The Role of Community Pharmacists in the Management of Hypertension

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Abstract

Background and aim

The rising workload in primary care and the declining general practitioner (GP) workforce has meant that new models of care to effectively manage long-term conditions, such as hypertension, are needed. Hypertension affects a third of adults in the UK and is the leading risk factor for cardiovascular events globally. Evidence from randomised controlled trials (RCTs) has shown that community pharmacist-led interventions significantly lower blood pressure (BP) over usual GP care. Despite this evidence, community pharmacists do not currently deliver hypertension management services.

This thesis investigated the extent to which the interventions from previous RCTs of community pharmacist-led hypertension management are translatable to current pharmacy practice in England.

Methods

The Consolidated Framework for Implementation Research (CFIR) was the theorectical framework used to direct the thesis. A mixed methods approach was used to address the thesis aim. First, semi-structured interviews were conducted with pharmacists to explore their views and experiences of delivering hypertension related care. Next, a systematic review and meta-analysis aimed to understand how pharmacy-measured BP compared to other BP measurement modalities. A qualitative analysis of 1,200 consultation notes was then conducted to understand the content of consultations between pharmacists and hypertensive patients in current practice. Finally, a multivariable logistic regression was undertaken on a

dataset of over 131,000 hypertensive ‘new medicine service’ (NMS) consultations to identify predictors for referral of hypertensive patients from pharmacies back to general practice.

Results

The interviews in Chapter 2 found that pharmacists prioritised services that provide financial remuneration over offering unfunded BP testing or monitoring. Participants outlined factors to consider before implementing hypertension services in pharmacies such as communication with GPs and access to patient clinical records. The systematic review (Chapter 3) suggested that using the 135/85 mmHg threshold for hypertension, rather than 140/90 mmHg, may be most appropriate for the community pharmacy setting due to the close association with daytime ambulatory BP readings. Analysis of routine pharmacy data found that the content of consultations closely resembled the interventions described in the RCTs of community pharmacist-led hypertension management (Chapter 4), and showed that pharmacists referred back 4% of patients to a GP during the first two weeks of new anti-hypertensive therapy (Chapter 5).

Overall, this thesis has identified that the interventions themselves are unlikely to be the barrier to hypertension service implementation at present.

Conclusion

The following recommendations to pharmacists and health service commissioners in relation to implementing future hypertension management services in community pharmacies can be made, based on the findings of this thesis:

1. Pharmacists require the reassurance of having local or national-level endorsement before delivering additional hypertension services. Ideally, this

should also include a funding stream to enable the redistribution of their other workload to other members of staff (Chapter 2).

2. Interpret pharmacy measured BP using the 135/85mmHg threshold and confirm pharmacy readings with home BP before making treatment or referral decisions if necessary (Chapter 3).
3. Further training for pharmacists to conduct hypertension management may not be required as pharmacists currently provide evidence-based advice related to hypertension management (Chapter 4).
4. A model of intervention that avoids referral back to a GP for final approval should be considered to minimise a GP's workload (Chapters 2 and 5). Alternatives could include referring to a general practice pharmacist or allowing community pharmacists to manage patients themselves through an agreed PGD if they do not possess the permissions to prescribe.

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My interest in research originated at Aston University, where I stayed back one summer as a pharmacy student to learn ‘how to do research’. I will always be thankful to Dr. Lindsay Marshall for spending time with me in her lab during the summer of 2013, and then taking me on as her Masters student. It is there that I considered that a career in research could be for me.

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Statement of contribution and dissemination statement

I was solely responsible for the studies conducted in this thesis, from conception to undertaking. I was, however, helped along the way by Dr. Jack O'Sullivan who second screened the studies from the systematic review in Chapter 3, and by Dr. Suman Prinjha who helped independently code some of the qualitative data discussed in this thesis (Chapters 2 and 4).

The results presented in Chapters 3 and 5 of this thesis have been published in peer-reviewed journals and therefore some sections, tables and figures of the publications have been reproduced within this thesis.(1,2) The remaining two results chapters from this thesis have been written up for journal publication and will be submitted in due course. Elements of other parts of this thesis have been reproduced for an editorial piece,(3) and a narrative review that I was invited to write,(4) both for the Clinical Pharmacist journal of the Royal Pharmaceutical Society during the course of my DPhil.

The results of this thesis have also been presented orally at the following conferences and scientific meetings:

2018 – British and Irish Hypertension Society (University of Cambridge)

Title of invited talk - *"Pharmacist management of hypertension".*

2018 – European Society of Hypertension (Barcelona, Spain)

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Title of talk - “A comparison of blood pressure in community pharmacies with ambulatory, home and general practitioner office readings: Systematic review and meta-analysis

2017 – South West Society for Academic Primary Care (University of Oxford)

Title of talk - “A comparison of blood pressure in community pharmacies with ambulatory, home and general practitioner office readings: Systematic review and meta-analysis”.

The work contained in this thesis has not been submitted for any other course or qualification at the University of Oxford or elsewhere.

Abbreviations and terms in this thesis

A-blockers – Alpha Adreno-receptor blockers

ABPM – Ambulatory Blood Pressure Monitoring

ACE-I – Angiotensin Converting Enzyme Inhibitors

AF – Atrial Fibrillation

ARBs – Angiotensin II Receptor Blockers

B-blockers – Beta Adreno-receptor blockers

BIHS – British and Irish Hypertension Society

BP – Blood Pressure

CCBs – Calcium Channel Blockers

CCG – Clinical commissioning group

CFIR – Consolidated Framework for Implementation Research

CI – Confidence Interval

CP – Community Pharmacist

CPBP – Community Pharmacy Blood Pressure

CVD – Cardiovascular Disease

DBP – Diastolic Blood Pressure

DDD – Defined Daily Dose

EQUATOR – Enhancing the Quality and Transparency of Health Research network

GP – General Practitioner/practice

GPP – General Practice Pharmacist

HBPM – Home Blood Pressure Monitoring

HLP – Healthy Living Pharmacy

mmHg – Millimetres of Mercury

MUR – Medicines Use Review

NHS – National Health Service

NICE – National Institute for Health and Care Excellence

NMS – New Medicine Service

PO – PharmOutcomes

PCPA – Primary Care Pharmacists Association

PGD – Patient Group Direction

PRISMA – Preferred Reporting Items for Systematic Reviews and Meta-Analyses

PROSPERO – International Prospective Register of Systematic Reviews

PSNC - Pharmaceutical Services Negotiating Committee

QUADAS-2 – Quality Assessment of Comparative Diagnostic Accuracy Studies-2 checklist

RCT – Randomised Controlled Trial

RPS – Royal Pharmaceutical Society

SBP – Systolic Blood Pressure

SCR – Summary Care Records

SRQR – Standards for Reporting Qualitative Research guidelines

UKCPA – United Kingdom Clinical Pharmacist Association

WHO – World Health Organisation

WMD – Weighted Mean Difference

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Chapter 1 – Background

1.1 Chapter overview

This chapter provides background and context to the topics covered in the thesis, beginning with the evolution of the community pharmacist's role over time and where this is today. It then describes hypertension epidemiology, aetiology, and treatment, highlighting the gap in current management strategies. Evidence from the latest systematic review of randomised controlled trials investigating the effectiveness of community pharmacist-led hypertension management is then presented.

The evidence to date is then considered along with implementation science theory to guide the direction of the subsequent chapters. From this, the emerging research questions from the literature are highlighted and their importance to answering the overall thesis aim is emphasised. The thesis' structure is then described with reference to the unanswered research questions followed by the rationale for taking a mixed methods approach.

1.2 Thesis aim

This thesis aims to investigate the extent to which the interventions from previous randomised controlled trials (RCTs) of community pharmacist-led hypertension management are translatable to current pharmacy practice in England.

1.3 Role of community pharmacists

A community pharmacist can be defined as a pharmacist working directly with patients in a local area, specifically, in a community pharmacy.(5) The role of the community pharmacist has evolved since the early 20th century. This section provides a brief history of the role since the early 1900s and its development up to the present day.

1.3.1 Historical roles

Three key eras in the evolution of the modern day community pharmacist over the past century were identified by Anderson (2007).(6) First, the pre-NHS era from the early 1900s to 1948, secondly the period from 1948 through to 1981, and finally from 1982 to the early 2000s.

1900s to 1948 (pre NHS)

During the pre-NHS era, the roles of pharmacists were to advise the public on the use of medications, and to ‘extemporaneously’ dispense medications on-site - i.e. the compounding and production of medications for individual patients.(6) In an era before free universal healthcare, the unaffordable nature of visiting a doctor made pharmacies a central hub for community care, with evidence of pharmacists even providing healthy lifestyle advice by the 1930s.(6)

1948 to 1981

After the introduction of the NHS in 1948, two major changes occurred that affected the role of the community pharmacist. Firstly, annual prescription volumes increased from 65 million items in 1937, to 250 million by 1950.(7) This meant that pharmacists became less visible to their patients as they began to spend more time in the back of pharmacies preparing medications according to the instructions of pre-written prescriptions. Secondly, during the 1950s and 60s, medications became more available in pre-formulated tablets and capsules at a larger scale.(6) This meant that the traditional role of pharmacists compounding raw ingredients on pharmacy premises became less necessary given the benefits for hygiene, consistency of dose and patient waiting times of industrially produced tablets.

1982 to early 2000s

After a transitionary period for the profession settling into a ‘dispensing role’ (or medication distribution role), the ‘*Ask your pharmacist*’ campaign, launched in 1982 by the National Pharmacy Association, was one of the first national efforts in the NHS era to raise public awareness of the wider potential of community pharmacists.(6) In particular, it advocated for the greater use of pharmacists for

general health, lifestyle and medication advice – a role that had been diluted since the NHS era began.

By 1983, the first ‘prescription-only medicines to pharmacy medicine’ switches (POM to P switches) occurred for drugs such as Ibuprofen and Loperamide.(8) This was followed in 1985 by a reduction in the number of medications allowable on NHS prescriptions (removal of cough remedies, certain indigestion remedies, laxatives and weak analgesics), further increasing pharmacist contact with patients through increased demand for over-the-counter medication sales.(8)

By 2005, the Department of Health published the “Choosing health through pharmacy 2005-2015 ” best practice guidance.(9) The document set out how pharmacists would take on a role to promote healthy living through smoking cessation services, sexual health services and work around substance misuse, while at the same time reducing health inequalities through their locations in the community and access to the wider public.(9) Subsequently, a move towards a more clinically oriented community pharmacy sector has grown, with particular emphasis on the potential for pharmacists to be involved in the management of long-term conditions.(10)

1.3.2 Current roles

NHS contractual framework

At present, the role of community pharmacists in England is largely dictated by the national contractual framework, agreed between the pharmacy sector and the NHS.(11) The Pharmaceutical Services Negotiating Committee (PSNC) is the

organisation that represents NHS pharmacy contractors in England and its role is to agree the terms of the contract between the NHS and pharmacies for the services being provided.(12) The pharmacy contract has three main categories:(11)

1. Essential services – a requirement of all pharmacy contractors, commissioned by NHS England. Examples include dispensing medications, public health promotion and disposal of unwanted medications.
2. Enhanced services – usually locally commissioned services via Local Authorities, Clinical Commissioning Groups or NHS England in response to local population need. Examples include smoking cessation services and free emergency hormonal contraception provision.
3. Advanced services – can be provided by all pharmacies once accreditation requirements have been met. The most commonly delivered advanced services are the New Medicine Service (NMS) and Medication Use Reviews (MURs).

The NMS targets patients taking medications for either hypertension, type 2 diabetes, asthma/COPD, or antiplatelets/anticoagulant medications, with a view to monitoring side effects and improving adherence to treatment.(13) MURs consist of annual medication reviews for patients taking medications for long-term conditions with a view to encouraging medication adherence and patient engagement with their health.(14) While both of these services are aimed at patients with long-term conditions, none of them offer long term management or ongoing monitoring for these conditions.

In the month of June in 2015, over 90 milllion prescription items were dispensed from community pharmacies in England compared to around 80 million items in

June 2011.(15) This increase, fuelled by the general increase in healthcare utilisation across the health service, has meant that pharmacists spend the majority of their time accuracy checking and clinically checking prescriptions at the end of the dispensing process.(16) This has meant that the role of community pharmacists most prominently consists of essential services, as defined in their NHS contract.

Further to the NHS-contracted services, the PSNC holds a local and national level service database of commissioned services, pilot studies and other ongoing projects across community pharmacies in England.(17) Between April 2013 and December 2019, several hypertension-related projects were reported on the PSNC database and these are summarised in Table 1 below. The largest of these projects are summarised in more detail here:

- Wakefield – "The Blood Pressure Drop In" was a 6 week pilot campaign in the Wakefield area focusing on the early detection of high blood pressure in 2014.(18) The campaign encouraged individuals over the age of 40 with no pre-existing diagnosis of high blood pressure to have a blood pressure test in a pharmacy. People with high blood pressure readings (greater than 140/90mmHg) were encouraged to visit their GP practice and offered lifestyle advice.
- Northamptonshire, Bedfordshire and Milton Keynes – a pilot screening programme for hypertension and atrial fibrillation (AF) in community pharmacy.(19) Patients over the age of 40 received advice on reducing their future risk of cardiovascular disease by addressing their modifiable risk factors (such as excess weight, dietary salt or alcohol), supporting a strategy of self-care. This scheme offered patients with a pharmacy blood pressure of ≥140/90mmHg, home testing to confirm the diagnosis of hypertension. The

pilot service ran from February 2018 for 3 months and also involved checking patient's pulse for those over 65 years, to screen for possible AF.

- Cheshire and Merseyside – a blood pressure screening programme for adults over 18 years, aiming to take a minimum of 3,000 BP screening measurements across 120 healthy living pharmacies (HLPs) by the end of March 2019.(17)

Table 1 – Hypertension related pilots or projects reported on the PSNC database

Location	Service name	Description provided on PSNC database	Status as of Dec '19
Cheshire & Merseyside	British Heart Foundation (BHF) Blood Pressure Innovation Award	Healthy Living Pharmacies (HLPs) to offer blood pressure and pulse screening.	Ongoing
Thurrock	Hypertension and Atrial Fibrillation Screening in Pharmacies	Screening high-risk patients for hypertension and atrial fibrillation.	Completed
Halton	Screening for Hypertension and Atrial Fibrillation in Community Pharmacy	Patients identified as at risk of developing hypertension will receive advice on reducing their future risk of cardiovascular disease. Those with a clinic blood pressure of 140/90 mmHg or higher will be offered ambulatory blood pressure monitoring to confirm diagnosis of hypertension from the pharmacy.	Completed
Kensington and Chelsea	Testing and Detection of High Blood Pressure	No information provided	Ongoing
Bedfordshire, Luton & Milton Keynes	Screening for Hypertension and Atrial Fibrillation in Community Pharmacy	Local Sustainability and Transformation Partnership developed a pilot service to target patients for hypertension and atrial fibrillation screening through community pharmacies.	Completed
Leeds	Leeds Blood Pressure Wise Service	Opportunistic blood pressure screening in community pharmacies for the detection of hypertension with an emphasis on atrial fibrillation	Ongoing
Wakefield	Blood Pressure Drop In Pilot	A 6-week pilot intervention was offering blood pressure testing to high-risk patients and provide appropriate information and local opportunities to individuals to encourage better lifestyle choices.	Completed

Wider 'non-dispensing' involvement

In 2008, a government White Paper - "*Pharmacy in England: building on strengths, delivering the future*" - described a vision to develop community pharmacies into the *"primary source of information and advice for healthy living and health improvement, [where] pharmacy is integrated into public health initiatives".*(20) This concept was later developed in Portsmouth in what is now known as the Healthy Living Pharmacy (HLP) scheme.(21) HLP provides a framework for pharmacies that aims to support the delivery of various public health initiatives. Public Health England stated the three main ways through which pharmacies wishing to become accredited as an HLP can deliver far reaching public health interventions: (22)

- "W*orkforce development – a skilled team to pro-actively support and promote behaviour change, improving health and wellbeing;*
- *A premises that is fit for purpose; and*
- *Engagement with the local community, other health professionals (especially GPs), social care and public health professionals and local authorities".*

There is currently a lack of evidence of clinical benefit of being an HLP over a non-HLP, with evaluations to date focussing on operational factors and on quantifying uptake of services (such as the number of smoking cessation consultations delivered rather than a comparison in successful 'quits' between HLP and non-HLP).(23) HLP status is part of the 'quality payments scheme' in England – a scheme whereby meeting certain 'quality' or 'gateway' criteria (such as HLP status, having an NHSmail account etc.), pharmacies can recoup some funding from the

cuts made to the sector by NHS England (described later in this chapter).(24) HLP accreditation, which in the initial phase involves self-accreditation based on a checklist provided by Public Health England, is a scheme that pharmacies are therefore financially incentivised to take part in.(22)

Cardiovascular disease (CVD) related public health initiatives offered by pharmacies include delivering the NHS health check screening programme.(25) The NHS Health Check consists of questions about lifestyle factors and family medical history as well as measurements of height, weight, blood pressure, cholesterol and, where appropriate, blood glucose levels.(25) In a study examining data from 190 NHS health checks performed in four pharmacies, 67 patients were referred to either weight support services, smoking cessation, alcohol reduction or exercise schemes, with 37 patients accepting these referrals.(26) Furthermore, of the 33 patients referred directly to their GP after the pharmacy health check due to >20% predicted 10-year cardiovascular risk or elevated BP (>140/90 mmHg), two were confirmed to have attended their referral. Commissioning of pharmacy NHS health checks occurs locally, therefore unlike the national coverage offered by general practices, the pharmacy checks are commissioned based on local population need.(26)

The next section presents an overview of hypertension and its management.

1.4 Hypertension background

1.4.1 Epidemiology

The term ‘blood pressure’ (BP) describes the force of blood pushing against the walls of arteries when the heart is beating (systolic blood pressure) and when the heart is relaxed (diastolic blood pressure).(27) Hypertension can be defined as persistently elevated blood pressure - elevated to levels that increase cardiovascular disease (CVD) risk - thus requiring lowering.(28) Rather than a ‘disease’ per se, hypertension is a risk factor associated with an increased risk of cardiovascular, cerebrovascular and renovascular events.(29) The mechanism behind which hypertension leads to such events stem from the damage it causes to both small and large blood vessels.(30) These result in structural and functional changes to vessel walls – such as impaired autoregulation of blood flow and altered capillary wall permeability.(31)

Epidemiological studies have shown that regardless of previous CVD status and baseline BP (at least greater than 110 mmHg systolic and 70 mmHg diastolic), reductions in blood pressure by 10 mmHg systolic or 5 mmHg diastolic result in relative risk reductions of coronary heart disease and stroke by 22% (95% CI, 17% to 27%) and 41% (95% CI, 33% to 48%) respectively.(32) While both elevated systolic and diastolic blood pressure are positively correlated with cardiovascular endpoints and renal disease, the association seen with systolic blood pressure is the stronger of the two in the general population.(33,34)

Across the population, blood pressures are normally distributed.(35) Globally, the prevalence of hypertension as the leading non-communicable 'disease' has increased, with an estimated 40% of all adults (more than 1 billion people) affected.(29) The World Health Organisation (WHO) has described this as a "global health crisis".(27) The most recent 'Health Survey for England' related to hypertension (2016) examined the prevalence of hypertension nationally.(36) The Health Survey for England deploys nurses to measure participant's BP in their homes.(36) The survey estimated that 28% of adults are hypertensive in England.(36) Further to the overall prevalence, 20% of men and 18% of women in England were thought to have uncontrolled and/or untreated (but diagnosed) hypertension, combined.(36) The true prevalence of undiagnosed hypertension (where blood pressure is elevated without detection) is unknown, though some estimates suggest that only half of the population who are hypertensive are aware that their blood pressure is elevated.(37,38) These data suggest that improvements are needed across the spectrum of hypertension, from awareness and detection, to management and follow-up.

1.4.2 Aetiology

Broadly, hypertension can be categorised in two main ways; primary or essential hypertension, and secondary hypertension.(30) Primary or essential hypertension is a classification reserved for cases where BP is elevated with no identifiable cause,(35) and this is thought to account for 90-95% of hypertensive cases.(27)

There are a number of modifiable and non-modifiable risk factors that predispose a person to hypertension, these include:

- Genetic predisposition and metabolic factors.(39)
- Dietary and lifestyle factors such as; high salt intake, high alcohol consumption, smoking, obesity, and a sedentary lifestyle.(40)
- Increasing age.(41)
- Social determinants such a low income and poor housing/living conditions.(42)

Secondary hypertension is estimated to make up the other 5-10% of hypertensive cases globally.(30) Some of the main causes of secondary hypertension are listed below, along with their prevalence in patients with secondary hypertension.

- Obstructive sleep apnoea – a breathing disorder characterised by episodes of complete or partial upper airway obstruction during sleep (>30% of secondary hypertension cases).(43)
- Primary hyperaldosteronism (Conn's syndrome) – excess production of aldosterone from the adrenal gland (6-23% of secondary hypertension cases).(43)
- Renal artery stenosis – a narrowing and hardening of the arteries carrying blood to the kidneys (2.5%-20% of secondary hypertension cases).(43)
- Pheochromocytoma – a tumour of the adrenal gland leading to excess production of adrenaline and noradrenaline (<1% of secondary hypertension cases).(43)

1.4.3 Blood pressure measurement

The measurement of blood pressure in primary care currently takes the form of a non-invasive, brachial artery cuff attached to either an automatic or manual blood pressure monitor.(28) For accurate readings, the British and Irish Hypertension Society (BIHS) recommend standardising BP measurement protocols for both home and clinic measured BP.(28,44) Their recommendations for patients and clinicians taking BP measurements include:

- Use of an appropriately sized cuff so as not to overestimate (cuff too small) or underestimate (cuff too large) blood pressure – placed 2cm above the elbow.
- Resting for 5mins prior to measurements.
- Not speaking or crossing legs during measurements.
- Supporting the measurement arm and keeping it level with the heart.
- Use of manual sphygmomanometers in patients with irregular heartbeats (measuring pulse prior to measurements).

Given that anti-hypertensive treatments are initiated and altered based on BP readings, inaccuracies (through poor measurement technique for example) can result in different treatment decisions and therefore outcomes for patients.(45) The requirement for consistent and accurate BP measurements is also important as long-term variability in BP is associated with increased cardiovascular and mortality outcomes over and above mean blood pressure alone.(46) Inaccurate readings could therefore skew these potentially prognostic trends.

Using a validated monitor is a requirement for accurate readings, and in the UK, the BIHS provide a list of validated blood pressure monitors for patients and clinicians.(47) In a cross-sectional study of 52 community pharmacies in England, 8 out of 62 BP monitors tested failed the BIHS accuracy test (>3 mmHg from validated reference device).(48) This error rate of 13% is in line with rates seen across general practice machines, and was most commonly due to monitors not undergoing recalibration every 12 months.(48)

In the UK, guidance on the diagnosis and management of hypertension is set by the National Institute for Health and Care Excellence (NICE).(49) NICE guidelines recommend out-of-office measurements, in the form of Ambulatory Blood Pressure Monitoring (ABPM), as the 'gold standard' for estimations of a patient's 'true' blood pressure, due to its closer correlation with cardiovascular events over home or clinic measurements, and due to the differences in BP readings obtained between different settings and operators.(50) ABPM is typically reserved for the diagnosis of hypertension, rather than ongoing condition monitoring due to cost and lack of acceptability in some patients.(51) ABPM involves placing a brachial cuff onto a patients arm, usually for a 24-hour period. Measurements are then automatically taken every 20-30mins in the day, and every 30mins in the night. A minimum of fourteen daytime (0700 – 2300h) ABPM readings are recommended to inform clinical decisions.(28) The multiple readings produced as a result of ABPM, the ability to capture diurnal variation and the reduced "white coat" or alerting effect of taking measurements at home, all contribute to the superior accuracy and prognostic value of this measurement modality over one-off clinic measurements.(52) If ABPM is not possible due to resource restrictions, or not tolerated by the patient, Home Blood Pressure Monitoring (HBPM) is

recommended.(28) For the diagnosis of hypertension, patients are instructed to monitor their BP every morning and evening for five consecutive days.(53) HBPM has also been shown to be more closely associated with future risk of cardiovascular events than clinic measurements alone.(54–56) When used in conjunction with GP clinic measurements, ABPM/HBPM (out-of-office measurements) make up the foundation of hypertension diagnosis and monitoring in the UK.(28)

1.4.4 Classification of hypertension

NICE guidance (2019) classifies hypertension into three stages: stage 1, where clinic BP is >140/90 mmHg and home or daytime ambulatory BP is >135/85 mmHg; stage 2, defined as a clinic reading of 160/100 mmHg or higher and subsequent daytime ambulatory or home monitoring average of 150/95 mmHg or higher; stage 3 or severe hypertension, a clinic blood pressure of 180 mmHg (systolic) or 120 mmHg (diastolic) or more.(49) For clinically important sub-populations such as diabetic patients, blood pressure targets were previously lower (140/80 mmHg) in the 2011 hyperetnsion guidance, however this is now in line with the general hypertensive population target of 140/90 mmHg in the 2019 guidance due to lack of evidence of benefit of lower BP.(57) Although cut-off points are largely arbitrary they are required for clinicians to know when to initiate and modify treatments.(35)

Guidance set by the European Society of Hypertension (ESH) in 2018 largely echo the NICE classifications however further stratify hypertensive categories - particularly in the so-called ‘pre-hypertensive stages’.(58) These additional

classifications are ‘optimal’ (less than 120/80mmHg clinic), ‘normal’ (120/80mmHg to 129/84mmHg clinic) and ‘high-normal’ (130/85mmHg to 139/89mmHg).(58)

In 2017, the American Heart Association and the American College of Cardiology (AHA/ACC) published updated hypertension guidance for the United States.(59) The guidance redefined hypertension to lower levels compared with British and European recommendations, lowering stage 1 hypertension to 130-139 mmHg systolic or 80-89 mmHg diastolic, and stage 2 hypertension to ≥140 mmHg systolic or ≥90 mmHg diastolic. This redefinition of hypertension is estimated to increase the proportion of adults defined as hypertensive in the US from 32% to 46%.(59)

The change in US guidance has been influenced by recent evidence advocating the benefits of more intensive blood pressure lowering on cardiovascular outcomes and mortality. For instance, a systematic review by Ettehad et al. (2016) of large-scale blood pressure reduction trials (defined as a minimum of 1000 patient-years of follow-up in each study arm) including the SPRINT trial,(60) showed ‘strong evidence’ for BP lowering to systolic levels of less than 130 mmHg.(61) Their meta-analysis of over 600,000 patients showed a significant relative risk reduction for both major CV events and all-cause mortality for every 10 mmHg reduction in BP from a baseline systolic BP of >160mmHg, 150-159 mmHg, 140-149 mmHg (a non-significant reduction in all-cause mortality), 130-139 mmHg and <130 mmHg. The results were most prominent in patients with higher baseline cardiovascular risk. Table 2 below summarises the new American thresholds and recommendations along with the UK and European guidance.

Table 2 – Summary of hypertension definitions from the UK, European and US guidelines.

BP level (mmHg)	**National Institute for Health and care excellence, UK, 2019** (49)		**European Society of Hypertension, 2018** (58)		**American Heart Association/ College of Cardiology, 2017** (59)	
	Definition	Treatment recommendation	**Definition**	Treatment recommendation	**Definition**	Treatment recommendation
<120/80	**-**	-	**Optimal**	Promote optimal lifestyle	**Normal**	Promote optimal lifestyle
120-129/80-84	**-**	-	**Normal**	Promote optimal lifestyle	**Elevated**	Non-pharmacological therapy
130-139/85-89	**-**	Promote optimal lifestyle	**High-normal**	Non-pharmacological therapy	**-**	-
130-139/85-89, no CVD and 10-year CVD risk <10%	**-**	-	**-**	-	**Stage 1a**	Non-pharmacological therapy
130-139/85-89 with CVD or 10-year risk ≥20%	**-**	-	**-**	-	**Stage 1b**	Non-pharmacological therapy and BP-lowering medication
≥140/90	**Stage 1**	Non-pharmacological therapy and BP-lowering medication if: target organ damage, CV/renal disease, diabetes, 10yr CV risk ≥10%	**Stage 1**	Non-pharmacological therapy and BP-lowering medication in combination ('poly-pill')	**Stage 2**	Non-pharmacological therapy and BP-lowering medication
≥160/100	**Stage 2**	Non-pharmacological therapy and BP-lowering medication	**Stage 2**	Non-pharmacological therapy and BP-lowering medication		
Systolic >180 Or diastolic >110	**Stage 3 (severe)**	Non-pharmacological therapy and BP-lowering medication	**Stage 3 (severe)**	Non-pharmacological therapy and BP-lowering medication		

In contrast to the findings of the Ettehad et al. meta-analysis, a 2018 systematic review by Brunstrom et al. showed evidence to the contrary, this time in a mostly primary-prevention population.(62) In their review, pooling results via a random effects meta-analysis rather than the fixed effects model used in the Ettehad review,(61) they found that while BP lowering was associated with a reduced risk for death and major cardiovascular events when systolic BP was 160mmHg or above, and between 140 to 159mmHg (RR, 0.93; 95% CI, 0.87-1.00 and RR, 0.78; 95% CI, 0.70-0.87 respectively), in trial populations with a baseline systolic BP of <140mmHg, treatment was not significantly associated with reduced mortality (RR, 0.98; 95% CI, 0.90-1.06) or reduced major cardiovascular events (RR, 0.97; 95% CI, 0.90-1.04).(62)

In addition to clinical outcomes, data concerning the adverse effects of intensive BP lowering are important in order to consider their full benefits and drawbacks.(63) Pooled data from studies that have included assessments of harms associated with lower treatment thresholds were assessed in a systematic review by Weiss et al. (2017).(64) Data regarding renal outcomes, cognitive impairment, quality of life measures and fall rates provide mixed results across the studies, and the heterogeneity of reporting and of reporting measures limited the ability of systematic review authors to combine data in meta-analyses.(64) However, data from the SPRINT trial (see Table 2) showed that lowering BP to a 120mmHg systolic target rather than a 140mmHg target resulted in a higher incidence of acute kidney injury or acute renal failure (HR 1.66, p=<0.001), hypotensive episodes (HR 1.70, p=<0.001) and syncope (HR 1.44, p=0.003).(60)

1.4.5 Hypertension treatment and management

Randomised controlled trials of blood pressure reduction

The first adequately powered, placebo controlled, randomised trials of blood pressure lowering were the Veterans Administration cooperative studies in 1967 and 1970.(65,66) These trials paved the way, both clinically and methodologically, for future trials of blood pressure lowering – some of which are summarised in Table 3. These trials have addressed some of the key questions in the field of hypertension treatment - the comparison of pharmacotherapy with placebo and of new pharmacotherapies with older treatments,(67) the contribution of dietary and lifestyle interventions on BP lowering,(68) and the thresholds for hypertension and treatment targets depending on relevant co-morbidities (such as diabetes) have all been explored to some degree to this point.(57) In addition, systematic reviews and meta-analyses have summarised the literature based on the above research areas. For instance, a 2009 systematic review aimed to determine the efficacy of different classes of blood pressure lowering drugs in preventing coronary heart disease (CHD) and stroke, and aimed to establish priority groups for treatment based on previous cardiovascular disease status and baseline BP.(32) The review found that all classes of blood pressure lowering drugs have a similar effect in reducing CHD events and stroke for a given reduction in blood pressure.(32)

Table 3 – Summary of key historical blood pressure lowering trials

Study	Year	Study information	Main conclusion
VA cooperative study phase 1 (65)	1967	Hydrochlorothiazide, reserpine, and/or hydralazine vs placebo in severe hypertension (diastolic BP 115–129 mmHg).	Reduction in diastolic BP could reduce mortality
Hypertension Detection and Follow-Up Program (69)	1979	Target driven and stepwise increases in therapy vs usual care (no target BP and flexible approach to up titrating care)	First study to demonstrate a mortality benefit (RRR 17%) of goal-directed BP targets and step-wise increases in BP treatment.
Medical Research Council Working Party Trial of treatment of mild hypertension (70)	1985	Treatment of mild hypertension in younger cohort (aged 35-64). 5 year follow-up	Significant reduction in stroke events and all CV events. No difference in all-cause mortality.
European Working Party for High BP in the Elderly (71)	1986	First major study of BP lowering exclusively in patients aged over 60yrs.	No significant difference in all-cause mortality.
Systolic Hypertension in the Elderly Program (SHEP) (72)	1991	First RCT investigating treatment of isolated systolic hypertension.	13% relative risk reduction in all-cause mortality, 36% RRR of stroke.
DASH - Dietary Approaches to Stop Hypertension (68)	1997	Trial of Mediterranean diet with or without salt restriction. Fruit and vegetables (9–10 servings/day), whole grain cereals, low fat dairy products and reduced saturated and total fat = DASH diet	Compared to the control with high salt diet, low salt reduced BP by 7.1 and 11.5 mmHg in normotensive and hypertensive participants, respectively.
Hypertension Optimal Treatment (HOT) trial (73)	1998	Compared benefits of lowering diastolic BP to 80 or 85 mmHg vs 90 mmHg on CV events.	No significant difference in lower diastolic levels. Diastolic threshold confirmed as 90 mmHg.
ALLHAT (67)	2002	Multi-arm trial of 42,000 patients comparing traditional treatment of thiazide-like diuretics vs ACE-I, CCB and A-Blockers.	No significant difference between the classes for primary outcome (fatal CHD or non-fatal MI).
ASCOT (74)	2005	Comparing calcium channel blockers plus ACE-inhibitors to B-blockers plus thiazide diuretics for control of blood pressure.	Lower CV events in CCB (amlodipine) plus ACE-I (perindopril) group.
ACCORD (57)	2010	Reduction of BP to <120mmHg vs 140mmHg systolic in diabetic population.	No significant difference in mortality, total CV events, or renal protection.
SPRINT (60)	2015	Reduction of BP to <120mmHg vs 140mmHg systolic in non-diabetic population.	27% reduction in all-cause mortality and 25% reductions in primary CV outcomes in lower BP group.

Current treatment

Diet and lifestyle

The treatment of patients identified as having raised BP follows a clearly defined path in the UK.(28) Diet and lifestyle modifications are recommended for all grades of hypertension and may include advice on: reduction of salt intake, increasing fruit and vegetable consumption, maintaining a healthy BMI, increasing exercise, and reducing alcohol and cigarette consumption.(28) At present, such advice are primarily delivered in general practice, where the majority of hypertension is detected and managed.(75)

A Cochrane review comparing average salt consumption (9-12g/day) with salt reduction (5-6g/day) found that reducing salt resulted in significant reductions in systolic BP (5.8 mmHg, 95%CI 2.5 to 9.2) in both hypertensive and normotensive individuals.(76) Furthermore, the Dietary Approaches to Stop Hypertension (DASH) study compared participants receiving 8-10 portions of fruit and vegetables per day, consuming whole grain cereals, low fat dairy products and reduced saturated and total fat, with those on a controlled diet (comparable to the average American diet), and showed an 11.4 mmHg (95%CI 6.9 to 15.9) reduction in systolic BP in the higher fruit and vegetable group (Table 3).(68) In addition to dietary approaches, regular exercise has been shown to reduce systolic BP by 4 mmHg or more,(77) and reductions in weight at rates of 1kg have been shown to reduce systolic BP in 1 mmHg increments.(78)

Pharmacological treatments

If healthy lifestyle advice alone leads to inadequate BP reduction, or if BP is sufficiently elevated to begin with, pharmacological treatment in the form of anti-

hypertensive medications are initiated.(28) Drug treatments for hypertension are available for generic prescribing in the UK and are some of the most widely prescribed drugs in general practice (Table 4).(79) They include Angiotensin Converting Enzyme Inhibitors (ACE-I, e.g. Ramipril or Lisinopril), Angiotensin II Receptor Blockers (ARBs, e.g. Candesartan or Losartan), Calcium Channel Blockers (CCBs, e.g. Amlodipine), Thiazide-like diuretics (e.g. Indapamide), and in some cases Beta Adreno-receptor blockers (B-blockers, e.g. Bisoprolol), Aldosterone antagonists (e.g. Spironolactone) and Alpha Adreno-receptor blockers (A-blockers, e.g. doxazosin).(28)

According to current NICE guidance, the first-line medication for patients under the age of 55 years is an ACE-I.(28) A troublesome dry cough occurs in approximately 10% of patients on an ACE-I.(80) If this or other side effects become intolerable to patients, the ACE-I is replaced with an ARB which are typically associated with fewer noticeable adverse effects.(81)

If target blood pressure is not reached with either an ACE-I or an ARB, second line therapy with a CCB is added - in particular, the Dihydropyridine CCBs such as Amlodipine or Felodipine.(28) The addition of a thiazide-like diuretic is the NICE recommended third line treatment for patients still not at blood pressure control after up titration of the first two pharmacological treatments. A fourth blood pressure lowering medication may be considered if clinic BP remains higher than 140/90 mmHg, and can include either Spironolactone, a Beta-Blocker or an Alpha-Blocker. If a patient's BP is still not adequately controlled after four anti-hypertensive medications (i.e. persistently >140mmHg systolic), and issues such as poor medication adherence have been checked with the patient, guidelines recommend

specialist advice to investigate possible ‘resistant hypertension’ or secondary causes.(28)

Genetic studies have shown that hypertensive patients over the age of 55 or those of African-Caribbean origin of any age are more likely to have so-called ‘low-renin hypertension’, meaning that medications acting on the Renin-Angiotensin system (ACE-I and ABRs) may be less effective and so are not first line therapies.(82) Instead, CCBs are used as first line, with ACE-I/ARBS as second line agents, followed by the same order of medications as per patients under the age of 55 years.

Table 4 – The most commonly used antihypertensive drug classes in England

Drug class and example (79)	**World Health Organisation Defined Daily Dose* (DDD)** (83)	**Expected BP reduction for DDD (mmHg, 95% CI)** (84)
Calcium Channel Blockers (Amlodipine)	5mg	Systolic 8.8 (8.3 to 9.2) Diastolic 5.9 (5.6 to 6.2)
Angiotensin Converting Enzyme Inhibitors (Ramipril)	2.5mg	Systolic 8.5 (7.9 to 9.0) Diastolic 4.7 (4.4 to 5.0)
Angiotensin II Receptor Blockers (Losartan)	50mg	Systolic 10.3 (9.9 to 10.8) Diastolic 5.7 (5.4 to 9.0)
Thiazide-like diuretic (Indapamide)	2.5mg	Systolic 8.8 (8.3 to 9.4) Diastolic 4.4 (4.0 to 4.8)

*refers to the DDD of the example drug from the table

Although treatments are primarily administered by GPs, the clear and protocol-driven nature of uncomplicated hypertension treatment means that pharmacists are

well placed to take on the management and up titration of antihypertensive therapies, given their medication and drug-monitoring expertise.(85)

Organisation of hypertension care

In the UK, the diagnosis and management of hypertension is predominantly undertaken in primary care, specifically, in general practice.(28) Elevated BP is usually detected through opportunistic screening in general practice.(86) NICE guidance recommends that a diagnosis based on clinic readings should be confirmed with ABPM or HBPM, using the protocols stated in section 1.4.3 previously.(28) After diagnosis, patients are recommended to monitor their BP at home on a monthly basis given the strong evidence for improved BP outcomes in doing so.(87) In patients with resistant hypertension, or hypertension with secondary causes, GPs are recommended to refer to specialists for further investigations and treatment recommendations.(28) Depending on the patient and the severity of the situation, continuation of care is either returned to general practice (usual care) or maintained in hospital outpatient clinics with an endocrinologist or cardiologist.(28)

Some blood pressure testing occurs in pharmacies also, though it is mainly reserved for screening undiagnosed patients on an ad-hoc basis rather than for the ongoing monitoring or management of hypertensive patients (see Table 1).(88)

1.4.6 A role for community pharmacists in hypertension management

The need for new models of care that include pharmacists

Demand for consultations in general practice has increased steadily over the past decade as a result of an aging population and a population living with more co-morbidities than ever before.(89) This increase in demand has not been matched by GP numbers which have decreased relative to population size for the first time since the 1960s in recent years.(90) There is therefore a clear mis-match in the current primary care model, with potential implications for patients with long-term conditions, such as hypertension, that require regular follow-up.

Health policy documents have acknowledged the potential for greater involvement of community pharmacists to bridge the gap between supply and demand in primary care. For instance, in 2014, NHS England published its 'five year forward view', a broad plan for the future of the NHS highlighting the actions that should be prioritised over the next five years.(91) In relation to primary care and community pharmacy, the forward view stated that there was a need to better integrate general practice with pharmacies and other disciplines in order to create *"Multispecialty Community Providers".*(91) Furthermore it stated the need for *"far greater use of pharmacists"* and in helping patients make more appropriate use of community pharmacies. The document did not, however, state how this should occur in practice.

In 2016, the community pharmacy sector published the 'Community Pharmacy Forward View' in response to the NHS and GP forward view documents.(92) The report set out pharmacy's intention to be *"the facilitator of personalised care and support for people with long-term conditions".* To achieve this, one of the

recommendations stated that patients could register with a specific pharmacy in order to facilitate continuity of care and a higher quality service for the management of long-term conditions in the future. Other reports and recommendations have been published by the Royal Pharmaceutical Society,(93) and the Chief Pharmaceutical Officer,(94) advocating ‘a greater clinical role’ for community pharmacy. However, again, no specific plan, timeline or funding stream for implementing this vision were outlined.

In 2016/17 NHS England and the Department of Health implemented a 6% drop in funding for the community pharmacy sector (£170m), followed by a further 6% cut in 2017/18.(95) This has resulted in 140 pharmacy closures to date and reductions in service provision such as free medication deliveries to the elderly – an apparent contradiction to the stated aims of the policy documents mentioned previously.(96) In addition, the 2019 “NHS long term plan” has provided little detail with regards to the future of community pharmacies in providing clinical services.(97) These factors have meant that the sustainability of many pharmacies is currently in question, with unclear consequences on future service development.

Despite these apparent uncertain conditions for the development of community pharmacy services, in the context of the growing strain on primary healthcare systems,(98) pharmacists have been described as an “*untapped resource”* and a potential solution to the workforce problem.(99) There are approximately 12,000 community pharmacies in England,(100) and their distribution within communities,(101) and the ability to see a pharmacist without an appointment,(102) make them a setting with the potential to deliver the care and follow-up required for hypertensive patients (see section 1.4.5 below). A large proportion of patients collect their medications from pharmacies on a monthly, two-monthly or quarterly

basis and thus present at regular intervals.(103) This may be in addition to other occasions where they may present for retail purposes or on behalf of others, making pharmacies one of the most frequently accessed healthcare settings.

Overall, the skills and abundance of pharmacists, coupled with their convenient community locations, suggest they have the potential to deliver hypertension management services in the community to meet the unmet clinical need.

Guidance on pharmacy-based hypertension management

In 2005, the World Health Organisation (WHO) produced a guideline proposing a community pharmacy-based hypertension model intended for use in any country.(104) The model consisted of three levels, where level 1 and 2 related to prevention and early detection of hypertension, and level 3 to ongoing hypertension monitoring. While the WHO stated that the model could be used in any country, it also acknowledged that every country has different legislation, populations, health priorities, available resources and skills, and therefore it did not envisage a uniform 'model' to be applicable to every region. The goals of the community pharmacy model were as follows:(104)

- To monitor patients with hypertension on treatment and to refer to the GP those who do not achieve adequate blood pressure control.
- To identify possible medication related problems and report them to the GP.
- To obtain and reinforce informed compliance.
- To provide health education to patients with hypertension about necessary lifestyle modifications.
- To advise on treatment regimen to patients with hypertension.
- To teach about self-measurement of blood pressure.

The model states the importance of the pharmacist's involvement in the follow-up of hypertensive patients, particularly between patient visits to the doctor, in order to complement the physician's role.(104) In addition to the general goals of the model, the WHO also attempted to provide guidelines for implementing this model and states the following as important factors to consider or have in place:

- Close cooperation with the local GPs.
- Consideration of the pharmacist's time and impact on their other tasks.
- Provision of relevant training, checklists and necessary forms.

To date, figures related to the uptake of the 'model' or evaluations of this programme are not readily available to examine and so its uptake, ease of implementation and efficacy are yet to be ascertained.

The section that follows presents the results of a review of community pharmacist-led hypertension management randomised controlled trials, in order to, firstly, explore the existing evidence of effectiveness pharmacist management, and secondly, to investigate the intervention models used.

1.5 Community pharmacist-led hypertension management - evidence of effectiveness

Section 1.4.1 presented data from the health survey for England that highlighted shortcomings with regards to hypertension detection, management and follow-up. Section 1.4.6 stated that with GPs already stretched to capacity, increasing the role of community pharmacists may be one solution to address these shortcomings. Together with the figures from Public Health England that hypertension-related appointments make up around 10% of GP consultations each year,(105) these sections point towards a hypothesis that community pharmacists could be utilised to manage the hypertension case load.

In order to assess whether community pharmacist-led interventions to reduce BP have been successful in the past, the evidence-based medicine hierarchy states that systematic reviews of randomised controlled trials are the 'gold standard' methodology to consult.(106) At the start of this thesis, RCTs of community pharmacist-led interventions to reduce BP were summarised in a systematic review by Cheema et al. (2014), identifying 16 RCTs.(107) Table 5 provides a summary of each study and their respective interventions.

Patients were recruited into the trials either via referral from their GP or opportunistically when presenting to the pharmacy to collect their medication. Interventions most commonly involved providing face-to-face consultations with patients in the pharmacy as well as providing feedback and results to the patient's GP to implement the necessary changes. The transfer of this information from community pharmacies to general practice occurred through letters or faxes to the

practice, via the patient verbally, or through email and telephone communication with the practice. All studies required the community pharmacist to either measure blood pressure in the pharmacy or to interpret readings before making clinical recommendations, however the threshold of ‘high’ or ‘normal’ BP varied between the studies (see Table 5).

In general, the interventions delivered by pharmacists were medication-related and included: establishing and improving adherence to BP medications, identification of drug related problems and side effects, making recommendations regarding medication choices to lower BP, and healthy diet and lifestyle advice including alcohol reduction and referral to smoking cessation schemes. Pharmacists received up to two days of training at the start of the trials to deliver the consultations.

Patients were required to report to their pharmacist every month or every two months throughout the study period. The time spent with each patient ranged from 5mins up to 60mins per consultation (Table 5). While more intensive interventions have been shown to result in better blood pressure outcomes than less intensive interventions in the literature,(108) the knock-on effect on other pharmacy tasks and services was not quantified in these RCTs.(107)

Finally, pharmacists made judgements as to whether the patients should be referred back to their GP – most commonly to implement the pharmacist’s recommendations. Therefore although described as ‘community pharmacist-led’ management of hypertension, none of the studies culminated with the community pharmacist implementing the medication or dosage changes themselves, therefore some form of co-intervention with the GP may have occurred in practice.

Across the RCTs, pooled systolic BP reductions in the pharmacy intervention arms were 6.1 mmHg lower than in the usual GP care groups (95% CI -8.4 to -3.8), with 'moderate' statistical heterogeneity observed in the meta-analysis (I^2=36%). In context, this level of BP lowering could equate to a risk reduction for coronary heart disease and stroke of 10% and 20% respectively.(32)

Table 5 – BP lowering randomised controlled trials based in community pharmacies – from Cheema et al (2014).(67)

Study details	Setting and country	Sample size (intervention/ control) and population	Components of pharmacist intervention	Intensity of intervention and follow-up duration	Method of communicating with/referring to GPs	BP threshold in the pharmacy	Mean systolic BP difference (mmHg, 95% CI)
McKenney et al, 1973 (109)	Community pharmacies (United States)	n=50 (25/25) Adults with hypertension	Patient education including advice on diet, physical activity, identification of drug related problems.	Monthly 6 minute consultations for 5 months.	Letters and verbal discussions	Diastolic BP <90 mmHg	-13 [not reported]
McKenney et al, 1978 (110)	Community pharmacies (United States)	n=136 (70/66) Adults with hypertension	Patient education including advice on diet, medication adherence, identification of drug related problems.	Frequency not stated (4 month duration)	Not stated	Not stated	–3.6 [–11.90 to 4.70]
Park et al, 1996 (111)	Community pharmacies (United States)	n=53 (27/26) Adults with hypertension	Blood pressure and heart rate assessments, counselling on lifestyle modifications and drug therapy.	Monthly for 4 months	Not stated	Not stated	–13.0 [–27.66 to 1.66]
Blenkinsopp et al, 2000(112)	Community pharmacies (United Kingdom)	n=180 (101/79) Adults with hypertension	Patient education, monitoring of pharmacological treatment - identification of drug related problems and advice to improve medication adherence.	Every 2 months for 6 months, lasting 7-12mins per consultation.	Speak to GP or refer patient directly.	<160/90 mmHg	Not reported
Garcao et al, 2002 (113)	Community pharmacies (Portugal)	n=82 (41/41) Adults with hypertension	BP monitoring, assess adherence to treatment, prevent, detect, and resolve drug-related problems, encourage non-pharmacological measures for blood pressure control	Monthly for 6 months	Not stated	Not stated	–18.3 [–29.90 to –6.70]

Sookaneknun et al, 2004 (114)	Community pharmacies (Thailand)	n=235 (118/117) Adults with hypertension	BP monitoring. Patient education - advice on diet, physical activity. Identification of drug related problems.	30-50 minutes monthly for 6 months	Letter sent to GP	<135/85 mm Hg	–4.6 [–9.36 to 0.04]
Zillich et al, 2005 (115)	Community pharmacies (United States)	n=117 (57/60) Patients with uncontrolled BP at baseline	Training in home blood pressure monitoring and giving recommendations to GP based on these. Patient education on high blood pressure, disease management, medication adherence, lifestyle advice.	4 pharmacy consultations in 3 months lasting 15 to 60 minutes.	Email with telephone follow-ups for clarification.	<140/90 mmHg (home blood pressure)	–4.6 [–13.38 to 4.18]
Fornos et al, 2006 (116)	Community pharmacies (Spain)	n=112 (56/56) Adults with type 2 diabetes	Patient education – advice on improving medication adherence, identification of drug related problems, diet, alcohol, physical activity.	Monthly for 13 months	Paper-based forms sent to GP	<140/90 mmHg	-10.0 [–19.92 to –0.08]
Krass et al, 2007 (117)	Community pharmacies (Australia)	n=289 (149/140) Adults with type 2 diabetes	Glucose self-monitoring training, adherence support, medication review, and diabetes self-management, lifestyle information focusing on physical activity and weight loss.	5 consultations over 6 months	Paper-based forms sent to GP	<130/80 mmHg	–4.8 [–9.53 to –0.07]
McLean et al, 2008 (118)	Community pharmacies (Canada)	n=227 (115/112) Adults with diabetes who had BP higher than 130/80mmHg	Reviewing BP as a risk factor, discussing the causes and consequences of high BP, explaining the effect of diabetes on high BP, and focusing on the lifestyle strategies the patient could undertake to improve BP. Team based care with nurses.	6-weekly intervals for 6 months	Faxed notes to GP	<130/80 mmHg	-5.6 (SD 2.1)
Doucette et al, 2009 (119)	Community pharmacies (United States)	n=78 (36/42) Adults with type 2 diabetes	Discussing medications, clinical goals, and self-care activities with patients and recommending medication changes to physicians when appropriate.	Every 3 months for 12 months	Faxed notes to GP	<130/80 mmHg	2.6 [–4.62 to 9.82]

Planas et al, 2009 (120)	Community pharmacies (United States)	n=52 (32/20) Adults with hypertension and diabetes	Patient education – diet and exercise advise. Monitoring of pharmacological treatment. Recommendations to physicians.	Monthly for 9 months	Not stated	<130/80 mm Hg	-14.6 (not stated)
Santschi et al, 2011 (121)	Community pharmacies (Canada)	n=89 (48/41) Adults with chronic kidney disease.	Medicines optimisation, information on the use of over-the-counter drugs and natural products	Month for 2 months, and then every 3 months for the remaining 12 months	Letter sent to GP	<130/80 mmHg in nurse-measured clinic	−11.6 (−21.3 to −1.8)
Ali et al, 2012 (122)	Community pharmacies (United Kingdom)	n=46 (23/23) Adults with diabetes	Diabetes education, medicines use review, lifestyle modification counselling. HbA1c, BMI, blood pressure, blood glucose and lipid profile measurements.	6 consultations in 12 months	Not stated	Not stated	−23.00 [−42.92 to −3.08]
Amariles et al, 2012 (123)	Community pharmacies (Spain)	n=714 (356/358) Adults with >1 drug for CVD or CV risk factor	Interviewing the patient and reviewing the drug and clinical records - drug history and results of clinical laboratory tests. Evaluate drug therapy goals (e.g BP lowering), personalised interventions.	5 consultations in 8 months	Intervention assessment forms sent to surgery.	<140/90 mmHg or <130/80 in presence of risk factors	−6.50 [−8.83 to −4.17]
Svarstad et al, 2013(124)	Community pharmacies (United States)	n=576 (276/300) Adults with hypertension.	Pharmacist and pharmacy technician teams implemented brief medication questionnaires, toolkits for enhancing medication adherence and provided pharmacist feedback to patients and physicians.	6 consultations in 12 months	Fax letter to GP	<140/90 mm Hg	−7.31 [−10.70 to −3.92]

1.5.1 Certainty of evidence from the randomised controlled trials

Although systematic reviews and meta-analyses of RCTs are considered to be the 'gold standard' for evaluating clinical interventions,(106) it is important to consider the applicability of RCT designs in the context of pharmacy practice research. For instance the inability to blind patients and practitioners to either the pharmacist intervention or usual care arm of a trial can introduce bias in the results.(125) As such, the 'quality' of evidence from the RCTs of community pharmacist interventions may be downgraded at the outset when compared to other intervention trials. Despite this, the quality assessment conducted in the Cheema et al. review showed that the 16 RCTs performed well across the Cochrane risk of bias assessment criteria.(107,126) Beyond the risk of bias for individual studies alone however, it is also important to consider the 'certainty' or strength of evidence presented in a review so as to make practical judgements regarding their conclusions.(127)

The Grades of Recommendation, Assessment, Development and Evaluation Working Group (GRADE) have developed an approach to grade the 'certainty' of evidence and their recommendations for individual outcomes in a systematic review or guideline.(128) The process assesses the following:

- Methodological flaws within the component studies.
- Consistency of results across different studies.
- Generalisability of research results to the wider patient base.
- How effective the treatments have shown to be.

GRADE specifies four levels of evidence ‘certainty’ - high, moderate, low, and very low.(127) The overall certainty of recommendations can be downgraded based on the following factors, classed as exhibiting ‘very serious’, ‘serious’ or ‘not serious’ biases:

- Limitations in the design and implementation of available studies suggesting high likelihood of bias.(129)
- Indirectness of evidence (in relation to population, intervention, control and outcomes).(130)
- Unexplained heterogeneity or inconsistency of results.(131)
- Imprecision of results.(132)
- Other considerations such as publication bias, effect size, confounding and/or a dose-response gradient.(133)

Evidence from 11/16 RCTs included in the meta-analysis of community pharmacist-led hypertension management were assessed via the GRADE criteria to assess the ‘certainty’ of the systolic and diastolic blood pressure results. The initial definition of ‘certainty’ for GRADE evaluations was thought to reflect the evaluator’s confidence in the point estimate for a particular outcome (in this case 6.1 mmHg reduction in systolic BP).(134) The GRADE working group have since clarified that the ‘certainty’ classification is a *“rating of how certain we are that the true effect lies within a particular range...”.*(134) The GRADE evaluation was therefore conducted with the clarified definition in mind.

The overall ‘certainty’ of evidence was classified as ‘moderate’ for both the systolic BP results and the corresponding diastolic BP results (Table 6). The certainty of evidence was downgraded from ‘high’ to ‘moderate’ due to concerns regarding the

‘directness of the evidence’ in relation to differences in intensity of interventions and follow-up durations used across the studies (see Table 6 for further details).

Overall, these results suggest that the previous RCTs of community pharmacist-led BP lowering provide a sound foundation from which to build this thesis’ investigation. The results also suggest that the addition of further evidence of effectiveness at this stage is unlikely to alter the conclusions of the Cheema at el. meta-analysis, and that work in relation to implementating existing interventions may be more pertinent than developing a new intervention.

Table 6 – GRADE of Cheema et al. systematic review BP outcomes

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Consistency (I^2)	Directness (study PICO)	Imprecision (95% CI)	Other considerations	Pharmacist care group	Usual care	Relative (95% CI)	Absolute (95% CI)		
Outcome - Systolic BP –6.13 [95% CI –8.44 to –3.81]												
11	Randomised trials	Not serious	Not Serious (36%)	Serious	Not serious –6.13 [95% CI –8.44 to –3.81]	Not serious[b]	1106	1134	MD 6.13mmhg lower (8.44 lower to 3.81 lower)	-	⊕⊕⊕◯ Moderate (*"The true effect is probably close to the estimated effect"*) (95)	Important
Outcome - Diastolic BP –2.51 [95% CI –3.46 to –1.55]												
11	Randomised trials	Not serious	Not serious (0%)	Serious	Not serious –2.51 [95% CI –3.46 to –1.55]	Not serious[b]	1106	1140	MD 2.51mmhg lower (3.46 lower to 1.55 lower)	-	⊕⊕⊕◯ Moderate (*"The true effect is probably close to the estimated effect"*) (95)	Important

CI: Confidence interval; **MD:** Mean difference; **PICO:** Population, Intervention, Comparator, Outcome(s); **I^2:** measure of statistical heterogeneity

[b] Publication bias not calculated

1.6 Implementation theory and evidence gaps

To date, the evidence from these RCTs has not translated into UK pharmacy practice.(11) This is despite demonstrating both clinically and statistically significant reductions in systolic BP over usual GP care.(107) Across healthcare, services and interventions that have been shown to improve patient outcomes in RCTs have not always translated into clinical practice.(135) This thesis aims to investigate the extent to which the interventions from previous RCTs of community pharmacist-led hypertension management are translatable to current pharmacy practice in England.

In a review summarising the key factors that limit the translation of research into practice, the following general barriers were identified by Glasgow et al:(136)

1. The context of intended target setting – competing demands on the clinician's time; a programme imposed from an external body; limited resources to deliver.
2. The intervention characteristics – intensive time demands; specific training and expertise required; lack of adaptability of interventions to local needs; the high cost of intervention delivery.
3. Research design – non-representative samples and settings; no economic evaluation; no assessment of implementation prior to introduction; failure to evaluate sustainability of delivering the intervention.

In addition to the factors summarised by Glasgow et al. the use of specific implementation science theories can help to guide the direction of this work in a systematic manner.(137) The role of implementation science can be to:

1. Describe the process of translating research into practice.
2. Understand or explain the factors influencing implementation outcomes.
3. Evaluate implementation.(138)

Nilsen (2015) highlighted the most frequently cited frameworks in a review of implementation science literature.(138) Of these, the Consolidated Framework for Implementation Research (CFIR) is most relevant to this thesis' investigation.(139) The CFIR acknowledges that many therories and frameworks have been developed over the years that overlap considerably, and that reviewing these to select the most appropriate one can be challenging. It therefore amalgamates 20 different sources, theories and frameworks to create one construct that can be applied to a variety of contexts and uses.(140) The CFIR includes five overarching domains:

1. The individuals involved – understanding the views of the people who are tasked with delivering the intervention.
2. The intervention characteristics – describing what the individuals involved in delivering the intervention have to do, and how often they have to do it.
3. The inner setting – the context through which the implementation process will proceed within that setting.
4. The outer setting – the economic, social, and political context within which the organisation/setting resides.
5. The process of implementation – the process of change aimed to achieve individual and organisational level use of the intervention.(139)

The CFIR is most commonly applied to studies that 'evaluate implementation', focussing on both initial implementation and longer term sustainability. For example, the CFIR was used to evaluate a large-scale weight management programme in

Veteran Affairs medical centres using semi-structured interviews with stakeholders.(141) The domains of the CFIR were sub-divided into ‘constructs’ or categories, and these were used to code the interviews, with each category’s influence on implementation rated as ‘high’ or ‘low’.(141) Categories such as developing networks and communication with other areas of healthcare (inner setting) and the strength of evidence showing clinical benefit (intervention characteristics) were reported as factors suggestive of an intervention that is more likely to be successfully implemented. In addition to ‘evaluating implementation’, the domians of the CFIR are also versatile enough to be used when trying to ‘understand or explain the factors influencing implementation outcomes’, and this is the context for its application in this thesis.

Overall, both the CFIR framework and the work of Glasgow et al highlight the importance of identifying and analysing the individual components of interventions in order to investigate their implementation potential. As described in section 1.5, patients were either recruited for the studies opportunistically as they presented to the pharmacy to collect their prescription, or would present to the pharmacy after a direct referral from the GP. The clinical components of the intervention was then composed of three main parts. These included an assessment of BP in the pharmacy followed by the provision of tailored medication and lifestyle advice/counselling to the patients based on their BP results. Finally, the pharmacists would make a judgement as to whether they could follow the patient up themselves at a later date, or whether the patient required the GP’s input. Figure 1 below summarises the typical clinical pathway for patients taking part in the RCTs of community pharmacist-led hypertension management from the Cheema et al review.

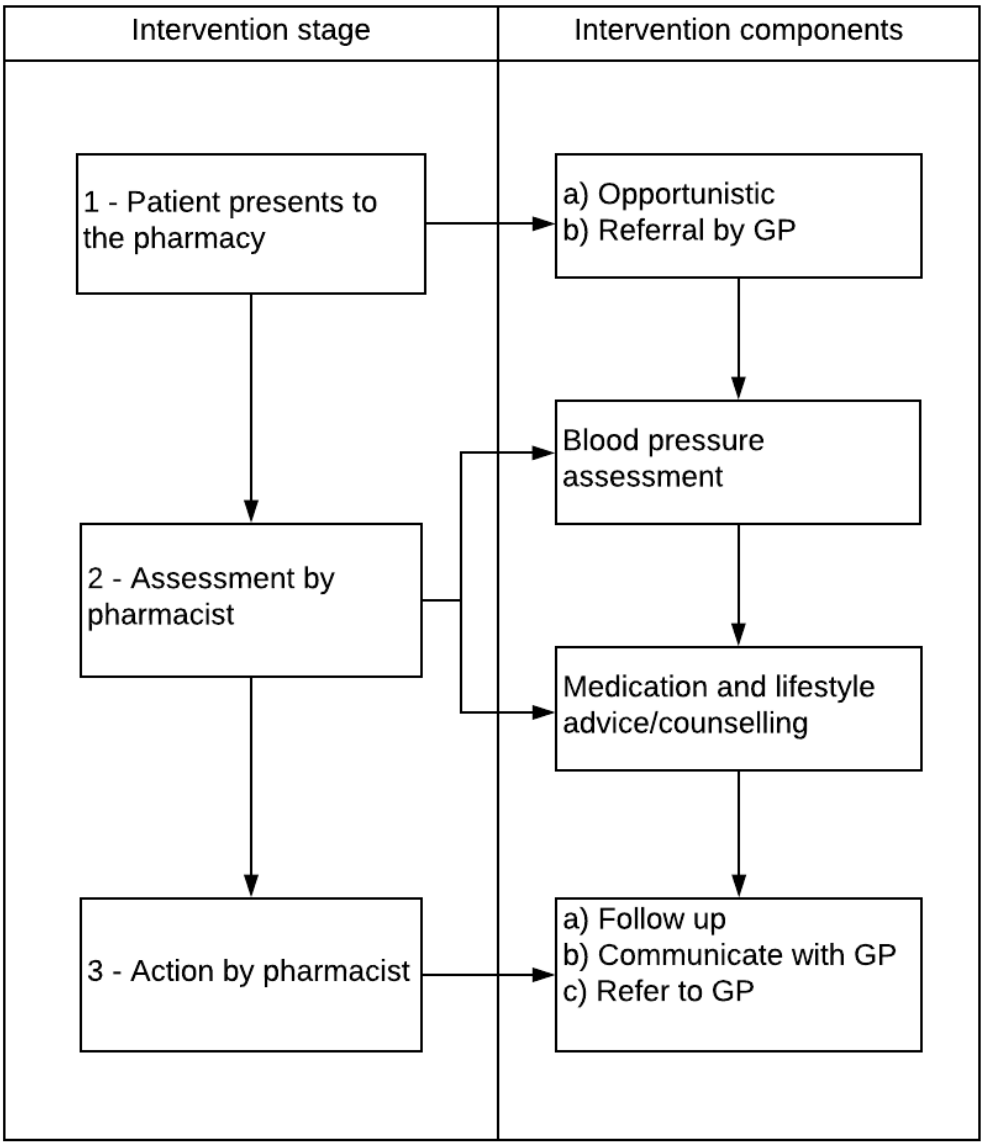

Figure 1 - Summary of the common model of intervention used across the RCTs of community pharmacist-led hypertension management

The series of interventions from the previous RCTs, prompted by the use of implementation theory, will therefore be used to guide the investigation of this thesis. These led to research objectives which are outlined and justified below.

1.6.1 Delivering hypertension management in pharmacies

The delivery of extended clinical services in community pharmacy has previously been explored in a study that gained the views of both pharmacists and GPs.(142) It found that pharmacists were broadly supportive of extended patient-facing roles but at the same time, stated that they did not want 'lines to be blurred' between their role and that of the GP. The study also described the perceived 'subordinate' position of pharmacists within the healthcare structure, and described GPs (as the 'dominant' medical occupation) as adopting exclusionary strategies towards the clinical expansion of pharmacists as a form of protectionism or demarcation of their own role. This study did not focus specifically on hypertension services, however. Subsequent studies have discussed the implementation of hypertension services in pharmacies in particular.(143,144) They highlight general factors such as the sustainability of extended pharmacist roles due to a lack of financial incentives, and a lack of collaboration with GPs as contributing factors to the lack of implementation of hypertension services.(143,144) More specific operational and context-specific considerations regarding the delivery of hypertension management in pharmacies, such as methods for communication and information sharing, and the interaction with the newer role of general practice based pharmacists, have not been well studied from the perspective of UK community pharmacists in the context of hypertension management. Furthermore, the extent to which pharmacists are willing to deliver these services in practice requires investigation.

The intervention components from the previous hypertension trials (Figure 1) can be placed into real-world context through discussion with the pharmacists who may be expected to deliver such services in the future. The CFIR highlights the

importance of understanding the views of the people who are tasked with delivering the intervention,(140) and further lends weight to an initial study within this thesis to set the context for a future hypertension management service in pharmacies.

This thesis will therefore examine the views and experiences of pharmacists on delivering hypertension management in community pharmacies and aim to better understand the barriers and facilitators to hypertension service implementation in this setting (Chapter 2). Specifically this work will focus on aspects not examined in previous studies including communication, information sharing, and the role of the GP based pharmacist i.e. practical factors beyond the intervention itself that require consideration for the service to be implemented.

1.6.2 Measuring blood pressure in pharmacies

All trials included in the systematic review by Cheema et al. (Table 5) required the community pharmacist to either measure blood pressure in the pharmacy or interpret readings before making clinical decisions.(107) Across these 16 RCTs, pharmacy BP thresholds varied from 135/85 mmHg,(114) 140/90 mmHg,(108,145) to 160/90 mmHg,(112) among non-diabetic cohorts. In current practice, BP measured in pharmacies is interpreted in line with the 140/90 mmHg threshold as suggested by the Royal Pharmaceutical Society,(146) and the World Health Organisation.(104) This recommendation, however, is not based on evidence from diagnostic accuracy studies comparing the relationship with other measurement modalities. Instead, it appears to make the assumption that pharmacies, as clinically related settings containing a healthcare professional, would be associated with a

similar ‘white coat’ effect as documented during GP measurements.(147) There is, however, reason to believe that the healthcare professional taking the BP reading may have an influence on the measurement. For example, a previous systematic review and meta-analysis examining differences between BP readings taken by a nurse and doctor (in the same setting) suggests systolic BP readings taken by nurses could be as much as 7 mmHg lower than those taken by a doctor.(148)

To date, there has been one systematic review that has attempted to compare pharmacy-measured BP with that of doctor-measured and home/ambulatory BP, and found 3 eligible studies in 2010.(149) No meta-analysis was possible due to lack of data and heterogeneity, therefore the clinical interpretation of pharmacy-measured BP is still unknown.

The potential clinical consequences of using different BP thresholds are over-treatment if the threshold is too low - leading to a potential increase in medication side effects, or under treatment if the threshold is too high - leading to an increase in preventable CV risk. The ability to reliably interpret BP readings in the context of what is known about clinic (140/90 mmHg) or out of office (135/85 mmHg) thresholds is therefore required for reliable clinical decision making for pharmacists. The prominence of BP measurement and interpretation in the previous RCTs (the first part of the assessment by pharmacists, Figure 1) adds further justification for a research study on this topic. This thesis will therefore investigate how pharmacy-measured BP readings compare to those taken in a GP clinic or via home/ambulatory BP monitoring, combining data from previous comparative studies in a systematic review and meta-analysis (Chapter 3).

1.6.3 Advice and counselling for hypertension

The successful interventions in the RCTs of community pharmacist-led hypertension management included the provision of medication and lifestyle advice/counselling (Figure 1).(107) Pharmacists gave recommendations in response to drug-related problems and side effects, recommended additional medications to lower BP, and gave healthy diet and lifestyle advice including alcohol reduction and referrals to smoking cessation schemes. Previous research has explored community pharmacists' experiences of providing lifestyle advice to patients with cardiovascular disease.(150) Pharmacists were reported to be reluctant to give lifestyle advice due to concerns about discussing sensitive topics such as weight, alcohol consumption and dietary intake, despite acknowledging that such conversations were part of their role as a community pharmacist. More broadly, community pharmacies in both the UK and across Europe conduct commissioned services that provide an opportunity to discuss diet, lifestyle and medication usage in patients with a long-term condition.(151) In England, this service is called the NMS (see section 1.3.2 and Chapter 4 for further details on the NMS).(13,152) NMS consultations are recorded via a paper-based system held in individual pharmacies.(153) This makes aggregated, national-level, information about the advice provided by pharmacists in current practice difficult to assess. The CFIR states that the intervention characteristics of trials should be examined in order to assess their implementation potential, and one way of doing this is to understand how the trial interventions compare to current practice.

Given the importance of providing medication and lifestyle advice and counselling for hypertension management, as evidenced in the successful trial interventions

(Table 5), an understanding of community pharmacist's current practice of this may provide insight into how (if at all) the previous trial interventions could be adapted to facilitate implementation. Chapter 4 therefore aims to examine the advice and counselling provided by pharmacists to hypertensive patients in routine practice by exploring the content of consultations conducted as part of the NMS in England.

1.6.4 Ongoing management of patients in pharmacies – referral or follow-up

All 16 RCTs of community pharmacist-led hypertension management culminated in either a recommendation to attend a follow-up appointment with the pharmacist or a referral to general practice (see Figure 1).(107) Current guidance available to practicing pharmacists from the RPS and the WHO make specific reference to referral to general practice in the context of high BP readings (>140/90mmHg) only.(104,146) Pharmacists are therefore expected to use their discretion when deciding when to refer hypertensive patients for reasons other than elevated blood pressure.

Previous research exploring the views of pharmacists considering either follow-up or referral to GP found that the lack of a clear referral pathway (i.e. the reasons they could refer for and what they may be expected to manage themselves) made the process challenging. Pharmacists stated that these barriers made them less likely to engange with additional clinical responsibilities.(154) Some data exist regarding the referral of patients from pharmacy to general practice in the context of various 'minor ailments' such as upper gastrointestinal symptoms,(155,156) as well as on elevated CVD risk calculations and BP levels (>140/90 mmHg).(157) However, the

types of presentations that pharmacists refer back to GP in the context of hypertension management is not well defined in the literature. A better understanding of the hypertensive patient groups most commonly associated with referral could contribute to the refinement of the interventions from previous RCTs in order to reduce referrals and subsequent workload on GPs.

Chapter 5 of this thesis will therefore investigate the reasons that pharmacists state for referring hypertensive patients to their GP and establish predictors for referral of hypertensive patients from pharmacies to general practice within the NMS service for hypertension.

1.7 Thesis structure

Thesis objectives

A summary of the thesis' objectives is presented below:

1. Explore the views and experiences of pharmacists regarding the delivery of hypertension related care, and understand the barriers and facilitators to hypertension service implementation in community pharmacies (Chapter 2).
2. Understand how pharmacy-measured blood pressure compares to other measurement modalities recommended in the NICE guidelines for hypertension (Chapter 3).
3. Understand the content of consultations between pharmacists and hypertensive patients drawing on data from a currently commissioned service - the New Medicine Service (NMS) in England (Chapter 4).

4. Establish predictors for referral of hypertensive patients from pharmacies to general practice during the NMS for hypertension (Chapter 5).

Sections 1.6.1 to 1.6.4 presented the research gaps that have emerged through the investigation of previous RCTs (summarised by the Cheema et al systematic review) and from previous hypertension literature, and was guided by the CFIR framework. Figure 2 below therefore depicts how the individual study chapters in this thesis relate to components of the trial interventions previously described, and presents the corresponding research questions that will be addressed in each.

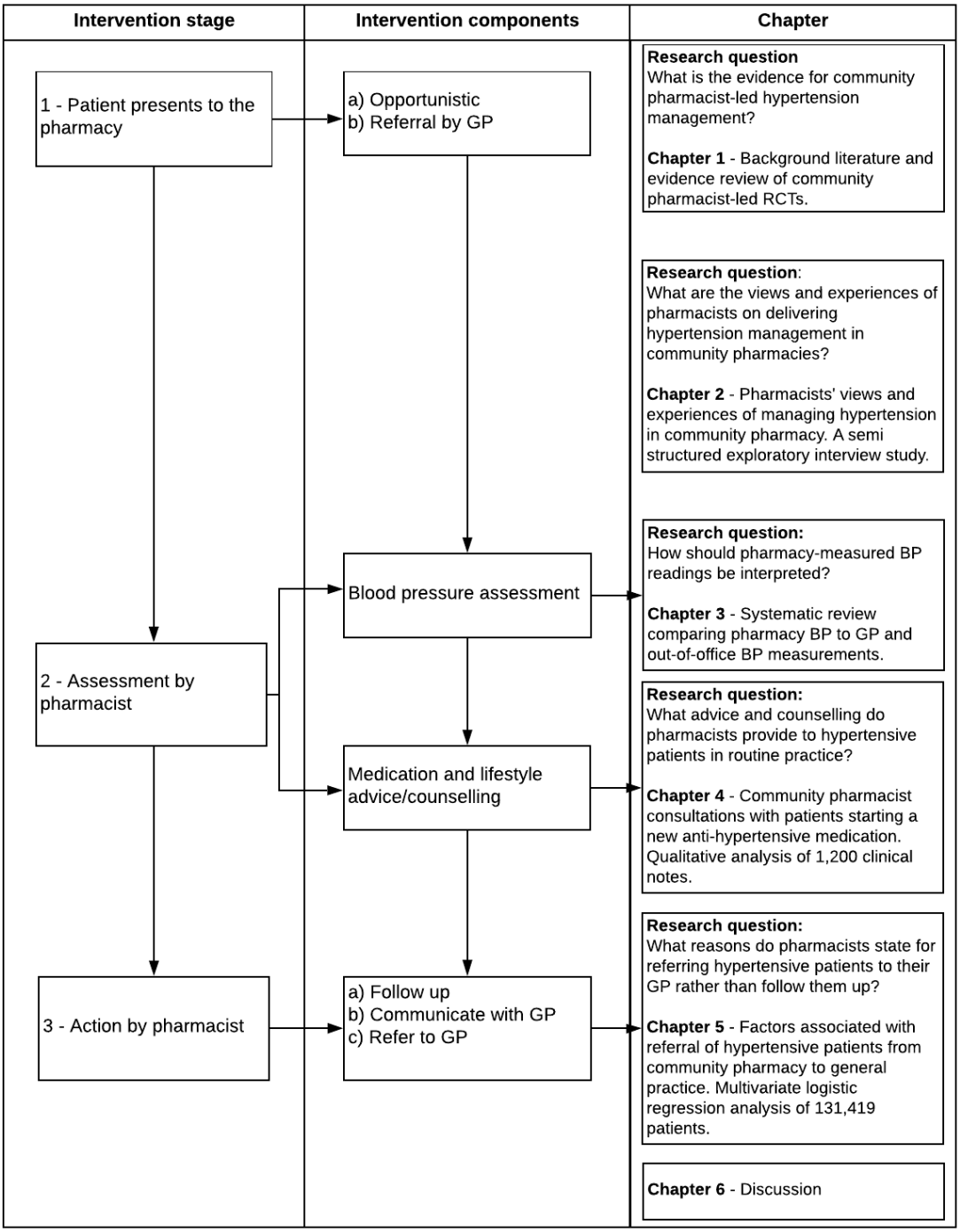

Figure 2 - Thesis structure in relation to previous trial interventions

1.8 Rationale for methodological approach

There are three broad research paradigms that cover the spectrum of approaches to answering research questions – qualitative approaches, quantitative approaches and mixed methods.(158) For the purposes of addressing the aim and objectives of this thesis, a mixed methods approach is used. Mixed methods studies combine both quantitative and qualitative components to answer a research question. The logic behind such an approach states that the respective components can complement each other to provide a comprehensive understanding of a topic – a concept termed 'triangulation' or 'convergence' by *Denzin* (1978).(159,160)

A mixed methods approach is pragmatic – the principle being that the researcher selects the most appropriate methodology to answering a research question rather than having an allegiance with a specific methodology.(161) For instance, when aiming to understand the context of working in a community pharmacy and establishing barriers and facilitators to new service development, qualitative methods may be more appropriate than quantitative methods. However, for analysing associations between interventions and clinical outcomes, quantitative research methods may be more suitable.(159)

Further reasons for including qualitative work with quantitative studies were identified by Greene et al. (1989),(162) and their relation to the chapters in this thesis are highlighted in parentheses:

- Expansion – the first phase of research may require qualitative explanation, or other previous findings may require either explanations or quantification. (Chapter 2 and 4)

- Exploration – an initial phase study to develop an intervention or develop hypotheses for future testing. (Chapter 2)
- Completeness – offsetting the inherent weaknesses of using one study design over the other (Chapter 2 and 4).

The overall rationale for the approach this thesis takes is to build on the existing evidence from RCTs of clinical effectiveness, with studies that broaden the understanding of the practice of pharmacists in routine practice. The specific research methods used in this thesis include qualitative interviews, a systematic review with meta-analysis, thematic analysis of routine consultation data, and a multivariable logistic regression of a large routine dataset. These are described further below.

1.9 Overview of results chapters

Chapter 2 – Pharmacists' views and experiences of managing hypertension in community pharmacy. An exploratory interview study.

This chapter provides context to the topic of community pharmacist-led hypertension management from the perspective of pharmacists. The interviews set the scene for the research by providing an insight into the issues faced by practicing pharmacists that may limit hypertension service development.

Chapter 3 – A comparison of blood pressure in community pharmacies with ambulatory, home and general practitioner office readings: a systematic review and meta-analysis

This chapter addresses objective 2 of the thesis – to understand how pharmacy measured blood pressure compares to other measurement modalities recommended in the NICE guidelines for hypertension.

It investigates how mean community pharmacy blood pressure (CPBP) measurements compare with GP clinic and out-of-office (home and ambulatory) blood pressure readings in the published literature.

Chapter 4 – Community pharmacist consultations with patients starting a new anti-hypertensive medication. Qualitative analysis of 1,200 clinical notes.

This chapter addresses objective 3 of the thesis – to understand the content of consultations between pharmacists and hypertensive patients drawing on data from a currently commissioned service (the New Medicine Service, NMS) in England.

It provides a qualitative analysis of consultation notes made by pharmacists during new hypertensive medication consultations. The chapter presents key themes identified from the consultations as reported by pharmacists, and stratifies the analysis by whether the patient was referred to general practice or not in order to identify any differences in themes between referred and non-referred patients. .

Chapter 5 – Factors associated with the referral of hypertensive patients from pharmacies to general practice. Multivariate logistic regression analysis of 131,419 patients.

This chapter addresses objective 4 of the thesis – to establish the reasons for referral of hypertensive patients from pharmacies to general practice during hypertensive NMS consultations.

The chapter utilises data from hypertensive patients reporting to a community pharmacy from the NMS in England (as per Chapter 4). Data were analysed with a view to identify the factors associated with patient referral from pharmacies back to general practice within the first two weeks of starting a new anti-hypertensive medication.

Finally, Chapter 6 provides an overall discussion and conclusion to the thesis.

Chapter 2 – Pharmacists' views and experiences of managing hypertension in community pharmacy. An exploratory interview study.

2.1 Chapter overview

The primary aims of the research presented in this chapter is to explore the views and experiences of pharmacists regarding the delivery of hypertension related care, and understand the barriers and facilitators to the implementation of pharmacist-led hypertension management in community pharmacies.

Pharmacists were predominantly recruited purposively and were included in the study based on their: role as a community pharmacist (CP), experience in commissioning of pharmaceutical services in primary care, and the pharmacy type in which they work (e.g. independent or multiple chain pharmacy). Additional interviews were conducted with general practitioners (GPs) and general practice-based pharmacists (GPPs) to explore the topic from a broader primary care perspective. In total, sixteen interviews were conducted with CPs (n=9), GPPs (n=3), primary care service commissioners (n=2) and GPs (n=2). All GPPs and both primary care service commissioners had been community pharmacists in the past. Interviews were conducted face-to-face (n=8) and via telephone (n=8) depending on participant preference and lasted for a mean of 35 minutes (range 21 to 54 minutes). Data were analysed using an inductive thematic analysis approach.

Community pharmacists did not consider the ongoing management of long-term conditions as a 'core duty'. One reason noted by CPs for this was the prioritisation

of other ‘additional services’, such as flu/travel vaccinations and medication use reviews – services that included financial remuneration and are included in the pharmacy contract. Pharmacists and service commissioners suggested several ways in which a hypertension management service could be implemented in the future, targeting areas such as communication and collaboration with general practice via use of GPPs as a liaison between the settings, and the expanded use of Summary Care Records to enhance information sharing.

The interviews highlighted the many operational factors that need to be considered when implementing hypertension services in pharmacies. While evidence of clinical effectiveness exists for such management from previous literature, the findings in this chapter place into context some of the reasons why this evidence has yet to be implemented into practice and how it could be taken forward in the future.

2.2 Introduction

Evidence from randomised controlled trials (RCTs) show that community pharmacist-led interventions can lower BP over usual care (see Chapter 1).(107) Despite this, no hypertension management provision currently exists in UK community pharmacies.(163) Previous qualitative literature has identified barriers to the implementation of hypertension services in pharmacies and states that the sustainability of 'extended' pharmacist roles, the lack of financial incentives, and a lack of collaboration with GPs may be contributing factors to the lack of implementation.(143,144) More specific operational and practical considerations regarding the delivery of hypertension management in pharmacies, such as communication and information sharing systems, and the willingness of pharmacists to take on hypertension management in addition to their current roles, have not been well studied from the perspective of community pharmacists in England. A better understanding of the context of working in a community pharmacy environment could help to elicit whether delivering hypertension management, akin to the interventions highlighted in Chapter 1 (Table 5), are implementable in current practice.

2.3 Chapter aim

The primary aims of this chapter are to explore the views and experiences of pharmacists regarding the delivery of hypertension related care, and understand

the barriers and facilitators to the implementation of pharmacist-led hypertension management in community pharmacies.

2.4 Methods

This study is reported according to the Standards for Reporting Qualitative Research (SRQR) guidelines, as recommended by the 'Enhancing the Quality and Transparency of Health Research' (EQUATOR) network.(164)

Ethical approval for this study was granted by the 'Medical Sciences Inter-Divisional Research Ethics Committee' at the University of Oxford (reference number R46769/RE003). Participant information sheets and consent forms were approved by the ethics committee before use. All participants gave written informed consent to participate.

2.4.1 Rationale for approach in this chapter

Qualitative research can be defined as:

> *"The investigation of phenomena, typically in an in-depth and holistic fashion, through the collection of rich narrative materials using a flexible research design".*(165)

Well-conducted semi-structured interviews should enable participants to guide the researcher to issues that they feel are important to the research topic.(166) The in-depth nature of the discussions allow for issues to be examined in detail over the

course of several questions that can encourage the participant to further explain their point of view.(166) The approach is also flexible as questions can be adapted based on the data collected in previous interviews.(167) The potential subtleties and complexities of delivering a new intervention in community pharmacies were therefore investigated through semi-structured interviews with community pharmacists. The inclusion of interviews with other stakeholders (general practice pharmacists, health service commissioners and general practitioners) were undertaken to provide a broader context from multiple perspectives.

2.4.2 Recruitment, participants and sampling

Potential participants were initially invited to take part in the study if they worked as a community pharmacist (CP). Diversity was sought in the following characteristics if possible:

- Length of time qualified as a pharmacist.
- Experience of primary care service commissioning (particularly in pharmaceutical services), or as a general practice pharmacist (GPP).
- Type of pharmacy employer – i.e. national chain, small chain and independently owned pharmacies.
- Demographic characteristics such as age, sex, ethnicity and geography.

Marshall (1996) outlined the three main strategies for sampling in qualitative research:(168)

- Convenience sampling – where the most easily accessible participants are recruited.
- Judgement sampling – also referred to as ‘purposive’ sampling, where the researcher selects participants based on characteristics that could influence their responses. This could be based on the researcher’s knowledge or on pre-existing literature.
- Theoretical sampling – mainly applicable to grounded theory, where subsequent participants are recruited based on a theory being developed by the researcher - iteratively from the previous interviews.

A combination of the first two strategies were used for this study, beginning with a convenience sample at the start of the research (3/16 interviews). Although the least methodologically rigorous form of sampling, it was used in order to begin the development of themes and to iteratively understand the characteristics that would need to be considered for the main stage of sampling.(168) A purposive sampling strategy was then used in order to generate maximum variation in responses based on the participant characteristics mentioned previously.(169) Potential participants were recruited through the ‘Prescribing with UKCPA (United Kingdom Clinical Pharmacist Association) and PCPA (Primary Care Pharmacists Association)’ event held on 14th December 2016 in London. This event was aimed at community pharmacists who were interested in commencing further professional development in primary care. The event also included pharmacists currently working in general practice (GPPs). Pharmacists at the UKCPA and PCPA were given a printed copy of the information sheet and were invited to get in contact if they were interested in participating or wanted to know more.

The GPPs interviewed for this study were asked to suggest colleagues who might also be interested in taking part. This 'snowballing method' of recruitment has been suggested by Biernacki et al. to be suitable when attempting to recruit participants with similar characteristics.(170)

2.4.3 Interviews and data collection

Participants were emailed a participant information sheet before the interview or presented with one on the day of interview (Appendix 1). They were given time to read and understand the study and any resulting queries were discussed prior to commencing the interview. The participant's understanding of the study was confirmed before asking them to sign a consent form (Appendix 2).

Interviews were conducted in a meeting room at the Nuffield Department of Primary Care Health Sciences (NDPCHS), at the participant's place of work (a consultation room or staff room in a pharmacy or general practice) or over the phone, depending on the participant's preference. Interviews were conducted face-to-face (n=8) and via telephone (n=8), and took place between August 2016 and September 2017.

The qualitative approach outlined below follow the methods described by Pope, Ziebland and Mays.(171) The semi-structured interviews began with open ended questions, asking the participant to describe their role in their own words and the aspects of their work that they enjoy most. After this initial period of familiarisation, questions were asked to elicit experiences of delivering blood pressure related consultations or interventions. Further questions covered a broad range of areas that were guided by the flow of the conversation – reflecting areas that the

participants felt were important. To conclude each interview, participants were asked if they wished to raise any additional points that they did not manage to cover, and to give some brief demographic details.

Interviews were guided by the study topic guide (Figure 3) that was developed prior to commencing data collection. The purpose of the topic guide was to act as a prompt if participants had little to say about a particular topic initially. Using the topic guide as a prompt, rather than a script, allowed flexibility and reflexivity in the interviewing approach whilst also serving to fill in any areas that were not covered in the natural flow of the conversation.

Interviews were audio recorded using an Olympus digital audio recorder and transcribed verbatim by a professional transcriber. The transcriber was external to the University and had read, understood and signed confidentiality forms with the department previously. Furthermore, audio recordings of the interviews were password protected before being securely sent via 'OxFile' – a programme run by the University of Oxford to securely transfer confidential information between users.

2.4.4 Researcher characteristics and reflexivity

The term reflexivity describes an acknowledgment that the researcher's characteristics and stance in relation to the participants or topic may have an influence on the research conducted or the resulting analysis.(172) The primary author (Ali Albasri, AA) planned, conducted and analysed all of the interviews presented in this study. AA has a professional background as a pharmacist, with most of his clinical work being conducted evenly between chain and independent

community pharmacies, as well as a more recent role as a general practice pharmacist. The study topic was approached with an open mind, and an inductive approach was used to thematic coding to minimise any biases that may have been brought to the analysis through pre-conceived themes.(173) Themes were discussed with the supervision team – in particular Dr. Suman Prinjha (SP), a senior qualitative researcher at the Department of Primary Care Health Sciences, University of Oxford.

All participants were aware that AA was a pharmacist. The main advantage of this was that interviewees were likely to feel comfortable discussing pharmacy related topics in detail and use technical language or abbreviations. It also meant that AA was able to probe for specific explanations if any answers stopped short of full descriptions. However, this had the potential to result in 'leading questions' given AA's prior knowledge of pharmacy.(174) The interviewer was conscious of this possibility during the interviews. Sword (1999) stated that no qualitative research is truly free of bias or pre-conceived assumptions, however an acknowledgement of their possible sources are the first step to minimising their impact on a qualitative piece of research.(175)

Prior to commencing this study, AA attended the Health Experiences Research Group's (HERG) training on conducting and analysing qualitative interviews at the University of Oxford.

Introduction

1. *Just to start us off, can you talk me through a typical working day for you?*
2. *What are the best aspects of community pharmacy, in your opinion?*
3. *What do you think are the most challenging aspects of being a pharmacist?*
4. *What do you think are the biggest challenges facing the community pharmacy sector today?*
5. *How much do you think about BP (blood pressure) or HTN (hypertension) in your everyday practice? Where would it rank in your list of priorities?*

Current practice

1. *What in your opinion are pharmacists currently doing to support patients with long-term conditions like HTN?*
2. *Are there any commissioned services that support patients with hypertension? – if there are, can you tell me about your experiences of them. If not, why not do you think?*
3. *Have there been any HTN related pilot schemes in your area that you know of? What was good/what was bad?*
4. *Can you think back to any BP tests you may have conducted as a pharmacist? Or any other experiences of conducting BP tests? Can you tell me about them?*

Views on extended hypertension management role

1. *What skills do you think pharmacists have, that can allow them to help HTN patients? And what do they lack?*
2. *How can community pharmacies efficiently target patients most in need of a HTN management service?*
3. *What would you like to see pharmacists being able to offer HTN patients that they may not currently be able to?*
4. *What would need to be changed or added to your practice to enable this to happen?*
5. *How do you think patients would feel about pharmacists offering a HTN management service? E.g. uptake of service, how to improve this?*
6. *How about the views of other primary care colleagues?*
7. *After delivering the service, how could pharmacists communicate these results to the patient's GP or to the patient?*
8. *Tell me about your experiences of current information transfer mechanisms between pharmacy and general practice.*

Is there anything else you can think of that you would like to mention?

Figure 3 – Interview guide

2.4.5 Data saturation

When undertaking an interview study, it is important to consider how many interviews may be needed to fulfil the study aims. The concept of 'data saturation' attempts to address this.(173) Data saturation can be described as the point where *"no additional data are being found whereby the [researcher] can develop properties of the category"*.(176)

Subsequent literature by Hennink et al. has subdivided the concept of saturation into 'code saturation' and 'meaning saturation'.(177) They defined these as:

- 'Code saturation' – the point in the analysis where no additional themes or sub-themes emerge from subsequent interviews.
- 'Meaning saturation' – the point where all themes and sub-themes are fully explored and *"no further dimensions, nuances, or insights of issues can be found"* from further interviews.(177)

Hennink et al. explored these two definitions of data saturation, and along with others exploring this concept, suggested that it is 'code saturation' that is most commonly achieved when analysing qualitative data, and that it could be achieved with between 7 and 16 interviews depending on the topic, the level of analysis, the depth of each interview and other individual study details.(178,179) However, Hennink states that reaching 'meaning saturation' for all themes and sub-themes would typically require a higher number of interviews and would be more difficult to quantify.

The interviews conducted in this chapter were exploratory in nature – they aimed to gauge the views of pharmacists on delivering services that are currently not delivered in community pharmacy. Both 'code saturation' and 'meaning saturation' were considered throughout conducting and analysing the interviews whilst also keeping in mind that the 'depth' of each interview, rather than number, would be key to making decisions regarding data saturation.(180)

A total sample of between 12 to 15 participants was expected to be sufficient to reach code saturation based on previous literature exploring similar topics,(21,22) and this range was stated in the ethics application where an estimate was required before study approval. Although an estimation of sample size is necessary for planning a qualitative study prior to starting,(180) ultimately the final number of interviews required was guided by continuously analysing transcripts throughout the study. In practical terms, this meant interviewing would stop once it was felt that no new themes were emerging from the interviews.

2.4.6 Data analysis

Transcripts were read and re-read as soon as they became available and were analysed in parallel to conducting subsequent interviews. Transcripts were transferred to the NVivo software package (version 11) for the organisation of thematic codes. Data were subsequently analysed using thematic analysis.(173) Thematic analysis encourages an inductive approach to data analysis, meaning themes are derived from the data with little or no pre-emption by the researcher prior to data collection.(184) This is in contrast to other popular approaches to

qualitative analysis, such as framework analysis.(185) A framework approach was less well suited to the broad exploratory aims of this chapter as it often begins with pre-generating themes in the form of a coding framework based on a pre-existing understanding of the topic *"rather than emerging from a reflexive research process"*.(185)

All new transcripts were constantly compared to previous transcripts in order to continually develop codes and to iteratively adapt the interview questions if necessary.(186) AA and SP discussed emerging themes after the first three interviews in order to begin the development of the coding framework. The next five interviews were also analysed independently by both AA and SP, before AA continued with subsequent recruitment and analysis.

2.5 Results

2.5.1 Characteristics of participants

Sixteen interviews were conducted with; current community pharmacists (n=9), general practice based pharmacists (n=3), primary care pharmacy service commissioners (n=2) and general practitioners (n=2). Participants involved in service commissioning were from a clinical commissioning group (CCG) and from the Pharmaceutical Services Negotiating Committee (PSNC). Both had worked as community pharmacists previously, as had all GPPs, making the final sample of participants with community pharmacy experience n=14. Participants ranged in age

from 26 to 62 years, worked in urban and rural parts of England, and worked in various pharmacy settings. Table 7 shows the characteristics of the sample.

Table 7 – Participant characteristics

Participant ID	Primary occupation	Setting and role	Age and gender	Area of work	Rurality of work
PH1	Community pharmacist	Multiple chain – relief manager	26, M	Derby	Urban
PH2	Service commissioning	Clinical commissioning group	42, M	Devon and Cornwall	Mixed
PH3	Community pharmacist	Independent pharmacy – locum	32, M	Birmingham	Urban
PH4	Community pharmacist	Multiple chain – relief manager	26, M	Bristol	Rural and suburban
PH5	General practice pharmacist	General practice	37, F	Oxfordshire	Suburban
PH6	Community pharmacist	Small chain – locum	57, F	Oxfordshire	Rural and suburban
PH7	Community pharmacist	Independent pharmacy – owner	62, M	Oxfordshire	Urban
PH8	General practice pharmacist	+ Independent pharmacy – owner	33, M	Birmingham	Suburban
PH9	General practice pharmacist	General practice	32, M	Birmingham	Suburban
PH10	Community pharmacist	Multiple chain – relief manager	28, F	Birmingham	Urban
PH11	Service commissioning	Pharmaceutical services negotiating committee	36, F	Nationally (England)	Mixed
PH12	Community pharmacist	Multiple chain – relief manager	26, M	Coventry	Urban and suburban
PH13	Community pharmacist	Various – locum	27, F	Birmingham	Suburban
PH14	Community pharmacist	Small chain – manager	28, F	Birmingham	Urban
GP1	General practitioner	General practice	38, M	Oxfordshire	Suburban
GP2	General practitioner	General practice	33, M	Oxfordshire	Urban

2.5.2 Thematic analysis

Four key themes emerged from the data:

1. Differing roles and expectations of pharmacists in primary care settings.
2. Priorities and variation in delivering hypertension-related interventions.
3. Barriers to pharmacist-led hypertension management.
4. Facilitators to pharmacist-led hypertension management.

Sub-themes were subsequently generated after re-analysing the four overarching themes in order to further describe the theme's meaning and any variation.(173)

Results are presented as themes and illustrated with quotes from the interviews. Participants are denoted through their unique study identification number (e.g. PH1, GP1), followed by details of their current occupation (e.g. service commissioning or community pharmacist). Table 8 shows each theme with their respective sub-themes. The themes and sub-themes are described in detail in the section that follows.

Table 8 – Thematic structure

Theme	**Sub-theme**
Differing roles and expectations of pharmacists in primary care settings	N/A
Priorities and variation in delivering hypertension related interventions	Initiating blood pressure related consultations
	Variation in service provision between pharmacies
Barriers to pharmacist-led hypertension management	Financial considerations
	Access to clinical records and communication with general practice colleagues
	Perceptions of pharmacists to patients and other health professionals
	Lack of professional autonomy
Facilitators to pharmacist-led hypertension management	Financial incentives
	Summary care records and 'NHSmail'
	Liaising with general practice pharmacists
	Staffing considerations

Differing roles and expectations of pharmacists in primary care settings

Pharmacists described the key tasks that they undertook on a typical day or week. A clear distinction became apparent between the roles of community pharmacists (CPs) and general practice pharmacists (GPPs). CPs generally prioritised tasks that involved the safe and efficient supply of medications, including offering advice on prescription and over the counter medication.

> *So my main duties really are [um]… So your usual dispensing and checking prescriptions, [um] seeing any patients, if they want any advice... Overseeing, the body of the pharmacy really, just making sure everything goes smoothly on the day.* (PH10 - community pharmacist)

Furthermore, some CPs had managerial duties that encompassed personnel management as well as process and dispensary management, such as organising and claiming prescriptions ready for monthly payment submissions.

> *Once that's done, just set up my team so that we know who's doing what for the day, who's on each job and then going forward…. claiming EPS [Electronic Prescription Service] tokens from the night before just to make sure, obviously, we're getting paid for prescriptions and that's about it normally.* (PH1 - community pharmacist)

Community pharmacists viewed long-term condition management and increased patient contact as areas that they wanted to engage with more often than is currently the case. They felt that these were the most enjoyable and professionally rewarding aspects of their job. However, most CPs reported that this occurred on an ad-hoc basis and was occasionally seen as disruptive to their other tasks.

> *Now it's great in theory, don't get me wrong, but, if you've got a queue full of patients, if you've got a (travel vaccination) clinic in about twenty minutes, you don't have time to take aside Mister X, Y or Z and give them a blood pressure check, diabetes test, etcetera. [Though] I'd love to, if I'm being honest.* (PH1 – community pharmacist)

Community pharmacists stated that the current services they conduct which relate to hypertension are MURs (Medication Use Reviews) and the NMS (New Medicine Service). Pharmacists stated that the fact they were paid to deliver these services made them integrate their delivery within what they perceived to be their core duties of dispensing and checking prescriptions.

> *And we provide that [the NMS] because there's remuneration attached to it, so it it's an incentive for us to set them up.* (PH7 – independent pharmacy owner)

In contrast to the responses of CPs, GPPs stated that the management of long-term conditions is one of their highest priorities and was in fact an expectation of their role in practices. A range of clinics for conditions such as hypertension, diabetes and asthma were noted as being a regular part of the GPP's typical week.

> *My role, throughout the time, has [er] sort of progressively increased, so initially I started off doing asthma clinics. From that I increased my competence to diabetes. So I did courses on diabetes and then started to do annual reviews on diabetic patients. That involves doing sort of reviewing their medication, looking at their concordance and things like that and [er] so yeah, so hypertension was what I originally you know, [er] was my original competence.* (PH9 – general practice pharmacist)

Priorities and variation in delivering hypertension related interventions

<u>Initiating blood pressure related consultations</u>

All pharmacists had some experience of taking blood pressure measurements, discussing anti-hypertensive medications with patients or referring patients to their GP if they felt BP was poorly controlled. According to participants, blood pressure readings taken in community pharmacies were most commonly conducted at the request of a patient rather than being offered by pharmacists or other members of

the pharmacy team. Community pharmacists stated that patients would ask for BP readings if they felt unwell or were just interested in knowing what their BP level was, irrespective of whether they were hypertensive or not.

> *In the pharmacy, in our pharmacy, we do have [a] blood pressure monitoring service but it is not [er] led by us. It's a patient led service. And what that means is, if somebody comes in and they ask for their blood pressure to be taken, [er] we would do that but we don't offer it to people that come and go and buy their paracetamol or pick up their medicines and things...* (PH7 – independent pharmacy owner)

> *When I've taken blood pressure, it's usually because they've come in just for a random check. Yeah, usually or it might be because the company is offering it and, therefore, you know, if people want it, we'll do it. Occasionally, it's been because somebody reports that their blood pressure has been high…I've had all sorts of things, their blood pressure monitor at home, they feel, might not be accurate. Or it might be they've been under a lot of stress recently and, you know, they don't feel too brilliant and could we do their blood pressure. [um] So in cases like that. [um] To people just wanting an annual check. [um] So it's usually been those.* (PH6 – community pharmacist)

In contrast, general practice pharmacists reported that encounters with hypertensive patients were less likely to be patient initiated. GPPs discussed the different methods in which patients were identified for hypertension related appointments. These ranged from a general practitioner allocating a cohort of patients to the GPP, to the GPP themselves taking charge of a group of hypertensive patients through practice list searches.

> *Generally, it tends to be the GPs who refer a patient with hypertension over to myself. [um] So the ones which I've had, have certainly been the case. [um] Sometimes it may be that they've been [um] discharged from hospital and they've been initiated on an antihypertensive.*
> *… we tend to have a list of patients which I can [um] target and then, so as long as the list is fairly clear, comprehensive then [um] the reception and administration staff can book patients like this in quite easily [um] and can target them quite easily as well. [um] They tend to, you know, they will speak over the phone to patients and say, the appointment will be with the clinical pharmacist.* (PH5 – general practice pharmacist)

Variation in service provision between pharmacies

Community pharmacists reported wide variation in the provision of BP measuring facilities on offer in a given pharmacy. This depended on the pharmacy employer or sometimes the particular pharmacy they were working in. For instance, one CP mentioned that some national, multiple chain pharmacies do not routinely keep equipment for BP measurement checks in their consultation rooms, whereas other pharmacy employers do.

> *The pharmacy I work in, [name removed], we don't do 'the blood pressure service', whereas I understand some pharmacies do. So sometimes we'll refer them (patients) to pharmacies that do provide the service such as [name of supermarket] and [name removed]. But I do know that in some [name removed] stores, for a handful of patients where they build a good rapport, they (pharmacists) do do blood pressure measurements for some of their regular patients. (PH12 – community pharmacist)*

Note: The 'blood pressure service' referred to by PH12 is the free blood pressure screening that some pharmacies offer, rather than a hypertension management service.

This variation was reported in other areas of practice too, and posed a difficulty for service commissioners when considering whether they should support community pharmacy led services:

> *If you commission a service from a GP practice, yeah, whatever it might be, pick one, Emergency Hormone Contraception (EHC) might be quite a good one, if you commission that service from a GP practice, you know the patient could turn up at that GP practice and will get an EHC. If you go to the community pharmacy, there's still a perception, there is a risk that, there's a locum in that day, who hasn't signed the protocol, who hasn't done the training or, you know, what I've seen as well, they've done the training in Somerset but that doesn't allow them to sign the protocol in Devon and so no EHC for that patient. (PH2 – service commissioner)*

Individual pharmacy owners and pharmacists working for independent pharmacies were concerned that they had less financial capability to withstand the current finding cuts to the community pharmacy sector, compared to larger chain competitors. Although they felt best placed to deliver long-term condition management, due to their more personal approach and better rapport with patients (compared to large multiple pharmacy chains), they felt that the cuts would affect their business viability disproportionately.

> *Now we will suffer most actually. Because [er] it's to do with the economies of scale and so on. If you're one of a lone single chemist shop, you suffer from a lot of disadvantages actually. [er] You don't have the buying power…You're talking about a tiny little community around your shop and you can't compete with larger buyers of products who can then, who will be offering bigger discounts…which they will be able to pass onto the customer possibly and, thereby, draw more people towards themselves. Whereas we can only buy a small amount at a higher price and end up selling it at a slightly higher price to the general public.* (PH7 – independent pharmacy owner)

The result of independent pharmacies closing, with only the larger chains remaining on the market would, in the opinion of the pharmacists interviewed, reduce the likelihood of successful hypertension management implementation for the sector. This view was echoed by a service commissioner, who described the mind-set of large multiple chains to be a barrier to the development of clinical services.

> *We don't do ourselves any favours as a profession because if you talk, this is just my experience right, but, if you talk to multiples about things, I spend my time talking to them about "patients", they will reply to me in the language of "customers". Not in patients. So while you have a corporate viewpoint that you have the "customers", not the "patients", you're not going to be having the correct ethos.* (PH2 – service commissioner)

However, pharmacists working for smaller chains or independent pharmacies felt that their relationship with their customers was the key to success as a business and an important part of their day-to-day practice. They stated that serving a local

population, often for many years, meant they gained the trust and loyaty of their patients, giving them an advantage over the pecieved 'less personal' approach of larger chain pharmacies.

> *What we do have in abundance is the personal touch and the care. And the conversations we have. [er] We're very, very lucky… I know most of my regular customers by first name and I have a conversation with all of them, [um] type of conversation that they want and I know what type of conversation I should be having with each one of them. [er] You can have a banter with somebody. You can have a political [er] discussion of sorts with somebody, [er] even talk about [er] Oxford University stuff with others and you can talk about serious health issues with others. [um] So you grow old with the community you serve and you get to know them personally [er] and [er] you have those lovely conversations with them and that's the part I love anyway. And that is why [er] I'm not retiring anytime soon.* (PH7 – independent pharmacy owner)

Pre-existing rapport and trust between the pharmacist and their patients were viewed as important for taking on an extended clinical role, given the importance of patient acceptance when offering an alternative model of hypertension management.(187)

Barriers to pharmacist-led hypertension management

Financial constraints

Pharmacists discussed several factors that they believed have contributed to the absence of hypertension management in community pharmacies to date. One recurring factor, expressed by both CPs and service commissioners, was the financial constraints placed on the sector by national funding cuts. As mentioned in theme 1, CPs did not necessarily view the ongoing clinical management of long-term conditions as a core duty. While CPs do provide additional services ("advanced" and "enhanced" services - see Chapter 1) they did so because these

services are associated with reimbursement, whereas hypertension management is currently not.

> *"There's no funding for it [hypertension management], we haven't been instructed. I mean any time someone has asked for us to do a blood pressure check, I'd never say no, but I'd never go out of my way to try and obtain a blood pressure check. We have to prioritise services that we get paid for."* (PH12 – community pharmacist)

> *We also try to weather this [national funding cuts] a little bit by adding on different services to the chemist. We provide a comprehensive travel service [er] for clients [er] for all kind of immunisations, we provide those. [um] Childhood vaccinations, which are not available on the NHS, we provide those, [er] the meningitis vaccine for children etcetera.* (PH7 – independent pharmacy owner)

Access to clinical records and communication with general practice

General practice pharmacists considered the lack of access to clinical records as a key barrier to the development of hypertension management services in community settings.

> *The first factor is that we have access to more patient records, so we have a more thorough [um] patient record. [er] So we can see all their bloods, as I said. We can see the previous blood pressure readings. We can see their other diagnoses and see their full history. [um] (*PH5 – general practice pharmacist).

Without access to clinical records or to prescribing clinicians, general practitioners also expressed some worry that community pharmacy interventions would focus solely on 'simple hypertension' or patients with fewer comorbidities and no polypharmacy. The result of this would mean that GPs would lose so-called "easy" workload, leaving them with patients that require longer appointments. This was described by one GP as detrimental to the morale of GPs, despite the potential for a reduction in overall consultation volume.

You know if they are seeing all the… the simple stuff which you can get out the door in in 7 minutes and save yourself 3 minutes, then [um] what you're left with is the more complex things which take 15 minutes. So, I'm sure it makes for overall - it is an efficiency - but I don't think it makes the GPs life any better. (GP1 – general practitioner)

Perceptions of pharmacists to patients and other health professionals

Pharmacists stated that they did not believe that other healthcare professionals or patients knew what their role entailed. They felt that this was an important point to address in order for a hypertension management services to be maintained once implemented. Pharmacists believed that if patients understood the role of the pharmacist, they may demand that these extended services be made available to them via pharmacies.

I think, I don't know why, but I think there's a perception with pharmacists, I think from GPs and even the public, I don't think [um] we have much of a reputation [um] in the public eye [um] and that's with I think even GP receptionists and doctors. I don't think they know that that, I don't know that they're very clear on what we actually do and how we can offer our services. Maybe that's because we are limited in the service that we can provide [um] or maybe that's because sort of we don't communicate often with practices, as much as we should do. So there's no real sort of [um] understanding how we can sort of help each other out sort of or complement each other. (PH12 – community pharmacist)

This view was reiterated in interviews with GPs, who both struggled to name any interventions or services delivered by pharmacists beyond medication reviews and dispensing.

In addition to misconceptions around their role, pharmacists and service commissioners described instances in the past where the trust of GPs in pharmacy had been shaken. These instances seemed to stem from issues around business/financial competition between the sectors.

> *The biggest barrier to overcoming this is nothing to do with hypertension, nothing to do with anything apart from this perception that currently exists, that pharmacies over-order (prescriptions) on behalf of patients…*
> *So I suppose the other thing about that is that you have to overcome resistance from GPs. So this isn't about hypertension models again, this is wider, we have seen, in the past, where community pharmacies have been commissioned to drive flu vaccines.* (PH2 – service commissioner)

Another pharmacist believed that the case of 'fighting over flu vaccination income' could not be compared to the more burdensome nature of ongoing long-term condition management. He believed that GPs may be more willing to delegate some of their long-term condition monitoring duties in the light of the lower 'yield' of such patients i.e. the time spent compared to the income received at the practice is lower than for a simple flu vaccination.

> *I think with flu vaccinations, I think the reluctance there has been because the practices have seen it as loss of income. All right and it's probably been loss of [um] relatively easy income. Right because they could just line up patients and go for it. [um] I don't think the same can be said of managing long term conditions. Right. I think they're much more time consuming. [er] And so, as I said, the demands, on them are greater.* (PH6 – community pharmacist)

<u>Lack of professional autonomy</u>

Community pharmacists reported a lack of autonomy to introduce changes to the services they provided for patients and found this frustrating. Some CPs suggested that they lacked the autonomy to offer hypertension clinics of their own accord. Instead, they reported that decisions about service and role expansion were often initiated by external authorities such as centralised pharmacy management or NHS directives, before changes are considered possible by individual pharmacists.

> *There's not a massive push for it as a service* [hypertension management] *and anytime we would experience any issues to do with hypertension and hypertensives is during any Medicines Use Reviews…or when a patient has encountered side-effects, which you can attribute to a particular drug…*

It's not something that's been highlighted by government bodies or even local authorities to pharmacists to make it a big thing. (PH3 – community pharmacist)

So it really depends, [er] as, the upper hand is with the government and, if the government sees this as how they're going to deliver any particular service, then that's how it shall be. And the rest of us will need to adapt and comply and change. [um] That's how it's always been, that's how it always will be. (PH7 – independent pharmacy owner)

Facilitators to pharmacist-led hypertension management

Financial incentives

Service commissioners and pharmacists were in favour of payment incentives that were based on the quality of care provided and achieving clinical targets, rather than a volume/quota based payment - as is the case with current 'advanced' pharmacy services such as MURs and NMS.

I just think that, while we base our contract on volume as the main area, then what we're going to end up with [is] what we're paying for, which is shovelling as much stuff down the pipe (as) possible, [and] get people out the shop. Whether, you know, you can talk about the, [er] you know neo-liberal obsession with targets…but the [um] while we, you know, we don't pay GPs for the number of patients they see. We pay them for the number of patients they have on their books [um] and we reward them for the quality, and I use that word advisedly…but I think, we are still, as a profession, I believe, in the main, focused on shovelling as many bits of paper out the door as we can. (PH2 – service commissioner)

So maybe something that doesn't just say, okay, just for doing a blood pressure check, you're going to get paid x amount… So, if you're helping managing a cohort of say, a hundred people to manage their blood pressure, [um], where they start off with forty per cent being outside the range and end with forty per cent being outside the range, they (pharmacists) are clearly not doing their job. So, whereas another pharmacy taking on the same group of patients, who make a significant decrease in that figure, you know, are effective, are doing their job and so (payment by) outcomes, yes…
(PH6 – community pharmacist)

The ‘Quality Payments Scheme’ was also discussed in the interviews. Introduced to community pharmacies in 2017, it requires pharmacies to meet certain criteria, known as ‘gateway’ or ‘quality criteria’, in order to become eligible for additional funding in an attempt to recoup some of the losses incurred from national budget cuts.(24) It is worth noting that the ‘quality payment scheme’ does not currently reward pharmacies for delivering on specific clinical outcomes such as blood pressure lowering or blood glucose control. The use of Summary Care Records (discussed below) was not only seen as a potential tool for improving communication and the delivery of clinical services but also has a financial reward associated with its appropriate use as part of the QPS ‘quality criteria’.

> *It’s one of the quality criteria [accessing Summary Care Records] so [um] community pharmacies, if they meet that criteria then, you know, they potentially earn money from increasing usage of SCR.* (PH11 – service commissioner)

Further gateway criteria include ‘healthy living pharmacy’ (HLP) status - described in Chapter 1. It was felt that pharmacies accredited (or indeed self-accredited) as HLPs would be empowered to proactively approach patients to initiate conversations around blood pressure management, rather than wait to be asked for BP measurements.

> *…with healthy living pharmacy, it is about having that more proactive approach and, you know, not waiting for patients to come and talk to you about their blood pressure… So I think healthy living pharmacies have kind of brought more into that ethos of being proactive…* (PH11 – service commissioner)

<u>Summary care records and ‘NHSmail’</u>

If closer collaboration between primary care settings were to be realised, the mode of communication between community pharmacy and general practice colleagues

would require optimisation. The introduction of Summary Care Records (SCR) have the potential to bridge this gap, according to one service commissioner. Currently, SCRs allow pharmacists to read limited patient information such as a complete medication list, doses and allergies, accessed via an NHS 'smart card' in a community pharmacy.(188) Access to these limited clinical records were seen by participants as a positive step towards more comprehensive access to patient notes in pharmacies. Given that access to SCR is a relatively new phenomenon (national pharmacy rollout began in June 2016), some pharmacists may be yet to use SCR, and this was acknowledged.

> *I think the more that it's used [Summary Care Records], then that gives a stronger case as well to get [um] 'write access' as well because, at the moment, it's only 'read access'. And then pushes the case forward more for getting shared care records. [um] And that all helps then, you know, community pharmacies can be adding the information on to that directly and not having to send notes across to GP surgeries.* (PH11 – service commissioner)

The use of 'NHSmail' accounts for pharmacies was discussed by CPs as a potential improvement to the communication between pharmacies and general practice – the subscription to which is another 'quality criteria' for the 'quality payment scheme'. The advantage these accounts hold are their end-to-end encryption, allowing confidential patient data to be transferred securely between healthcare professionals and settings.

<u>Liaising with general practice pharmacists (GPPs)</u>

Pharmacists suggested that greater collaboration between community and general practice settings could facilitate the delivery of hypertension management in community pharmacies. Service commissioners anticipated that the national rollout

of GPPs could be the catalyst for this collaboration. Service commissioners and CPs felt that this collaboration would work best if GPPs made appropriate use of their community colleagues, and vice versa, in a two-way process.

> *I would hope that, if we were going to be referring to them (to the general practice pharmacist) and the patient is found to be hypertensive, then you could say that we'd provide new medicines support [um] to this group of patients. So can you please let them know that this is available so that, when you're prescribing a new medicine, get them prepared to accept that service, right. So, if they mention it, then the patient is going to come in, you know, with an open mind to it. Rather than, what's this? Why are they wasting my time? [laughs].* (PH6 – community pharmacist)

> *I think that they can help to bridge the gap between pharmacists, [er] between pharmacists and GP surgeries. [but] there's a risk that they don't do it, don't do that and they, just, depending where they've come from, they may not understand community pharmacies either..* (PH11 – service commissioner)

The notion that GPPs could be the key to enhancing collaboration and communication between general practice and community pharmacy was also acknowledged by GPPs themselves. They believed the mechanism responsible for this improved collaboration could be the fact that a large percentage of GPPs may have once been CPs themselves, meaning that they would better understand one other from the outset.

> *The main thing is trying to bridge that gap between [um] community pharmacy and [um] and GP practice, so that we can build a better relationship. …when they (CPs) ring up the surgery and they need to speak to someone with more of a complicated issue… if they do get put through to me, then they know almost like we're speaking the same language so to speak. So that's kind of like reassuring for them and [um] and [um] and issues tend to get solved quite easily and quite quickly as well.* (PH5 – general practice pharmacist)

<u>Staffing considerations</u>

Pharmacists reported that appropriate use of other members of the pharmacy team would be vital in enabling them to deliver more clinically oriented hypertension

management. The measurement of blood pressure itself was seen as a task suitable for appropriately trained pharmacy technicians, dispensers or healthcare assistants, while the subsequent advice and recommendations were viewed as more of a pharmacist's job. This model was put forward in order to make the best use of scarce pharmacist time, which they reported to be limited due to balancing the growing number of prescriptions to deal with as well as the other tasks/services they are contracted to deliver.

> *…It probably wouldn't need to be a pharmacist anyway. You know, you'd have a trained member of staff, whether it's counter or dispenser but one of them could do the blood pressure check and pass the results to the pharmacist, who'd then review and decide what needs to be done, then has that chat with the [er] with the patient, as necessary. So that would make most use of each person's time.* (PH6 – community pharmacist)

In addition to making use of other members of the pharmacy team, some pharmacists felt strongly that pharmacies should routinely operate with two pharmacists, particularly if the profession as a whole is required to take on roles that are more clinical.

> *I think an acceptance that we need second pharmacists more in pharmacies. [um] You know, if not on a full time basis then on a part time basis. It then frees up one of them to go away and do the services… And I think, if we're taking on rather more of a clinical role, that support becomes even more important. You don't have many surgeries these days where it's just one doctor, and how many times, you know, does one doctor pop into another one just to get a quick second opinion. It's very common and it's accepted in that profession and I think it should be something that's accepted in ours as well, you know, hospitals have it, let's bring it out into the community.* (PH6 – community pharmacist)

2.6 Discussion

2.6.1 Summary of findings

This chapter has presented the findings from 16 semi-structured interviews, predominantly with community pharmacists, but also with general practice pharmacists, service commissioners and general practitioners. The analysis provides insights into the wider operational considerations needed for the adoption of evidence based, pharmacist-led interventions for the management of hypertension. Community pharmacists generally did not view the ongoing management of long-term conditions as a core part of their current role, primarily due to time restrictions and to prioritising other tasks that are associated with either medication supply/advice or financial reimbursement (flu and travel vaccinations or medication use reviews, for example). Most encounters for blood pressure measurements were reported to be initiated by patients themselves rather than being offered by the pharmacist or pharmacy team.

Pharmacists felt that the future development of a hypertension management service could be hindered by the lack of co-operation and co-ordination between community pharmacies and general practice. However, they believed that the role of GPPs could facilitate the collaboration and communication needed between the settings for such an intervention to run. The secure data sharing capabilities now available to community pharmacy, such as Summary Care Records and NHSmail, were seen as important facilitators for service delivery. In addition, pharmacists felt less willing

to deliver services unless they were specifically commissioned at either a local or national level by their pharmacy employer or the NHS directly.

2.6.2 Strengths and limitations

Participants in this study varied in the number of years since professional qualification and in their roles in community pharmacy and wider primary care. This diversity, predominantly enabled through purposive sampling, generated a wide range of views, reflected in the themes and sub-themes presented in this chapter. A further strength of this interview study was the depth of the interviews, which allowed the topic to be explored thoroughly from the point of view of each participant.

The analysis presented in this study identified several perceived barriers and facilitators to the development and implementation of community pharmacist-led hypertension management. In doing so, it has highlighted contextual factors in relation to community pharmacy that require consideration before implementation of the trial evidence summarised in Chapter 1 (Table 5).(107) A key strength of this study therefore also lies in its contribution to the wider thesis, as it begins to address the context within which the trial interventions discussed in Chapter 1 could be implemented – a step recommended in the literature on translating evidence to practice.(136)

The results of qualitative research are intended to be study specific rather than produce generalisable findings, mainly due to the trade-off between small sample sizes and depth of investigation.(189) The question of how many interviews may be

enough is still debated among social scientists, with different interpretations of how this is judged leading to different interpretations as to their consequences on a qualitative study.(180) In this study, no new themes emerged during the twelfth pharmacist interview. A further two pharmacists were interviewed to confirm this, where, again, no new themes were identified. Ritchie and Lewis (2003) outlined several factors that may influence the required sample size in qualitative studies including the heterogeneity of the sample and the number of 'samples within the sample'.(167) Given the heterogeneity of the sample, and the fact that 'multiple samples' were included in this study (CPs, GPPs, GPs, service commissioners), the idea that 'meaning saturation' could have occurred with 16 interviews is open to interpretation, however it is likely that 'code saturation' was reached. It is worth noting that 16 interviews are a comparable number to the sample sizes of other qualitative literature investigating hypertension or other extended services in the pharmacy setting.(181,190,191)

As previously discussed, qualitative research is primarily concerned with the richness and depth of the data and how these data describe the research topic.(173) Although the participants interviewed provided a wide range of opinions and experiences, resource limitations prevented the recruitment of pharmacists from wider geographical areas of the country. National recruitment was attempted through attendance of the UKCPA (United Kingdom Clinical Pharmacist Association) and PCPA (Primary Care Pharmacists Association) event held in London, however this yielded few participants. Consequently, the views of pharmacists from the north of England and London, for example, were not represented in this exploratory study. Whilst qualitative research does not purport to be concerned with the number of participants or generalisability of findings,(189)

a greater breadth of views may have been collected if more pharmacists from other regions of the country participated in the study.

In retrospect, given the potential role of other pharmacy staff as ‘facilitators’ to the delivery of hypertension management in community pharmacies, interviews with healthcare assistants, dispensers or pharmacy technicians could have been conducted to better understand their views of a role in hypertension management. This limitation could be addressed in future research focussing specifically on the views of these groups. In addition, further exploration of GP (n=2) and service commissioner views (n=2) would also be areas of future research to gain deeper understanding of the broader primary care context to pharmacy service development.

2.6.3 Comparison with previous literature

A systematic review of qualitative literature published between 1990-2001 explored the views of community pharmacists regarding their perceived contribution to public health.(191) In the twelve studies identified, pharmacists reported being more likely to offer advice to patients in response to direct requests for such information rather than opportunistically. They also stated that a barrier to their wider participation in a 'public health role' was limited by their extensive medication supply duties (clinical and accuracy checking of prescriptions). These barriers were similarly prominent in the interviews conducted in this chapter. This suggests that little may have changed in terms of the attitudes and barriers facing community pharmacists over the past few decades. This assumption is further reinforced by the fact that few (if any) duties have been added to the community pharmacy contract over the same time period that contribute to the management and ongoing monitoring of chronic conditions.(6,11)

More recently, in 2015, a qualitative study of 15 community pharmacists explored their experiences of delivering cardiovascular disease related advice.(150) Thematic analysis of pharmacist responses from supermarket, multiple and independent pharmacy backgrounds highlighted that CPs felt unsure and sometimes uneasy about providing 'additional services' without remuneration. This point, mentioned on numerous occasions in the interviews discussed in this chapter, highlights the 'commercial vs healthcare' identity conflict of the pharmacy setting.(192) As external contractors to the NHS, pharmacies are private business contractors much like GP surgeries. The sales façade and transaction processes occurring at the tills of pharmacies were seen as somewhat undermining of the

healthcare environment by some of the pharmacists interviewed in this chapter and in the 2015 study. Against a background of a tighter fiscal environment for pharmacies,(95) pharmacists felt that they were often torn between extending the clinical services they provided to patients and business survival.

In a study of general practice pharmacists, Butterworth et al. interviewed 16 GPPs via telephone to explore their views on the emerging role of pharmacists in general practice.(181) One of the roles that GPPs stated they would expect to perform was 'liaising with community pharmacists'. This was a role that the CPs and GPPs also mentioned in this chapter as a potential facilitator for the development of clinical services in community pharmacies. Specifically, participants in this chapter stated that this collaboration could overcome some of the historical communication barriers between the two primary care settings.(122) A critique of this perspective is that pharmacists working in hospital settings and community settings have co-existed for several decades yet do not necessarily collaborate any more closely on matters such as patient discharge medications, despite their common professional background. Nonetheless, this counter argument does not take into account the fact that many GPPs were once CPs themselves, whereas this may be less likely to be the case for secondary care pharmacists (with exceptions either way).(193)

In this study, pharmacists felt less willing to deliver services unless they were specifically commissioned at either a local or national level by their pharmacy employer or by the NHS directly. Interestingly, this finding is in contrast to previous literature exploring the general barriers to the translation of evidence into practice (section 1.6, Chapter 1) which states that a programme imposed from an external body is likely to be a barrier to implementation.(136) In this chapter, the pharmacists did not feel empowered to develop or implement their own services and so were

reliant on direction from employing authorities to decide their role. This suggests that while it may be a barrier in other sectors or settings, introducing a service into pharmacies via the NHS or through the employing organisation may not be a barrier in community pharmacies, and is in fact the way the sector operates currently via the NHS-community pharmacy contractual framework.(11)

As well as corroborating/contradicting the findings of previous literature on this topic, this chapter also provided some novel insights. For instance, the variation in provision of equipment in pharmacies, driven by variation in pharmacy-chain owner policies, has not previously been discussed in the literature as a barrier to the uptake of clinical services in pharmacies. Other insights such as the 'quality payments scheme' and 'healthy living pharmacies', were also potentially useful considerations to service development given that they may be more realistic than recommending large funding increases to the sector to provide financial incentives for hypertension service implementation.(96)

2.6.4 Implications for clinical practice

Pharmacists stated that blood pressure measurements and other hypertension related consultations are currently *"a patient-led service*" (PH7) in community pharmacy. That is, patients ask for such consultations rather than being offered to them by pharmacists. This approach was seen as a potential barrier to the uptake of extended hypertension services in pharmacies. A possible solution to this was the concept of 'Healthy Living Pharmacies' (HLP). Participants involved in service commissioning thought that HLP status would encourage pharmacists and pharmacy teams to proactively approach patients about long-term condition

management. As of December 2017, around 8,300 community pharmacies (~70%) reached the basic level to self-accredit as ‘stage 1’ HLPs by the Royal Society of Public Health in England.(21) However while the HLP concept has shown initial promise in areas such as provision of smoking cessation services, there are currently a lack of data from randomised trials of HLPs vs conventional pharmacy models to suggest that HLP status alone could facilitate provision of hypertension management in community pharmacies.(194,195) As HLP status is part of the remuneration package associated with the ‘quality payments scheme’, HLPs appear to have the potential to contribute to the implementation of a hypertension management service by providing some level of financial remuneration. NHS England has stated that the future of the quality payments scheme is being constantly re-evaluated, placing into question the longevity and reliance on such schemes as ‘facilitators’ of service provision in pharmacies.(188)

The provision of additional, financially rewarding, services such as private vaccination clinics were reported to be prioritised over clinical services such as blood pressure checks that are not financially reimbursed. The overall burden of blood pressure consultations on a pharmacist’s time was also felt by pharmacists to contribute to this lack of prioritisation. Upskilling other pharmacy workers, such as healthcare assistants and pharmacy technicians, was reported by several pharmacists in this study to have the potential to rebalance this prioritisation, but would require investment to train these staff. The appointment of a “health champion” in the HLP model encourages training of other pharmacy staff, suggesting that the relevant training infrastructure is currently available for pharmacy teams to utilise.

A further consideration for clinical practice is the view that "*one size does not always fit all*" (PH2) in terms of service development. Despite a nationwide problem with sub-standard hypertension control,(36) some areas of the country may have to make commissioning decisions based on the need of their local population in order to ration scarce resources. This consideration means that rather than a nationally commissioned or 'advanced' service under the community pharmacy contract, hypertension management could begin as an 'enhanced' service – i.e. locally commissioned by an NHS England area team, on a locality-by-locality basis, based on need and opportunity-cost. If clinically and economically evaluated, this could also serve as a 'proof of concept' for wider uptake of community pharmacist-led hypertension management in the future.

2.6.5 How this chapter fits within the wider thesis

This chapter has provided information regarding 'the context of intended target setting' referred to in section 1.6 of this thesis by Galsgow et al, and also the section of the CFIR framework relating to understanding the views of the people who are tasked with delivering the intervention (Chapter 1). Community pharmacists stated that they did not consider hypertension management to be one of their core duties as they felt the need to prioritise services that were associated with remuneration, and enjoyed the reassurance of services that were included in their contract, as they viewed this as endorsement for their work. Given these sentiments, the feasibility of conducting monthly or two monthly hypertension follow-ups in clinical practice, lasting between 5 and 60mins (as delivered in the previous RCTs, see Chapter 1,

Table 5) should be considered, along with the opportunity-cost for the pharmacy's viability of providing this instead of other services that may be associated with financial remuneration. The choice between delivering long-term condition management to patients (unfunded), or providing the services that are stipulated (and funded) via the community pharmacy NHS contract, is clearly problematic but appears to be a decision pharmacists are making. Even if pharmacists were funded to deliver hypertension management, this would still not guarantee its uptake into practice given the other factors such as volume of dispensing and other tasks that take up a pharmacist's time and resources. Therefore both funding and additional personnel in the pharmacy, such as a second pharmacist, may be required for implementing extended hypertension services.

With regards to the 'intervention characteristics' identified in section 1.6 (Chapter 1), 'programs imposed from an external body' were stated to be a component of interventions that are associated with low uptake into practice.(136) The participants in this chapter stated that they felt uncomfortable if a new intervention was not recommended to them by an NHS body or local authority, and were in fact more likely to deliver interventions on the basis of external recommendations. It is unclear whether this view was due to a level of inertia (i.e. only delivering interventions if told to); symptomatic of the lack of autonomy community pharmacists have with regards to the services they offer; or whether this is a realistic view of how services and interventions are commissioned and delivered in UK pharmacy practice today. These factors require further consideration when thinking about the delivery of hypertension management in this setting and its long-term sustainability.

2.7 Conclusion

This chapter has provided important context to begin this thesis' investigation into the role of community pharmacists in hypertension management. It has highlighted barriers and facilitators to the development of future hypertension services and has identified some practical and operational factors to consider, such as the need to situate a new intervention into a pharmacist's already busy schedule.

While evidence of clinical effectiveness exists for pharmacist-managed hypertension from the trials described in Chapter 1, the findings from this chapter place into context some of the reasons why this evidence has yet to be implemented into pharmacy practice, and ways this can be taken forward.

Chapter 3 - A comparison of blood pressure in community pharmacies with ambulatory, home and general practitioner office readings: a systematic review and meta-analysis

3.1 Chapter overview

This chapter presents the results of a systematic review and meta-analysis of literature comparing community pharmacy BP (CPBP) readings with ambulatory BP monitoring (ABPM), home BP monitoring (HBPM) and general practitioner (GP) clinic readings.

Mean CPBP readings were compared with these other measurement modalities and summarised using random-effects meta-analyses. The primary outcome was to compare CPBP with 'gold standard' ABPM readings.

Searches generated 3,815 studies of which eight were included in the meta-analyses. The mean systolic CPBP-daytime ABPM difference was small [+1.6mmHg (95% confidence interval (CI) -1.2 to 4.3) three studies, n=319]. CPBP was significantly higher than 24-h ABPM [+7.8mmHg (95% CI 1.5 to 14.1) three studies n=429]. Comparisons with general practitioner clinic readings (six studies, n=2100) were inconclusive with significant heterogeneity between studies. Overall, CPBP and HBPM readings (five studies, n=1,848) were not significantly different. Diastolic comparisons mirrored systolic comparisons in all but the CPBP-daytime ABPM comparison, where CPBP was significantly higher.

Current evidence around the clinical interpretation of CPBP is inconclusive. As a result, a threshold of 135/85mmHg for hypertension might be considered reasonable and potentially result in a higher sensitivity for detecting patients with truly raised BP in pharmacies. Future research should consider the impact of this lower threshold on increased referrals to general practice clinics.

A manuscript of this chapter has been published in the *Journal of Hypertension,*(196) and can be found in Appendix 3

3.2 Introduction

All trials included in the systematic review by Cheema et al. (Table 5, Chapter 1) required the community pharmacist to either measure blood pressure in the pharmacy or interpret readings before making clinical decisions.(107) Across the 16 trials, pharmacy BP thresholds varied from 135/85 mmHg,(114) 140/90 mmHg,(108,145) and 160/90 mmHg (112) among non-diabetic cohorts.

Both the Royal Pharmaceutical Society (RPS) in the UK and the World Health Organisation have previously suggested that the standard clinic 140/90 mmHg threshold for hypertension is appropriate for interpreting pharmacy measured BP.(104,146) This recommendation, however, is not based on evidence from diagnostic accuracy studies comparing this relationship. Instead, it appears to make the assumption that pharmacies, as clinically related settings containing a healthcare professional, would be associated with a similar 'white coat' effect as documented during GP measurements.(147) While a systematic review conducted in 2009 identified three studies comparing CPBP with other measurement modalities, no meta-analysis was conducted due to sparsity of data.(149) Contrary to RPS guidance, recent studies have suggested that pharmacy BP readings may be comparable with home or ambulatory readings.(197,198)

If pharmacists are to deliver blood pressure services in community pharmacies, the fundamentals of interpreting the readings taken in pharmacies should be established in order for appropriate clinical decisions to be made.

This systematic review was devised in order to establish the mean differences between pharmacy-measured BP and measurements from other modalities and settings used in the diagnosis and management of hypertension.

3.3 Chapter aim

This study aimed to systematically review all existing literature comparing BP readings taken in community pharmacies with ABPM, HBPM and GP clinic readings taken in the same patients.

3.4 Methods

The current study is reported according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses guidelines (PRISMA).(199) The study protocol was registered on the International Prospective Register of Systematic Reviews (PROSPERO) and can be found online (registration number CRD42016032518) and in Appendix 4.

3.3.1 Rationale for approach

A systematic review can be described simply as a review of the literature prepared using a systematic approach to minimise bias.(200) This approach aims to ensure

that study selection bias and any author bias does not unduly influence the narrative or results of the review.

A meta-analysis is a statistical analysis used to combine data from sufficiently similar studies.(201) The aim of a random effects meta-analysis (employed in this chapter) was to estimate the average blood pressure difference between pharmacy measured BP and BP measured using other modalities. A random effects model assumes the 'true differences' in blood pressure would differ from study to study even if individual studies were infinitely large in sample size.(202) This is due to methodological and population heterogeneity between included studies (described later in this chapter). The combined study effects or summary estimates in the forest plots of a meta-analysis therefore represents the mean of the population of 'true effects'.(203) In contrast, if a fixed-effects meta-analysis had been used, this would assume that any difference between the constituent study results would be due to chance differences derived from the sampling of patients, and not from between-study heterogeneity arising from different blood pressure measurement protocols, for example.(202) The summary estimate from a fixed effects meta-analysis would therefore assume that there is one true effect or difference between pharmacy and other measurement modalities.

3.3.2 Search strategy

A literature search in the EMBASE, CINAHL and MEDLINE databases was conducted to identify studies which compared CPBP readings to those of ABPM, HBPM or GP clinic readings. While the EMBASE and MEDLINE databases are likely

to pick up the majority of general medical literature, the CINAHL database focuses on nursing and 'allied health' literature, encompassing pharmacist based studies, hence its inclusion in the search strategy.

No language limit or study design filters were set. Searches were conducted on articles from January 2009 to December 2015 in MEDLINE and EMBASE (updating the search from December 2009 by Sabater-Hernandez et al.(149)) and from inception to December 2015 in CINAHL. Further studies were identified through searching references of full text articles screened and of the previous systematic review on the topic.(149). The first set of key search terms related to pharmacists, pharmacies or community pharmacies, were connected with the Boolean operator 'OR'. The second set of key search terms related to blood pressure, hypertension and white coat or masked hypertension. The two sets of terms were grouped with the Boolean operator 'AND'. The full MEDLINE search strategy can be found in Appendix 5.

3.3.3 Selection of studies, inclusion and exclusion criteria

Titles, abstracts and full texts were independently reviewed by two members of the review team (Ali Albasri (AA) and Jack O'Sullivan (JOS)). Any conflicts were resolved through discussion, or through involvement of a third member of the review team (Dr. James Sheppard (JPS)) if necessary. Studies screened by title, abstract and full text were eligible for inclusion if they met all of the following criteria:

1. BP measured in a community pharmacy;

2. Pharmacy BP readings compared with any of ABPM, HBPM or GP clinic BP readings in the same patients;
3. Participants aged 18 years or older.

Studies were excluded if any of the following applied:

1. Participants had their BP measured in a pharmacy as part of a wider intervention or package of care to reduce or control BP – for example, patients who received more regular monitoring, or condition or medication advice before or after comparator measurement.
2. Patients who had atrial fibrillation or were pregnant.
3. Clinic or pharmacy BP readings from secondary care or outpatient clinic settings.

3.3.4 Outcomes measured

The primary outcome of this review was to compare the mean systolic blood pressure (SBP) difference between measurements taken in community pharmacy and those from mean daytime ABPM readings - measured as the difference between published estimates of mean CPBP and ABPM. As previously stated, ABPM is considered to be the 'gold standard' for blood pressure estimations given its closer correlation with cardiovascular endpoints.(50) Daytime ABPM measurements were selected as the primary outcome since these are more acceptable to patients (than 24-hour ABPM) and are recommended in current NICE hypertension guidelines.(28)

Secondary outcomes explored the mean differences between SBP measured in the pharmacy, 24-hour ABPM readings, HBPM readings and GP clinic readings, as well as corresponding diastolic comparisons.

3.3.5 Data extraction

Data were independently extracted and verified by two members of the review team (AA and JOS). Data on mean blood pressure values and standard deviations (SD), number of visits to the relevant setting, number of measurements per visit, the profession of the operator taking the BP reading, the BP monitor used, patient demographics, medication history and hypertensive status were extracted where available. Where data were not available from the published articles, authors were contacted and the outstanding data requested. Discrepancies in data extraction were discussed and resolved with the third reviewer (JPS) if necessary.

3.3.6 Quality assessment

Included articles were independently assessed for quality by two members of the review team (AA and JOS). The Quality Assessment of Comparative Diagnostic Accuracy Studies-2 (QUADAS-2) checklist was used to assess methodological quality.(204) The QUADAS-2 checklist considers ‘risk of bias’ and ‘applicability’ concerns regarding patient selection, index test and reference test conduction, as well as flow and timing of patients through a study. Specifically, individual studies were considered to have a low risk of bias based on the four QUADAS-2 domains:

1. Patient selection - use of consecutive or random sampling methods.
2. Index test - index test results interpreted without knowledge of the reference standard results and vice versa.
3. Reference standard test - all patients receiving the same reference test.
4. Flow and timing - patients randomly allocated to receive pharmacy BP testing before other measurements or vice versa.

Studies were judged to be at low, high, or unclear risk of bias primarily on the above criteria. The QUADAS-2 tool does not provide guidance for how researchers should attribute an 'overall risk of bias' to a study, however it states that when such overall judgements are made, they should be explicit, applied consistently and take into account individual review contexts.(204) An example of a context-specific decision taken in this review to downgrade evidence occurred when a non-validated BP monitor (wrist BP device) was used. In the absence of such context specific study limitations, primary literature were classed as 'high risk' of bias if they scored 'high risk' in two or more of the QUADAS-2 domains. All seven sub-domains can be found in Table 11. Low risk studies were classed as such by virtue of scoring one or fewer 'high risk' scores and through taking into account specific risk of bias regarding BP measurement methods. 'Unclear' was reserved for occasions where there was insufficient information to make a judgement of risk.

To aid the process of assessing bias, the following "signalling questions" are provided by the QUADAS-2 tool to aid the researcher's assessments:(204)

"Participant Selection:

1. *Were participants recruited randomly or consecutively into the study?*

2. *Was a case-control design avoided?*
3. *Did the study avoid inappropriate patient exclusions?*

Index Test:

1. *Were the index test results interpreted without knowledge of the results of the reference standard?*
2. *If a threshold for the test result was used, was it pre-specified?*

Reference standard:

1. *Is the reference standard likely to correctly classify the target condition?*
2. *Were the reference standard results interpreted without knowledge of the results of the index test?*

Flow and timing:

1. *Was there an appropriate interval between the index test and reference standard?*
2. *Did all participants receive a) a reference standard test and b) was the reference standard the same tests for all participants?*
3. *Were all participants included in the analysis?"*

The impact of studies of a lower quality, according to reviewer consensus, were assessed in sensitivity analyses by excluding them from the meta-analysis. Furthermore, the influence of individual studies on the overall summary estimate was assessed using an influence analysis. An influence analysis re-runs the meta-analysis command in STATA using the '*metaninf*' command, and re-estimates the summary estimate after omitting each study in turn.(205) This method can identify whether a particular study drove the overall summary estimate to its position or not.

Where possible, publication bias was assessed via an Egger's test.(206)

3.3.7 Data synthesis

Data were analysed using a random effects meta-analysis of the weighted mean differences (WMDs) between measurement modalities using STATA statistical software (StataCorp 2011, Release 12; StataCorp, College Station, Texas, USA). Where the 'standardised mean difference' combines study outcomes measured in different ways - such as combining overall medication adherence using different scales or questionnaires, the WMD combines studies that compare the same outcome (BP) in the same way (brachial cuff BP monitor with results presented in mmHg).(207) The sum of the differences of individual studies are combined and 'weighted' according to individual study precision (standard deviations).

A random-effects model was used to account for heterogeneity in baseline population characteristics, sample sizes and BP measurement protocols between studies.(208) Statistical heterogeneity was quantified by using the I^2 statistic, produced when using the '*metan*' command in STATA, and interpreted using the guidelines presented by the Cochrane Handbook.(207) A sensitivity analysis using a fixed-effects model (Appendix 6) was conducted in order to highlight any differences in interpretation when using a random effects model.

Mean BP and SDs from relevant studies were synthesised comparing: pharmacy and daytime ABPM (primary outcome), as well as pharmacy and 24-h ABPM, pharmacy and HBPM and pharmacy and general practitioner clinic. *A priori* subgroup analyses taking into account study quality (i.e. excluding studies exhibiting high risk of bias) and baseline hypertensive status (hypertensive vs non-

hypertensive or mixed cohorts) were conducted on all comparisons where possible. Studies including non-hypertensive patients at baseline have been shown to exhibit higher rates of masked hypertension i.e. higher office BP than home or ambulatory BP,(209) hence the inclusion of this sub-group analysis.

Data are presented as means with SD or WMD with 95% CIs (confidence intervals) unless otherwise stated.

3.5 Results

3.5.1 Study selection

After removal of 677 duplicate records, 3,138 unique studies were identified from the literature searches. An additional three records were found from citation searches. A total of 2,577 studies were excluded at title screening and 534 studies were excluded after abstract screening, resulting in 30 studies eligible for full-text review (Figure 4).

Twenty-one articles screened at the full-text stage were excluded because they either: examined CPBP as part of a wider package of care, such as incorporating measurements during interventions to reduce BP (n=5); examined the BP measurements in a different setting such as pharmacy outpatient clinics (n=4); presented no comparator setting (n=4); used a different comparator (e.g. compared pharmacy readings with secondary care BP readings, n=2); or did not present

primary data (n=6). In total, nine studies were eligible for inclusion in the review, eight of which were included in the data-synthesis (Figure 4).

One eligible study could not be included in the meta-analysis as no data relating to BP readings taken in a pharmacy or home setting were presented, despite reporting conducting these measurements in their methods.(210) The corresponding author was contacted on three occasions without reply.

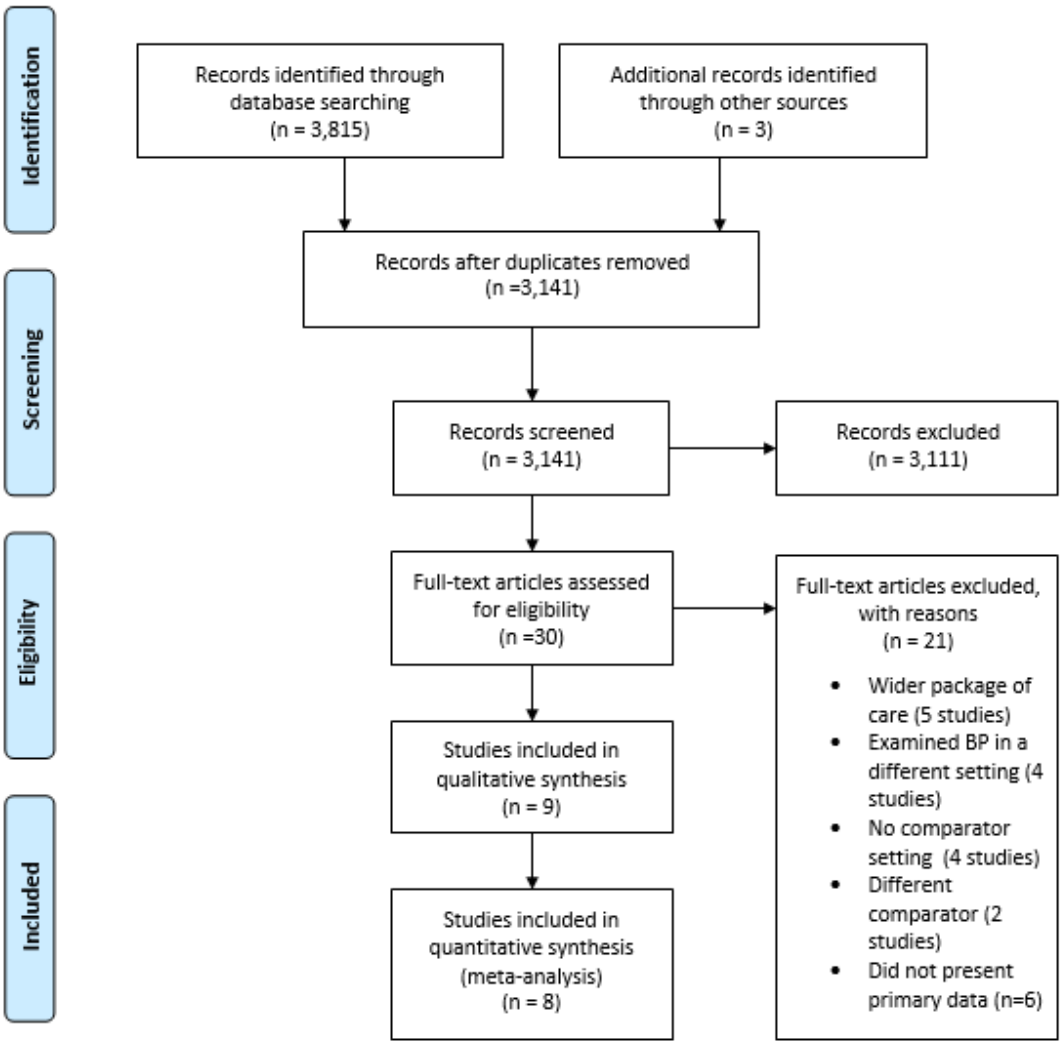

Figure 4 – PRISMA flow diagram of study selection

3.5.2 Study characteristics

A total of three studies compared CPBP and daytime ABPM readings (n=319), five studies compared CPBP and HBPM readings (n=1848) and six studies compared CPBP and general practitioner clinic readings (n=2100) (Table 9).

Studies were conducted in Spain (n=4), Canada (n=2), Turkey (n=1) and Switzerland (n=1). The mean age of study participants included in the quantitative synthesis was 58.6 years and mean proportion of women 53.5%. Four studies included only hypertensive patients, (197,198,211,212) whereas four other studies recruited a mixed cohort of hypertensive and normotensive individuals.(210,213–215) One study did not specify the baseline blood pressure status of participants.(216)

BP readings taken in the pharmacy were conducted by a pharmacist (n=5), (197,198,210,213,217) pharmacist or pharmacy technician (n=2) (211,215) or via automated machine with no member of the pharmacy team (n=2) (Table 10).(212,214) Studies included in this review varied in pharmacy BP measurement protocols, with different numbers of visits to the pharmacy (one to five visits), different number of readings per visit (two to six readings) and different operators responsible for conducting the BP readings (pharmacist, pharmacy staff or unattended kiosk).

Table 9 – Study characteristics

Study	Sample size	Mean systolic CPBP, mmHg (SD)	Mean Age, years (SD)	Population	Measurement modalities compared	% female	Location
Division et al 2001	96	131.4 (24.5)	57.3 (SD not reported)	Not stated	CP, GP clinic	63	Spain
Botomino et al 2005	50	129.0 (19)	53.7 (14)	Mixed	CP, ABPM, HBPM	58	Switzerland
Aleman et al 2008	1399	157.0 (13.4)	60.1 (9.7)	Hypertensive	CP, HBPM, GP clinic	50	Spain
Sabater-Hernandez et al 2011	169	128.3 (14.7)	56.4 (10.6)	Hypertensive	CP, ABPM, HBPM	60	Spain
Sendra-Lillo et at 2012	70	128.0 (14.8)	61.8 (12.4)	Hypertensive	CP, HBPM, GP clinic	44	Spain
Chambers et al 2013 (group A)	136	121.8 (14.1)	75.9 (6.5)	Mixed	CP, GP clinic	49	Canada
Chambers et al 2013 (group B)	139	127.6 (16.5)	75.9 (6.8)	Mixed	CP, GP clinic	53	Canada
Chung et al 2014 *	1838	Not stated	66 (10.0)	Mixed	CP, HBMP	62	Not stated
Padwal et al 2014	100	137.8 (13.7)	59.7 (12.8)	Hypertensive	CP, ABPM, GP clinic	53	Canada
Mutlu et al 2015	160	145.7 (12.9)	44.4 (15.3)	Mixed	CP, ABPM, HBPM and GP clinic	46	Turkey

CP= community pharmacy, HBPM = home blood pressure monitoring, ABPM= ambulatory blood pressure monitoring, GP = general practitioner, BP= blood pressure, SD = standard deviation. *Study not included in quantitative synthesis due to lack of data presented

Table 10 – Blood pressure measurement methods in included studies

Study	Setting	Nº readings per visit	Nº of visits	Protocol for calculating mean	Measured by
Division et al 2001	Pharmacy	3	1	Mean of three readings	Pharmacist
	GP clinic	3	1	Mean of three readings	Nurse
Botomino et al 2005	Pharmacy	2	1	Mean of two readings	Pharmacist
	ABPM	54	1 day	Mean of daytime readings	Automatic
	HBPM	4	4 days	Mean of days two to four	Patient
Aleman et al 2008	Pharmacy	2	3	Mean of two readings per visit	Pharmacist/ technician
	HBPM	3	3 mornings	Mean of all readings per sitting	Patient
	GP	2	3	Mean of two readings per visit	Patient
Sabater-Hernandez et al 2011	Pharmacy	3	4	Discarded first reading from each visit, mean over all four visits	Pharmacist
	ABPM	45	1 day	Mean daytime and 24-hour readings	Automatic
	HBPM	6	4 days	Discarded day one readings and first readings each morning and evening	Patient
Sendra-Lillo et at 2012	Pharmacy	3	5	Mean of all readings from first three visits	Pharmacist
	HBPM	6	4 days	Mean of days two to four	Patient
	GP clinic	3	3	Mean of all readings	GP and nurse
Chambers et al 2013	Pharmacy	6	1	Mean of readings two to six	Automated
	GP clinic	6	1	Mean of readings two to six	Automated
***Chung et al 2014**	Pharmacy	3	4	Mean of last two measurements from all four visits	Pharmacist
	HBPM	6	12 days	Discarded day one readings and first morning and evening readings thereafter	Patient
Padwal et al 2014	Pharmacy	3	4	Mean of each visit, as well as overall mean	Automated (kiosk)
	ABPM	45	1 day	Mean daytime and 24-hour readings	Automatic
	GP clinic	3	1	All readings	Research assistant
Mutlu et al 2015	Pharmacy	Not stated	1	Not stated	Pharmacy employees
	ABPM	Not stated	1 day	Mean of 24-hour readings	Automatic
	HBPM	Not stated	1 day	Not stated	Patient
	GP clinic	Not stated	2	Not stated	GP

HBPM = home blood pressure monitoring, ABPM= ambulatory blood pressure monitoring, GP = general practitioner.
* = not included in quantitative synthesis due to lack of data

3.5.3 Quality assessment

Risk of bias for each study is presented in Table 11. All studies had some degree of bias or lack of clarity in methodological reporting.

All but two studies (214,217) used a suitable reference standard to accurately estimate patient's out-of-office BP (i.e. ABPM or HBPM). The timing of index and reference measurements, with respect to each other, was generally poorly reported, with only one study randomising the order in which patients received the index test (CPBP) and reference test (in this case GP clinic BP).(214) Seven out of eight studies included in the meta-analysis used validated BP monitors, with the other using a non-validated wrist device.(215)

As none of the pooled analyses included 10 or more studies, the extent of publication bias could not be reliably assessed using an Egger's test as originally planned.(31)

Table 11 – QUADAS-2 assessment of study quality

Study	Risk of bias				Applicability concerns			Overall risk of bias
	Patient selection	Index test	Reference standard	Flow and timing	Patient selection	Index test	Reference standard	
Division et al 2001	High	High	High	Unclear	High	High	Unclear	High
Botomino et al 2005	High	Unclear	Unclear	Low	High	High	Low	High
Aleman et al 2008	Unclear	Unclear	High	Low	High	Low	Low	Unclear
Sabater-Hernandez et al 2011	Low	Unclear	Low	Unclear	Low	Low	Low	Low
Sendra-Lillo et al 2012	Low	Unclear	Unclear	Unclear	Low	Low	Low	Low
Chambers et al 2013	High	High	High	Low	Unclear	Low	High	High
***Chung et al 2014**	Unclear	Low	Unclear	Low	Low	Low	Low	Low
Padwal et al 2014	High	Unclear	Low	Low	Low	Low	Low	Low
Mutlu et al 2015	High	Unclear	Low	Low	High	Low	Low	High

*= not included in quantitative synthesis due to lack of data

3.5.4 Main results

Pharmacy and daytime ambulatory blood pressure readings

Three studies (n=319, mean age 57.0 years) reported data comparing CPBP and daytime ABPM readings in the primary analysis (Figure 5).(197,212,213) Daytime readings were defined inconsistently in the included studies, with two studies using readings from 0700 to 2200 h,(197,212) and one study using measurements from 0600 to 1800 h.(213) All studies included more than the minimum of 14 daytime (0700–2300 h) ABPM readings required by UK guidelines.(28,51)

Overall, pooled analysis of systolic CPBP and daytime ABPM readings (Figure 5) showed no significant difference between the two measurement modalities [WMD 1.6mmHg (95%CI -1.2 to 4.3), statistical heterogeneity I^2=34.6%, P=0.22].

Pharmacy and 24-hour ambulatory blood pressure readings

Three studies (197,212,215) (n=429, mean age 52.7 years) reported a comparison of CPBP and 24-h ABPM (Figure 5). All readings were from a single 24-h period. Mean systolic BP recorded in pharmacies were significantly higher than 24-h ABPM readings [WMD 7.8mmHg (95% CI 1.5–14.1)]. However, there was evidence of considerable statistical heterogeneity between included studies (I^2=92.1%, P<0.001) [28].

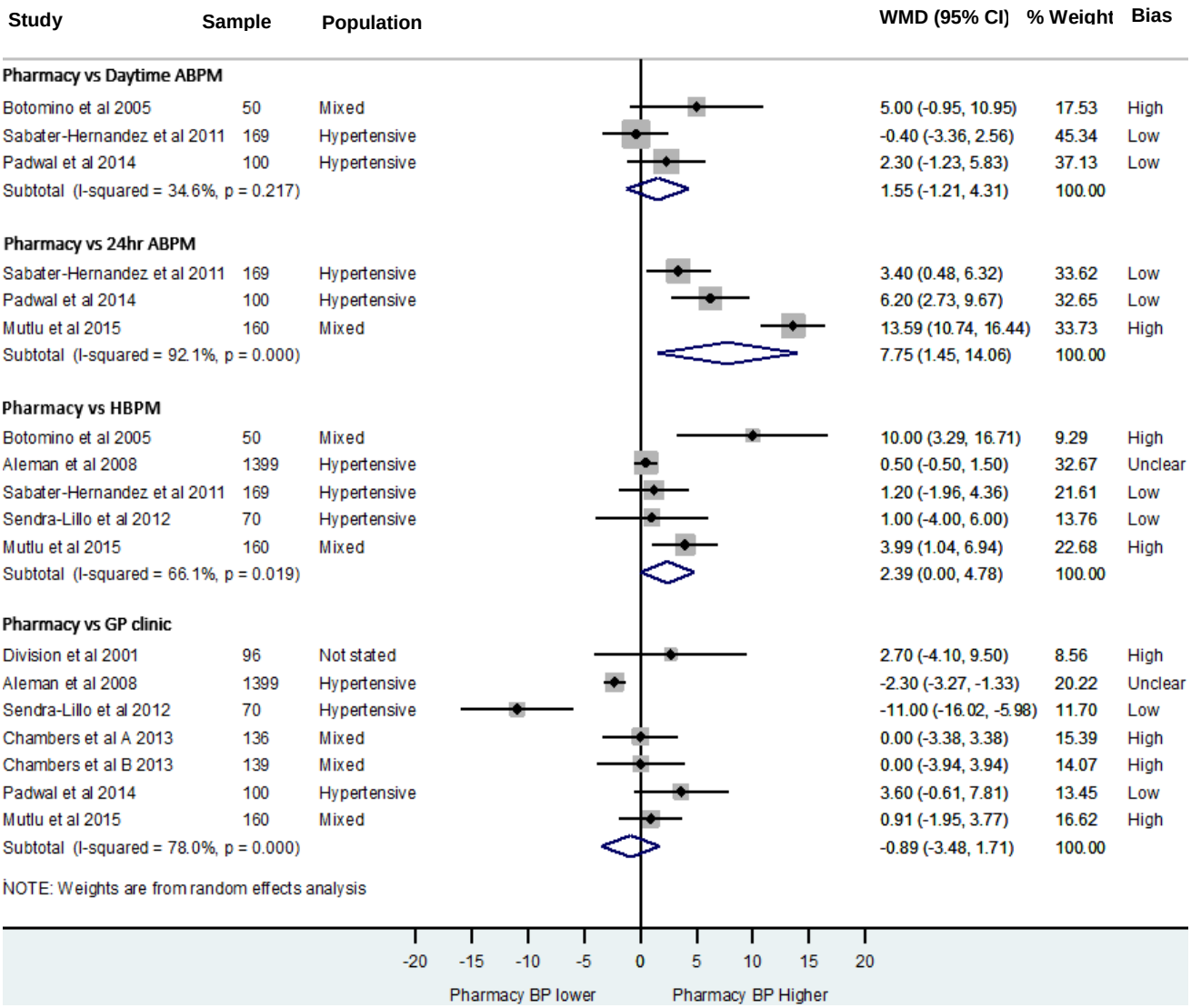

Figure 5 - Forest-plot showing weighted mean systolic blood pressure differences between; Pharmacy and daytime ABPM, Pharmacy and 24hour ABPM, Pharmacy and Home, and Pharmacy and GP clinic readings.

WMD= Weighted mean difference, Bias= Risk of bias, GP= General Practitioner, ABPM= Ambulatory blood pressure monitoring, HBPM= Home blood pressure monitoring

Pharmacy and home blood pressure readings

Five studies (197,198,211,213,215) compared mean systolic CPBP readings with HBPM (n=1848, mean age 58.3 years) (Figure 5). A sixth study stated that a CPBP–HBPM comparison was made but did not report this data in their analysis [24]. Mean systolic BP in pharmacy was 2.4mmHg (95% CI 0.0–4.8) higher than HBPM readings, with differences ranging from 0.5 to 10.0mmHg between studies. The observed statistical heterogeneity was significant (I^2=66.1%, P=0.02).

Pharmacy and general practitioner clinic readings

Across the six studies comparing mean systolic CPBP to general practitioner clinic measurements (n=2100, mean age 60.9 years),(198,211,212,214,215,217) there was no evidence of a difference between the two measurement modalities [WMD -0.9mmHg (95% CI -3.5 to 1.7)] (Figure 5). One study reported findings from two separate cohorts of patients and so is included separately in the meta-analysis as Chambers et al. group A and Chambers et al. group B.(214) Mean differences between studies ranged from -2.3mmHg (pharmacy readings lower than general practitioner) to 11.0mmHg (pharmacy readings higher than general practitioner), and there was evidence of considerable statistical heterogeneity between included studies (I^2=78.0%, P<0.001).

Diastolic comparison

Corresponding diastolic BP comparisons (Figure 6) show CPBP to be significantly higher than both daytime ABPM [WMD 2.96mmHg (95% CI 1.27to 4.64)] and 24-h ABPM [WMD 6.52mmHg (95% CI 5.19 to 7.85)]. There was no significant difference between CPBP and HBPM [WMD 1.61mmHg (95% CI -0.63 to 3.84)] or between CPBP and general practitioner clinic readings [WMD -0.24mmHg (95% CI -1.50 to

1.02)]. The diastolic comparisons exhibited less statistical heterogeneity compared to the corresponding systolic comparisons.

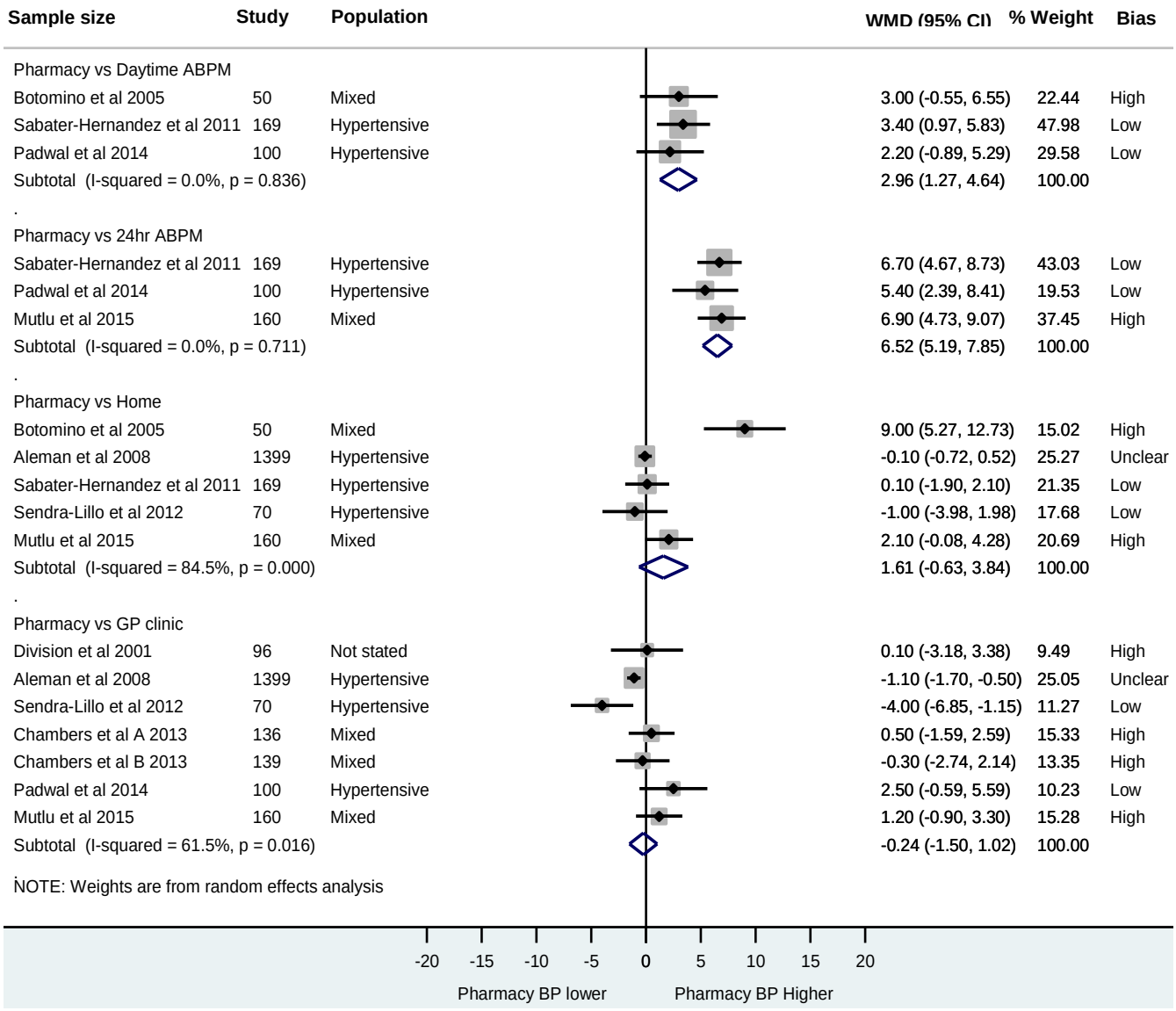

Figure 6 - Forest-plot showing weighted mean diastolic blood pressure differences between; Pharmacy and daytime ABPM, Pharmacy and 24hour ABPM, Pharmacy and Home, and Pharmacy and GP clinic readings.

WMD= Weighted mean difference, Bias= Risk of bias, GP= General Practitioner, ABPM= Ambulatory blood pressure monitoring, HBPM= Home blood pressure monitoring, CI = confidence interval

3.5.5 Subgroup and sensitivity analyses

The impact of excluding studies considered to exhibit high risk of bias was explored through sensitivity analyses. Figure 7 shows pooled estimates of all comparisons after removal of 'high risk' of bias studies. As with the primary analyses, these results show no difference between CPBP and daytime ABPM readings [WMD 0.8mmHg (95% CI -1.9 to 3.4)] and CPBP and HBPM [WMD 0.6mmHg (-0.4 to 1.5)]. Heterogeneity was reduced for the 24-h ABPM (92% to 32%) and HBPM comparisons (66% to 0%). CPBP remained significantly higher than 24-h ABPM readings.

Removal of 'high-risk' studies narrowed confidence intervals across CPBP and daytime ABPM, 24-h ABPB and HBPM. The interpretation of CPBP in relation to general practitioner clinic readings remained unchanged by this analysis, with no difference observed.

Further subgroup analysis, accounting for baseline hypertensive status (hypertensive or mixed cohorts) across all four modality comparisons did not significantly alter the study findings (Appendix 7).

Influence analyses, whereby each study is omitted in turn within each comparison, did not significantly alter the interpretation of the summary estimates (Appendix 8) suggesting that no one study had undue influence on the summary estimates above all others. This is despite the fact that 1,399 of 2,100 patients in the CPBP-GP clinic comparison (67%) came from one study,(211) whose results suggested that pharmacy readings were significantly lower than general practitioner clinic measurements [WMD -2.30mmHg (95% CI -3.27 to -1.33)].

The conclusions of this chapter were largely unchanged by the results of the sensitivity analysis by fixed effects (Appendix 6) in all but the pharmacy-GP comparison. Here, the fixed effects model, driven largely by the Aleman et al. study (n=1399, 67% of the total population in that analysis), showed pharmacy measured BP to be lower than corresponding GP readings [WMD -1.72mmHg (95% CI -2.55 to -0.89)].

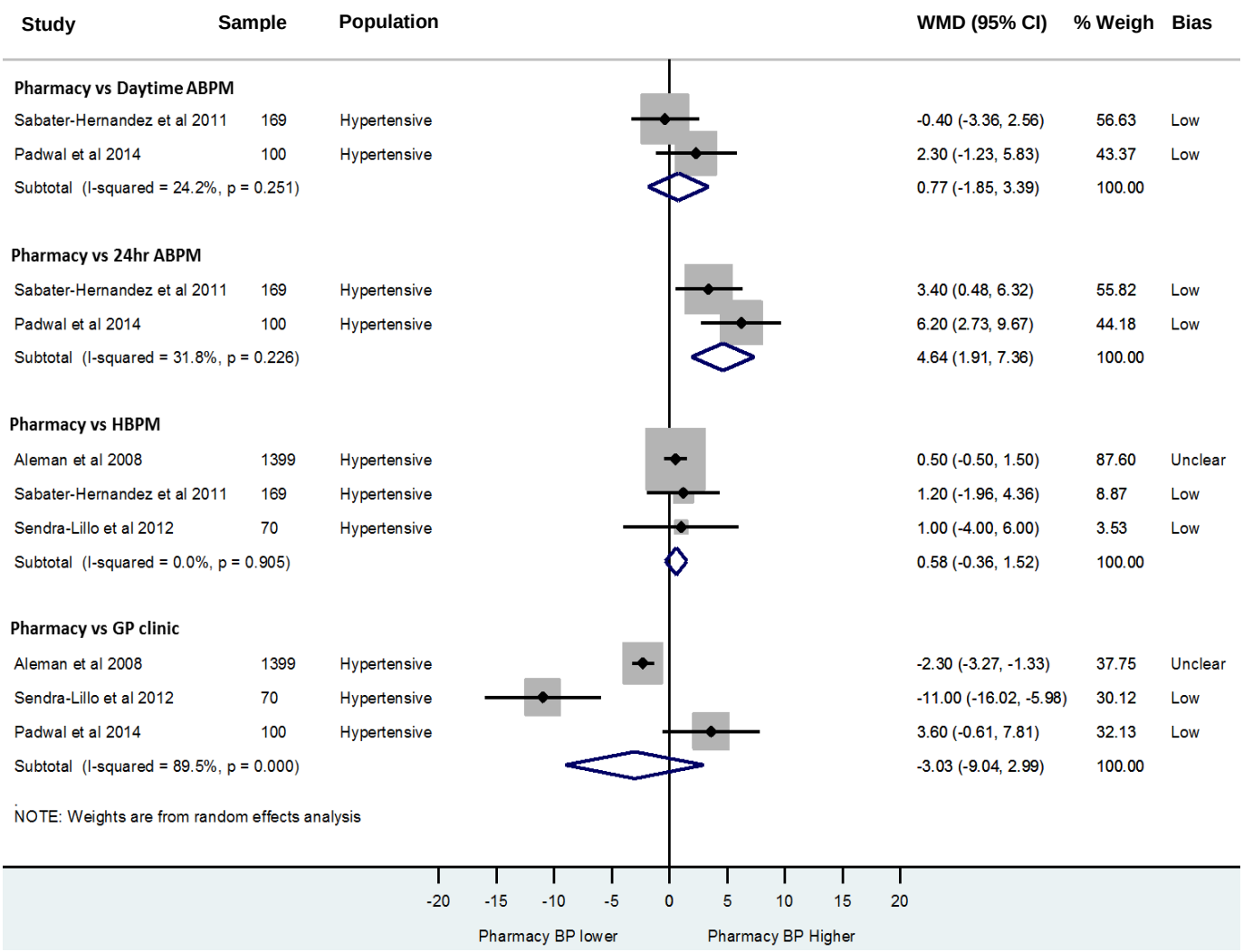

Figure 7 - Forest-plot showing weighted mean systolic blood pressure differences between; Pharmacy and daytime ABPM, Pharmacy and 24hour ABPM, Pharmacy and Home, and Pharmacy and GP clinic readings after removal of studies exhibiting 'high risk' of bias

WMD= Weighted mean difference, Bias= Risk of bias, GP= General Practitioner, ABPM= Ambulatory blood pressure monitoring, HBPM= Home blood pressure monitoring

3.6 Discussion

3.6.1 Summary of findings

This systematic review identified existing literature comparing BP measurements in community pharmacies with ambulatory, home and general practitioner clinic readings in the same patients. Pooled summary estimates from eight studies included 2,319 patients. There was evidence of no significant difference between systolic CPBP and daytime ABPM, and this result was unchanged by the removal of studies exhibiting high risk of bias. CPBP was significantly higher, both statistically and clinically, than 24-h ABPM readings [+7.8mmHg (95% CI 1.5–14.1)]. Given that 24-h ABPM readings include night time measurements and the associated night-time BP dip,(219) and that CPBP is measured during the day, it is unsurprising that the pharmacy–24-h ABPM comparison showed this.

Currently, BP readings taken in community pharmacies result in either referral to the general practitioner or advice to the patient, rather than formal diagnosis or regular patient follow-ups. These recommendations are based on the 140/90mmHg threshold.(146) Given this context and the inconclusive nature of the data from the primary studies in this review, the presented evidence suggests that CPBP readings may be best interpreted using the daytime ABPM threshold for the diagnosis and management of hypertension (135/85mmHg). This cautious approach would likely result in a higher sensitivity for detecting hypertension when referring patients to their general practitioner with borderline elevated BP, albeit at the expense of specificity.

3.6.2 Strengths and limitations

This is the first meta-analysis comparing CPBP readings to guideline recommended BP measurement techniques. The comprehensive and systematic search strategy meant that it was unlikely to have missed any relevant articles.

The interpretation of mean BP differences in this review was affected by inconsistent methodology between included studies, particularly in the measurement of CPBP. Four of the eight studies calculated mean pharmacy BP from one visit,(213–215,217) whereas all other studies used three or more visits. One study measured pharmacy and GP clinic BP using a non-validated wrist monitor.(215) Given so few studies were included in this review, it was deemed inappropriate to conduct post-hoc sensitivity analyses based on different BP measurement protocols.

Studies where mean CPBP was calculated from eight (197) or twelve (212) BP readings over several pharmacy visits correlated more closely with daytime ABPM than studies where CPBP was calculated from two readings at a single visit.(213) Importantly, however, readings from a single pharmacy visit may be most closely related to currently used BP measurement protocols in pharmacies.(146) Furthermore, in two studies comparing CPBP with GP clinic BP,(198,217) nurses were fully or partially involved in the clinic BP measurements rather than a GP. A systematic review comparing nurse with general practitioner measured BP estimated that BP taken by a nurse can be up to 7 mmHg lower on average than general practitioner measured readings.(148) Further studies in this analysis used automated devices that either take several BP readings continuously (BpTRU device) with an operator in the room,(214) or without an operator present.(212) The

use of automated blood pressure devices such as BpTRU have been shown to correlate more closely with daytime ABPM than clinic measurements where an operator is present or where each reading is manually taken.(220) These variations in measurement protocols are the likely to have contributed to the heterogeneity observed in the analyses.(221)

The largest study eligible for inclusion (n=1838) did not publish mean BP values for pharmacy and home readings, nor did the authors respond to any attempts to be contacted for their results.(210) Given the size of the study, it is unclear how inclusion of this study could have affected the 'pharmacy vs. home' comparison [currently +2.4mmHg (95% CI 0.0 to 4.8)] or the heterogeneity in that comparison.

Where no difference was seen between measurement modalities, the issue of whether sufficient statistical power was available to detect a true difference should be considered.(222) Three studies compared CPBP with daytime ABPM and only two of these presented a sample size calculation to adequately power their study,(197,212) with only one study recruiting a sufficient number of participants to meet their power calculation target.(212) Although pooling data from multiple, similar studies as part of a meta-analysis has the advantage of increasing the power to detect a 'true difference' in BP between measurement modalities, it is still possible that even with these additional data, the comparisons may have remained underpowered. The wide pooled confidence intervals in all systolic comparisons (all ~5 mmHg or higher) suggests this may have been the case.

Furthermore, it was not possible to extract mean differences of individual patients from the articles in this review, resulting in mean differences between measurement modalities being estimated from the overall mean BP data presented in each study.

This method results in larger standard errors, and thus, wider confidence intervals than if individual patient mean differences were available.(223) As such, the findings of this review are likely to be conservative in their estimations of how CPBP compares with other measurement modalities.

3.6.3 Comparison with previous literature

One previous systematic review conducted in 2009 compared pharmacy BP readings with ABPM, HBPM and GP clinic readings and found three studies but were unable to conduct a meta-analysis due to lack of available data and heterogeneity.(149) The current review presents pooled data from a further five studies (i.e. eight in all) combined in a random effects meta-analysis due to the heterogeneity between studies.

A 2011 systematic review by Hodgkinson et al. compared the diagnostic accuracy of home and general practitioner clinic BP readings with that of ABPM readings.(224) Their meta-analysis included two studies comparing HBPM with ABPM, six comparing general practitioner clinic BP with ABPM and one study comparing all three measurement methods. Their overall findings suggested neither clinic nor home measurement could be recommended as a single diagnostic test and therefore recommended that clinic readings should not be relied upon alone for the diagnosis of hypertension without ABPM measurements as confirmation. For the diagnostic accuracy of CPBP measurements to be ascertained, a receiver operating characteristic curve of its sensitivity and specificity for diagnosing hypertension would be required,(225) and although sought, these data were not sufficiently reported in the primary studies in this review.

Despite daytime ABPM readings typically being lower than clinic readings,(28) other literature have placed caveats on this broad assessment. For instance, a study comparing 888 non-hypertensive patients with a mean age of 45 years and a without history of cardiovascular disease, found that daytime ABPM was 7 mmHg higher on average than corresponding clinic readings.(209) Furthermore, a previous systematic review has also suggested that daytime ABPM readings were higher than office readings in patients until the age of 51 years, after which, office readings became higher - as per convention.(226) The interpretation of CPBP in the context of out-of-office measurements may therefore require investigation in a variety of sub-populations (e.g. based on age) in order to understand whether similar such caveats apply.

3.6.4 Implications for clinical practice

Findings from this meta-analysis suggest that CPBP may be best interpreted using daytime ABPM thresholds for hypertension diagnosis and management. In the absence of additional high-quality and adequately powered studies, using the 135/85mmHg threshold for hypertension is likely to ensure a higher sensitivity for detecting and referring patients with true underlying hypertension to their general practitioner or for out-of-office measurements, than the current 140/90 mmHg threshold. For example, if a patient's CPBP was measured as 137/85mmHg, using this threshold would likely result in the patient being advised to see their GP, encouraged to monitor their BP at home and/or given healthy lifestyle advice. If however the 140mmHg threshold was employed, this patient could be less likely to

get such advice. The former approach is more conservative but would likely benefit more patients whose clinic and out-of-office measurements would later suggest a persistently high BP. On the other hand, a lower threshold could increase GP workload through more false positive referrals. This could be minimised by pharmacies referring patients for HBPM or daytime ABPM directly to further refine referral criteria. The presented analyses do not support the utilisation of CPBP as an alternative to current out-of-office BP measures due to lack of data and certainty in the results. Instead, CPBP could be used to complement out-of-office BP monitoring.

Overall, the results of this chapter could be used by the NICE hypertension guidance committee as the best currently available evidence for interpreting CPBP – particularly as they do not currently have a position on this measurement modality.(49)

3.6.5 How this chapter fits within the wider thesis

While mean BP differences between GP clinic and out-of-office settings have been combined in a meta-analysis previously,(224) comparisons with pharmacy measured BP have not. All trials included in the systematic review by Cheema et al. (Table 5, Chapter 1) required the community pharmacist to either measure blood pressure in the pharmacy or interpret readings before making clinical decisions.(107) In order to consider pharmacies as suitable locations for ongoing hypertension monitoring and management, addressing the fundamental question of

how to interpret the blood pressure readings in a pharmacy was addressed in this chapter.

In addition to comparing BP differences between settings and aiding the interpretation of community pharmacy BP measurements, this chapter has also highlighted the variation in BP measurement protocols used in community pharmacies (number of visits, number of readings taken, person taking the readings). This highlights a wider lack of practical guidance for pharmacists in conducting BP measurements in community pharmacies. Such guidance would be important for improving the consistency of BP measurements taken in pharmacies and therefore aid its subsequent comparison with GP or out-of-office measurements. Following the BIHS guidance on how to measure BP could be a one way of improving consistency,(44) and further pharmacy-specific guidance could be used to reinforce this.

3.7 Conclusion

Studies comparing mean CPBP with general practitioner clinic and out-of-office measurements of BP were generally small, underpowered and exhibited important methodological differences in the way mean BP was estimated. Given the limitations of these studies CPBP readings should be cautiously interpreted using the daytime ABPM threshold for the diagnosis and management of hypertension (i.e. 135/85mmHg), until more adequately powered studies become available. Furthermore, the combination of these results with patient home measurements

could be considered before making decisions to refer patients their GP for treatment.

Chapter 4 – Community pharmacist consultations with patients starting a new anti-hypertensive medication: Qualitative analysis of 1,200 clinical notes

4.1 Chapter overview

This chapter presents a qualitative study exploring the content of clinical consultation notes made during the 'New Medicine Service' (NMS) for hypertension in England. The interventions across the 16 randomised controlled trials of community pharmacist-led hypertension management (Table 5, Chapter 1) provided some level of advice and counselling to patients but little is known about the nature of pharmacists' current consultations with hypertensive patients or their skills at providing such advice in routine clinical practice.

The overall aim of this study was to understand the nature and content of consultations between pharmacists and hypertensive patients drawing on data from a currently commissioned service (NMS) in England.

The content of 1,200 anonymised consultation notes were analysed thematically. Four main themes emerged from the analysis of patients who were subsequently referred to the GP after the pharmacist consultation (n=600): medication side effects; adherence and medication changes; discussing blood pressure readings; and patient uncertainty. Four main themes were identified from the analysis of non-referred patients: monitoring and follow-up; information and counselling; other medications and conditions; and discussing blood pressure readings.

The evidence from this study suggests that participating pharmacists provided a range of relevant information; advice and other hypertension related counselling to patients within the first two weeks of therapy in the NMS structure. The content of the consultations appeared comparable to the medication and lifestyle advice/counselling component in the interventions of the previous RCTs highlighted in Table 5 (Chapter 1). This suggests that pharmacists do have the required skills to deliver the types of interventions from these previous trials with little or no additional training required.

4.2 Introduction

As established in Chapter 1 of this thesis, community pharmacies do not routinely provide hypertension management in the UK. They do, however, conduct services aimed at discussing medications used for the management of long-term conditions such as hypertension.(151)

In England, the New Medicine Service (NMS) is a nationally commissioned 'Advanced Service' under the community pharmacy contract aimed at providing support for patients within the first month of starting a new medication.(13,152) It has been delivered in over 90% of community pharmacies in England since its introduction in 2011 and covers four therapeutic areas: hypertension; type 2 diabetes; asthma/chronic obstructive pulmonary disease; and anti-coagulation/anti-platelet therapy.(13) The NMS involves the following three stages:(227)

1. Patient engagement stage – a pharmacist would explain the service, provide initial advice to the patient about the medicine and its use, and agree a method and time for the intervention consultation (between 7-14 days after patient engagement).
2. Intervention stage (the focus of this chapter) – assess the patient's adherence to the medicine, identify problems, determine the patient's need for further information and support, and agree on one of the following steps with the patient based on three scenarios:
    a. If the patient is adherent and no problems are identified, follow up in between 7-14 days.

b. Problems are identified but intervention by the patient's GP is not required – agree the time and location for the follow up and any appropriate steps in the meantime.

c. Problems are identified and it is the clinical judgement of the pharmacist that intervention by the patient's GP is required – explain this to the patient, complete the NMS feedback form and refer the matter to the patient's GP practice. At this point the service will have been completed.

3. Follow up – pharmacist to provide advice and further support at this stage and agrees one of the following next steps with the patient based on three possible scenarios:

   a. Patient adhering to regimen – service completed.

   b. Problem identified – pharmacist and patient agree solution. At this point the service will have been completed.

   c. Problem identified – referral to the GP practice for review. At this point the service will have been completed.

The previous RCTs reviewed in Chapter 1 (Table 5) included medication and lifestyle advice/counselling as a key part of their interventions.(107) It is unclear, however, how applicable these interventions are to real-world practice, or to what extent they are already being delivered to patients. In relation to the overall thesis, the interventions delivered by pharmacists included assessments of blood pressure (addressed Chapter 3) as well as medication and lifestyle advice/counselling (addressed in this Chapter), and subsequent actions to follow-up with the patient or refer to their GP (Chapter 5, that follows) - as summarised in Figure 1 previously.

4.3 Chapter aim

The aim of this study was to understand the content of consultations between pharmacists and hypertensive patients – drawing on routine data from a service currently commissioned and delivered in England (the NMS).

4.4 Methods

4.4.1 Rationale for approach

This qualitative chapter used a thematic analytical approach, as described in Chapter 2 of the thesis (section 2.4). The analysis sought to describe the content of the consultation notes made by pharmacists. Although usually used in purely inductive approaches in the analysis of interviews,(173) thematic analyses are flexible enough to be used for other types of textual data as used in this study.(186) The predominant approach to analysis in this study was inductive – that is, themes were allowed to emerge from the data with little or no pre-emption from the researchers.(228) A deductive approach to thematic generation was not used in order to allow this analysis of pragmatic data to highlight the current practice of pharmacists delivering hypertension-related consultations.

Given the large number of consultation notes eligible for analysis (67,583 patients with consultation notes attached to their records), this chapter focussed on analysing a sample of these. No clearly agreed methodology exists regarding the

sampling of a large dataset of clinical notes for the purpose of qualitative evaluation. This chapter therefore describes the methods used to sample referred and non-referred patients (to general practice), controlling for demographic characteristics and blood pressure medications. By sampling and comparing themes between referred and non-referred patients, this chapter attempted to compare and contrast the differences (if any) between the two groups in terms of pharmacist interventions and patient presentations. Further details regarding the sampling strategy can be found in the corresponding section of the methods below.

4.4.2 Data source

Anonymised patient and consultation data were recorded by pharmacists using 'PharmOutcomes' software in pharmacies as part of the NMS service, and were subsequently sent to the Pharmaceutical Services Negotiating Committee (PSNC).

'PharmOutcomes' is a web-based platform available to all community pharmacies in England to record data on service provision, such as influenza vaccination provision.(229) Pharmacists recorded information regarding patient age, sex, ethnicity, the anti-hypertensive drug and dosage. The consultation-related information was recorded in two forms – free text data analysed in this chapter, and fixed field data relating to the boxes ticked by pharmacists after the consultations (analysed in the chapter that follows). The full data collection form for pharmacists conducting the NMS can be found in Appendix 9.

Data were obtained via a request to the PSNC who provided the data based on a plan of analysis (described in this chapter). Since this was an analysis of routinely collected and fully anonymised data, no ethical approval was required.

4.4.3 Sampling

Patients were excluded from this analysis if they:

- Withdrew consent for subsequent pharmacist interventions/follow-ups after recruitment
- Could not be contacted for subsequent appointments after enrolling in the service
- Had a recorded age of under 18 years or no age recorded
- Contacted the pharmacist to say that their medication had been stopped prior to their first NMS consultation
- Had no recorded consultation notes

A flow chart quantifying the reasons for exclusion is depicted in Figure 8. To produce a sample of consultation notes to meet the study objectives, first, a random sample of four hundred referred patients and four hundred non-referred patients was generated using STATA statistical software (StataCorp. 2015. *Stata Statistical Software: Release 14*. College Station, TX: StataCorp LP). Individual patient data were placed in ascending order according to study identification number, and the *'sample'* command in STATA was used to generate the random sample – controlling for demographic factors and the medication class prescribed via the '*sample'*

command. At stage two of sampling, a further two hundred referred and two hundred non-referred patient consultations were randomly identified in the same way as described above.

The two-stage process allowed for the assessment of thematic saturation by confirming or contradicting themes generated from the first sample (n=800) with the second sample (n=400). If further themes emerged after stage two, a further sample of 200 would have been taken, and would have continued to be taken until no new themes were identified. It is worth noting that the themes generated were broad and were intended to portray the topic of the consultations, rather than to provide an account of all clinical scenarios that could have been encountered across the dataset or current practice.

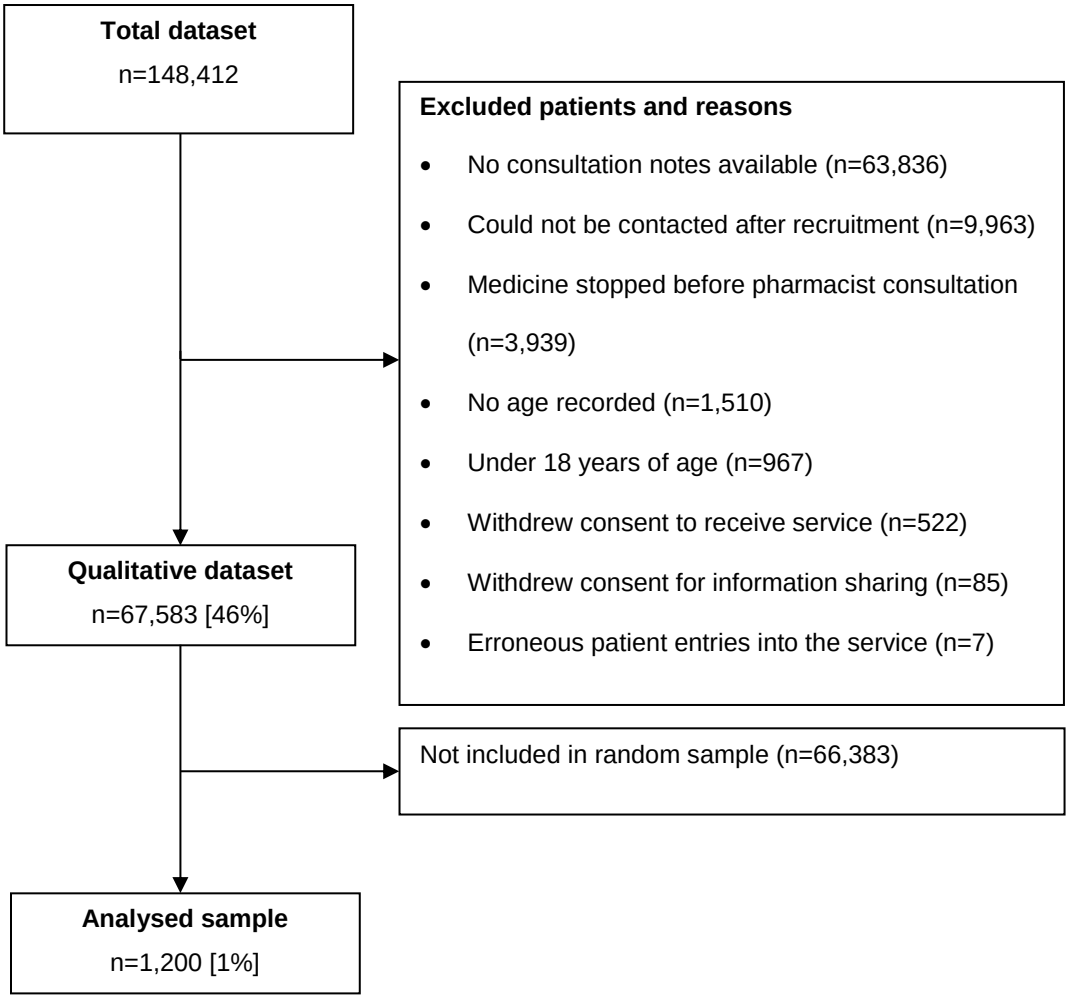

Figure 8 - Derivation of sample flow diagram

4.4.4 Data analysis

Data were analysed using thematic analysis, as described in Chapter 2.(173) A thematic analysis encourages an inductive approach to data analysis i.e. themes are derived from the data with little or no pre-emption of themes by the researcher prior to data collection.(184) This type of analysis is appropriate when existing theory or literature on a phenomenon is limited – as is the case for routine consultations between pharmacists and hypertensive patients. Researchers are expected to immerse themselves in the data by reading and re-reading the content,

utilising the constant comparison method (described below) to allow new insights to emerge as transcripts are being analysed.(230)

After random sampling, data were read and re-read independently by the author Ali Albasri (AA, a pharmacist and doctoral research student) and by Dr. Suman Prinjha (SP, DPhil supervisor and senior qualitative researcher) in parallel to ensure familiarity with the style and breadth of the consultation notes. All consultation notes were constantly compared to previous notes in order to ensure consistency in thematic development and to ensure that themes encompassed the breadth of the consultation data.(186) Data were transferred to NVivo 11, a qualitative data-indexing package that facilitated analysis and organisation of codes (NVivo QSR International Pty Ltd. Version 11, 2015).

Data were available for all three stages of the NMS process outlined in section 4.4.2 above. Analysis focused on pharmacist-reported consultations occurring during the intervention stage of the NMS process (up to two weeks after medication initiation). This was in order to select a time point where the pharmacist had to make a decision as to either follow up a patient or refer them back to their GP. Analysis of the follow up phase of the NMS does not specify that a pharmacist has the option of further follow up as they are not paid to do so, therefore pharmacists do not have to make the same decisions at that time point compared to the intervention stage.

Since this was an analysis of anonymised routinely collected data, no ethical approval was required.

4.5 Results

4.5.1 Characteristics of sample

Of the 148,412 hypertensive patient consultations recorded on the PharmOutcomes database for the NMS, 67,583 (46%) matched the inclusion criteria of this study (Figure 8). Consultation notes from 1,200 hypertensive patients (600 referred and 600 non-referred), recorded by community pharmacists between October 2011 and September 2012, were randomly sampled and analysed.

The age, sex, ethnicity and number of anti-hypertensive medications prescribed in the two sample groups were similar to that of the overall dataset (Table 12). Table 13 presents the frequency of patient reported issues in the analysed sample. The average number of words per consultation was 19, therefore approximately 22,800 words were analysed in this study (equivalent to approximately 65 A4 pages of text). Demographic characteristics of the samples closely matched those of the overall dataset.

Patients are denoted through their assigned identification number (e.g. p33 = patient number 33), followed by gender (M or F), anti-hypertensive drug class prescribed (e.g. ACE-I = angiotensin converting enzyme inhibitor) and patient age (years).

Table 12 below provides a full breakdown of the patient characteristics in this analysis.

Table 12 – Patient Characteristics

	Overall dataset* n= 131,419	**Qualitative dataset** n=67,583 (51%)**	**Referred sample n= 600**	**Non-referred sample n=600**
Referral to General Practice, n (%)	5,895 (4)	4,395 (7)	600 (100)	0 (0)
Mean length of consultation note (words)	n/a	20	19	19
Age, mean (SD)	65 (13)	68 (13)	66 (13)	64 (12)
Ethnicity, n (%)				
White	112,194 (85)	58,686 (87)	504 (84)	511 (85)
South Asian	4,586 (4)	1,988 (3)	22 (4)	20 (3)
Black/African-Caribbean	2,760 (2)	1,239 (2)	20 (3)	9 (2)
Not stated	10,234 (8)	4,894 (7)	46 (8)	50 (8)
Other	1,645 (1)	776 (1)	8 (1)	10 (2)
Gender, n (%)				
Male	61,146 (47)	30,362 (45)	299 (50)	304 (51)
Female	70,273 (53)	37,221 (55)	301(50)	296 (49)
Medication class prescribed, n (%)				
CCB	41,372 (32)	21,618 (32)	185 (31)	188 (31)
ACE-I	34,497 (26)	17,769 (26)	139 (23)	162 (27)
ARB	17,415 (13)	8,900 (13)	75 (13)	84 (14)
Thiazide-like diuretic	16,211 (12)	7,824 (12)	83 (14)	66 (11)
B-blocker	15,487 (12)	7,926 (12)	71 (12)	74 (12)
A-blocker	5,264 (4)	2,938 (4)	40 (7)	18 (3)
Other	1,173 (1)	608 (1)	1 (0.3)	8 (1)

*= Consented and followed-up patients; **= patients with consultation note data. CCB = calcium channel blocker; ACE-I = Angiotensin converting enzyme inhibitor; ARB = angiotensin II receptor blocker; B-blocker = beta-blocker; A-blocker = alpha-blocker.

4.5.2 Key themes - referred patients

A sample of six hundred consultation notes between pharmacists and hypertensive patients, subsequently referred to their GP, was analysed. Four main themes emerged from the data:

1. Medication side effects
2. Adherence and medication changes
3. Concerns about blood pressure readings
4. Patient uncertainty

Medication side effects

The discussion of medication side effects was an overarching theme throughout the NMS consultations and is relevant to each theme presented in this analysis. A standalone theme reporting the scope of discussions related to side effects was nonetheless warranted.

Pharmacists used the consultations as an opportunity to identify potentially serious medication related problems or side effects before a patient's next scheduled GP appointment.

> *"Rash on hand developed. A risk of angioedema"* (p519 – M, B-blocker, 59yrs)

The urgency of the referral back to the GP was emphasised by pharmacists in instances they deemed severe enough – in some cases contacting the patient's GP surgery on the same day:

"Called GP on 13.04.2012 at approx. 2.30pm. Spoke with receptionist and addressed my concerns. Receptionist took patients phone number to make arrange appointment with the GP." (p175 – M, ACE-I, 48yrs)

Pharmacists described patients as reporting 'negative feelings' in the fixed field boxes of the NMS form. These negative feelings were often reported to be in relation to medication side effects.

"Negative feelings due to side effects. Swollen ankles. Has stopped taking" (p36 – M, CCB, 60yrs)

Referrals due to side effects ranged from serious and immediate referrals (such as for suspected angioedema – shown previously) to referrals due to more common medication side effects.

"Patient experiencing headache similar to one she had when prescribed amlodipine, stopped taking them (Lacidipine) and headache went, re-started and headache came back, referred to GP." (p46 – F, CCB, 68yrs)

"The patient had usual side effect of the tablet which is constant unbearable headache. He had tried to overcome with Paracetamol but didn't work." (p80 – M, CCB, 43yrs)

On occasion, patients were referred to their GP after reporting side effects or other complaints that they had attributed to the new medication, despite these not being listed as an adverse effect of the drug. These cases appeared not to have been discussed or corrected by the pharmacists and so the negative feelings toward the medication that some patients reported were not discussed.

"Pain in the feet for the last four days since he started taking Losartan, which is now worse than usual pain he feels" (p55 – M, ARB, 57yrs)

"Is getting flu like symptoms 30 minutes after taking the tablet" (p49 – M, Thiazide, 71yrs)

Adherence and medication changes

Issues relating to medication side effects led to pharmacists reporting non-adherence (patients stopping the medication) and other changes to the use of the newly prescribed anti-hypertensive. In cases where the new medication had replaced a previous anti-hypertensive drug, pharmacists reported that some patients reverted to their old medications, presumably from old stock left at home, in response to either inadequate BP reductions or unacceptable side effects.

> *"Patient has a blood pressure machine at home and has been monitoring his blood pressure. He tells me that his blood pressure was very high with amlodipine so he has reverted back to his previous drug valsartan. The Dr is unaware of this." (p162 – M, CCB, 58yrs)*

> *"Took one tablet and felt very sick. Bladder problems, leg cramps so stopped it and went back to losartan tablets." (p159 - F, Thiazide, 78yrs)*

Pharmacists reported on instances where dosing recommendations were discussed in light of falls – an adverse event related to anti-hypertensive drugs rather than a medication side effect per se. Given that pharmacists in community do not have the prescribing authority to make dosage adjustments, these patients were referred to their GP.

> *"Patient had a fall on Wednesday - 2 days after starting medication - dose due to be increased on Sunday to 2 a day but have advised pt to see gp before doing that." (p394 – F, ARB, 90yrs)*

There were some examples of pharmacists identifying medication non-adherence in instances unrelated to side effects or adverse events. In the example below, the patient reported taking a 'complementary medicine' for an unspecified indication and therefore felt that their newly prescribed Ramipril was incompatible.

"Taking complementary medication and took one dose of Ramipril and then stopped. Doesn't want to mix the two types of medication and therefore will not use medication." (p22 – M, ACE-I, 42yrs)

While the pharmacist reported this in the consultation notes, it is unclear whether attempts were made to discuss the patient's medication beliefs and perceptions.

Concerns about blood pressure readings

Consultations discussing BP with referred patients were mainly centred on self-monitored/home BP readings rather than on measurements taken in the pharmacy or GP clinics. Although the recommended questions during NMS consultations focus on the early identification of side effects and establishing adherence patterns (Appendix 9), pharmacists appeared to use patient's self-monitored BP readings as an additional guide to decision making.

"Swelling around ankles increased aching and numbness in body and not much difference in BP reading - patient measures daily. Referred to GP." (p151 – M, ACE-I, 48yrs)

"Seems to be causing sleep disturbances and measures own BP which at the last reading was 168/80" (p104 – F, ARB, 68yrs)

Referrals were recommended in cases where patients reported unsatisfactory BP results (either too high or too low) in the absence of adverse medication affects.

"Patient monitors blood pressure every day and not decreasing." (p86 – M, ACE-I, 67yrs)

The extent to which pharmacists trained patients to take home BP or interpret their readings was unclear from the consultation notes. However, one patient was referred back to the GP for expressing an interest in self-managing their BP, suggesting that such training was variable if present at all.

Wants to manage BP by self-management. Concerned about potential risk of exacerbation of psoriasis. (p224 – M; B-Blocker; 74yrs)

While the interpretation of BP levels in relation to threshold was not explicitly clear from the consultation notes, there did appear to be some interpretations of BP that were not in line with current NICE guidance, particularly with regards to diastolic readings.

Last BP 140/66 - too low!! Lost 20kg recently, wants to lose another 15kg. Doing 10,000 steps per day. Told to speak to GP about coming off tablet - also not happy to take it anymore. (p126 – M; CCB; 63yrs)

Patient uncertainty

Pharmacists indicated that some patients reported measuring their BP before and after taking their new medication and made judgements regarding its efficacy based on this.

"Patient does not think that medication is working, he did BP measurement on 26/07/2012 and it was 139/90." (p383 – M, ACE-I, 32yrs)

"Patient feels that the medication isn't working. He has said that his BP has increased since starting them. Could possibly be due to incorrect use of BP monitor." (p332 – M, CCB, 74yrs)

Rather than uncertainty relating only to drug efficacy, pharmacists also reported that patients raised doubts about whether they needed to start their new anti-hypertensive medications at all. For instance, pharmacists stated that some patients acknowledged the fact that a reliable diagnosis of hypertension may require more than one BP measurement in the GP's clinic.

"Concerned that diagnosis was made on one blood pressure reading at surgery that was elevated." (p293 – F, Other, 58yrs)

"Concerned that medicine is not required as diagnosis was made on a one off measurement during a house move etc. Does not want to take…" (p367 – F, ACE-I, 59yrs)

"Has stopped taking. Went to GP with sinus problem. BP was checked and amlodipine prescribed. This has caused sinus problem to worsen and caused flushing etc. ...does not understand why prescribed so has stopped taking." (p390 – M, CCB, 52yrs)

Patient uncertainty towards the perceived need for the new medication was also linked with the continuity of care from their regular GP. Some patients given a new mediation or a new diagnosis of hypertension by a GP other than their own were reported to show reluctance to taking their medication.

"Medication prescribed by different GP, patient not convinced about the medication. Waiting for her GP to come back to confirm/cancel the medication." (p50 – M, Thiazide, 56yrs)

4.5.3 Key themes - non-referred patients

Six hundred consultation notes between pharmacists and hypertensive patients who were not subsequently referred back to their GP were analysed. Four main themes were identified from the data:

1. Monitoring and follow-up
2. Information and counselling
3. Discussing other medications and conditions
4. Discussing blood pressure readings

Monitoring and follow-up

Some pharmacists demonstrated a 'watchful waiting' approach, particularly in relation to the management and monitoring of adverse drug effects. In particular, they were willing to use subsequent consultations within the NMS process as an opportunity to follow-up patients, rather than refer to a GP.

> *Patient taking medication regularly in the mornings, however in the last day or so has been experiencing slight light-headedness. Hasn't affected patient too much. Will keep taking medication and I will follow up in a couple of weeks. (p53 – M; CCB; 60yrs)*

Further examples followed a similar pattern, whereby pharmacists recorded a common side effect such as dizziness or gastrointestinal disturbances, and would recommend that the patient should continue for now to see whether this was a transient issue, or something that would require further clinical input.

> *"Has had a cough will see if it carries on as a side effect or is just a cough." (p60 – F; ACE-I; 66yrs)*

Some pharmacists reported shared decision making with patients on decisions about referral or follow-up. These consultations appeared to discuss balancing the side effects of the drug with its efficacy, concluding in a judgement based on this balance.

> *Feels dizzy sometimes, but tablet seems to help a lot with her water retention. So she is quite happy with them for that. Advised patient to continue taking tablets, if problem still persist on next follow up. Might recommend MR* [modified release] *preparation that may be useful to help with her dizziness. (p313 – F; Thiazide; 47yrs)*

Information and counselling

Pharmacists reported on a range of patient concerns regarding their new treatment. These included patient queries about adverse medication effects, the efficacy of the new medication, how the medication should be taken (e.g. with food/at night), why the medication was needed, possible interactions with other medications, and advice on monitoring BP. Providing information about medication side effects was common whether patients were referred back to their GP or not, and included information on common side effects as well as side effects that are not usually associated with the medication. Pharmacists were able to offer advice to help patients overcome some of the common, and potentially transient, medication adverse effects.

> *"Causes dizziness, advised to take at bedtime"* (p21; F; CCB; 55yrs; not referred)

Counselling offered by pharmacists also included dietary and lifestyle recommendations, including the benefits of non-pharmacological measures to reducing blood pressure and the positive effect this would have on overall health. Other lifestyle advice related to hydration, exercise, smoking and alcohol.

> *"Patient started medication and having taken blood pressure at home after a week on Bendroflumethiazide, there was a significant reduction. Patient also took my exercise and diet advice and has reduced alcohol consumption."* (p407; M; Thiazide; 61yrs; not referred)

Pharmacists counselled patients regarding the risk/benefit trade-offs of taking long-term blood pressure lowering medications, and of the likelihood of experiencing side effects.

> *"Concerned about having to take long-term medication and the effect this may have. Reassured that safe to do so long-term and the benefits will*

outweigh the risks of leaving the BP untreated" (p81 – F, ACE-I, 42yrs, not referred)

Some pharmacists reported addressing the concerns of patients who had read the medication information leaflet. These pharmacists acknowledged that reading a long list of possible adverse effects, regardless of prevalence, could cause anxiety in some patients,(231) and so this was addressed during the consultations – in contrast to the actions reported in the referred cohort.

"…did not start taking the Ramipril straight away as she read in the leaflet that it may cause vertigo which she already suffers from. I reassured her that she is taking the smallest available dose which will gradually be increased…" (p198 – F, ACE-I, 63yrs, not referred)

Pharmacists also reported providing information regarding medication conversions. Some patients recruited on the NMS were previously taking an anti-hypertensive medication but may have been switched to an alternative due to poor tolerability or side effects, for instance. Given that medications with the same class have different potencies, the doses (the numerical number of milligrams needed to elicit the equivalent therapeutic effect) may differ.

"Patient asked about increase in milligrams for losartan, reassured him that this was the equivalent of his previous candesartan. BP 128/72 weighs 17.5 stone, plays golf for exercise and is actively losing weight as knows this will help BP." (p30 – M, ARB, 44yrs)

Discussing other medications and conditions

Although the NMS consultations are aimed at a single new medication, there was evidence that pharmacists engaged in discussions about other medications and conditions to hypertension. Discussion of other medications included identifying the possible source of side effects that patients were experiencing.

> *"Patient has been taking antibiotics in addition to amlodipine this last week and is unsure whether gastric side effects are related to the new medicine."* (p99 – F, CCB, 41yrs, not referred)

Further examples showed evidence that some pharmacists discussed the new medication or new diagnosis of hypertension in the context of comorbidities that are directly related to an increased cardiovascular risk, such as diabetes. In addition, pharmacists also provided evidence that they dealt with confused polypharmacy patients or patients with other medication related queries, within the NMS consultations:

> *"Patient has had so many changes to his medication recently he is getting a bit confused as to what is going on, have been through all meds and reassured…"* (P49; M; ACE-I; 92yrs; not referred)

> *"Wanted to talk about Diclofenac to Naproxen change."* (p186; M, ACE-I; 72yrs)

Additional examples showed that some pharmacists engaged in discussions addressing lifestyle choices such as excessive alcohol consumption.

> *"…drinks 4 half pint glasses of Vodka once a week. Counselled regarding lifestyle and regarding alcohol intake..."* (p52 – F, B-blocker, 59yrs, not referred*)*

Discussing blood pressure readings

In contrast to the referred sample, consultations discussing BP readings among the non-referred sample originated from a variety of measurement modalities. These included patient self-monitored readings as well as GP measured BP, pharmacy measured BP and nurse measured BP.

> *Dizziness with first few doses. Ok now. BP check with GP confirmed BP has already reduced.* (p223 – F, ARB, 49yrs)

> *Taking medication every day and not experiencing any problems. Had BP checked by nurse and has reduced.* (p284 - F, CCB, 61yrs)

Where patients measured BP at home, some pharmacists took the opportunity to confirm the readings by taking measurements in the pharmacy.

> *"…BP measured, patient has been monitoring at home am and pm has found a drop in BP. BP measured in pharmacy 4.35pm 155/90 and 145/85 average 150/88. Will re-check in 2 weeks…"* (p170 – F, Thiazide, 71yrs)

Given the asymptomatic nature of hypertension, some pharmacists used the BP readings to counsel patients who may have been unsure about the efficacy and need for their new medication. On some occasions, pharmacists were able to demonstrate the efficacy of new BP medication by discussing BP readings taken before starting the medication with those taken subsequently.

> *"BP at recruitment (28/05/2012) 163/84; BP at intervention (07/06/2012) 149/72…"* (p253 – M, A-blocker, 82yrs)

Table 13 – Frequency of patient reported issues in the analysed samples

Patient reported issues	**Qualitative dataset [n=67,583]**	**Referred sample Frequency, n (%) [n= 600]**	**Non-referred sample Frequency, n (%) [n= 600]**
Using medicine as prescribed	57,700 (85)	266 (44)	532 (89)
Side effects	21,238 (31)	454 (75)	144 (24)
Negative feelings towards new BP medication	4,541 (7)	170 (28)	26 (4)
Uncertainty whether medicine working	5,864 (9)	64 (11)	53 (9)
More information about medication needed	4,449 (7)	39 (7)	52 (9)
Not using medication as prescribed	4,264 (6)	222 (37)	20 (3)
Missed dose in the past 7 days	978 (1)	42 (7)	4 (1)
Not yet started the medication	642 (1)	21 (4)	2 (0.3)
Concerns about remembering to take medication	586 (1)	6 (1)	7 (1)

4.6 Discussion

4.6.1 Summary of findings

This study analysed the content of 1,200 pharmacist consultation notes from the intervention stage of hypertensive NMS consultations.

In the referred sample of 600 patients, four key themes emerged from the data: medication side effects; adherence and medication changes; blood pressure readings; and patient uncertainty. Discussions regarding medication side effects ranged from identifying potentially serious manifestations such as angioedema, to addressing misconceptions around the side effects of their new medication. Pharmacists reported on instances where patients would either stop their medication or revert to previously prescribed anti-hypertensive drugs, usually because of medication side effects or adverse events. Patient uncertainty resulted from three main areas: uncertainty about the circumstances in which hypertension was diagnosed; uncertainty about the prescriber making the recommendations; and uncertainty regarding the efficacy of the new medication.

A further four themes were identified from the 600 non-referred patients analysed: monitoring and follow-up; information and counselling; other drugs and conditions; and discussing blood pressure readings. Monitoring and follow-up highlighted cases where pharmacists used the next stage of the NMS process (the follow-up stage) as a safety net for re-examining the patient's concerns or side effects. For some side effects, such as dizziness upon medication initiation, pharmacists advised patients to wait until the next appointment in the NMS to discuss a decision to refer

or continue. Pharmacists demonstrated evidence of providing information and counselling to patients experiencing side effects, such as elevating ankles that were swollen from calcium channel blockers. Other instances of counselling included providing information to the patient regarding the benefits and risks of taking long-term medications, and information where medications or doses had been changed. Other consultations demonstrated instances where the patient's hypertension was discussed in the context of their co-morbidities or other medications, or where the NMS consultations were used as an opportunity to discuss medications or conditions that were not hypertension-related. Finally, where BP readings were discussed, they were used either to confirm home readings with pharmacy measurements, or to inform patients who may have been uncertain as to their need for the new medication.

4.6.2 Strengths and limitations

This chapter provides the only detailed exploration of routine hypertension NMS practice beyond the descriptive data presented by the PSNC in 2012.(229) The analysis included a large sample (1,200 consultation notes) that controlled for demographic characteristics and prescribed antihypertensive drug class. The study sample was representative of the wider cohort of 67,000 patients.

The average length of each consultation note analysed was nineteen words. As a result, the depth of analysis possible was limited. Despite this, the breadth of the sample, the number of consultation notes analysed, and the comparison between

referred and non-referred patients allowed themes to be explored across a wide range of patient presentations, thus capturing a diversity of cases.

Due to the limited amount of patient data collected during the NMS, it was not possible to further sample patients based on the number of anti-hypertensive medications taken, the severity of their blood pressure readings, nor by relevant co-morbidities. Such analyses could have provided an insight into how pharmacists manage particular patient sub-groups. Although blood pressure levels are not routinely recorded in the NMS (Appendix 9), analysis of the consultation notes suggested that BP readings were discussed with patients. Furthermore, data on co-morbidities and polypharmacy were not routinely recorded in the NMS dataset, yet evidence from this chapter suggests that these were discussed with some patients.

Given that this study analysed routinely collected consultation data documented by pharmacists, the results only reflect pharmacists' reported views of the consultations. The presented themes can therefore not be used to explain the impact of the consultations on the patient – i.e. whether the provision of advice and information by the pharmacist was sufficient or directly resulted in the patient feeling reassured. Furthermore, the overlap of concepts and themes within consultations required subjective judgements to be made in order to classify the consultation note into one sub-theme rather than another during analysis. While this could be interpreted as a limitation of qualitative research in general, it may also be reflective of clinical practice, as patients and their presentations are seldom compartmentalised or clear-cut. Analysis in this study was conducted independently by two researchers in order to minimise bias, as per established qualitative methodology.(173)

Of the 148,412 potentially eligible patients, 67,583 (46%) had consultation notes associated with their record. Consultations where no clinical notes were written do not necessarily mean that no transfer of information or meaningful conversation took place. Equally, notes where certain consultation techniques or features were not explicitly reported do not necessarily mean that they did not occur. While differences between individual pharmacists or specific patient presentations may be used to explain some of the decisions to refer rather than follow-up, it is not possible to determine causality from these observational data. In addition, this analysis is unable to establish whether patient referral or non-referral (follow-up) was clinically appropriate, nor did it attempt to.

A further limitation of this study relates to the patient population investigated. It is unclear how these consultations would differ between patients presenting with repeat medications rather than new medications for hypertension. NMS consultations are not necessarily representative of hypertension management as the service does not involve clinical condition monitoring, for example. Instead, the NMS focusses on medication tolerance and adherence, and occurs during the first month of treatment only. These factors must therefore be considered when assessing the generalisability of these findings to hypertension management.

4.6.3 Study findings in the context of previous literature

A randomised controlled trial of pharmacists providing new medicine consultations showed that these can lead to improvements in medication adherence at 10-week follow-up,(152) though it is unclear if this persists in the longer term.(232)

Pharmacists delivering new medicine consultations have previously stated in interviews that they feel able to contribute to patient care, particularly with regards to providing medication related information, advice on side effects, and reassurance when presented with patient uncertainty towards taking their medication.(154) This and other literature have suggested that pharmacist-patient interactions primarily focus on the medicine rather than engaging in discussions around patient's health values and beliefs.(233) The analysis in this chapter also found this to be the case, though some evidence of pharmacists providing more holistic consultations when discussing newly prescribed anti-hypertensive medications was also observed.

A systematic review by Marshall et al. (2012) synthesised 53 qualitative studies exploring patient perspectives of having hypertension and taking anti-hypertensive medications.(187) The patient-reported concerns described in the presented chapter closely resembled those reported across the 53 studies reviewed. For instance, the Marshall et al. synthesis described how patients would intentionally avoid or reduce treatment in response to a lack of hypertension symptoms or a belief that their medications were ineffective at reducing blood pressure. This was a theme noted in this chapter, in particular when discussing blood pressure readings and uncertainty towards the medication's efficacy.

In a survey of 258 patients starting a new medication for a range of chronic conditions, 43% reported *'concerns about the new medication'* in the first ten days after the prescription was issued.(234) The authors concluded that more than half of the patients expressed a need for *"sustained and substantial information"* regarding their medications beyond this period, and that approximately a third of patients were *'intentionally non-adherent'* to their new drug as a result. While the expanding roles of pharmacists in primary care settings have the potential to resolve

medication related issues, particularly in providing information and counselling in the early stages of treatment, the evidence for this from routinely collected data has been lacking until now.(235) As this chapter has demonstrated, NMS consultations for hypertension predominantly consist of information and counselling.

4.6.4 How this chapter fits within the wider thesis

With regards to future service development, the CFIR (introduced in Chapter 1, section 1.6) states that the intervention characteristics of trials should be examined in order to assess their implementation potential. Understanding what pharmacists currently do and to what extent this differs from the successful interventions delievered in the previous RCTs can highlight the extent to which trial interventions need to be tailored in order to improve their implementation chances. The second component of the previous 16 RCT interventions of community pharmacist-led hypertension management (summarised in Figure 1, Chapter 1) consisted of medication and lifestyle counselling/advice, and pharmacists received dedicated training to deliver this.(107) To recap, medication advice included reinforcement of medication adherence, a review of all medications taken by the patient, and identification of drug-related problems including side effects. Healthy lifestyle advice included alcohol and smoking cessation, dietary advice and exercise/weight loss referrals and recommendations.

This chapter has shown evidence that the medication and lifestyle advice/counselling observed in these trials, with the exception of formal medication reviews and referral to external weight loss organisations, occurs in routine practice

during the NMS. Pharmacists are not required to undergo specific training to deliver the NMS,(236) therefore the data described in this study are from pragmatic, routinely delivered interventions. Pharmacists, therefore, are currently delivering similar medication and healthy lifestyle advice used in the trials without the associated prior training. This may be a ‘facilitator’ for the implementation of future hypertension management services in community pharmacy given that the need to organise training may not be required.(237)

4.7 Conclusion

Currently, pharmacists are not responsible for the ongoing management of hypertension in the community setting. The evidence from this study, however, suggests that pharmacists are delivering consultations with hypertensive patients that include providing drug information and recommendations, BP readings, and counselling – all without extra training. In relation to the trial interventions from Table 5 (Chapter 1), and the overall thesis investigation (Figure 2, Chapter 1), this chapter has provided evidence that routine interventions currently delivered by pharmacists are comparable to those delivered in the trials, suggesting that the ‘assessment by pharmacist’ stage of the intervention is deliverable in current practice.

Chapter 5 - Factors associated with referral of hypertensive patients from pharmacies to general practice.

5.1 Chapter overview

The aim of this chapter was to identify factors associated with referral of patients from pharmacy to general practice during hypertensive NMS consultations.

Analyses were conducted on 131,419 hypertensive patients. Fifteen predictors were included in a multivariable logistic regression model and were grouped into three categories: demographic factors, patient reported factors and medication related factors. Patient referral to general practice (yes or no) was the primary outcome.

The mean patient age was 65 (±13) years and 85% of patients were of white ethnicity. A total of 5,895 (4%) patients were referred by a pharmacist to a GP within the first two weeks of starting a new anti-hypertensive medication. Patients reporting side effects (adjusted OR 11.60 [95% CI 10.80-12.40]) were most likely to be referred. Prescriptions for alpha-blockers were associated with referral (adjusted OR 1.28 [95% CI 1.12-1.47]) while patients receiving angiotensin-II receptor blockers were less likely to be referred (adjusted OR 0.89 [95% CI 0.80-0.99]).

The majority of patients in this study were followed up by pharmacists without the need for referral to their GP. These data suggest that additional pharmacist involvement in hypertension care does not currently increase medical workload appreciably. As a result, the appropriate clinical expansion of the NMS may have the potential to contribute to both better blood pressure outcomes and a better use of primary care resources.

A version of this chapter has been published in the *British Journal of General Practice* and can be found in Appendix 10.(2)

5.2 Introduction

The reasons for referring hypertensive patients from pharmacies to general practice are not well defined in the published literature. Guidance available to pharmacists from the Royal Pharmaceutical Society and the World Health Organisation make specific reference to referral only in the context of high BP readings (>140/90mmHg, see Chapter 3).(104,146) Pharmacists are therefore expected to use their discretion when deciding when to refer hypertensive patients for reasons other than elevated blood pressure.

Previous research exploring referral from pharmacy to general practice has focussed on upper gastrointestinal symptoms,(155) and a systematic review of community pharmacy triage services reported reasons for referrals for a variety of other minor ailments.(156) Much of these data were collected using surveys or questionnaires that rely on participant recall rather than more objective sources of data. In order to gain an understanding of referral in the context of hypertension, this chapter analysed pharmacists' reasons for referring patients using routinely collected data from a nationally commissioned service in pharmacies – the New Medicine Service (NMS).

All 16 RCTs of community pharmacist-led hypertension management culminated in either a recommendation to attend a follow-up appointment in the pharmacy or a referral to general practice (see Figure 1, Chapter 1).(107) The intervention stage of the NMS culminates with the choice of one of the same two outcomes, and was therefore analysed in this chapter.

5.3 Chapter aim

This study aimed to establish the predictors of referral of hypertensive patients from pharmacies to general practice.

5.4 Methods

This study is reported according to the 'REporting of studies Conducted using Observational Routinely collected health Data' (RECORD) statement extension to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines.(238)

5.4.1 Study design and data source

This was a cross-sectional study of hypertensive patients presenting to a community pharmacy in England with a newly prescribed anti-hypertensive medication. The data used for this analysis was described in Chapter 4. Briefly, anonymised patient and consultation data from 148,412 hypertensive patients, collected from 1st October 2011 to 30th September 2012, were routinely recorded by community pharmacists in England using 'PharmOutcomes' software.(229) These data were extracted by the Pharmaceutical Services Negotiating Committee (PSNC), who subsequently supplied them for research purposes based on a plan of analysis (described in this chapter). The dataset included only the hypertensive cohort of the NMS.

Data were available for all three stages of the NMS process: the ‘patient engagement stage’ (upon prescription collection), the ‘intervention stage’ (1-2 weeks post prescription), and the ‘follow-up stage’ (3-5 weeks post prescription). Analysis focused on the intervention stage of the NMS process (one to two weeks after a medication is initiated).

Since this was an analysis of routinely collected, anonymised data, no ethical approval was required.

5.4.2 Participants

Eligible patients were those starting a new antihypertensive medication with no differentiation possible between newly diagnosed or pre-existing hypertension from the data available. No age, co-morbidity or previous cardiovascular disease restrictions were in place for eligibility to the NMS.(13)

Patients were excluded in this study if they:

- Withdrew consent for subsequent pharmacist consultations after recruitment.
- Could not be contacted for appointments after enrolling in the service.
- Had a recorded age of under 18 years or had no age recorded.
- Contacted the pharmacist to say that their medication had been stopped prior to their first NMS consultation.

5.4.3 Primary outcome

The primary outcome for this study was to establish factors associated with patient referral from community pharmacies to general practice within the first two weeks of starting a new anti-hypertensive medication (the intervention stage of the NMS). The NMS service specification states that during the intervention stage, pharmacists should aim to identify medication related problems with patients and take one of the following two actions: a) arrange a follow-up consultation as part of the NMS, or b) refer the patient directly to their general practitioner.(227) Given that following a patient up is an option, the choice to refer to a GP at this stage would suggest that the pharmacist could not manage the patient's presenting complaint – hence making the variables associated with this potentially valuable to identify.

Referral to a GP was the outcome variable - defined as any instance where "referral" was explicitly marked on the pharmacist-completed NMS form (Appendix 9).

5.4.4 Statistical analysis

Logistic regression can be defined as a method to calculate the chance of a binary outcome variable occurring, based on the presence of one or more (independent) predictor variables.(239) This analysis examined multiple predictors of referral and therefore a multivariable logistic regression model was used.

Logistic regression analyses depend on two main assumptions:(240)

1. The outcome variable is binary (coded "0" for non-referral and "1" for referral in this analysis).

2. The predictor variables are independent of each other, with correlation below approximately r=0.5 when tested in a correlation matrix (although no official threshold exists in the literature) - see section 5.4.7.

All analyses were conducted using STATA statistical software (StataCorp 2015, Release 14; StataCorp, College Station, Texas, USA). The *"logistic"* command, followed by the outcome "referral" and the list of variables was used to carry out the primary analysis in STATA.(241)

Odds ratios (OR) with 95% confidence intervals (95% CI) were used to describe the effect of predictor variables on the outcome variable (referral to general practice). The OR signifies the odds of the outcome occurring in the presence of a predictor variable in relation to the odds of the outcome occurring in the absence of that predictor.(242) For example, an OR of '3' for a predictor variable means that the outcome is 3 times more likely to occur in the presence of that variable, than in its absence. Adjusted odds ratios were presented in this analysis to show the effect of the predictor variables on the outcome whilst holding all other independent variables constant, adjusting for their potential confounding effects.(243) Appendix 11 provides the results of the unadjusted ORs for completeness.

5.4.5 Predictor selection

The lack of previously published literature on predictors of referral from community pharmacies meant that predictor selection was dictated solely by the available data on the NMS form that were clinically relevant to the outcome. Given the small

number of predictors, the large number of outcome cases and the large sample size of the dataset, no attempt was made to reduce the model through predictor selection.(240) All predictor variables that were available in the dataset were included in the model.(244)

Predictors were classified into three categories: demographic predictors, patient reported factors and medication class. Demographic predictors were age, gender and ethnicity. White ethnicity was chosen as the reference standard against which all other ethnicities were measured. Age categories were split in the following way: <40 years (comparator category), 40-49 years, 50-59 years, 60-69 years, 70-79 years, 80 years and over. Age was not examined as a continuous variable in order to examine any non-linear effects. The selection of below 40 years as the reference category is in line with the starting age for eligibility for the NHS health checks screening programme (40 years and over) indicating a lower CVD risk in this comparator age group.(245)

Patient reported predictors were those included on the NMS form:

- Side effects
- Not using the medicine as prescribed
- Negative feelings towards the new BP medication
- Uncertain whether the medicine is working
- Not having started the medication since being prescribed
- Concerns with remembering to take the medication
- Difficulty with the medication's formulation
- Prescriber stopping the medication
- More information requested about the new medication
- A missed dose in the past seven days
- Using the medicine as prescribed

All patient reported predictors were binary variables (e.g. side effects reported – yes or no). No further detail regarding these reported factors were available for quantitative analysis. For instance, the nature or severity of the side effects and any specific details regarding the negative feelings reported by patients were not available. The qualitative analysis in Chapter 4 does however provide some detail regarding these factors.

Medication related predictors were the anti-hypertensive drug class newly prescribed. Calcium Channel Blockers (CCBs) were selected as the reference medication class against which other medication classes were compared. This was because they were the most commonly prescribed drug class in the dataset and the average age of the sample was 65 years, meaning that CCBs are recommended as first line treatments by NICE for the majority of the cohort.(28)

5.4.6 Data management, missing data and sample size

Data management was conducted with reference to the STATA data management manual.(246) The original dataset was imported into STATA from a .csv file (Microsoft Excel) in preparation for data coding. This involved recoding variables such as gender from strings (M for males and F for females) to a numerical format (F=0 and M=1). This allowed the statistical package to use '0' (F) as the baseline comparator with which to analyse the effect of '1' (M) on the outcome variable. Such data coding was required for all variables included in this analysis.

Of the 148,412 patients in the original dataset, age data were missing for 1,510 patients (1.0%). No other missing data were known to be present among the other

dataset variables. Given the low overall level of missing data in the dataset, imputation of missing age data was not attempted and therefore these patients were omitted from the analysis.(247) No formal sample size calculation was used for this study, however each predictor included in the analysis had at least 10 outcome events (referral) associated with them, satisfying the general rule of thumb used for logistic regression.(248)

5.4.7 Other analyses

To satisfy one of the assumptions of logistic regression (independence of predictor variables) correlation between predictors were checked using the STATA command '*pwcorr*'.(249) This command displays all pairwise correlation coefficients (r-value) between the included variables, displaying correlation between the values of -1 (perfect inverse relationship) and +1 (perfect positive linear relationship). In general, an r value of greater than -0.5 or +0.5 between two variables indicates that the inclusion of both into the regression may not be necessary as they display high levels of correlation.(250) Appendix 12 shows the correlation matrix for the included variables. The most closely correlated variables were 'not using medication as prescribed' and 'missed dose in the past seven days' with a value of 0.45 - meaning they could both be included in the analysis as separate variables without violating the assumptions of the logistic regression model.

Pre-specified interactions between side effects and both age and gender were examined. These interaction terms were explored to test whether the impact of one predictor variable on 'referral' is affected by different levels of another variable.(251)

Further interactions were examined post-hoc (side effects and being offered additional information about the medication). These are reported using ORs and 95% CIs.

It is worth noting the difference between ‘interaction’ and ‘correlation’ between variables. An interaction between two variables occurs when their effect on each other are not constant i.e. the effect differs at different values of the other. Correlation between two variables means the values of one variable generally co-occur with values of the other, resulting in difficulty interpreting their ORs as their independence cannot be guaranteed.(252)

5.5 Results

5.5.1 Inclusion of participants

Anonymised data from 148,412 hypertensive patients were available - collected from 1st October 2011 to 30th September 2012. Over this period the total number of NMS completed in England for all four therapeutic areas (hypertension, type 2 diabetes, asthma/COPD and anti-platelets/anti-coagulants) was 481,744 with approximately half of these for hypertension (~240,000).(253) Of the 148,412 hypertensive patient records in the dataset (62% of all hypertensive consultations), 131,419 patients (88.6%) matched the inclusion criteria for this analysis. The data included in this analysis therefore represents approximately 55% of all hypertensive NMS consultations in England from October 2011 to September 2012. A flow chart

of excluded patients can be found in Figure 9. The characteristics of the excluded participants are shown in Appendix 13.

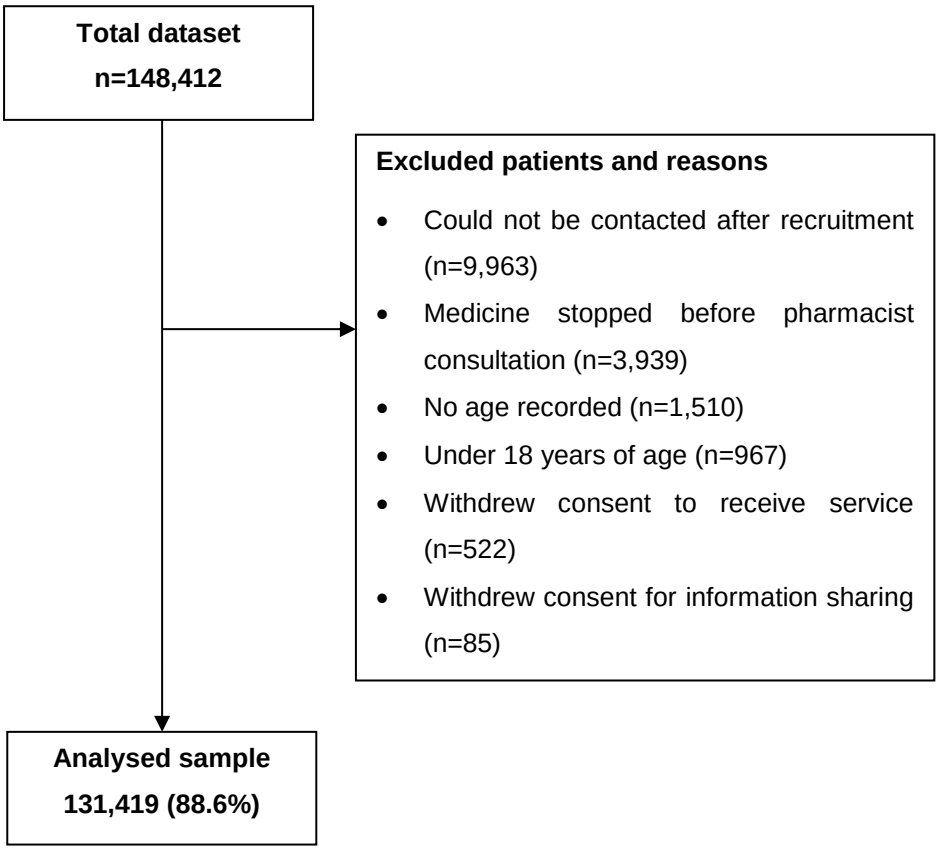

Figure 9 - Sample selection

5.5.2 Descriptive analysis

Patients attended pharmacies based in all nine regions of England (Table 14). Mean patient age was 65 (±13) years. The majority of patients were of white ethnicity (85%), with the rest South Asian (4%), black/African-Caribbean (2%), 'not stated' (8%) or 'other' (1%).

Proportions of the BP lowering medications prescribed closely reflected the order of prescribing stated in the current National Institute for Health and Care Excellence (NICE) guidelines, 2011 (28) – with CCBs most common [41,372 (32%)], followed by Angiotensin Converting Enzyme inhibitors [ACEi, 34,497 (26%)], Angiotensin II Receptor Blockers [ARBs, 17,415 (13%)], Beta adrenoceptor blockers [B-Blockers, 16,211 (12%)], Thiazide diuretics [15,487 (12%)], Alpha adrenoceptor blockers [A-blockers, 5,264 (4%)] and 'other anti-hypertensives' such as centrally acting anti-hypertensives [1,173 (1%)]. Centrally acting drugs included Methyldopa, Clonidine and Moxonidine.

Side effects were reported by 24,992 (19%) patients, while 5271 (4%) reported that they were not using their new anti-hypertensive medication according to their prescriber's instructions. Patients also reported uncertainty towards the efficacy of their new medication (n= 8,344, 6%) and, negative feelings towards their new BP medication (n= 5,038, 4%) Table 15 shows the frequencies of all predictor variables.

Table 14 – Data characteristics

Total population	n= 131,419
Age (mean, SD)	65 (13)
Ethnicity, n (%)	
White	112,194 (85)
South Asian	4,586 (4)
Black/African-Caribbean	2,760 (2)
Not stated	10,234 (8)
Other	1,645 (1)
Gender, n (%)	
Male	61,146 (47)
Female	70,273 (53)
Medication class, n (%)	
CCB	41,372 (32)
ACEi	34,497 (26)
ARB	17,415 (13)
B-Blocker	16,211 (12)
Thiazide diuretic	15,487 (12)
A-blocker	5,264 (4)
Other	1,173 (1)
Region of pharmacies in England that contributed to dataset (%)	
North East	6
North West	16
Yorkshire and the Humber	10
East Midlands	9
West Midlands	10
East Anglia	5
Greater London	15
South East	15
South West	14

CCBs= calcium channel blockers; ACEi= angiotensin converting enzyme inhibitor; ARB= angiotensin II receptor blocker, B-Blocker= beta-blockers; A-blocker= alpha-blockers

5.5.3 Main analyses

A total of 5,895 patients (4%) were referred back by a pharmacist to a GP within the first two weeks of starting a new anti-hypertensive medication (Table 15).

Demographic factors

Neither age nor ethnicity were significant predictors of referral, with the exception of the 40-49 years age bracket (OR 0.77 [95% CI 0.63 – 0.93]) which was associated with non-referral. Males were less likely to be referred than females (OR 0.85 [95% CI 0.80-0.91]).

Patient reported factors

Patients reporting side effects from their new medication were most likely to be referred to their GP of all factors included in the analysis (adjusted OR 11.6 [95% CI 10.8-12.4]) (Figure 10 and Table 15). Other patient reported factors such as expressing negative feelings towards the anti-hypertensive drug (adjusted OR 3.29 [95% CI 3.01-3.60]) and reporting uncertainty regarding the efficacy of the new medication (adjusted OR 1.50 [95% CI 1.35-1.68]) were significantly associated with referral. In contrast, patients who requested more information about their new medication from the pharmacist (adjusted OR 0.45 [95% CI 0.39-0.52] n= 7,276, 6%) and those using their medication as prescribed (adjusted OR 0.20 [95% CI 0.18-0.21] n=107,989, 82%) were less likely to be referred to their GP.

Medication related factors

Alpha-blockers were associated with referral (OR 1.28 [95% CI 1.12-1.47]) while patient's prescribed an ARB were significantly less likely to be referred (OR 0.89 [95% CI 0.80-0.99]). No other drug classes were associated with referral.

5.5.4 Interaction analyses

No interaction was found between age and side effects (OR 1.01 [95% CI 1.00-1.01]) meaning the likelihood of referral was not significantly affected by the reporting of side effects as age increased. However, males reporting medication side effects were more likely to be referred than females reporting side effects (OR 1.19 [95% CI 1.06-1.34]).

Additional post-hoc analysis showed that patients who reported side effects and were offered additional information about their medication/condition were less likely to be referred to their GP than those reporting side effects without requesting additional information from the pharmacist (OR 0.42 [95% CI 0.32-0.54]).

Table 15 – Results of a logistic regression model of factors associated with referral from Pharmacy to General Practice

	Total n (%) (N=131,419)	Number referred, n (%)	Adjusted OR (95% CI)
Outcome variable	–	–	–
Referrals from Pharmacy to General Practice	5,895 (4)	–	–
Predictor variables	–	–	–
Demographic factors	–	–	–
Age (years, <40 years as reference)	–	–	–
40 – 49	12,987 (10)	463 (4)	0.77 (0.63 – 0.93)*
50 – 59	23,451 (18)	951 (4)	0.89 (0.75 – 1.06)
60 – 69	37,312 (28)	1,548 (4)	0.87 (0.74 – 1.03)
70 – 79	34,895 (27)	1,680 (5)	0.93 (0.78 – 1.10)
80 and over	17,975 (14)	1,045 (6)	1.05 (0.88 – 1.25)
Ethnicity (White as reference)	–	–	–
South Asian	4,586 (4)	227 (5)	1.14 (0.97-1.35)
Other	1,645 (1)	91 (6)	1.25 (0.97-1.62)
Not stated	10,234 (8)	476 (5)	1.12 (1.00 – 1.26)
Black/Afro-Caribbean	2,760 (2)	127 (5)	0.94 (0.75-1.17)
Gender, Male (Females as reference)	61,146 (47)	2,172 (4)	0.85 (0.80 - 0.91)*
Patient reported factors	–	–	–
Side effects	24,992 (19)	4155 (17)	11.60 (10.85 - 12.41)*
Not using the medicine as prescribed	5271 (4)	2,236 (42)	5.83 (5.23 - 6.52)*
Negative feelings towards new BP medication	5,038 (4)	1,292 (26)	3.29 (3.01 - 3.60)*
Uncertainty whether medicine working	8,344 (6)	555 (7)	1.50 (1.35 - 1.68)*
Not yet started the medication	823 (0.6)	230 (28)	1.23 (1.02 - 1.50)*
Concerns with remembering to take medication	965 (1)	60 (6)	0.91 (0.68 - 1.24)
Difficulty with medication formulation	149 (0.1)	13 (9)	0.81 (0.41 - 1.60)
Prescriber stopping the medication	777 (0.6)	313 (40)	0.75 (0.62 - 0.91)*
More information about medication requested	7,276 (6)	301 (4)	0.45 (0.39 - 0.52)*
Missed dose in the past 7 days	1,166 (1)	415 (36)	0.42 (0.36 - 0.50)*
Using medicine as prescribed	107,989 (82)	2,354 (2)	0.20 (0.18 - 0.21)*
Medication related factors (CCB as reference)	–	–	–
A-Blocker	5,264 (4)	411 (8)	1.28 (1.12-1.47)*
B-Blocker	16,211 (12)	777 (8)	1.10 (0.99-1.21)
Thiazide	15,487 (12)	800 (5)	1.02 0.92-1.13)
ACEi	34,497 (26)	1312 (4)	0.94 (0.86-1.02)
ARB	17,415 (13)	622 (4)	0.89 (0.80-0.99)*
Other	1,173 (1)	53 (5)	0.77 (0.56-1.06)

OR= odds ratio; CI= confidence interval; CCBs= calcium channel blockers; ACEi= angiotensin converting enzyme inhibitor; ARB= angiotensin II receptor blocker, B-Blocker= beta-blockers; A-blocker= alpha-blockers. *= p<0.05

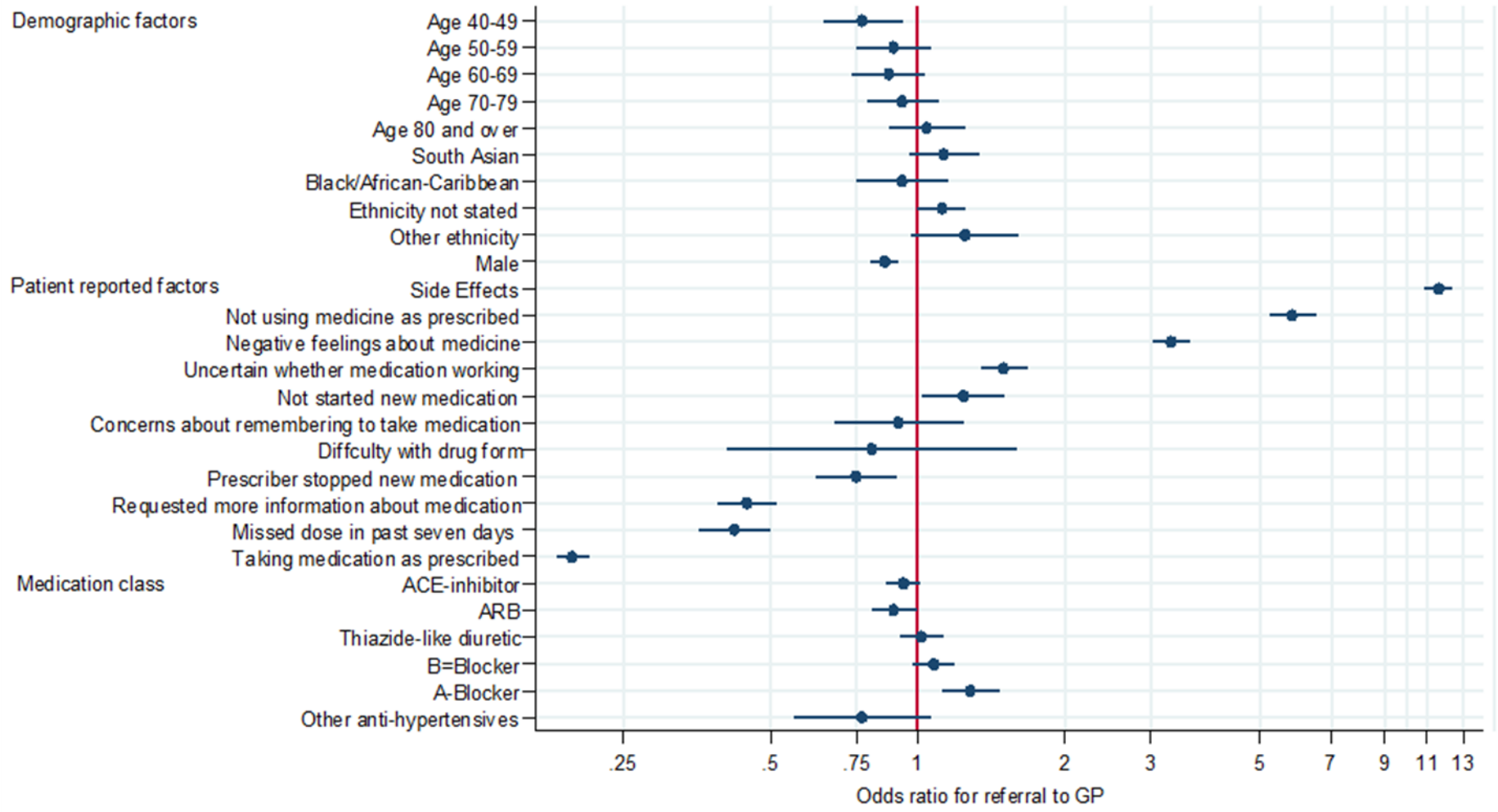

Figure 10 - Coefficient plot showing adjusted odds ratios for referral to general practice.

Reference categories – Age = <40 years; Ethnicity = White; Sex = female; Medication class = Calcium channel blockers. Data presented on a logarithmic scale.

5.6 Discussion

5.6.1 Summary of findings

This study examined reasons for the referral of hypertensive patients from pharmacies to general practice from routine hypertension NMS consultations. The results indicate that within the first two weeks of starting a new anti-hypertensive medication, the majority of hypertensive patients (96%) were reviewed without further recourse to their general practitioner. Side effects, uncertainty regarding the efficacy of treatment, and negative feelings towards the newly prescribed anti-hypertensive drug were among the patient reported factors most associated with referral. A-blockers were the anti-hypertensive drug class most associated with referral, while ARBs were least associated. Males were less likely to be referred than females. When patients were provided with 'more information' about their new medication by a pharmacist, they were less likely to be subsequently referred (OR 0.45 [0.39 - 0.52]. Additional analysis showed that patients who reported side effects and were offered additional information about their medication were less likely to be referred to their GP than those reporting side effects without receiving additional information from a pharmacist (OR 0.42 [95% CI 0.32-0.54]).

This chapter has provided real-world evidence in relation to the decisions pharmacists are making when consulting with hypertensive patients. The results show that pharmacists delivering the NMS in its current form are unlikely to add appreciable workload onto GPs through re-referral during early pharmacotherapy, and shows that pharmacists seem able to take on the responsibility to follow-up

patients by using the final consultation stage of the NMS process, even when patients report a variety of medication and non-medication related issues.

5.6.2 Strengths and limitations

This is the first study exploring factors associated with referral from pharmacies to general practice in patients that were newly prescribed an anti-hypertensive medication. Key strengths of this work include the large sample size and national coverage of the data used. Where previous studies assessing referral from pharmacies to general practice have used survey data,(156) this study was able to access and use the only routinely collected dataset from a nationally commissioned service for hypertension in English pharmacies.

The full range of factors associated with referral from pharmacies to general practice were limited by the lack of data on patient comorbidities, the total number of anti-hypertensive medications prescribed to each patient and consistent information regarding other prescribed medications. Previous studies have suggested that polypharmacy is associated with non-adherence to anti-hypertensive medications and hence possible increases in GP visits,(254) but this could not be examined here.

The trials of community pharmacist-led hypertension management each involved the assessment of BP, with subsequent decisions to refer to GP or follow up based almost solely on this.(107) The omission of patient BP readings within the dataset meant that this potentially important confounding factor was not accounted for in the analysis. In addition, information regarding drug interactions were discussed with

9,538 (7%) of patients in this dataset, however, data were not recorded on the attribution of drug interactions to referral which therefore prevented further analysis of drug interactions as a possible predictor. Other potential confounders such as age, sex and ethnicity were however taken into account.

A further limitation, inherent with routinely collected data, was the inability to verify the quality and accuracy of data entry into the dataset.(255) For example, where fixed-box fields were not ticked in the dataset, they were assumed not to be applicable to the patient. However, it is not possible to guarantee that instances where boxes should have been ticked were ticked, and vice versa. It is unclear what the impact of these theoretical, yet unaccountable, data entry errors could have had on the results of this analysis.

An inherent limitation within the delivery of the NMS is the potential for pharmacists to select patients who are more engaged with their health, or for more engaged patients to accept the service being offered. Given that the NMS is predominantly pharmacist-initiated rather than patient-initiated,(227) information on patients who may have rejected the service would have strengthened the findings of these data by allowing the generalisability of the results to be understood more clearly. In Chapter 2, pharmacists reported that blood pressure related conversations were, in their experience, most often initiated by patients. Pharmacists stated that a lack of time and financial constraints were some of the reasons why they did not initiate BP related consultations. In contrast, the NMS is financially incentivised, with the pharmacy earning between £20 and £28 for each completed NMS.(13) Knowledge of the proportion of patients accepting/rejecting the NMS for hypertension could give an indication as to the attitudes and acceptance of patients towards pharmacist-led services more generally.

5.6.3 Study findings in the context of previous research

The RCTs of community pharmacist-led hypertension management involved referral to GP as a possible outcome to their interventions (Table 5, Chapter 1). In one of these RCTs,(112) 20% of the 101 patients in the intervention group informed their pharmacist that they were experiencing intolerable side effects and asked the pharmacist to inform their GP. A further 15 of these patients were referred with a specific recommendation from the pharmacist to consider either a change in medication, a change in dose or frequency or a change in dosage form. Although the study did not find a significant association between patients reporting side effects and medication adherence (p=0.78) they reported that the study was underpowered to detect this association and that future work may look to study this.(112) In comparison, 19% of all patients in this chapter reported side effects, with 17% of these being referred to the GP for this reason.

A survey of 1,782 hypertensive patients stated that patient reported problems such as difficulty accepting their diagnosis or frustration with treatment, were associated with higher levels of self-reported medication non-compliance.(256) These data, in line with the results in this chapter showing the relationship between patient-reported problems and referral to general practice, further highlight the importance of pharmacists incorporating patient reported problems in interventions to manage hypertension – in addition to BP levels.

ARBs were the drug class least associated with referral (adjusted OR 0.89 [95% CI 0.80-0.99]). This could be due to the lower association with adverse events over other anti-hypertensive drug classes, as evidenced in a systematic review by

Thomopoulos et al.(81) Their meta-analysis found that ARBs were the only anti-hypertensive drug class which do not significantly increase adverse event rates over placebo [risk ratio 1.13 (0.78–1.62)]. Alpha-blockers were the drug class most associated with referral to GP (adjusted OR 1.28 [95% CI 1.12-1.47]). Alpha-blockers are often the fourth anti-hypertensive medication added to a patient's regimen, tending to be reserved for patients with resistant hypertension or where other medications are not tolerated.(28) They can cause pronounced postural hypotension and dizziness, particularly within the first few days of initiating.(257) Thomopoulos et al showed that the prevalence of BP medication discontinuation due to adverse events is proportional to the number of anti-hypertensive medications a patient takes. Therefore the association between Alpha-blockers and referral in this chapter could be due to their side effect profile or due to the fact that they serve as a proxy for patients taking multiple BP lowering medications.

A systematic review of 18 trials (n=4,168 patients) indicated that the time taken to reach 50% of the maximum estimated BP lowering effect across anti-hypertensive drug classes was 1 week, with full effects becoming evident after 4 weeks.(258) This suggests that pharmacists should exercise caution when referring patients back to their GP due to lack of drug efficacy 1-2 weeks after initiation of a new medication, as observed in this chapter. Given that the clinical interpretation of BP readings taken in community pharmacies is less well defined in comparison to home readings,(1) the most appropriate source of BP results from which to base drug efficacy decisions should be carefully considered.(259,260)

The concept of the NMS itself was originally based on research showing that pharmacists delivering telephone advice and follow-up could result in improved medication adherence.(229) This then led to a randomised controlled trial of an

NMS intervention for patients with a new prescription for a long-term condition (hypertension, type 2 diabetes, asthma/COPD or taking anti-platelets/anti-coagulants).(152) This trial was undertaken two years after the NMS was first introduced into practice in 2011. Critical evaluation reveals two key issues with the trial. First, the trial did not report adherence outcomes at 6 months even though this was a primary outcome stated in the trial protocol.(261) Instead, only 6 week and 10 week adherence data were published despite post-publication requests for the reporting of the 6 month adherence data.(232) This raises doubts as to the efficacy of these interventions. Secondly, the studies leading to the NMS trial did not follow how the NMS was eventually implemented. For instance, all pharmacists delivering the NMS in the studies were provided with one or two days of face-to-face training on how to deliver the intervention.(261) In contrast, the delivery of the NMS in clinical practice requires the pharmacist to self-assess their ability to deliver the service, without compulsory training.(236)

5.6.4 Implications for clinical practice

Patients reporting side effects from their new medication were the most likely to be referred to their GP in this cohort of 131,419 patients (adjusted OR 11.6 [95% CI 10.8-12.4]). The likely responses from clinicians to the development of side effects could include dose reductions or switching to alternative medications.(112) Recommending such changes are within a pharmacist's capability, however actioning such changes would currently require a further prescribing qualification under current regulations.(262) Currently, only 11% (~6,188) of pharmacists have completed the independent prescribing course since its introduction in 2006.(263)

Furthermore, approximately one-third of those pharmacists have either never used their qualification to prescribe or do so only annually or less.(263) In addition, the provision of pharmacist prescribing in community pharmacies can only currently occur privately, as no pharmacy presently has an NHS drug prescribing budget.(264) This suggests that pharmacist prescribing in community pharmacies may not to be a solution to the delivery of hypertension management in the short term, therefore alternative facilitators should be considered. Efficient communication systems between pharmacists and general practitioners could result in reduced patient referrals by allowing changes to medications or doses to be approved in a more timely manner, without the need for an appointment.(144) The participants in Chapter 2 mentioned the introduction of NHSmail and 'read and write' summary care records access in pharmacies as ways in which this could begin to occur. The reporting of negative feelings towards the new medication and uncertainty as to their efficacy were also independent predictors of referral in this study. These concerns could be managed via blood pressure measurements, advice, or reassurance, and do not require a pharmacist to have a prescribing qualification.

Health service policy makers state that a key driver for the development and maintenance of pharmacy services is their potential to relieve pressure from other areas of the NHS, such as general practice.(10,265) The impact on general practice workload of pharmacy services such as the NMS is therefore an additional consideration for discussion. The incidence of new hypertension cases in England is eight people per 1000 per year,(266) meaning approximately 52 new hypertension cases per practice, annually.(267) The 4% prevalence of referral shown in this chapter is therefore likely to contribute only two patients per practice

per year in additional GP appointments. Without knowing the rate of patient re-presentation to GP outside of the NMS in the same time period and circumstances, it is difficult to determine whether a 4% referral rate would indeed represent an improvement or worsening of the current situation, however these numbers appear low.

5.6.5 How this chapter fits within the wider thesis

The final component of the trial interventions of community pharmacist-led hypertension management involved pharmacists making decisions to either refer a patient to the GP or continue monitoring the patient without further GP recourse (Figure 1, Chapter 1). This chapter has provided real-world evidence in relation to the decisions pharmacists are making when consulting with hypertensive patients in current practice. The rationale for this chapter was to provide a better understanding of the hypertensive patient groups most commonly associated with referral, with a view target future interventions to reduce referrals to GP, and hence reduce the workload on general practice. The results show that pharmacists are able to take on the responsibility of following patients up by using the final consultation stage of the NMS process, even when patients report a variety of medication-related issues. Given that the factor most associated with refer was medication side effects, future interventions should empower pharmacists to either reduce doses or switch to alternative medications to reduce referrals.

5.7 Conclusion

This study of national NMS data has provided real-world evidence in relation to the decisions pharmacists are making when consulting with hypertensive patients. It highlighted that the majority of patients with a newly prescribed medication for hypertension can be followed up by pharmacists in the early phase of treatment. It also identified several factors associated with patient referral from pharmacy to general practice such as medication side effects, negative feelings towards the new medication, and patients reporting uncertainty about its efficacy. It is likely that either improved communication with general practice or allowing pharmacists to make medication alterations can reduce referrals, and workload, to general practice.

Chapter 6 Discussion

6.1 Chapter overview

The final chapter presents an overall discussion for this thesis. The aims and objectives of the work are restated and the findings in relation to the CFIR framework are summarised by chapter. The strengths and limitations of the thesis as a whole are then presented.

Other evidence related to pharmacist-led hypertension management are then discussed. This is followed by a discussion of literature related to the barriers and facilitators to delivering hypertension services in pharmacies in the context of this thesis' findings.

The implications of this work on future hypertension provision in pharmacies is then discussed, followed by recommendations for future research. The thesis is concluded with some final remarks to summarise the findings.

6.2 Introduction

In the context of the growing strain on primary healthcare systems in recent years,(98) pharmacists have been described as an "*untapped resource"*.(99) The introduction of Medicines Use Reviews (2005) and the New Medicine Service (2011) were intended to pave the way for the transformation of community pharmacists' role from a predominantly medication supply function, towards a more clinical and patient-facing role.(11) However the predominant role of community pharmacists (measured as a proportion of their daily tasks) has remained the supply of medications through prescriptions.(192,268,269)

There is a clinical need to investigate novel strategies to manage hypertension given its scale (affecting approximately one third of adults in the UK) and its consequences on health outcomes.(29) The long-term monitoring requirements of hypertensive patients and the lack of capacity in general practice also emphasises the requirement to investigate alternative settings for its management.(98) There are approximately 12,000 community pharmacies in England,(100) and their distribution within communities and accessibility to patients make them a setting with the potential to deliver the care and follow-up required for hypertensive patients.(101)

Overall, the research questions addressed in this thesis resulted from trial evidence showing that community pharmacist-led management of hypertension results in significantly lower BP over usual GP care.(107) Despite showing evidence of clinical effectiveness, the interventions from the trials have not yet translated into pharmacy practice in England.

6.3 Restatement of aim, objectives and thesis structure

Thesis aim

This thesis aimed to investigate the extent to which the interventions from previous RCTs of community pharmacist-led hypertension management are translatable to current pharmacy practice in England.

Thesis objectives

The following objectives were addressed in the chapters specified in parentheses:

1. Explore the views and experiences of pharmacists regarding the delivery of hypertension related care, and understand the barriers and facilitators to hypertension service implementation in community pharmacies (Chapter 2).
2. Understand how pharmacy-measured blood pressure compares to other measurement modalities recommended in the NICE guidelines for hypertension (Chapter 3).
3. Understand the content of consultations between pharmacists and hypertensive patients drawing on data from a currently commissioned service (the New Medicine Service, NMS) in England (Chapter 4).
4. Establish predictors for referral of hypertensive patients from pharmacies to general practice during the NMS for hypertension (Chapter 5).

Recap of thesis structure

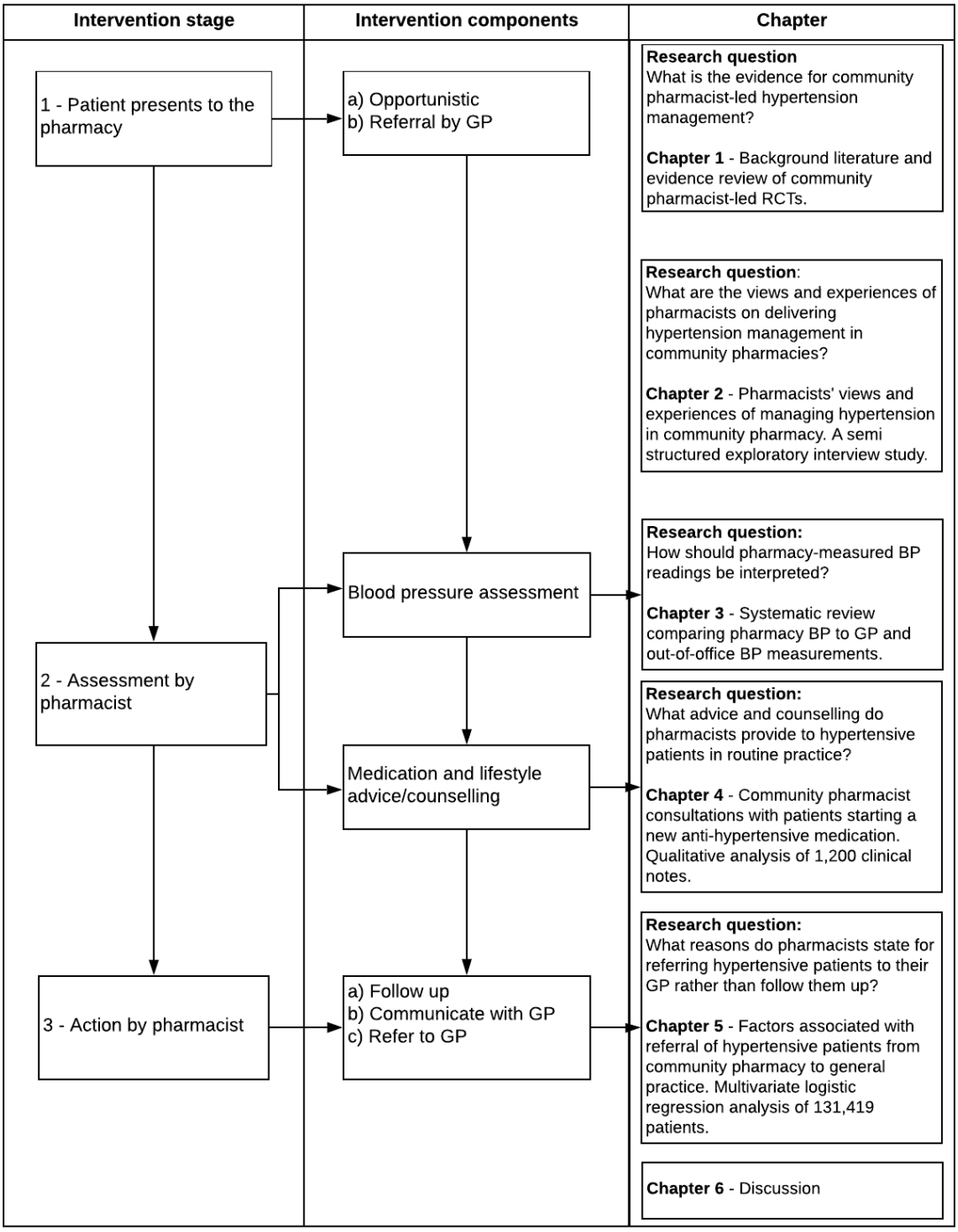

Figure 2 - Thesis structure in relation to previous trial interventions (reproduced from Chapter 1)

6.4 Reflection on thesis findings

The work conducted in this thesis investigated the interventions from previous RCTs of community pharmacist-led hypertension management to assess their potential implementation in current practice. While the interventions do appear to be translatable into current pharmacy practice in England, there are several important requirements that need to be addressed for such interventions to be delivered in practice, and these are discussed within this chapter - particularly in section 6.6.2.

Results in the context of the CFIR

As stated in Chapter 1, the Consolidated Framework for Implementation Research (CFIR) was identified as a suitable guide to the direction of this thesis' investigation.

To recap, the CFIR contains five overarching domains:

1. The individuals involved – understanding the views of the people who are tasked with delivering the intervention.
2. The intervention characteristics – describing what the individuals involved in delivering the intervention have to do, and how often they have to do it.
3. The inner setting – the context through which the implementation process will proceed within that setting.
4. The outer setting – the economic, social, and political context within which the organisation/setting resides.
5. The process of implementation – the process of change aimed to achieve individual and organisational level use of the intervention.(139)

The thesis primarly focused on the intervention characteristics domain. This was a context-specific decision as there are limited data examining previous hypertension trial interventions in community pharmacy and their potential for implementation. Furthermore, the work of Glasgow et al (see section 1.6) highlights that the characteristics of interventions can hinder the translation of research into practice, particularly if they are found to be too time-consuming, complicated or require multiple follow-ups by the people delivering them.(136) Despite this, other domains of the CFIR were also addressed in this thesis given that many of the issues connected with implementation are interdependent. For example, the individuals involved and the inner setting domains were discussed in Chapter 2, and section 6.6.2 of this chapter outlines some of the inner and outer setting implementation factors relevant to community pharmacy in more detail. Table 16 shows how each results chapter of this thesis related to its corresponding CFIR domain.

The process of implementation domain – i.e., the process of change aimed to achieve individual and organisational level use of the intervention - was the least covered in this thesis, and could therefore be the subject of future work. In particular, mapping the commissioning process of pharmacy services, including an understanding of typical timelines from evidence gathering to implementation, and the identity and roles of the stakeholder groups involved in the process, could help with understanding how an optimised intervention could be commissioned and then delivered.

Table 16 - Results in the context of the CFIR domains

Results Chapter	**CFIR domain**	**Relevant findings**
Chapter 2 – Interviews	The individuals involved and the inner setting	• Lack of access to patient clinical records and efficient communication with GPs is limiting the clinical expansion of pharmacy services. • Current pharmacy workload will require redistribution in order for pharmacist to deliver hypertension management. This may require additional pharmacist support or upskilling other staff members. • Endorsement of hypertension services in local or national pharmacy contracts may be needed before they are taken on by pharmacists.
Chapter 3 – Systematic review	The intervention characteristics	• As the first component of the previous trial interventions, pharmacy BP readings can now be interpreted in the context of an evidence-based meta-analysis which was not previously possible. • Pharmacy-measured BP may be a useful addition to clinic and out-of-office BP measurements.
Chapter 4 – Qualitative NMS	The intervention characteristics	• Pharmacists provide similar advice and counselling in current practice as delivered within the previous trial interventions. • It is therefore unlikely that further training is required for pharmacists to deliver this component of the successful BP lowering interventions from the trials.
Chapter 5 – Quantitative NMS	The intervention characteristics	• The majority of patients with a newly prescribed medication for hypertension can be followed up by a pharmacist without the need for referral back to the GP. • Referrals were commonly made due to medication side effects, negative feelings towards the medication(s), and uncertainty about their efficacy. • If community pharmacists were able to prescribe and therefore alter medications, measure BP in the pharmacy routinely and arrange regular follow-up appointments, referrals to general practice could be reduced, leading to a more independent hypertension management service in pharmacies.

As a result of the work conducted within this thesis, the following four areas, highlighted as the research questions to be answered in Chapter 1, have been addressed:

1. The specific operational and practical considerations regarding the delivery of hypertension management in pharmacies, including the barriers, facilitators and willingness of pharmacists to deliever hypertension management.
2. The threshold for interpreting community pharmacy-measured BP.
3. The type of advice that pharmacists give in current practice and how this compares to evidence from previous trials.
4. The number of, and reasons for, hypertension referrals from pharmacies to general practice in a nationally commissioned pharmacy service, and therefore how future interventions could be targeted and developed to minimise these referrals.

A summary of these results and their relation to the implementation of future hypertension services in pharmacies is now presented.

Chapter 2 - Pharmacists' views and experiences of hypertension management in community pharmacy. An exploratory interview study

This chapter explored the views and experiences of pharmacists regarding the delivery of hypertension related care, and some of the barriers and facilitators to implementating hypertension services in community pharmacies.

Community pharmacists felt that the ongoing management of long-term conditions was not a ‘core duty’ of their role. One reason for this was the prioritisation of other services such as flu/travel vaccinations and MURs – services that not only included financial remuneration but were also endorsed in contractural frameworks for pharmacies. Pharmacists and service commissioners suggested several ways in which a hypertension management service could be implemented in the future, with areas such as communication and collaboration with general practice via use of GPPs, and extended rights for the use of Summary Care Records, as important facilitators.

This chapter discussed the topic of hypertension management with the individuals that are expected to be involved with the delivery of the service, as per guidance from the CFIR framework. The interviews shed light on some of the many operational factors that need to be considered when implementing hypertension services that are specific to community pharmacy. For instance, we learnt that pharmacists appear less willing to take on further roles and services if they are not endorsed in the pharmacy-NHS contract (or local equivalent). This adds to previous literature that stated pharmacists would only take on additional roles if they were funded to do so (see Chapter 2). National, or at least local-level endorsement would appear to act as reassurance to the pharmacists and hence may increase the chances of successful implementation of hypertension services. The willingness of pharmacists to incorporate hypertension management within existing services, with pre-existing national endorsement and funding (i.e. the NMS), is an area that was not explored in this chapter, and could therefore be the topic of future research (see section 6.8 for further details).

Chapter 3 - A comparison of blood pressure in community pharmacies with ambulatory, home and general practitioner office readings: a systematic review and meta-analysis

Given the uncertainty regarding how pharmacy-measured BP should be interpreted, the aim of Chapter 3 was to understand how pharmacy-measured blood pressure compares to other measurement modalities recommended in the NICE guidelines for hypertension.(49)

Nine studies were identified in the systematic review – eight of which were included in the meta-analyses. Studies varied in pharmacy BP measurement protocols, with different numbers of visits to the pharmacy (one to five visits), different number of readings per visit (two to six readings) and different operators responsible for conducting the BP readings (pharmacist, pharmacy staff or unattended kiosk).

The mean systolic CPBP-daytime ABPM difference was small [+1.6mmHg (95% CI -1.2 to 4.3) three studies, n=319]. CPBP was significantly higher than 24-h ABPM [+7.8mmHg (95% CI 1.5 to 14.1) three studies, n=429]. Comparisons with GP clinic readings (six studies, n=2100) were inconclusive with significant heterogeneity in the pooled analysis. CPBP and home BP monitoring readings (five studies, n=1,848) were not significantly different. Diastolic comparisons mirrored systolic comparisons in all but the CPBP-daytime ABPM comparison, where CPBP was significantly higher.

Although inconclusive, data from Chapter 3 suggests a threshold equivalent to the daytime ABPM threshold of 135/85mmHg might be considered reasonable for interpreting BP measured in pharmacies. This raises doubts about the validity of the

current 140/90 mmHg threshold used in pharmacies, as the possibility of missing truly elevated BP is greater than if the 135/85 mmHg threshold was being used.

In the context of the CFIR, this chapter provides evidence for pharmacists to deliver the first stage of hypertension management from the previous RCTs, and more reliably interpret the BP readings they take in pharmacies. An understanding of what the BP results mean is fundamental to delivering an evidence-based hypertension service in pharmacies, something that was not possible prior to this systematic review. Although this study demonstrates that pharmacy readings are likely to be different from GP clinic readings, further studies are needed to quantify the exact difference. This idea is taken forward in section 6.8 (recommendations for future research).

Chapter 4 - Community pharmacist consultations with patients starting a new anti-hypertensive medication: Qualitative analysis of 1,200 clinical notes

The aim of Chapter 4 was to understand the nature and content of consultations between pharmacists and hypertensive patients within the New Medicine Service (NMS) across England. Investigating this would determine the extent to which pharmacists are able to give healthy lifestyle advice and counselling to hypertensive patients in current practice – a key element of hypertension management interventions used in the trials.

The content of 1,200 consultation notes were analysed from 600 referred and 600 non-referred patients, encompassing a broad range of patient presentations. Four main themes emerged from the analysis of referred patients: medication side effects; adherence and medication changes; concerns about blood pressure readings; and patient uncertainty. A further four themes were identified from the

analysis of non-referred patients: monitoring and follow-up; information and counselling; discussing other medications and conditions; and discussing blood pressure readings.

This chapter showed that pharmacists routinely provide advice on medication side effects, adherence to treatment, and healthy diet and lifestyle to patients with hypertension, in the context of a commissioned service. The results also showed that pharmacists provide similar advice and counselling during the NMS to those delivered within the trial interventions without specific prior training. When analysing the characteristics of the interventions from previous trials, CFIR suggests that comparisons with current practice can give an indication to the extent to which interventions need to be adapted for implementation in practice. Given the similarity between the content of advice and counselling provided in the trials and in current practice, pharmacists are unlikely to require further training to deliver the second part of the BP-lowering interventions (see Figures 1 and 2). This potentially overcomes a barrier to implementation - the further training of pharmacist to deliver hypertension services in the community.

Chapter 5 - Factors associated with referral of hypertensive patients from pharmacies to general practice

The aim of Chapter 5 was to establish the factors associated with hypertensive patient referrals from pharmacies to general practice to understand how future hypertension interventions by pharmacists can be targeted to minimise GP workload.

Analyses were conducted on 131,419 hypertensive patients (mean age 65 (±13) years from the NMS for hypertension in England. A total of 5,895 (4%) patients were

referred by a pharmacist to a GP within the first two weeks of starting a new anti-hypertensive medication. Patients reporting side effects to their anti-hypertensive medications (adjusted OR 11.60 [95% CI 10.80-12.40]) were most likely to be referred. Prescriptions for alpha-blockers were associated with referral (adjusted OR 1.28 [95% CI 1.12-1.47]) while patients receiving angiotensin-II receptor blockers were less likely to be referred (adjusted OR 0.89 [95% CI 0.80-0.99]).

This chapter showed that the majority of patients with a newly prescribed medication for hypertension can be followed up by a pharmacist without the need for referral back to the GP. It also identified factors associated with referral to general practice such as medication side effects, negative feelings towards the new medication, and uncertainty about its efficacy. When making recommendations about implementing trial interventions, the findings of this chapter indicate that the interventions may need to be adapted towards empowering pharmacists to manage patient presentations that are currently associated with referral. This can be achieved through facilitators such as pharmacist prescribing to enact medication changes in a timely manner, or through improved communication and information sharing between pharmacies and general practice. As per the findings of Chapter 2, including a hypertension service specification in the pharmacy contract is likely to be the best way of highlighting these enabling factors for pharmacy and primary care teams to implement locally. A discussion of how this can be achieved can be found in section 6.6.2 of this chapter.

6.5 Strengths and limitations

The specific strengths and limitations of each study have been discussed in their respective Chapters (2 to 5). This section discusses the strengths and limitations of the thesis as a whole.

6.5.1 Strengths

A mixed methods approach to addressing the overall research aim was adopted in this thesis (Chapter 1, section 1.8). This approach provided evidence from current practice in the form of qualitative interviews, collated data from published literature in a systematic review, and utilised a routine dataset of pharmacy services. A key advantage of using mixed methods is that it provides strengths that counteract the disadvantages of both qualitative and quantitative methodologies when used alone.(270) Quantitative methods do not account for the social context in which the phenomenon being researched occurs, whereas qualitative research can.(271) The interviews conducted in Chapter 2 provided rich data in relation to the context of delivering hypertension interventions in the community pharmacy setting. Quantitative methods may not have elicited these insights. Qualitative research can, however, be criticised for being non-generalisable whereas well conducted quantitative research can avoid this weakness.(272) As an example, Chapter 4 used qualitative methods to examine the consultation notes made by pharmacists during hypertension NMS consultations. Due to the study design, it was not possible to conclude that a certain patient presentation or a pharmacist response was

associated with referral to GP. The quantitative approach in Chapter 5 was, however, able to do so through its larger sample size and statistical methods that adjusted for confounders.(239)

This thesis presented a broad range of views about the potential of community pharmacists to deliver hypertension management. The views of pharmacists interviewed in Chapter 2 were generally more negative about the prospect of hypertension management in pharmacies than the results of Chapters 4 and 5, which showed that pharmacists currently deliver similar interventions, in practice, to those seen in the previous RCTs.(107) It should be noted, however, that discussing a fully-fledged hypertension management service is not the same as observations from the NMS given the extra responsibility and time that full hypertension management would require. Factors such as measuring BP and monitoring renal function and electrolytes longitudinally are not part of the NMS, and in contrast to the NMS, a clear funding structure to support hypertension management does not currently exist in pharmacies.

Finally, the research questions that related to the second and third intervention components (medication and lifestyle advice/counselling and follow up by pharmacist or referral to GP) were investigated using the largest routine dataset for a nationally commissioned pharmacy service in England (Chapters 4 and 5).(2) The conclusions regarding the implementation of these intervention components were therefore grounded in the current framework of community pharmacy service delivery, improving the external validity of the findings.

6.5.2 Limitations

The observational data gathered and analysed throughout this thesis are likely to be prone to biases such as participant selection bias, recall bias, social desirability bias and confounding.(273,274) For instance the interviews in Chapter 2, although providing rich data, are likely to exhibit recall bias and social desirability bias – as with any interview study.(275) One way this could have been mitigated is through the direct observation of a pharmacist's practice in the community setting in an ethnographic study.(276) Although still observational, this approach could have overcome the recall bias, though social desirability bias may have remained during observations.

The national NMS dataset used in Chapters 4 and 5, although large, represented approximately 55% of all hypertension NMS consultations conducted in England over the time period of data collection.(253) It is therefore unclear whether systematic differences exist between the pharmacies selected to use PharmOutcomes to record the consultations and pharmacies using paper-based reporting (current practice). Furthermore, during the anonymisation of the dataset by the PSNC (prior to data management and analysis) data regarding the pharmacy's postcode and details of the pharmacist (age, sex, years qualified) were removed. This further limited the ability to describe the data's generalisability and limited sub-group analyses by area or pharmacist characteristics.

Long-term follow-up of routine pharmacy interventions were not measured in this thesis due to the cross-sectional nature of the NMS and a lack of suitable other pharmacy data sources and services. Furthermore, the external validity of using the NMS data in this thesis may be limited as they are only applicable to patients in the first few weeks of starting a new anti-hypertensive medication. They are therefore not necessarily applicable to patients who have been on anti-hypertensive

medications for several years. It is unclear how a pharmacist's advice would differ temporally through treatment, and whether reasons for referral to general practice would differ at further time points. In addition, NMS consultations are typically conducted over the phone for feasibility reasons in practice, whereas the previous RCTs mostly involved face-to-face consultations. This difference may reduce the external validity of the findings of Chapters 4 and 5, given the different dynamics of remote consultations.(277)

The impact of community pharmacists delivering ongoing hypertension management on a patient's journey through the healthcare system was also not explored in this thesis. Patients with hypertension commonly present with co-morbidities and polypharmacy given their average age and increased cardiovascular risk.(278) For the purposes of illustration, a particular hypertensive patient may also have type 2 diabetes and take anti-coagulant therapy (e.g. Warfarin). In this example, the patient may be asked to have their hypertension followed-up or supported through the community pharmacy, their diabetes managed by a practice nurse, their INR managed through an outpatient clinic, and any other health issues overseen and managed by their GP. This fragmented system has the potential to lead to errors and oversights in patient care,(279) and its acceptability to patients and the clinicians involved need to be carefully explored. On the other hand, rather than being viewed as 'fragmenting' services, such a model may alternatively be viewed as a multi-disciplinary approach to healthcare, utilising all health workers with appropriate skills and specialities to maximise patient benefit efficiently.(280)

Other potential study designs and topics could have been considered to address the overall thesis aim to investigate how previous trial interventions are translatable

to current practice. The first could have been to conduct an analysis of medicines use reviews (MURs), the most frequently conducted ‘advanced service’ in the community pharmacy contract.(14) Conducting analyses, akin to those in chapters 4 and 5 of this thesis, of MURs that focussed on anti-hypertensive medications may have added to the understanding of pharmacist’s current practice with regards to delivering interventions to hypertensive patients. This may have improved the understanding of how implementable a new hypertension management service may be in relation to the RCT interventions. No national dataset of MURs is currently available for analysis, therefore such a study would have relied on primary data collection which was beyond the resources of this DPhil.

Secondly, understanding the health economics of implementing a hypertension management service would have aided the understanding of how implementable such a service would be and hence address this thesis’ aim. The knock-on effect on the pharmacist’s time (with regards to the opportunity-cost of not conducting other services) could have been investigated, along with the cost-effectiveness of the intervention itself.

6.6 Thesis in the context of previous literature

6.6.1 Other evidence for pharmacist management of hypertension

Santschi et al. 2014

Further to the evidence for community pharmacist-managed hypertension, a systematic review and meta-analysis by Santschi et al. (2014) included evidence from primary care, hospitals, army medical centres, academic health centres as well as community pharmacies.(281) In most studies (23/39) the pharmacist led the intervention. In the other 16 studies, the pharmacist intervened in close collaboration with doctors, nurses or dietitians (team-based care). The pharmacist interventions included the following:

1. Pharmacist-measured blood pressure - 13 studies.
2. Patient education and counselling about lifestyle, medication and adherence - 35 studies.
3. Medication management (including drug monitoring with adjustment or change in medication) - 34 studies.
4. Feedback to health care professionals (e.g. recommendation to primary care physician for medication change, team meeting and development of treatment plan) - 35 studies.

This pattern of intervention resembles those described in Figure 1 (Chapter 1) of this thesis as the ‘common intervention’ schedule from previous community

pharmacy hypertension trials, and therefore supports the overall structure of this thesis.

Pharmacist interventions showed greater reductions in systolic BP (−7.6 mmHg [95% CI −9.0 to −6.3 mmHg]) and in diastolic BP (−3.9 mmHg [95% CI −5.1 to −2.8 mmHg]) than usual care across the studies included by Santschi et al.(281) These BP reductions are similar to the Cheema et al. systematic review findings (-6.13 mmHg [95% CI -8.44 to - 3.81] systolic, and -2.51 mmHg [95% CI -3.46 to -1.55] diastolic).(107)

However, significant heterogeneity was found in the meta-analysis and the review authors stated that the source of this heterogeneity could not be clearly identified from the trials. Interventions led by the pharmacist and conducted at least monthly were more effective than less frequent interventions.(281)

It is worth noting that the Santschi et al. meta-analysis contained only 4 community pharmacist-led trials, whereas Cheema et al. included 11, hence the reason for using the Cheema et al. review from the beginning of this thesis.

Clark et al. 2019

Since the completion of this thesis, a more recent review has been conducted in the form of a 2019 Cochrane review of 'allied health professional' interventions to reduce BP *(provisionally accepted for publication)*.(282) This review by Clark et al showed that both nurse and pharmacist models of care are more effective than usual GP care for lowering BP, achieving BP targets and improving adherence to antihypertensive medications. The results were consistent across community pharmacy, primary care and secondary care settings and appeared applicable across a wide range of ethnicities and co-morbid populations.(282) The review

authors concluded that interventions were more likely to be effective if delivered face to face, as telephone contact alone did not appear to improve outcomes. No evidence was found of an increase in patient adverse events attributable to the pharmacist's interventions. The review also highlighted the lack of economic analyses across the RCTs. Lack of economic evaluation was a 'research design' consideration (highlighted in Chapter 1, section 1.6) as a factor that hinders the translation of evidence into practice, as service commissioners are required to allocate finite resources to maximise health outcomes.(136)

Overall, the Cochrane review added one new community pharmacist-led BP lowering trial to those summarised in Table 5 from the Cheema et al. systematic review. In this additional trial,(283) the pharmacist assessed CVD risk and BP control, counselled on and reviewed anti-hypertensive medications, and had the prescribing authority to make changes to existing medications and initiate new anti-hypertensive drugs – a key difference between this trial and the previous RCTs from Cheema et al. The patient's doctor was notified of any test results and medication changes either via fax or in person. Patients were followed up at monthly intervals until their BP was at target for 2 consecutive visits and thereafter at 3-month intervals for the duration of the study period, with a total of 6 months of follow up.(283) The study resulted in a 6.6 mmHg reduction in systolic BP over usual care (±1.9 mmHg, p=0.0006),(283) closely matching the conclusions of the Cheema et al meta-analysis.(107) These results appear to suggest that community pharmacists are able to effect similar BP reductions regardless of their ability to prescribe. This inference is however contradicted by the overall conclusion to the 2019 Cochrane review that stated:

> *"Allied health professional-led interventions that include the ability to prescribe, or at least advise prescription of changes to antihypertensive medications… result in greater reductions in blood pressure than those which do not."* (282)

This conclusion covers all pharmacist and nurse-led interventions across a variety of settings, however. Furthermore, the likely benefits of pharmacist-prescribing in the community could be evaluated via other metrics to BP reduction alone, such as the effect on subsequent GP workload or on patient satisfaction with their consultation.

6.6.2 Delivering extended services in community pharmacies

The sections that follow highlight the current and future implementation challenges for delivering community pharmacy hypertension management services, as identified in this thesis and the broader literature. The factors identified are also discussed in the context of the CFIR implementation framework.

Intervention intensity

As per the Santschi et al. review, the 2019 Cochrane review also found that monthly follow up appointments were associated with improved blood pressure outcomes over less frequent monitoring, and this has been further shown in previous community pharmacy-hypertension literature.(115) In Chapter 2, pharmacists felt strongly about the potential burden of fitting in routine BP management on their time. Pharmacists reported that this stopped them from prioritising the development and uptake of hypertension services. They also reported reluctance to engage with additional services in general if they were not associated with financial

remuneration. The effect of diverting the pharmacist's time from other essential pharmacy tasks were not estimated in the RCTs from the Cheema et al review,(107) however Table 5 (Chapter 1) described the intervention intensities of the individual trials, demonstrating considerable variation in frequency and durations of appointments.

The process of dispensing, from the point of view of the pharmacist, involves clinically checking the drug and dose for the patient and accuracy-checking the dispensed label and item processed by the dispenser.(284) This labour-intensive task accounts for over 80% of community pharmacy income and is therefore vital to the viability of a pharmacy.(100) The steady increase in prescription volumes from around 80 million items per year in England in 2011 to over 90 million items per year in 2015, and falling prescription item income, has cemented this role for pharmacists.(15) A possible consequence of diverting a pharmacist away from their medication distribution/dispensing role may therefore be to threaten the financial viability of the community pharmacy. Evaluations of this are therefore required in order to mitigate such impact, for example by evaluating the cost/benefit implications of introducing a second pharmacist in the pharmacy (a suggestion made in Chapter 2), which may improve the deliverability of hypertension interventions whilst maintaining other essential pharmacy tasks. In a study of how additional services have been embedded into everyday practice (in particular, MURs) one pharmacist exemplified this point:

> *"You can't switch off from the fact that you know that's going on* (prescriptions piling up whilst conducting an MUR in the consultation room)*. And that's in the back of your mind, when you know that you're exceptionally busy, it puts you under a pressure and you really just want to get through those questions* (the MUR) *as quickly as possible. Because, you know you're going to go back to bedlam. You can't switch off from that, because that's part of your responsibility as well."*(285)

Upskilling other pharmacy workers, such as healthcare assistants and pharmacy technicians, was viewed by pharmacists in Chapter 2 as having the potential to rebalance pharmacist workload towards more patient-facing services. Furthermore technological innovations in the pharmacy sector, namely hub-and-spoke models of dispensing (automated, offsite dispensing) have also been proposed, developed and implemented in a limited capacity in recent years.(286) Currently, the evidence demonstrating their ability to free-up pharmacist time to conduct patient facing clinics has been limited.(286)

As with many of the factors to be outlined in this section of the thesis, the intensity of the intervention is a factor that relates to more than one component of the CFIR framework.(140) Fundamentally, it is an intervention characteristic, however it requires consideration from both an inner setting (the balance and opportunity-cost of other pharmacy tasks) and outer setting (training and funding for other pharmacy staff or automated dispensing to facilitate the process) perspective in order to optimise the balance between the clinical benefits of more intensive interventions, and the burden this would place on individual pharmacists and the pharmacy business.

Scope of practice

Medico-legal constraints in the UK mean that pharmacists are unable to adapt existing prescriptions (change doses or strengths) or initiate new prescription medications in community pharmacies without the approval and signature of a prescriber (usually the GP).(287) In Chapter 5, pharmacists referred patients to their GP after they reported side effects that may have required either lower doses or a

change in medications. Other than independent prescribing pharmacists, who are currently too few to fulfil these roles and do not typically operate in community pharmacies,(263) strategies such as Patient Group Directions (PGDs) could be used to enable a pharmacist to add, switch or titrate anti-hypertensive medications. PGDs can however take a significant amount of time and resource to develop and implement.(288) Alternatively, patient specific directions (for the care of a named patient rather than a group of patients that fit a broader definition) could be used to devolve management to a pharmacist on a case-by-case basis. In both circumstances, a pre-agreed protocol for both up and down titrations of treatments, such as those used in patient self-management trials,(260) could be devised between GPs, pharmacists, patients and the required approving organisations. In addition to this, the ability of a pharmacist to order or view routine blood and urine markers relevant to hypertension are also barriers to independent, long-term, hypertension follow up that require addressing.

Other countries have found solutions to these issues that could be used as a precedent for the UK. In Canada for example, all 10 provinces permit community pharmacists to reauthorise repeat prescriptions, and 6 out of 10 provinces allow pharmacists to make dosage alterations (as of 2017).(289) Furthermore, 6 out of 10 provinces allow pharmacists to order and access laboratory monitoring such as urea and electrolyte levels that are required for annual ACE-inhibitor monitoring, for example.(289) For context, the first province to allow pharmacists to reissue prescriptions (Nova Scotia) did so in 2005.(290) Compared to the UK, where such a policy would be managed nationally rather than devolved to specific regions,(291) Canadian provincial health authorities can make changes to legislation that affect their locality only.(290) Although this can lead to inconsistencies in service provision

across a country, such devolution is argued to reduce bureaucracy in some instances, speeding up the implementation of services.(292)

This outer setting factor from the CFIR (section 1.6) has, in recent times, been the subject of some change in community pharmacies with the introduction of more private prescribing taking place.(293) However, this has largely been in the area of minor ailaments rather than for chronic conditions, and requires patients to pay for their medications and consultations. An NHS 'prescribing budget' allocated to community pharmacies is not likely to be considered until the next pharmacy contract is negotiated and therefore more timely changes to medications by GPs may be a more realistic prospect for optimising hypertension medications.

Communication and information sharing

Improving communication between pharmacy and general practice, and the lack of access to patient clinical records available to the community pharmacist are further areas that require addressing (see Chapter 2). This was also recognised by the Royal Pharmaceutical Society who stated in their "Shaping Pharmacy for the future" document in 2015, that:

> *"Access to the patient health record will allow pharmacists to make more informed clinical decisions, in partnership with patients and other health and social care professionals, about the pharmaceutical care that patients receive."*(294)

In Chapter 2 pharmacists stated that communication with GPs was often challenging due to a lack of collaboration between the professions, and previous literature has found that factors such as past negative encounters and the busyness of both settings also contribute to poor inter-professional communication.(295) Some methods of communication used in current practice between pharmacies and

GP surgeries were noted in the consultation notes from Chapter 4, where pharmacists reported that referrals to the GP were made directly over the phone (via receptionists) in urgent cases or via written communication for the patient to pass on in less urgent cases. The consequences of poor communication between pharmacies and general practice risks duplicating work between the settings as neither are up-to-date with the latest care received by the patient, wasting resources. Poor communication has also been associated with a reduction in the ability of pharmacists to make clinical decisions.(294) Methods of communication between pharmacists and GPs were described in 11/16 community pharmacy BP trials in the Cheema et al. systematic review.(107) In those trials, pharmacists did not have access to the full clinical record, reflecting clinical practice in English community pharmacies today.(294) The trials varied with how pharmacists communicated results and recommendations with GPs, ranging from written notes to the patient to pass on, letters directly to the practice, periodical face-to-face meetings with the GP, phone calls to the GP, or faxing letters. The participants interviewed in Chapter 2 suggested the use of other communication tools such as NHSmail and 'read-write' access to summary care records as more efficient alternatives. Currently in England, pharmacists have access to a patient's summary care record (SCR) which contains a full list of the patient's prescribed medications, allergies and contact details – if the patient consents to share this information.(296) However, further information such as co-morbidities, previous consultations with the GP, laboratory results and secondary care letters are not present. While pharmacists currently have 'read' access to the SCR, they cannot write in the records after consultations with patients. To combat this shortcoming, some areas of Europe have introduced fully integrated primary care records, such as in

Valencia, Spain, where both GPs and pharmacists have combined their records onto a shared system.(297) Such data has allowed for the better monitoring of patient compliance for instance, whereby the prescriber can view if the patient has collected their prescription in a given month.(298) In addition, community pharmacists in Valencia are able to view the full clinical data needed to deliver clinical services as well as make consultation entries into the record.(298) An integrated computer system in England is likely to lead to similar such benefits, and could facilitate the delivery of community pharmacist-led hypertension management. The bureaucracy and permissions needed to set up and deliver such a system, however, makes this apparently unfeasible at present in the UK.

Community pharmacy's identity

A further challenge to delivering extended services in community pharmacies is the 'commercial vs healthcare' identity problem that the setting faces. This was highlighted in Chapter 2, where a commissioner described speaking to pharmacy chains in the language of 'patients', while they spoke back in the language of 'customers'. In a survey of all primary care trusts (now CCGs, clinical commissioning groups) in England, engagement with extended pharmacy services occurred disproportionately in larger pharmacy chains than independent or small chain pharmacies, and this was primarily driven by commercial and corporate pressures to achieve financial targets.(299) Bush et al. referred to this as the 'corporatisation' of community pharmacy, whereby the needs of the business are put ahead of patient or wider NHS priorities.(300) This has the potential to create a conflict between the healthcare professional role of pharmacists and the assumed business priorities of those who own the pharmacy chain. In the past, pharmacists have reported feeling pressurised to conduct services, such as MURs, in order to meet

targets, and this can result in lower quality patient care and inappropriate use of resources.(285) These literature provide a contrast to the thoughts of some of the pharmacists interviewed in Chapter 2, that felt the more personal approach of independent community pharmacies would be a key facilitator for delivering hypertension management services in pharmacies.

Community pharmacy contractual framework

As introduced in Chapter 1, activities conducted in community pharmacy are largely dictated by the national contractual framework agreed with the NHS.(11) The pharmacy contract does not currently include payment for hypertension screening or ongoing management, meaning that pharmacists are unable to dedicate significant periods of time to these activities. This thesis has highlighted two key points in relation to the contract's influence on the future of community pharmacy-led hypertension services. First, the current contract is predominantly 'based on volume' *(PH2 – service commissioner)* rather than quality measures (such as the percentage of hypertensive patients achieving BP control).(11) The pharmacists interviewed in Chapter 2 suggested that this would need to change to a 'quality' based system of remuneration for a future hypertension service in community pharmacy to be feasible and acceptable to all stakeholders. Specifically, this was perceived to facilitate GPs and service commissioners to trust that patient care would be put above profits if a hypertension service was to be introduced (see also 'Community pharmacy's identity' section above). Second, pharmacists in Chapter 2 acknowledged that without national-level endorsement in the contract, they were not prepared to take on hypertension services. Financially, the rationale for this view is clear – if they are not being paid for an activity, the current austere climate means that they are unable to conduct the service. However beyond finances alone,

pharmacists also felt that hypertension 'wasn't being pushed' *(PH3 – community pharmacist)* – i.e. they placed less importance on hypertension as a condition because of its exclusion from the contractual framework. Therefore the contract appeared to not only serve as a guide to what they would be paid for, but it may also have a role in influencing their views and attitudes regarding the national importance of certain conditions – in this case hypertension. While other literature suggests that pharmacists are willing to conduct hypertension services,(295) changes in the contract, as stated above, appear to be warrented in order to facilitate this.(150)

6.7 Implications

This thesis has identified that the interventions themselves are unlikely to be the barrier to hypertension service implementation at present. The limited role for community pharmacists in hypertension management is likely to continue, however, unless the challenges discussed in this chapter are addressed. Currently, approximately 80% of a community pharmacy's income is derived from dispensing prescriptions,(100) and with their overall income becoming eroded,(95) the introduction of tasks that take community pharmacists away from their current core function require both funding and a reorganisation of work in the pharmacy. Nevertheless, there are some potential implications for practice beyond outlining the factors to consider before implementing hypertension management services.

Pharmacists delivering blood pressure measurements in community pharmacy may now have a better idea of how to clinically interpret the readings that they generate

as a result of the systematic review and meta-analysis in Chapter 3.(196,301) Although data were sparse and heterogeneous, the novel findings suggested that pharmacy readings were closer to daytime ambulatory and home measurements than could be reliably said for the comparison with GP readings - if the data were to be interpreted cautiously. While future high quality studies are needed to confirm the 135/85mmHg threshold in pharmacies, pharmacists may be able to use these data as a guide to making clinical decisions particularly as the previous threshold (140/90mmHg) was not based on published evidence.

The results presented in Chapters 4 and 5 of this thesis (analysis of consultations and outcomes from hypertensive NMS in pharmacies) may also have an influence on future practice. One such recommendation resulting from Chapter 5 stemmed from the finding that patients who reported uncertainty towards the efficacy of their new anti-hypertensive medication were more likely to be referred back to their GP than those who did not.(2) To avoid such referrals, the NMS could include BP readings as part of the consultation in order to reassure patients. However, given that the majority of NMS consultations occur over the phone, pharmacists could instead consider encouraging patients to report home blood pressure readings, given the strong evidence for pharmacist-supported self-monitoring of BP.(87) Although Chapter 4 found that BP readings were discussed with some patients in pharmacies at present, this was not widespread and is not part of the consultation template used by pharmacists for the NMS (Appendix 9). Discussing BP readings could reassure patients of the efficacy of their new medication in the short term, but may also improve BP outcomes in the longer term when combined with pharmacist counselling.(302) Importantly, with regards to implementation in practice, encouraging home BP readings within NMS consultations is unlikely to require

substantial further work for the pharmacist, reducing their additional workload when delivering hypertension care.

Given the short-term nature of the NMS (consultations cover the first month of treatment only) an extension of this to include periodic follow-ups could be a further progression towards full hypertension management in community pharmacies in the future. At present, extending the existing hypertension NMS may be a more realistic prospect than funding an altogether new service, given the funding already allocated to pharmacies for delivering the NMS and the budget cuts experienced by the sector at present.(13,95) Recommendations for an extended hypertension service are described in section 6.8 that follows.

In summary, the following recommendations to pharmacists and health service commissioners in relation to implementing future hypertension management services in community pharmacies can be made, based on the findings of this thesis:

1. Pharmacists require the reassurance of having local or national-level endorsement before delivering additional hypertension services. Ideally, this should also include a funding stream to enable the redistribution of their other workload to other members of staff (Chapter 2).
2. Interpret pharmacy measured BP using the 135/85mmHg threshold and confirm pharmacy readings with home BP before making treatment or referral decisions if necessary (Chapter 3).
3. Further training for pharmacists to conduct hypertension management may not be required as pharmacists currently provide evidence-based advice related to hypertension management (Chapter 4).

4. A model of intervention that avoids referral back to a GP for final approval should be considered to minimise a GP's workload (Chapters 2 and 5). Alternatives could include referring to a general practice pharmacist or allowing community pharmacists to manage patients themselves through an agreed PGD if they do not possess the permissions to prescribe.

6.8 Recommendations for future research

The feasibility and efficacy of an 'extended' hypertension NMS that includes longitudinal evaluations of BP, at 6 and 12 months for example, could be established in a future study. The design of an extended NMS study should attempt to follow the evidence based intervention schedule shown in Figure 1, whilst attempting to overcome some of the implementation barriers mentioned previously in this thesis. For instance, a prescribing model whereby the prescriber in general practice was an independent prescribing pharmacist rather than a GP could be trialled in order to action any recommendations made by the community pharmacist. This novel collaboration between community pharmacists referring to prescribing pharmacists in general practice has not been explored in the literature to date,(107,282,303) and was hypothesised to improve collaboration and communication between community pharmacy and general practice by the participants in Chapter 2. In addition, the use of NHSmail or read/write summary care records to communicate BP readings and consultations between the settings could also be formally trialled for feasibility. The existing funding model associated with the NMS could be used or extended to accommodate the extra consultations proposed at month 6 and 12. An associated health economic analysis would be required in parallel in order to decipher cost

implications to the health service and to the pharmacy's business viability. The 2019 Cochrane review of allied health professional-led interventions for improving BP (see section 6.6.1 above) concluded that the costs of the interventions, where reported, were more than usual care, however no analysis of cost-effectiveness was undertaken in the review due to inconsistent reporting.(282) The findings from a future health economic study could be used to inform policy on the most appropriate funding stream to sustain a new model of hypertension management in the community.

Secondly, an adequately powered study is needed to confirm the relationship between pharmacy-measured BP and corresponding GP and out-of-office measures. Although the systematic review in Chapter 3 concluded that pharmacy-measured BP could be interpreted at the current home level (135/85 mmHg), the meta-analysed results exhibited heterogeneity and included few primary studies per comparison.(196) In addition, of the three included studies presenting a sample size calculation, only two were adequately powered to answer the research question.(197,212) None of the eight meta-analysed studies were from the UK and, given the differences in pharmacy models between the UK, the rest of Europe and North America, a UK study may be worth conducting.(289) A future primary study should aim to randomise the order in which patients received the pharmacy, GP, home and ambulatory measurements in light of evidence that BP regresses to the mean as measurements are repeated.(304) Only one study in the systematic review from Chapter 3 randomised the order in which patients received the different BP measurements.(214)

6.9 Concluding remarks

Previous research has shown that community pharmacist-led interventions can significantly reduce blood pressure over usual care.(107) Despite evidence of effectiveness, and the requirement for new models of care for patients with long-term conditions,(97) no community pharmacist-led hypertension management service is currently delivered in UK pharmacies.(11) This thesis has investigated the extent to which the interventions from previous RCTs of community pharmacist-led hypertension management are translatable to current pharmacy practice in England.

The four results chapters contained within this thesis were devised in order to provide context for hypertension-related service delivery in pharmacies (Chapter 2) and to address the three common intervention components from the previous RCTs that showed clinical effectivness: measuring and interpreting BP in the pharmacy; offering advice and counselling related to blood pressure control; and making decisions to refer or to follow-up patients (Chapters 3-5).

This thesis has shown that components of the interventions used in the RCTs are currently being delivered to some extent in community pharmacies, particularly with regards to the provision of medication and healthy lifestyle advice and counselling. This suggests that the previous trial interventions are implementable in practice. However, the wider operational, financial and legal factors highlighted in this thesis need to be taken into consideration before hypertension management services can be implemented and maintained in community pharmacies. These challenges may

require national-level change in both legislation and infrastructure for tanglible progress to be made.

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Appendices

Appendix 1 – Participant Information Sheet for Chapter 2 interviews



NUFFIELD DEPARTMENT OF
PRIMARY CARE
HEALTH SCIENCES

Participant information sheet

Optimising the management of hypertension in Pharmacies: an interview study of Pharmacists

You are being invited to take part in an interview as part of a research study. Before you decide if you are willing to be interviewed it is important for you to understand why the research is being done and what it will involve.

Please take the time to read the following information carefully and discuss it with friends and relatives if you wish. If there is anything that is not clear or you would like more information, please ask the researcher.

What is the purpose of the study?

This study is a component of a wider body of work aimed at putting pharmacists at the heart of creating, developing and implementing a service for hypertensive patients most in need of blood pressure management support.

Elevated blood pressure increases the risk of stroke and heart disease, therefore making adequate blood pressure control a public health priority. It is estimated that approximately half of people with high blood pressure are poorly controlled. Poor adherence to long term medications and clinical inertia (lack of optimal therapy) have been cited as two of the major factors contributing to the sub-standard control.

The aim of these interviews is to guide the development of a novel and feasible blood pressure intervention aimed at addressing these factors in hypertensive patients visiting community pharmacies.

This study will inform the development of a subsequent study in community pharmacies.

The research forms part of a DPhil (PhD) project in the Nuffield Department of Primary Care Health Sciences at the University of Oxford.

Why have I been invited?

You have been invited because of your experience and role within (and related to) community pharmacy. We would like to interview pharmacists with varying years of experience, geographic locations, and from different employment and store types.

What will happen to me if I decide to take part?

Interviews will take place in a meeting room in the Nuffield Department of Primary Care Health Sciences at the University of Oxford. If this is inconvenient, then a suitable professional location can be arranged nearer to you (such as a meeting room at your place of work).
Before the interview, the researcher will go over the study and will answer any questions you may have. At this point you will be asked to sign an informed consent form to confirm you agree to participate. You will be given a copy of this to keep.

V1.1 20/07/2016

Initially, you will be asked some background questions about yourself, particularly regarding your job and link to community pharmacy. Subsequently, pharmacists will be asked to share their expertise and experiences to help inform ways in which they can identify and assist hypertensive patients with medication adherence problems, and with identifying and overcoming clinical inertia.

In addition, pharmacists will be invited to speak about barriers to service implementation in pharmacies and to share their experiences of delivering services.

The interviews should last no longer than 45 minutes. The interviews will be audio recorded and then transcribed for analysis.

Reasonable travel expenses will be remunerated on production of receipts or tickets. Please note, taxi fares will not be reimbursed.

Do I have to take part?

It is up to you to decide whether or not you take part in the interview. If you decide to take part you are still free to withdraw at any time and without giving a reason.

What will happen to my data?

The transcribed interviews will be anonymised by removing any information that could identify you. Extracts from your interview may be quoted in reports or publications arising from the research, but again these will be anonymous.

Will my taking part in the study be kept confidential?

In accordance with the Data Protection Act 1998 the information you give us in the interviews (recordings and transcripts) will be kept securely for a period of 10 years after the study ends and then destroyed.

Responsible members of the University of Oxford [and the relevant NHS Trust(s)] may be given access to data for monitoring and/or audit of the study to ensure that the research is complying with applicable regulations.

Are there any possible disadvantages or risks from taking part?

Participant interviews will be anonymised and pseudonyms will be used in transcripts. Any identifying details will be altered in order to prevent any chance of confidentiality breaches. No personal information will be passed on beyond the research team, and data will be stored in line with the Data Protection Act (i.e. on a password protected hard-drive and records deleted after 10 years).

It could be that you are not comfortable talking about certain aspects of the pharmacy profession, pharmacy services, your particular experience or a particular question in the interview, for example. You are free not to answer any question or stop the interview at any point if you wish.

What are the possible benefits of taking part?

You may feel passionate about the role of pharmacists in primary care, therefore adding to the evidence base of pharmacy interventions may be both fulfilling and interesting to you. Once the study is finished the information you have given may help to improve the management of patients with hypertension.

What will happen if I don't want to carry on with the study?

Participation is voluntary and you are free to change your mind at any point during the interview or at a later stage. You are free to withdraw without penalty. You can withdraw your data from the study at any point up until the time of analysis, which is likely to be around 6 months after your interview.

Who is organising and funding the research?

This research is organised by the Nuffield Department of Primary Care Health Sciences.

The study is funded by a scholarship awarded to Mr. Ali Albasri by the University of Oxford, Oxford Primary Care Research Trust and CLARHC (Collaboration for Leadership in Applied Health Research and Care).

Who has reviewed the study?

This study has been reviewed by, and received ethics clearance through, the University of Oxford Central University Research Ethics Committee (CUREC).

What if there is a problem?

If you have a concern about any aspect of this study, please speak to the relevant researcher [01865 289323] or their supervisor [01865 617852], who will do their best to answer your query. The researcher should acknowledge your concern within 10 working days and give you an indication of how they intend to deal with it. If you remain unhappy or wish to make a formal complaint, please contact the chair of the Research Ethics Committee at the University of Oxford who will seek to resolve the matter in a reasonably expeditious manner:

Chair, **Medical Sciences Inter-Divisional Research Ethics Committee**; Email: ethics@medsci.ox.ac.uk; Address: Research Services, University of Oxford, Wellington Square, Oxford OX1 2JD'

Further information and contact details.

If you have any questions about this study, please contact:

Mr Ali Albasri

Postal address: Nuffield Department of Primary Care Health Sciences, University of Oxford, Gibson Building, 1st Floor, Radcliffe Observatory Quarter, Woodstock Road, Jericho, Oxford, OX2 6GG

Email: ali.albasri@gtc.ox.ac.uk Telephone: 01865 289323

Thank you for reading this information.

Appendix 2 – Participant consent form for Chapter 2 interviews

Professor Richard McManus
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PARTICIPANT CONSENT FORM

CUREC Approval Reference: R46769/RE001

Optimising the management of hypertension in Pharmacies: an interview study of Pharmacists

Purpose of Study: to guide the development of a novel and feasible blood pressure intervention aimed at hypertensive patients visiting community pharmacies.

		Please initial each box
1	I confirm that I have read and understand the information sheet version 1.1 dated 20/07/2016 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 reason, and without any adverse consequences or academic penalty.	☐
3	I understand that research data collected during the study may be looked at by designated individuals from the University of Oxford where it is relevant to my taking part in this study. I give permission for these individuals to access my data.	☐
4	I understand that this project has been reviewed by, and received ethics clearance through, the University of Oxford Central University Research Ethics Committee.	☐
5	I understand who will have access to personal data provided, how the data will be stored and what will happen to the data at the end of the project.	☐
6	I understand how this research will be written up and published.	☐
7	I understand how to raise a concern or make a complaint.	☐
8	I consent to being audio recorded	☐
9	I give permission for my anonymised quotes to be used in the research publication	☐
10	I agree to take part in the above study.	☐

Name of Participant	Date	Signature
Name of person taking consent	Date	Signature

Review

OPEN

A comparison of blood pressure in community pharmacies with ambulatory, home and general practitioner office readings: systematic review and meta-analysis

Ali Albasri[a], Jack W. O'Sullivan[a], Nia W. Roberts[b], Suman Prinjha[a], Richard J. McManus[a], and James P. Sheppard[a]

See editorial comment on page 1948

Background: Blood pressure (BP) readings are traditionally taken in a clinic setting, with treatment recommendations based on these measurements. The clinical interpretation of BP readings taken in community pharmacies is currently unclear. This study aimed to systematically review all literature comparing community pharmacy BP (CPBP) readings with ambulatory BP monitoring (ABPM), home BP monitoring and general practitioner clinic readings.

Method: Studies were included if they compared CPBP with at least one other measurement modality used for the diagnosis or management of hypertension. Mean CPBP readings were compared with other measurement modalities and summarized using random-effects meta-analyses. The primary outcome was to compare CPBP with gold standard ABPM readings.

Results: Searches generated 3815 studies of which eight were included in the meta-analyses. The mean systolic CPBP-daytime ABPM difference was small [+1.6 mmHg (95% confidence interval −1.2 to 4.3) three studies, $n = 319$]. CPBP was significantly higher than 24-h ABPM [+7.8 mmHg (95% confidence interval 1.5–14.1) three studies $n = 429$]. Comparisons with general practitioner clinic readings (six studies, $n = 2100$) were inconclusive with significant heterogeneity between studies. CPBP and home BP monitoring readings (five studies, $n = 1848$) were nonsignificantly different. Diastolic comparisons mirrored systolic comparisons in all but the CPBP-daytime ABPM comparison, where CPBP was significantly higher.

Conclusion: Current evidence around the clinical interpretation of CPBP is inconclusive. Although this review suggests that adopting the 135/85 mmHg threshold for hypertension might be reasonable and potentially result in a higher sensitivity for detecting patients with truly raised BP in pharmacies, the impact of this lower threshold on increased referrals to general practice clinics must be considered.

Keywords: ambulatory, blood pressure, clinic, general practitioner, home, hypertension, pharmacy

Abbreviations: ABPM, ambulatory blood pressure monitoring; BP, blood pressure; CI, confidence interval; CPBP, community pharmacy blood pressure; GP, general practitioner; HBPM, home blood pressure monitoring; WMD, weighted mean difference

INTRODUCTION

Hypertension is the most common, preventable risk factor for cardiovascular events [1], with almost a third of all adults in England affected [2]. Hypertension-related appointments make up approximately one in 10 of all general practitioner consultations each year [3] and with the workload of general practitioners thought to be nearing saturation point [4]; alternative models of care are needed to ensure appropriate management of hypertension in the community.

National guidelines in the United Kingdom recommend out-of-office measurements, in the form of ambulatory blood pressure (BP) monitoring (ABPM), as the 'gold standard' for the diagnosis of hypertension [5]. Where ABPM is not possible, home BP monitoring (HBPM) is recommended, but even this is not acceptable to all patients with hypertension [6]. These measurement modalities have shown to be more closely associated with patient's future risk of cardiovascular events than clinic BP [7,8], and when combined with general practitioner clinic measurements, make up the foundation of hypertension diagnosis and monitoring. Thresholds of 140/90 (clinic) and 135/85 mmHg (daytime ABPM/HBPM) are widely accepted

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Appendix 4 – Prospero systematic review protocol title page Chapter 3

PROSPERO
International prospective register of systematic reviews

NHS National Institute for Health Research

Print | PDF

A comparison of blood pressure readings taken in community pharmacies with; ambulatory, home, and general practitioner office blood pressure readings: a systematic review and meta-analysis

Ali Albasri, Jack O'Sullivan, James Sheppard, Nia Roberts, Richard McManus

Citation

Ali Albasri, Jack O'Sullivan, James Sheppard, Nia Roberts, Richard McManus. A comparison of blood pressure readings taken in community pharmacies with; ambulatory, home, and general practitioner office blood pressure readings: a systematic review and meta-analysis. PROSPERO 2016 CRD42016032518 Available from: http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42016032518

Review question

How do community pharmacy blood pressure (CPBP) readings and ambulatory blood pressure monitoring (ABPM) readings compare?

How do CPBP readings and home blood pressure monitoring (HBPM) readings compare?

How do CPBP readings and general practitioner (GP) office blood pressure readings compare?

Searches

The MEDLINE and EMBASE electronic databases will be searched. Relevant articles from 01/01/2009 to 16/12/15 will be searched in addition to the references of relevant reviews and articles that meet selection criteria published before and after 2009. No language limits will be applied.

Types of study to be included

All study types with extractable data comparing mean blood pressure readings, mean difference or a measure of correlation/agreement between community pharmacy and any of; ABPM, HBPM or GP clinic readings. Studies will be excluded if pharmacy readings were taken alone and not compared to one of the above reading types mentioned. Studies will also be excluded where participants had their BP measured in a pharmacy as part of a wider intervention or package of care to reduce or control BP e.g received more regular monitoring, condition or medication advice…over participants receiving usual care and being followed up by their general practitioner

Appendix 5 – Medline search strategy for systematic review Chapter 3

((((((pharmacy[Title/Abstract])

OR pharmacies[Title/Abstract])

OR pharmacist*[Title/Abstract]))

OR ((((("Pharmacy"[Mesh]))

OR "Pharmacies"[Mesh])

OR "Community Pharmacy Services"[Mesh])

OR "Pharmacists"[Mesh])

OR "Pharmaceutical Services"[Mesh:NoExp])))

AND

((((hypertension[Title/Abstract])

OR "blood pressure"[Title/Abstract]))

OR (((((("Hypertension"[Mesh:NoExp])

OR "Masked Hypertension"[Mesh])

OR "White Coat Hypertension"[Mesh])

OR ("Blood Pressure Determination"[Mesh]

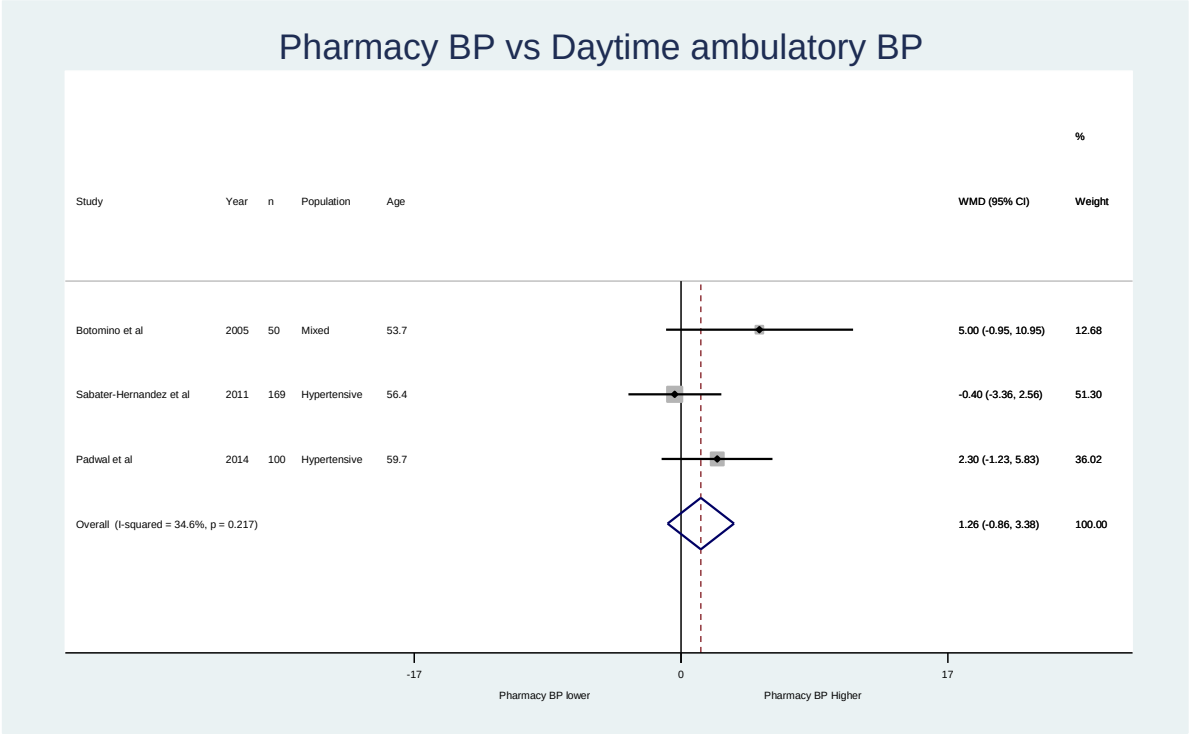
OR "Blood Pressure"[Mesh]))

OR "Blood Pressure Monitors"[Mesh]))

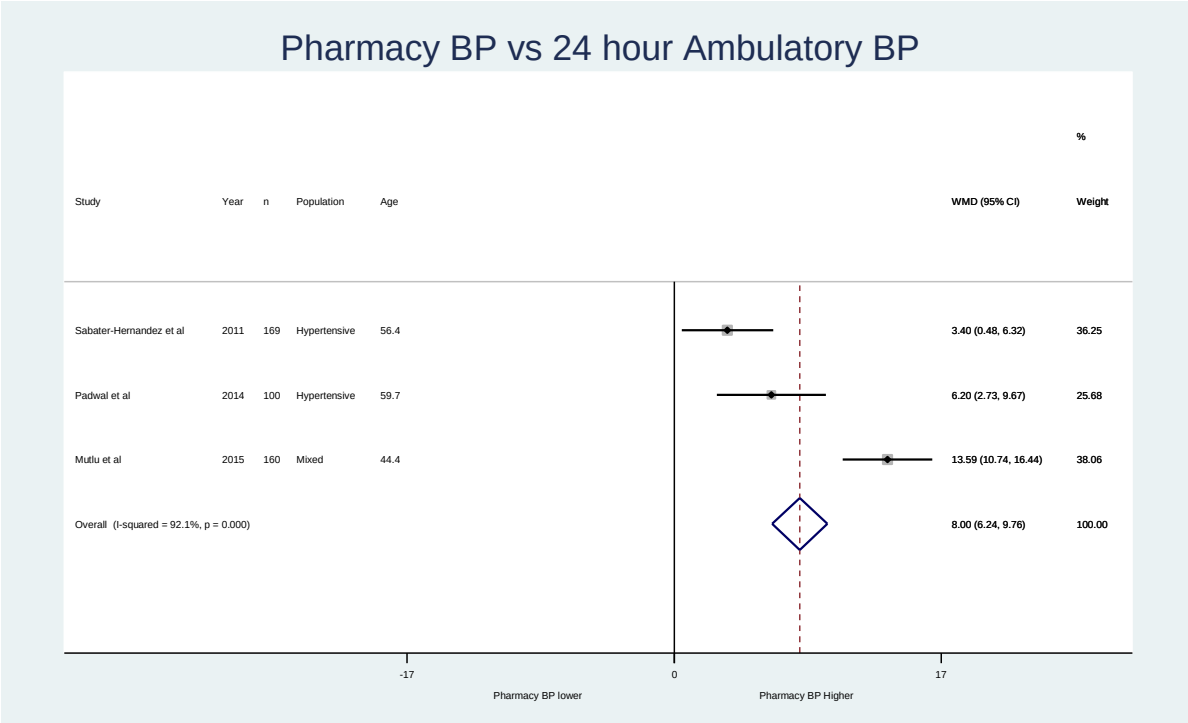
Filters: Publication date from 2009/01/01 to 2015/12/31

Appendix 6 – Sensitivity analyses of systolic BP results using a Fixed Effects meta-analysis, Chapter 3

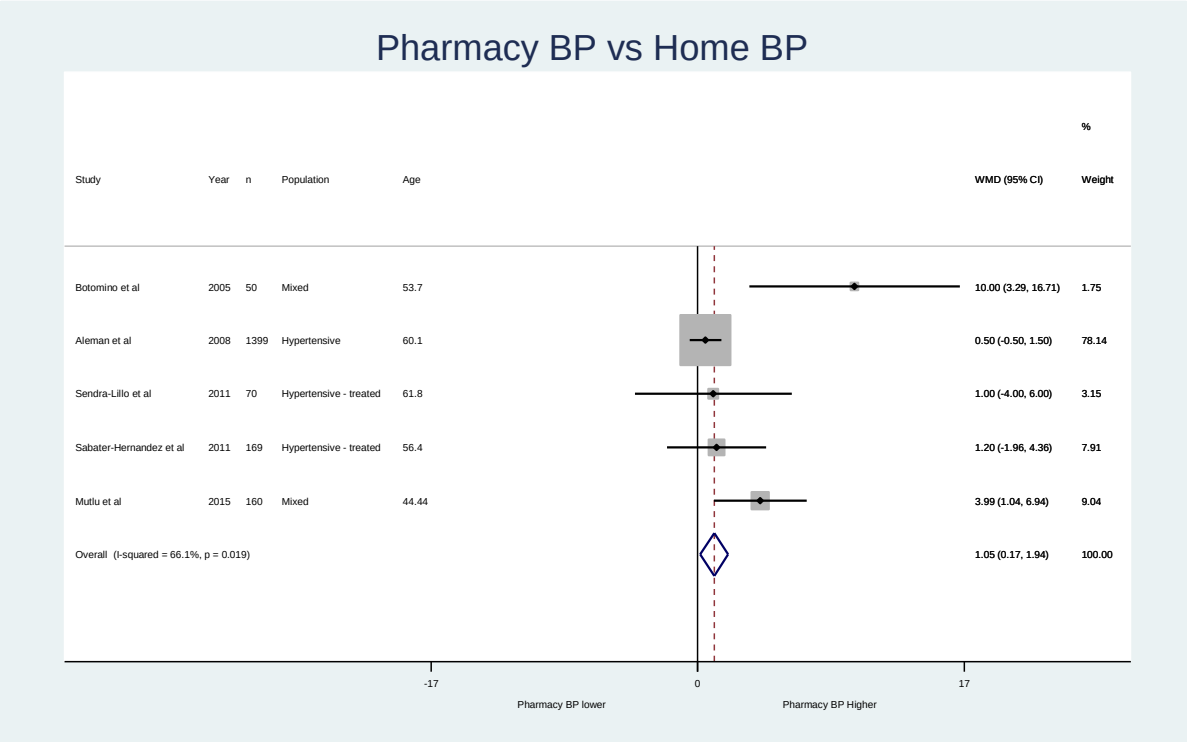
a)



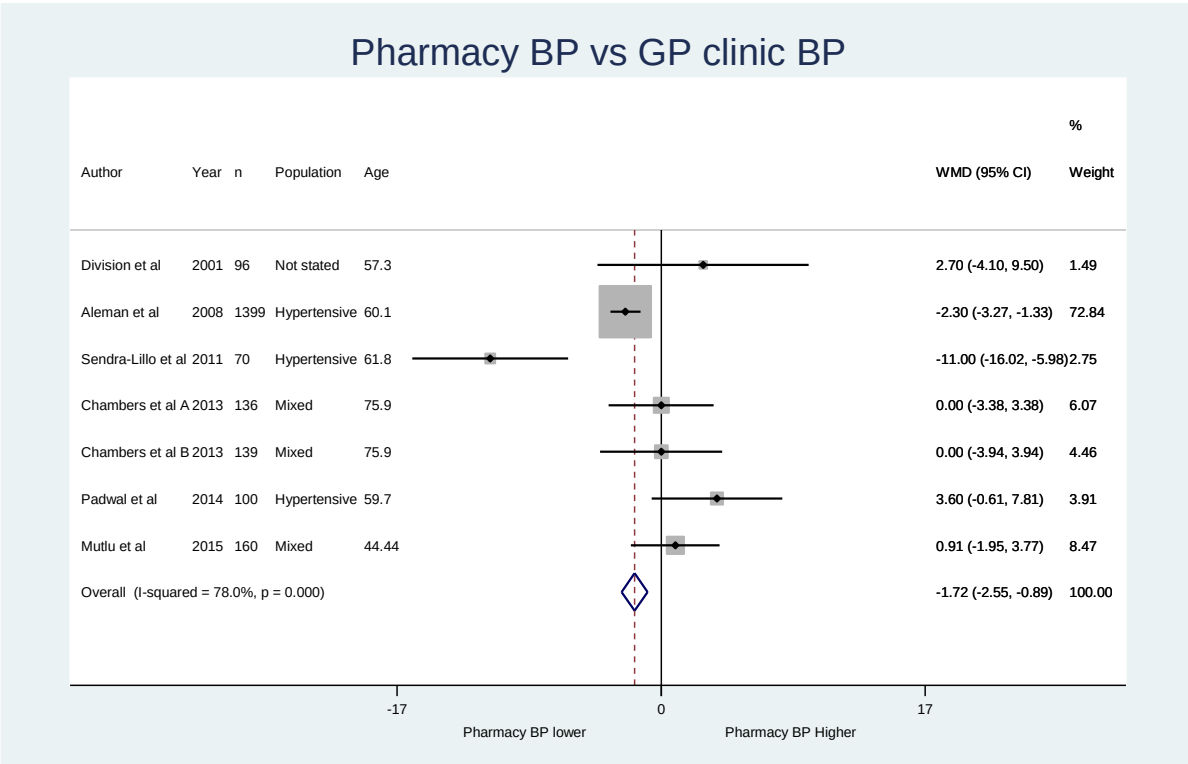
b)



c)

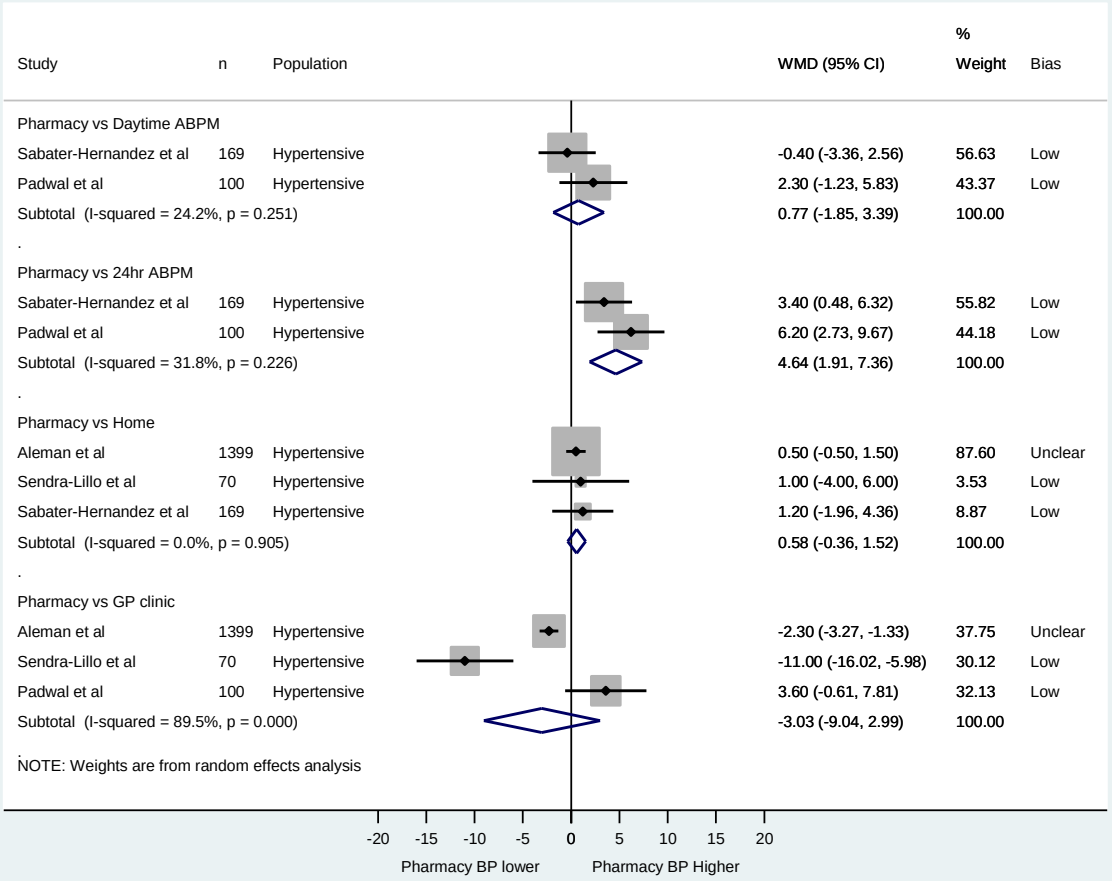

Pharmacy BP vs Home BP
Study
Year
n
Population
Age
WMD (95% CI)
%
Weight
Botomino et al 2005 50 Mixed 53.7 10.00 (3.29, 16.71) 1.75
Aleman et al 2008 1399 Hypertensive 60.1 0.50 (-0.50, 1.50) 78.14
Sendra-Lillo et al 2011 70 Hypertensive - treated 61.8 1.00 (-4.00, 6.00) 3.15
Sabater-Hernandez et al 2011 169 Hypertensive - treated 56.4 1.20 (-1.96, 4.36) 7.91
Mutlu et al 2015 160 Mixed 44.44 3.99 (1.04, 6.94) 9.04
Overall (I-squared = 66.1%, p = 0.019) 1.05 (0.17, 1.94) 100.00
-17
0
17
Pharmacy BP lower
Pharmacy BP Higher

d)

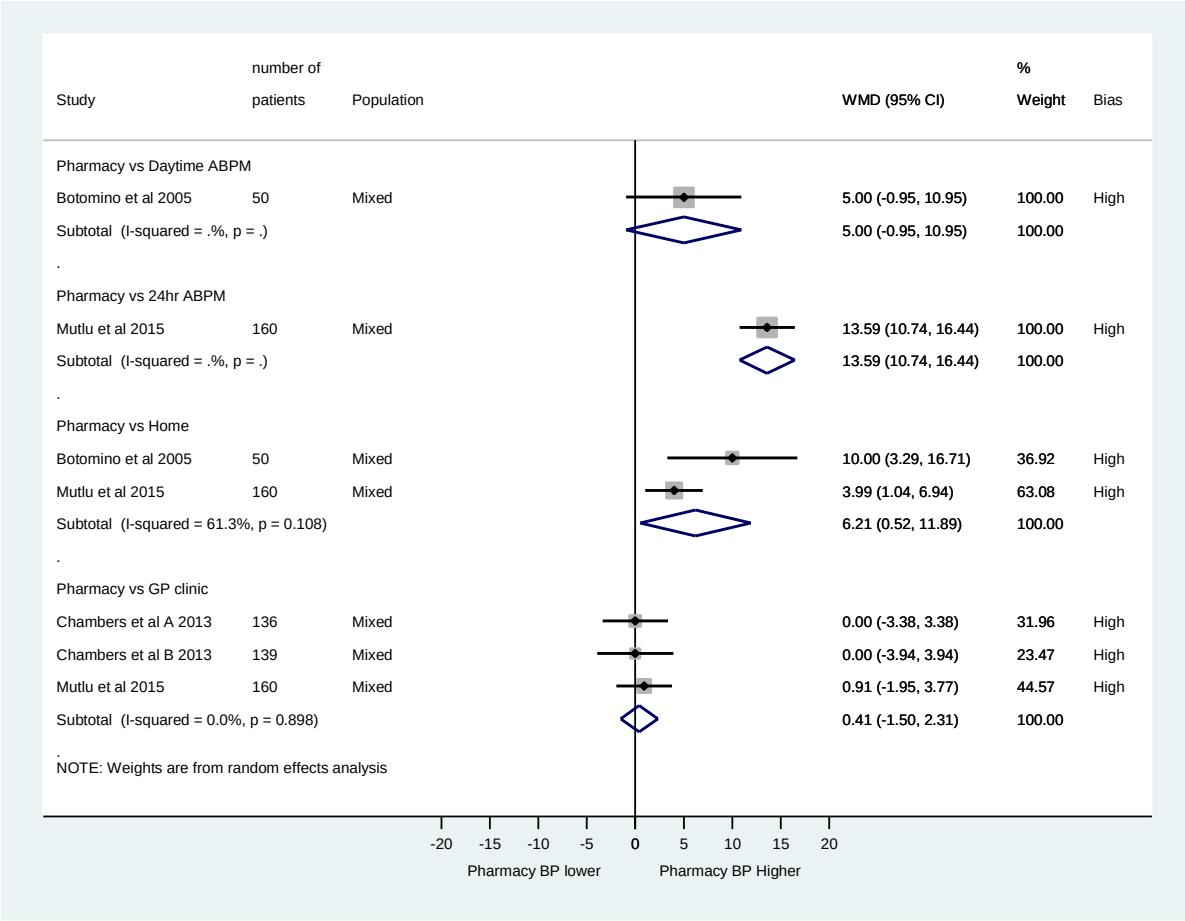

Pharmacy BP vs GP clinic BP
Author
Year
n
Population
Age
WMD (95% CI)
%
Weight
Division et al 2001 96 Not stated 57.3 2.70 (-4.10, 9.50) 1.49
Aleman et al 2008 1399 Hypertensive 60.1 -2.30 (-3.27, -1.33) 72.84
Sendra-Lillo et al 2011 70 Hypertensive 61.8 -11.00 (-16.02, -5.98) 2.75
Chambers et al A 2013 136 Mixed 75.9 0.00 (-3.38, 3.38) 6.07
Chambers et al B 2013 139 Mixed 75.9 0.00 (-3.94, 3.94) 4.46
Padwal et al 2014 100 Hypertensive 59.7 3.60 (-0.61, 7.81) 3.91
Mutlu et al 2015 160 Mixed 44.44 0.91 (-1.95, 3.77) 8.47
Overall (I-squared = 78.0%, p = 0.000) -1.72 (-2.55, -0.89) 100.00
-17
0
17
Pharmacy BP lower
Pharmacy BP Higher

Appendix 7 – Sub group analyses, Chapter 3

a) Sub-group analysis – hypertensive patients only

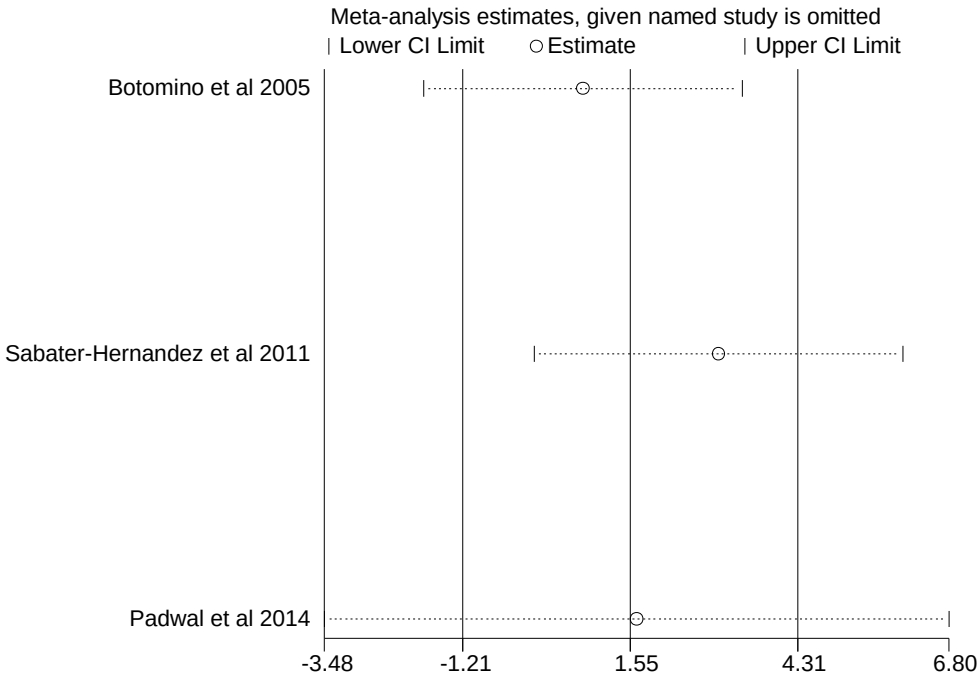


b) Sub-group analysis mixed cohorts only



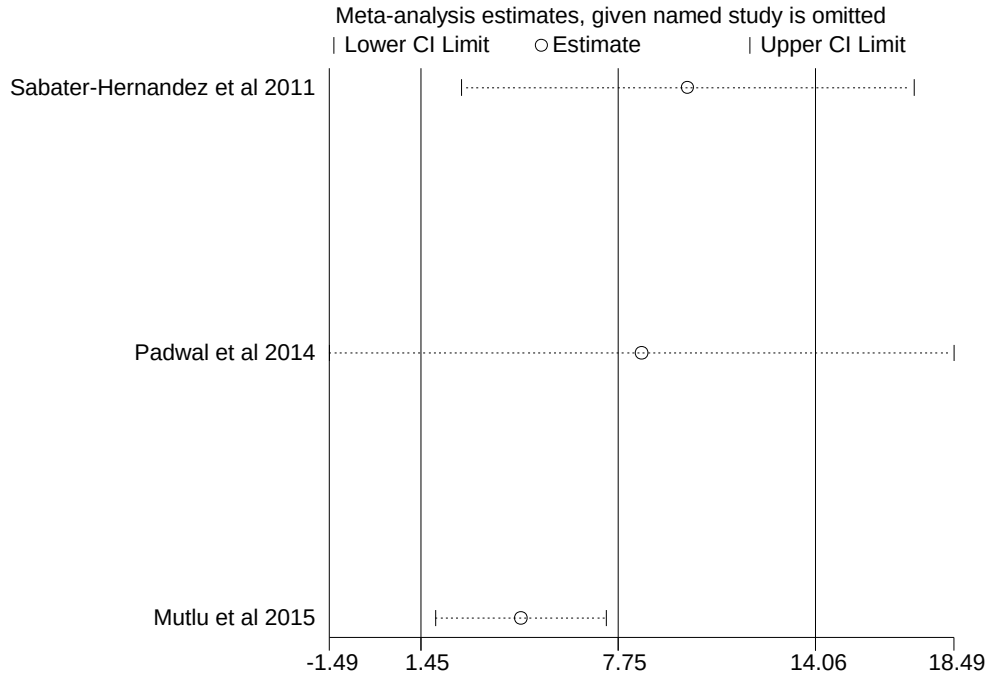
Appendix 8 – Influence analysis, Chapter 5

a) Pharmacy vs Daytime ABPM



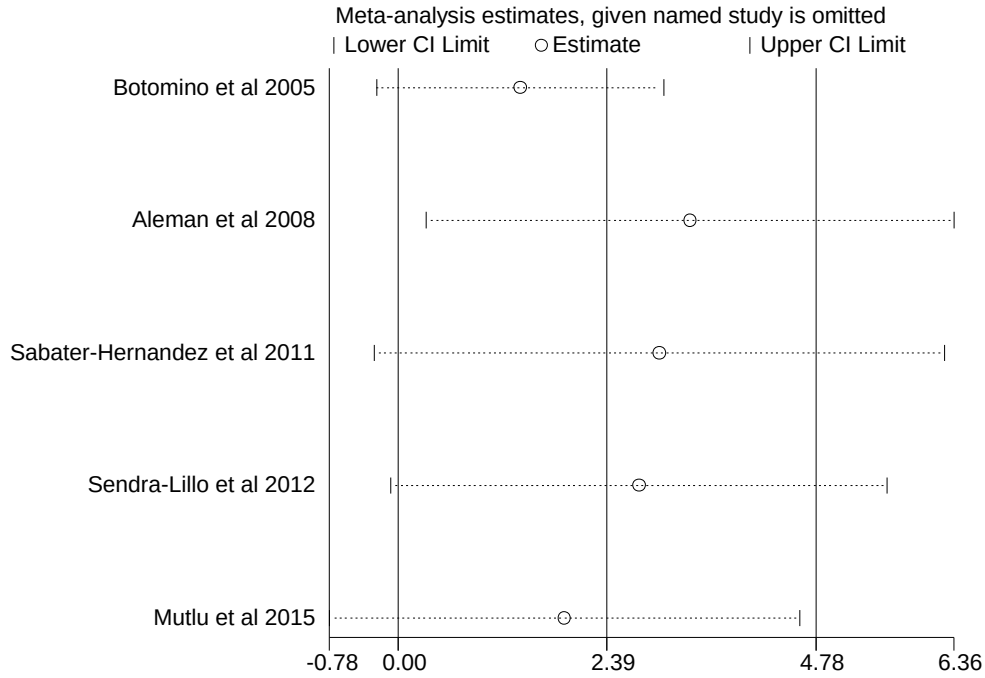
Study omitted	Estimate	[95% Conf.	Interval]
Botomino et al 2005	.77090049	-1.8516585	3.3934593
Sabater-Hernandez etal 2011	3.0030186	-.03376865	6.0398059
Padwal et al 2014	1.6572837	-3.4824934	6.7970605
Combined	1.5490726	-1.2112734	4.3094187

b) Pharmacy vs 24hr ABPM



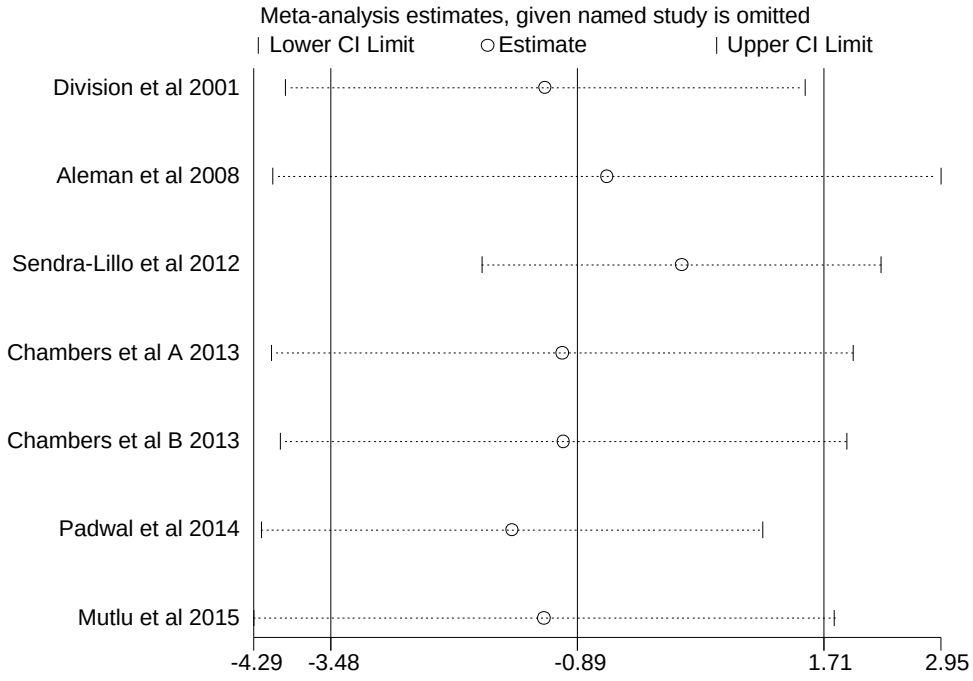
Study omitted	Estimate	[95% Conf.	Interval]
Sabater-Hernandez et al 2011	9 .9639187	2.7231128	17.204725
Padwal et al 2014	8.5001717	-1.4858342	18.486177
Mutlu et al 2015	4.6369181	1.9116533	7.3621831
Combined	7.7515859	1.446265	14.056907

c) Pharmacy vs Home



Study omitted	Estimate	[95% Conf.	Interval]
Botomino et al 2005	1.4016708	-.23659065	3.0399325
Aleman et al 2008	3.3403513	.32474157	6.3559613
Sabater-Hernandez et al 2011	2.9890139	-.26888627	6.2469139
Sendra-Lillo et al 2012	2.7563651	-.07942593	5.5921559
Mutlu et al 2015	1.9066255	-.77650213	4.5897532
Combined	2.3935821	.00408071	4.7830834

d) Pharmacy vs GP clinic



Study omitted	Estimate	[95% Conf.	Interval]
Division et al 2001	-1.2231871	-3.9586985	1.5123243
Aleman et al 2008	-.57429051	-4.0936413	2.9450605
Sendra-Lillo et al 2012	.21220227	-1.8885365	2.3129411
Chambers et al A 2013	-1.0451097	-4.10952	2.0193005
Chambers et al B 2013	-1.0310435	-4.0171752	1.9550883
Padwal et al 2014	-1.5729132	-4.2122922	1.0664659
Mutlu et al 2015	-1.2362955	-4.293551	1.8209603
Combined	-.88519466	-3.4801519	1.7097626

Appendix 9 – NMS intervention form, Chapters 4 and 5

NHS New Medicine Service
Intervention Worksheet

PHARMACY
the Heart of our Community

Patient:		DOB:		Consultation: ☐ in pharmacy ☐ by telephone
Pharmacist:		Date:		
Medicine:		Dosage:		

Intervention questions	Consultation notes
1. Have you had the chance to start taking your new medicine yet?	
2. How are you getting on with it?	
3. Are you having any problems with your new medicine, or concerns about taking it?	
4. Do you think it is working? (Prompt: is this different from what you were expecting?)	
5. Do you think you are getting any side effects or unexpected effects?	
6. People often miss taking doses of their medicines, for a wide range of reasons. Have you missed any doses of your new medicine, or changed when you take it? (Prompt: when did you last miss a dose?)	
7. Do you have anything else you would like to know about your new medicine or is there anything you would like me to go over again?	

After the consultation use the following sections to code your discussion with the patient

Matters identified with patient

Patient reports:

☐ Using the medicine as prescribed	☐ Not using the medicine as prescribed
☐ Not having started using the medicine	☐ Prescriber has stopped the new medicine
☐ Not using the medicine in line with the directions of the prescriber	☐ Missing a dose in the past 7 days
☐ Need for more information about the medicine	☐ Side effects
☐ Negative feelings about the medicine	☐ Uncertainty on whether the medicine is working
☐ Concern about remembering to take the medicine	☐ Difficulty using the medicine due to its pharmaceutical form/formulation
☐ Other (record detail in 'Other notes' overleaf)	

PSNC

CONFIDENTIAL

Outcomes of the discussion with the patient

Advice provided:

- ☐ Reminder strategies to support use of medicine
- ☐ Change to timing of doses to support adherence
- ☐ How to manage or minimise side effects

Information provided:

- ☐ Interactions with other medicines
- ☐ Why am I using the medicine / what is it for
- ☐ How to use the medicine
- ☐ Correct dose of the medicine
- ☐ Effects of the medicine on the body / how it works
- ☐ Why should I take the medicine
- ☐ Timing of the dose
- ☐ Interpretation of side effect information

Agreed patient actions:

- ☐ Carry on using medicine as prescribed
- ☐ Use medicine as agreed during the intervention
- ☐ Submit Yellow Card report to MHRA
- ☐ Other (record detail in 'Other notes')

Actions taken by pharmacist:

- ☐ Referral (record details below)
- ☐ Yellow card report submitted to MHRA
- ☐ Reminder chart / MAR chart provided
- ☐ Other (record detail in 'Other notes')

Referral reasons

- ☐ Drug interaction(s)
- ☐ Potential side effect(s) / ADR preventing use of medicine

Patient reports:

- ☐ Not using medicine any more
- ☐ Never having started using medicine
- ☐ Difficulty using the medicine - issue with device
- ☐ Difficulty using the medicine - issue with formulation
- ☐ Lack of efficacy
- ☐ Problem with dosage regimen
- ☐ Unresolved concern about the use of the medicine
- ☐ Other issue (detail below)

Further information / comments / possible action regarding referral:

Other notes

Healthy living advice

- ☐ Diet & nutrition
- ☐ Smoking
- ☐ Physical activity
- ☐ Alcohol
- ☐ Sexual health
- ☐ Weight management

Research

Ali Albasri, Suman Prinjha, Richard J McManus and James P Sheppard

Hypertension referrals from community pharmacy to general practice:

multivariate logistic regression analysis of 131 419 patients

Abstract

Background
The burden of hypertension in primary care is high, and alternative models of care, such as pharmacist management, have shown promise. However, data describing outcomes from routine consultations between pharmacists and patients with hypertension are lacking.

Aim
To identify factors associated with referral of patients from pharmacies to general practice within the first 2 weeks of starting a new antihypertensive medication.

Design and setting
Multivariate logistic regression conducted on data from community pharmacies in England.

Method
Data were obtained from the New Medicine Service between 2011 and 2012. Analyses were conducted on 131 419 patients. In all, 15 predictors were included in the model, grouped into three categories: patient-reported factors, demographic factors, and medication-related factors.

Results
Mean patient age was 65 years (±13 years), and 85% of patients were of white ethnicity. A total of 5895 (4.5%) patients were referred by a pharmacist to a GP within the first 2 weeks of starting a new antihypertensive medication. Patients reporting side effects (adjusted odds ratio [OR] 11.60, 95% confidence interval [CI] = 10.85 to 12.41) were most likely to be referred. Prescriptions for alpha-blockers were associated with referral (adjusted OR 1.28, 95% CI = 1.12 to 1.47), whereas patients receiving angiotensin-II receptor blockers were less likely to be referred (adjusted OR 0.89, 95% CI = 0.80 to 0.99).

Conclusion
Most patients were followed up by pharmacists without the need for referral. Patient-reported side effects, medication-related concerns, and the medication class prescribed influenced referral. These data are reassuring, in that additional pharmacist involvement does not increase medical workload appreciably, and support further development of pharmacist-led hypertension interventions.

Keywords
general practice; hypertension; logistic regression; new medication; pharmacists; referral.

INTRODUCTION

The New Medicine Service (NMS) is a nationally commissioned NHS contractual service aimed at providing support for patients within the first month of starting a new medication.[1] It has been delivered in >90% of community pharmacies in England since its introduction in 2011, and covers four therapeutic areas: hypertension, type 2 diabetes, asthma and chronic obstructive pulmonary disease (COPD), and anticoagulation and antiplatelet therapy.[1] The NMS aims to improve patient adherence to long-term medications by encouraging engagement with their new medication.[1,2]

Hypertension-related appointments make up almost one in 10 of all GP consultations each year.[3] With the workload of GPs thought to be nearing saturation point,[4] alternative models of hypertension management such as pharmacist-led care have the potential to alleviate this increasing burden on primary healthcare systems. Evidence from systematic reviews shows that such interventions can significantly reduce blood pressure compared with usual GP care.[5,6]

To explore the potential of implementing extended pharmacist roles in the management of hypertension in community settings, detailed assessments of current interventions such as NMS are required to identify patient groups and presentations that pharmacists are able to manage independently, without referral to a GP. Previous research exploring reasons for referral from pharmacies to general practice has focused on upper gastrointestinal symptoms,[7] and a systematic review of community pharmacy triage services reported reasons for referrals for a variety of other minor ailments.[8] Much of these data were collected using surveys or questionnaires, relying on participant recall, rather than from routine datasets, and hence may not capture the true impact of such services.

Routinely collected data were analysed from 131 419 patients with hypertension reporting to a community pharmacy with a new antihypertensive medication. This study aimed to establish factors associated with patient referral from pharmacies to general practice within the first 2 weeks of starting a new antihypertensive medication.

METHOD

Study design and data source

This was a cross-sectional study of patients with hypertension presenting to a community pharmacy in England with a newly prescribed antihypertensive medication. Anonymised patient and consultation data were recorded by pharmacists using PharmOutcomes software in pharmacies as part of the NMS service, and were subsequently sent to the Pharmaceutical Services Negotiating Committee (PSNC).

The data collection form for pharmacists

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Appendix 11 – Unadjusted logistic regression model, Chapter 5

	n (%) (N=131,419)	Number referred n (%)	Unadjusted OR (95% CI)
Outcome variable			
Referrals from Pharmacy to GP	5,895 (4)	–	–
Predictor variables			
Patient reported factors			
Side effects	24,992 (19)	4155 (17)	12.00 (11.32 - 12.71)
Not using the medicine as prescribed	5271 (4)	2,236 (42)	24.66 (23.14 – 26.29)
Negative feelings towards new BP medication	5,038 (4)	1,292 (26)	9.12 (8.51 - 9.79)
Uncertainty whether medicine working	8,344 (6)	555 (7)	1.57 (1.44 - 1.72)
Not yet started the medication	823 (0.6)	230 (28)	8.55 (7.32 - 9.98)
Concerns with remembering to take medication	965 (1)	60 (6)	1.42 (1.09 – 1.84)
Difficulty with medication formulation	149 (0.1)	13 (9)	2.04 (1.15 -3.60)
Prescriber stopping the medication	777 (0.6)	313 (40)	15.11 (13.06 – 17.49)
More information about medication requested	7,276 (6)	301 (4)	0.91 (0.81 - 1.02)
Missed dose in the past 7 days	1,166 (1)	415 (36)	12.59 (11.13 – 14.23)
Using medicine as prescribed	107,989 (82)	2,354 (2)	0.13 (0.12 - 0.13)
Demographic factors			
Age (years, <40 years as reference)			
40 – 49	12,987 (10)	463 (4)	0.82 (0.69 – 0.96)
50 – 59	23,451 (18)	951 (4)	0.93 (0.80 – 1.09)
60 – 69	37,312 (28)	1,548 (4)	0.96 (0.82 – 1.10)

70 – 79	34,895 (27)	1,680 (5)	1.12 (0.96 – 1.29)
80 and over	17,975 (14)	1,045 (6)	1.36 (1.17 – 1.59)
Ethnicity (White as reference)			
South Asian	4,586 (4)	227 (5)	1.12 (0.98-1.29)
Other	1,645 (1)	91 (6)	1.26 (1.02-1.56)
Not stated	10,234 (8)	476 (5)	1.05 (0.95-1.16)
Black/Afro-Caribbean	2,760 (2)	127 (5)	1.04 (0.87-1.25)
Gender, Male (Females as reference)	61,146 (47)	2,172 (4)	0.66 (0.62 - 0.69)
Medication related factors (CCB as reference)			
A-Blocker	5,264 (4)	411 (8)	1.74 (1.56-1.94)
B-Blocker	16,211 (12)	777 (8)	1.03 (0.95-0.13)
Thiazide	15,487 (12)	800 (5)	1.11 (1.03-1.22)
ACEi	34,497 (26)	1312 (4)	0.81 (0.76-0.87)
ARB	17,415 (13)	622 (4)	0.76 (0.69-0.83)
Other	1,173 (1)	53 (5)	0.05 (0.74-1.29)

Appendix 12 – Correlation matrix of variables from Chapter 5

	age2	sex	Ethnic~B	medici~2	uncert~g	negati~s	SideEf~d	needsm~o	notsta~d	notusi..	missed~s	concer~d	diffcu~m	prescr~d	usinga~d
age2	1.0000														
sex	-0.0833	1.0000													
EthnicityB	-0.1316	0.0015	1.0000												
medicine2	0.0313	-0.0070	0.0012	1.0000											
uncertainw~g	0.0090	0.0016	-0.0109	0.0118	1.0000										
negativefe~s	0.0246	-0.0394	-0.0049	0.0238	0.1125	1.0000									
SideEffect~d	0.0201	-0.0750	-0.0075	-0.0026	0.0611	0.1768	1.0000								
needsmorei~o	0.0130	-0.0110	-0.0022	0.0183	0.1247	0.1385	0.0837	1.0000							
notstarted~d	-0.0034	-0.0089	0.0052	0.0075	-0.0167	0.1168	-0.0279	0.0360	1.0000						
notusingas~d	0.0178	-0.0340	0.0135	0.0269	-0.0095	0.1864	0.1399	0.0187	0.3751	1.0000					
misseddose~s	0.0011	-0.0162	0.0129	0.0074	0.0143	0.1011	0.0832	0.0136	0.0017	0.4554	1.0000				
concernabo~d	-0.0055	-0.0039	0.0070	-0.0017	0.0584	0.0432	0.0280	0.0891	-0.0012	0.0228	0.0384	1.0000			
diffcultyw~m	0.0017	-0.0047	0.0029	-0.0048	0.0339	0.0286	0.0217	0.0413	0.0002	0.0116	0.0113	0.0819	1.0000		
prescriber~d	0.0144	-0.0154	-0.0005	0.0101	-0.0091	0.0161	0.0640	-0.0148	0.0052	0.3636	0.0255	-0.0043	0.0033	1.0000	
usingaspre~d	-0.0032	0.0215	-0.0090	-0.0255	0.0634	-0.0881	-0.0094	0.0459	-0.1702	-0.4388	-0.2006	-0.0077	-0.0020	-0.1625	1.0000

Appendix 13 – Characteristics of excluded patients from Chapter 5

Category	Included patients	Excluded patients
Population	131,419	16,993
Age (mean, SD)	65 (13)	N/A
Gender (%)		
Male	61,146 (47)	7,580 (45)
Female	70,273 (53)	9,413 (55)
Medication class (%)		
CCB	41,372 (32)	5,312 (31)
ACE-I	34,497 (26)	4,396 (26)
ARB	17,415 (13)	1,816 (11)
Thiazide	16,211 (12)	2,147 (13)
B-Blocker	15,487 (12)	2,342 (14)
A-Blocker	5,264 (4)	799 (5)
Other	1,173 (1)	181 (1)
Ethnicity (%)		
White	112,194 (85)	14,163 (83)
South Asian	4,586 (4)	479 (3)
Black/African- Caribbean	2,760 (2)	360 (2)
Not stated	10,234 (8)	1,736 (10)
Other	1,645 (1)	255 (2)