attributed to new medications and incorrect use of medications as common, addressable problems.

The largest category of drug-related issues identified by pharmacists in this study appeared to be incorrect use of medications by patients. It is noteworthy that pharmacists identified 10% of the patients with incorrect use of their medications. Further research is needed to investigate two major questions arising from this aspect of service evaluation: how to prevent the initial occurrence of medication-related problems such as the adverse effects and efficacy issues with medications prescribed for long-term conditions; and, what would make interventions by community pharmacists more effective, when aiming to resolving medication-related problems?

Hypertension was the most common condition treated (51%) among the four medical conditions eligible for the NMS. (31%) patients were prescribed a new medication for asthma or COPD, (13%) for new treatment for diabetes and (5%) for new antiplatelet or anticoagulant

treatment. Such dominance of hypertension and asthma or COPD as the largest target disease areas within NMS was also reported in the recent evaluation work carried out on behalf of Department of Health, UK (Elliott et al., 2014).

A high prevalence of ADRs (18%) was reported by patients during NMS consultations with the pharmacists. The incidence of ADRs was reported to be highest (25% each) for anti-diabetic medications and anti-hypertensive medications. A high incidence of ADRs with anti-diabetic (17%) and anti-hypertensive medications (15%) was previously reported in the PSNC NMS summary data report (PSNC, 2012). 22 patients who reported ADRs in this study were referred to their GP by the pharmacists. A weakness of the NMS is that no outcome data is recorded for NMS interventions by pharmacist. Within the current service specifications of the NMS, there is an opportunity to establish contact with an individual patient by conducting an MUR after six months. This is a potential weakness of the NMS as lack of validation means that pharmacists are unaware if their advice to patients and GPs is acted upon. As evident from the findings of this study, some NMS consultations will necessitate recommendations being made to GPs e.g. a change in formulation or inhaler device or perhaps because an adverse drug reaction is reported. In the absence of any feedback on their recommendations, community pharmacists would be unaware of the impact of their clinical advice to prescribers. A separate study would be needed with ethical approval to approach and track patients to obtain objective evidence of effectiveness of the NMS in practice.

The NMS provides a specific prompt to report ADRs using the national Yellow Card reporting system (PSNC, 2013). However, despite recording 51 ADRs, none of the pharmacists who took part in this evaluation reported submitting a Yellow Card for a suspected ADR. This finding is in contrast to the findings of previous evidence which

suggested that following the introduction of the NMS in October 2011, over 700 new Yellow Cards were reported by pharmacists over a 12 month period (Jadeja & McCreedy, 2012). Prompt reporting of suspected ADRs is fundamental in the post-marketing surveillance of medicines and helps in ensuring medicine safety (MHRA, 2014). Pharmacists should therefore use the opportunity provided in the NMS to report suspected ADRs to the MHRA.

Successive recent governments in the UK have initiated schemes for extensions in the role of community pharmacists, through independent prescribing, medication use reviews, and health promotion (Coggans, McKellar, Bryson & Parr, 2001; Department of Health, 2005; Sinclair, Bond, Lennox, Silcock, Winfield & Donnan, 1998). The NMS continues this strategy, with providing lifestyle advice as a major component (PSNC, 2013); in addition to identifying and managing ADRs, and ensuring that medications are being used appropriately. However only one in four patients in this analysis was reported to have been given lifestyle advice by pharmacists. Lifestyle advice should be provided at both intervention and follow up stage of NMS. Previous systematic reviews and meta-analysis have demonstrated that community pharmacists can significantly improve blood pressure control of hypertensive patients by giving advice related to medications as well as advice on lifestyle (Machado et al., 2007; Morgado et al., 2011; Santschi et al., 2011a; Santschi et al., 2014).

Although the NMS consultations can be conducted both over the telephone and in the consultation room, telephonic consultations were the most popular method of NMS contact in this study. There is some evidence to suggest that telephonic consultations can achieve better compliance to treatment as compared to face-to-face consultations (Mohr, Ho, Duffecy, Reifler, Sokol, Burns et al., 2012). Telephonic consultations can be a preferable method of contact both for patients who do not live close to the pharmacy and for pharmacists as it can

allow them to conduct consultations at less busy times (Wells, Thornley, Boyd & Boardman, 2014).

The identification of the incorrect use of medicines by asthmatic patients reported in this study, would have important implications for improving the healthcare outcome of patients with asthma. Several studies involving community pharmacy-led asthma interventions have demonstrated a positive impact on patients' asthma-related quality of life and peak expiratory flow rates (Barbanel, Eldridge & Griffiths, 2003; Cordina, McElnay & Hughes, 2001; Herborg, Soendergaard, Jorgensen, Fonnesbaek, Hepler, Holst, 2001; Narhi, Airaksinen & Enlund, 2001; Schulz, Verheyen, Muhlig, Muller, Muhlbauer, Knop-Schneickert et al., 2001).

Internationally, community pharmacists are actively engaged in improving the healthcare outcomes of patients by improving medicines adherence and by promoting healthy lifestyle (Pharmaceutical Group of the European Union [PGEU], 2008). For example in Finland, a nationwide asthma programme was introduced whereby a community pharmacist helps the prescriber in delivering guidance to asthmatic patients on their medication (PGEU, 2008). Similarly in Denmark, an asthma specific pharmaceutical care programme was associated with a reduction in inhalation errors and improved drug prescribing (PGEU, 2008). There is an obvious scope to extend initiatives like NMS to other countries as it has a great potential to improve new medication use in patients with long-term conditions. Evidence from this report recognises this potential and supports the need for continuing this service in the long-term. However, more work involving an active participation from community pharmacists needs to be done to demonstrate the clinical value of this service.

This study has several key limitations. Although this study demonstrated the contribution of NMS in detecting ADRs and incorrect use of medicines by patients; these findings could have been explained by confounding. Any known or unknown confounding factors are better controlled by using an RCT to establish causality. This study had no control group and therefore, it cannot be assumed that the positive impact on patient healthcare outcomes reported in this study was produced by pharmacists' interventions. Another limitation of this study was the lack of objective clinical data on patient outcomes. However, it should be pointed that like MURs, NMS is a review of medicines use and is not a clinical review. Recording clinical data for patients is outside the scope of NMS and is a weakness of the NMS in its current format. This study had a very low response rate from pharmacists. However, the participation of pharmacists from all sectors of community pharmacy including large multiples, small multiples, supermarkets and independents suggest that the findings of this study are likely to be generalisable across the wider community pharmacy sector.

Summary of chapter

The findings of this chapter demonstrate the contributions of community pharmacists within NMS in detecting both a high rate of ADRs attributed to new medications and incorrect use of medications by patients. However, the very low response rate from pharmacists in this study coupled with the absence of a control group suggested that this chapter did not fully meet the second objective of the thesis.

4.6 Conclusion

This evaluation provides support for the NMS as an opportunity to improve detection and resolution both of ADRs and incorrect use of medications by patients. However, the very low response rate from pharmacists in this study coupled with the absence of a control group suggests that the findings of this study may not be generalizable across the wider community sector. Further research using an RCT would be required to compare the effectiveness of the NMS interventions in the clinical practice.

The next chapter evaluates the level of ADR reporting by pharmacists in the UK.

Chapter Five

5 Reporting of ADRs by community pharmacists in UK: a questionnaire-based audit to identify the barriers towards spontaneous reporting

This chapter aims to address the third objective of the thesis by evaluating the current understanding of community pharmacists about ADRs, level of ADR reporting and barriers to ADR reporting.

5.1 Abstract

This chapter was aimed to evaluate the level of ADR reporting by community pharmacists and to identify the barriers to ADR reporting. A questionnaire based audit was conducted in the UK from April to September 2012. Statistical analysis was performed with the Fisher's exact test. A total of 139 questionnaires were returned (78 females and 61 males). Two important factors for reporting an ADR were identified: being confident of which ADRs to report (odds ratio 1.8, 95% CI 1.1 to 3.0 $p = 0.011$ Fisher's exact test) and being confident of how to report (odds ratio 4.3, 95% CI 2.5 to 7.5 $p < 0.0001$). Lack of time and uncertainty about the seriousness of an ADR were among the barriers to spontaneous reporting. This study highlights barriers to spontaneous reporting of ADRs. There is a need to provide explicit education and training to pharmacists at both undergraduate and professional level to improve their understanding and awareness of ADRs.

5.2 Background

ADRs are a major public health problem. They are a significant cause of hospital admissions and prolonged hospital stay (Meier et al., 2014; Pirmohammed et al., 2004) and increase the cost of disease management in patients. Evidence from a meta-analysis of 25 prospective observational studies (Kongkaew, Noyce & Ashcroft, 2008) reported that approximately 5.3% of hospital admissions were directly related to ADRs.

A large proportion of ADRs can be prevented by improved drug prescribing, administration and importantly through consistent and prompt recording and reporting (MHRA, 2014). Some predictable ADRs occur when patients are prescribed the same medications to which they have previously experienced an ADR (Shenfield, Robb & Duguid, 2001). Prompt reporting of suspected ADRs is fundamental in the post-marketing surveillance of medicines and helps in ensuring medicine safety (MHRA, 2014). Community pharmacists in particular are well placed to identify and report ADRs, as they have frequent interaction with the public (PSNC, 2013). However, despite this frequent interaction with the public, the number of ADR reports submitted by community pharmacists remains low (Jadeja & McCreedy, 2012).

Although, a lot of work has been done to explore the knowledge, perception and barriers towards ADR reporting by community pharmacists worldwide (Elkalmi, Hassali, Ibrahim, Jamshed & Al-Lela, 2014; Granas, Buajordet, Stenberg-Nilsen, Harg & Horn, 2007; Irujo, Beitia, Bes-Rastrollo, Figueiras, Hernández-Díaz & Lasheras, 2007), very little is known about the factors which could prevent community pharmacists in UK from reporting an ADR (Green et al., 1999; Whittlesea & Walker, 1996). More work therefore needs to be done to evaluate the level of ADR reporting by community pharmacists in the UK.

5.3 Methods

This study was a questionnaire based audit and was conducted in the UK from April to September 2012.

5.3.1 Study development

A questionnaire approach was used in this study (see Appendix G for questionnaire). The style and format of some of the questions were adopted from a previous questionnaire-based survey in the Netherlands (Eland, Belton, Grootheest, Meiners, Rawlins & Stricker, 1999). The questionnaire was piloted among a group of six community pharmacists.

5.3.1.1 Ethical approval

Based on the University of Warwick research code of practice, this project fell within the category of an audit and therefore ethics approval was not required. The study was completely anonymous as the researchers did not request any personal data from pharmacists such as name, date of birth and ethnicity which could identify the participants. All information collected from this study was kept strictly confidential. The procedures for handling, processing, storage and destruction of the data complied with the Data Protection Act 1998. Only members of the research team had access to the completed questionnaires.

5.3.2 Study procedure

5.3.2.1 Questionnaire distribution and data collection

Community pharmacists were invited to participate in the study by giving 10 minutes presentation at two Local Pharmacy Committee (LPC) meetings in the West Midlands area. As a result, the local management of the largest pharmacy chain in the UK agreed to arrange

the distribution of questionnaires among their 230 pharmacist employees based in the West Midlands area. In order to further increase the capacity to recruit and to have a large database, management of the PSNC were approached to request the online distribution of the questionnaire to the local pharmacy committees.

5.3.2.2 Statistical analysis

Statistical analysis was performed with IBM SPSS Statistics (version 22). The results are presented as odds ratios, percentage frequencies and 95% confidence intervals, where appropriate. A step wise multivariable linear regression analysis was undertaken to explore the influence of various explanatory or independent variables including the reasons for not reporting ADRs (listed in Table 5.1) and the ADRs reported by pharmacists as the dependent variable.

5.4 Results

A total of 139 pharmacists returned the completed questionnaires. The mean age of participants was 34 years, 78 (56%) were females and 61 (44%) were males. 32 (23%) of the respondents were pharmacy managers, 59 (42%) were store based pharmacists and 48 (35%) were relief pharmacists. 12 (9%) of the respondents had been qualified as a pharmacist for less than a year, 56 (40%) had an experience of 1-5 years, 18 (13%) had an experience of 6-10 years, 20 (14%) had an experience of 11-20 years and 33 pharmacists (24%) had been qualified for more than 20 years.

5.4.1 Level of reporting by community pharmacists

Pharmacists were asked if they had ever reported an ADR. Just over a half (51%) of the pharmacists said that they had reported an ADR before, while the remaining 68 (49%) said

they never reported an ADR. 104 (75%) of the pharmacists expressed confidence in how to report an ADR while the remaining 35 (25%) did not have the confidence to report a suspected an ADR. 89 (64%) of the participating pharmacists were confident of which ADRs to report, while 50 (36%) felt they were not confident enough of which ADRs to report. Two important factors for reporting an ADR were identified: being confident of which ADRs to report (odds ratio 1.8, 95% CI 1.1 to 3.0 p = 0.011 Fisher's exact test) and being confident of how to report an ADR (odds ratio 4.3, 95% CI 2.5 to 7.5 p < 0.0001. Figure 5.1 presents the percentage of ADRs reported by 71 pharmacists.

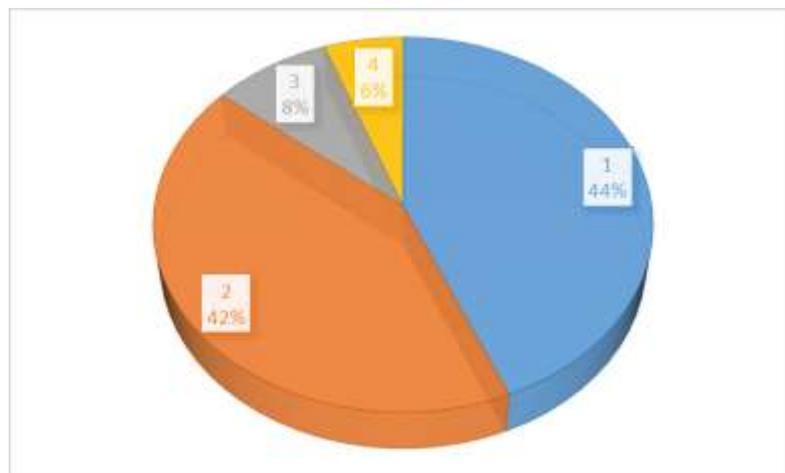


Figure 5-1 Number and proportion of ADRs reported by 71 pharmacists.

The questionnaire required the pharmacists to record when they last reported a suspected ADR. 40 (56%) of the 71 pharmacists who stated to report an ADR did it more than a year ago, 16 (23%) reported more than six months ago, 6 (8%) reported more than three months ago and five (7%) reported an ADR more than a month ago. The remaining four (6%) pharmacists did not remember when they last reported a suspected ADR.

5.4.2 Nature and severity of ADRs recorded by pharmacists

Of the 71 pharmacists who reported a suspected ADR, 30 (42%) of them considered the reaction to be serious while 20 (28%) did not consider the reaction to be serious. The

remaining 21 (30%) of the pharmacists did not respond to this question. Some of the ADRs reported by pharmacists included swelling of tongue suspected with gabapentin, severe cramps with rivaroxaban, severe myalgia with simvastatin, breathlessness with finasteride, fainting with ramipril, pruritus with dipyrimadole, severe allergy with tiotropium, severe urticaria with metformin and blotching with amlodipine. A severe ADR suspected from St. Johns wart resulted in patient hospitalisation. Three pharmacists reported suspected ADRs from OTC medications including ibuprofen and pholcodine.

5.4.3 Reporting of ADRs in adults

Pharmacists were asked which suspected ADRs they would consider for reporting in adults: 1) report a serious reaction from a Prescription Only Medicine (POM); 2) a serious reaction from a herbal drug; 3) a serious reaction from an OTC medicine; 4) a serious reaction from a drug with black triangle; 5) a mild reaction from a drug with black triangle; and 6) a mild reaction from an existing drug. A total of 137 pharmacists responded to this question.

Majority of the pharmacists (97%) stated that they would report a serious reaction from a drug with a black triangle. 126 (92%) stated they would report a serious reaction from POM, while 121 (88%) said they would report a serious reaction from an OTC medicine. As far as the reporting of a serious reaction from a herbal drug was considered, 112 (82%) agreed to reporting such reactions, while 104 (76%) considered to report a mild reaction from a drug with black triangle. Only 18 (13%) of the respondents agreed to report a mild reaction from an existing drug.

5.4.4 Reporting of ADRs in children

With regards to reporting of suspected ADRs in children, almost all (99%) of the 137 respondents considered to report a serious reaction from a drug with black triangle. Majority

of them (98 and 96%) agreed to report serious reactions suspected from a POM and OTC medicines, respectively. 123 (89%) stated to report a serious reaction suspected with herbal medicines. Similarly, 118 (86%) also agreed to report a mild reaction from drug with black triangle. However, only 53 (39%) of the pharmacists said they would consider to report a mild reaction from an existing drug.

5.4.5 Barriers to reporting

Pharmacists were asked to provide reasons for not reporting ADRs. Just over a half of the respondents (53%) cited lack of time as a reason for not reporting ADRs. Table 5.1 presents the complete list of factors that were considered as barriers by pharmacists to report ADRs. Unable to report an ADR due to lack of certainty about the drugs responsible for suspected ADR had a significant linear association with reporting an ADR ($p = 0.01$). None of the other variables showed any significant association with ADR reporting.

Table 5-1 Reasons considered by pharmacists for not reporting a suspected ADR

<i>Reason</i>	<i>Percentage</i>
Did not report because was not clear what ADR is	11 (9%)
Did not report because did not know how to report	15 (13%)
Did not report because did not consider duty to report	2 (2%)
Did not report because did not have time to report	63 (53%)
Did not report because did not have access to internet	19 (16%)
Did not report because considered reaction too well known to report	51 (43%)
Did not report because did not consider reaction too serious to report	51 (43%)
Did not report because was not sure which drugs were responsible for ADRs	33 (28%)
Did not report because did not have complete information to report	35 (29%)

5.4.6 Future training and support

Pharmacists were asked to state what training and support would be helpful to improve reporting of ADRs in future. They were provided with the option of choosing one or more of the options which were: 1) information about what to report, 2) information about how to report and 3) IT access to ADR reporting system. Information about what to report was the most frequently cited response to this question as 89 (79%) of the pharmacists favoured this option. Access to reporting system through IT (option 3) was also considered by many to be helpful (75%), while 66 (58%) considered information about how to report to be useful in improving ADR reporting.

5.4.7 Confounding and its control

Although this study suggested an association between awareness about what to report and reporting of suspected ADRs; such association could have been explained by confounding. Potential confounders in this study that were not considered in data analysis included the ethnicity of pharmacists, their job title, level of education and level of experience. These confounding factors along with any other unknown confounders are better controlled by using an RCT to establish causality.

5.5 Discussion

This chapter presents the current level of ADR reporting by pharmacists and the challenges to spontaneous reporting of ADRs. Awareness about what to report and how to report was associated with an increased tendency to report suspected ADRs. Lack of time and uncertainty about the seriousness of ADR were among the barriers to spontaneous reporting. There was a major consensus among the pharmacists that access to online resources and provision of further education on what to report would be helpful in improving the reporting of suspected ADRs.

Just over a half (51%) of the pharmacists who participated in this study said that they had reported an ADR before, while the remaining 68 (49%) said they never reported an ADR. This finding is in contrast to the findings of two previous studies that reported 4% (Green et al., 1999) and 21% (Whittlesea & Walker, 1996) of ADR reporting by community pharmacists in the UK. Although this study reported an improvement in ADR reporting among community pharmacists, the national reporting numbers by community pharmacists remain low and static. Around 370 ADR reports are submitted annually by community

pharmacists that accounts for 3 to 4% of all direct health professional yellow card reporting in the UK (Jadeja & McCreedy, 2012).

According to the NHS Business Services Authority figures, there were 11,495 community pharmacies in England on 31st March 2013 (Health and Social Care Information Centre UK, 2013). If each yellow card received by MHRA was from an individual community pharmacy, this suggests that less than 2% of pharmacies in England reported suspected ADRs. ADRs are not hard to find in the community. Evidence from a cohort study involving 167 patients at a Veterans Affairs Medical Centre in the United States reported that up to 35% of the patients experienced an adverse drug event (Hanlon, Schmader, Koronkowski, Weinberger, Landsman, Samsa et al., 1997). The incidence of ADRs has been reported to be even higher amongst nursing home residents (Gurwitz, Field, Avorn, McCormick, Jain, Eckler et al., 2000).

Knowledge about which ADRs to report and the confidence in how to report was reported to have a positive association with the number of ADRs reported by pharmacists in this study. Although majority of the pharmacists were aware of how to report, around a third of the pharmacists expressed their lack of confidence in which ADRs to report. A previous study in the UK that explored the knowledge and attitudes of 322 hospital pharmacists towards ADR reporting also reported the lack of ability of pharmacists in diagnosing a suspected ADR (Green, Mottram, Rowe & Pirmohamed, 2001).

Majority of the respondents in this study stated that they would report a serious reaction from a drug with a black triangle and POM in both adults and children. While there was consensus among the participants in reporting serious reactions in both adults and children, only three

quarters of the participants considered to report mild reactions from new drugs in adults. As far as the reporting of mild reactions from existing drugs in children was concerned, only (39%) of the pharmacists said they would consider to report such reactions. A very small proportion of the respondents (13%) in this study stated to report a mild reaction from an existing drug. These findings are in parallel with the findings of previous two studies that reported that pharmacists do not consider minor reactions worthy enough to be reported (Green et al., 1999; Green et al., 2001). However, this study reported a higher percentage of pharmacists who were in agreement to report OTC medicines both in adults and children as opposed to a small proportion of pharmacists found to report such reactions in a previous study involving community pharmacists in the UK (Green et al., 1999).

Lack of time, well known reactions and reactions not serious enough to be reported were among some of the main reasons cited by pharmacists for not reporting suspected ADRs. Such barriers or deterrents to reporting of ADRs have not only been reported in studies conducted in the UK (Belton, Lewis, Payne, Rawlins & Wood, 1995; Green et al., 1999; Sweis & Wong, 2000; Whittlesea & Walker, 1996), but also studies conducted outside the UK (Eland et al., 1999; Khalili, Mohebbi, Hendoiee, Keshtkar & Dashti-Khavidaki, 2012).

The findings of this study underscore the importance of providing explicit education and training to improve the understanding and awareness of ADRs among pharmacists at both undergraduate and professional level. Previous studies aimed at investigating the extent of pharmacovigilance education provided to medical and pharmacy students suggest an increased devotion to the time spent on pharmacovigilance education (Smith & Webley, 2013) and involvement of MHRA in the development of such education (Cox, Marriott, Wilson & Ferner, 2004). Research indicates that training is associated with an increased

likelihood to ADR reporting (Green et al., 2001; Sweis & Wong, 2000). A recent study in Denmark demonstrated the capabilities and competencies of trained pharmacy students in the identification and reporting of ADRs experienced by patients (Christensen, Sondergaard, Honore & Bjerrum, 2011).

There is a need to nurture the culture of reporting along with the strengthening and re-enforcement of the pharmacovigilance education to community pharmacists. The general attitude towards reporting adverse events is variable among various healthcare professionals (Kingston, Evans, Smith & Berry, 2004; Lawton & Parker, 2002; Stanhope, Crowley-Murphy, Vincent, O'Connor & Taylor-Adams, 1999). As far as pharmacists are concerned, a previous experimental study in the UK involving 223 community pharmacists and 52 members of support staff concluded that community pharmacists and their support staff are unlikely to report an adverse event in the community pharmacy (Ashcroft, Morecroft, Parker & Noyce, 2006). This culture of reporting needs to change and will only be possible if all stakeholders including pharmacy professional bodies and pharmacy schools play a proactive role in promoting and fostering the culture of spontaneous reporting.

This study has some key limitations. Although this study suggested an association between awareness about what to report and reporting of suspected ADRs; such association could have been explained by confounding. Any known or unknown confounders are better controlled by using an RCT to establish causality. No power calculation was undertaken prior to the commencement of this study. However, it may be argued that this study was a descriptive study with no hypothesis testing. Therefore, the sample size used in this study was based on available resources. Another important limitation of this study was the use of an adopted questionnaire from a previously validated study. However, this adaptation was

necessary to ensure the inclusion of questions that were suitable to address the research outcomes. The questionnaire relied on self-reported responses from the participants, therefore the actual number of pharmacists not reporting an ADR could be higher or vice versa.

Summary of chapter

This chapter has identified lack of time and uncertainty about the seriousness of ADRs as some of the barriers to ADR reporting. Furthermore, it has also suggested an association between the awareness about what to report and how to report with the reporting of ADRs. However, the use of an adapted questionnaire indicates that the findings of this study should be viewed with caution. This chapter therefore fails to effectively address the third objective of the thesis.

5.6 Conclusion

This chapter highlighted important barriers towards spontaneous reporting of ADRs by community pharmacists. However, the use of an adapted questionnaire indicates that the findings of this study should be viewed with caution.

Pharmacists reported a number of ADRs that were suspected with anti-hypertensive medications. The suspected incidence of ADRs with anti-hypertensive medications can lead to poor adherence to anti-hypertensive medications by patients. Community pharmacists appear to be an important resource for improving hypertension control. The next chapter assesses the role of community pharmacists in the management of hypertension and its treatment.

Chapter Six

6 The impact of interventions by pharmacists in community pharmacies on control of hypertension: a systematic review and meta-analysis of randomised controlled trials

This chapter aims to address the fourth objective of the thesis by conducting a systematic review and meta-analysis of the impact of pharmacist interventions on blood pressure control. The aim of this review is to extend previous assessment of the impact of community pharmacist interventions on blood pressure control by limiting the analysis to RCTs and by evaluating studies in patients with hypertension with or without cardiovascular co-morbidities.

6.1 Abstract

Hypertension is a major health problem, yet its control is poor in the community. A systematic review and meta-analysis of RCTs was conducted to assess the impact of community pharmacist-led interventions on blood pressure control. Eight electronic databases were searched up to 30th November 2013, with no start date (Web of Science, Embase, The Cochrane Library, Medline Ovid, Biomed Central, Biosis, Citation Index, CINAHL, PsycINFO). All studies included were RCTs involving patients with hypertension, with or without cardiovascular-related co-morbidities, with difference in blood pressure as an outcome. Data collected included study design, baseline characteristics of study populations, types of interventions, and outcomes. The Cochrane tool was used to assess risk of bias. From 340 articles identified on initial searching, 16 RCTs (3,032 patients) were included.

Pharmacist-led interventions included patient education on hypertension, management of prescribing and safety problems associated with medications, and advice on lifestyle. These interventions were associated with significant reductions in systolic (11 studies [2,240 patients]; -6.1 mm Hg [95% CI, -3.8 to -8.4]; $p < 0.00001$) and diastolic blood pressure (11 studies [2,246 patients]; -2.5 mm Hg [95% CI, -1.5 to -3.4; $p < 0.001$). Community pharmacist-led interventions can significantly reduce systolic and diastolic blood pressure. These interventions could be useful for improving clinical management of hypertension

A paper related to this chapter has been published in the British Journal of Clinical Pharmacology: Cheema, E., Sutcliffe, P. and Singer, D. R. J. (2014). The impact of interventions by pharmacists in community pharmacies on control of hypertension: a systematic review and meta-analysis of randomized controlled trials. *British Journal of Clinical Pharmacology*, 78: 1238–1247. doi: 10.1111/bcp.12452.

6.2 Background

Despite benefits of blood pressure control for reducing risk of stroke and coronary heart disease and other serious cardiovascular events (Lewington et al., 2002; Cook et al., 1995), hypertension continues to be poorly controlled in the community (WHO, 2011). It has been reported that pharmacist-led interventions can lead to significant reductions in blood pressure in patients seen in a range of healthcare settings (Machado et al., 2007; Morgado et al., 2011), including secondary care, community health clinics and community pharmacies (Santschi et al., 2011a; Santschi et al., 2014). However, previous systematic reviews and meta-analysis of blood pressure control have been limited by including very short-term studies (Machado et al., 2007), and by including observational studies (Machado et al., 2007; Morgado et al., 2011). Furthermore, these reviews have largely confined outcomes to hypertensive patients with no reported cardiovascular problems including diabetes, kidney disease, stroke, atrial fibrillation, myocardial infarction and/or heart failure (Machado et al., 2007; Morgado et al., 2011) and by being unclear about the specific role of community pharmacists in improving the management of high blood pressure (Santschi et al., 2014).

Increasingly in clinical practice, patients with hypertension have an associated range of cardiovascular co-morbidities. The aim of this systematic review and meta-analysis was to extend previous assessment of the impact of community pharmacist interventions on blood pressure control by limiting the analysis to RCTs and by evaluating studies in patients with hypertension with or without cardiovascular co-morbidities. Heterogeneity in pharmacist interventions was minimized by including data only from RCTs, by being specific about the setting for pharmacist intervention i.e. community pharmacies, and by standardizing the nature of active pharmacist interventions.

6.3 Methods

6.3.1 Search strategy for identification of studies

A literature search of published articles with no start date restrictions, was undertaken in November 2013 in eight electronic health-related databases: MEDLINE, Web of Science, the Cochrane library, EMBASE, Biosis Citation Index and Biomed Central, CINAHL and PsycINFO. Articles were retrieved up to 30th November 2013. Search terms included "community pharmacy", "hypertension", OR "blood pressure", "randomised controlled trial" and "intervention" (see Appendix H for complete search strategy).

In addition reference lists were screened of all included articles retrieved at full paper and the first 100 results of this search strategy applied to Google Scholar. Reference list of another systematic review and meta-analysis published in April 2014 was screened for additional eligible RCTs (Santschi et al., 2014).

6.3.2 Types of studies

RCTs and systematic reviews of RCTs evaluating the clinical impact of community pharmacist interventions on patients with hypertension were included. Systematic reviews were searched to identify additional eligible RCTs. RCTs were included if they had a control group receiving standard or usual care, compared with the care in intervention groups.

6.3.3 Types of participants

All participants were adults (18 years or older) participating in an RCT of treatment for their hypertension in community pharmacies. A study was included if it had a minimum of 80% of the population meeting the inclusion criteria for study participants. Studies were also included which had participants with co-existing cardiovascular-related medical conditions (e.g., high cholesterol, diabetes, renal disease, and clinical cardiovascular disease, including cerebrovascular disease and peripheral arterial disease).

6.3.4 Types of interventions

Pharmacological interventions were defined as interventions concerning education on drug treatment of blood pressure, advice to patients to improve medication adherence, identifying drug adverse effects and drug prescribing issues, and liaising with prescribers about concerns of drug treatment. Non-pharmacological interventions were defined as those concerning education about hypertension, and education about lifestyle, such as advice to patients on healthy lifestyle, including, diet, weight management, alcohol consumption and smoking cessation.

6.3.5 Types of outcome measures

6.3.5.1 Primary outcomes

Reduction in systolic blood pressure (SBP) and diastolic blood pressure (DBP) measured in the community pharmacies or at home.

6.3.5.2 Secondary outcomes

Improvement in adherence to anti-hypertensive medications measured by tablet count, by pharmacy dispensing records, by use of the four point Morisky questionnaire (Morisky, Green & Levine, 1986) and by prescription claims data.

Identification and management of drug-related problems. Drug-related problems were defined as concerns about adverse drug effects expressed by the patient or the pharmacist.

Methodology for assessing this was non-standard across included studies. Inappropriate drug selection or dose was based on pharmacist access to formularies and guidelines: sources for these were not clear across the studies.

Impact on cardiovascular risk factors: smoking, alcohol consumption, weight, cholesterol level (mmol/L) and HbA1c (%).

6.3.6 Exclusion criteria

Studies with multidisciplinary interventions in which pharmacist's intervention within the team was not clearly defined were excluded. In addition, conference proceedings or abstracts only, systematic reviews of RCTs containing less than 50% of eligible studies, and articles published in languages other than English were also excluded.

6.3.7 Data extraction, risk of bias and quality assessment

Two reviewers (E.C, P.S) independently reviewed titles and abstracts of all potentially relevant papers. Papers which met inclusion criteria were retrieved at full paper and these two reviewers checked each paper for inclusion. Any differences were agreed through discussion or resolved by a third reviewer D.S. E.C independently extracted data and P.S checked all extraction sheets (see Appendix I for characteristics of included studies).

Criteria for quality assessment of included systematic reviews were based on those of the NHS Centre for Reviews and Dissemination (CRD), (1999). E.C along with P.S rated each paper using the Cochrane Risk of Bias tool (Higgins & Green (Eds), 2011) to assess RCTs on their randomisation procedure, allocation concealment, blinding of participants, reporting of incomplete outcome data, selective reporting, or any other biases that did not fit into the above mentioned categories. Other sources of bias explored in this review included possibility of cross-contamination between study groups, recruitment of participants from a selected population, and non-compliance of researchers to study protocol. For each included study, a risk of bias graph and a risk of bias summary were generated. The use of power calculations was recorded. A critical appraisal of the review was conducted with the CASP tool.

6.3.8 Statistical analysis

A narrative overview and analysis of included RCTs and systematic reviews was undertaken and supplemented with further meta-analyses. A cumulative meta-analysis of studies was used to identify changes in blood pressure control overtime. Meta-analyses were undertaken with random effects models (Rev Man version 5.2). Mean differences [SD] and 95% confidence intervals were used to estimate effects. Because of differences in study population, sample size and methods of blood pressure measurement, a random effects model was used, and tau squared recorded. To minimize heterogeneity in the meta-analysis, studies using three similar interventions were used (patient education on disease management, identification and management of prescribing and safety problems associated with anti-hypertensive medications, and advice on lifestyle). Heterogeneity was measured by Cochrane's test. Statistical heterogeneity beyond that expected through chance was investigated using I². Heterogeneity was further explored with sensitivity analysis by repeating meta-analysis after excluding a single outlying study, and by using both random and fixed-effect models.

6.4 Results

A total of 340 studies were identified (see Figure 6.1 for Prisma flow diagram), 330 from electronic databases and 10 from reference lists of previous reviews. 53 duplicates were removed. 287 records were screened at title level, with 143 irrelevant titles removed. The remaining 144 records were screened at abstract level. After eliminating abstracts not meeting inclusion criteria, 70 full text studies were assessed for eligibility. 54 studies did not meet inclusion criteria. Reasons for exclusion included: not RCTs, different study settings, systematic reviews containing < 50% of eligible studies, intervention not provided by community pharmacists, < 80% study population hypertensive, blood pressure not a study

outcome, studies not defining details of community pharmacist roles, and studies with published protocol only. 16 RCTs contributed to the systematic review (Ali, Schifano, Robinson, Phillips, Doherty, Melnick et al., 2012; Amariles, Sabater-Hernandez, Garcia-Jimenez, Rodriguez-Chamorro, Prats-Mas, Marin-Magan et al., 2012; Blenkinsopp, Phelan, Bourne & Dakhil, 2000; Doucette, Witry, Farris & McDonough, 2009; Fornos, Andres N, Andres J, Guerra & Egea, 2006; Garcao & Cabrita, 2002; Krass, Armour, Mitchell, Brilliant, Dienaar, Hughes et al., 2007; McKenney, Slining, Henderson, Devins & Barr, 1973; McKenney, Brown & Necsary, 1978; McLean, McAlister, Johnson, King, Makowsky, Jones et al., 2008; Park, Kelly, Carter & Burgess, 1996; Planas, Crosby, Mitchell & Farmer, 2009; Santschi, Lord, Berbiche, Lamarre, Corneille, Prud'homme et al., 2011b; Sookaneknun, Richards, Sanguansermisri & Teerasut, 2004; Svarstad, Kotchen, Shireman, Brown, Crawford, Mount et al., 2013; Zillich, Sutherland, Kumbera & Carter, 2005). Of these, 11 studies were included in the meta-analysis (Ali et al., 2012; Amariles et al., 2012; Doucette et al., 2009; Fornos et al., 2006; Garcao & Cabrita, 2002; Krass et al., 2007; Mckenney et al., 1978; Park et al., 1996; Sookaneknun et al., 2004; Svarstad et al., 2013; Zillich et al., 2005).

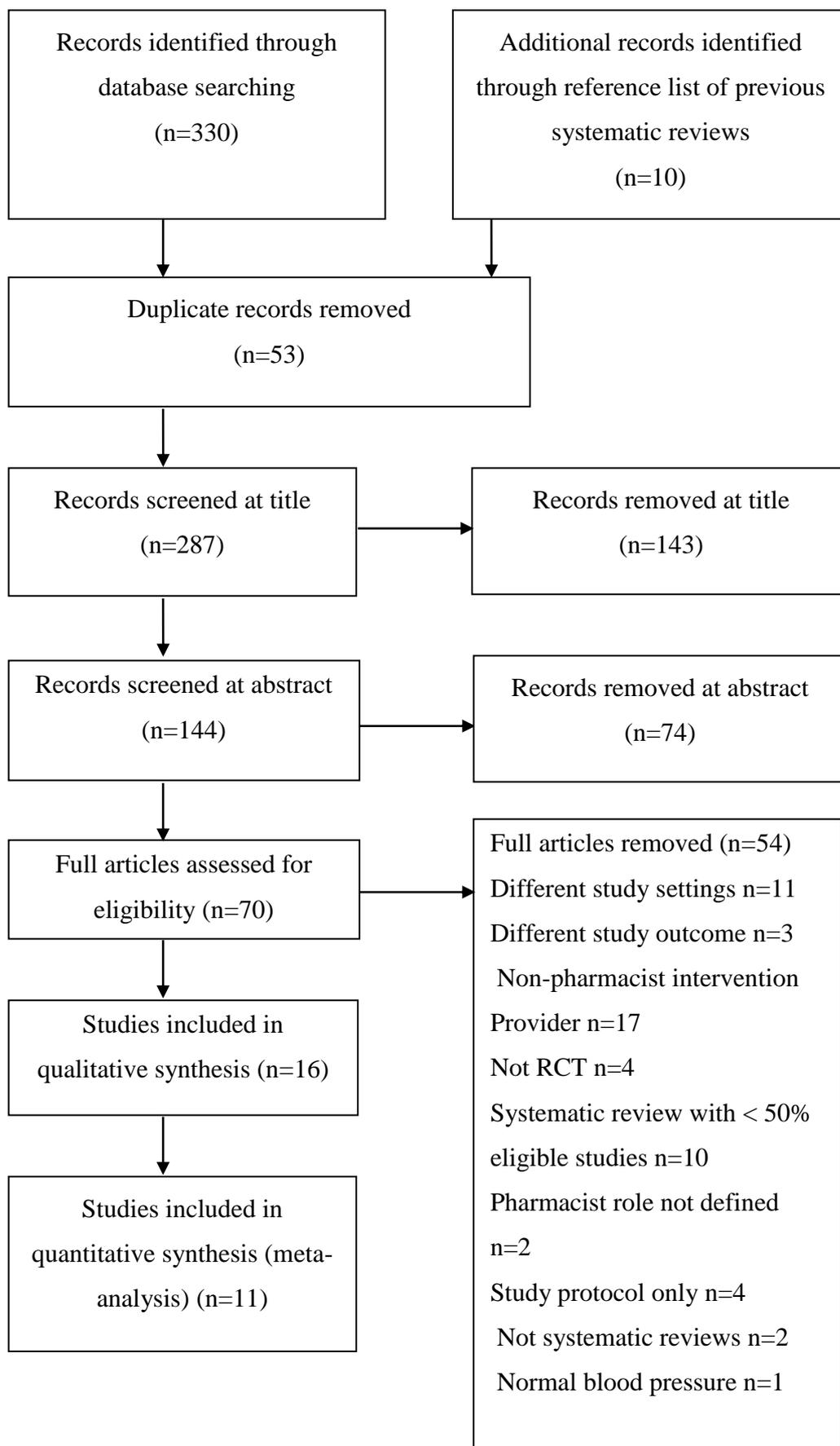


Figure 6-1 Prisma flow diagram.

6.4.1 Study characteristics

All 16 studies included were RCTs conducted in community pharmacies. These trials were conducted in Australia (Krass et al., 2007), Canada (McLean et al., 2008; Santschi et al., 2011b), Portugal (Garcao & Cabrita, 2002), Spain (Amariles et al., 2012; Fornos et al., 2006), Thailand (Sookaneknun et al., 2004), United States (Doucette et al., 2009; Mckenney et al., 1973; Mckenney et al., 1978; Park et al., 1996; Planas et al., 2009; Svarstad et al., 2013; Zillich et al., 2005) and United Kingdom (Ali et al., 2012; Blenkinsopp et al., 2000). All 16 studies used intervention groups receiving a selection from the following interventions by community pharmacists: patient education on disease management, identification and management of prescribing and safety problems associated with anti-hypertensive medications, and advice on lifestyle, compared to a control group receiving usual care. No systematic reviews meeting the inclusion criteria were identified.

Length of intervention ranged from three months (Zillich et al., 2005) to 13 months (Fornos et al., 2006). The studies included 3,034 patients, individual study size ranging from 50 (Mckenney et al., 1973) to 714 (Amariles et al., 2012). Mean age ranged from 53 (Svarstad et al., 2013) to 72 years (Santschi et al., 2011b). Additional medical conditions included dyslipidemia, diabetes mellitus, heart failure, angina pectoris, and atrial fibrillation.

There was heterogeneity among studies for interventions, outcomes, population characteristics, study duration, and methods for measuring outcomes. Only three out of seven studies that measured adherence to anti-hypertensive medications reported using a similar assessment method (pill count) (Mckenney et al., 1973; Park et al., 1996; Sookaneknun et al.,

2004). Only four studies reported measuring impact of pharmacists' interventions on other cardiovascular disease risk factors (Amariles et al., 2012; Doucette et al., 2009; Fornos et al., 2006; Krass et al., 2007).

6.4.2 Study quality

The quality of included studies assessed by Cochrane Risk of Bias tool is shown in Figure 6.2 and Figure 6.3. Only three (18%) out of 16 studies reported details of allocation concealment (Amariles et al., 2012; McLean et al., 2008; Svarstad et al., 2013). It was unclear in the remaining 13 studies whether they had used adequate allocation concealment. Only four (25%) studies reported using single blinding of participants (Fornos et al., 2006; Garcao & Cabrita, 2002; Park et al., 1996; Svarstad et al., 2013). Only nine (56%) studies reported using power calculations (Ali et al., 2012; Amariles et al., 2012; Doucette et al., 2009; Fornos et al., 2006; Garcao & Cabrita, 2002; Krass et al., 2007; Park et al., 1996; Sookaneknun et al., 2004; Svarstad et al., 2013).

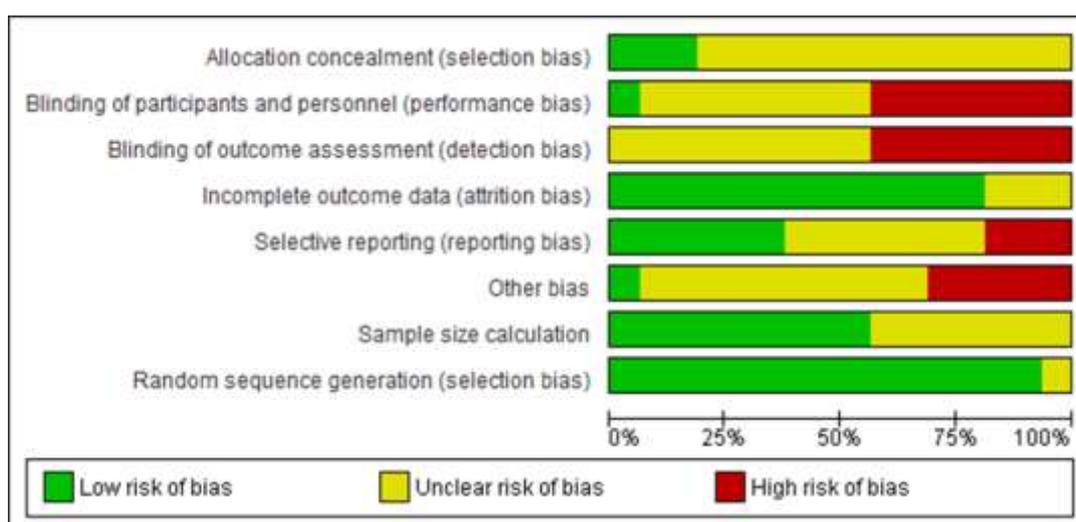


Figure 6-2 Cochrane risk of bias graph. Author's judgement about each risk of bias item presented as percentages across all included studies.

	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias	Sample size calculation	Random sequence generation (selection bias)
#Ali 2012	?	?	?	?	?	?	+	+
#Amariles 2012	+	-	-	+	+	?	+	+
#Doucette 2009	?	?	?	+	+	?	+	+
#Fornos 2006	?	-	-	+	+	?	+	+
#Krass 2007	?	?	?	+	-	?	+	?
#Zillich 2005	?	-	-	?	?	-	?	+
Blenkinsopp 2000	?	?	?	+	+	-	?	+
Garcao 2002	?	-	-	+	?	-	+	+
Mckenney 1973	?	?	?	+	-	?	?	+
Mckenney 1978	?	?	?	+	-	-	?	+
Mclean 2008	+	-	-	+	?	?	?	+
Park 1996	?	-	-	+	?	-	+	+
Planas 2009	?	?	?	?	?	?	?	+
Santschi 2011	?	-	-	+	+	+	?	+
Sookanekum 2004	?	?	?	+	?	?	+	+
Svarstad 2013	+	+	?	+	+	?	+	+

Figure 6-3 Cochrane risk of bias summary. Author's judgement about each risk of bias item for each included study.

indicates studies including patients with cardiovascular related co-morbidities.

6.4.3 Impact of pharmacist interventions on outcome measures

All 16 studies included in this systematic review measured systolic and diastolic blood pressure at baseline and end of study. None measured ambulatory blood pressure. In 14 studies, measurements were in the community pharmacy and in one study home blood pressure recordings were used (Zillich et al., 2005). One study (Blenkinsopp et al., 2000) reported improved blood pressure based on measurements in general practice, but did not report quantitative blood pressure results.

Of these 16 studies, eleven were included in the meta-analysis of effects on systolic (2,240 patients) and diastolic blood pressure (2,246 patients) (Ali et al., 2012; Amariles et al., 2012; Doucette et al., 2009; Fornos et al., 2006; Garcao & Cabrita, 2002; Krass et al., 2007; Mckenney et al., 1978; Park et al., 1996; Sookaneknun et al., 2004; Svarstad et al., 2013; Zillich et al., 2005). Absence of quantitative blood pressure data (one study) (Blenkinsopp et al., 2000) and limitations in interventions were reasons to exclude the remaining four studies from meta-analysis (Mckenney et al., 1973; McLean et al., 2008; Planas et al., 2009; Santschi et al., 2011b).

6.4.4 Meta-analysis

All eleven studies included in meta-analysis used three similar interventions: patient education on hypertension and the importance of its treatment, identification of drug-related problems, and lifestyle advice.

6.4.4.1 Systolic blood pressure – all subjects

Meta-analysis of data from the above eleven studies showed a significant benefit in favour of community pharmacist interventions, with a pooled effect of 6.1 mm Hg reduction in systolic blood pressure (95% CI -3.8 to -8.4, $p < 0.001$) using a Random Effect model. Heterogeneity among studies for differences in systolic blood pressure was low to moderate (chi-squared = 15.73, d.f. = 10, $p = 0.11$, $I^2 = 36\%$: (see Figure 6.4).

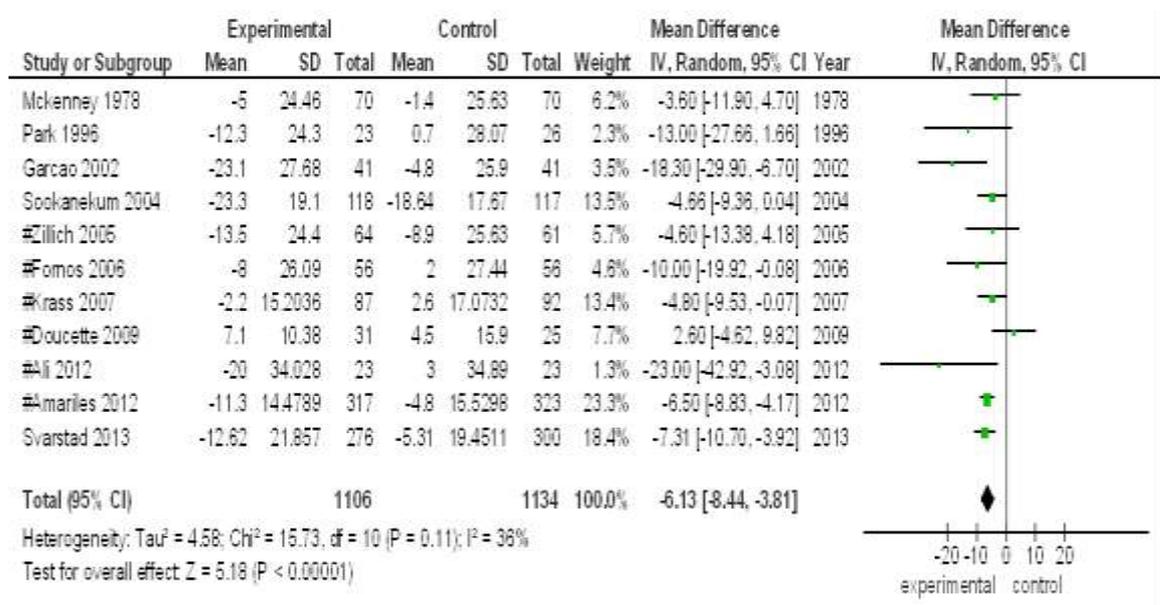


Figure 6-4 Forest plot comparisons of experimental (intervention) vs. control groups in 11 studies for systolic blood pressure.

indicates studies including patients with cardiovascular related co-morbidities

6.4.4.2 Diastolic blood pressure – all subjects

Meta-analysis of data from the above eleven studies showed a significant benefit in favour of community pharmacist interventions with a pooled effect of 2.5 mm Hg reduction in diastolic blood pressure (95% CI -1.5 to -3.4, $p < 0.00001$) using a Random Effect model. There was

no heterogeneity among the studies for differences in diastolic pressure chi-squared = 8.58, d.f. = 10, p = 0.57, I2 = 0%: (see Figure 6.5).

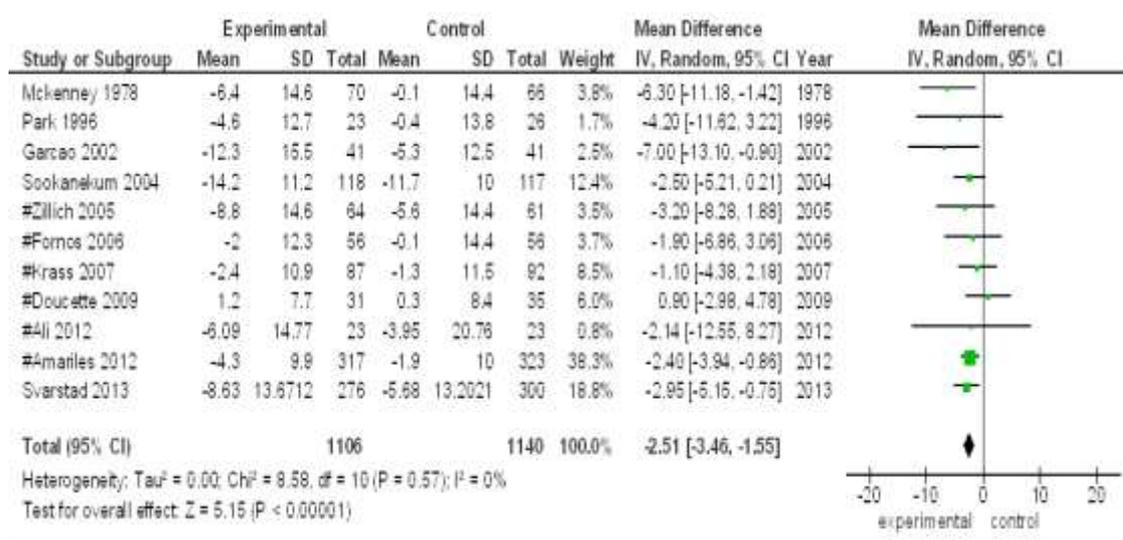


Figure 6-5 Forest plot comparisons of experimental (intervention) vs. control groups in 11 studies for diastolic blood pressure.

indicates studies including patients with cardiovascular related co-morbidities

6.4.4.3 Sensitivity meta-analysis for blood pressure effects

Two approaches were used to test the robustness of the results (Higgins & Green (Eds), 2011). No significant difference was found between the results of fixed effect model meta-analysis (systolic -6.2 mm Hg 95% CI -4.7 to -7.8 mm Hg; diastolic -2.5 mm Hg 95% CI -1.6 to -3.5 mm Hg) vs. the above random effect model analysis. Results of random effects model meta-analysis after removal of the outlier were similar for systolic (-6.6 mm Hg 95% CI -5.0 to -8.2 mm Hg) and diastolic blood pressure (-2.7 mm Hg 95% CI -1.7 to -3.7 mm Hg). Cumulative meta-analysis identified no significant changes overtime in the impact of pharmacist interventions on blood pressure control.

6.4.4.4 Blood pressure effects for 5 studies in hypertension without cardiovascular problems

Pooled reduction in systolic blood pressure with active interventions in 528 patients without cardiovascular-related co-morbidities vs. 554 controls (Garcao & Cabrita, 2002; Mckenney et al., 1978; Park et al., 1996; Sookaneknun et al., 2004; Svarstad et al., 2013) was 7.2 mm Hg (95% CI -3.6 to -10.8 mm Hg; $p = 0.004$). Heterogeneity was low to moderate (chi-squared = 5.91, d.f. = 4, $p = 0.21$, $I^2 = 32\%$).

Pooled reduction in diastolic blood pressure with active interventions in 528 patients without cardiovascular-related co-morbidities vs. 550 controls (Garcao & Cabrita, 2002; Mckenney et al., 1978; Park et al., 1996; Svarstad et al., 2013) was 3.4 mm Hg (95% CI -1.9 to -5.0 mm Hg; $p < 0.00001$). There was no significant heterogeneity (chi-squared = 3.32, d.f. = 4, $p = 0.51$, $I^2 = 0\%$).

6.4.4.5 Blood pressure effects for 6 studies in hypertension with cardiovascular problems

Pooled reduction in systolic blood pressure with active interventions in 578 patients with cardiovascular-related co-morbidities vs. 580 controls (Ali et al., 2012; Amariles et al., 2012; Doucette et al., 2009; Fornos et al., 2006; Krass et al., 2007; Zillich et al., 2005) was 5.3 mm Hg (95% CI -1.7 to -8.9 mm Hg; $p < 0.0001$). Heterogeneity was moderate (chi-squared = 9.34, d.f. = 5, $p = 0.10$, $I^2 = 46\%$).

The pooled reduction in diastolic blood pressure with active interventions in patients with cardiovascular-related co-morbidities was 1.9 mm Hg, (95% CI -0.7 to -3.1 mm Hg, n = 578 intervention v. 590 controls, p = 0.002). There was no significant heterogeneity (chi-squared = 2.88, d.f. = 5, p = 0.72, I² = 0%).

This trend for a smaller blood pressure reduction from community pharmacists interventions in patients with compared to those without co-morbidities was not significant (systolic difference 1.9 mm Hg: 95% CI -3.1 to -6.9 mm Hg, p = 0.46; diastolic difference 1.5 mm Hg: 95% CI -0.4 to -3.4 mm Hg, p = 0.127).

6.4.5 Problems with blood pressure medications

Pharmacists recorded drug-related problems in five studies. On entry to these studies, 822 medication-related problems were recorded in 337 patients; no medication-related data was recorded in 132 of the control patients. Categories of medication problems included patients not prescribed a relevant anti-hypertensive medicine, patients not benefiting from effects of medicine(s), and patients experiencing adverse effects from anti-hypertensive medications (Doucette et al., 2009; Fornos et al., 2006). Within intervention groups (240 patients, 5 studies), pharmacists reported resolving 205 of 539 problems (38%) by advice to prescribers and patients.

6.4.6 Medication adherence

Seven studies reported the impact of pharmacists' interventions on adherence to anti-hypertensive medications (Blenkinsopp et al., 2000; Mckenney et al., 1973; Mckenney et al., 1978; Planas et al., 2009; Sookaneknun et al., 2004; Svarstad et al., 2013; Zillich et al., 2005).

Three studies used pill counting, one used pharmacy dispensing records, two used self-reported adherence questionnaires and one study used prescription claims data. One study (Blenkinsopp et al., 2000) used a pharmacist-administered questionnaire based on a Medication Adherence Report Scale (Horne, 1997). Another study (Zillich et al., 2005) used self-reported adherence using the four item Morisky questionnaire (Morisky, Green & Levine, 1986). Three studies reported an increase in medication adherence in intervention compared to control groups (Blenkinsopp et al., 2000; Planas et al., 2009; Sookaneknun et al., 2004). One study reported increased adherence ($p < 0.005$) but provided no quantitative data. For the remaining six studies, adherence in intervention groups increased from 203 (56%) to 246 (68%) of 360 participants, and from 190 (59%) to 195 (61%) of 320 participants in the control group. Thus there was an increase in adherence of 43 from 158 poorly adherent subjects in intervention groups and four of 132 poorly adherent subjects in control groups (Odds Ratio 12.1: 95% CI 4.2 to 34.6, $p < 0.001$).

6.4.7 Reduction in cardiovascular risk factors

Three studies reported results for total cholesterol levels (Amariles et al., 2012; Fornos et al., 2006; Krass et al., 2007). One study (Fornos et al., 2006) reported a reduction in total cholesterol levels by 0.52 mmol/L ($p < 0.001$) in the intervention group. Two studies reported outcomes for LDL-cholesterol (Doucette et al., 2009; Fornos et al., 2006). Both these studies reported a mean reduction in LDL-C for both intervention and control groups. Three studies measured HbA1c% (Doucette et al., 2009; Fornos et al., 2006; Krass et al., 2007). Two studies reported a mean reduction in HbA1c% by 0.5 and 1.0% in patients in intervention groups (Fornos et al., 2006; Krass et al., 2007).

6.5 Discussion

These findings show that compared with usual blood pressure management, active interventions by pharmacists working in community pharmacies were associated with important improvement in control of hypertension, whether or not associated with cardiovascular co-morbidities. Compared to patients receiving usual care, both systolic and diastolic pressure decreased, and adherence improved, as did control of other cardiovascular risk factors, including both diabetes mellitus and cholesterol.

Previous analyses have assessed the impact of community pharmacist interventions on blood pressure control in hypertensive patients without cardiovascular problems (Machado et al., 2007; Morgado et al., 2011) or of a wide range of clinical and other pharmacists working within in-patient and out-patient settings (Santschi et al., 2011a; Santschi et al., 2014). The present study is the first meta-analysis to evaluate the specific impact of community pharmacist interventions delivered in community pharmacies both in hypertensive patients without cardiovascular problems as well as in patients with cardiovascular co-morbidities, including dyslipidaemia, diabetes mellitus, chronic kidney disease, and clinical vascular disease. Of note, Santschi et al. (2014) do not differentiate between the impact of different types of pharmacists working across a range of healthcare settings including primary care health centres, hospitals, army medical centres, academic health centres, community pharmacies, community based hypertension clinics and hospital outpatient clinics. Furthermore, in addition to all four studies in community pharmacies identified by Santschi et al. (2014), a further seven studies not referenced in that study were also included in this meta-analysis (Santschi et al., 2014).

The evidence presented in this review together with previous reviews (Machado et al., 2007; Morgado et al., 2011; Santschi et al., 2011a; Santschi et al., 2014) provides an important message to health professionals and policy makers about the potential for community pharmacists to ease the burden for physicians in primary and secondary care of the management of hypertension. The results of this review show that interventions by community pharmacists were associated with important reductions in both systolic and diastolic blood pressure within a wide range of international geographical regions from North America to Europe, South East Asia and Australia.

The improvement in blood pressure control appeared to occur irrespective of the length of intervention, across included studies whose duration ranged from three to 13 months. In the meta-analysis, in studies published from 1978 to 2013, there was also no obvious trend in degree of impact on blood pressure by year of publication. Community pharmacists appeared to be similarly effective in improving blood pressure control both for patients with high blood pressure alone (Garcao & Cabrita, 2002; Mckenney et al., 1978; Park et al., 1996; Sookaneknun et al., 2004; Svarstad et al., 2013) as well as for patients with hypertension coupled with serious cardiovascular problems (Ali et al., 2012; Amariles et al., 2012; Doucette et al., 2009; Fornos et al., 2006; Krass et al., 2007; Zillich et al., 2005).

The largest category of preventable causes of poor blood pressure control across the studies included in this review appeared to be incorrect use of medicines by prescribers and patients. In the five studies which recorded this information, it was noteworthy that pharmacists reported only being able to resolve 38% of these problems by making suggestions to prescribers and patients, although expertise in resolving these problems is an expected core usual clinical activity of community pharmacists (Hepler & Strand, 1990). Further work is

needed to investigate two major questions arising from this aspect of the meta-analysis. How to prevent the initial occurrence of medication-related problems such as errors of omission and commission when prescribing for hypertension, and adverse effects from anti-hypertensive medications? Secondly, what would make interventions by community pharmacists more effective, when aiming to resolving medication-related problems? Possible reasons for the high proportion of unresolved medicine-associated problems include time pressure on community pharmacists providing clinical services within busy commercial settings (De Simoni, Mullis, Clyne & Blenkinsopp, 2012) and challenges to effective inter-professional working arrangements between community pharmacists and other clinical practitioners (Kelly, Bishop, Young, Hawboldt, Phillips & Keough, 2013).

There were limitations in this review. Although rigorous and systematic, it did not include unindexed and unpublished research. Studies were of variable quality, with low to moderate heterogeneity for systolic blood pressure. Home blood pressure monitoring (HBP) was used only in one of studies in this systematic review (Zillich et al., 2005). There is however, high quality evidence from a meta-analysis of 18 RCTs involving 1359 patients with essential hypertension that reported better blood pressure control with HBP as compared to standard blood pressure monitoring in health care systems (Cappuccio, Kerry, Forbes & Donald, 2004). Furthermore recent research from a cluster randomised clinical trial of 450 adults with uncontrolled blood pressure in the United States suggested that HBP is also a useful adjunct to pharmacist-supported management of hypertension within family doctor centres (Margolis, Asche, Bergdall, Dehmer, Groen, Kadrmas et al., 2013). Secondly, there are well-established lifestyle approaches for improving control of hypertension (Appel, Champagne, Harsha, Cooper, Obarzanek, Elmer et al., 2003). However details of life-style interventions were unclear in many of the studies included in this systematic review. This review could not

establish if specific lifestyle advice was provided to patients such as advice on reducing dietary salt and increasing fruit and vegetable intake. Future studies could for example evaluate formal use of established DASH-2 lifestyle approaches (Sacks, Svetkey, Vollmer, Appel, Bray, Harsha et al., 2001) within community pharmacist interventions aimed at blood pressure control.

The reductions in systolic and diastolic blood pressure reported in this meta-analysis, if sustained in clinical practice, would have important implications for primary and secondary prevention of cardiovascular morbidity and mortality. For example, evidence from a meta-analysis involving one million adults in USA reported that every 1 mm Hg reduction in systolic blood pressure could prevent about 10,000 deaths related to coronary heart disease in the US each year (Lewington et al., 2002). Another analysis suggests that a sustained 2 mm Hg reduction in diastolic blood pressure would be expected to result in a 6% reduction in the risk of coronary heart disease and 15% decrease in stroke (Cook et al., 1995).

There are international differences in the extent to which community pharmacy services are embedded within usual clinical care of long-term medical conditions. In the NHS in the UK, a new contractual framework for community pharmacy was introduced in 2005, with the intention of moving pharmacists towards a more clinical service-oriented role (National Pharmacy Association & British Medical Association, 2009). For example, UK community pharmacies can provide Health Checks for people aged 40-74 years. Within these health checks, pharmacists can carry out a full vascular risk assessment and provide advice and support to help to reduce the risk of heart disease, strokes, diabetes and obesity (National Pharmacy Association & British Medical Association, 2009).

However, such extensions in activities and services delivered by community pharmacists may conflict with the work of general practice and health professionals working in hospitals. There is a need for formal links to ensure coherence of treatment approaches and evidence-based integration of pharmacy-delivered services with other health services (Blenkinsopp, 2007).

6.5.1 Critical appraisal of the review

Did the review address a clearly focussed question?

Yes (see the abstract for the concise question). The population included in the systematic review is described as adults (18 or over) and who were receiving treatment for hypertension in community pharmacies. The review compared pharmacist-led interventions (both pharmacological and non-pharmacological) with usual care. A clear definition of both pharmacological and non-pharmacological interventions was provided. See the methods section for the outcomes considered (see the methods section for the types of interventions). The primary outcome was reduction in systolic blood pressure (SBP) and diastolic blood pressure (DBP) measured in the community pharmacies or at home. Secondary outcomes: improvement in adherence to anti-hypertensive medications, identification and management of drug-related problems and impact on cardiovascular risk factors: smoking, alcohol consumption, weight, cholesterol level (mmol/L) and HbA1c (%).

Did the authors look for the right type of papers?

Yes (see the methods section for the types of studies). The inclusion and exclusion criteria for studies was explicitly stated. Only RCTs and systematic review of the RCTs evaluating the clinical impact of community pharmacist interventions on patients with hypertension were included. Studies with multidisciplinary interventions in which the role of pharmacists with the team was not clear were excluded.

Do you think all the important, relevant studies were included?

Not clear (see the methods section for the search strategy). Eight electronic health-related databases: Literature search with no start date restrictions was undertaken in MEDLINE, Web of Science, the Cochrane library, EMBASE, Biosis Citation Index and Biomed Central, CINAHL and PsycINFO were searched. In addition reference lists were screened of all included articles retrieved at full paper and the first 100 results of this search strategy applied to Google Scholar. Two reviewers (E.C, P.S) independently reviewed titles and abstracts of all potentially relevant papers. Papers which met inclusion criteria were retrieved at full paper and these two reviewers checked each paper for inclusion. Any differences were agreed through discussion or resolved by a third reviewer D.S. Personal contact with experts was not used. Studies published in English language only were included.

Did the review's authors do enough to assess the quality of the included studies?

Yes (see the methods section for quality assessment). Criteria for quality assessment of included systematic reviews were based on those of the NHS Centre for Reviews and Dissemination (CRD), (1999). Two reviewers (E.C, P.S) rated each paper using the Cochrane Risk of Bias tool (Higgins & Green (Eds), 2011) to assess RCTs on their randomisation procedure, allocation concealment, blinding of participants, reporting of incomplete outcome data, selective reporting, or any other biases that did not fit into the above mentioned categories. Other sources of bias explored in this review included possibility of cross-contamination between study groups, recruitment of participants from a selected population, and non-compliance of researchers to study protocol. For each included study, a risk of bias graph and a risk of bias summary were generated. The use of power calculations was recorded.

If the results of the review have been combined, was it reasonable to do so?

Not clear (see the results section). There was heterogeneity among studies for interventions, outcomes, population characteristics, study duration, study quality and methods for measuring outcomes. However, the reasons for these variations in included studies have not been provided in the review. To minimize heterogeneity in the meta-analysis, studies using three similar interventions were used (patient education on disease management, identification and management of prescribing and safety problems associated with anti-hypertensive medications, and advice on lifestyle). Because of these differences, a random effects model was used. Two approaches were used to test the robustness of the results (Higgins & Green (Eds), 2011). No significant difference was found between the results of fixed effect model meta-analysis. Results of random effects model meta-analysis after removal of the outlier were similar for both systolic and diastolic blood pressure.

What are the overall results of the review?

Mean differences [SD] and 95% confidence intervals were used to identify changes in blood pressure control over time. The results of each study included in the meta-analysis were presented in a graphic form together with their respective confidence intervals (see results section for the forest plots). Significant reductions in systolic (11 studies [2,240 patients]; -6.1 mm Hg [95% CI, -3.8 to -8.4]; $p < 0.00001$) and diastolic blood pressure (11 studies [2,246 patients]; -2.5 mm Hg [95% CI, -1.5 to -3.4; $p < 0.001$) was reported.

How precise are the results?

Not precise. The wide Confidence Intervals reported for the blood pressure outcome for all but two studies (Amariles, 2012; Svarstad, 2013) suggest the lack of certainty about the true

effect of the study intervention. In other words, it indicates that these studies were not powered enough to estimate the precise effect size. Studies included in the review were of variable quality, with low to moderate heterogeneity for systolic blood pressure. The findings of this review should therefore be interpreted with caution.

Can the results be applied to the local population?

Not clear. The reduction in the systolic and diastolic blood pressure was similar for patients with or without cardiovascular related medical conditions (see the results section for the subgroup analysis). Since the review only assessed the impact of pharmacist-led interventions in community pharmacies, it remains to be established whether the findings of this review are generalizable to population visiting other healthcare settings including primary care health centres, hospitals, army medical centres, academic health centres, community based hypertension clinics and hospital outpatient clinics.

Were all important outcomes considered?

Not clear. The review did not consider the policy implications of pharmacist-led interventions including the cost effectiveness analysis of these approaches and their sustainability in long-term in clinical practice. It also needs to consider the type, mode and frequency of interventions in relation to differences in age, gender, ethnicity and other variables of potential importance in the selection and response to the management of hypertension.

Are the benefits worth the harms and costs?

Yes. The interventions considered by pharmacists in this review are not expected to harm the patients (non-invasive interventions). Although this review did not undertake the cost-

effectiveness analysis of pharmacist-led interventions, it is reasonable to conclude that the benefits of these interventions outweigh any risks associated with these interventions if any.

Summary of chapter

The findings of this chapter show that compared with usual blood pressure management, active interventions by pharmacists working in community pharmacies were associated with important improvement in control of hypertension. However, this review did not determine the particular pharmacist intervention responsible for the reductions in systolic and diastolic blood pressure. Furthermore, the limitations of this review such as the exclusion of unindexed and unpublished research coupled with the variable quality of the included studies suggests that this chapter has only partially addressed the fourth objective of the thesis.

6.6 Conclusions

The findings of this review highlight the significant potential benefits of community pharmacist led interventions in the management of high blood pressure whether or not associated with significant cardiovascular co-morbidity. Although the systematic review was rigorous and systematic, it did not include unindexed and unpublished research. Studies included in this review were of variable quality, with low to moderate heterogeneity for systolic blood pressure. The findings of this review should therefore be interpreted with caution.

Future work needed to address the policy implications of pharmacist led interventions includes cost effectiveness analysis of these approaches, and their sustainability in the long-term in clinical practice. Research is also needed into the type, mode and frequency of interventions in relation to differences in age, gender, ethnicity and other variables of potential importance in the selection and response to the management of hypertension.

The next chapter assesses the impact of written pharmacist-led education on the management of blood pressure control. It aims to determine whether structured education provided to patients verbally and in writing by community pharmacists about blood pressure and its treatment will be a) better retained and b) be associated with improved blood pressure control.

Chapter Seven

7 A feasibility study of the impact on blood pressure control of supplementing community pharmacist services with structured information on blood pressure and its treatment

This chapter aims to address the final objective of the thesis by conducting a feasibility study of a new pharmacist supported method for a more effective use of medicines by patients with hypertension. It aims to determine whether structured education provided to patients verbally and in writing by community pharmacists about blood pressure and its treatment will be a) better retained and b) be associated with improved blood pressure control.

7.1 Abstract

A RCT was conducted in four community pharmacies in the West Midlands area. The study had two groups (an active or intervention group where participants received verbal NMS intervention as well as written information on blood pressure and its treatment; and a control group where participants received verbal NMS intervention only). Participants in both groups were required to attend four visits in total over a period of six months (at week 0, 2, 4 and 26). They were required to complete a questionnaire during all four visits. Blood pressure of all participants was also recorded during all four visits. In addition, a participant satisfaction survey was conducted at the six-month follow up. A total of 66 participants were recruited between January 2014 and June 2014.

There was an overall mean reduction in systolic blood pressure from baseline in both intervention group $F(3, 24) = 3.17, p = 0.04$ and control group $F(3, 30) = 3.4, p = 0.02$.

However, there was no statistically significant difference between the two groups in treatment effect $F(1, 54) = 0.17, p = 0.91$. There was an overall mean reduction in diastolic blood pressure from baseline during the study in both intervention group $F(3, 24) = 3.17, p = 0.02$ and control group $F(3, 30) = 3.9, p = 0.01$. As observed for systolic blood pressure, there was no difference between the two study groups in treatment effect $F(1, 54) = 0.36, p = 0.78$. However, compared to participants in the control group, there was a significant improvement in the knowledge about hypertension and its treatment in the intervention participants. The participants of this study gave a positive response about the involvement of pharmacists in the management of long-term medical conditions such as hypertension.

7.2 Background

Long-term medical conditions including hypertension and diabetes require patient education to achieve adequate blood pressure control (Williams, Baker, Parker & Nurss, 1998). Lack of adequate knowledge about high blood pressure, twice daily dosage instead of once daily regimens and the cost of anti-hypertensive medications have been reported as barriers to medication adherence by hypertensive patients (Osterberg & Blaschke, 2005). A study was conducted in the UK to assess the understanding of the knowledge and awareness about blood pressure (Slark, Khan, Bentley & Sharma, 2014). The study involved a total of 1019 participants from a selected population (Slark et al., 2014). This study reported that more than half (52%) of the total study population was unable to correctly estimate an acceptable range of blood pressure. Furthermore, the mean systolic blood pressure of participants who had correctly estimated the acceptable range of blood pressure was 3 mm Hg lower (147 mm Hg) than those who had estimated the incorrect acceptable range of blood pressure (150 mm Hg) ($p < 0.04$) (Slark et al., 2014).

In 2001, a systematic review and meta-analysis was conducted to assess the impact of three behavioural interventions including patient-centred counselling, self-monitoring of blood pressure and structured training courses on blood pressure control (Boulware, Daumit, Frick, Minkovitz, Lawrence & Powe, 2001). Pooled results from 15 studies involving 4072 patients reported that patient-centred counselling led to an additional reduction of 11.1 mm Hg in systolic and 3.2 mm Hg reduction in diastolic blood pressure (Boulware et al., 2001). Evidence from this meta-analysis suggested that patient-centred counselling offers better blood pressure control as compared to ordinary care. Similar findings were reported in a cluster randomised controlled study in the United States (Roumie, Elasy, Greevy, Griffin, Liu,

Stone et al., 2006). This study involving 1341 patients with essential hypertension assessed the impact of targeted patient education on blood pressure control (Roumie et al., 2006). Patients receiving education experienced a reduction of 8 mm Hg in systolic blood pressure and achieved a better blood pressure control.

In the UK, the NMS and MURs are established schemes which fund community pharmacists to review and explain medicine use to patients, with hypertension a common condition for which advice is given within these schemes. Within these schemes, advice is verbal and unstructured, with no specific written information provided on drugs or the disease being treated. Research suggests that provision of written medical advice to patients about a disease and its treatment is better retained by patients than verbal information (Victoria, 1981).

7.3 Methods

7.3.1 Study aims

The aim of this study is to determine whether structured information provided to patients verbally and in writing by community pharmacists about blood pressure and current medicine(s) within NMS and MUR reviews will be retained and will be associated with improved blood pressure control.

7.3.2 Study objectives

- 1) To assess whether information about blood pressure and current medicines provided to participants verbally and in writing by community pharmacists will be better retained than in current NMS.
- 2) To assess the impact of this structured written information on blood pressure in participants with hypertension.

- 3) To assess the impact of blood pressure in terms of participants' characteristics including age, gender, BMI and medical conditions.
- 4) To assess the impact of this study on the frequency and severity of ADRs in active and control arm participants.

7.3.3 Overall study design

This study was a six months RCT conducted across four community pharmacies in the West Midlands area. The trial was registered on ClinicalTrials.gov (Identifier: NCT01939860). The study had two groups (an active or intervention group where participants received verbal NMS intervention as well as written information on blood pressure and its treatment; and a control group where participants received verbal NMS intervention only). Eligible participants were recruited during a six-month period between January 2014 and June 2014 and subsequently randomised to either a control or an intervention group. Randomisation was conducted by a computer-generated randomised list. Random allocation of participants to study arms was done to help reduce researcher bias. Both groups were then followed up to see the difference in retention of information and on blood pressure control. Participants in both groups were required to attend four visits in total over a period of six months (at week 0, 2, 4 and 26). They were required to complete a questionnaire during all four visits. Blood pressure of all participants was also recorded during all four visits (see Figure 7.1 for the study flow diagram). In addition, all participants were required to complete a participant satisfaction survey at the end of their final visit to the study site.

7.3.3.1 Primary outcome:

1. Whether information about blood pressure and current medicines provided to patients verbally and in writing by community pharmacists will be better retained than in current New Medicine Service?

2. If provision of structured written information will be associated with improved blood pressure control in patients with hypertension?

7.3.3.2 Secondary outcome:

1. Impact of blood pressure in terms of participants' characteristics including age, gender, and ethnic background?

2. To assess the impact of this study on the frequency and severity of ADRs in active and control arm participants.

Day 1: Patient presents with a prescription for a new blood pressure medicine

Are they eligible for this study?

Patient is eligible for this study if

1. 18 years or over, male or female
2. Patient has agreed to take part in the NMS

Stage 1 (Patient engagement)

Dispense medicine as normal. Inform patient of the study and hand a letter introducing the study, patient information sheet and a consent form

Patient agrees to participate?

No. Patient excluded from the study

Yes. Patient randomised to study groups

Intervention group

Control group

Week 0: (4-7 days after engagement)

1. Written consent will be obtained
2. Blood pressure will be measured
3. Patients complete a validated questionnaire on blood pressure and its treatment
4. Patients will then be provided with validated verbal and written information on hypertension and its treatment
5. Date arranged for NMS intervention

Week 0: (4-7 days after engagement)

1. Written consent will be obtained
2. Blood pressure will be measured
3. Patients complete a validated questionnaire on blood pressure and its treatment
4. Patients will then be provided with validated verbal and written information on NMS
5. Date arranged for NMS intervention

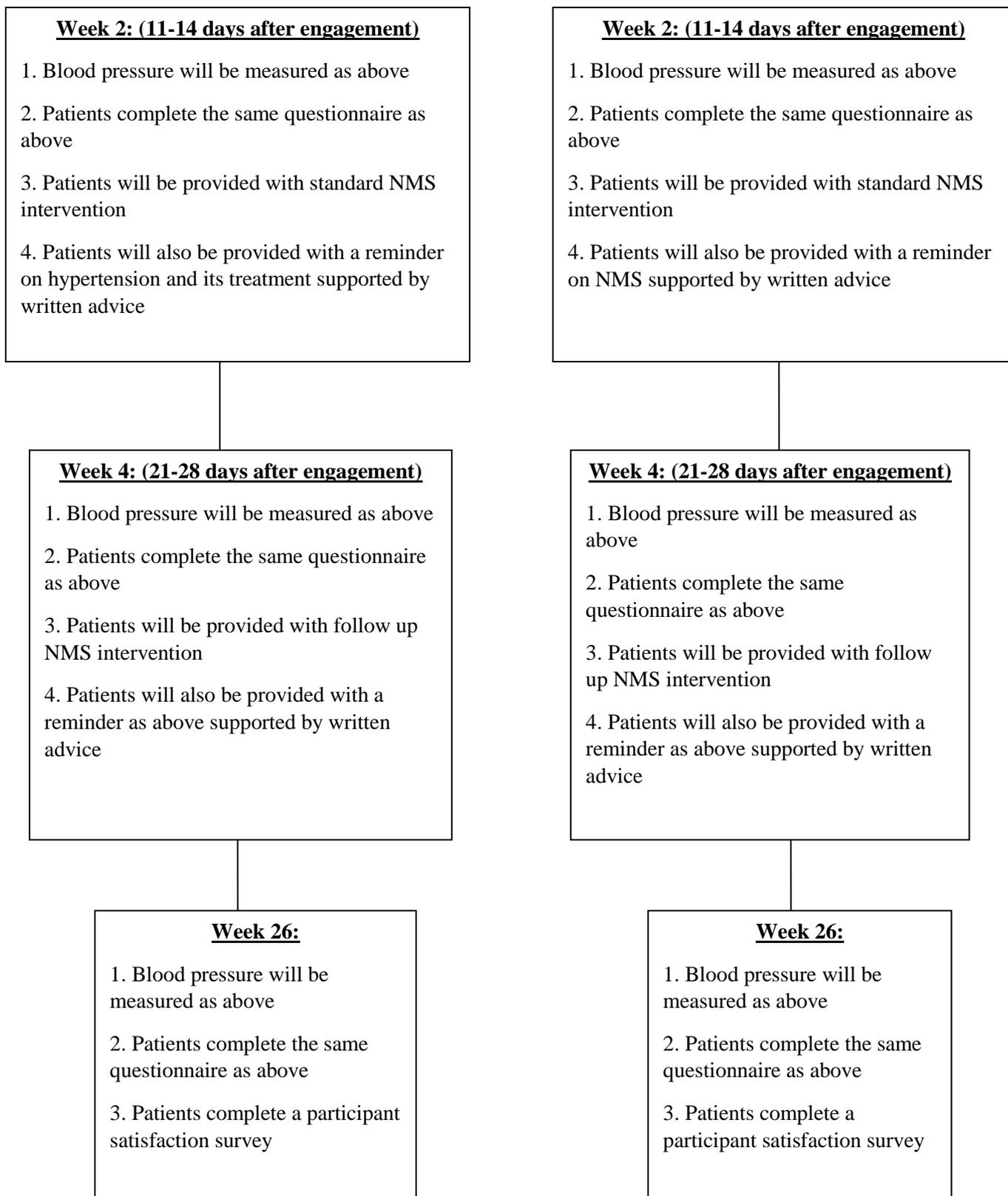


Figure 7-1 Study flow diagram.

7.3.4 Study development

7.3.4.1 Development of study protocol

A study protocol was developed with the support and guidance of the supervisors (see Appendix J for study protocol). Two meetings were held with Dr Richard Crossman (Research Fellow for the Statistics and Epidemiology Unit, Division of Health Sciences) to ensure that the sample size calculations were accurate. Feedback was also obtained from Mr Mark Galloway, a pharmacist and head of Medicines Management (NHS Coventry & Rugby CCG) for an independent review of the study protocol.

7.3.4.2 Pharmacists Advisory Group

A total of six community pharmacists were invited in writing to form a West Midland's Pharmacist Expert Advisory Group. The aim of the pharmacist advisory group was to seek the advice of pharmacists in the development of research projects that would investigate ways to improve education of patients about their medications and their potential adverse effects. The invited pharmacists represent large high street multiples, supermarkets and independent pharmacies in the West Midlands area. All these pharmacists had more than five years of working experience and had been involved in the provision of NHS services including NMS and targeted MURs. These pharmacists provided feedback on the questionnaire, timing of the visits and on the supporting written education material on blood pressure and its treatment.

7.3.4.3 Patient feedback

In addition to the feedback from pharmacists, feedback was also obtained from the patients on development of both proposed questionnaire and for written educational information on blood pressure and on treatments. To obtain patient advice, two approaches were used: 1) feedback

from the Expert Hypertension Patient Advisory Group established by Professor Singer; and 2) individual feedback from outpatients who were being started on a new treatment while attending the Blood Pressure Clinic at UHCW NHS Trust and patients attending community pharmacies. These patients were helpful in supporting development of patient information sheets for the Local Ethics Committee application for the study.

7.3.4.4 Development of questionnaire

A questionnaire was developed using questions from the previous audit presented in chapter 3 (audit no: 1421) and 6 questions drawn from a 12-item questionnaire designed at the National Institutes of Health for assessment of knowledge about high blood pressure among non-medical individuals (Martins, Gor, Teklehaimanot & Norris, 2001). The primary intent of the questionnaire was to explore participants' basic knowledge of blood pressure including awareness about ideal blood pressure targets, the risks associated with high blood pressure, the role of lifestyle measures in reducing high blood pressure, knowledge about the participants' new blood pressure medicine and awareness about potential adverse effects of their new blood pressure medicine (see Appendix K for the questionnaire). The questionnaire also recorded participants' demographics including age, gender, weight, height, ethnicity and history of chronic conditions. The questionnaire was developed in English language only and the questions were not anticipated to be sensitive, embarrassing, threatening or distressing to the respondents.

7.3.4.5 Development of participant consent form, information sheet and invitation letter

A participant's consent form, the participant information sheet and invitation letter were developed with the help and support of the supervisors (see Appendix L for consent form, Appendix M for information sheet and Appendix N for invitation letter).

7.3.4.6 Development of information sheets on blood pressure and its treatment

The information sheets containing structured advice on blood pressure and on nine classes of blood pressure medications were developed (see Appendix O for information sheets on blood pressure). These information sheets were prepared using guidance CG 127 (National Clinical Guideline Centre, 2011) and Blood Pressure UK, 2014. These information sheets were provided to participants in the intervention group. A separate information sheet containing information on the NMS was prepared using guidance produced by (PSNC, 2013). This information sheet was provided to participants assigned to the control group (see Appendix P for information sheet on NMS).

7.3.4.7 Piloting of the questionnaire and other study materials

The questionnaire along with the other study materials were piloted on a group of 20 patients that included patients attending the Blood Pressure Clinic at the UHCW and patients attending one of the participating pharmacies in Birmingham. The aim of this pilot work was to ensure that the content, length and layout of the questionnaire and other study materials were clear, simple and understandable. Based on the feedback obtained during pilot work, wording of some of the questions of the questionnaire were edited to make the questions simpler and easier to understand. The final questionnaire had a Flesch-Kincaid reading grade level of 5.8 (Flesh, 1948).

7.3.4.8 Development of interview schedule for participating pharmacists

A complete interview guide was developed for the pharmacists participating in this study (see Appendix Q for interview guide). All participating pharmacists were instructed to follow this guide in the delivery of study interventions.

7.3.4.9 Sample size calculation

Based on the previous audit presented in chapter 3 (audit number 1421), it was expected that 55% of patients will be aware of adverse risks of their medicines. A sample size of 54 per group will provide a power of 80% at the 5% level in a 2-tailed test to detect an increase from 55% to 80% of participants aware of adverse risks of their medicines. This will result in the need to recruit 66 per group, based on planning for a 20% drop-out rate during the study.

A sample size of 54 per group completing the study will also provide a power of 80% at the 5% level in a 2-tailed test to detect a reduction of a size equal to 0.6 standard deviations in systolic and diastolic pressure as assessed by an Omron BHS approved device (www.bhsoc.org). The SD will depend on the results for the study sample e.g. for a typical SD between visits of 7 mm Hg in systolic pressure in patients with hypertension, this would represent an 80% power to detect a 4 mm Hg reduction in systolic pressure.

7.3.4.10 Participant satisfaction survey

A separate questionnaire was developed for the participant satisfaction survey. The style and format of some of the questions were adopted from a previous patient satisfaction survey published in the MUR service evaluation report (National Pharmacy Association, 2010) (see Appendix R for the participant satisfaction questionnaire). The primary intent of this questionnaire-based survey was to capture participants' views about this study and the future involvement of community pharmacists in blood pressure control. The questionnaire had four questions that included two closed and two open questions. The inclusion of closed and open questions in the questionnaire was aimed to conduct both the descriptive and qualitative analysis of the data.

7.3.4.11 Ethical approval

The ethics application was prepared under the guidance of the supervisors. Following the interview, the ethics committee proposed minor changes to the study protocol that were addressed to the satisfaction of the ethics committee. In addition, approval was also obtained from NHS R&D prior to recruiting study participants.

7.3.5 Study participants

7.3.5.1 Pharmacy recruitment

A total of eight community pharmacies offering NHS services including NMS and MURs were invited in writing to take part in the study. Seeking R & D approvals from the respective management of these pharmacies was a time consuming process. Six of the invited pharmacies agreed to take part and confirmed their participation. All participating pharmacies were approved as research sites by the Coventry and Warwickshire ethics committee

following site-specific assessment. Two pharmacies withdrew before the commencement of the study. The remaining four participating pharmacies included two independent pharmacies in Coventry and two pharmacies from a large multiple company in the Birmingham area. It was expected that participating pharmacies will act as Participant Identification Centres in this study i.e. they will identify potential research participants who will be invited to participate in the study.

7.3.5.2 Training of the participating pharmacists

Study interventions were carried out by the pharmacists of four participating pharmacies. Participating pharmacists were not offered any financial incentive for carrying out the study interventions. No additional resources were employed during the study. All participating pharmacists were provided 30 minute training by the chief investigator of the study. The training involved explanation of the study background and study design, interview schedule, delivery of study interventions, questionnaire administration. In addition, training was provided to dispensers on measuring blood pressure. Pharmacists were specifically instructed not to provide any help with answering the questions as the same questionnaire was used during all four visits. However, pharmacists were allowed to assist the participants in understanding the questions when needed. In addition, each participating pharmacy was provided the same model of OMRON blood pressure monitor (705CP-II HEM-759-E2) to record the measurements of the study participants.

7.3.5.3 Impact of the study on participating pharmacies

The risks and burden to the participating pharmacies was expected to be minimal. The participant study materials (study invitation letter, information sheet and consent form) were all placed together in individual packs so that the dispensary staff can conveniently hand to the eligible participants. Thus, the administrative burden on participating pharmacies had been designed to cause minimum disruption to the daily pharmacy operations.

7.3.5.4 Participant recruitment

All participants 18 years or over, male or female, had been started on a blood pressure medication, had agreed to take part in the NMS and capable of giving written consent to the study were eligible for the study. Participants referred by their GP or a secondary care prescriber were also eligible for the study. Exclusion criteria included patients under 18 years, being too ill to participate and patients not capable of giving a written consent. Eligible participants were identified by a member of the dispensary team including a dispenser and the pharmacist. Participants interested in the study were handed a pack containing a letter introducing the study, a consent form, participant information sheet and a questionnaire.

The advertising posters were displayed in the participating pharmacies, at the local GP surgeries, at the outpatient blood pressure clinic at UHCW and at the Consulate of Pakistan in Birmingham. In order to encourage participant recruitment at the GP surgeries, over 30 local GP surgeries in the West Midlands area were contacted to inform them about the study. A reminder was also sent to all the local surgeries to promote participant recruitment. In addition, a request was made to the local press including Coventry Telegraph and Express and Star to report this study as a news story:

http://www2.warwick.ac.uk/fac/med/news/news/how_pharmacists_can/ (Accessed 28 April, 2014) in their respective newspapers. An appearance was made in a live interview at the BBC radio Coventry and Warwickshire to promote recruitment of the participants in the study. The complete interview with the BBC radio can be found at:

http://www2.warwick.ac.uk/fac/med/news/news/how_pharmacists_can/ (Accessed 25 April, 2014). All study participants were offered £10 to cover travelling expenses for each of the four visits to the pharmacy.

7.3.6 Study procedure

7.3.6.1 Blood pressure measurement

All patients had their blood pressure measurements recorded during all four visits (weeks 0, 2, 4 and 26). Blood pressure was recorded electronically by trained dispensers using a British Hypertension Society (BHS) approved Omron blood pressure monitor (Assaad, Topouchian, & Asmar, 2003). Three readings of systolic and diastolic pressure were recorded for both intervention and control groups in accordance with the guidelines produced by British Hypertension Society (British Hypertension Society, 2013). As per the BHS guidelines, the final two readings of both systolic and diastolic blood pressure were used to calculate the average readings.

7.3.6.2 Anticipated participant study time

It was expected that participants would spend an average 15 minutes in total during their visit to the pharmacy apart from the first visit which was expected to take around 25-30 minutes.

This was estimated as follows:

Visit 1:

- 1) Obtaining consent: 5 minutes.
- 2) Completion of a questionnaire: 5 minutes
- 3) Recording of blood pressure: 5 minutes
- 4) Provision of written and verbal information: 10 minutes

Visit 2, 3:

- 1) Completion of a questionnaire: 5 minutes
- 2) Recording of blood pressure: 5 minutes
- 3) Provision of written and verbal information: a range up to 10 minutes
- 4) Verbal NMS intervention: 5 minutes

Visit 4:

- 1) Completion of a questionnaire: 5 minutes
- 2) Recording of blood pressure: 5 minutes
- 3) Completion of participant satisfaction survey: 5 minutes

7.3.6.3 Written consent

A written consent to participate was obtained from all participants. The consent form was provided by the dispensary team of the participating pharmacy at the time patients brought their prescriptions. Eligible participants were asked to complete the consent form themselves.

7.3.6.4 Anonymity

Returned questionnaires were assigned a unique study number for electronic analysis that was only known to the research team. All analyses and reports were anonymous. Patients entered the study on the day written consent was obtained.

7.3.6.5 Confidentiality

All information collected from this study was kept strictly confidential. Written consent was obtained from the participants to contact their GP when needed. The procedures for handling, processing, storage and destruction of the data complied with the Data Protection Act 1998. Only members of the research team had access to the completed questionnaires.

7.3.6.6 Sponsorship and Indemnity

Sponsorship for the study was provided by the University of Warwick. The University of Warwick has in force a Public and Products Liability Policy which provides cover for claims of “negligent harm” and the activities here are included within that coverage subject to the terms, conditions and exceptions of the policy.

7.3.6.7 Information Governance

All information collected from the study participants was stored in accordance with the Data Protection Act (1998) and the University of Warwick policies. Completed questionnaires and consent forms were only accessed by members of the research team. Data from the completed questionnaires was stored in an anonymous form in a secure password-protected network location that was only accessible by the research team. A unique code number was used to identify each participant.

7.3.6.8 Data Management and Analysis

Questionnaire responses were coded and entered into SPSS version 22. Data was single-entered. Summary descriptive statistics were generated from the questionnaire data using SPSS. Summary data are presented in tables and figures, as appropriate. One-way ANOVA (repeated measures) was used to calculate the mean difference in systolic and diastolic blood

pressure (in mm Hg) from baseline across all study visits. Sub-group analysis was conducted using one-way ANOVA (repeated measures) to assess the impact of blood pressure in terms of participants' characteristics including age, gender, BMI, medical conditions, ethnicity and number of medications. Bonferroni correction (post-hoc test) was used to set more stringent significance levels to reduce the risk of a type 1 error. It was only restricted to explore the impact on systolic and diastolic blood pressure and was not used on the knowledge outcome. Bonferroni correction adjusted at 5% significance level ($0.05/3 = 0.016$) was used to further explore the impact on systolic and diastolic blood pressure. Cross tabulation was used to analyse the responses to hypertension knowledge questions.

A stepwise multivariable regression analysis was conducted to explore the influence of various explanatory or independent variables including age, gender, BMI, ethnicity, medical conditions, knowledge about hypertension including knowledge about top blood pressure number, lower blood pressure number, the risk of heart attack with hypertension, risk of stroke with hypertension, risk of kidney disease with hypertension, risk of asthma with hypertension, risk of cancer with hypertension, effect of reducing weight on hypertension, effect of reducing salt on hypertension, effect of reducing alcohol on hypertension, importance of taking anti-hypertensive medications for the long-term, frequency of anti-hypertensive medications, correct recall of the name of new anti-hypertensive medication, correct recall of the dose of new anti-hypertensive medication and the mechanism of action of anti-hypertensive medication in the body with average systolic and diastolic blood pressure as response or dependent variables.

Advice was obtained from a statistician (Dr Nick Parsons) to confirm the choice of the statistical methods used in the analysis of the study data. A qualitative analysis was undertaken using the inductive method of thematic analysis (Braun & Clarke 2006).

The five steps of the qualitative analysis were:

Step 1: familiarising with the data

A thorough reading and re-reading of the entire data was done to familiarise with the participants' responses. Initial ideas were then identified and noted.

Step 2: Generating initial codes

After familiarising with the data set, initial codes were manually generated from the data in a systematic way. The coding process was independently verified by an expert (AL) in qualitative methods to ensure rigour in the analysis. Any variations in the coding process were resolved through discussion.

Step 3: searching for themes

After the generation of initial codes, codes were then assigned to potential themes.

Step 4: reviewing themes

Themes were reviewed to ensure they were appropriate in relation to the codes. Some of the initially developed themes were discarded as the data was not large enough to support those themes.

Step 5: defining and naming themes

Themes were checked again by AL and EC and names were assigned to each theme.

The quantitative data of this survey was analysed using SPSS.

7.3.6.9 Third party interim analysis

A Third party interim analysis was performed after 50% of the initial projected sample size had completed the six month study interventions. The term 'interim analysis' is used to

describe an evaluation of the current data from an ongoing trial, in which the primary research question is addressed, and which has the potential for modifying the conduct of the study (Whitehead J, Todd, Whitehead A & Stallard, 2001). The aim of the interim analysis was to confirm that the power calculations were appropriate in practice.

7.4 Results

A total of 66 participants were included in the study (see Figure 7.2 for the flow of participants through the study).

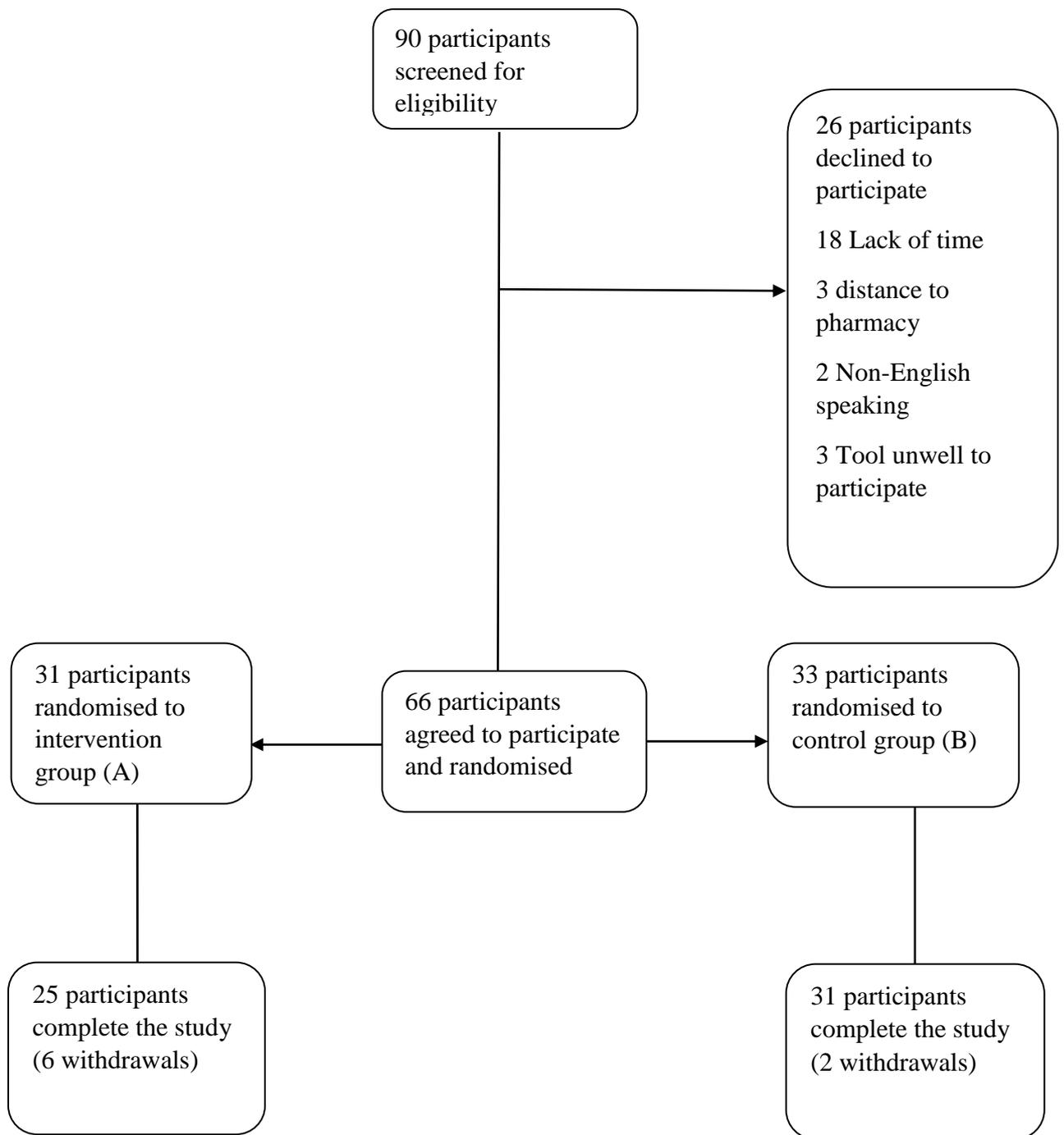


Figure 7-2 Flow of participants through the study.

7.4.1 Participant demographics

At baseline, no statistically significant differences were found between the participants in the intervention and the control groups (see Table 7.1). Some of the participants in both study groups had multiple cardiovascular co-morbidities (CVCs) including diabetes, stroke, heart failure, kidney disease and heart attack.

Table 7-1 Participant demographics. BMI= Body Mass Index (calculated as weight in kilograms divided by height in meters squared). All data are given in numbers (percentages) unless otherwise indicated

<i>Variables</i>	<i>Intervention</i>	<i>Control</i>
Mean age years (SD)	64.7 (10.5)	60.0 (9.3)
<u>Gender</u>		
Male	14 (45%)	18 (55%)
Female	17 (55%)	15 (45%)
<u>Ethnicity</u>		
White Caucasian	24 (78%)	25 (76%)
South Asian	5 (16%)	6 (18%)
African Caribbean	2 (6%)	2 (6%)
Mean BMI kg/m ² (SD)	29.0 (5.9)	30.3 (5.2)
Systolic blood pressure mm Hg (SD)	142.0 (17.0)	143.4 (16.9)
Diastolic blood pressure mm Hg (SD)	79.5 (11.4)	83.0 (12.9)
Other medical conditions (self-reported)	6 (19%)	7 (21%)
Diabetes	1(3%)	0

Heart failure	1 (3%)	1 (3%)
Kidney disease	1 (3%)	4 (13%)
Heart attack	1 (3%)	1 (3%)
Stroke	21 (67%)	20 (60%)

7.4.2 Impact on systolic blood pressure

A one-way ANOVA (repeated measures) analysis was conducted to explore the differences in systolic blood pressure from baseline both within and between the study groups. Normality of data was checked before undertaking the analysis. The data satisfied the assumption of Normality (Kolmogorov-Smirnov test was non-significant $p = 0.20$). Mauchly's test of sphericity was non-significant ($p = 0.31$) that satisfied the assumption of sphericity. There was an overall significant reduction in systolic blood pressure from baseline in both intervention group $F(3, 24) = 3.17, p = 0.04$ and control group $F(3, 30) = 3.4, p = 0.02$. "F" ratio represents the variance between the intervention and control group divided by the variance within the groups. However, based on the Bonferroni correction adjusted at 5% significance level ($p = 0.016$), the overall effect on systolic blood pressure in both study groups was not significant. There was a significant mean reduction in the systolic blood pressure from baseline at visit 3 in the intervention group which remained significant after Bonferroni correction ($p < 0.016$). There was no change in the systolic blood pressure between visit 3 and 4 in the intervention group. For control group, systolic blood pressure was decreased from baseline at visit 2, but did not change in the following visits. None of these reductions in systolic blood pressure achieved the significance level after Bonferroni corrections. Table 7.2 presents the change in systolic blood pressure for both groups across 4 study visits.

There was no overall difference between the two study groups in treatment effect $F(1, 54) = 0.17, p = 0.91$. After adjustment of co-variates including age $F = 0.46, p = 0.71$, gender $F = 0.10, p = 0.95$, BMI $F = 0.33, p = 0.79$, ethnicity $F = 0.15, p = 0.92$ and medical conditions $F = 0.16, p = 0.92$, there remained no significant differences between the two study groups. Figure 7.3 presents the changes in systolic blood pressure in both study groups during the study. As shown in Figure 7.3, apart from visit 3, a similar trend of reduction in systolic blood pressure was observed in both study groups during the study.

Table 7-2 Systolic blood pressure measurements in mm Hg of intervention and control group participants across 4 visits of the study. All data are given with standard deviation (SD)

<i>Study arm</i>	<i>Visit 1 (Baseline)</i>	<i>Visit 2</i>	<i>p-value*</i>	<i>Visit 3</i>	<i>p-value*</i>	<i>Visit 4 (6 month follow-up)</i>	<i>p-value*</i>
Intervention group	142.0 (17.0)	137.4 (15.0)	$p = 0.08$ CI 95% (-0.7-9.9)	134.3 (20.7)	$p = 0.009$ CI 95% (2.1-13.3)	134.7 (13.6)	$p = 0.01$ CI 95% (1.8-12.7)
Control group	143.4 (16.9)	137.7 (18.5)	$p = 0.01$ CI 95% (1.2-10.0)	137.2 (18.1)	$p = 0.02$ CI 95% (0.6-11.7)	136.1 (16.6)	$p = 0.02$ CI 95% (1.1-13.6)

***Unadjusted p values with 95% Confidence Interval (CI) representing differences in blood pressure between study visits.**

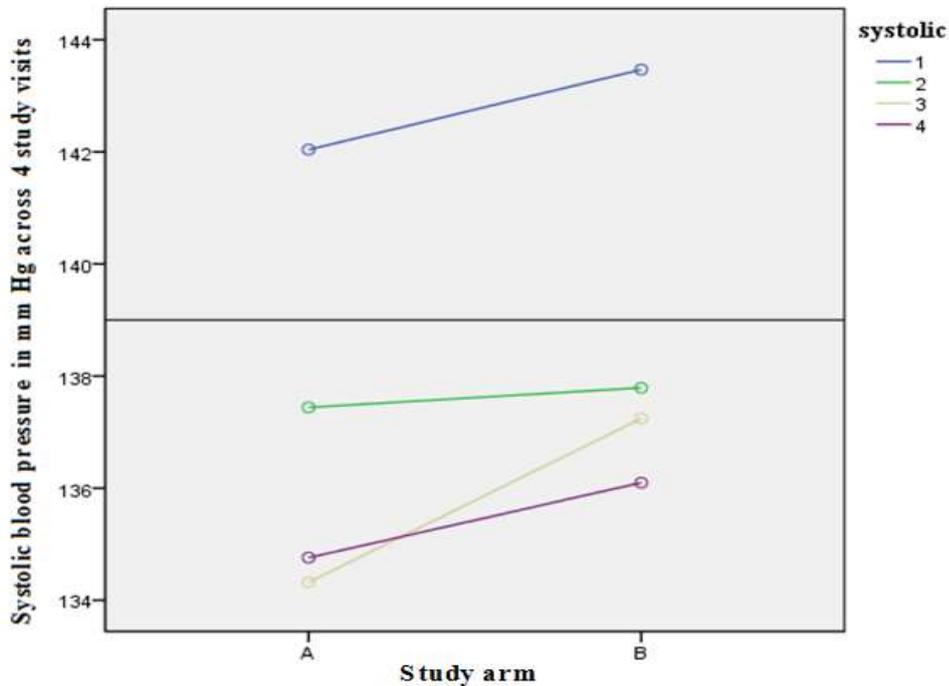


Figure 7-3 Changes in systolic blood pressure in the study arms A (intervention arm) and B (Control arm) across four study visits.

7.4.3 Impact on diastolic blood pressure

A one-way ANOVA (repeated measures) analysis was conducted to explore the difference in diastolic blood pressure from baseline both within and between the study groups. Mauchlys' test of sphericity was non-significant ($p = 0.09$) that satisfied the assumption of sphericity. There was an overall significant reduction in diastolic blood pressure from baseline during the study in both intervention group $F(3, 24) = 3.17, p = 0.02$ and control group $F(3, 30) = 3.9, p = 0.01$. However, based on the Bonferroni correction adjusted at 5% significance level ($p = 0.016$), the effect on diastolic blood pressure in both study groups was not significant ($p > 0.016$). There was a significant mean reduction in diastolic blood pressure from baseline at visit 4 in both study groups that remained significant after Bonferroni correction adjusted at 5% significance level. Apart from visit 4, none of other reductions in diastolic blood pressure

at other visits achieved the significance level after Bonferroni corrections. Interestingly, the diastolic blood pressure was increased between visit 2 and 3 in the intervention arm before reducing again at visit 4. No such patterns of change in diastolic blood pressure were observed in the control arm. Table 7.3 presents the diastolic blood pressure measurements for both groups across 4 study visits.

As observed for systolic blood pressure, there was no difference between the two study groups in treatment effect. $F(1, 54) = 0.36, p = 0.78$. After adjustment of co-variates including age $F = 0.46, p = 0.70$, gender $F = 0.46, p = 0.70$, BMI $F = 0.56, p = 0.63$, ethnicity $F = 0.36, p = 0.77$ and medical conditions $F = 0.37, p = 0.77$, there remained no significant differences between the two study groups. Figure 7.4 presents the changes in diastolic blood pressure in both study groups during the study.

Table 7-3 Diastolic blood pressure measurements in mm Hg of intervention and control arm participants across 4 visits of the study. All data are given with standard deviation (SD)

<i>Study arm</i>	<i>Visit 1 (Baseline)</i>	<i>Visit 2</i>	<i>p-value*</i>	<i>Visit 3</i>	<i>p-value*</i>	<i>Visit 4 (6 month follow-up)</i>	<i>p-value*</i>
Intervention group	79.5 (11.4)	76.9 (10.9)	$p = 0.10$ CI 95% (-0.5-5.7)	77.2 (11.7)	$p = 0.11$ CI 95% (-0.6-5.1)	75.0 (9.7)	$p = 0.008$ CI 95% (1.2-7.7)
Control group	83.0 (12.9)	79.4 (11.5)	$p = 0.03$ CI 95% (0.2-6.9)	78.7 (9.6)	$p = 0.01$ CI 95% (0.9-7.6)	77.9 (8.1)	$p = 0.009$ CI 95% (1.3-8.8)

***Unadjusted p values with 95% Confidence Interval representing differences in blood pressure between study visits.**

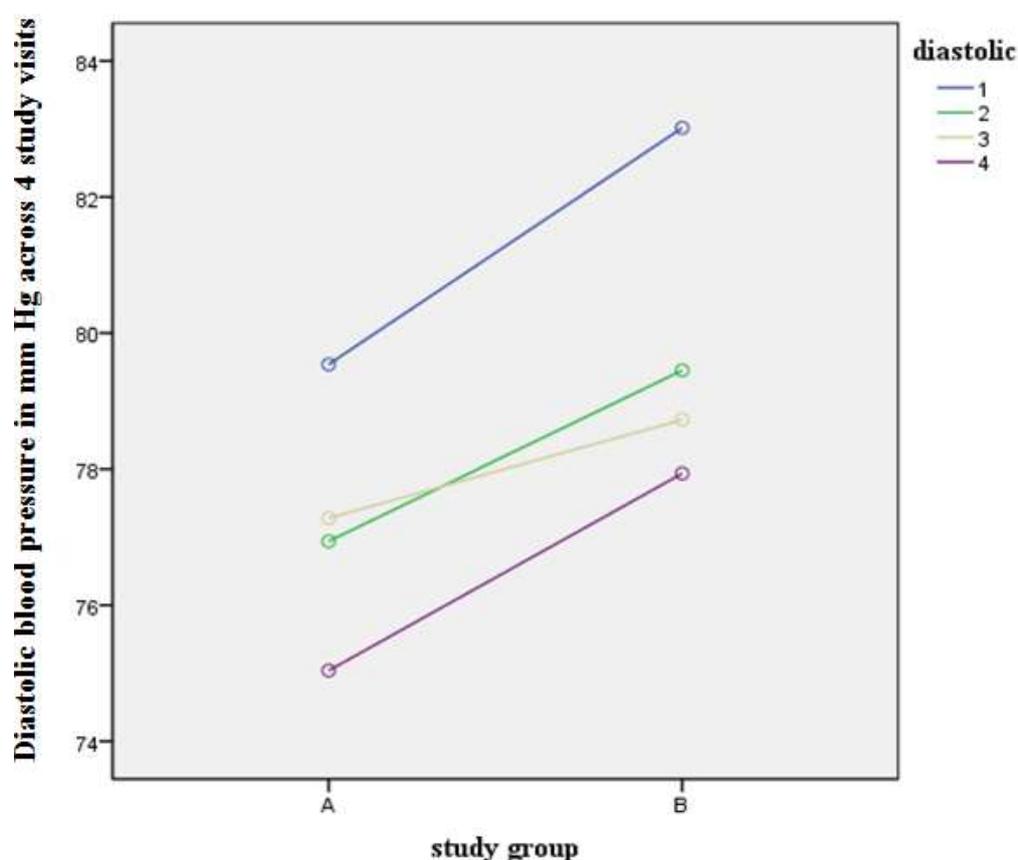


Figure 7-4 Changes in diastolic blood pressure in the study arms A (intervention arm) and B (Control arm) across four study visits.

7.4.4 Knowledge about hypertension and its treatment

Cross tabulation was used to analyse the responses to hypertension knowledge questions by participants of intervention and control groups. The questions were related to the ideal hypertension targets, risk factors of hypertension, the impact of lifestyle changes on hypertension control and the awareness about adverse effects of anti-hypertensive medications. A significant overall improvement was observed in the knowledge of intervention participants for 12 out of 18 questions. In the control group, no significant change was observed in the knowledge of participants with the exception of one question

only. However, difference between the two groups was significant at visit 4 for 5 questions only. These questions included awareness about top and bottom blood pressure targets, expected duration of hypertension disease, awareness about the adverse effects of hypertension and how anti-hypertensive medication works (Table 7.4).

Table 7.4. Percentages of participants correctly answering each hypertension knowledge question

Question	Intervention arm (n= 25)					Control arm (n=31)					Difference between groups expressed by p-value+			
	Visit 1 baseline	Visit 2	Visit 3	Visit 4	Overall difference within group p-value*	Visit 1 baseline	Visit 2	Visit 3	Visit 4	Overall difference within group p-value*	Visit 1	Visit 2	Visit 3	visit 4
Top blood pressure number should be under 140?	16 (64%)	16 (64%)	19 (76%)	24 (96%)	p = 0.01	18 (58%)	19 (61%)	25 (80%)	23 (74%)	p = 0.25	p = 0.65	p = 0.40	p = 0.74	p = 0.02
Lower blood number should be under 90?	15 (60%)	18 (72%)	21 (84%)	24 (96%)	p = 0.02	21 (68%)	22 (71%)	24 (77%)	24 (77%)	p = 0.85	p = 0.54	p = 0.43	p = 0.40	p = 0.04
Hypertension is a lifelong disease?	11 (44%)	23 (92%)	25 (100%)	25 (100%)	p < 0.001	20 (65%)	24(77%)	26 (84%)	25 (84%)	p = 0.29	p = 0.12	p =0.14	p = 0.03	p =0.02
Hypertension can cause heart attacks?	11 (44%)	21 (84%)	22 (88%)	25 (100%)	p < 0.001	20 (65%)	25 (80%)	26 (84%)	25 (84%)	p = 0.51	p = 0.99	p = 0.68	p = 0.19	p = 0.19
Hypertension can cause strokes?	21 (84%)	22 (88%)	23 (92%)	25 (100%)	p = 0.03	26 (84%)	29 (94%)	29 (94%)	29 (94%)	p = 0.09	p = 0.47	p = 0.55	p = 0.53	p = 0.36
Hypertension can cause kidney disease?	21 (84%)	21 (84%)	23 (92%)	25 (100%)	p = 0.20	21 (68%)	21 (68%)	23 (74%)	25 (80%)	p = 0.30	p = 0.87	p = 0.78	p = 0.08	p = 0.36
Hypertension does not cause asthma?	14 (56%)	16 (64%)	21 (84%)	23 (92%)	p = 0.03	18 (58%)	20 (65%)	22 (71%)	22 (71%)	p = 0.20	p = 0.68	p = 0.87	p = 0.41	p = 0.12
Hypertension does not cause cancer?	12 (48%)	18 (72%)	21 (84%)	19 (76%)	p = 0.02	13 (42%)	14 (45%)	20 (65%)	18 (58%)	p = 0.18	p = 0.87	p = 0.68	p = 0.11	p = 0.14
Losing weight reduces high blood pressure?	15 (60%)	20 (80%)	23 (92%)	23 (92%)	p = 0.005	12 (39%)	18 (58%)	18 (58%)	16 (52%)	p = 0.39	p = 0.04	p = 0.24	p = 0.23	p = 0.41
Cutting salt reduces high blood pressure?	20 (80%)	22 (88%)	22 (88%)	24 (96%)	p = 0.004	26 (84%)	28 (90%)	31 (100%)	29 (94%)	p = 0.44	p = 0.70	p = 0.68	p = 0.38	p = 0.25
Cutting alcohol reduces high blood pressure?	19 (76%)	24 (96%)	25 (100%)	25 (100%)	p = 0.18	28 (90%)	29 (94%)	30 (97%)	30 (97%)	p = 0.65	p = 0.27	p = 0.24	p = 0.36	p = 0.41

Anti-hypertensive should be taken daily?	19 (76%)	22 (88%)	23 (92%)	25 (100%)	p = 0.002	28 (90%)	29 (94%)	30 (97%)	30 (97%)	p = 0.79	p = 0.04	p = 0.23	p = 0.21	p = 0.19
Anti-hypertensive should be taken long-term?	22 (88%)	23 (92%)	23 (92%)	25 (100%)	p = 0.45	28 (90%)	28 (90%)	28 (90%)	28 (90%)	p = 0.34	p = 0.27	p = 0.41	p = 0.11	p = 0.11
Name of your new blood pressure medicine?	20 (80%)	22 (88%)	23 (92%)	25 (100%)	p = 0.01	28 (90%)	28 (90%)	28 (90%)	28 (90%)	p = 0.35	p = 0.96	p = 0.19	p = 0.08	p = 0.43
Dose of your new blood pressure medicine?	16 (64%)	20 (80%)	21 (84%)	20 (80%)	p = 0.08	20 (65%)	23 (74%)	23 (74%)	22 (71%)	p = 0.81	p = 0.81	p = 0.08	p = 0.43	p = 0.25
How your new blood pressure medicine works?	17 (68%)	21 (84%)	21 (84%)	21 (84%)	p = 0.09	22 (71%)	23 (74%)	30 (97%)	22 (71%)	p = 0.03	p = 0.07	p = 0.07	p = 0.02	p = 0.01
Awareness about adverse effects?	6 (24%)	17 (68%)	21 (84%)	21 (84%)	p < 0.001	7 (23%)	11 (35%)	15 (48%)	11 (35%)	p = 0.21	p = 0.90	p = 0.01	p = 0.002	p < 0.001
Incidence of adverse effects?	10 (40%)	11 (44%)	5 (20%)	5 (20%)	p = 0.12	8 (26%)	9 (29%)	11 (35%)	6 (19%)	p = 0.55	p = 0.39	p = 0.37	p = 0.32	p = 1.00

. * Chi-square test at p < 0.05.

P-value* indicates the difference within the study groups and **P-value+** indicates the difference between the study groups.

7.4.5 Sub group analysis

7.4.5.1 Impact of difference in gender on blood pressure control (male vs. female participants)

7.4.5.1.1 Systolic blood pressure

A one-way ANOVA (repeated measures) analysis was conducted to explore the difference in systolic blood pressure from baseline between males and females. Mauchly's test of sphericity was non-significant ($p = 0.81$) that satisfied the assumption of sphericity. There was an overall significant reduction in systolic blood pressure from baseline in females $F(3, 28) = 4.97, p = 0.008$ that remained significant after Bonferroni correction adjusted at 5% significance level ($p < 0.016$). No significant reduction in systolic blood pressure was observed for males $F(3, 26) = 2.02, p = 0.15$. Based on the Bonferroni correction adjusted at 5% significance level, there was a significant mean reduction in the systolic blood pressure from baseline at visit 3 and 4 in females ($p < 0.016$). In male participants, there was an increase in their systolic blood pressure between visit 2 and 3. Table 7.5 presents the systolic blood pressure measurements for both genders across 4 study visits.

Table 7-5 Systolic blood pressure measurements in mm Hg of male and female participants across 4 visits of the study. All data are given with standard deviation (SD)

<i>Study arm</i>	<i>Visit 1 (Baseline)</i>	<i>Visit 2</i>	<i>p-value*</i>	<i>Visit 3</i>	<i>p-value*</i>	<i>Visit 4 (6 month follow-up)</i>	<i>p-value*</i>
Males	140.6 (16.4)	135.5 (18.9)	p = 0.03 CI 95% (0.5-9.6)	136.7 (18.3)	p = 0.14 CI 95% (-1.4-9.1)	135.3 (16.9)	p = 0.07 CI 95% (-0.5-10.9)
Females	145.2 (17.2)	139.8 (14.5)	p = 0.04 CI 95% (0.2-10.4)	135.0 (20.5)	p = 0.001 CI 95% (4.4-15.8)	135.6 (13.6)	p = 0.003 CI 95% (-3.5-15.6)

***Unadjusted p values with 95% Confidence Interval representing difference in blood pressure between study visits.**

7.4.5.1.2 Diastolic blood pressure

A one-way ANOVA (repeated measures) analysis was conducted to explore the difference in diastolic blood pressure from baseline between males and females. Mauchly's test of sphericity was non-significant ($p = 0.5$) that satisfied the assumption of sphericity. There was an overall significant reduction in diastolic blood pressure from baseline in females $F(3, 28) = 4.6, p = 0.01$. However, this effect did not remain significant after Bonferroni correction adjusted at 5% significance level ($p > 0.016$). No significant reduction in diastolic blood pressure was observed for males $F(3, 26) = 1.2, p = 0.35$. Based on the Bonferroni correction adjusted at 5% significance level, there was a significant mean

reduction in the diastolic blood pressure from baseline at visit 3 and 4 in females ($p < 0.016$). As observed for systolic blood pressure, there was an increase in the diastolic blood pressure of male participants between visit 2 and 3. Table 7.6 presents the diastolic blood pressure measurements for both genders across 4 study visits.

Table 7-6 Diastolic blood pressure measurements in mm Hg of male and female participants across 4 visits of the study. All data are given with standard deviation (SD)

<i>Study arm</i>	<i>Visit 1 (Baseline)</i>	<i>Visit 2</i>	<i>p-value*</i>	<i>Visit 3</i>	<i>p-value*</i>	<i>Visit 4 (6 month follow-up)</i>	<i>p-value*</i>
Males	80.2 (12.3)	77.7 (11.3)	p = 0.12 CI 95% (-0.7-5.7)	78.2 (11.2)	p = 0.17 CI 95% (-0.9-5.0)	77.1 (10.1)	p = 0.07 CI 95% (-0.3-6.5)
Females	82.7 (12.3)	78.9 (11.3)	p = 0.02 CI 95% (0.5-7.1)	77.9 (9.9)	p = 0.006 CI 95% (1.4-8.1)	76.0 (7.5)	p = 0.001 CI 95% (-3.1-10.2)

***Unadjusted p values with 95% Confidence Interval representing differences in blood pressure between study visits.**

7.4.5.2 Impact of difference in age on the blood pressure control (participants ≥ 65 years vs. participants < 65 years)

7.4.5.2.1 Systolic blood pressure

A one-way ANOVA (repeated measures) analysis was conducted to explore the difference in systolic blood pressure from baseline between participants aged > 65 and participants aged < 65 years. Mauchly's test of sphericity was non-significant ($p = 0.36$) that satisfied the assumption of sphericity. There was an overall significant reduction in systolic blood pressure from baseline in participants < 65 $F(3, 33) = 9.1, p < 0.001$ that remained significant after Bonferroni correction adjusted at 5% significance level ($p < 0.016$). No

significant reduction in systolic blood pressure was observed for the other group $F(3, 21) = 1.9, p = 0.16$. Based on the Bonferroni correction adjusted at 5% significance level, there was a significant mean reduction in the systolic blood pressure from baseline at visit 3 and 4 in participants < 65 ($p < 0.016$). There was an increase in the systolic blood pressure of participants > 65 years between visit 2 and 3. Table 7.7 presents the systolic blood pressure measurements for both groups across 4 study visits.

Table 7-7 Systolic blood pressure measurements in mm Hg of participants > 65 and < 65 years across 4 visits of the study. All data are given with standard deviation (SD)

<i>Study arm</i>	<i>Visit 1 (Baseline)</i>	<i>Visit 2</i>	<i>p-value*</i>	<i>Visit 3</i>	<i>p-value*</i>	<i>Visit 4 (6 month follow-up)</i>	<i>p-value*</i>
Participants ≥ 65 years	145.5 (17.7)	137.6 (17.0)	$p = 0.02$ CI 95% (1.3-14.4)	140.3 (22.3)	$p = 0.2$ CI 95% (-3.1-13.4)	139.7 (16.8)	$p = 0.17$ CI 95% (-2.7-14.3)
Participants < 65 years	141.0 (16.2)	137.6 (17.1)	$p = 0.06$ CI 95% (-0.1-7.0)	133.0 (16.6)	$p < 0.001$ CI 95% (4.2-11.7)	132.7 (13.8)	$p < 0.001$ CI 95% (4.2-12.6)

***Unadjusted p values with 95% Confidence Interval representing differences in blood pressure between study visits.**

7.4.5.2.2 Diastolic blood pressure

A one-way ANOVA (repeated measures) analysis was conducted to explore the difference in diastolic blood pressure from baseline between participants aged > 65 and < 65 years. Mauchly's test of sphericity was non-significant ($p = 0.32$) that satisfied the assumption of sphericity. There was an overall significant reduction in diastolic blood pressure from baseline in participants < 65 $F(3, 33) = 4.6$, $p = 0.008$ that remained significant after Bonferroni correction adjusted at 5% significance level ($p < 0.016$). No significant reduction in diastolic blood pressure was observed for the other group $F(3, 21) = 1.7$, $p = 0.19$. Based on the Bonferroni correction adjusted at 5% significance level, there was a significant mean reduction in the diastolic blood pressure from baseline at visit 3 and 4 in participants < 65 ($p < 0.016$). As observed for systolic blood pressure, there was an increase in the diastolic blood pressure of participants > 65 years between visit 2 and 3. Table 7.8 presents the diastolic blood pressure measurements for both groups across 4 study visits.

Table 7-8 Diastolic blood pressure measurements in mm Hg of participants > 65 and < 65 years across 4 visits of the study. All data are given with standard deviation (SD)

<i>Study arm</i>	<i>Visit 1 (Baseline)</i>	<i>Visit 2</i>	<i>p-value*</i>	<i>Visit 3</i>	<i>p-value*</i>	<i>Visit 4 (6 month follow-up)</i>	<i>p-value*</i>
Participants ≥65 years	76.9 (14.0)	72.4 (12.2)	$p = 0.03$ CI 95% (0.3-8.7)	74.0 (12.5)	$p = 0.15$ CI 95% (-1.2-7.1)	73.0 (9.2)	$p = 0.07$ CI 95% (- 0.4-8.4)
Participants < 65 years	84.3 (10.2)	82.1 (8.8)	$p = 0.10$ CI 95% (- 0.4-4.8)	80.7 (8.2)	$p = 0.008$ CI 95% (1.0-6.2)	79.0 (7.9)	$p = 0.001$ CI 95% (2.3-8.3)

***Unadjusted p values with 95% Confidence Interval representing differences in blood pressure between study visits.**

7.4.5.3 Impact of difference in BMI on blood pressure control (participants with BMI \geq 30 vs. participants with BMI < 30)

7.4.5.3.1 Systolic blood pressure

A one-way ANOVA (repeated measures) analysis was conducted to explore the difference in systolic blood pressure from baseline between participants with a BMI > 30 kg/m² and participants with < 30 kg/m². Mauchly's test of sphericity was non-significant ($p = 0.33$) that satisfied the assumption of sphericity. There was an overall significant reduction in systolic blood pressure from baseline in participants with a BMI < 30 $F(3, 33) = 6.0$, $p = 0.002$ that remained significant after Bonferroni correction adjusted at 5% significance level ($p < 0.016$). No significant reduction in systolic blood pressure was observed for the other group $F(3, 21) = 0.9$, $p = 0.41$. Based on the Bonferroni correction adjusted at 5% significance level, there was a significant mean reduction in the systolic blood pressure from baseline at all study visits for participants with a BMI < 30 ($p < 0.016$). In the participants with a BMI > 30 , there was an increase in their systolic blood pressure at visit 4 of the study. Table 7.9 presents the systolic blood pressure measurements for both groups across 4 study visits.

Table 7-9 Systolic blood pressure measurements in mm Hg of participants with a BMI > 30 and < 30 across 4 visits of the study. All data are given with standard deviation (SD)

<i>Study arm</i>	<i>Visit 1 (Baseline)</i>	<i>Visit 2</i>	<i>p-value*</i>	<i>Visit 3</i>	<i>p-value*</i>	<i>Visit 4 (6 month follow-up)</i>	<i>p-value*</i>
Participants with ≥ 30 BMI	139.3 (14.4)	136.3 (15.6)	p = 0.24 CI 95% (-0.9-9.2)	132.7 (21.2)	p = 0.10 CI 95% (3.1-15.3)	136.3 (18.2)	p = 0.38 CI 95% (0.2-9.9)
Participants with < 30 BMI	145.0 (18.0)	138.5 (17.8)	p = 0.005 CI 95% (1.8-10.9)	137.9 (17.8)	p = 0.001 CI 95% (2.8-11.0)	134.9 (13.3)	p < 0.001 CI 95% (5.2-15.6)

***Unadjusted p values with 95% Confidence Interval representing differences in blood pressure between study visits.**

7.4.5.3.2 Diastolic blood pressure

A one-way ANOVA (repeated measures) analysis was conducted to explore the difference in diastolic blood pressure from baseline between participants with a BMI > 30 kg/m² and participants with < 30 kg/m². Mauchly's test of sphericity was non-significant ($p = 0.70$) that satisfied the assumption of sphericity. There was an overall significant reduction in diastolic blood pressure from baseline in participants with a BMI < 30 $F(3, 33) = 5.17, p = 0.005$ that remained significant after Bonferroni correction adjusted at 5% significance level ($p < 0.016$). No significant reduction in diastolic blood pressure was observed for the other group $F(3, 21) = 0.8, p = 0.48$. Based on the Bonferroni correction adjusted at 5% significance level, there was a significant mean reduction in the diastolic blood pressure from baseline at visit 3 and 4 for participants with a BMI < 30 ($p < 0.016$). Table 7.10 presents the diastolic blood pressure measurements for both groups across 4 study visits.

Table 7-10 Diastolic blood pressure measurements in mm Hg of participants with a BMI > 30 and < 30 across 4 visits of the study. All data are given with standard deviation (SD)

<i>Study arm</i>	<i>Visit 1 (Baseline)</i>	<i>Visit 2</i>	<i>p-value*</i>	<i>Visit 3</i>	<i>p-value*</i>	<i>Visit 4 (6 month follow-up)</i>	<i>p-value*</i>
Participants with ≥ 30 BMI	84.5 (11.9)	82.0 (11.7)	p = 0.23 CI 95% (-0.5-7.2)	82.4 (10.3)	p = 0.26 CI 95% (-0.1-6.4)	81.0 (8.1)	p = 0.11 CI 95% (0.3-8.2)
Participants with < 30 BMI	79.4 (12.3)	75.9 (10.4)	p = 0.01 CI 95% (0.5-6.2)	75.2 (9.9)	p = 0.004 CI 95% (1.3-7.0)	73.8 (8.3)	p < 0.001 CI 95% (2.7-8.8)

***Unadjusted p values with 95% Confidence Interval representing difference in blood pressure between study visits.**

7.4.5.4 Impact of co-morbidities on blood pressure control (participants with co-morbidities vs. participants without co-morbidities)

7.4.5.4.1 Systolic blood pressure

A one-way ANOVA (repeated measures) analysis was conducted to explore the difference in systolic blood pressure from baseline between participants with and without CVCs.

Mauchlys' test of sphericity was non-significant (p = 0.86) that satisfied the assumption of sphericity. There was an overall significant reduction in systolic blood pressure from baseline in both participants with CVCs $F(3, 22) = 3.4, p = 0.03$ and participants without CVCs $F(3, 32) = 5.7, p = 0.003$. However, based on the Bonferroni correction adjusted at 5% significance level (p = 0.016), only participants without CVCs achieved significant reduction in systolic blood pressure (p < 0.016). There was a significant mean reduction in

the systolic blood pressure from baseline at visit 3 and 4 in participants without CVCs ($p < 0.016$). For participants with CVCs, they only achieved significant reduction at visit 2 after Bonferroni correction. An increase in the systolic blood pressure was observed between visit 3 and 4 in participants with CVCs. Table 7.11 presents the systolic blood pressure measurements for both groups across 4 study visits.

Table 7-11 Systolic blood pressure measurements in mm Hg of participants with and without CVCs across 4 visits of the study. All data are given with standard deviation (SD)

<i>Study arm</i>	<i>Visit 1 (Baseline)</i>	<i>Visit 2</i>	<i>p-value*</i>	<i>Visit 3</i>	<i>p-value*</i>	<i>Visit 4 (6 month follow-up)</i>	<i>p-value*</i>
Participants with CVCs	143.2 (19.3)	135.1 (20.7)	p = 0.008 CI 95% (2.3- 13.8)	138.8 (22.9)	p = 0.21 CI 95% (-2.6- 11.3)	136.4 (18.4)	p = 0.07 CI 95% (-0.8- 14.3)
Participants without CVCs	142.3 (15.2)	139.3 (13.7)	p = 0.11 CI 95% (-0.8- 7.1)	133.8 (16.2)	p = 0.001 CI 95% (4.1- 13.2)	134.8 (12.9)	p = 0.003 CI 95% (2.8- 12.5)

***Unadjusted p values with 95% Confidence Interval representing difference in blood pressure between study visits.**

7.4.5.4.2 Diastolic blood pressure

A one-way ANOVA (repeated measures) analysis was conducted to explore the difference in diastolic blood pressure from baseline between participants with and without CVCs.

Mauchly's test of sphericity was non-significant ($p = 0.38$) that satisfied the assumption of sphericity. There was an overall significant reduction in diastolic blood pressure from baseline in participants without CVCs $F(3, 32) = 5.8$, $p = 0.003$ that remained significant after Bonferroni correction ($p < 0.016$). No significant reduction in diastolic blood pressure was observed for participants with CVCs $F(3, 22) = 0.8$, $p = 0.49$. Based on the Bonferroni

correction adjusted at 5% significance level, there was a significant mean reduction in the diastolic blood pressure from baseline at visit 3 and 4 in participants without CVCs ($p < 0.016$). For participants without CVCs, no significant reduction was achieved for any study visit after Bonferroni correction. The diastolic blood pressure of participants with CVCs was increased between visit 2 and visit 3. Table 7.12 presents the diastolic blood pressure measurements for both groups across 4 study visits.

Table 7-12 Diastolic blood pressure measurements in mm Hg of participants with and without CVCs across 4 visits of the study. All data are given with standard deviation (SD)

<i>Study arm</i>	<i>Visit 1 (Baseline)</i>	<i>Visit 2</i>	<i>p-value*</i>	<i>Visit 3</i>	<i>p-value*</i>	<i>Visit 4 (6 month follow- up)</i>	<i>p-value*</i>
Participants with CVCs	77.4 (12.4)	74.91 (12.7)	p = 0.21 CI 95% (-1.5- 6.5)	76.0 (11.6)	p = 0.45 CI 95% (-2.3- 5.0)	75.2 (8.9)	p = 0.24 CI 95% (-1.5- 5.9)
Participants without CVCs	84.2 (11.5)	80.7 (9.9)	p = 0.01 CI 95% (0.8-6.3)	79.4 (9.2)	p = 0.001 CI 95% (2.0-7.5)	77.6 (8.9)	p < 0.001 CI 95% (3.4-9.8)

***Unadjusted p values with 95% Confidence Interval representing differences in blood pressure between study visits.**

7.4.5.5 Impact of differences in ethnic origin on blood pressure control (White participants vs. Non-White participants)

7.4.5.5.1 Systolic blood pressure

Due to the limited number of South Asian and African-Caribbean participants in the study, they were placed in one group. A one-way ANOVA (repeated measures) analysis was conducted to explore the difference in systolic blood pressure from baseline between White and non-White participants. Mauchly's test of sphericity was non-significant ($p = 0.23$) that satisfied the assumption of sphericity. There was an overall significant reduction in systolic blood pressure from baseline in both non-White participants $F(3, 14) = 13.5, p < 0.001$ and White participants $F(3, 40) = 3.1, p = 0.03$. However, after Bonferroni correction adjusted at 5% significance level ($p < 0.016$) only non-White participants achieved significant reduction in systolic blood pressure. No significant reduction in systolic blood pressure was observed for the other group. Based on the Bonferroni correction adjusted at 5% significance level, there was a significant mean reduction in the systolic blood pressure from baseline at visits 3 and 4 for non-White participants ($p < 0.016$). White participants achieved a significant reduction from baseline at visit 2 only. There was no change in their blood pressure between the remaining study visits. Table 7. 13 presents the systolic blood pressure measurements for both groups across 4 study visits.

Table 7-13 Systolic blood pressure measurements in mm Hg of White and non-White participants across 4 visits of the study. All data are given with standard deviation (SD).

<i>Study arm</i>	<i>Visit 1 (Baseline)</i>	<i>Visit 2</i>	<i>p-value*</i>	<i>Visit 3</i>	<i>p-value*</i>	<i>Visit 4 (6 month follow-up)</i>	<i>p-value*</i>
White participants	142.6 (17.2)	136.3 (16.0)	p = 0.005 CI 95% (2.0-10.4)	136.5 (20.1)	p = 0.02 CI 95% (1.0-11.2)	136.7 (16.3)	p = 0.03 CI 95% (0.5-11.2)
Non-White participants	143.4 (16.4)	141.0 (19.4)	p = 0.31 CI 95% (-2.4-7.2)	134.4 (17.1)	p < 0.001 CI 95% (4.8-13.1)	132.1 (11.9)	p < 0.001 CI 95% (6.3-16.2)

***Unadjusted p values with 95% Confidence Interval representing difference in blood pressure between study visits.**

7.4.5.5.2 Diastolic blood pressure

A one-way ANOVA (repeated measures) analysis was conducted to explore the difference in diastolic blood pressure from baseline between White and non-White participants.

Mauchlys' test of sphericity was non-significant ($p = 0.10$) that satisfied the assumption of sphericity. There was an overall significant reduction in diastolic blood pressure from baseline in White participants $F(3, 40) = 3.7, p = 0.02$. However, after Bonferroni correction adjusted at 5% significance level, this effect in White participants did not remain significant ($p > 0.016$). No significant reduction in diastolic blood pressure was observed

for the other group $F(3, 14) = 1.6, p = 0.22$. Based on the Bonferroni correction adjusted at 5% significance level, there was a significant mean reduction in the diastolic blood pressure from baseline at visit 4 for White participants only ($p < 0.016$). Table 7.14 presents the diastolic blood pressure measurements for both groups across 4 study visits.

Table 7-14 Diastolic blood pressure measurements in mm Hg of White and non-White participants across 4 visits of the study. All data are given with standard deviation (SD).

<i>Study arm</i>	<i>Visit 1 (Baseline)</i>	<i>Visit 2</i>	<i>p-value*</i>	<i>Visit 3</i>	<i>p-value*</i>	<i>Visit 4 (6 month follow-up)</i>	<i>p-value*</i>
White participants	80.9 (12.6)	77.3 (11.6)	p = 0.01 CI 95% (0.6-6.5)	77.3 (10.9)	p = 0.01 CI 95% (0.8-6.3)	76.0 (8.4)	p = 0.002 CI 95% (1.9-7.8)
Non-White participants	82.9 (11.7)	81.9 (11.7)	p = 0.16 CI 95% (-0.8-4.5)	80.1 (9.6)	p = 0.12 CI 95% (-0.8-6.5)	78.3 (10.1)	p = 0.05 CI 95% (-0.1-9.3)

***Unadjusted p values with 95% Confidence Interval representing difference in blood pressure between study visits**

7.4.5.6 Impact of difference in the number of blood pressure medications taken by participants on blood pressure control (participants taking one medication vs. participants taking more than one medication)

7.4.5.6.1 Systolic blood pressure

A one-way ANOVA (repeated measures) analysis was conducted to explore the difference in systolic blood pressure from baseline between participants taking a single anti-hypertensive medication (monotherapy) and participants taking more than a single medication (multiple therapy). Mauchly's test of sphericity was non-significant ($p = 0.57$) that satisfied the assumption of sphericity. There was an overall significant reduction in systolic blood pressure from baseline in participants on multiple therapy $F(3, 29) = 5.6$, $p = 0.004$ that remained significant after Bonferroni correction ($p < 0.016$). No significant reduction in systolic blood pressure was observed for the other group $F(3, 26) = 1.1$, $p = 0.32$. Based on the Bonferroni correction adjusted at 5% significance level, there was a significant mean reduction in the systolic blood pressure from baseline at visits 3 and 4 for participants with multiple therapy only ($p < 0.016$). There was an increase in the systolic blood pressure of participants taking a single medication between visit 3 and 4. Table 7.15 presents the systolic blood pressure measurements for both groups across 4 study visits.

Table 7-15 Systolic blood pressure measurements in mm Hg of participants taking single and multiple anti-hypertensive medications across 4 visits of the study. All data are given with standard deviation (SD)

<i>Study arm</i>	<i>Visit 1 (Baseline)</i>	<i>Visit 2</i>	<i>p-value*</i>	<i>Visit 3</i>	<i>p-value*</i>	<i>Visit 4 (6 month follow-up)</i>	<i>p-value*</i>
Multiple therapy	143.2 (18.2)	136.8 (19.8)	p = 0.12 CI 95% (-0.4-8.2)	135.2 (19.2)	p = 0.001 CI 95% (1.3-12.0)	134.1 (13.2)	p = 0.001 CI 95% (1.7-11.4)
Monotherapy	142.3 (13.7)	138.5 (13.1)	p = 0.11 CI 95% (1.3-11.8)	136.7 (19.5)	p = 0.10 CI 95% (1.2-13.0)	137.0 (17.5)	p = 0.13 CI 95% (1.0-15.1)

***Unadjusted p values with 95% Confidence Interval representing difference in blood pressure between study visits.**

7.4.5.6.2 Diastolic blood pressure

A one-way ANOVA (repeated measures) analysis was conducted to explore the difference in diastolic blood pressure from baseline between participants taking a single anti-hypertensive medication (monotherapy) and participants taking more than a single medication (multiple therapy). Mauchly's test of sphericity was non-significant ($p = 0.5$) that satisfied the assumption of sphericity. There was an overall significant reduction in diastolic blood pressure from baseline in participants on multiple therapy $F(3, 29) = 3.7$, $p = 0.02$ that did not remain significant after Bonferroni correction ($p > 0.016$). No significant reduction in diastolic blood pressure was observed for the other group $F(3, 26) = 1.5$, $p = 0.23$. Based on the Bonferroni correction adjusted at 5% significance level, there was a significant mean reduction in the diastolic blood pressure from baseline at visit 4 for participants with multiple therapy only ($p < 0.016$). Table 7.16 presents the diastolic blood pressure measurements for both groups across 4 study visits.

Table 7.16 Diastolic blood pressure measurements in mm Hg of participants taking single and multiple anti-hypertensive medication across 4 visits of the study. All data are given with standard deviation (SD)

<i>Study arm</i>	<i>Visit 1 (Baseline)</i>	<i>Visit 2</i>	<i>p-value*</i>	<i>Visit 3</i>	<i>p-value*</i>	<i>Visit 4 (6 month follow-up)</i>	<i>p-value*</i>
Multiple therapy	82.9 (11.0)	79.2 (10.9)	p = 0.03 CI 95% (-0.5-4.3)	78.5 (9.7)	p = 0.01 CI 95% (-0.9-4.5)	77.2 (8.7)	p = 0.002 CI 95% (-0.5-5.7)
Monotherapy	79.7 (13.6)	77.3 (11.7)	p = 0.11 CI 95% (0.5-8.4)	77.5 (11.6)	p = 0.09 CI 95% (1.4-8.7)	75.9 (9.52)	p = 0.04 CI 95% (3.4-11.0)

***Unadjusted p values with 95% Confidence Interval representing difference in blood pressure between study visits**

7.4.6 Multivariable linear regression analysis

7.4.6.1 Systolic blood pressure

Only BMI was found to have a significant linear association with systolic blood pressure (R^2 0.024, $p = 0.02$, $F = 5.32$). However, as suggested by the small R^2 value, BMI only accounted for 2.4% of the variation in systolic blood pressure. None of the other included variables showed any significant association with the systolic blood pressure.

7.4.6.2 Diastolic blood pressure

Only BMI (R^2 0.17, $p < 0.001$, $F = 23.3$) and age (R^2 0.11, $p < 0.001$, $F = 27.0$) were found to have a significant linear association with diastolic blood pressure. None of the other included variables showed any significant association with the diastolic blood pressure.

7.4.7 Participant satisfaction survey

7.4.7.1 Description of the quantitative data

A total of 53 participants completed the participant satisfaction survey. Participants were not asked to provide any personal details including age, gender or ethnicity. Participants were asked to strongly disagree, disagree, agree or strongly agree to the statements described in Table 7.17.

Table 7-17 Quantitative description of the participants' satisfaction with the study

<i>Question</i>	<i>Strongly disagree</i>	<i>Disagree</i>	<i>Agree</i>	<i>Strongly agree</i>
The pharmacist clearly explained the purpose of the study to me?	0	0	14 (26.4%)	39 (73.6%)
The advice given to me by pharmacist was useful?	0	0	15 (28.3%)	38 (71.7%)
I feel that taking part in the study has improved my high blood pressure?	0	4 (7.5%)	20 (37.7%)	28 (52.8%)
I am happy with the number of appointments I had with the pharmacist?	0	0	17 (32%)	36 (67.9%)
I would recommend others to take part in the study?	0	0	10 (18.9%)	43 (81.1%)

Participants were asked to provide reasons for taking part in the study. They were required to choose from four statements. These were: 1) I was concerned about my high blood pressure, 2) I wanted to learn about high blood pressure and its risks, 3) I wanted to learn about the new blood pressure medicine I was using and 4) I was confident that my pharmacist would give me good advice. More than half of the study participants (n =27, 51.0%) selected all of the four above statements. Ten (19%) of the study participants selected statement 4 only, 4 (7.5%) selected statements 2,3,4. Three (5.7%) of the study participants selected statements 1,3,4 and statements 2,4, respectively. Two(3.8%) of the study participants selected statements 1,2,4 and the remaining four participants each selected statements 3, statements 1,2 and statements 3,4, respectively.

7.4.7.2 Qualitative analysis

7.4.7.2.1 Participants views about approaching pharmacists for getting advice on medical conditions

The qualitative data extracted from participants' responses was classified into two broad themes: participants' confidence to approach pharmacists in future and participants' preference to use pharmacists as their first port of call before GPs. **Figures 7.5-7.7** describes the steps taken to reach the final two themes.

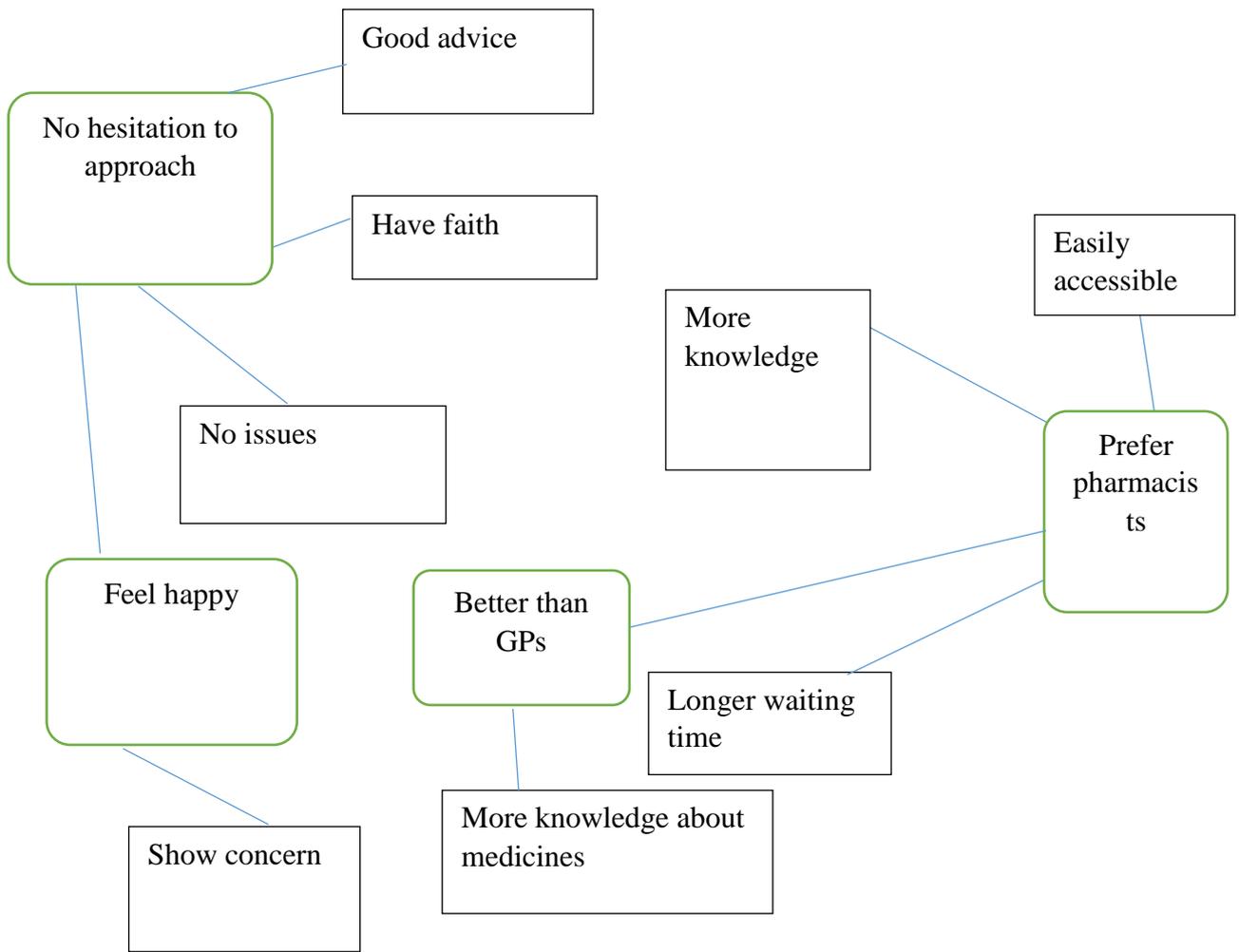


Figure 7.5: Initial thematic map, showing four main themes

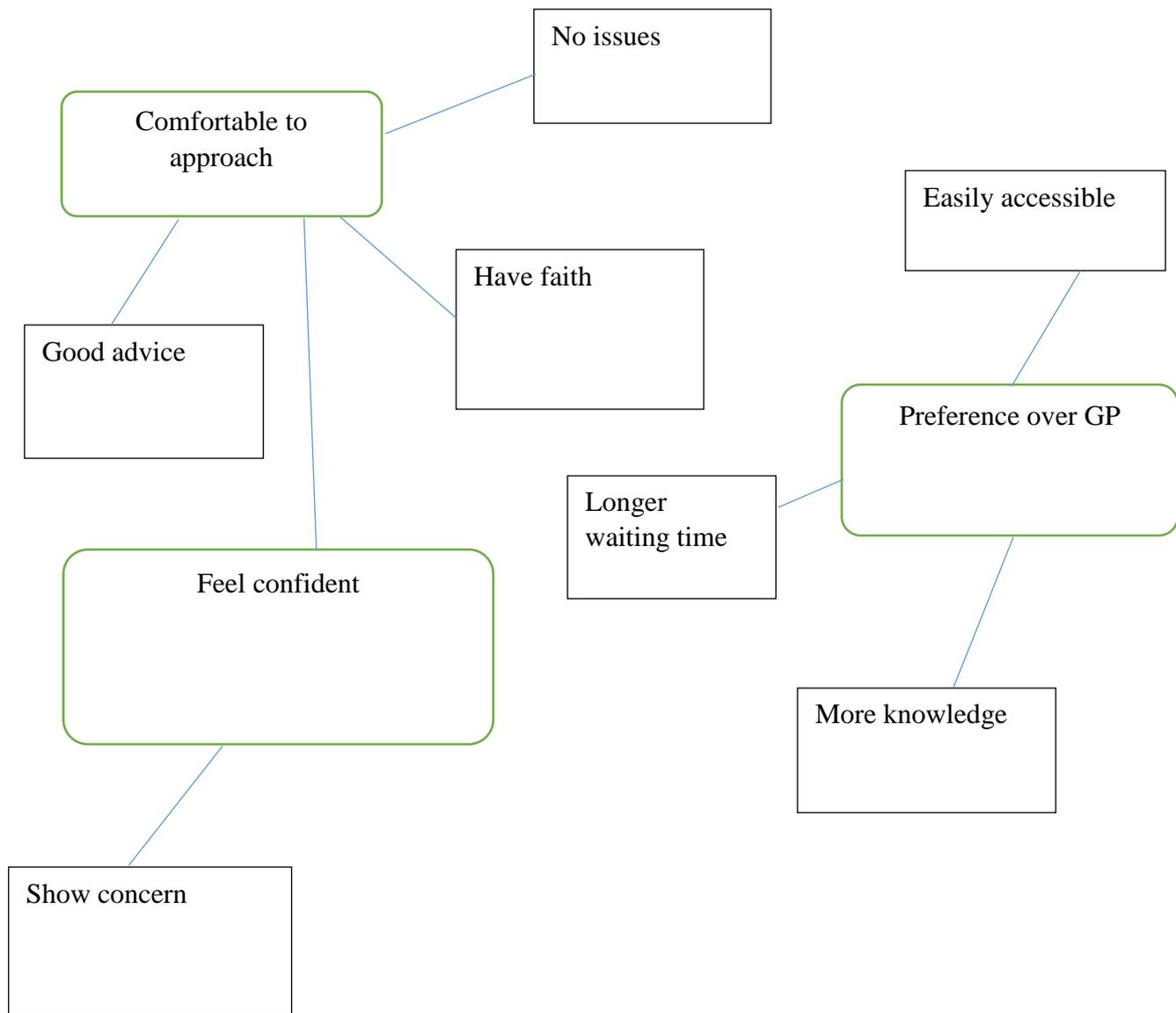


Figure 7.6: Developed thematic map, showing three main themes

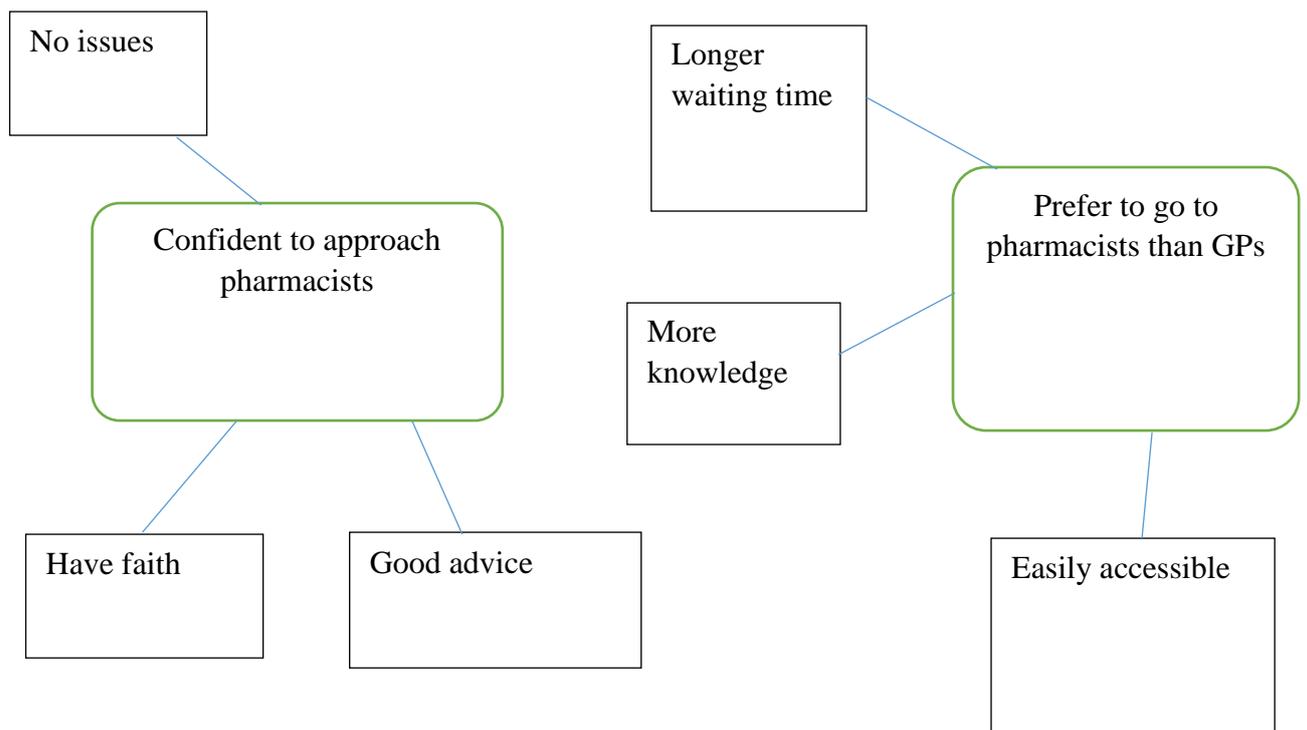


Figure 7.7: Final thematic map, showing final two main themes

Confident to approach pharmacists in future

Participants felt confident to approach pharmacists in future. Their expression of confidence in pharmacists appears to have been based on the level of trust in pharmacists' advice. Participants expected to receive good advice from pharmacists based on their knowledge and understanding about medicines. The expression of confidence in pharmacists' skills was also shared in the findings of the quantitative analysis of this survey where more than 70% of participants felt confident that they would get good advice from the pharmacists. Some of the participant's comments were:

"I would approach my pharmacist anytime. He is exceptionally good"

"I know that I can always approach my pharmacist. Don't even have to think about it"

"Quite confident that I would be given the correct advice"

"I would feel strongly in the future to get more advice about my treatment"

"Feel confident in asking pharmacists. No problem in approaching pharmacists"

"Would definitely ask the pharmacists for their advice on blood pressure"

"Very confident. Pharmacist is very helpful and knowledgeable"

These comments reflect participants' level of satisfaction with pharmacists' advice and also highlight participants' lack of hesitation in approaching pharmacists for their health-related issues. Convenient and easier accessibility of pharmacists was another reason for some of the participants to approach them. Some of the comments included:

"Feel very confident and can approach my local pharmacist any time when needed"

"Wouldn't think about speaking to pharmacist. Don't need to book an appointment to speak to pharmacist about something very important"

"Easier to come and see the pharmacist than GP for advice. Have complete faith in the pharmacist advice"

"Very confident to approach pharmacist without any hesitation. Approachable at any time of the day as no need to make appointment. Pharmacists have willingness to help"

Preference to go to Pharmacists than GPs

Participants seemed to use community pharmacists as the first port of call due to convenience. Others believed that pharmacists had better understanding and knowledge about medicines than GPs. Some of these comments included:

"I feel very confident in asking pharmacists. I prefer to go to pharmacists than GPs because the advice I had from pharmacist was impartial. Pharmacists have more understanding and knowledge about medicines. It not only applies to blood pressure but also applies to other conditions"

"I feel that sometimes pharmacists make more sense than doctors. Pharmacists explain the medication use in detail as compared to doctors"

"Feel very confident discussing with the pharmacist. You get more advice from pharmacists than doctors"

"You get more advice from pharmacists than GPs. It is easier to come to pharmacists than GPs due to delays in getting appointments"

"Would approach pharmacists if needed. I would approach pharmacists first before going to GP if experienced any side-effects"

The above comments reflect participants' frustration over the delays in getting appointment with the GPs. These comments also appear to restore their confidence in the knowledge and skills of pharmacists. However, not all the participants appear to use pharmacists as their first port of call.

Comment:

"I have no issues with pharmacist advice but would always go to my GP first.

7.4.7.2.2 Participants views about taking part in the study

Majority of the study participants gave a positive response about the study. According to some participants, their participation in the study allowed them to develop a better understanding and relationship with the pharmacists. Participants found the pharmacists' advice to be very useful and helped participants to bring the recommended changes in their lifestyle. Some participants appreciated the concern and care shown towards their health by pharmacists. The participants' sense of satisfaction with their experience of study was also reflected in the findings of the quantitative analysis of this survey. As described in the Table 7.17, more than 80% of the participants said that they would recommend others to take part in the study. However, one participant expressed his concern on the amount of time spent with the pharmacists. Some of these comments included:

"Don't have any problems in asking pharmacists after taking part in the study. Found the advice very useful and the information of weight and alcohol on blood pressure. After getting advice from pharmacist, I reduced my weight and cut alcohol. It did not take a long time to participate in this study and the study helped to improve my blood pressure"

"Very easy to understand the information from pharmacist. Fully satisfied with the consultation with the pharmacist and was happy that my blood pressure was checked regularly for me and the care shown in reminding me about the appointments"

"Improved my knowledge about blood pressure and its treatment. I know more about my medication after taking part in the study. The pharmacist told me about the consequences of high blood pressure which I wasn't previously aware of"

7.5 Discussion

The findings of this study show that interventions by pharmacists working in community pharmacies are associated with important improvements in hypertension control, whether or not associated with cardiovascular co-morbidities. Both systolic and diastolic blood pressure decreased, but the mean difference between the intervention and control group was not statistically significant. However, compared to participants in the control group, there was a significant improvement in the knowledge about hypertension and its treatment in the intervention participants. The participants of this study gave a positive response about the involvement of pharmacists in the management of long-term medical conditions such as hypertension.

7.5.1 Key findings

Provision of structured and written education on hypertension and its treatment was associated with a significant improvement in the knowledge of intervention participants and was sustained throughout the six month study. The improvement in the knowledge about hypertension reported in this study would have important implications for improving medication adherence to anti-hypertensive medications. For example, a study involving 525 hypertensive patients in the United States suggested that poor knowledge about hypertension was a significant impediment to adequate medication adherence by hypertensive patients (Knight, Bohn, Wang, Glynn, Mogul & Avon, 2001). Patient education plays an important role in facilitating patients' acceptance of their condition and helps them to embrace the behavioural changes required for an adequate adherence with their treatment (Grueninger, 1995).

Although provision of written education to the intervention participants led to an improvement in their awareness about hypertension and its treatment, it did not lead to a better blood control as compared to the control participants. The weak association of knowledge with blood pressure control has also been reported in a British study that involved 552 hypertensive patients (Watkins, Papacosta, Chinn & Martin, 1987). In this 12-month study, patients randomised to the study group received an educational booklet on hypertension and were compared to the usual care (Watkins et al., 1987). No significant difference in systolic or diastolic blood pressure was reported between the groups; however the study reported better knowledge about hypertension in the study patients as compared to the usual care (Watkins et al., 1987).

It also needs to be acknowledged that the meta-analysis presented in chapter 6 (Cheema et al., 2014), reported a 6.1 mm Hg reduction in systolic blood pressure and 2.5 mm Hg reduction in the diastolic blood pressure. However, the meta-analysis considered multifaceted pharmacist-led interventions including patient education on hypertension and the importance of its treatment, identification of drug-related problems and lifestyle advice. Compared to the meta-analysis, this study only assessed the impact of pharmacist-led patient education on blood pressure control. In addition, the meta-analysis included over 2000 patients as compared to the 56 patients included in the RCT. Therefore, the results of the two studies could not be compared.

Compared to males, females had a greater and significant mean reduction in both systolic and diastolic blood pressure in this study. The evidence of lower blood pressure levels in females has also been previously reported in a Danish study that involved 352 participants aged 20 to 79 years (Wiinber, Hoegholm, Christensen, Bang, Mikkelsen, Nielsen et al.,

1995). The study by Wiinber et al. (1995) reported that although systolic blood pressure increased with aging in both genders, men had a significantly higher 24-hour mean systolic blood pressure than women. However, the evidence of better blood pressure control in women compared to men has not been supported by a meta-analysis of 31 RCTs (Turnbull, Woodward, Neal, Barzi, Ninomiya, Chalmers et al., 2008). The review involving 103,268 men and 87,349 women who were assessed for their response towards anti-hypertensive medications did not report any difference between the two genders in their response to anti-hypertensive medications (Turnbull et al., 2008).

In this study, participants < 65 years achieved a greater and significant mean reduction in their systolic and diastolic blood pressure from baseline as compared to the participants > 65 years. Blood pressure is known to increase with age (Kotchen, McKean & Kotchen, 1982; Weinberger & Fineberg, 1991). Age-related changes in blood pressure are mainly ascribed to an increase in systolic blood pressure and evidence suggest that people over the age of 65 years have almost 90% risk of developing hypertension due to rise in systolic blood pressure (Franklin, 2006). Importantly, the mean systolic blood pressure at six-month follow-up in participants > 65 years in this study was just below the target level of 140 mm Hg specified in the NICE guidelines (National Clinical Guideline Centre, 2011). The successful achievement of the target systolic blood pressure level by the elderly participants in this study implies an adequate adherence to their anti-hypertensive medications.

The multiple linear regression analysis conducted in this study found a significant linear association of BMI with both systolic and diastolic blood pressure. A greater body weight is one of the major risk factors for hypertension (Landsberg, Aronne, Beilin, Burke, Igel, Lloyd-Jones et al., 2013). Evidence suggests that in the United States, the prevalence of

hypertension in obese individuals (BMI \geq 30 kg/m²) is 42.5% compared with 27.8% for overweight individuals (BMI 25.0–29.9 kg/m²) and 15.3% for those with BMI < 25 kg/m² (Wang & Wang, 2004). The findings of the sub-group analysis conducted in this study also confirmed the implication of a higher BMI with hypertension. The results suggest that participants with a BMI of < 30 kg/m² achieved better blood pressure control as compared to participants with BMI > 30 kg/m².

The findings of the sub-group analysis demonstrate the importance of weight reduction in achieving better blood pressure control. According to the Coronary Artery Risk Development in Young Adults (CARDIA) study in the United States, young adults (mean age 25 years at baseline) who maintained a stable BMI (within 2 kg/m² of baseline) during 15 years had no significant change in their systolic and diastolic blood pressure (Lloyd-Jones, Liu, Colangelo, Lijing, Yan, Klein et al., 2007). However those who had an increase in their BMI \geq 2 kg/m² had significant increase in their blood pressure (Lloyd-Jones et al., 2007). Specific lifestyle advice such as advice on reducing dietary salt and increasing fruit and vegetable intake should be provided to patients. Future research could for example evaluate formal use of established DASH-2 lifestyle approaches (Sacks, et al., 2001) within community pharmacist interventions aimed at blood pressure control.

Compared to monotherapy (use of single medication), participants taking multiple anti-hypertensive medications in this study achieved greater reductions in both systolic and diastolic blood pressure. These findings are in parallel with the findings of a meta-analysis that included 354 RCTs (Law, Wald, Morris & Jordan, 2003). Evidence from this meta-analysis by Law et al. (2003) suggested that blood pressure lowering effect of various anti-hypertensive medications was additive when used in combination. Another study that

compared the effects of monotherapy and combination therapy on systolic blood pressure supported the use of combination therapy for the treatment of hypertension (Everett, Glynn, Danielson & Ridker, 2008). This study by Everett et al. (2008) concluded that combination therapy led to a significantly greater reduction in systolic blood pressure than monotherapy. Furthermore, this study reported that apart from a greater increase in dizziness when compared to monotherapy, combination therapy was well tolerated (Everett et al., 2008).

Both systolic and diastolic blood pressure was reduced in participants with or without CVCs such as diabetes, kidney disease, stroke and heart failure. However, a greater mean reduction in systolic as well as diastolic blood pressure was achieved by participants without CVCs as compared to participants with CVCs. These findings have been supported by a previous study in the United States that assessed the prevalence, treatment and control of hypertension in adults with or without CVCs (Wong, Lopez, L'Italien, Chen, Kline, Franklin, 2007). The study that involved 4646 participants reported that around three-fourth of adults with CVCs in the United States have hypertension (Wong et al., 2007). The study by Wong et al. (2007) further reported that isolated systolic hypertension was common in patients with CVCs and the average systolic blood pressure was 20 mm Hg above the target level. However, it needs to be recognised that the potential effects of subject characteristics such as age, gender, BMI, ethnicity, CVCs and number of medications on systolic and diastolic blood pressure would require a test for an interaction to measure the impact of pharmacist-led intervention on the two study groups.

7.5.2 Critique of the qualitative analysis in the context of previous research

The findings of this study suggest that patients have the confidence and trust to approach pharmacists for not only discussing issues related to medicines but also to explore

additional health-related problems. These findings are in contrast to the findings of a cross-sectional study conducted at 13 general practices in the UK (Hammond et al., 2004). This study involved nearly 4000 patients and was aimed to explore the prevalence of patients' visits to the General Practitioners (GPs) (Hammond et al., 2004). GPs classified 260 (7%) of the patient visits as unnecessary and believed that these visits could have been managed by a community pharmacist (Hammond et al, 2004). Of the 260 patients whom GPs believed could have been managed by a community pharmacist, majority of these patients (59%) did not agree with the GPs' opinion and believed that visiting the pharmacist would not have been appropriate for their problem.

Although, the findings of this study may imply that the public perception about seeking pharmacists' advice may have changed, the results of the two studies are not comparable due to difference in the study settings. This study was conducted in community pharmacies only that may had positively influenced participants' willingness to seek pharmacists' advice on health-related problems. This study did not involve people who do not interact with pharmacy or pharmacists (non-pharmacy users). The representation of non-pharmacy users would have helped to gain an insight into the factors that would encourage them to interact with the pharmacists.

Majority of the participants in this study indicated their preference to visit pharmacists rather than GPs. However, these findings contradict the findings of a qualitative study conducted in the UK (Gidman, Ward & McGregor., 2012). This study used focus groups of people including both users and non-users of community pharmacy. The findings of this study reported a greater patients' trust and faith in their GPs than in pharmacists. The participants of this study associated pharmacists primarily with the supply of medicines.

Furthermore, the awareness of people about the extended role of pharmacists was reported to be low in this study (Gidman et al., 2012).

For a majority of participants of this study, the biggest strength of pharmacists is their convenient and easier accessibility besides their sound knowledge and understanding about medicines and its adverse effects. This study was also viewed by some as an opportunity to enhance patient pharmacist relationships. However, unlike the study by Gidman et al. (2012), this study used a questionnaire approach to seek patients view about the involvement of pharmacists in the management of long-term medical conditions. It must be acknowledged, that questionnaires have a limited ability to provide an in-depth information from the target population. On the contrary, a focus group can provide a more flexible and participatory approach to explore public views and beliefs (Adams & Cox, 2008).

7.5.3 Study limitations

This study has some important limitations. The study failed to recruit the desired number of participants as per the planned sample size calculations. This was attributed to a number of factors predominantly due to the withdrawal of two participating pharmacies from the study. Although compensation was offered to the eligible participants to take part in the study, no such financial incentive was offered to the participating pharmacists. The lack of financial incentive for pharmacists along with the time pressure on them to provide other pharmacy services may have contributed to the challenges in participant recruitment. Participant recruitment was further constrained by the lack of interest from the local surgeries. No patient referrals were made by the local GPs in this study despite repeated contacts with the local surgeries. Owing to the nature of pharmacists' interventions in this study, participants and the investigators could not be blinded to the study intervention.

The very wide Confidence Intervals reported for the blood pressure outcome in this study indicate the lack of certainty about the true effect of the study intervention. In other words, it indicates that this study was not powered enough to estimate the precise effect size. It also suggests that the variability in the study population.

Another limitation of the study was to use selective Bonferroni correction to the blood pressure outcome. It should be acknowledged that if a Bonferroni correction was to be used, it should have been applied to both primary outcome measures. The use of multiple outcome measures in a study is itself problematic. Zhang, Quan & Stepanavage (1997) recommends the use of a single primary outcome measure as a practical method to maintain the overall type I error rate. The main problem attributed to the use of multiple testing of multiple outcome measures at multiple time points is that multiple tests may falsely identify additional statistically significant results that may have been produced by chance and thus may not be true effects of the intervention studied (Gelman, Hill & Yajima, 2012).

7.5.4 Study strengths

This study has several strengths. It was a well-designed RCT that was informed by prior evidence and was developed using input from both patients and pharmacists. A sample size calculation was undertaken prior to the study that was independently verified by a statistician. Exclusion and inclusion criteria were rigorously applied to ensure that the study population was representative of the target population. Participants were randomly allocated to the study arms through a set of computer generated numbers to minimize selection bias. Randomisation was carried out by an external person who was not involved in the study. The primary outcome (blood pressure) was measured by trained dispensers

who were blinded to the study group. The measurement of blood pressure by dispensers in both groups with the same validated automated device was done to ensure the elimination of any investigator bias in the study.

7.5.5 Implications for clinicians and policymakers

The important reductions in blood pressure by pharmacist-led interventions have important implications for primary and secondary prevention of cardiovascular morbidity and mortality. For example, evidence from a meta-analysis involving one million adults in USA reported that every 1 mm Hg reduction in systolic blood pressure could prevent about 10,000 deaths related to coronary heart disease in the US each year (Lewington et al., 2002). Another analysis suggests that a sustained 2 mm Hg reduction in diastolic blood pressure would be expected to result in a 6% reduction in the risk of coronary heart disease and 15% decrease in stroke (Cook et al., 1995). This evidence provides an important message to clinicians and policy makers about the potential of community pharmacists in primary and secondary care of chronic disease management in the context of hypertension. The positive response of participants about the role of pharmacists as healthcare professionals should encourage pharmacists to continue to support and educate patients.

Summary of chapter

Despite the failure in the recruitment of the desired number of participants, this chapter has achieved the final objective of the thesis by introducing a new pharmacist supported method for a more effective use of medicines by patients with hypertension.

7.5.6 Conclusion

The findings of this study reported that provision of written information to patients was associated with a significant improvement in their knowledge about hypertension and its treatment. Furthermore, both systolic and diastolic blood pressure was reduced, however the mean difference between the intervention and control group was not statistically significant. The participants of this study gave a positive response about the involvement of pharmacists in the management of long-term medical conditions such as hypertension.

Both GPs and pharmacists play an important role in the management of long-term medical conditions. Many patients use pharmacists as a first port of call for advice, not just for their medicines but also to discuss their other health problems. The combined and coordinated efforts of GPs and pharmacists can be very useful in ensuring the provision of optimum care to patients.

Chapter Eight

8 Overall discussion

This chapter aims to summarise all the key findings of this research and discusses their implications for practice and for future research.

The overall aim of this thesis was to determine whether studying patients' knowledge about their medicines and pharmacists' systems for interacting with patients may lead to identifying ways in which pharmacists' role can be improved in patient care. On reflection, this thesis has only partly achieved its overall aim. This thesis has attempted to define the role of pharmacists in terms of what pharmacists could and should be doing during their interactions with patients. This research recognises that although pharmacists may have a role in improving patient care, this role cannot be simply put in place without due consideration of other healthcare professionals in particular the GPs.

The first objective of this thesis was to explore the challenges to effective medicines reconciliation in patients attending the ED and by gaining an insight into their medications and their experience of ADRs. The audit based study demonstrated the challenges in capturing information from high risk patients about their medications. It also suggested the possible association of the lack of knowledge about medications with increased incidence of self-reported ADRs. However, in the absence of an independent verification of the information provided by patients through an adapted questionnaire, this study partially addressed the first objective of the thesis.

It attempted to address the second objective of the thesis by analysing the spectrum of medicines considered in the NMS, points for actions identified and outcomes within 30 days of these interventions. This study demonstrated the contributions of community pharmacists within NMS in detecting both a high rate of ADRs attributed to new medications and incorrect use of medications by patients. However, the very low response rate from pharmacists in this study coupled with the absence of a control group suggested that this study did not fully meet the second objective of the thesis.

Following the NMS evaluation, this research then aimed to address the third objective of this thesis by evaluating the current understanding of community pharmacists about ADRs, level of ADR reporting and barriers to ADR reporting. This study identified lack of time and uncertainty about the seriousness of ADR as some of the barriers to ADR reporting by pharmacists. Furthermore, it also suggested an association between the awareness about what to report and how to report with the reporting of ADRs. However, the use of an adapted questionnaire indicated that the findings of this study should be viewed with caution. This study therefore failed to effectively address the third objective of the thesis.

Using hypertension as a test of concept, this research aimed to address the fourth objective of this thesis by conducting a systematic review and meta-analysis of the impact of pharmacist interventions on blood pressure control. This review reported that compared with usual blood pressure management, active interventions by pharmacists working in community pharmacies were associated with important improvement in control of hypertension. However, this review did not determine the particular pharmacist intervention responsible for the reductions in systolic and diastolic blood pressure. Furthermore, the

limitations of this review such as the exclusion of unindexed and unpublished research coupled with the variable quality of the included studies suggested that this study only partially addressed the fourth objective of the thesis.

Finally, this research used the findings of the initial studies to address to the fifth and final objective of this thesis. The findings of this study reported that provision of written information to patients was associated with a significant improvement in their knowledge about hypertension and its treatment. Furthermore, both systolic and diastolic blood pressure was reduced, however the mean difference between the intervention and control group was not statistically significant. The participants of this study gave a positive response about the involvement of pharmacists in the management of long-term medical conditions such as hypertension. Despite the failure in the recruitment of the desired number of participants, this study achieved the final objective of the thesis by introducing a new pharmacist supported method for a more effective use of medicines by patients with hypertension.

This chapter discusses the key findings of this research and their implications in practice. It also highlights the limitations and strengths of this research and the goals of future research.

8.1 Key findings

This research reported challenges in obtaining an accurate and up to date medication history from patients attending the ED of a hospital. Similar finding have been reported in a previous study that highlighted the discrepancies in medication lists produced at the hospital (Caglar et al., 2011). These findings suggest major scope to improve the system of

medicines reconciliation. Patients are not known to be accurate historians of their medication history (Rodehaver & Fearing, 2005) and may not have the desired literacy to maintain or communicate a list of their current medicines (Kutner, Greenberg & Jin, 2006). Healthcare professionals should therefore assume the responsibility of maintaining the accurate and updated medication history of patients (Barnsteiner, 2008).

There should be an integrated record of a patient's medication history available for both primary and secondary care healthcare professionals including pharmacists (Royal Pharmaceutical Society Scotland & Royal College of General Practitioners Scotland, 2012). Pharmacists are a common source of OTC medications which were found to be very common among the study population of medicine reconciliation audit (chapter 3). The current GP lists do not provide information on what may potentially be important unrecognized OTC use of these drugs. As reported from the findings of pharmacists audit on ADR reporting (chapter 5), a number of ADRs reported by pharmacists were potentially associated with OTC medicines. Patient's records should therefore include an updated and comprehensive list of all medications prescribed by GPs and dispensed by pharmacists. This list should record sales of the OTC medicines as well as medicines prescribed through pharmacy services such as the minor ailment scheme.

The integration of primary and secondary patient records might also help in raising awareness and recognition of pharmacy services among other important stakeholders including GPs. As reported in the findings of the NMS service evaluation (chapter 4) and the RCT (chapter 7), none of the patients who received advice from pharmacists were referred by the GPs. These findings appear to suggest that either GPs are not aware of pharmacy services or they do not recognise the potential of pharmacy services in patient

care. The findings of the systematic review (chapter 6) and the RCT (chapter 7) have important implications for the prevention of primary and secondary care. For example, evidence from a meta-analysis involving one million adults in USA reported that every 1 mm Hg reduction in systolic blood pressure could prevent about 10,000 deaths related to coronary heart disease in the US each year (Lewington et al., 2002). Another analysis suggests that a sustained 2 mm Hg reduction in diastolic blood pressure would be expected to result in a 6% reduction in the risk of coronary heart disease and 15% decrease in stroke (Cook et al., 1995). The evidence presented in this review provides an important message to health professionals and policy makers about the potential for community pharmacists to ease the burden for physicians in primary and secondary care of chronic disease management.

Both systematic review and RCT reported that provision of education to patients about hypertension and its treatment was associated with a significant improvement in the knowledge and management of hypertension. Patient education plays an important role in facilitating patients' acceptance of their condition and helps them to embrace the behavioural changes required for an adequate adherence with their treatment (Grueninger, 1995). In an attempt to raise public awareness about hypertension, the National Heart, Lung and Blood institute in the United States coordinated the establishment of a National High Blood Pressure Education Programme (NHBPEP). The aim of NHBPEP is to reduce the morbidity and mortality associated with high blood pressure through patient education (National high blood pressure education programme United States, 1993). In Canada, collaboration between Blood Pressure Canada, the Heart and Stroke Foundation of Canada, the Canadian Hypertension Society and the Canadian Hypertension Education Program has been formed to improve public and patient awareness and knowledge of hypertension

(Campbell, Petrella & Kaczorowski, 2006). Similarly, in the UK, the British Hypertension Society (BHS) provides educational resources on hypertension and cardiovascular disease (British Hypertension Society, 2014). Healthcare professionals should therefore use these educational resources to disseminate information about hypertension to their patients with the aim of reducing the burden of this disease in the UK.

The findings of the NMS evaluation demonstrated the important contributions of community pharmacists within the NMS including both detecting a high rate of ADRs attributed to new medications and incorrect use of medications as common, addressable problems. These findings have important implications in the management of long-term medical conditions that are imposing an increasing burden on health care systems. For example, in England alone, around 15 million people are estimated to have a long-term condition requiring medication and other therapies (Department of Health, 2010). Furthermore, adherence to medicines for long-term conditions is poor and evidence suggests 30 to 50% of medicines prescribed for long-term conditions are not taken as intended (WHO, 2003). With the service currently commissioned until 31st March, 2015, the findings of this study provide support for the continuation of this service beyond the current commissioned date.

The NMS provides a specific prompt to report ADRs using the national Yellow Card reporting system (PSNC, 2013). However, none of the pharmacists reported submitting a Yellow Card in this study. This finding is in contrast to the findings of previous evidence which suggested that following the introduction of the NMS in October 2011, over 700 new Yellow Cards were reported by pharmacists over a 12 month period (Jadeja & McCreedy, 2012). Time pressure on pharmacists to deliver a number of pharmacy services may also

explain the under reporting of ADRs by pharmacists in this study. These findings may complement the findings of chapter 5 that reported lack of time and uncertainty about the seriousness of ADR as major barriers to spontaneous reporting. Organisations employing pharmacists should provide adequate resources to support the delivery of quality care to patients. These findings also underscore the importance of providing explicit education to improve the understanding and awareness of ADRs among pharmacists at both undergraduate and professional level. Research has shown that training is associated with an increased likelihood to ADR reporting (Green et al., 2001; Sweis & Wong, 2000).

Participants of this study appeared to recognise pharmacists as an important part of the healthcare team. Participants showed trust and confidence in pharmacists' advice and did not seem to have any hesitation in approaching pharmacists in future for health-related issues. This study was seen by some as an opportunity to enhance patient pharmacist relationships. These findings are in contrast to the findings of previous research that did not share the same public opinion about pharmacists (Hassell et al., 1998; Hammond et al., 2004). Pharmacists must therefore continue to remain actively engaged with patients to ensure the delivery of better care to patients.

8.2 Implications for research

The White paper titled "A vision for pharmacy in the new NHS" outlines the government's vision for community pharmacy (Department of Health, 2003). It calls for using pharmacy strengths towards the delivery of a safer, effective and more patient-centred care (Department of Health, 2003). The introduction of the new community pharmacist contract in 2005 is the first step that attempts to move pharmacists towards a more clinically oriented role. The evidence presented in this thesis aligns with the government's vision for

community pharmacy. However, it recognises the challenges in the complex transition of pharmacists' role from their traditional responsibility of dispensing towards the delivery of a greater personalised patient care.

The findings of this research suggest that pharmacists would need to engage more effectively with the patients about their medicines and their adverse effects. Pharmacists may need to undertake specific training to improve their communication skills. The UK Department of Health's version of patient-centred care emphasises on improving those things that really matter to patients (Department of Health 2010). Pharmacists would therefore be required to learn how to anticipate patient concerns and address those concerns to the satisfaction of patients. There can be many approaches that can help pharmacists to effectively engage with patients. One of these approaches includes the provision of short but focussed information leaflets to patients. As demonstrated from the findings of the final study, written and focussed information was better retained by patients. Pharmacists could also consider the use of digital means such as CDs (Compact Disks) or DVDs (Digital Video Disks) for providing information to patients.

The NMS is another approach that gives pharmacists the opportunity to engage with patients about their chronic medicines. However, as reported in the findings of the service evaluation, pharmacists do not always adhere to the specifications of this service. These include the limited provision of lifestyle advice to patients and under-reporting of suspected ADRs to the MHRA. Deviation from these important service specifications of NMS may reflect the organisational pressure within community pharmacies to deliver a certain number of NMS consultations. Commercial organisations should provide adequate

resources to pharmacists to improve the quality of these services and to allow pharmacists to promptly report suspected ADRs.

The findings of this research highlight the important potential of pharmacists in the management of long-term medical conditions such as hypertension. However, any such extension in the activities of pharmacists would very much rely on the support from other stakeholders in particular the GPs. The lack of patient referrals by GPs to pharmacists reported in this research seem to suggest that either GPs are not aware of pharmacists' potential or they do not recognise the importance of community pharmacy services. These findings suggest the need for formal links to ensure coherence of treatment approaches and evidence-based integration of pharmacy-delivered services with other health services (Blenkinsopp & Bond 2007).

Against the backdrop of these developments in pharmacy practice, community pharmacists would need to bring a cultural and behavioural change to adjust them to this new role. This adjustment would imply that pharmacists would be required to broaden their current contributions towards patient care and thus would need to assume greater responsibility than they currently do (Department of Health, 2003).

8.3 Limitations

This research has some important limitations. No power calculations were undertaken prior to the commencement of studies described in chapter 3, 4 and 5. However, it may be argued that these studies were all descriptive studies with no hypothesis testing. In these studies, participants were recruited on their willingness and ability to participate.

Therefore, the sample size used in these studies was based on available resources.

Another important limitation of this research was the poor quality of questionnaires used in chapter 3, 4 and 5. Future questionnaire based studies involving patients must ensure that the questionnaire has been designed in consultation with the healthcare professionals as well as patients and their carers. The content and language of the questionnaire should be clear, unambiguous, understandable and in simple English. The questionnaire should be piloted on the appropriate population to demonstrate that they are effective for the purpose of revalidation before implementation (General Medical Council, 2012). The pilot work should aim to determine the time taken to complete the questionnaire and to identify any additional support required for participants with literacy or learning difficulties.

Furthermore, the questionnaire must include a preamble detailing information and instructions about how to complete the questionnaire, the purpose of the questionnaire, whether the questionnaire responses will be anonymous or confidential and the choice provided to respondents who choose not to complete the questionnaire (General Medical Council, 2012).

In chapter 3, there was no independent verification of the information provided by patients on their medications and history of ADRs. Thus a patient could have listed their medications incorrectly or could have stated incorrectly that they knew the reason of taking their medications. The service evaluation described in chapter 4 did not have a control group. Therefore it cannot be assumed that any positive impact on patient healthcare outcomes reported in this study was associated with the pharmacists' interventions. Another limitation of this study was the lack of objective clinical data on patient outcomes. However, it should be borne in mind that recording clinical data for patients is outside the scope of NMS and is a weakness of the NMS in its current format.

Although the systematic review was rigorous and systematic, it did not include unindexed and unpublished research. Studies included in this review were of variable quality, with low to moderate heterogeneity for systolic blood pressure. The findings of this review should therefore be interpreted with caution. Finally, the RCT that assessed the impact of pharmacists-led education on blood pressure failed to recruit the desired number of participants as per the planned sample size calculations.

8.4 Strengths

This research has several strengths. It is rigorous, innovative, comprehensive, thorough, transparent and appropriate. It was informed by prior evidence, patient focus groups, pharmacists' advisory group, GPs and other stakeholders. It has used a series of studies involving various methodological approaches including audits, service evaluation, systematic review and meta-analysis as well as an RCT. These studies have helped to address the aims and objectives of this research. Additionally, these studies have helped in acquiring the skills and tools necessary for an all-round researcher. The limitations of the initial studies have contributed in the development of a well-designed RCT (chapter 7). Similarly, the methods used to assess the quality of studies included in the systematic review and meta-analysis can serve as a benchmark for future studies. This research for example can extend the scope of pharmacist interventions on the management of other long-term medical conditions.

The studies presented in this thesis have led to several research presentations at national and international meetings and an important publication in the British Journal of Clinical Pharmacology. These findings not only support the existing pharmacy-based evidence but also add new knowledge to the current evidence base.

8.5 Goals of future research

The findings of this research have set some clear goals for future research. An appropriately designed RCT would be required to compare the groups of patients who receive education and support on the recognition of ADRs with those who don't receive such support. This will help to further supplement the findings of chapters 3, 4 and 7 and will be helpful in reducing the severity of preventable ADRs. Furthermore, this research should supplement the subjective data collected from patients with self-reported ADRs (chapter 3) by data obtained from their primary and secondary care patients' records. This verification would be helpful in exploring the differences between patients' recollections of their ADR-related events and the perspectives of healthcare professionals about these events.

Qualitative work involving pharmacists' focus groups would be needed to gather pharmacists' views and perspectives about pharmacists' existing communication and consultation skills. Such qualitative research should ideally employ semi-structured interviews with pharmacists. This will help to understand pharmacists' future learning requirements and will help to identify any gaps in the knowledge. These focus groups should also cover the topic of effective time management while delivering pharmacy services in the busy commercial settings.

An observational study involving a cohort of patients who receive NMS consultations from pharmacists should be conducted to address the limitations of this service. As reported in chapter 4, the current NMS does not record any outcome data for patients receiving NMS interventions. Pharmacists are therefore unaware if their interventions have been acted upon by patients or GPs. This research will be helpful to validate the effectiveness of NMS in

practice. It will also help to create more awareness and understanding of pharmacy led services among both patients and GPs.

A prospective observational study would be needed to assess the impact of ADR specific education on the level of ADR reporting by pharmacists. This will help to identify further training and support required by pharmacists in improving their current level of ADR reporting. Finally the important contributions of pharmacists in the management of high blood pressure (chapter 6, 7) should be extended to the management of other long-term medical conditions including obesity, diabetes and ischaemic heart disease. This research may again take the form of RCT involving intervention and control groups.

Future research should also aim to explore collaborative partnerships between GPs and pharmacists and assess the impact of their combined efforts on patient healthcare outcome. This shall help in the development of better understanding between GPs and pharmacists that would ultimately be very useful in the delivery of effective healthcare to patients.

8.6 Conclusions

The overall aim of this thesis was to determine whether studying patients' knowledge about their medicines and pharmacists' systems for interacting with patients may lead to identifying ways in which pharmacists' role can be improved in patient care. On reflection, this has only been achieved partly as part of this process. The evidence presented in this research suggests that pharmacists may have the potential to play a bigger role in patient care. However, this research suggests that pharmacists would also require the support and recognition from other stakeholders in particular the GPs. Both pharmacists and GPs would

need to develop a clear understanding and recognition of each other's role and should work together towards the common goal of providing optimum care to patients.

Patients appear to be willing to seek pharmacists' advice on health-related issues. However, pharmacists would need to actively engage with patients. Pharmacists would need to identify their specific learning needs to help them deliver a more patient-centred care.

Future research is required to develop better co-ordination between GPs and pharmacists with the aim of delivering more effective healthcare to patients.

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Appendices

A) Audit project proposal form

Clinical Audit & Effectiveness Department
 5th Floor, East Wing
 University Hospital
 Tel: 02476 968262
 Fax: 02476 968261



CLINICAL AUDIT & EFFECTIVENESS DEPARTMENT (CAED) CLINICAL AUDIT PROJECT PROPOSAL FORM

Office Use Only:
 R&M Non-R&M

Surgery Number:

1. PROJECT LEAD

This should detail the staff member who is to be the main contact for this audit project.

Title (eg Mr, Mrs, Ms, Professor, Dr, etc)	PROFESSOR
Last Name	SINGER
Forename(s)	DONALD
Grade	
Specialty (in which audit project will be undertaken)	Clinical Pharmacology & Therapeutics
Bleep	
Telephone	02476968665/6097
Email Address	donald.singer@uhcw.nhs.uk

When will you be leaving your current post (i.e. your next rotation date):

Please note if your project is not completed or handed over to another member of staff before you leave the Trust, the project will be abandoned.

2. JOINT WORKING

Please provide details of staff members involved in this project.

1. Name	DR MAGDY SAKR
Grade	Consultant, Honorary Associate Professor
Division/Specialty	EMERGENCY MEDICINE
Role within the project - e.g. data collection, advisory	CO-SUPERVISOR
2. Name	DR BUDDHAVARAPU MURTHY
Grade	CLINICAL DIRECTOR - CRITICAL CARE
Division/Specialty	CRITICAL CARE
Role within the project - e.g. data collection, advisory	
3. Name	
Grade	
Division/Specialty	
Role within the project - e.g. data collection, advisory	

Please continue on a further sheet if more than 3 staff members are involved in this project.

3. PROJECT TITLE

This should be no more than two sentences and should clearly and concisely state the focus of the proposed project.

RECONCILIATION OF MEDICINES IN PATIENTS ADMITTED FOR URGENT MEDICAL CARE

4. BACKGROUND / RATIONALE

Briefly describe the reasons for undertaking this piece of work e.g. evidence of a serious quality problem in the topic area, subject of recent clinical incidents, evidence of variations in practice etc.

ADRs are a major health problem. They are a significant cause of hospital admissions and increase the cost of disease management in patient (BMJ 2004, Pirmohammed). According to this study, two thirds of these ADRs are serious and can be prevented. Therefore there is a need clearly for more studies that can provide ways to improve identification and prevention of ADRs.

5. OBJECTIVE/S

What will the audit tell us? Please specify what you hope to demonstrate by undertaking this particular piece of work e.g. (1) to ensure patients are assessed appropriately (e.g. as per guidelines)

Objective 1: HIGHLIGHT THE INCIDENCE OF ADRs

Objective 2: IMPROVE RECOGNITION OF ADRs

Objective 3: IDENTIFY WAYS TO PREVENT ADRs

Objective 4: HIGHLIGHT THE ROLE OF PHARMACISTS IN REDUCTION/PREVENTION OF ADRs

6. METHODOLOGY

How will the audit be undertaken? Please consider the points below:

Who/what is your population? e.g. all patients with heart failure, all patients with IDDM?
PATIENTS ADMITTED TO EMERGENCY DEPTT AND ICU

How will you identify the patients you are including in the audit?

Prospectively Departmental database Clinical Coding Clinic lists Other, please state below:

What time period will your sample be chosen from?

Date Start: 08-01-2012

Date Finish: 08-01-2014

Approximately how many cases will there be during this time period?

How many of these cases will you review? E.g. all, randomised sample etc

1,600 as winter and summer. 1 week samples in 2012 and 2013.

Where will you collect the relevant data from?

Health records Database, please state below: Directly from patients (questionnaire) Other, please state below:

7. STANDARDS / GUIDELINES

What are you measuring practice against? Please specify the guidance you will be using below e.g. UHCW NHS Trust Guideline for Antibiotic Prophylaxis (2007) or NICE guideline for Falls Prevention (2006). The guidance should have been implemented in the specialty for at least 3 months prior to audit.

Title and author of guidelines/standard document *

1) NICE CG 76 MEDICINE ADHERENCE 2) BMJ 2004, PIRMOHAMMED

*A copy of all standards/guidelines and a completed table "Standards for Clinical Audit" must be attached to the registration form on submission (see last page).

8. REPORTING MECHANISMS/FEEDBACK

Who needs to know about this audit project? In what meetings do you plan to present/feedback this project?

Proposed date of presentation: SPRING 2012, 2013, 2014 Meeting: GRAND ROUND

Please state all of the specialties this audit could impact upon either whilst it is being undertaken or when action is required on completion of the project:

1. ALL MEDICAL SPECIALITIES
2. _____
3. _____

9. TIME SCALE

What is your deadline for this project? i.e. the date when the final report can be submitted to the Clinical Audit Department, to include all discussion following presentation and an action plan.

Anticipated completion date:
FIRST REPORT SEPT 2012, FINAL REPORT APRIL 2014

10. DATA PROTECTION

This information is required to ensure that (1) data collection is undertaken in line with Caldicott principles (2) data storage and the sharing of information meets the requirements of the Data Protection Act.

NB. Completion of this section of the form is mandatory.

SECTION 1

From the list below please select fields/data items that you are collecting as part of your audit project (tick all applicable)

Please note that the majority of audit projects require collection of PID only, you should only collect data which is essential in order to meet the objectives of the project.

a) Identification data (please)		c) Family circumstances	
PID	<input checked="" type="checkbox"/>	Current marriage or partnership	<input type="checkbox"/>
Name	<input type="checkbox"/>	Marital history	<input type="checkbox"/>
Address	<input type="checkbox"/>	Details of other family, household members	<input type="checkbox"/>
DOB	<input checked="" type="checkbox"/>	Other social contacts	<input type="checkbox"/>
Postcode	<input type="checkbox"/>		
GP	<input type="checkbox"/>	d) Social circumstances	
Ethnicity	<input checked="" type="checkbox"/>	Accommodation or housing	<input type="checkbox"/>
Any other personal identifiers	<input type="checkbox"/>	Property, professions	<input type="checkbox"/>
Identifiers issued by public bodies	<input type="checkbox"/>	Immigration status	<input type="checkbox"/>
		Travel, movement details	<input type="checkbox"/>
		Leisure activities, interests	<input type="checkbox"/>
b) Personal characteristics		Lifestyle	<input checked="" type="checkbox"/>
Personal details	<input type="checkbox"/>	Complaint, incident, accident details	<input type="checkbox"/>
Physical description	<input checked="" type="checkbox"/>		
Habits	<input type="checkbox"/>	e) Other	
Personality, character	<input type="checkbox"/>	Consultant in charge of care	<input type="checkbox"/>
		Other staff names	<input type="checkbox"/>

SECTION 2

To be signed by ALL people who are undertaking the project:

Please indicate by signing below that you agree/will comply with the following statements:

- The computer that is to be used for analysis / storage of patient data belongs to UHCW NHS Trust
- Data will not be stored on a portable / laptop computer
- Data will not be stored on any removable device (eg Floppy disk, CD, Data stick)
- Data will only be stored on the Network drive at UHCW (eg your H drive)
- I will surrender all copies of proformas/surveys/questionnaires used in this project to the Clinical Audit & Effectiveness Department on completion of the audit
- I will surrender all copies of databases/datasets/electronic information used in this project to the Clinical Audit & Effectiveness Department on completion of the audit
- I will not, at any time, remove any audit data pertaining to University Hospitals Coventry and Warwickshire staff, patients or practices off Trust premises without the prior permission of the Clinical Audit & Effectiveness Manager.
- I will not publish or present any of the data I collect as a result of this audit outside University Hospitals Coventry and Warwickshire without the prior permission of the Clinical Audit & Effectiveness Manager
- I understand that this form will be retained in the Clinical Audit & Effectiveness Department for future reference.

Project Lead:

1. Name:	PROF. DONALD SINGER	Position held:	Prof. of Clinical Pharm. & Therapeutics
Signature*:	<i>Donald R S Singer</i>	Date:	19/12/2011
Please tick the box to confirm that you agree to each of the statements above:			<input type="checkbox"/> Agree <input checked="" type="checkbox"/> I AGREE

*By signing this form I agree to ensure that this project is completed and a report is given to the Clinical Audit & Effectiveness Department.

Project Team:

1. Name:	DR. MAGDY SAKR	Position held:	EMERGENCY CONSULTANT
Signature:	M Sakr	Date:	4/1/2012
Please tick the box to confirm that you agree to each of the statements above:			<input checked="" type="checkbox"/> Agree <input type="checkbox"/> I AGREE
2. Name:	EJAZ CHEEMA	Position held:	PHD RESEARCH STUDENT
Signature:	<i>Ejaz Cheema</i>	Date:	12/12/2011
Please tick the box to confirm that you agree to each of the statements above:			<input type="checkbox"/> Agree <input checked="" type="checkbox"/> I AGREE
3. Name:	DR BUDDHAVARAPU MURTHY	POSITION	CLINICAL DIRECTOR - CRITICAL CARE
Signature:		Date:	
Please tick the box to confirm that you agree to each of the statements above:			<input type="checkbox"/> Agree

Consultant Lead (e.g. Educational Supervisor or Clinical Audit Lead):

****The Consultant Lead must sign below before the project will be considered for registration****

By signing this form I confirm that I give my full support to this project. I will monitor the progress of the project where possible and lead the development and implementation of an action plan on completion of the project in order to obtain improvements in the quality of care provided.

1. Name:	PROF. DONALD SINGER	Position held:	Prof of Clinical Pharm. & Therapeutics
Signature:	<i>Donald R S Singer</i>	Date:	19/12/2011
Please tick the box to confirm that you agree to each of the statements above:			<input type="checkbox"/> Agree <input checked="" type="checkbox"/> I AGREE

Please return completed registration forms to:
Clinical Audit & Effectiveness Department, 5th Floor, East Wing, University Hospital,
Clifford Bridge Road, Walsgrave, Coventry, CV2 2DX

Tel: 02476968262 Fax: 02476968261

Developed and produced by the Clinical Audit & Effectiveness Department, University Hospitals Coventry & Warwickshire NHS Trust

CLINICAL AUDIT & EFFECTIVENESS DEPARTMENT

STANDARDS FOR CLINICAL AUDIT

Please complete the following table to show the standards you are auditing against (taken from the guideline) and any exceptions to these. Assistance with this is available via surgery appointments – please dial 26282 for an appointment.

Standard (what aspect of the guideline will you measure adherence to)	Criteria (where will you find this information)	Exceptions (when) would this standard not apply
<i>E.g. 1. All patients to receive Clexane 40mg for 10 days post-op</i>	<i>E.g. 1. Documented evidence on Drug Kardex</i>	<i>E.g. 1. Documented contraindication</i>
<i>E.g. 2. Patients must give their informed consent to surgery</i>	<i>E.g. 2. Documented evidence on the Trusts consent Form</i>	<i>E.g. 2. Documented evidence patient is unable to give informed consent.</i>
NICE CG 76 MEDICINE ADHERENCE	Print out of current prescription	No access to objective source of medicines used.
BMJ 2004, PIRMOHAMMED	Documented evidence from patient's GP prescribing record.	

B) Approval of clinical audit project

From: "Woodhouse Hanna (RKB) Quality & Effectiveness Facilitator"
<Hanna.Woodhouse@uhcw.nhs.uk>
Subject: Clinical Audit Project 1421: Reconciliations of Medicines in Patients Admitted for Urgen Medical Care
Date: 26 January 2012 09:34:38 GMT
To: "Singer Donald (RKB) Professor Of Pharmacology" <Donald.Singer@uhcw.nhs.uk>

Dear Professor Singer,

Many thanks for meeting with me earlier this week to discuss your clinical audit.

The audit has now been registered as number 1421; please find attached the Trust Clinical Audi Report and presentation templates.

I have enquired within the department about whether there are any equivalent members of staff within the PCT and we don't believe that there are.

I would be grateful if you could keep me updated on the progress of the audit.

Kind regards,
Hanna Woodhouse
Quality and Effectiveness Facilitator

University Hospitals Coventry and Warwickshire NHS Trust
Clifford Bridge Road
Coventry
CV2 2DX

Tel: 02476 968 276 Ext: 28276
Email: hanna.woodhouse@uhcw.nhs.uk

C) Questionnaire on medicines reconciliation

The purpose of this questionnaire is to understand what you know about your medicines and their side effects. Please complete all the questions below. For some questions you may be asked to give added written details. It is important that you complete all the questions. If you have any questions about the questionnaire please ask a member of the research team.

*Confidential history for medicines.
It should take around five to ten minutes. To be completed by patient or a next-of-kin.
If you run out of room, use the 'additional information' box overleaf*

PATIENT NAME AND DATE OF BIRTH:

GENDER: Male Female

WEIGHT: stones/pounds _____ or kg _____

HEIGHT: feet/inches _____ or metres _____

1) Please list what medications you are currently taking:

Medicine 1: _____

State any expected or advised side-effects:

What condition is it for:

Advice from whom?
GP Hospital doctor Pharmacist Nurse

Medicine 2: _____

State any expected or advised side-effects:

What condition is it for:

Advice from whom?
GP Hospital doctor Pharmacist Nurse

Medicine 3: _____

State any expected or advised side-effects:

What condition is it for:

Advice from whom?
GP Hospital doctor Pharmacist Nurse

Medicine 4: _____

State any expected or advised side-effects:

What condition is it for:

Advice from whom?
GP Hospital doctor Pharmacist Nurse

Medicine 5: _____

State any expected or advised side-effects:

What condition is it for:

Advice from whom?
GP Hospital doctor Pharmacist Nurse

Medicine 6: _____

State any expected or advised side-effects:

What condition is it for:

Advice from whom?
GP Hospital doctor Pharmacist Nurse

Medicine 7: _____

State any expected or advised side-effects:

What condition is it for:

Advice from whom?
GP Hospital doctor Pharmacist Nurse

2) Do you take any herbal remedies or other supplements (including St. John's Wort)

YES NO → [If NO, go to Question 3]

Name	How often?	Duration	Source

3) Do you take any of the following medicines that you have bought and have not been prescribed by a doctor?

Name	How often?	Duration	Source
Ibuprofen			
Aspirin			
Paracetamol			
Statin			
Voltarol			

PTO

4) Have you ever had a side effect or unwanted effect from a medication?

YES NO → [if NO, go to Question 5]

Medicine name	Dose	How long?	Side-effect	Source

5) Have you ever smoked? YES NO

If NO, go to Question 6

What age did you start smoking? _____

Do you still smoke? _____

If NO, what age did you stop smoking? _____

Type of smoking?

Cigarettes YES NO
 Cigars YES NO
 Pipe YES NO

Average number of packets of 20 cigarettes /week since you started smoking: _____

Current packets of 20 cigarettes/week: _____

Other tobacco:

Cigars per week: _____
 Tobacco oz. per week: _____

6) Do you drink alcohol? YES NO

If NO, go to Question 7

Type(s) of alcoholic beverage:

Red wine White wine
 Beer Cider
 Lager Bitter
 Spirit Liqueur
 Sherry Port

Other(s): _____

Please list for a typical week how much of each type of alcohol (ml or units):

7) Foods – how often do you eat:

	YES	NO	Per month?
Broccoli	<input type="checkbox"/>	<input type="checkbox"/>	_____
Spinach	<input type="checkbox"/>	<input type="checkbox"/>	_____
Asparagus	<input type="checkbox"/>	<input type="checkbox"/>	_____
Grapefruit	<input type="checkbox"/>	<input type="checkbox"/>	_____

	YES	NO	Glasses/day
Grapefruit juice	<input type="checkbox"/>	<input type="checkbox"/>	_____

8) What do you think your current main problem is?

Have you had this before?

9) Do you or have you had any of the following medical conditions:

High blood pressure	<input type="checkbox"/>	Stroke	<input type="checkbox"/>
High cholesterol	<input type="checkbox"/>	Asthma	<input type="checkbox"/>
Angina/heart attack	<input type="checkbox"/>	Cancer	<input type="checkbox"/>
Kidney disease	<input type="checkbox"/>	Liver disease	<input type="checkbox"/>
Epilepsy	<input type="checkbox"/>	Migraine	<input type="checkbox"/>

Deep vein thrombosis	<input type="checkbox"/>
Pulmonary embolism	<input type="checkbox"/>
Hormonal disorder (e.g. thyroid)	<input type="checkbox"/>
Diabetes mellitus (type I or II)	<input type="checkbox"/>

10) Any non-drug allergies? If YES, to what and what happened?

11) Are there any medical problems in your family? If YES, what medical problem and which family member?

Are you aware of any drug or other allergies in your family? If YES, to what and what happened?

12) Did you find it easy to complete the questionnaire?

YES NO

If NO, what do you think would improve the questionnaire?

Additional information:

D) Clarification on ethical approval

From: Singer, Donald [mailto:D.R.Singer@warwick.ac.uk] **Sent:** 13 December 2011 19:30
To: Jones Ceri (RKB) Head of R&D
Cc: Mills, Penny; cheemaejaz@hotmail.com; Magdy Sakr
Subject: Re: Data Collection

Dear Ceri

The intention was that this phase of Ejaz studies should be a clinical audit within the expected national framework for Medicines Reconciliation, expected from all NHS Trusts since ~Dec 2007 and ADR reporting, with the 2004 Liverpool audit as template.

This off course needs to comply with Clinical Audit rules for which there is a draft in preparation.

That should help in providing background. I'm happy to discuss this with the named ethics contact below.

Best wishes

Donald

Donald RJ Singer

Professor of Clinical Pharmacology & Therapeutics

02476 966097

From: "Prinsloo Deirdre (RKB) PA to Professor Singer"
<Deirdre.Prinsloo@uhcw.nhs.uk>
Subject: Data Collection - Email from Ceri Jones 14.12.11
Date: 27 March 2013 10:34:51 GMT
To: "Prinsloo Deirdre (RKB) PA to Professor Singer" <Deirdre.Prinsloo@uhcw.nhs.uk>

From: Ceri.Jones@uhcw.nhs.uk
To: D.R.Singer@warwick.ac.uk
CC: P.M.Mills@warwick.ac.uk; cheemaejaz@hotmail.com;
Magdy.Sakr@warwick.ac.uk
Date: Wed, 14 Dec 2011 08:33:12 +0000
Subject: RE: Data Collection

Hi Donald –

Thanks for the clarification! As such, he will need to run it past audit, we (and ethics) do not not need to be involved!

Best wishes,

Ceri

Ceri Jones
Head of Research & Development
Research & Development Department
First Floor Rotunda (opposite Cardiac)
University Hospitals Coventry & Warwickshire NHS Trust
University Hospital
Clifford Bridge Road
Coventry
CV2 2DX

02476 966196 (extn. 26196)
07766 780642
ceri.jones@uhcw.nhs.uk

E) Questionnaire on the service evaluation of NMS

The purpose of this questionnaire is to evaluate the NMS. Please complete this questionnaire with data from one single completed NMS patient for all four categories of NMS if possible (Please use separate sheets for each category).

Tick your type of pharmacy

1) Large multiple (>50 pharmacies) 2) Small multiple (< 50 pharmacies) 3)

Single pharmacy

Intervention

Gender: Male Female

Age of the patient _____

Name of medicine _____

Dose _____

Any problems? Yes No

If yes please specify:

Is medicine working? Yes No

Any side effects? Yes No

If yes please specify:

Any missed doses?

Yes

No

Advice provided by the pharmacist

Yes

No

If yes, briefly specify the advice e.g. counselling on how to use, side effects, how it works,
reason for its use

Referral to GP?

Yes No

If yes, please specify reason for referral

Healthy living advice provided (Tick the following which applies):

Diet & nutrition Smoking Alcohol Weight management Exercise

Follow up

Is the patient still taking the medicine?

Yes No

If no reason for stopping:

Any problems raised during intervention resolved?

Yes No

If no, please specify

Any other concerns?

Yes No

If yes, please specify

F) Guidance on obtaining ethical approval

Audit, Service Evaluation or Research?

Comparison:

	In research studies:	In audits:	In service evaluations:
Intent:	Primary aim is to derive new knowledge; discovering the right thing to do	To produce information to inform delivery of best care against a current standard	To define or judge current care without reference to a current standard
Treatment:	May test a new practice, therapy/drug which may lead to change in clinical practice	Only use treatment (intervention) arising from evidence-based clinical judgement & necessity	Only use treatment (intervention) arising from evidence-based clinical judgement & necessity
Allocation:	Only research allocates treatment by a protocol	No allocation: health professional & patient have chosen intervention before audit	No allocation: health professional & patient have chosen intervention before service evaluation
Randomisation:	Only used in research	N/A	N/A

Out of Remit / No Review

- Secondary analysis of published or other freely available data
- Clinical Audits
- Service Evaluation and Development Projects within the NHS
- Minor amendments to previously approved projects
- Undergraduate projects with primarily an educational purpose, including projects for the purpose of research methods training, provided they do not:
 - Seek to recruit participants beyond the students' social circle, family, peers, or colleagues
 - Receive external funding
 - Include any form of deception or coercion
 - Involve the administration of any substance
 - Involve participants being subjected to any invasive procedure

G) Audit Questionnaire on the reporting of ADRs by community pharmacists

The purpose of this questionnaire is to evaluate your understanding and level of ADR reporting to the MHRA. Please complete all the questions below. For some questions you may be required to tick more than one box. For any questions, please ask a member of the research team.

Audit on adverse drug reactions –Clinical Pharmacology and Therapeutics, University of Warwick

Male: Female: Age: _____

Pharmacy manager

Store based pharmacist

Relief pharmacist

Other: _____

No. of years qualified as a pharmacist:

<1 1-5 6-10 11-20 >20

How many ADRs have you reported?

None 1 2-5 6-10 >10

When did you last report an ADR:

In the past week > 1 week ago

> 1 month ago > 3 months ago

> 6 months ago > 1 year ago

Describe the most recent ADR you have reported:

Details of reaction _____

Name of suspected drug(s) _____

Gender _____ Age (approx) _____

Did you consider the reaction serious?

Yes No

If yes, describe its severity _____

What ADR would you consider reporting in adults?
(Tick all that apply)

Serious reaction from a POM

Serious reaction from a herbal drug

Serious reaction from an OTC medicine

Serious reaction from a drug with black triangle

Mild reaction from a drug with black triangle

Mild reaction from an existing drug

Other: _____

What ADR would you consider reporting in children?
(Tick all that apply)

Serious reaction from a POM

Serious reaction from a herbal drug

Serious reaction from an OTC medicine

Serious reaction from a drug with black triangle

Mild reaction from a drug with black triangle

Mild reaction from an existing drug

Other: _____

What reporting systems are you aware of?

Paper

Online

Other: _____

Which factors prevented you reporting an ADR? (Tick all that apply)

Not clear what an ADR is

Not clear how to report

Did not consider your duty to report it

Lack of time

Lack of access to internet

Considered reaction to be too well known

Did not consider reaction serious enough to report

Not sure which drug(s) responsible

Did not have complete information for making the report

Other: _____

Confident which ADRs to report: Yes No

Confident how to report: Yes No

What training and support would be helpful?

Information about what to report

Information about how to report

IT access to reporting system

Other: _____

Other comments:

If happy to be contacted about future questions on medicines, please provide contact details:

Name: _____

Email address: _____

H) Search strategies used in the major electronic databases

Embase:

- 1) Hypertension.mp.
- 2) Blood pressure.mp. Or exp blood pressure/
- 3) 1 or 2
- 4) Exp pharmaceutical care/ or exp pharmacy/ or exp pharmacist/
- 5) pharmac*.mp.
- 6) 4 or 5
- 7) Exp community/ or communit*.mp.
- 8) Intervention*.mp.
- 9) 3 and 6 and 7 and 8
- 10) limit 9 to (English language and randomized controlled trial and (adult <18 to 64 years> or aged <65+ years>))

Medline Ovid:

- 1) Hypertension.mp.
- 2) Exp Hypertension/ or hypertension.mp.
- 3) Blood pressure.mp. or exp Blood Pressure/
- 4) 1 or 2 or 3
- 5) 1 or 3
- 6) Exp Community Pharmacy Services/ or community pharmac*.mp.
- 7) Intervention*.mp.
- 8) 5 and 6 and 7
- 9) 4 and 6 and 7

10) limit 8 to (English language and ("all adult (19 plus years)" or "adolescent (13 to 18 years)") and randomized controlled trial)

Web of Science:

1) Pharmacist OR pharmacists OR pharmaceutical AND

2) Hypertension

The Cochrane Library:

1) Pharmacists OR pharmacist interventions

Biosis Citation Index:

Pharmacist OR pharmacists OR pharmaceutical AND

1) Hypertension AND

RCTs

CINAHL:

Pharmacists or pharmacist or pharmaceutical AND

1) Hypertension AND

2) Systematic review AND

3) RCTs

Biomed Central:

1) Pharmacists interventions ALL WORDS

2) Essential Hypertension AND

3) Randomised controlled trial AND

PsycINFO:

Pharmacists and hypertension

Additional limits: Population (Female, Male)

Age group: (Adulthood (18 Yrs & Older), Aged (65 Yrs & Older), Middle Age (40-64 Yrs), Thirties (30-39 Yrs), Very Old (85 Yrs & Older), Young Adulthood (18-29 Yrs)

Language: English

I) Characteristics of included studies

Source; Year of publication and country usual care	Study setting	Study Design duration	Sample size, (Intervention usual care)	Participants; Mean age (intervention/ usual care)	Key components of Pharmacist intervention	Intervention providers	Compari son	Outcomes assessed
Ali et al, 2012 United Kingdom	Community pharmacies	RCT 12 months	46 (23/23)	Adults with diabetes, (66.4/66.8)	Provision of pharmaceutical care package including diabetes monitoring and education programme	Community pharmacists	Usual care	BP, HbA1C LDL-C, Total cholesterol BMI
Amariles et al, 2012 Spain	Community pharmacies	RCT 08 months	714 (356/358)	Adults with CVD or CVD risk factors such as high BP, Diabetes, High cholesterol, heart failure MI, (63.0/62.6)	Provision of Dader method of pharmaceutical care: patient education about CVD medications, identification of drug-related problems, advice on lifestyle changes, suggestions to physicians on treatment	Community pharmacists	Usual care	BP, HbA1C LDL-C, Total cholesterol

Blenkinsopp et al, 2000 United Kingdom	Community pharmacies	RCT 06 months	180 (101/79)	Adults with high blood pressure, (NR)	Patient education, monitoring of pharmacological treatment including identification of drug related problems, advice to improve medication adherence	Community pharmacists	Usual care	BP, Medication adherence, Patient satisfaction with Pharmacy services
Doucette et al, 2009 United States	Community pharmacies	RCT 12 months	78 (36/42)	Adults with type 2 diabetes, other conditions not reported (58.7/61.2)	Patient education including specific advice on food, physical activity, identification of drug related problems, recommendations to physicians	Community pharmacists	Usual care	BP, HbA1C LDL-C, Total cholesterol
Fornos et al, 2006 Spain	Community pharmacies	RCT 13 months	112 (56/56)	Adults with type 2 diabetes and high blood pressure, other conditions not reported (62.4/64.9)	Patient education including advice on improving medication adherence, identification of drug related problems, advice on diet advice on alcohol, physical activity, recommendations to physicians	Community pharmacists	Usual care	BP, HbA1C LDL-C, Total cholesterol BMI

Garcao et al 2002 Portugal	Community pharmacies	RCT 06 months	82 (41/41)	Adults with essential hypertension (66.5/63.4)	Patient education including advice on alcohol, physical activity, identification of drug related problems, recommendations to physicians	Community pharmacists	Usual care	BP
Krass et al, 2007 Australia	Community pharmacies	RCT 06 months	289 (149/140)	Adults with type 2 diabetes (62.0/62.0)	Patient education including advice on diet, physical activity, weight management, smoking cessation , drug related problems, recommendations to physicians	Community pharmacists	Usual care	BP, HbA1C LDL-C, triglycerides Total cholesterol BMI
Mckenney et al, 1973 United States	Community pharmacies	RCT 06 months	50 (25/25)	Adults with essential hypertension (62.0/58.0)	Patient education including advice on diet, physical activity, identification of drug related problems, recommendations to physicians	Community pharmacists	Usual care	BP, Medication adherence
Mckenney et al, 1978	Community pharmacies	RCT 04 months	136 (70/66)	Adults with essential	Patient education including advice on diet, advice on	Community pharmacists	Usual care	BP, Medication adherence

United States				hypertension (62.0/58.0)	medication adherence, identification of drug related problems, recommendations to physicians			
Mclean et al, 2008 Canada	Community pharmacies	RCT 06 months	227 (115/112)	Adults with diabetes, hypertension (66.2/63.7)	Patient education including advice on lifestyle, blood pressure monitoring, recommendations to physicians	Community pharmacists	Usual care	BP
Park et al, 1996 United States	Community pharmacies	RCT 04 months	53 (27/26)	Adults with hypertension (57.3/63.0)	Patient education including advice on lifestyle	Community pharmacists	Usual care	BP, Medication adherence
Planas et al, 2009 United States	Community pharmacies	RCT 09 months	52 (32/20)	Adults with diabetes, hypertension (64.2/65.2)	Patient education including advice on diet, advice on exercise, monitoring of pharmacological treatment, recommendations to prescribers	Community pharmacists	Usual care	BP, Medication adherence
Santschi et al, 2011	Community pharmacies	RCT 06 months	89 (48/41)	Adults with chronic kidney	Lifestyle advice including advice on diet, advice on weight	Community pharmacists	Usual care	BP, LDL, total triglycerides

Canada				disease (71.9/73.3)	management			BMI
Sookaneknun et al, 2004 Thailand	Community pharmacies	RCT 06 months	235 (118/117)	Adults with hypertension (63.2/63.2)	Patient education including advice on diet, physical activity, identification of drug related problems, recommendations to physicians	Community pharmacists	Usual care	BP, Medication adherence
Svarstad et al, 2013 United States	Community pharmacies	RCT 12 months	576 (276/300)	Adults with hypertension (53.2/52.8)	Team education, adherence monitoring programme	Community pharmacists	Usual care	BP, Medication refill adherence rates
Zillich et al, 2013 United States	Community pharmacies	RCT 03 months	125 (64/61)	Adults with hypertension, diabetes, kidney disease, cerebrovascular disease, high cholesterol	Patient education on high blood pressure including advice about disease management, medication adherence, lifestyle advice, technique on using a home systolic blood pressure monitoring device and	Community pharmacists	Usual care	BP, Medication adherence

				(64.0/66.6)	recommendations to prescribers			
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NR= not reported, BMI= body mass index, LDL= low density lipids, CVD= cardiovascular disease, RCT= randomised controlled trial,

MI= myocardial infarction

J) Study protocol

1. Study Overview

1.1 Research Question

Primary research questions:

1. Whether information about blood pressure and current medicines provided to patients verbally and in writing by community pharmacists will be better retained than in current New Medicine Service?
2. If provision of structured written information will be associated with improved blood pressure control in patients with hypertension?

Secondary research questions:

1. Impact on the above outcomes in terms of participants' characteristics including age, gender, and ethnic background?
2. Impact of this study on the frequency and severity of Adverse Drug Reactions in active Vs control arm participants?

2.2 Background

Hypertension or high blood pressure is a major health problem and accounts for an estimated 7.5 million deaths per year worldwide. [1] However, its control is unsatisfactory. One of the reasons for such a high prevalence of this disease includes poor compliance to treatment by patients. It is believed that approximately 30 % of newly diagnosed hypertensive patients stop taking their blood pressure medication by six months [2] and 50 % stop by 12 months.

Evidence from two systematic reviews suggests that community pharmacist-led interventions can improve the management of hypertension. [3, 4] Interventions by

pharmacists included education about the disease and medicines to treat it, as well as identifying medication errors and adverse drug reactions. However, it is not clear which particular intervention by pharmacists contributed to improved blood pressure control [3, 4].

The government is keen to encourage community pharmacists to play an active role in participation of services that can improve patient adherence to their medications. The New Medicines Service (NMS) and targeted Medicines Use Reviews (MUR) are such recently established services which fund community pharmacists to review and explain medicine use to patients, with hypertension a common condition for which advice is given within these schemes.

The NMS is designed to provide early support to patients to maximise the benefits of medications they have been prescribed. [5] Targeted MURs aim to improve patient's knowledge, understanding and use of their medications. Unlike NMS, where patients have been newly prescribed a medication, patients receiving a targeted MUR are likely to have been taking their medicine for a longer period of time.

Within NMS and MUR schemes, advice is verbal and unstructured, with no specific written information provided on drugs or the disease being treated. Provision of written medical advice to patients about a disease and its treatment is better retained by patients than verbal information. [6]

3. Methods

3.1 Aim

To determine whether structured information provided to patients verbally and in writing by community pharmacists about blood pressure and current medicine(s) within NMS and MUR reviews will be retained and will be associated with improved blood pressure control.

3.2 Objectives

- 1) To conduct a six months randomised controlled trial.
- 2) To assess whether information about blood pressure and current medicines provided to patients verbally and in writing by community pharmacists will be better retained than in current New Medicine Service.
- 3) To assess the impact of this structured written information on blood pressure in patients with hypertension.
- 4) To assess the impact of blood pressure in terms of participants' characteristics including age, gender, and ethnic background.
- 5) To assess the impact of this study on the frequency and severity of Adverse Drug Reactions in active and control arm participants.

3.3 Pharmacy recruitment

This study will involve participation of patients attending community pharmacies in Coventry and Birmingham area. Participating pharmacies will act as Participant Identification Centres in this study i.e. they will identify potential research participants who will be invited to participate in the study. The advertising posters will be displayed in the participating pharmacies, at the local GP surgeries, local press and at the outpatient clinic at University Hospital Coventry and Warwickshire. The local press and radio stations will also be used to recruit participants. Five community pharmacies offering NHS services including New Medicines Service (NMS) and targeted Medicines Use Review have been invited in writing to take part in the study. These pharmacies are located in Coventry and in Birmingham area. All these pharmacies have agreed to take part in this study.

3.4 Participant recruitment

All participants (18 or over, male or female and have been started on any blood pressure medication) visiting one of the five participating pharmacies will be informed of the study by the dispensary staff. Participants interested in the study will be handed a pack containing a letter introducing the study, a consent form, participant information sheet and a questionnaire.

3.5 Study design

The study is a randomised controlled trial and will have two arms (an active arm where participants would receive verbal NMS intervention as well as written information on blood pressure and its treatment; and a control arm where

participants would receive verbal NMS intervention only). Interested participants would be randomly allocated to the active and control arms. Random allocation of participants to study arms would help in reducing researcher bias. Both groups would then be followed up to see the difference in retention of information and on blood pressure.

Participants in both arms would attend 4 visits in total over a period of 6 months (at week 0, 2, 4 and 26). They would be required to complete a questionnaire during all four visits. It is estimated that the questionnaire would take approximately 5 minutes to complete and overall study involvement would be around 15 minutes. In addition to this, blood pressure of all participants would also be recorded during all four visits.

3.6 Study development

Feedback would be obtained from patients and pharmacists on the development of both proposed questionnaire and for written educational information on blood pressure and on treatments. To obtain feedback, we shall use a combination of focus groups and semi-structured individual interviews separately for pharmacists. To obtain patient advice, we shall use two approaches: 1) feedback from the Expert Hypertension Patient Advisory Group established by Professor Singer; and 2) individual feedback from outpatients who are being started on a new treatment while attending the Blood Pressure Clinic at UHCW NHS Trust and patients attending community pharmacies. These patients will also be helpful in supporting development of patient information sheets for the Local Ethics Committee application for the study.

3.7 Consent

Consent to participate and for data collected during the study will be sought from all participants by a self-completion consent form.

3.8 Interventions

The pharmacists will deliver a total of four patient interactions (at week 0, week 2, 4 and at 26 weeks). Figure 1 shows an overview of the study.

All participants

On each of the four visits, patients will complete a validated questionnaire about hypertension, the benefits of treating it and the risks of any treatment(s) currently used by each patient. This questionnaire will include validated questions from my previous audit (reference no: 1421) on patient knowledge about medicines. All patients will also receive the standard verbal advice expected within NMS and MUR assessments, including advice on healthy lifestyle based on the guidance produced by NICE (CG127, 2011).[7] All patients will also receive routine dispensing and general advice.

Blood pressure

All patients will have blood pressure measurements recorded during all four visits (weeks 0, 2, 4 and 26). Blood pressure will be recorded electronically using a BHS approved Omron blood pressure monitor. Three readings of systolic and diastolic pressure will be recorded for both intervention and control groups in accordance with the guidelines produced by British Hypertension Society, 2011 (5 readings for patients with arrhythmias).[8]

Active arm

Week 0:

- i) Consent will be obtained.
- ii) Blood pressure will be measured as above.
- iii) Participants will complete a validated questionnaire on blood pressure and its treatment.
- iv) Participants will then be provided with validated verbal and written information on hypertension and its treatment, including information about class (es) of anti-hypertensive medication(s) used by each patient, and their common side-effects. The written material will be based on validated patient information leaflets from the British Heart Foundation and the Blood Pressure Association.
- v) Prescription issued and date arranged for NMS intervention in two weeks.

Week 2:

- i) Blood pressure will be measured as above.
- ii) All participants complete the questionnaire again.
- iii) Standard NMS verbal intervention. Participants will also be provided with a reminder supported by written advice, based on the results of their questionnaire and further copies of the previously provided written material will be provided to them.

Week 4:

- i) Blood pressure will be measured as above.
- ii) All participants complete the questionnaire again.

- iii) Standard NMS verbal intervention follow-up.
- iv) Participants will be provided with a reminder of advice, based on the results of their questionnaire and further copies of the previously provided written material will be provided to them.

Week 26:

- i) Blood pressure will be measured as above.
- ii) All participants complete the questionnaire again.

Control arm

Week 0:

- i) Consent will be obtained.
- ii) Blood pressure will be measured as above.
- iii) Participants will complete a validated questionnaire on blood pressure and its treatment.
- iv) Participants will then be provided with validated verbal and written information on New Medicine Service.
- v) Prescription issued and date arranged for NMS intervention in 2 weeks.

Week 2:

- i) Blood pressure will be measured as above.
- ii) All participants complete the questionnaire again.
- iii) Standard NMS verbal intervention. Participants will then be provided with further copies of written information on New Medicine Service.

Week 4:

- i) Blood pressure will be measured as above.
- ii) All participants complete the questionnaire again.

- iii) Standard NMS verbal intervention follow-up. Participants will then be provided with further copies of written information on New Medicine Service.

Week 26:

- i) Blood pressure will be measured as above.
- ii) All participants complete the questionnaire again.

3.9) Patient satisfaction survey:

All participants taking part in the study will be asked to complete a short survey at the end of their final visit to the pharmacy. The purpose of this survey is to find out what participants thought about the study and the involvement of community pharmacists in blood pressure control.

3.10) Sample size calculation:

Plan for a 20% drop-out rate during the study. Based on our previous audit (reference number 1421), we expect that 55% of patients will be aware of adverse risks of their medicines. A sample size of 54 per group will provide a power of 80% at the 5% level in a 2-tailed test to detect an increase from 55% to 80% of participants aware of adverse risks of their medicines. This will result in the need to recruit 66 per group, based on planning for a 20% drop-out rate during the study.

A sample size of 54 per group completing the study will also provide a power of 80% at the 5% level in a 2-tailed test to detect a reduction of a size equal to 0.6 standard deviations in systolic and diastolic pressure as assessed by an Omron BHS approved device (www.bhsoc.org). The SD will depend on the results for the study

sample e.g. for a typical SD between visits of 7mmHg in systolic pressure in patients with hypertension, this would represent an 80% power to detect a 4mmHg reduction in systolic pressure.

3.11. Data Management and Analysis

Questionnaire responses will be coded and entered into SPSS (PASW Statistics) as completed questionnaires are received. Data will be single-entered. Data will be analysed both as intention to treat as well as per protocol. Data will be checked for missing and invalid responses prior to commencing analysis. Summary descriptive statistics will be generated from the questionnaire data using SPSS. Summary data will be presented in tables and figures, as appropriate. Third party interim analysis will be performed after 50% of our initial projected sample size have completed the six month study interventions.

4. Research Approval

NHS Research Ethics Committee and relevant NHS R&D approvals will be sought prior to recruiting practices.

5. Risks and Ethical Issues

There are no risks to researchers through involvement in this study. The questionnaire topics are not anticipated to be sensitive, embarrassing, threatening or distressing to the respondents. It is extremely unlikely that criminal or other disclosures requiring action will occur during the study. The questionnaire is only available in English and it is not possible to provide copies in other languages. Patients will be informed that they may seek the assistance of friends, carers or

relatives in completing the questionnaire. Professional telephone interpretation will also be available for participants who request this.

6. Sponsorship and Indemnity

Sponsorship for the study will be provided by the University of Warwick, The University has in force a Public and Products Liability Policy which provides cover for claims of “negligent harm” and the activities here are included within that coverage subject to the terms, conditions and exceptions of the policy.

7. Information Governance

All information will be stored in accordance with the Data Protection Act (1998) and University of Warwick policies. Completed questionnaires and consent forms will only be accessed by members of the research team only and will be stored in a lockable filing cabinet in Warwick Medical School. Participants who request to receive a report at the end of the study will have been asked to provide their name and contact details on the consent form. Data from the completed questionnaires will be stored in an anonymous form in a secure password-protected network location that will only be accessible by the research team. A unique code number will be used to identify each participant. Participant personal details from consent forms will not be stored with other data collected during the study. All study documentation and data will be retained for two and a half years after completion of the study and then destroyed.

8. Research Management

The research team will accept overall responsibility for the study and its conduct.

The research group comprising all investigators will meet monthly during the study period, and will be responsible for ensuring that the study is conducted in accordance with research governance frameworks and the study protocol.

8.1 Timescales

Anticipated start date: December 2013 (following REC and R&D approvals)

Duration: 18 months finish date 04.06.2015 (excluding REC and R&D approvals)

9. Dissemination

The findings of this research, and any implications or suggestions for future practice and patient care, will be publicised in the NHS and wider healthcare community via a number of routes:

1. A summary report, in lay language, will be sent to patients that requested this.
2. A paper will be submitted for publication in a relevant peer-reviewed journal.
3. The research findings will be submitted for presentation at an appropriate conference.

Research questions arising from the findings will be explored in terms of further research funding applications.

10. Compensation to patients:

Patients participating in the study will be offered GB 10 pounds per visit. Patients already recruited shall be paid retrospectively.

References

1. Mathers C, Stevens G, Mascarenhas M. Global health risks: mortality and burden of disease attributable to selected major risks. Geneva, Switzerland: World Health Organization; 2009.
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3. Machado M, Bajcar J, Guzzo GC, et al. Sensitivity of patient outcomes to pharmacist interventions. Part two: Systematic review and meta-analysis in hypertension management. *Ann Pharmacother*. 2007; 41 (11): 1770-1781.
4. Morgado MP, Morgado SR, Mendes LC, et al. Pharmacist interventions to enhance blood pressure control and adherence to antihypertensive therapy: Review and meta-analysis. *Am J Health Syst Pharm*. 2011; 68 (3): 241-253.
5. NHS New Medicine Service. PSNC. 2011. psnc.org.uk. (accessed online 03.06.2013)
6. Victoria G. Written advice: compliance and recall. *J R Coll Gen Pract*. 1981; 31(230): 553–556.
7. Hypertension. NICE. <http://www.nice.org.uk/CG127> (accessed online 20.08.2013).
8. Blood pressure management. British Hypertension society. http://www.bhsoc.org/files/8413/4390/7770/BP_Measurement_Poster_-_Electronic.pdf (accessed online 20.08.2013)

K) Questionnaire on blood pressure and its treatment

For questions 1, 2, 18, 19, 20, 22 and 23 please give as many answers as relevant to you. For all other questions, please tick one box. For some questions you may be asked to give added written details. It is important that you complete all the questions. If you have any questions about the questionnaire please ask a member of the research team.

NAME _____

DATE OF BIRTH _____

Surgery details:

Name of GP _____

Address _____

GENDER: Male Female

WEIGHT: stones/pounds __or kg_____

HEIGHT: feet/inches __or metres____

How would describe yourself as (e.g.

White/Caucasian, Asian, Black African)?_____

*1) Do you or have you had any of the following medical conditions?

Diabetes YES NO

Stroke YES NO

Heart failure YES NO

Kidney disease YES NO

Heart attack/angina YES NO

*2) What does the term hypertension mean?

High blood pressure

High level stress/tension

High blood sugar

Over activity

Don't know

3) Did your doctor or nurse tell you what your blood pressure reading should be?

YES NO don't know

4) What should be your top blood pressure number?

Under 140 140 over140
don't know

5) What should be your bottom blood pressure number?

Under 90 90 over 90
don't know

6) Do you think that hypertension is a life-long disease?

YES NO don't know

7) Can hypertension cause heart attacks?

YES NO don't know

8) Can hypertension cause strokes?

YES NO don't know

9) Can hypertension cause kidney problems?

YES NO don't know

10) Can hypertension cause asthma?

YES NO don't know

11) Can hypertension cause cancer?
YES NO don't know

12) Does losing weight help reduce high blood pressure?
YES NO don't know

13) Does cutting salt help reduce high blood pressure?
YES NO don't know

14) Does cutting alcohol help reduce high blood pressure?
YES NO don't know

15) How often should people with high blood pressure take their medicine?
Daily Few times a week
When needed don't know

16) Should people with high blood pressure take their medicine long term?
YES NO don't know

17) What is the name and dose of your new blood pressure medicine?
Name _____ or don't know
Dose _____ or don't know

*18) Do you know how your new blood pressure medicine works?
YES NO
If yes, please explain _____

*19) What side effects (if any) have you been warned to look out for, when taking your new blood pressure medicine? _____
None told

*20) What is your source of advice on side effects?

GP Hospital doctor Pharmacist
 Nurse Package leaflet Friend
 other

21) Have you suffered any side effects from your new blood pressure medicine?
YES NO
If yes, please explain _____

*22) If you have answered yes to the above question, please explain how the side effect affected you?
Mild or slightly uncomfortable
Uncomfortable or irritating but able to carry on with daily activities
had short term effect that was bad enough to affect daily activities
Bad enough to be admitted to hospital
 not serious

*23) Do you take any other blood pressure medication (s)?
If yes, please list them below
1) _____
2) _____

24) Do you know if new medicine service offered through your pharmacy (chemist) is a free NHS service?
YES NO don't know

25) Did you find it easy to complete the questionnaire?
YES NO

Thank you for taking the time to complete this questionnaire

For Office use only:
Name of new blood pressure medicine _____ Dose _____

Patient allocated to study arm A B

Issues raised YES NO

L) Participant consent form

CONSENT FORM

Title of Study: Impact of community pharmacists on blood pressure control

The purpose of this sheet is to ensure that you have read and understood the information about the study and are fully aware of your rights should you decide to take part. If you would like to take part, please indicate this by reading the following questions and **writing your initials in the boxes**, where appropriate. Then **sign and add today's date** in the space provided.

Your name, and address if you give this, will not be recorded with the questionnaire responses.

1. I confirm that I have read and understand the information sheet, **Local Version** dated **10th August 2013**, for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.

2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reasons and without my medical care or legal rights being affected.

3. I understand that data collected during the study may be looked at by individuals from the University of Warwick, from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to the relevant sections of my medical notes and data collected during the study.

4. I agree that my GP may be informed of my participation in the study.

5. I agree to take part in the above study.

Your name

Date

Signature

M) Participant information sheet



Title of Study: Impact of community pharmacists on blood pressure control

Invitation to take part in our research study

You are being invited to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. You are welcome to discuss it with others if you wish. Please contact us if anything is not clear or if you would like more information.

What is the purpose of this study?

Community pharmacists can help patients to control their high blood pressure. Community pharmacists have two schemes where they can help to review and explain medicine use to patients. These are: The New Medicines Service (NMS) and targeted Medicines Use Reviews (MURs). Within these schemes, advice is verbal and written information is not provided to patients. The aim of our study is to assess the impact of pharmacist-based intervention, supported by written information and find out whether blood pressure control is different depending on how information is provided to you.

Why have I been invited?

You are being invited to take part in this study because you have been started on a new medicine to treat high blood pressure and have agreed to have advice on this

from your pharmacist under the New Medicine Service. Your participation will help us to understand ways to improve control of blood pressure.

Do I have to take part?

No. It is up to you to decide whether or not to take part.

What will happen to me if I take part?

Taking part will involve being seen at time convenient to you. You will be randomly assigned to two different groups. You will receive advice from your pharmacist on four occasions over six months. On each visit you will be asked to complete a short questionnaire and your blood pressure will also be measured.

What will I have to do?

You should continue to take your prescribed medicine(s) or over the counter drugs. It is important that you attend all the scheduled visits during the study.

What are the possible benefits of taking part?

You will have your blood pressure checked for you 4 times over the 6 months study. You will also receive written education from the pharmacist. The information from this study will help us to identify new ways to help patients with their medicines and improve their blood pressure control.

Are there any disadvantages to taking part in this research?

We do not anticipate any disadvantages.

Will my involvement in this study be kept confidential?

All information collected from this study will be kept strictly confidential. Your GP may be informed of your participation in the study. Our procedures for handling, processing, storage and destruction of the data comply with the Data Protection Act 1998. This means that information about your contact details will be kept in a secure location separate from the other information you provide. The responses to the questionnaires are anonymous and will be stored in an anonymous form using a code number for reference. You will not be asked to provide your name or anything that could identify you on the questionnaire. All information you provide on the questionnaire will be stored in a computer file at Warwick Medical School at the University of Warwick and at the University Hospital in Coventry and Warwickshire. These computers are password protected. Only members of the research team will have access to the completed questionnaires.

What if there is a problem?

If you have a concern about any aspect of this study, please speak to the research team, using the contact details on the front of this sheet, in the first instance. If you remain unhappy and wish to complain formally, you can do this through the University of Warwick Complaints Procedure. Details can be obtained from the University Deputy Registrar, Ms Jo Horsburgh, University of Warwick, Coventry CV4 8UW (tel: 024 7652 2785)

Study publication

We intend to publish the results of this study in scientific journals and at scientific conferences. These papers will be made available on a research website maintained

by Professor Singer. Individual volunteer details will not be identified in reports to be published.

Who is organising and funding the research?

We aim to apply for research funding from Medical Research Charities.

Who is providing sponsorship and professional indemnity for the study?

Sponsorship and professional indemnity are provided by the Research Support Services (RSS), The University of Warwick, CV4 7AL.

Who has reviewed the study?

This study has been reviewed by a panel of community pharmacists based in the West Midlands area and by the Local Research Ethics Committee. It has also been reviewed by Expert Hypertension Patient Advisory Group established by Professor Singer at University Hospital Coventry and Warwickshire (UHCW) and by patients attending blood pressure clinics at the UHCW and community pharmacies in the West Midlands area.

Further information and contact details

If you have any questions, or would like more information about the study, please contact us using the contact details on the front of this sheet.

N) Participant invitation letter

Title of Study: Impact of community pharmacists on blood pressure control

Dear Patient

We are writing to ask for your help in a research study in which your pharmacy is taking part, and which is being run by Warwick Medical School.

The purpose of this study is to understand the effect of pharmacist-based intervention, supported by written information and find out whether blood pressure control is different depending on how information is provided to you. Your participation will help us to understand ways to improve control of blood pressure.

You are being invited to take part because you have been started on a new medicine to treat high blood pressure and have agreed to have advice on this from your pharmacist under the New Medicine Service. Taking part will involve being seen at time convenient to you. You will be randomly assigned to two different groups. You will receive advice from your pharmacist on four occasions over six months. On each visit you will be asked to complete a short questionnaire and your blood pressure will also be measured.

If you do choose to take part, any information that you provide will be treated in complete confidence, and we will not use any details that could identify you in any reports that we write about the study.

Before you make up your mind please read the enclosed information sheet which provides details about the study, and what is involved. If you decide that you would like to take part please sign the consent form inside the envelope provided. You can either hand the envelope back to the dispensary team, who will forward it on to the research team on your behalf, or you can bring it with you on the first day of your appointment with the research pharmacist.

If you have any questions, or would like more information about the study, please contact the lead researcher, Prof Donald Singer, using the contact details at the top of this letter. Alternatively, you can speak to a member of the local research team using the contact details above.

Thank you for taking the time to read this letter and the information sheet, and for considering taking part. Your help is greatly appreciated.

Yours faithfully

O) Information sheet for intervention group

Information on blood pressure and ACE inhibitors

What is blood pressure?

When your heart beats, it pumps blood round your body to give it the energy and oxygen it needs. As the blood moves, it pushes against the sides of the blood vessels. The strength of this pushing is your blood pressure.

What do the numbers mean?

Every blood pressure reading consists of two numbers or levels. They are shown with the higher number given first e.g. 140/90. The first (or higher) number is your systolic blood pressure. It is the highest level your blood pressure reaches when your heart beats. The second (or lower) number is your diastolic blood pressure. It is the lowest level your blood pressure reaches as your heart relaxes between beats.

What is high blood pressure / hypertension?

High blood pressure – or hypertension – means that your blood pressure is usually higher than the recommended level. You probably have high blood pressure (hypertension) if your blood pressure readings are consistently 140 over 90, or higher. If you are diabetic or have heart or kidney disease, a blood pressure above 130 over 80, would be high.

How dangerous is hypertension to your health?

High blood pressure is a risk factor for future cardiovascular disease such as heart attack or stroke.

Can changing lifestyle help to lower your blood pressure?

Yes. For example 1) Lose weight if you are overweight: Blood pressure can fall by up to 2.5/1.5 mm Hg for each excess kilogram which is lost. 2) Do physical activity as much as possible. The more the better. 3) Lower salt intake as much as possible. Use herbs and spices rather than salt to flavour food. 4) Consume less alcohol. A maximum of one large glass of wine or one pint of mild beer per day.

How does your blood pressure medicine work?

Your blood pressure medicine belongs to a group of drugs called ACE inhibitors. These medicines help to control hormones that affect blood pressure. This allows arteries to relax and helps to reduce blood pressure.

How do I take my medicine?

Your doctor will advise you how to take your medication. In some people the first dose can cause a drop in blood pressure immediately. Stay indoors for about four hours, as occasionally some people feel dizzy. If you do feel dizzy, sit or lie down and it will usually ease off.

What is the usual length of treatment?

Most people with hypertension need to take medication for life. Ask your doctor for further advice.

What are the possible side-effects?

A common side-effect associated with an ACE inhibitor is dizziness. If you become dizzy you should report this to your doctor. Around one in ten people who take an ACE inhibitor have a persistent dry cough. **Note:** Please see the leaflet that comes with this medicine for a full list of possible side-effects and cautions.

Information on blood pressure and direct renin inhibitors

What is blood pressure?

When your heart beats, it pumps blood round your body to give it the energy and oxygen it needs. As the blood moves, it pushes against the sides of the blood vessels. The strength of this pushing is your blood pressure.

What do the numbers mean?

Every blood pressure reading consists of two numbers or levels. They are shown with the higher number given first e.g. 140/90. The first (or higher) number is your systolic blood pressure. It is the highest level your blood pressure reaches when your heart beats. The second (or lower) number is your diastolic blood pressure. It is the lowest level your blood pressure reaches as your heart relaxes between beats.

What is high blood pressure / hypertension?

High blood pressure – **or hypertension** – means that your blood pressure is usually higher than the recommended level. You probably have high blood pressure (hypertension) if your blood pressure readings are consistently 140 over 90, or higher. If you are diabetic or have heart or kidney disease, a blood pressure above 130 over 80, would be high.

How dangerous is hypertension to your health?

High blood pressure is a risk factor for future cardiovascular disease such as heart attack or stroke.

Can changing lifestyle help to lower your blood pressure?

Yes. For example 1) Lose weight if you are overweight: Blood pressure can fall by up to 2.5/1.5 mm Hg for each excess kilogram which is lost. 2) Do physical activity as much as possible. The more the better. 3) Lower salt intake as much as possible. Use herbs and spices rather than salt to flavour food. 4) Consume less alcohol. A maximum of one large glass of wine or one pint of mild beer per day.

How does your blood pressure medicine work?

Your blood pressure medicine (aliskiren) belongs to a group of drugs called **direct rennin inhibitors**. These medicines work by blocking the effects of a chemical called renin. Renin is involved in producing a hormone called angiotensin, which raises your blood pressure. By blocking renin, aliskiren reduces the amount of angiotensin in your body.

How do I take my medicine?

Your doctor will advise you how to take your medication.

What is the usual length of treatment?

Most people with hypertension need to take medication for life. Ask your doctor for further advice.

What are the possible side-effects?

Aliskiren is a relatively new medicine and not much is yet known about its possible side-effects. The most common known side-effect of aliskiren is diarrhoea

Note: Please see the leaflet that comes with this medicine for a full list of possible side-effects and cautions.

Information on blood pressure and alpha blocker

What is blood pressure?

When your heart beats, it pumps blood round your body to give it the energy and oxygen it needs. As the blood moves, it pushes against the sides of the blood vessels. The strength of this pushing is your blood pressure.

What do the numbers mean?

Every blood pressure reading consists of two numbers or levels. They are shown with the higher number given first e.g. 140/90. The first (or higher) number is your systolic blood pressure. It is the highest level your blood pressure reaches when your heart beats. The second (or lower) number is your diastolic blood pressure. It is the lowest level your blood pressure reaches as your heart relaxes between beats.

What is high blood pressure / hypertension?

High blood pressure – or **hypertension** – means that your blood pressure is usually higher than the recommended level. You probably have high blood pressure (hypertension) if your blood pressure readings are consistently 140 over 90, or higher. If you are diabetic or have heart or kidney disease, a blood pressure above 130 over 80, would be high.

How dangerous is hypertension to your health?

High blood pressure is a risk factor for future cardiovascular disease such as heart attack or stroke.

Can changing lifestyle help to lower your blood pressure?

Yes. For example 1) Lose weight if you are overweight: Blood pressure can fall by up to 2.5/1.5 mm Hg for each excess kilogram which is lost. 2) Do physical activity as much as possible. The more the better. 3) Lower salt intake as much as possible. Use herbs and spices rather than salt to flavour food. 4) Consume less alcohol. A maximum of one large glass of wine or one pint of mild beer per day.

How does your blood pressure medicine work?

Your blood pressure medicine belongs to a group of drugs called **Alpha blockers**. They work by relaxing blood vessels. This allows blood and oxygen to circulate more freely around your body, lowering blood pressure and reducing strain on your heart.

How do I take my medicine?

Your doctor will advise you how to take your medication, including how often. In some people the first dose can cause a drop in blood pressure immediately. If you do feel dizzy, sit or lie down and it will usually ease off.

What is the usual length of treatment?

Most people with hypertension need to take medication for life. Ask your doctor for further advice.

What are the possible side-effects?

Although side-effects are uncommon, they occur in some people. Side-effects are more likely to occur in the first two weeks of treatment, and usually go away on their own. The most common side-effects are slight drowsiness, headaches and dizziness. **Note:** Please see the leaflet that comes with this medicine for a full list of possible side-effects and cautions.

Information on blood pressure and Angiotensin receptor blockers

What is blood pressure?

When your heart beats, it pumps blood round your body to give it the energy and oxygen it needs. As the blood moves, it pushes against the sides of the blood vessels. The strength of this pushing is your blood pressure.

What do the numbers mean?

Every blood pressure reading consists of two numbers or levels. They are shown with the higher number given first e.g. 140/90. The first (or higher) number is your systolic blood pressure. It is the highest level your blood pressure reaches when your heart beats. The second (or lower) number is your diastolic blood pressure. It is the lowest level your blood pressure reaches as your heart relaxes between beats.

What is high blood pressure / hypertension?

High blood pressure – **or hypertension** – means that your blood pressure is usually higher than the recommended level. You probably have high blood pressure (hypertension) if your blood pressure readings are consistently 140 over 90, or

higher. If you are diabetic or have heart or kidney disease, a blood pressure above 130 over 80, would be high.

How dangerous is hypertension to your health?

High blood pressure is a risk factor for future cardiovascular disease such as heart attack or stroke.

Can changing lifestyle help to lower your blood pressure?

Yes. For example 1) Lose weight if you are overweight: Blood pressure can fall by up to 2.5/1.5 mm Hg for each excess kilogram which is lost. 2) Do physical activity as much as possible. The more the better. 3) Lower salt intake as much as possible. Use herbs and spices rather than salt to flavour food. 4) Consume less alcohol. A maximum of one large glass of wine or one pint of mild beer per day.

How does your blood pressure medicine work?

Your blood pressure medicine belongs to a group of drugs called **Angiotensin receptor blockers**. Angiotensin receptor blockers work by blocking the effect of a hormone (angiotensin II) on the blood vessel walls. This helps to reduce blood pressure.

How do I take my medicine?

Your doctor will advise you how to take your medication, including how often. In some people the first dose can cause a drop in blood pressure immediately. Stay indoors for about four hours, as occasionally some people feel dizzy. If you do feel dizzy, sit or lie down and it will usually ease off.

What is the usual length of treatment?

Most people with hypertension need to take medication for life. Ask your doctor for further advice.

What are the possible side-effects?

A common side-effect associated with this medication is low blood pressure. It may make you feel dizzy. If you become very dizzy you should report it to your doctor. **Note:** Please see the leaflet that comes with this medicine for a full list of possible side-effects and cautions.

Information on blood pressure and beta blockers

What is blood pressure?

When your heart beats, it pumps blood round your body to give it the energy and oxygen it needs. As the blood moves, it pushes against the sides of the blood vessels. The strength of this pushing is your blood pressure.

What do the numbers mean?

Every blood pressure reading consists of two numbers or levels. They are shown with the higher number given first e.g. 140/90. The first (or higher) number is your systolic blood pressure. It is the highest level your blood pressure reaches when your heart beats. The second (or lower) number is your diastolic blood pressure. It is the lowest level your blood pressure reaches as your heart relaxes between beats.

What is high blood pressure / hypertension?

High blood pressure – or **hypertension**– means that your blood pressure is usually higher than the recommended level. You probably have high blood pressure (hypertension) if your blood pressure readings are consistently 140 over 90, or higher. If you are diabetic or have heart or kidney disease, a blood pressure above 130 over 80, would be high.

How dangerous is hypertension to your health?

High blood pressure is a risk factor for future cardiovascular disease such as heart attack or stroke.

Can changing lifestyle help to lower your blood pressure?

Yes. For example 1) Lose weight if you are overweight: Blood pressure can fall by up to 2.5/1.5 mm Hg for each excess kilogram which is lost. 2) Do physical activity as much as possible. The more the better. 3) Lower salt intake as much as possible. Use herbs and spices rather than salt to flavour food.4) Consume less alcohol. A maximum of one large glass of wine or one pint of mild beer per day.

How does your blood pressure medicine work?

Your blood pressure medicine belongs to a group of drugs called **Beta Blockers**. They work by blocking the transmission of certain nerve impulses which then reduce blood pressure.

How do I take my medicine?

Your doctor will advise you how to take your medication, including how often. In some people the first dose can cause a drop in blood pressure immediately. If you do feel dizzy, sit or lie down and it will usually ease off.

What is the usual length of treatment?

Most people with hypertension need to take medication for life. Ask your doctor for further advice.

What are the possible side-effects?

Sometimes the heart rate can go too slowly. This can make you dizzy or feel faint or make you short of breath. The tablet can also make you wheezy. If you have diabetes you need to be aware that beta-blockers may dull the warning signs of a low blood sugar level (hypoglycaemia - often called a hypo)

Information on blood pressure and calcium channel blockers

What is blood pressure?

When your heart beats, it pumps blood round your body to give it the energy and oxygen it needs. As the blood moves, it pushes against the sides of the blood vessels. The strength of this pushing is your blood pressure.

What do the numbers mean?

Every blood pressure reading consists of two numbers or levels. They are shown with the higher number given first e.g. 140/90. The first (or higher) number is your systolic blood pressure. It is the highest level your blood pressure reaches when

your heart beats. The second (or lower) number is your diastolic blood pressure. It is the lowest level your blood pressure reaches as your heart relaxes between beats.

What is high blood pressure / hypertension?

High blood pressure – or **hypertension** – means that your blood pressure is usually higher than the recommended level. You probably have high blood pressure (hypertension) if your blood pressure readings are consistently 140 over 90, or higher. If you are diabetic or have heart or kidney disease, a blood pressure above 130 over 80, would be high.

How dangerous is hypertension to your health?

High blood pressure is a risk factor for future cardiovascular disease such as heart attack or stroke.

Can changing lifestyle help to lower your blood pressure?

Yes. For example 1) Lose weight if you are overweight: Blood pressure can fall by up to 2.5/1.5 mm Hg for each excess kilogram which is lost. 2) Do physical activity as much as possible. The more the better. 3) Lower salt intake as much as possible. Use herbs and spices rather than salt to flavour food. 4) Consume less alcohol. A maximum of one large glass of wine or one pint of mild beer per day.

How does your blood pressure medicine work?

Your blood pressure medicine belongs to a group of drugs called **calcium channel blockers**. They work by reducing the amount of calcium that goes into heart

muscle cells. This causes these muscle cells to relax, which reduces the blood pressure.

How do I take my medicine?

Your doctor will advise you how to take your medication, including how often. In some people the first dose can cause a drop in blood pressure immediately. If you do feel dizzy, sit or lie down and it will usually ease off.

What is the usual length of treatment?

Most people with hypertension need to take medication for life. Ask your doctor for further advice.

What are the possible side-effects?

Because of their action to relax and widen blood vessels (arteries), some people develop flushing and headache. These tend to ease over a few days if you continue to take the tablets. Mild ankle swelling is also quite common. Constipation is also quite a common side-effect.

Information on blood pressure and centrally acting drug

What is blood pressure?

When your heart beats, it pumps blood round your body to give it the energy and oxygen it needs. As the blood moves, it pushes against the sides of the blood vessels. The strength of this pushing is your blood pressure.

What do the numbers mean?

Every blood pressure reading consists of two numbers or levels. They are shown with the higher number given first e.g. 140/90. The first (or higher) number is your systolic blood pressure. It is the highest level your blood pressure reaches when your heart beats. The second (or lower) number is your diastolic blood pressure. It is the lowest level your blood pressure reaches as your heart relaxes between beats.

What is high blood pressure / hypertension?

High blood pressure – or **hypertension** – means that your blood pressure is usually higher than the recommended level. You probably have high blood pressure (hypertension) if your blood pressure readings are consistently 140 over 90, or higher. If you are diabetic or have heart or kidney disease, a blood pressure above 130 over 80, would be high.

How dangerous is hypertension to your health?

High blood pressure is a risk factor for future cardiovascular disease such as heart attack or stroke.

Can changing lifestyle help to lower your blood pressure?

Yes. For example 1) Lose weight if you are overweight: Blood pressure can fall by up to 2.5/1.5 mm Hg for each excess kilogram which is lost. 2) Do physical activity as much as possible. The more the better. 3) Lower salt intake as much as possible. Use herbs and spices rather than salt to flavour food. 4) Consume less alcohol. A maximum of one large glass of wine or one pint of mild beer per day.

How does your blood pressure medicine work?

Your blood pressure medicine belongs to a group of drugs called **centrally acting drugs**. They work by reducing the resistance to flow of blood and hence reduce blood pressure.

How do I take my medicine?

Your doctor will advise you how to take your medication, including how often. In some people the first dose can cause a drop in blood pressure immediately. If you do feel dizzy, sit or lie down and it will usually ease off.

What is the usual length of treatment?

Most people with hypertension need to take medication for life. Ask your doctor for further advice.

What are the possible side-effects?

This medicine can cause sedation and drowsiness, dry mouth and sexual dysfunction in men.

Note: The above is not the full list of side-effects for these medicines. Please see the leaflet that comes with your particular brand for a full list of possible side-effects and cautions.

Information on blood pressure and diuretics

What is blood pressure?

When your heart beats, it pumps blood round your body to give it the energy and oxygen it needs. As the blood moves, it pushes against the sides of the blood vessels. The strength of this pushing is your blood pressure.

What do the numbers mean?

Every blood pressure reading consists of two numbers or levels. They are shown with the higher number given first e.g. 140/90. The first (or higher) number is your systolic blood pressure. It is the highest level your blood pressure reaches when your heart beats. The second (or lower) number is your diastolic blood pressure. It is the lowest level your blood pressure reaches as your heart relaxes between beats.

What is high blood pressure / hypertension?

High blood pressure – or hypertension – means that your blood pressure is usually higher than the recommended level. You probably have high blood pressure (hypertension) if your blood pressure readings are consistently 140 over 90, or higher. If you are diabetic or have heart or kidney disease, a blood pressure above 130 over 80, would be high.

How dangerous is hypertension to your health?

High blood pressure is a risk factor for future cardiovascular disease such as heart attack or stroke.

Can changing lifestyle help to lower your blood pressure?

Yes. For example 1) Lose weight if you are overweight: Blood pressure can fall by up to 2.5/1.5 mm Hg for each excess kilogram which is lost. 2) Do physical activity as much as possible. The more the better. 3) Lower salt intake as much as possible. Use herbs and spices rather than salt to flavour food. 4) Consume less alcohol. A maximum of one large glass of wine or one pint of mild beer per day.

How does your blood pressure medicine work?

Your blood pressure medicine belongs to a group of drugs called **Diuretics**.

Diuretics work by increasing the amount of salt and fluid that you pass out in your urine. This has some effect on reducing the fluid in the circulation, which reduces blood pressure. They may also have a relaxing effect on the blood vessels, which reduces the pressure within the blood vessels.

How do I take my medicine?

Your doctor will advise you how to take your medication, including how often. In some people the first dose can cause a drop in blood pressure immediately. If you do feel dizzy, sit or lie down and it will usually ease off.

What is the usual length of treatment?

Most people with hypertension need to take medication for life. Ask your doctor for further advice.

What are the possible side-effects?

They can cause gout attacks in a small number of users, or can make gout worse if you already have gout. Impotence develops in some users. **Note:** Please see the leaflet that comes with this medicine for a full list of possible side-effects and cautions.

Information on blood pressure and direct acting vasodilators

What is blood pressure?

When your heart beats, it pumps blood round your body to give it the energy and oxygen it needs. As the blood moves, it pushes against the sides of the blood vessels. The strength of this pushing is your blood pressure.

What do the numbers mean?

Every blood pressure reading consists of two numbers or levels. They are shown with the higher number given first e.g. 140/90. The first (or higher) number is your systolic blood pressure. It is the highest level your blood pressure reaches when your heart beats. The second (or lower) number is your diastolic blood pressure. It is the lowest level your blood pressure reaches as your heart relaxes between beats.

What is high blood pressure / hypertension?

High blood pressure – **or hypertension** – means that your blood pressure is usually higher than the recommended level. You probably have high blood pressure (hypertension) if your blood pressure readings are consistently 140 over 90, or higher. If you are diabetic or have heart or kidney disease, a blood pressure above 130 over 80, would be high.

How dangerous is hypertension to your health?

High blood pressure is a risk factor for future cardiovascular disease such as heart attack or stroke.

Can changing lifestyle help to lower your blood pressure?

Yes. For example 1) Lose weight if you are overweight: Blood pressure can fall by

up to 2.5/1.5 mm Hg for each excess kilogram which is lost. 2) Do physical activity as much as possible. The more the better. 3) Lower salt intake as much as possible. Use herbs and spices rather than salt to flavour food. 4) Consume less alcohol. A maximum of one large glass of wine or one pint of mild beer per day.

How does your blood pressure medicine work?

Your blood pressure medicine belongs to a group of drugs called **potent direct vasodilators**. They work by relaxing blood vessels that reduce blood pressure.

How do I take my medicine?

Your doctor will advise you how to take your medication, including how often. In some people the first dose can cause a drop in blood pressure immediately. If you do feel dizzy, sit or lie down and it will usually ease off.

What is the usual length of treatment?

Most people with hypertension need to take medication for life. Ask your doctor for further advice.

What are the possible side-effects?

This medicine can cause headache, nasal stuffiness and fluid retention.

P) Information sheets for control group

Information on New Medicine Service

Do you know what is the New Medicine Service?

The New Medicine Service is a free NHS service, offered through your pharmacy (chemist), to help you understand your condition and get the most out of your new medicine.

Who is it for?

The service is for people who have received their first prescription for a medicine to treat medical conditions including asthma/lung conditions such as chronic bronchitis and emphysema, type 2 diabetes, high blood pressure and conditions where you take a medicine to control the way your blood clots.

How will the service help you?

The service will:

- help you to find out more about the new medicine you are taking
- help to sort out any problems you are having with your new medicine
- give you a chance to ask questions about your medicine and discuss any concerns
- help to improve the effectiveness of your new medicine, for example, there may be an easier or better way to take it

help you to make your own decisions about managing your condition help you to improve your health, which could lead to fewer GP and hospital visits.

How does the service work?

When you are given your new medicine you will be asked if you want to sign up to the service, which will be provided in three parts. If you agree, you will need to sign a consent form to allow your pharmacist to share your information with other parts of the NHS.

Why do I need to sign a consent form?

In order to receive this service, you will be asked to give your consent for your pharmacist to share information from your New Medicine Service discussions with: your GP your primary care trust (PCT – the local NHS authority), to make sure that the service is being provided properly by your pharmacist your PCT, the NHS Business Services Authority and the Secretary of State for Health, to make sure your pharmacy is being paid the correct amount by the NHS for the service they have provided you.

How can you prepare for your discussion with the pharmacist?

Read the leaflet that comes with your new medicine. Make a note of questions you want to ask about your new medicine. Make a note of any concerns about your new medicine that you may want to discuss with your pharmacist. Bring your new medicine to the meeting with your pharmacist.

What happens after two discussions?

Everything may be fine with your new medicine and nothing else may need to happen. •If you have had problems with the medicine, you may agree with your pharmacist to change the way you take it. •Your pharmacist may recommend that

your doctor reviews your new medicine. If this is needed your pharmacist will send a note to your doctor explaining the issues raised. You can have a copy of this note.

Q) Interview schedule for pharmacist

Impact of community pharmacists on blood pressure control

Interview Schedule

Week 0:

1. Introduction:

Hi. My name is _____ and as a member of the research team, I would be conducting this consultation with you.

2. Purpose of the study:

As explained in the information sheet given to you by my colleague a few days ago, the purpose of this study is to understand the effect of pharmacist-based intervention, supported by written information and find out whether blood pressure control is different depending on how information is provided to you.

3. Patient journey:

Taking part will involve being seen at time convenient to you. You will be randomly assigned to two different groups. You will receive advice from the pharmacist on four occasions over six months. On each visit you will be asked to complete a short questionnaire and your blood pressure will also be measured. Each visit is expected to take about 15 minutes. You should continue to take your prescribed medicine(s) or over the counter drugs. It is important that you attend all the scheduled visits during the study. All information collected from you will be kept strictly confidential.

4. Patient consent:

If you would like to take part, please indicate this by reading the following questions and writing your initials in the boxes, where appropriate. Then sign and add today's date in the space provided.

5. Measuring blood pressure:

Thank you for agreeing to take part in the study. Firstly, I would measure your blood pressure.

Take three blood pressure readings using OMRON device.

6. Administration of the questionnaire:

I would now ask you to complete this questionnaire. Kindly, complete this questionnaire as far as practical.

7. Provision of structured information verbally and in writing:

I would now go through with you this information sheet. If you are not sure about anything, feel free to ask any questions.

Read out and explain the contents of the information sheet to the participant and provide this copy of information sheet to the participant.

8. Arrange the date for the NMS intervention:

Do you have any questions at this stage or is there anything you would like me to go over again? Thank you for your time and I would like to see you

on_____

Securely place the participant's blood pressure readings log, completed questionnaire record of participants' allocation to study arm along with details of participant's next visit in the folder provided to you.

Week 2:

Introduction:

Hi. Do you have any questions from our previous consultation or is there anything you would like me to go over again?

1. Measuring blood pressure:

If no questions, let me start by measuring your blood pressure.

Take three blood pressure readings using OMRON device.

2. Administration of the questionnaire:

I would now ask you to complete this questionnaire. Kindly, complete this questionnaire as far as practical.

Administer the same questionnaire which was completed by the participant in week 0.

3. Provision of structured information verbally and in writing:

I would now go through with you this information sheet. If you are not sure about anything, feel free to ask any questions.

Read out and explain the contents of the same information sheet which was handed to the participant in week 0 and provide this copy of information sheet to the participant.

5. Standard NMS intervention:

Conduct the standard verbal NMS intervention.

Do you have any questions at this stage or is there anything you would like me to go over again? Thank you for your time and I would like to see you on_____

Securely place the participant's blood pressure readings log, completed questionnaire along with details of participant's next visit in the folder provided to you.

Week 4:

1. Introduction:

Hi. Do you have any questions from our previous consultation or is there anything you would like me to go over again?

2. Measuring blood pressure:

If no questions, let me start by measuring your blood pressure.

Take three blood pressure readings using OMRON device.

3. Administration of the questionnaire:

I would now ask you to complete this questionnaire. Kindly, complete this questionnaire as far as practical.

Administer the same questionnaire which was completed by the participant in week 0.

4. Provision of structured information verbally and in writing:

I would now go through with you this information sheet. If you are not sure about anything, feel free to ask any questions.

Read out and explain the contents of the same information sheet which was handed to the participant in week 0 and provide this copy of information sheet to the participant.

5. Standard NMS follow up:

Conduct the standard verbal NMS follow up consultation.

Do you have any questions at this stage or is there anything you would like me to go over again? Thank you for your time and I would like to see you on_____

Securely place the participant's blood pressure readings log, completed questionnaire along with details of participant's next visit in the folder provided to you.

Week 26:

1. Introduction:

Hi. Do you have any questions from our previous consultation or is there anything you would like me to go over again?

2. Measuring blood pressure:

If no questions, let me start by measuring your blood pressure.

Take three blood pressure readings using OMRON device.

3. Administration of the questionnaire:

I would now ask you to complete this questionnaire. Kindly, complete this questionnaire as far as practical.

Administer the same questionnaire which was completed by the participant in week 0.

4. Conclusion of study:

Do you have any questions at this stage or is there anything you would like me to go over again? Thank you for your time and if you would like to receive a summary of the results of this study, we will send them to you in post in due course.

Securely place the participant's blood pressure readings log, completed questionnaire along with any other participant's data next in the folder provided to you.

R) Patient satisfaction survey

Thank you for taking part in the above study at your local pharmacy. We would like you to complete a short survey about the study. The purpose of this survey is to find out what you thought about the study and the involvement of community pharmacists in blood pressure control.

Please complete all the questions below. Your responses will remain confidential. For question 1, please tick the most appropriate option for each statement. For question 2, please tick all that apply to you. For questions 3 and 4 please provide as much information as you can. If you have any queries about the survey or would like to provide any additional feedback, please speak to a member of the research team.

1. Please rate how strongly you AGREE or DISAGREE with each of the following statements by ticking in the most appropriate box.

- a) The pharmacist clearly explained the purpose of this study to me?
Strongly disagree Disagree Agree Strongly agree
- b) The advice given to me by the pharmacist was useful?
Strongly disagree Disagree Agree Strongly agree
- c) I feel that taking part in this study has improved my high blood pressure?
Strongly disagree Disagree Agree Strongly agree
- d) I am happy with the number of appointments I had with the pharmacist?
Strongly disagree Disagree Agree Strongly agree
- e) I would recommend others to take part in this study?
Strongly disagree Disagree Agree Strongly agree

2. Why did you decide to participate in this study? (You may tick more than one box)

- I was concerned about my high blood pressure
- I wanted to learn about high blood pressure and its risks to my health
- I wanted to learn about the new blood pressure medicine I was using
- I was confident that my pharmacist would give me good advice
- Other (please state) _____

Participants' views

3. How would you feel about approaching pharmacists in future for getting advice on medical conditions including high blood pressure and its treatment? _____

Other comments

4. Do you have any other comments about this study? If yes, please write your comments below.

Thank you for taking the time to complete this questionnaire