IMPACT OF MOTIVATIONAL INTERVIEWS WITHIN PHARMACY CARE UPON ADHERENCE TO CARDIOVASCULAR MEDICINES: A FEASIBILITY PILOT CONTROLLED TRIAL

Thesis submitted in accordance with the requirements of University College London for the degree of Doctor of Philosophy by

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Declaration

This thesis describes research conducted in UCL School of Pharmacy, between November 2011 and November 2015 under the supervision of Professor Felicity Smith and Professor David Taylor. I, [Zahraa Sabeeh MohammedAli Al Jalal] confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.'

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Signature Date

Abstract

Background

Non adherence to medication in myocardial infarction patients ranges from 13-60% (Garavalia et al, 2009). Consistent use of secondary prevention medication after a coronary event is associated with lower adjusted mortality and higher survival rates compared with patients who are not compliant (Newby et al, 2006). Strategies to tackle the burden of non adherence could involve pharmacy care and services including Medication Use Review and the New Medicine Service with a motivational interview as part of the counselling session of a community pharmacist.

Objective

To investigate the feasibility and potential impact of a pharmacy care intervention involving motivational interviews and referral to the community pharmacy services, amongst patients with acute coronary syndrome, on adherence to medication and on health outcomes.

Methods

This thesis reports a prospective, intervention, controlled feasibility/pilot study. Seventy one patients discharged from a London Heart Attack Centre following acute treatment for a coronary event were enrolled and followed up for six months. Thirty two pharmacies in London were allocated into intervention or control sites. The intervention was delivered by community pharmacists face-to-face in the pharmacy, or by telephone as part of the New Medicine Service or a Medication Use Review. The consultation included a 15-20 minute motivational interviewing session aimed at improving protective cardiovascular medicine adherence. As this was a feasibility study, measures of uptake, workability and acceptability were gathered from all stakeholders. A measure of fidelity to the intervention was also performed. The primary outcome measure was adherence to secondary prevention medication using a self report adherence measure. Secondary

clinical outcomes included blood pressure and LDL-C. Data collection of outcome measures took place at baseline, 3 months and 6 months. An intention-to-treat analysis was conducted for the outcome measures.

Results

Given a small sample size, the feasibility study was not powered to measure clinical outcomes. However, at 3 and 6 months there was a statistically significant difference in adherence between the intervention group and the control group (P= 0.026), (P=0.004) respectively. In addition, there was a statistically significant relationship between the level of adherence at 3 months and beliefs regarding medicines (P=0.028). Patients who reported better adherence expressed positive beliefs regarding the necessity of taking their medicines. However, given the small sample size, no statistically significant outcome difference in terms of recorded blood pressure and LDL-C was observed over the six months of the study.

Conclusion

The feasibility, acceptability and potentially positive clinical outcome of the intervention was demonstrated, along with a high level of patient acceptability. It had a significant impact on cardiovascular medicine taking adherence. But these findings must be interpreted with caution. The intervention should be tested in a larger trial to ascertain its full clinical utility.

List of Abbreviations

ACE inhibitors	Angiotensin Converting Enzymes inhibitors
A&E	Accident and Emergency
ACS	Acute Coronary Syndrome
ACT	Asthma Control Test
AHA	American Heart Association
ANF	Portuguese Pharmacy Association
ARBs	Angiotensin Receptor Blockers
B.P	Blood Pressure
BMQ	Beliefs about Medicines Questionnaire
CABG	Coronary Artery Bypass Graft
CAD	Coronary Artery Disease
CASP	Critical Appraisal Skills Programme
CCGs	Clinical Commissioning Groups
CHDs	Coronary Heart Diseases
COPD	Chronic Obstructive Pulmonary Disease
CVDs	Cardiovascular Diseases
DUR	Drug Usage Review
EMR	Eastern Mediterranean Region
FIP	International Pharmaceutical Federation
GP	General Practitioner
GPP	Good Pharmacy Practice
HbA1c	Glycosylated Hemoglobulin
HDL	High Density Lipoprotein
HLP	Healthy Living Pharmacies
IHD	Ischemic Heart Disease
IRAS	Integrated Research Application System
KNMP	The Royal Dutch Pharmacist Association
LDL-C	Low Density Lipoprotein-Cholesterol
LPC	Local Pharmaceutical Committee
MARS	Medication Adherence Report Scale
MEMS	Medication Event Monitoring System
MeSH	Medical Subject Headings
MI	Myocardial Infarction
MITI	Motivational Interviewing Treatment Integrity
MMAS	Morisky Medication Adherence Score
MONICA	Monitoring trends and determinants in cardiovascular disease
MRP	Medication Related Problems

MTM	Medication Therapy Management
MUR	Medication Usage Review
NCCPC	National Collaborating Centre for Primary Care
NCD	Non Communicable Disease
NELLPC	North East London Local Pharmaceutical Committee
NHLBI	National Heart Lung Blood Institute
NHS	National Health Service
NICE	National Institute for Health and Clinical Excellence
NMS	New Medicine Service
NSF	National Service Framework
NSTEMI	Non ST-Elevation Myocardial Infarction
PCI	Percutaneous Coronary Intervention
PCTs	Primary Care Trusts
PDC	Proportion of days covered
PHLink	Pharmacy Health Link
PMAS	Community Pharmacy Based Minor Ailment Scheme
PSNC	Pharmaceutical Services Negotiating Committee
RPS	Royal Pharmaceutical Society
SBPM	Self Blood Pressure Monitor
SCR	Summary Care Record
SIGN	Scottish Intercollegiate Guidelines Network
STEMI	ST-Elevation Myocardial Infarction
TAB	Tools for Adherence Behaviour Screening
TB	Tuberculosis
UCLSOP	University College London School of Pharmacy
WHO	World Health Organisation

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A special thanks to my family especially my sisters Fatima and Miriam who always encouraged me. Words cannot express how grateful I am to my mother Layla, for all of the sacrifices that you've made on my behalf. Your prayer for me was what sustained me thus far. I would also like to thank all of my friends who supported me in writing and encouraged me to strive towards my goal, especially my friend Kathryn King who was always there for me. At the end I would like to express appreciation to my beloved husband Dr. Mazin who was always my support in the moments when there was no one to answer my queries. Finally, I would like to dedicate my work to my two handsome sons' Yousif and Sammy I hope mummy has made you proud.

Publications from this thesis

Publications

- Zahraa S Jalal, Felicity Smith, David Taylor, Katherine Finlay, Hemant Patel and Sotiris Antoniou, Impact of pharmacy care upon adherence to cardiovascular medication a feasibility controlled trial. *Eur J Hosp Pharm* 2016;10.1136/ejhpharm-2015-000790.
- David Taylor, Zahraa S Jalal and James Davies (2015). Pharmacy and the Public Health Policy. In: K. Taylor and G. Harding, ed., 2nd ed. London, pp.33-59.
- Zahraa S Jalal, Felicity Smith, David Taylor, Katherine Finlay, Hemant Patel and Sotiris Antoniou, Pharmacy care and adherence to primary and secondary prevention cardiovascular medication: a systematic review of studies, 2014; *Eur J Hosp Pharm* doi:10.1136/ ejhpharm-2014-000455.
- Zahraa S. Jalal, David Taylor, Sotiris Antoniou, Katherine Finlay and Felicity Smith; 2013, ClinicalTrials.gov: Impact of Motivational Interviews within Pharmacy Care upon Adherence to Cardiovascular Medicines (Pharmacy care) NCT01920009.

Future potential publications from this thesis

- Results of the feasibility study interviews and questionnaires with stakeholders (a supplementary article to the main pilot study).
- Interviews with South Asians in the UK and adherence to cardiovascular medication after Coronary Heart Disease (an article to raise awareness for a larger study).

Chapter One

Introduction and Background

This chapter will discuss the epidemiology of cardiovascular disease around the world including the context of epidemiological transition. It will provide an overview of cardiovascular disease and its risk factors. There will be a particular focus on coronary heart disease, which is the disease studied in this thesis, and its prevention and management. The chapter will explore the role of medicines in secondary prevention, and include a discussion on adherence, reasons for non-adherence, measurement of adherence and strategies, in particular, behavioural approaches (motivational interviewing) in addressing non-adherence.

1.1-Introduction

Cardiovascular diseases (CVDs) account for more than 17 million deaths globally each year (30% of all deaths); a figure which is expected to grow to 23.6 million by 2030 (Wong *et al*, 2014). The WHO projections suggest that non communicable diseases will be responsible for a significantly increased number of deaths in the next decade; with the greatest increases in the WHO regions of Africa, South-East Asia and the Eastern Mediterranean (WHO, 2015). It is also noteworthy that many deaths occur in people under 70 years of age, in the more productive period of life. The WHO believes that population based strategies, lifestyle changes and encouraging people to adhere to their medicines and regimens may be effective for both people with established disease and for those at high risk of developing disease (WHO, 2015).

1.2-Recognition of the importance of cardiovascular prevention worldwide

Since the 1920s cardiovascular disease has been identified as a significant cause of death worldwide. Articles from the 1930s and 1940s suggested hypertension, cholesterol, poor nutrition, obesity, smoking, physical inactivity, and psychosocial stress as important factors contributing to heart disease, but they at that time did not provide strong evidence to support this assertion (Mensah and Brown, 2007).

A rising prevalence of CVD was similarly noted in the 1930s and 1940s in the USA (Fuster and Kelly, 2010). This lead to the establishment of the Framingham Heart Study under the direction of the National Heart Institute (now known as the National Heart, Lung, and Blood Institute or NHLBI) (www.framinghamheartstudy.org). The Framingham Heart Study became a joint project of the National Heart, Lung and Blood Institute and Boston University. The aim was to identify the common factors that contribute to cardiovascular diseases, and it focused on participants whom did not yet have obvious cardiac diseases. The study recruited 5,209 men and women ages between 30- 62 from the town Framingham, Massachusetts. In the period between 1948 and 2003 participants and their generations (children and grandchildren) were enrolled and followed-up. The Framingham heart study led to identification of the major risk factors for cardiovascular diseases; high blood pressure, high blood cholesterol, smoking, obesity, diabetes, and physical inactivity as well as providing information on the effects of related factors such as blood triglyceride and HDL cholesterol levels, age, gender, and psychosocial issues (Fuster and Kelly, 2010). From this time the concept of CVD risk factors has become an essential part of the modern medicine and has led to the identification and development of effective treatment and preventive strategies in clinical practice.

Another important epidemiology study was the Seven Countries Study in 1958 to establish if there was a relationship between hypercholesterolemia and coronary heart disease (Keys, 1980). The study included 16 cohorts, in seven countries, in four regions of the world (United States, Northern Europe, Southern Europe, and Japan). In total, 12,763 men, 40-59 years of age, were enrolled between 1958 and 1964 and followed for 15 years in a prospective design (Keys, 1980). The study demonstrated that hypercholesterolemia increases cardiovascular risk both at the population level, individual level and in different cultures. The researchers recommended a healthy diet, avoiding obesity and promotion of physical activity, which all became major aspects for prevention of cardiovascular disease.

After World War II there was a notable rise in coronary heart disease (CHD) in Western countries, although in some countries a decline in rates of disease was observed in the following decades (Keil, 2005). In the 1980s and 1990s, the WHO MONICA (Monitoring trends and determinants in cardiovascular disease) project was conducted to assess trends and determinants of cardiovascular mortality, incidence and case fatality. Altogether some 13 million people from 21 countries in Western Europe and also Russia, Iceland, Canada, China and Australia were monitored over a 10 year period. 166,000 myocardial infarction patients were registered and more than 300,000 men and women were recruited and monitored for their cardiovascular risk factors and other health data. The study also gathered data on mortality, morbidity, coronary care and population-based risk factor surveillance. The findings provided information for disease treatment and prevention of CVD in developed countries. The MONICA study also showed that other factors (in addition to established risk factors of cardiovascular disease: obesity, smoking, blood pressure and cholesterol) such as unrest, poverty and social and economic change could have an effect on contribution to the incidence of heart disease, a role that was not valued at that time. The study produced mass data for cardiovascular diseases around the world and remains the largest cardiology study.

Other important epidemiological studies can be found in the Table 1.1 below. It is beyond the scope of this chapter to describe all the epidemiological studies conducted over the last decades. Nevertheless, cardiovascular epidemiological studies conducted over the past 70 years have made important contributions to our knowledge of disease distribution, and highlighted the importance of risk factors and subclinical disease in predicting cardiovascular events. This has led to the development of methods for estimating the individual's 'global' risk of CHD and CVD. This information has been used to guide the initiation and intensity of preventive therapies (Wong, 2014).

Table 1.1 Major global and national epidemiological studies of cardiovascular disease adapted from (Wong, 2014)

Study	Year commenced	Location	Population studied
The Minnesota Businessmen study	1946	Minnesota, USA	281 men aged <55 years
INTERHEART	1999	Global	15,152 patients with MI and 14,820 age-matched and sex-matched control individuals
The PURE study	2002	17 countries	153,996 adults aged 35–70 years
The Ni–Hon–San study	1965	Japan; Hawaii, USA; San Francisco, CA, USA	20,000 Japanese men aged 45–69 years
The Whitehall and Whitehall II studies	1967 and 1985	UK	18,403 male civil servants aged 40–64 years, and 10,314 male and female civil servants aged 35–55 years
The Rejkavik study and AGES	1968 and 2003	Iceland	9,141 and 2,499 men aged 34–79 years

The PROCAM study	1979	Germany	4,043 men and 1,333 women aged 50–65 years
The CARDIA study	1984	Four communities in the USA	5,115 African American and white men and women aged 18–30 years
ARIC	1987	Four communities in the USA	15,792 African American and white men and women aged 45–64 years
The Strong Heart study	1989	13 American Indian tribes in the USA	4,549 Native American men and women aged 45–75 years
The Cardiovascular Health study	1989	Four communities in the USA	5,888 African American and white men and women aged 65–102 years
The Jackson Heart study	2000	Jackson, MS, USA	5,302 African American men and women aged 21–94 years
MESA	2000	Six communities in the USA	6,814 African American, Chinese, Hispanic, and white men and women aged 45–80 years
The Hispanic Community Health study/Study of Latinos	2006	Four communities in the USA	15,079 Hispanic men and women aged 18–72 years

The epidemiology of cardiovascular disease facts and application to the UK

Despite the significant decline in mortality in the UK, CVD has a tremendous burden on health and costs. Both primary and secondary prevention measures are considered necessary to reduce both the burden of CVD and inequalities in CVD mortality and prevalence (Bhatnagar *et al*, 2015). In 2012 cardiovascular disease was the most common cause of death in the UK for women (28% of all female deaths), but not for men, where cancer was the most common cause of death (32% of all male deaths) (Bhatnagar *et al*, 2015). Mortality from CVD varies widely throughout the UK, with the highest age-standardised CVD death rates in Scotland (347/100 000) and the North of England (320/ 100 000 in the North West). Prevalence of coronary heart disease is also highest in the North of England (4.5% in the North East) and Scotland (4.3%). Men have a greater risk of myocardial infarction than women.

Around 73,000 deaths in the UK each year are attributed to coronary heart disease and there are an estimated 2.3 million people living with the condition, who need secondary prevention medication (NHS, 2014). Prescriptions and surgical interventions for CVD have substantially increased over the last two decades. The National Health Service in England spent around £6.8 billion on CVD in 2012/2013, the majority of which came from spending in secondary care (Bhatnagar *et al*, 2015).

1.3-Epidemiological transition

At the beginning of the 20th century, cardiovascular disease was responsible for fewer than 10% of all deaths worldwide. Today, that figure is about 30%, with 82% of the burden now occurring in developing countries (Gaziano *et al*, 2011). Gaziano, 2005 and Gaziano *et al*, 2011 (Please see Appendix 1) argue that social and economic transition in the world had a major impact on cardiovascular disease prevalence worldwide. This transition has lead to a shift in the cause of death from infectious diseases and malnutrition before 1900 to CVD and cancer currently in most high income countries. Increases in wealth that lead to better availability of food, improved sanitation, and access to vaccines and antibiotics, contributed to increased lifespan and a greater incidence of CVD. As the average lifespan increased beyond 50 years; mortality from CVD in particular and other non communicable diseases exceeded mortality from malnutrition and infectious diseases. The predominant form of CVD is coronary heart disease, but ischemic stroke also emerges as a significant cause of mortality and morbidity.

In the age of delayed degenerative diseases, age-adjusted CVD mortality tends to decline because of widespread primary and secondary prevention efforts such as smoking cessation programs and effective blood pressure control, acute hospital management, and technological advances such as the availability of bypass surgery (Gaziano *et al*, 2011).

However, congestive heart failure prevalence increases because of the improved survival of those with ischemic heart disease. New trends suggest that many developed countries could be entering a fifth as-yet-unnamed phase of the epidemiological transition, characterized by an epidemic of obesity and diabetes prevalence. This trend is not unique to developed countries, however, according to recent WHO data, there are about 1.1 billion overweight adults in the world, with 115 million of them known to be living with obesity related problems in the developing world (Gaziano *et al,* 2011), (WHO, 2015). The so called "epidemiological transition" is taking place because of the rapid aging of the developing world's populations, progressive urbanization and socioeconomic transformation, and changed dietary habits (Jabbour *et al,* 2012), (Gaziano *et al,* 2011).

Governments in the Eastern Mediterranean Region (EMR) are not believed to have placed a sufficiently high priority on addressing the high and rising prevalence of non-communicable diseases, with variations in policies between countries and overall weak implementation (Rahim *et al,* 2014). In the next two decades it is anticipated that the EMR will be overwhelmed by stroke, heart disease and diabetes (Jabbour *et al,* 2012) (please see Appendix 2). However, some EMR countries have recognised this escalating risk and started to look for solutions to decrease the CVD burden. Examples of these solutions are the Abu Dhabi Cardiovascular Program, "Weqaya" (Hajat *et al*, 2010) and the Isfahan Healthy Heart Program in the Islamic Republic of Iran (Sarrafzadegan *et al*, 2009).

1.4-Early onset of cardiovascular diseases

Established cardiovascular diseases are often witnessed in middle-aged or elderly men and women. However, if focusing on atherosclerosis, risk factors in adulthood for CVD have been correlated with increasing severity of asymptomatic coronary and aortic atherosclerosis in young people. Thus, the process is believed to start at an early age, through adolescence and early adulthood (Berenson, 2001; Zieske *et al*, 2002; Sternby *et al*, 1999; Tell and Vellar, 1988) suggesting that cardiovascular disease prevention and promotion of healthy lifestyles should commence in childhood.

1.5-Potential for prevention

Four stages of prevention can be identified, corresponding to different phases in the development of disease (Alwan, 1997), (Donovan *et al*, 2015). Stage one 'primordial prevention' aims to avoid the emergence and establishment of the social, economic and cultural patterns of living that are known to contribute to an increased risk of disease. For Non Communicable Diseases (NCDs) primordial prevention should include national policies on food and nutrition, comprehensive programmes to discourage smoking and promotion of regular physical activity. It addresses broad health determinants rather than preventing personal exposure to risk factors, which is the goal of primary prevention.

Stage two 'primary prevention' seeks to prevent the onset of specific diseases via risk reduction. The purpose of primary prevention is to limit the incidence of disease by focusing on known causes and risk factors, e.g. efforts to discourage unhealthy eating habits, reduce obesity, promote physical activity and reduce smoking. It involves two strategies that are often complementary. It can focus on the whole population, with the aim of reducing average risk (population strategy) or on people at high risk as a result of particular exposures.

Stage three 'secondary prevention', aims to cure patients and/or reduce the more serious consequences of disease through early diagnosis and treatment. It comprises the measures available to individuals and populations for early detection and prompt and effective intervention. It is directed at the period between onset of disease and the normal time of diagnosis, and aims to reduce the prevalence of disease.

Stage four 'tertiary prevention', is aimed at reducing the progress or complications of established disease and is an important aspect of therapeutic and rehabilitation medicine. It consists of measures intended to reduce impairment and disability, to minimise suffering caused by departure from good health and to promote patient adjustment to incurable conditions. The key goal for tertiary prevention is to enhance quality of life.

1.6-Benefits of screening for cardiovascular risk

Many people are unaware of their cardio-vascular risk status. Opportunistic and other forms of screening by health care providers are therefore, a potentially useful means of detecting risk factors, such as raised blood pressure, abnormal blood lipids and blood glucose (WHO, MONICA study, 2005). The predicted risk of an individual can be a useful guide for making clinical decisions on the intensity of preventive interventions; when dietary advice should be strict and specific, when suggestions for physical activity should be intensified and individualized, and when and which drugs should be prescribed to control risk factors. Such a risk stratification approach is particularly suitable to settings with limited resources, where saving the greatest number of lives at lowest cost becomes necessary (WHO report, 2002). A systematic review (Sheridan *et al*, 2010) assessed the effect of providing CHD risk information to adults and identified 20 articles including 14 randomized controlled studies. The review showed that CHD risk information alone or with accompanying education, could increase the accuracy of perceived risk and probably increase intent to start therapy among individuals at moderate to high risk (Sheridan *et al*, 2010).

Sheridan *et al*, (2010) also found that providing risk information at only one point in time seemed ineffective, and that repeated instances of counselling were needed to achieve small but significant reductions in predicted CHD risk (absolute differences, −0.2% to −2% over 10 years in studies using risk estimates derived from Framingham equations).

Opportunistic comprehensive CVD risk assessment in primary care for all adults over 40 years, who have no history of CVD or diabetes, and who are not already on treatment for blood pressure or lipids, has been advocated (Joint British Society, 2014). Younger adults (under 40 years) with a family history of premature atherosclerotic disease should also have their cardiovascular risk factors measured (Joint British Society, 2014). Moreover, the American Heart Association's 2014 guidelines (Goff *et al*, 2014) recommend risk factor assessment in adults at age 20 years and that all adults at age 40 years or above should know their absolute risk of developing CHD; and 10-year CVD risk should be used as the basis for recommendations to reduce the risk (Goff *et al*, 2014). Risk assessment should include ethnicity, smoking habit history, family history of CVD and measurements of weight, waist circumference, blood pressure, lipids (total cholesterol and high-density lipoprotein (HDL) cholesterol) and glucose (Goff *et al*, 2014). The American Heart Association guidelines also recommend recording the pulse rate and rhythm to screen for atrial fibrillation (Goff *et al*, 2014). Once all risk factors have been identified cardiovascular risk charts or calculators should be used to estimate the total risk of developing CVD over the following 10 years. A total CVD risk of over 20% over 10 years is defined as high-risk. People with moderate-to-high risk are more likely to be compliant with lifestyle changes and preventative medication if given information about their individual cardiovascular risk (Sheridan *et al*, 2010). There are several risk calculators available to estimate both 10-year risk and lifetime risk of CVD, such as the JBS 3 risk assessment tool (Joint British Society, 2014) and the QRISK2 (www.qrisk.org) calculator.

The National Institute for Health and Clinical Excellence (NICE) 2014 does not recommend any particular risk calculator. However, calculators which are based on the Framingham risk equation may overestimate risk in UK populations. This may be as much as 5% for UK men. There are other coronary heart disease-cardiovascular disease risk calculators (please refer to Appendix 3).

1.7-Role of medications in primary and secondary prevention of cardiac diseases

Major advances have been made in understanding the pathogenesis of cardiovascular diseases. For example in coronary syndromes (unstable angina, myocardial infarction, and coronary death) recognition that rupture of plaques, leading to coronary thrombosis, accounts for most acute coronary syndromes and that the risk of plaque rupture and its consequences can be substantially reduced by medical intervention (Grundy, 1999), (Kumar and Cannon, 2009). Thus preventive medical therapies are now available to reduce risk factors for disease, before it becomes clinically manifest and appropriate selection of patients for aggressive primary prevention emerges as a crucial issue (Kumar and Cannon, 2009). Both NICE, 2014 and JBS3, 2014 clinical guidelines recommend pharmacological therapy for individuals with high lifetime CVD and with high 10-year CVD risk, in whom lifestyle changes alone are considered insufficient by the physician and person concerned. These therapies include the following: statins are recommended as they are highly effective at reducing CVD events with evidence of benefit to LDL-C levels <2 mmol/L. Statins are safe, with trial evidence showing no effects on non-cardiovascular mortality. Pharmacological treatment for patients with hypertension should follow current NICE guidance (CG127) treatment algorithm.

For secondary prevention all patients post-myocardial infarction NICE, (2014) recommendations include**:** indefinite antiplatelet therapy with low dose aspirin (75–100 mg). In patients with true aspirin intolerance, clopidogrel 75 mg should be considered as an alternative. More potent antiplatelet agents (such as prasugrel or ticagrelor) are recommended as dual antiplatelet therapy in combination with aspirin in patients with acute coronary syndromes. Dual antiplatelet therapy is recommended for up to 12 months post-MI with a minimum of 1 month for patients also receiving a bare metal stent and 6 months for patients also receiving a drug eluting stent. Lipid lowering therapy should include intensive statin therapy which is recommended in all patients following myocardial infarction, in the absence of a contraindication or intolerance, irrespective of initial cholesterol values. Thus statins should be prescribed with a 'lower is better' approach to achieve values of at least <2.5 mmol/L for non-HDL-C (equivalent to <1.8 mmol/L for LDL-C). In addition, β-blockers, ACE inhibitors/ARBs, aldosterone antagonists post-MI are recommended in line with existing NICE guidance.

Adherence to medicines regimens in patients with cardiovascular diseases

Evidence on rates of non-adherence to cardiovascular medicine

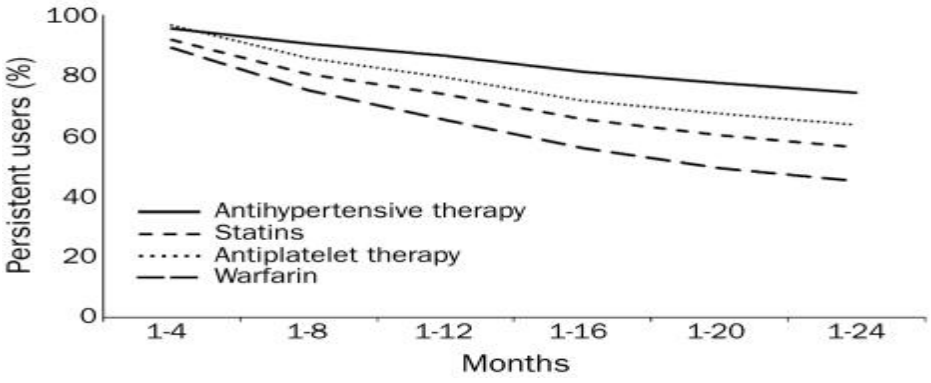
There is considerable evidence that adherence to prescribed medicines for secondary prevention of cardiovascular disease is sub–optimal and that this adversely impacts on clinical outcomes. Despite the importance of secondary prevention, non-adherence rates for myocardial infarction patients ranges from 13-60% for prescribed, evidence-based medicines (Garavalia *et al*, 2009). The main concern is not with compliance alone (and the wastage of medicines) but also the implications of discontinuation and the lack of clinical benefit and possible serious consequences.

Furthermore, studies conducted in the USA and the UK show that approximately one fourth of cardiac patients do not fill their cardiac medications (Jackevicius *et al*, 2002) (Jackevicius *et al*, 2008) (Carter *et al*, 2003). Jackevicius *et al*, 2002 showed that only 40% of patents were still taking statins 2 years after hospitalization for acute coronary syndrome, adherence was even lower for patients taking statins for chronic coronary disease. A second study by Jackevicius *et al*, 2008 showed that among patients discharged, after being hospitalized for acute myocardial infarction, 24% did not fill their cardiac medications by day 7 of discharge.

Studies examining long term adherence to primary and secondary prevention cardiovascular medication show that persistence also remains poor. Both Chapman *et al*, 2005 and Glader *et al*, 2010 give evidence that adherence to cardiovascular medication declines sharply following treatment initiation. Chapman *et al*, 2005 looked at patterns of adherence with concomitant antihypertensive and lipid-lowering therapy and found that the percentage of patients' adherent to both medications declined sharply following treatment initiation, with 44.7% of patients' adherent at 3 months and 35.8% at 12 months, respectively. Glader *et al*, 2010 found that persistence declines with secondary prevention medication in the 24 months after ischemic stroke as shown in figure 1.1.

Figure 1.1 Persistence to secondary prevention medication after ischemic stroke

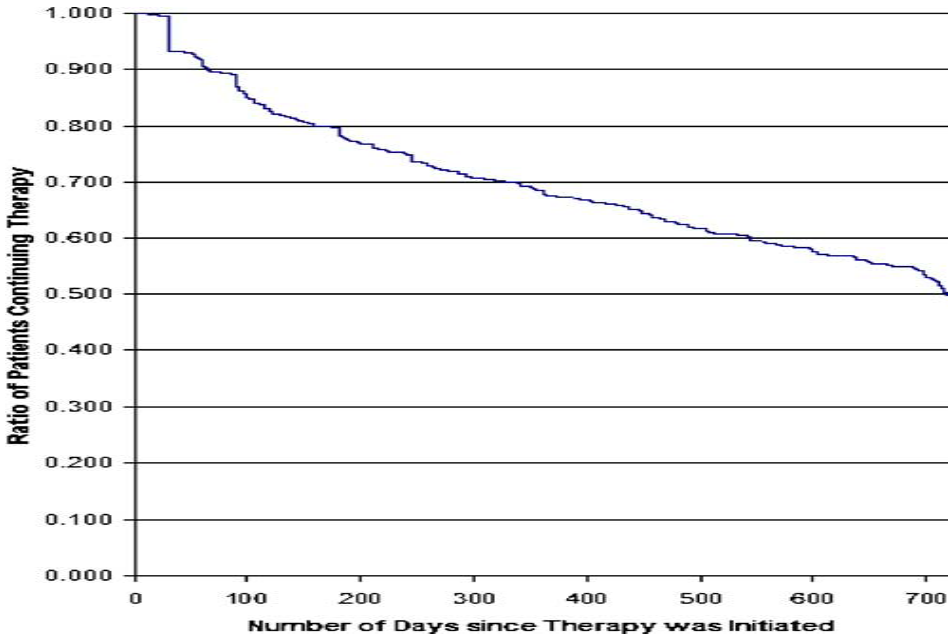
Adapted from Glader EL, Sjölander M, Eriksson M, *et al.* (2010) Persistent use of secondary preventive drugs declines rapidly during the first 2 years after stroke, *Stroke*; 41(2):397-401.



Discontinuation rates of secondary prevention medication after a myocardial infarction in practice follow the pattern shown in the figure 1.2 (Akincigil, *et al*, 2007). Nevertheless, it is important to also take into consideration physicians, stopping or changing medicines during the course of treatment, because this would not be related to non-adherence. Thus after a myocardial infarction NICE, 2014 guidelines recommend that aspirin plus a second antiplatelet drug is usually advised for up to 12 months after a myocardial infarction.

Figure 1.2 Discontinuation rates of secondary prevention medication after a myocardial infarction (Akincigil, *et al*, 2007).

Adapted from Akincigil A, Bowblis JR, Levin C *et al*. (2007) Long-Term Adherence to Evidence Based Secondary Prevention Therapies after Acute Myocardial Infarction, J Gen Intern Med; 23(2):115–21.



In summary, this suggests that many patients initiating primary and secondary therapy may receive no or limited benefit from the medication because of premature discontinuation.

Effect of non-adherence to medication on the outcomes of cardiovascular diseases

Consistent use of secondary prevention medication after a coronary event is associated with lower adjusted mortality and higher survival rates compared with patients who are not compliant (Newby *et al*, 2006). Blackburn *et al*, (2005) investigated the association between cardiovascular morbidity and non adherence to statin therapy in a study involving 1056 patients and found that patients in the adherent group were half as likely to experience a subsequent myocardial infarction as the patients in the non adherent group. A similar finding was reported by McGinnis *et al*, (2009) in a study in which 2201 patients were followed regarding their adherence to statin therapy. McGinnis *et al*, (2009) found that risk of any-cause death was lower among patients who were adherent compared with non adherent patients. In a further study, Gehi *et al*, (2007) followed 1015 outpatients with established coronary heart disease; non adherent participants were more likely than adherent participants to develop cardiovascular events during 3.9 years of follow-up.

Furthermore, medications like aspirin and clopidogrel if stopped early can lead to short term consequences for instance rehospitalisation and even increased risk of death (Garavalia *et al*, 2009). In the Prospective Registry Evaluating Myocardial Infarction Event Recovery (PREMIER) 16% of patients were reported to have ceased their clopidogrel 30 days after their Percutaneous Coronary Intervention procedure (PCI) (Spertus *et al*, 2006). The mortality rate over the next 11 months of those who stopped thienopyridine therapy was 7.5% compared with 0.7% in those still taking clopidogrel 30 days after PCI. This represented a significant increase in risk of event rates (hazard ratio 9.02, 95% CI 1.3 to 60.6) (Spertus *et al*, 2006). Thus, there is considerable evidence of the effect of non-adherence on coronary heart disease outcomes, suggesting that interventions to improve adherence may be effective in improving treatment outcomes, evidence is summarised in the tables 1.2 and 1.3.

Table 1.2 Evidence of suboptimal adherence to secondary prevention medication after a coronary artery disease	
Chodick *et al*, 2008	Evaluated a cohort of 93 866 Israeli patients with CAD who initiated statin treatment between 1998 and 2006. Over the study period, patients took, on average, 59% of their prescribed pills (i.e. PDC 0.59), and greater than 75% of patients discontinued their statins within 2 years of the initial prescription.
Turley *et al*, 2008	Post coronary artery bypass graft (CABG) surgery patients had suboptimal rates of beta-blocker (79%) and ACEI/ARB (61.5%) use.
Newby *et al*, 2006	For the years 1995 to 2002. US researchers analyzed data for medication adherence in 31,750 patients these patients had undergone a cardiac procedure for coronary artery bypass surgery or had more than 50% coronary artery blockage. Nearly half of the CAD patients self reported that they did not consistently take beta blockers, lipid lowering therapy and antiplatelets. In 2002, 83% of patients reported using aspirin, 61% beta blockers, 63% lipid lowering therapy, 54% used aspirin and beta blockers and 39% regularly took all three. Among patients without heart failure 39 % reported ACE inhibitor use.
Ho *et al*, 2006	Among patients with prescriptions for aspirin, statin, and beta-blockers after an acute myocardial infarction 34% stopped at least 1 medication and 12% stopped all 3 medications within one month of hospital discharge.
Insull, 1997	Discontinuation rates of secondary prevention medication in practice range from 50% after 1 year and 85% after 2 years.
Shepherd *et al*, 1995	In the West of Scotland Coronary Prevention Study a quarter of participants were classed as non compliant, defined as taking less than 75% of the medication they were prescribed.
Jackevicius *et al*, 2008	Patients discharged after hospitalization for acute myocardial infarction approximately one fourth of the patients 24% did not fill their cardiac medications by day 7 of discharge.
Jackevicius *et al*, 2002	Only 40% of patents were still taking statin medications 2 years after hospitalization for acute coronary syndrome and adherence was even lower for patients taking statins for chronic coronary disease.

Table 1.3 Studies demonstrating the association between medication adherence and outcomes	
Mc Dermott *et al*, 1997	Non compliance is one of the most important reasons for hospital readmission for CHD and 43% of hospitalized patients are non compliant to their medication. In addition patients who were not compliant with prescribed treatment were twice likely to die as those who were compliant.
Spertus *et al*, 2006	Patients discontinuing clopidogrel within 1 month after hospital discharge for acute myocardial infarction and drug eluting stent placement were significantly more likely to have an adverse outcome, including rehospitalization and mortality, in the subsequent 11 months.
Rasmussen *et al*, 2007	31, 455 elderly Acute Myocardial Infarction survivors between 1999 and 2003 in Ontario. All patients filled a prescription for statins, Beta-blockers or calcium channel blockers. Patient adherence was subdivided into 3 categories high (proportion of days covered, >80%), intermediate (proportion of days covered, 40%-79%), and low (proportion of days covered, <40%) and compared with long-term mortality (median of 2.4 years of follow-up) using multivariable survival models. Among statin users, compared with their high-adherence counterparts, the risk of mortality was greatest for low adherers *P*=.001) and was intermediary for intermediate adherers; *P*=.03). A similar but less pronounced dose-response–type adherence-mortality association was observed for beta blockers. Mortality was not associated with adherence to calcium channel blockers.
Newby *et al*, 2006	Consistent use of medication was associated with lower adjusted mortality and higher survival rates compared with patients who never used them. Patients who were consistent in the use of aspirin showed a 42% reduction in risk of death. Reduction in the risk of death was 37% and 48% for beta blockers and lipid lowering therapy use respectively and 33% reduction when using all three medications.

1.8-Medication-Taking Behaviour-Definitions

A. Definitions

The World Health Organization in 2003 framed a definition for adherence that includes health-related behaviours that extend beyond taking prescribed medications. Examples of these behaviours are seeking medical attention, filling prescriptions, taking medication appropriately and attending follow-up appointments. Different terms are used regarding medication-taking behaviours, including: compliance, adherence and concordance.

Compliance has been defined as 'the extent to which the patient's behaviour matches the prescriber's recommendations.' However, its use is declining as it implies lack of patient involvement; this approach has negative connotations and allows for the interpretation of non-adherence as deviant behaviour (Horne, 2005). In addition, compliance suggests that the patient is passively following the doctor's orders and that the treatment plan is not based on a therapeutic alliance or contract established between the patient and the physician (Osterberg, and Blaschke, 2005).

Adherence has been defined as 'The extent to which the patient's behaviour matches agreed recommendations from the prescriber.' It has been adopted by many as an alternative term to compliance, in an attempt to emphasise that the patient is free to decide whether to adhere to the doctor's recommendations and that failure to do so should not be a reason to blame the patient; adherence develops the definition of compliance by emphasising the need for agreement (Horne, 2005). Thus adherence shifts the balance between professional and patient to suggest there should be agreement between professional and patient about the prescriber's recommendation (NICE, 2009).

The WHO adopted the following definition of adherence to long-term therapy 'The extent to which a person's behaviour – taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider.' (WHO, 2003), adherence, now commonly replaces compliance as a preferred term (Horne, 2005).

Concordance is a term that is used in the United Kingdom. Concordance was first introduced by a joint working group assembled by the Royal Pharmaceutical Society of Great Britain in 1995. The 'concordance' construct recognized the need for patients and health care providers to cooperate in the definition of a mutually agreed treatment programme, acknowledging that patients and providers may have differing views (Virjens *et al*, 2012). Its definition has changed over time from one which focused on the consultation process, in which doctor and patient agree therapeutic decisions that incorporate their respective views, to a wider concept which stretches from prescribing communication to patient support in medicine taking. Concordance is sometimes used, incorrectly, as a synonym for adherence (Horne, 2005). Thus the term concordance has infrequently, and not always appropriately, replaced the terms compliance or adherence.

Compliance and adherence share the property of being quantifiable parameters, which detail when doses are taken and how much drug each dose provides, while concordance implies a certain meeting of the minds/perspectives of carers/caregivers and patients regarding a treatment plan suitable for a course of pharmacotherapy, during which the patients and/or carers/caregivers bear the responsibility for correct administration of the medicine(s) (Virjens *et al*, 2012).

Persistence describes the duration of continuation with therapy (Elliot *et al*, 2008), non persistence referring to patients stopping their medication earlier than the prescriber's recommendation.

Furthermore, medication non-adherence may occur at different points in a patient's decision-making process. It may occur at the start of therapy, if a patient receives the initial prescription but does not fill it (primary non-adherence), or it may occur after therapy has started if the patient fails to follow the instructions or fails to refill the prescription (secondary non-adherence) (Jackevicius et al, 2008).
Adherence will be used in this thesis as a term for medication taking behaviour as concluded by expert panels and consultation groups (Horne, 2005; Virjens *et al*, 2012).

Intentional and unintentional non-adherence

Non-adherence to medications has been identified as intentional or unintentional. Unintentional non-adherence arises from capacity and resource limitations that prevent patients from implementing their decisions to follow treatment recommendations as a consequence of individual restrictions and their environment characteristics (Horne, 2005). Examples of unintentional non-adherence include poor recall or difficulties in understanding the instructions, problems with using the treatment, inability to pay for the treatment, or simply forgetting to take it (NICE, 2009). Intentional non-adherence arises from the beliefs, attitudes and expectations that influence patients' motivation to begin and persist with the treatment regimen (Horne, 2005). Addressing non-adherence is not about getting patients to take more medicines. It starts with an understanding of patients' perspectives of medicines and the reasons why they may not want or are unable to use them (NICE, 2009). It is important to distinguish between these two types of non-adherence because research has shown the underlying causes of these two types of non-adherence are different (Clifford *et al*, 2010).

Understanding the reasons behind non-adherence may be helpful in designing appropriate interventions. Interventions addressing unintentional non-adherence may need to focus on simplifying the regimen, reminding patients to take their medication, and supporting

patients in making the intake of medication part of their daily routine (Hugtenburg *et al,* 2013). On the other hand patients with intentional non-adherence may become doubtful about their medication because of side effects and other disadvantages, such as drug dependency, or reduced long-term efficacy (Hugtenburg *et al,* 2013). In addition, using certain medication can be stigmatizing or remind patients that they are ill. These factors may contribute to a lack of motivation to use the necessary medication. Therefore, interventions such as increasing knowledge about the disease and its treatment and addressing patient concerns or fears about potential side effects may provide solutions for intentional non-adherence (Hugtenburg *et al,* 2013). However, research also indicates that there may be more to unintentional non-adherence than pure forgetfulness, patients reporting intentional versus unintentional non-adherence have been found to be similar to one another in terms of their adherence-related knowledge and motivation (Gadkari and McHorney, 2012). Unintentional non-adherence has also been recently linked to perceived need for medications, medication concerns, and beliefs about treatment efficacy, which suggests that interventions focusing on patients' medication beliefs may be required to address both intentional and unintentional non-adherence (Gadkari and McHorney 2012). Thus the two types of non adherence could be overlapping and there is a need to adapt a patient centred approach that encourages informed adherence (NICE, 2009).

B. Measurements of adherence

The difficulties of valid and reliable measurements have been the focus of much discussion and research. Many different approaches have been taken to the measurement of adherence. There is currently no 'gold standard' measure of adherence (Vik *et al*., 2004; Horne *et al*, 2005). Interpreting studies comparing the performance of various adherence measures is therefore difficult because different studies have used different methods. Each of the available methods has certain flaws which limit the accuracy (Horne *et al*, 2005).

Adherence measures have been distinguished as direct and indirect measurements, each method has advantages and disadvantages (Osterberg, and Blaschke, 2005), (more details can be found in Appendix 4).

Direct methods

Direct methods include observing people taking medication, or the measurement of medicine, metabolites, or biological markers in the blood (Please see Appendix 4). Although objective and accurate, direct adherence measures are often impractical or too expensive (Osterberg, and Blaschke, 2005). Direct measures are considered by some to be more reliable and accurate than indirect measures. However, they are labour-intensive and costly and also if patients are being observed, they might tend to change behaviour and this can give a false impression of adherence (Osterberg, and Blaschke, 2005).

Biological Assays

Biological assays are part of direct methods and measure the concentration of a drug, its metabolites, or tracer compounds in the blood or urine of a patient. These are invasive, costly, patients are aware that they are been tested so maybe more inclined to adhere. Therefore, biological assays are not a good measure of normal adherence patterns. A number of factors can affect the results like physiological differences, food interactions (Vik *et al*, 2004).

Pill Counts

This is often considered as a straightforward approach to the measurement of adherence. Pill counts are a simple method involving counting the number of pills remaining in a container (Williams *et al*, 2012). Pill counts may not provide an accurate reflection of medication taking behaviour and they may be manipulated by people if they are aware that the pills are being counted (e.g., pill dumping). Thus, they do not necessarily mean that medication has been taken at the correct time (Glynn *et al*, 2011).

Pill counts have been described as an "objective" measure of adherence, because they don't rely on subject's self-report (Glynn *et al*, 2011), (Williams *et al*, 2012). Moreover, pill count based adherence measures may provide an estimate of adherence on average over a given period of time. Consecutive days without medication and other variations in the pattern of medication use are not captured by this method (Williams *et al,* 2012). When relying on the patient to bring medication to a scheduled visit or when making a scheduled home visit, there is the possibility that the patient will dispose of surplus pills to avoid the discovery of non-adherence. Further, even in the most well-intentioned of circumstances, it is possible that pills stored elsewhere may inadvertently not be included in the count, leading to an over estimation of adherence (Williams *et al*, 2012).

Electronic Monitoring

There are a number of electronic monitors capable of recording the time of opening bottles, dispensing drops (e.g. eye drops) or activating a canister (e.g. metered dose inhaler for asthma) that can give a measure of adherence (Jimmy and Jose, 2011). Most commonly used, is the Medication Event Monitoring System (MEMS). This is a container that has an electronic chip in the lid that records the time of each opening (Garfield *et al*, 2011). Electronic monitoring methods have greatly advanced in recent years and allow recordings of the timing and frequency of accessing the container. However, they are expensive, and there is no guarantee that opening of the medication container is followed by ingestion of the correct dose. Thus, opening or emptying of containers does not necessarily reflect what the patient has taken. These devices may therefore be considered as measures of variables indicative of adherence rather than absolute measures of medication use (Garfield *et al*, 2011). It could also be argued that placing an electronic cap to measure adherence is an intervention in itself, which will influence medication-taking behaviour (a Hawthorne effect) as people are aware that they are being monitored, rather than provide a measure reflective of normal behaviour (Glynn *et al*, 2011).

Furthermore, MEMS is also not suitable for all formulations and medications. It may be more useful for a single solid dosage medication being delivered and monitored as part of a clinical trial than multiple drug use in routine primary care (Garfield *et al,* 2011). Advantages of MEMS include measurement of adherence in real time, tracking the timing of missed doses, avoidance of error due to recall or memory associated with self-report, evaluating medication dose response and the ability to identify patterns of adherence behaviour that would be difficult to detect with other types of measures (e.g. self-report, pharmacy refill) (Williams *et al,* 2012). Disadvantages associated with electronic monitoring include, in addition to their high cost, the possibility of malfunction, possible interference with routine adherence activities, inability to confirm ingestion of the medication, inconsistent use of the electronic monitoring device, and the need to censor data (Williams *et al,* 2012). Despite these disadvantages electronic monitoring data has been considered the reference standard when validating other measures of adherence (Pearson *et al,* 2007), (Garfield *et al,* 2012).

Pharmacy Records and Prescription Claims

Prescribing data, such as the rate of prescription refills or cessation of refills (discontinuation rate) can often be obtained through pharmacies, but require a closed-pharmacy system to be accurate (Glynn *et al*, 2011). Also, they cannot be regarded as equivalent to measures of the ingestion of medication. Interpretation of pharmacy refill data relies heavily on the assumption that the pharmacy record is complete, comprehensive, exclusive and accurate. So long as these assumptions hold true, pharmacy refill data can be an effective method to measure medication adherence (Williams *et al,* 2012). However, pharmacy refills, whilst possibly a prerequisite for adherence, cannot provide assurances or detail on what medications are taken, and when and how (Williams *et al,* 2012).

Self report adherence measures

In clinical practice there is a need to measure adherence in a cheap and relatively unobtrusive way which can be used routinely (Garfield *et al,* 2011). There is also a need to distinguish between intentional and unintentional non-adherence, which have different underlying causes and therefore require different interventions; self report is the only measure which is able to meet these criteria (Garfield *et al,* 2011). Self report has been considered the method of choice for clinical use (Garfield *et al,* 2011). NICE guidelines have identified that whilst other types of measures are useful for clinical trials of new drugs, self report is an appropriate tool for clinical practice (NICE, 2009). However, patients are known to overestimate their level of adherence (Horne, 2005). Therefore, self report method is often combined with other methods used to achieve a valid measure of adherence. Nevertheless, triangulation of self report adherence measure with other methods of measuring adherence may not be practical for regular clinical use (Garfield *et al,* 2011). In addition, recent reviews have shown that self report has moderate correlation with electronic monitoring, although self reported adherence levels are higher than adherence levels derived from MEMS (Garfield *et al,* 2011).

Self-report measures can be classified into patient-kept diaries, patient interviews and questionnaires. Self-reported adherence measures range from highly specific inquiries concerning the number of medication doses people have taken (or missed) to general estimates of how much or how often medication was taken as prescribed, which may be anchored by a specified period of time (Williams *et al,* 2012). Similarly diverse, the methods for administering these measures include individual structured interviews, computer delivered assessments, paper and pencil measurement, Short Message Service (SMS) text prompts, voice response systems, and web-based data collection (Williams *et al,* 2012).

Patient Estimates of Adherence

Direct questioning of patients to assess adherence can be an effective method. Patients who admit to non adherence have been found to be accurate in their self-assessment. However, patients who claim adherence may be underreporting their non adherence to avoid caregiver disapproval (Vik *et al*. 2004).

Patient diaries and Surveys

Diaries in which patients record details of medicines-taking might provide relevant information but may also be viewed as an intervention which influences their medication-taking behaviours (because the patient is completing the diaries and taking the medication concomitantly) (Fairman *et al*, 2000). Thus, their validity as a measurement tool might be questionable.

A large number of self report measures have been used to measure adherence, few are summarised briefly below (Lam and Fresco, 2015):

Hill-Bone Compliance Scale (Hill-Bone)

As a measure of reviewing patient's medication-taking behaviour and barriers to adherence, Hill-Bone has limited generalizability since it targets patients with antihypertensive medication only. This scale has been suggested as suitable for use in studies specific for hypertension in a predominantly black population (Lam and Fresco, 2015).

Eight-Item Morisky Medication Adherence Scale (MMAS-8)

Morisky *et al.* developed this 8-item MMAS (MMAS-8) in 2008. The first seven items are Yes/No responses while the last item is a 5-point Likert response. The additional items (additional to the MMAS-4) focus on medication-taking behaviours, especially related to underuse, such as forgetfulness, so barriers to adherence can be identified more clearly.

93% sensitivity and 53% specificity were reported while validating in "a sample of low income minority patients treated for hypertension". It is probably the most commonly used self-report measure for adherence to medication (Lam and Fresco, 2015). The Morisky Scale will be discussed further in chapter 4 of this thesis.

The Self-Efficacy for Appropriate Medication Use Scale (SEAMS)

The SEAMS is a 13-item, 3-point Likert-type scale focusing on self-efficacy in chronic disease management while measuring barriers to medication adherence. It may be difficult to carry out at the point of care because of its length. However, this scale has been validated in various chronic conditions. Reliability of this scale was measured by its internal consistency, coefficient alpha reliability at 0.89 and 0.88, on low and high literacy populations, respectively (Lam and Fresco, 2015).

Medication Adherence Report Scale (MARS)

MARS assesses both beliefs and barriers to medication adherence. It consists of 10 questions with a simple scoring to evaluate patient's adherence behaviour, attitude towards medication, and general disease control during the past week. It was designed and first validated for patients with schizophrenia (Lam and Fresco, 2015).

Diagnostic Adherence to Medication Scale (the DAMS)

Garfield *et al,* 2012 developed a theory based adherence scale (the DAMS) and established its content and preliminary construct validity. The DAMS is a relatively new and short self-report measure (consists of 6 questions). The DAMS was developed for routine monitoring of adherence in clinical practice. The authors concluded that it was acceptable to patients taking single or multiple medication and valid when tested against other adherence measures. Adherence ratings of the DAMS were significantly associated with levels of self reported adherence on all other measures Spearman Rho 0.348-0.719, ($p < 0.01$) (Garfield *et al,* 2012).

Self report measures have the advantage of being simple and inexpensive, quick and easy to administer, and able to identify those who are non adherent (as it is likely those reporting non-adherence are being truthful). Self-reporting can also gather social, situational and behavioural factors including revealing patterns of medicine use and what leads to non-compliance (NICE, 2009). In addition, to the problem of self-report over-estimating adherence, other disadvantages include inaccurate self-reporting as a consequence of poor recall, social desirability bias and errors in self-observation. The timeframe of the adherence recollection may also affect the accuracy of recall. Wording of questions, how this is expressed, and the skills of the interviewer may influence the accuracy of the response. However, being non-judgmental, e,g, by giving a preamble before adherence questions, and asking about specific behaviours may improve the validity of responses (NICE, 2009).

In conclusion, a perfect measure of adherence does not exist and therefore, when choosing a suitable measure researchers balance reliability, practicality and cost effectiveness of the chosen method; in addition a multi measure approach could also be a current solution (Lam and Fresco, 2015).

Reasons for non- adherence to cardiac medication

The World Health Organization (2003) categorized potential reasons for medication non adherence into 5 broad groupings listed in the table below, these factors are summarised and described below:

Table 1.4 Reasons for medication non adherence cited in (Ho *et al,* 2009) and cited in (WHO, 2003).

Table. Reasons for Medication Nonadherence

Categories of Nonadherence	Examples
Health system	Poor quality of provider-patient relationship; poor communication; lack of access to healthcare; lack of continuity of care
Condition	Asymptomatic chronic disease (lack of physical cues); mental health disorders (eg, depression)
Patient	Physical impairments (eg, vision problems or impaired dexterity); cognitive impairment; psychological/behavioral; younger age; nonwhite race
Therapy	Complexity of regimen; side effects
Socioeconomic	Low literacy; higher medication costs; poor social support

Health system factors

These are structural or operational factors of health care system that may create barriers to adherence. These may include, poorly developed health services, inadequate or non-existent reimbursement by health insurance plans, poor medication distribution systems, lack of knowledge and training for health care providers on managing chronic diseases, overworked health care providers, lack of incentives and feedback on performance, short consultations, weak capacity of the system to educate patients and provide follow-up, inability to establish community support and self-management capacity, and lack of knowledge on adherence and of effective interventions for improving it (WHO, 2003).

Condition-related factors

Condition-related factors reflect particular illness-related demands faced by the patient. Some strong determinants of adherence are those related to the severity of symptoms, level of disability (physical, psychological, social and vocational), rate of progression and severity of the disease, and the availability of effective treatments (WHO, 2003). Their impact depends on how they influence patients' risk perception, the importance of following treatment, and the priority placed on adherence. Co-morbidities, such as depression (in diabetes or HIV/AIDS), and drug and alcohol abuse, are important modifiers of adherence behaviour (WHO, 2003).

Patient-related factors

Patient-related factors represent the resources, knowledge, attitudes, beliefs, perceptions and expectations of the patient, patients' knowledge and beliefs about their illness, motivation to manage it, confidence (self-efficacy) in their ability to engage in illness-management behaviours, and expectations regarding the outcome of treatment (WHO, 2003).

Therapy-related factors

There are many therapy-related factors that affect adherence. Most notable are those related to the complexity of the medical regimen, duration of treatment, previous treatment failures, frequent changes in treatment, the immediacy of beneficial effects, side-effects, and the availability of medical support to deal with them (WHO, 2003).

Socioeconomic factors

Socioeconomic factors that may contribute, include poor socioeconomic status, poverty, illiteracy, low level of education, unemployment, lack of effective social support networks, unstable living conditions, long distance from treatment centre, high cost of transport, high cost of medication, changing

environmental situations, culture and lay beliefs about illness and treatment, and family dysfunction (WHO, 2003).

Many studies have examined factors associated with non-adherence and discontinuation of medication for cardiovascular disease (Sonali *et al*, 2005) (Gazmararian *et al*, 2006) and have reported association of poorer existence of adherence with the following factors: age, gender (female), marital status (unmarried), low education and health literacy. Other studies also investigating barriers to medication adherence in CVD have reported factors such as side effects of the cardiac medication (Garavalia *et al*, 2009), (Fried *et al*, 2011), regimen complexity (Melloni *et al*, 2009), economic factors and payer policies in which patients were unable to afford expensive cardiac medicines (Doshi *et al*, 2009). Clinicians should be aware that reasons may vary between patients (Garavalia *et al*, 2009) and that adherence interventions should be tailored to the needs of the patient in order to achieve maximum impact (WHO, 2003).

1.9- Strategies to tackle non adherence

Strategies and interventions to tackle non-adherence to cardiac medication are numerous and can be related to areas as shown previously of patient, healthcare practitioner and health system. In this thesis three strategies will be studied these include pharmacy care, communication between health providers that could aim to tackle both factors of healthcare practitioner and health system and behavioural interventions that could aim to address patient related factors such as knowledge and motivation. These three strategies will be examined with the potential of been utilised in a study to improve adherence to cardiovascular medication. The following sections will show evidence of effectiveness of these three strategies.

1-Pharmacy care

Effects of hospital pharmacist interventions on outcomes of cardiovascular disease

The addition of a pharmacist to a multidisciplinary team to improve outcomes of cardiovascular diseases has been addressed in a number of studies and in several diseases including dyslipidemia, heart failure and hypertension. Traywick *et al*, 2003 in a retrospective cohort study examined the effect of the addition of a pharmacist to the interdisciplinary medical team for management of dyslipidaemia. There were two groups; the pharmacist group was associated with a significant reduction in mean low-density lipoprotein (LDL, 18.5%) compared to the cohort that did not have a pharmacist as the primary manager of dyslipidemia (LDL, 6.5%, P=0.049). Moreover, Gattis *et al*, (1999) developed an intervention evaluated in a randomized trial, to assess the role of a pharmacist as a member of the multidisciplinary heart failure team, in this trial pharmacists optimized ACE inhibitors doses, the study found that all cause mortality and heart failure events were significantly lower in the pharmacist group compared with the control group (4 vs 16; P = .005). Bogden *et al*, 1998 in a randomised control trial randomised Hawaiian hypertensive patients, who failed to meet the national standard blood pressure goals into an intervention group that had a pharmacist as part of the team and a control group with no pharmacist. The percentages of patients achieving national goals in the intervention and control arms were 55% and 20% respectively (p <0.001).

Effects of community pharmacist interventions on outcomes of cardiovascular disease

There are presently approaching 12,000 community pharmacies in England and there are around 30,000 community pharmacists (Colin-Thome *et al*, 2016). Pharmacists are trained in therapeutics and are trained to deal with patients. They are skilled to identify and address patients' problems with medicines including adherence (Holland *et al*, 2007). Furthermore, the role of community pharmacists within the UK is changing to include supporting patients in managing medicines to achieve optimal clinical outcomes (Jaffray *et al*, 2007). Therefore they are a resource to support patients who have a chronic disease in regards to their medication.

A systematic review (Watson *et al*, 1998) of community pharmacist interventions in CHD provides; evidence of benefits of pharmacists' interventions in improvements in blood pressure, cholesterol, anticoagulation control, and smoking cessation rates. Several randomised control trials conducted in the UK (Goodyer and Miskelly, 1992, Blenkinsopp *et al*, 2000, Jaffray *et al*, 2007, Holland *et al*, 2007) have evaluated the role of community pharmacists in improving outcomes of cardiovascular diseases and increasing adherence for patients with hypertension, heart failure and coronary heart diseases. In addition, local initiatives such as the Community Pharmacy Future (CPF) project collaboration between Boots UK, The Co-operative Pharmacy, Lloyds Pharmacy and Rowlands Pharmacy have highlighted the potential value of extended pharmaceutical care (Colin-Thome *et al*, 2016), in which community pharmacists screened and identified patients with undiagnosed chronic obstructive pulmonary disease. Pharmacists in this project (CPF) made significant improvements to medicines adherence and quality of life for older patients on multiple medicines, leading to better medicines optimisation. However, further research in the UK is needed to evaluate and promote the role of community pharmacists as new extended roles are proposed, all with their challenges. Pharmacy care as a strategy to tackle non adherence to cardiovascular medication, will be researched in detail in a systematic review discussed in chapter two of this thesis.

2-Communication of health care professionals across the primary-secondary care interface

Evidence has shown that when patients move between care providers the risk of miscommunication between health providers and unintended changes to medicines remain a significant problem. In 2010 a UK audit across 50 acute trusts involving over 8600 patients found that when medicines were checked after admission most patients had at least one omitted drug or wrong dose (Dodds, 2010).

Earlier UK studies suggest that between 30 and 70% of patients have either an error or an unintentional change to their medicines when their care is transferred (NPSA, 2007). More recent studies reveal that this problem also exists in other countries. For example a study in Australia (Belleli *et al,* 2013) showed that only 55% of the discharge summaries of patients are received by GPs before the first post-discharge visit. Moreover, a review in USA (Kripalani *et al,* 2007) involving 73 studies showed that direct communication between hospital and primary care physicians occurs infrequently (3%-20%) and the availability of a discharge summary at the first post discharge visit is low (12%-34%) and remains poor at 4 weeks (51%-77%). Thus deficits in communication and information transfer at hospital discharge are common and may adversely affect patient care. In 2012 the Royal Pharmaceutical Society (RPS) published a report "Keeping patients safe when they transfer between care providers" the report was based on an early adopter programme encouraging organizations to adapt a multidisciplinary approach. The programme aimed to improve the transfer of information about medicines and included a series of workshops involving clinicians, front-line staff, practitioners, community pharmacists, patients and managers.

Some of the core recommendations of the RPS report include: (1) IT systems in hospitals and general practice should ensure that their systems are able to effectively transfer the recommended core content of records for medicines (2) all community pharmacies should have an NHS.net website address to enable secure communications between secondary and primary care (3) the most effective ways of signposting patients treated in secondary care to the post discharge Medicines Use Review Service and New Medicine Service offered by community pharmacists should be shared nationally to ensure that patients are able to optimise their outcomes from medicines. There are examples of good communication practices such as a recent project in 2014 "PharmOutcome" which is an example of a referral technology developed between hospital and community pharmacies. This project endorsed by the Local Pharmaceutical Committee in North East and North

Cumbria is an Academic Health Science Network project. This involves a web-based application and a secure method of data transfer to all community pharmacies in the area. In addition, there are numerous pilots of collaborations between hospital and primary care to facilitate and improve medicines management over the interface and these are taking place in several areas around the UK (The Pharmaceutical Journal, 2004). Therefore, it is important to establish a link between hospital pharmacists and community pharmacists as part of a continuation of patient care; because miscommunications across the primary/secondary care interface have been numerous and many studies as mentioned earlier have shown how this has had a negative impact on patient care. Thus in order to work efficiently; community pharmacies need to have links with pharmacies in secondary and tertiary care and also with other members of the primary health care team (www.dhsspsni.gov.uk/makingitbetter04_sect3.pdf).

Communication of health providers with patients

Good communication between healthcare professionals and patients is needed for involvement of patients in decisions about medicines and for supporting adherence (NICE, 2009). NICE, 2009 guidelines on adherence provide recommendations to healthcare professionals, to help patients adhere to their medicines. These involve urging healthcare professionals to adapt their consultation style to the needs of patients, establish effective ways of communication with each patient individually and encourage patients to be involved and ask questions about their conditions. Over the years, much has been published in the literature on this important topic (Fong *et al*, 2010). In one study Garavalia *et al*, (2011) the researchers recognised traditional views of adherence where the patient is viewed as a passive recipient of instructions rather than an active decision maker and developed a tool for communication between cardiac patients and clinicians (Medicine Discussion Questions- MedDQ). Garavalia *et al*, 2011 suggested that this tool can be easily used by community pharmacists to help identify patients at risk of non-

adherence to cardiac medication. However, the authors reported that more research is needed before expanding the MedDQ's application in clinical settings.

3- Behavioural interventions to improve adherence

Evidence from meta-analyses of different interventions (including behavioural interventions) to improve adherence

Improving adherence to cardiac medication in clinical practice remains modest and challenging (Ho *et al,* 2009). This statement is based on evidence from numerous meta-analyses. A meta–analysis by Schroeder, 2005 determined the effectiveness of interventions aiming to increase adherence to blood pressure lowering medication. Thirty eight studies testing 58 different adherence interventions on 15,519 patients were included in the meta-analysis. The interventions included the following; education of caregivers and patients (e.g. health education) in six studies but education alone seemed unsuccessful, only one of six studies improved adherence. Simplification of dosage regimens was used in nine studies and seven of these trials showed improvement in adherence with a relative small increase in adherence of 8% to 19%. Complex health and organizational interventions, including interventions in combination, increased adherence in eight of the eighteen studies with an increase of 5%-41%. Motivational strategies including patient motivation and support were successful in 10 out of 24 of the studies reviewed, with an increase in adherence up to 23% (Schroeder, 2005). The meta-analysis concluded that simplification of dosing regimens appeared to be the most promising intervention to increase adherence to blood pressure–lowering medication and that the evidence of the effect of motivational and more complex interventions was mixed and inconclusive (Schroeder, 2005).

A second meta-analysis by Peterson (2003), evaluated 484 articles and studied multiple interventions, including; behavioural, educational, combined interventions and interventions including mail reminders, this analysis concluded that; the data from these studies are not homogeneous hence conclusions were difficult to be derived. The meta-analysis revealed an increase of 4-11 % in adherence and concluded that no single strategy appeared to be best.

Evidence from meta-analyses of behavioural interventions to improve adherence

Despite the challenges to improve adherence reported above, there is strong evidence that behavioural and motivational strategies could be effective after all (Roter *et al,* 1998), (Easthall *et al,* 2013). Older evidence such as a meta-analysis (Roter *et al,* 1998), of adherence-enhancing interventions demonstrated that comprehensive interventions, combining cognitive, behavioural, and affective motivational components, were more effective than single-focused interventions including information alone. In addition, more recent evidence from meta-analysis of 26 RCTs (Easthall *et al,* 2013) supported the use of motivational interviewing and other cognitive-based behaviour change techniques as interventions to improve medication adherence. Much of health care today involves helping patients manage conditions whose outcomes can be greatly influenced by behaviour change. Patient related factors are a determinant of adherence behaviour as discussed in earlier sections of this chapter, the patient's perceived value of adhering, with the patient's intrinsic motivation could be targeted along with providing education to increase knowledge of the medications (WHO, 2003). Motivational strategies and behavioural support are becoming increasingly more common to use in healthcare settings to promote behavioural change. Therefore, a behavioural approach to enhance adherence is selected to be investigated with a focus on motivational interviewing.

The coming sections will provide a discussion of the theory of motivational interviewing, followed by evidence of its application and use to improve adherence, by different healthcare professionals including pharmacists:

Motivational interviewing

Motivational interviewing refers to a counselling approach in part developed by clinical psychologists Professor William R Miller and Professor Stephen Rollnick. The concept of motivational interviewing evolved from experience in the treatment of problem drinkers and was first described by Miller (1983) in an article published in Behavioural Psychotherapy. These fundamental concepts and approaches were later elaborated by Miller and Rollnick (1991) in a more detailed description of clinical procedures (Miller *et al,* 1991). In 2004 Miller further described motivational interviews as "a way of being with people which is also directive in seeking to move the person toward change by selectively evoking and strengthening the patient's own reasons for change". Motivational interviewing is a client-centred, directive style of counselling. Clinical trials have established motivational interviews as an efficacious method for facilitating behaviour change as well as increasing adherence to treatment. This method is intended for use particularly when patient motivation and adherence are important for treatment to be effective (Bisono *et al,* 2006).

Numerous studies have shown that motivational interviewing has been successfully used to improve adherence to medication in diseases such as chronic illnesses like diabetes, psychiatric disorders, HIV and asthma (Smith *et al,* 1997), (Kemp *et al,* 1998), (Daley *et al,* 1998), (Dilorio *et al,* 2003), (Rosen *et al,* 2002), (Schmaling *et al,* 2001) (Miller, 2004). Moreover, research has shown that even one session of motivational interviewing at early stages of treatment can improve adherence and outcomes of many diseases (Miller, 2000). Regarding time, the application of such techniques to practice requires little additional time and can be very effective.

A skilled provider can use motivational interviewing for 5–10 minutes per session per patient and achieve desirable outcomes (Possidente *et al*, 2006). Motivational interviewing is based on four key principles (Bisono *et al*, 2006), these principles are outlined in figure 1.3 and then further described below;

Figure 1.3 Description of Motivational Interviewing Principles (Bisono *et al*, 2006)

Adapted from Bisono A.M, Manuel J K, Forcehimes A.A, (2006) Promoting Treatment Adherence Through Motivational Interviewing05-O'Donohue-(V-5).qxd 6/9/2006 10:39 AM Page 71.

MI Principle	*Brief Description*
Express empathy	Actively listen to the patient and understand his or her perspective
Develop discrepancy	Develop a discrepancy between the patient's goals and current behavior Reflect the patient's ambivalence about change Patient should give reasons or arguments for change
Roll with resistance	Reflect resistance from the patient Arguing with the patient for change is counterproductive
Support self-efficacy	Enhance the patient's confidence to change The patient should initiate change in behavior and the practitioner should support the patient's ability to initiate change

1. Express empathy: expressing empathy involves actively listening to the patient and conveying an understanding of the patient's perspective, without judging, criticizing, or blaming. In motivational interviewing, ambivalence about change is regarded as normal and a part of the change process; therefore empathic listening is used to understand and accurately reflect this ambivalence (Miller, 2004), (Bisono *et al*, 2006).

2. Develop discrepancy: a goal in motivational interviewing is for patients to see a discrepancy between their personal goals and their present behaviour. The objective is for the practitioner to direct the discussion in such a way that the patients perceive this discrepancy and the reasons to change their behaviour without pressure from the practitioner (Bisono *et al*, 2006).

3. Roll with resistance: avoiding pushing against resistance to change is a third principle. Rather than arguing with a patient who is resistant to change, practitioners roll with this resistance. Arguing in favour of a certain position with the patient, for instance, arguing to persuade patients to take medications will likely result in defensiveness on his or her part, a decreased desire to take the medication, and lower medication compliance. Practitioners can roll with resistance by reflecting or rephrasing the patient's arguments against change (Bisono *et al*, 2006).

4. Support self-efficacy: self-efficacy, a person's confidence in his or her ability to achieve a specific goal, is an important predictor of a successful treatment outcome. If a practitioner believes that the patient is able to change his or her behaviour and expresses this support, the patient may feel empowered by the idea that change is possible (Miller, 2004), (Bisono *et al*, 2006). Motivational interviewing has been contrasted with traditional pharmacist consultations as demonstrated in the figure 1.4 below:

Figure 1.4 Comparison of Motivational Interviewing with a traditional pharmacist consultation –Possidente *et al*, 2005.

Adapted from Possidente C.J, Bucci K. K and Mcclain W.J (2005) Motivational interviewing: A tool to improve medication adherence? *Am J Health-Syst Pharm*.; 2005; 62:1311-4.	
Traditional pharmacist consultation	Motivational interviewing
Practitioner is an expert and assumes that the patient needs more knowledge, provides advice and anticipates that patient will follow the instructions.	A partnership is developed between practitioner and patient, to reach an informed decision. Patient decides own care.
Information is given to patient by practitioner.	To develop discrepancy practitioner provides patient with information.
Practitioner dictates healthcare behaviour.	Behaviour is negotiated between practitioner and patient to reach an agreement.
The aim is to motivate the patient.	The aim is to elicit commitment to change behaviour.
Practitioner convinces patient to change behaviour.	Practitioner understands, in addition accepts patient's behaviour.
Practitioner expects respect.	Practitioner must earn respect.
Practitioner saves patient.	Patient saves self.

Evidence of use of motivational interviewing in cardiovascular diseases by healthcare professionals other than pharmacists

Research suggests that it is possible to train healthcare professionals to offer motivational interviewing (The Health Foundation, 2011) the section below shows evidence of motivational interviewing delivered by healthcare professionals other than pharmacists to improve adherence to medications in cardiovascular disease:

A review in 2011 by Thompson *et al*, examined motivational interviewing delivered by nurses, as a method for improving modifiable coronary heart disease risk factors. The review included one systematic review, three literature reviews of motivational interviewing, four meta-analyses and five primary studies of motivational interviewing pertaining to cardiovascular health. This review suggested with strong evidence that motivational interviewing is an effective behavioural approach and that it focuses on eliciting the individual's own intrinsic motivation for change of behaviour that offers a promise in improving cardiovascular health status.

Randomised control trials such as Hardcastle *et al*, 2013 evaluated, in a primary –care setting, the effectiveness of a six-month low-intensity motivational interviewing intervention in maintaining reductions in CVD risk factors at 12 months post-intervention. This included five face-to-face motivational interviewing session delivered (by a physical activity specialist and a registered dietician) to 203 patients, compared to 132 patients in the control group who received standard information. The intervention included patient-centred, tailored counselling sessions which incorporated principles and strategies from motivational interviewing. Consistent with the underpinning 'spirit' of motivational interviewing, personal motives to change cardiovascular risk factors were identified by the patient and not imposed by the practitioner. Outcome measures included; risk factors for cardiovascular disease; body mass index, bodyweight, blood pressure, cholesterol and physical activity.

The results revealed significant differences between the two groups for cholesterol and walking. Obese and hypercholesterolemic patients exhibited significant improvements in body mass index and cholesterol respectively. However, post-intervention improvements in other health-related outcomes including blood pressure and weight were not maintained. Based on these findings, the study recommended that future interventions should be conducted in a primary care setting to target patients with high risk of CVD. Training on motivational interviewing in Hardcastle *et al,* 2013 included two 4 hours training sessions and the consultations were audio-recorded. Another recent RCT included a USA study Palacio *et al,* (2015) in ethnic minorities' patients after a coronary stent placement, 452 patients were randomised to receive either four motivational interviewing telephone calls over a 12 month period or a one-time mailed DVD video containing educational information on antiplatelets medication. The consultation was delivered by nurses trained on motivational interviewing in a 3 day workshop. The intervention aimed to elicit individual values, preferences, arguments for change, and reasons for past failures and to empower patients to resolve ambivalence and develop a behaviour modification plan. The nurses succeeded to establish rapport with patients, and used open-ended questions. The results showed statistically significant results on adherence to antiplatelet therapy; measured by both self report Morisky scale and by prescription refills ($P = 0.01$).

Evidence of use of motivational interviewing in cardiovascular diseases by pharmacists

For motivational interviewing in CVDs delivered by pharmacists, only four studies were found, it is worth to mention that these studies were not published before the design of this pilot study. Three trials were published in scientific journals (Binaso *et al,* 2012), (Hedegaard *et al,* 2014), (Pringle *et al,* 2014) and one trial (still recruiting patients) was published on ClinicalTrials.gov (NCT02102503).

These studies were conducted in countries other than the UK and they implemented varying approaches on using motivational interviewing including consultation timings and modes of delivery. Two involved community pharmacists delivering the intervention in a community pharmacy setting (Binaso *et al,* 2012), (Pringle *et al,* 2014) and two employed hospital pharmacists in a hospital clinic setting (Hedegaard *et al,* 2014), (NCT02102503). Three of these studies are RCTs (Binaso *et al,* 2012), (Hedegaard *et al,* 2014), (NCT02102503) and one is a quasi-experimental (Pringle *et al,* 2014). These studies are summarised in the following section:

Binaso *et al,* 2012 in an RCT recruited 10 community pharmacy sites across the United States and enrolled 216 patients with diabetes. During a 6 month period pharmacists delivered a behavioural intervention to improve patient adherence to diabetes medication therapy. The intervention consisted of structured communication sessions using motivational interviewing techniques to facilitate discussions with patients; in a quick, simple, interactive, and patient-centred way. The interventions were developed to be easily incorporated into community pharmacy workflow. Patients in the intervention group showed a 6% increase in adherence compared with previous 180 days pre-intervention and a 28% increase in adherence compared with control group.

In Denmark; Hedegaard *et al,* 2014 conducted an intervention that focused on pharmacists' medication review and a motivational interviewing consultation. This study included 211 patients randomised after a stroke/TIA. The intervention was divided into a 30-minutes face-to-face patient interview, to support adherence and lifestyle changes and 3 follow-up telephone calls that lasted for 6 months. The aim of the interview was to help the patients' identify goals in relation to their medication/disease and to facilitate behaviour change by exploring ambivalence and by mobilizing the patients' intrinsic values for behaviour change.

To assist the pharmacist in adhering to a standardized approach, an interview guide was developed. The primary outcome was adherence, measured by prescription refills. Results showed that despite patients been satisfied with the service and reported increased knowledge about the medications; no statistically significant differences were found for adherence and persistence to specific thrombopreventive agents. The authors attribute the absence of an intervention effect, to the unintentional use of some elements of the intervention in the control group (i.e. contamination).

A large-scale community pharmacy study was conducted in Pennsylvania –USA (Pringle *et al*, 2014). The design of the study was quasi-experimental in which the control group received standard care from a community pharmacist which comprised information on medication during refills, whilst the intervention group additionally were offered a brief screen that indicates a patient risk of non-adherence, followed by a pharmacist-led brief intervention provided to patients at elevated risk. The brief interventions were pharmacist-led; two-to-five-minute conversations using motivational interviewing principles with a focus on exploring and resolving a patient's ambivalence and centred on motivational processes within the individual that facilitated change. This study involved 283 pharmacists in the intervention group delivering the brief intervention to 29,042 patients with chronic diseases compared to 295 control group pharmacists and 30,454 patients. The intervention significantly improved medication adherence for all classes of medication under study, ranging from 4.8% difference in adherence for oral diabetes medicine to 3.1% for beta blockers measured by prescription refills.

In Pringle *et al,* (2014) the authors reported that the project was implemented under real-world conditions, with very limited extra funding to community pharmacies. Furthermore, the brief intervention was stably integrated into the standard workflow process without affecting the normal pharmacy operation or requiring additional staffing. In this large study pharmacists' training and also assessment of proficiency of the skills were mentioned. However, the study was not a randomised control trial, where measures such a randomisation, concealment and blinding were employed. This can raise concerns with internal validity and also the possibility of convincingly demonstrating a causal link between the intervention and observed outcomes. Finally, a recently commenced Swedish randomised control trial registered on ClinicalTrials.gov (NCT02102503), is investigating if an intervention can improve patients' medication adherence. The intervention will involve a medication review and a motivational interviewing counselling session, delivered by hospital pharmacists, at three months post-discharge and a follow-up phone call two weeks later for patients on secondary prevention medication after a myocardial infarction. The primary outcome will include targets of LDL-C and secondary outcomes are adherence to secondary prevention medication and blood pressure control. The trial, currently recruiting, aims to recruit 585 patients and is estimated to be completed in 2018. The authors were contacted by the PhD student (researcher) for preliminary results, but the authors reported that no results are available.

In conclusion, from the evidence described above, there is evidence that motivational interviewing interventions can be effectively delivered by pharmacists, to improve adherence to medication, in the cardiovascular population. However, the evidence is still limited. Therefore, there is a need for multi-centred randomised controlled trials that could provide conclusive evidence about the impact of motivational interviewing on adherence to cardiovascular medications across different settings, ethnicity, age and socio- demographic populations.

End of Chapter One

Overview of the thesis

1- Background literature on cardiovascular diseases and the importance of adherence to medication to improve outcomes, this was reviewed in chapter one.

2- Examine previous evidence and review literature to identify trials examining pharmacy services with an aim to improve adherence and clinical outcomes to cardiovascular diseases. This was by conducting a systematic literature review in chapter two.

3- Review the evidence to identify pharmacy services and pharmacy roles in the UK. To be able to design an intervention, which can be incorporated into community pharmacy this was studied in chapter three.

4- Employ conclusions from previous and existing evidence of pharmacy services to design a pilot feasibility study that can be incorporated into UK community pharmacy services. This was designed in chapter four.

5- Chapters five and six will show results of the feasibility study and chapter seven will include a discussion of the results.

Chapter Two

Pharmacy Care and Adherence to Primary and Secondary Prevention Cardiovascular Medication- A systematic review of studies

2.1-Introduction

As discussed in chapter 1, adherence has been defined as the 'active, voluntary, and collaborative involvement of the patient in a mutually acceptable course of behaviour to produce a therapeutic result' (Ho *et al*, 2009). Non-adherence to medications has been documented to occur in >60% of patients with cardiovascular disease (Baroletti *et al*, 2010). Primary non adherence (not initially filling the prescription) leads to a significant increase in 1-year mortality after hospitalization for myocardial infarction (Jackevicius *et al*, 2008). Secondary non-adherence (failure to follow the instructions or to refill the prescription) has been shown to increase mortality, hospitalisations and costs (Baroletti *et al*, 2010). Therefore, it is crucial to promote adherence to improve outcomes in these groups of patients. Evidence-based data have demonstrated that pharmacists deliver clinical services that improve cost effective quality of care in patients with cardiovascular diseases (Giberson *et al*, 2013). It is estimated that poor adherence costs US$100 billion annually in the USA (Vermeire *et al*, 2005) and the cost of unwanted medications exceeds £100 million annually in the UK (Clifford *et al*, 2010).

Pharmacists are believed to have an increasingly important role in improving adherence. This role can be achieved through services in hospitals (example, medicines reconciliation and monitoring) and in the community (in the UK: Medication Usage Reviews and the New Medicine Service; in the USA: Medication Therapy Management (MTM); in Australia and Canada: MedsCheck program). Moreover, pharmacists have reduced healthcare costs by minimizing adverse clinical events (hospitalisations, emergency room visits, etc) and reduced outpatient visits (Giberson *et al*, 2013). Advanced patient care services, delivered by pharmacists, decrease drug-related morbidity and mortality (Giberson *et al*, 2013). Therefore, it is accepted that pharmacists are well placed to support patients with their medication use. This review aimed to explore existing evidence on if and how healthcare delivery could be improved through the use of pharmacist-delivered patient care with a focus on cardiovascular diseases.

Research question: can pharmacy care improve adherence to primary and secondary cardiovascular medication?

2.2-Aim and Objectives

To determine if pharmacy service intervention can lead to enhanced adherence to primary and secondary cardiovascular medication and improve outcomes of cardiovascular diseases.

- To establish if there is an effect of pharmacy service intervention, on improving adherence to medications and outcomes of cardiovascular diseases.
- To identify types of interventions found to be effective in clinical trials in improving adherence to cardiovascular medication that could be implemented in practice.

2.3-Materials and Methods

Search strategy and data resources

A systematic search of articles published in peer reviewed healthcare-related journals was performed. The literature was systematically searched in order to identify articles describing and evaluating pharmacist delivered interventions to improve outcomes and adherence measures to cardiovascular medication. Data bases Pubmed central UK, Pubmed, Cochrane Library, CINAHL, PsycINFO, EMBASE, International Pharmaceutical Abstracts and Google Scholar were searched for the period from 01/01/1990 to 19/11/2013 (please refer to Figure 2.1- Study selection chart below). The review commenced with three main key words: pharmacy care, adherence and cardiovascular disease. These were included in the databases searched, first without search restriction and second with search restrictions to randomised control trials, the specified period and English language.

The following key words were used (pharmacy care, adherence, cardiovascular disease or diseases), (pharmacy care, compliance, cardiovascular disease), (pharmaceutical care, adherence, cardiovascular disease), (pharmacists, cardiac disease, adherence), (adherence, pharmacists, cardiovascular disease) and (adherence, pharmacist interventions, cardiovascular disease). In addition, search terms related to the type of diseases (adherence, pharmacists, hypertension or hyperlipidemia, or diabetes, or coronary heart disease, or heart failure). Following this search the other key words were generated from MeSH (medical subject heading) terms in PubMed and term mapping database EMBASE. Key words not listed as MeSH or Map Terms were searched as phrases using the free text search mode. A further list of search terms was generated by referring to a key review, Cutrona *et al*, 2010, which studied modes of delivery for interventions to improve cardiovascular medication adherence. The reference list of relevant papers was also searched in order to identify any additional studies. Duplicate articles were removed if they were found in the different databases. Two articles published study protocols, therefore the authors were contacted for the results.

Selection criteria

The articles were selected through screening of titles and abstracts. The criteria for relevant studies were: randomised control trials; interventions aiming to enhance adherence to cardiovascular medications; trials evaluating clinical outcomes of cardiovascular diseases in which adherence was the secondary outcome; studies delivered in hospital or community settings and studies in English language.

Data extraction

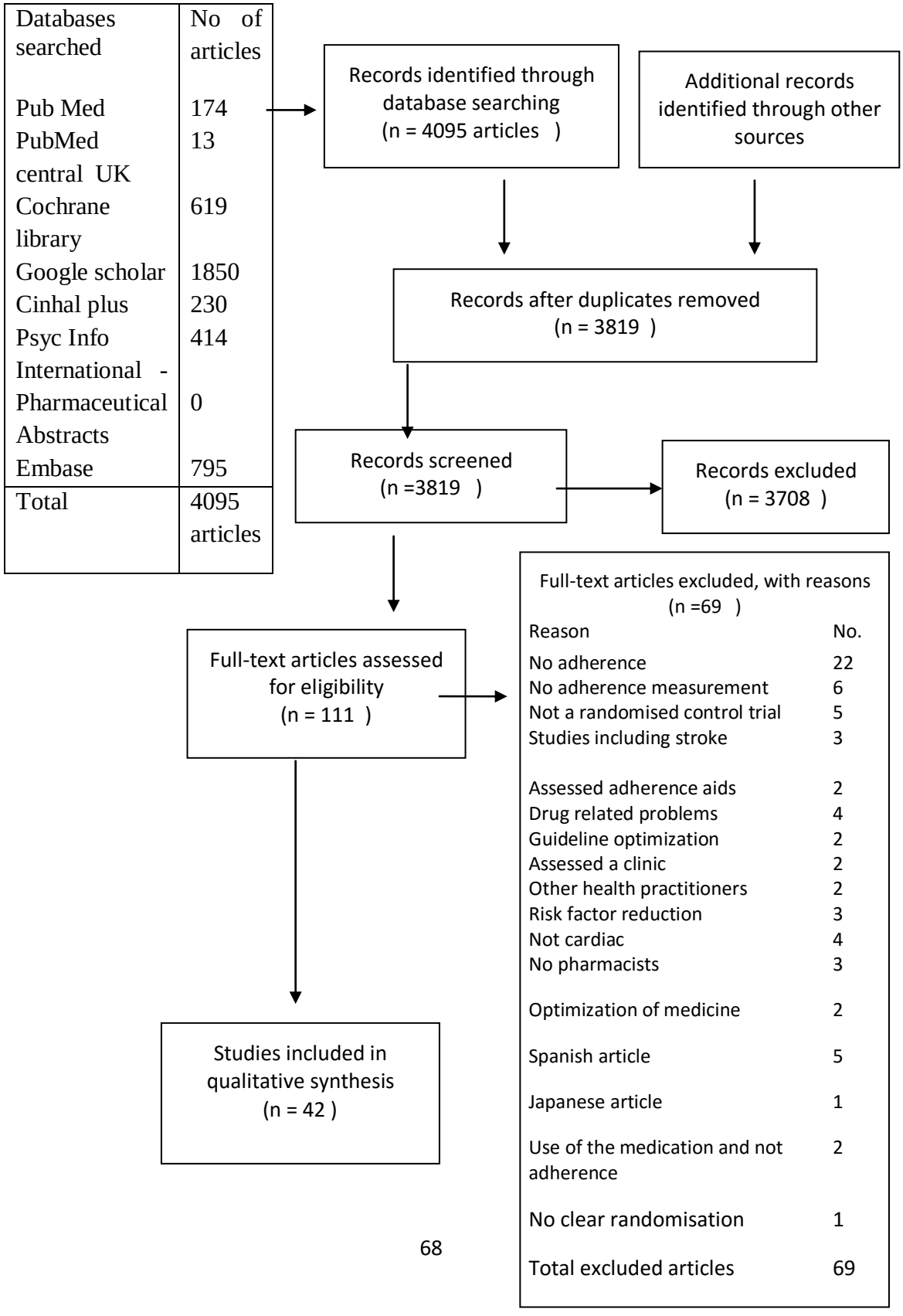
Electronic data bases were searched to identify studies that matched the inclusion criteria. After application of the key words the databases yield the following number of articles; Pub Med (n=174), Pub Med Central UK (n=13), Cochrane library (n=619), Google scholar (n=1850), CINAHL plus (n=230), PsycINFO (n=414), International Pharmaceutical Abstracts (n=0), EMBASE (n=795). The search gave a total number of 4095 citations. The titles and/or abstracts of these articles were reviewed and 111 full text articles matched the inclusion criteria and were retrieved either electronically or on paper copy for assessment; 39 articles were identified. The reference lists of the relevant 39 articles were also searched and an additional 3 articles were found. Therefore, a total of 42 randomised controlled trials were included in this review (Figure 2.1 Study selection chart below). In total, 69 articles were excluded for the following reasons: did not study adherence (n=22), no adherence measurement (n=6), not a randomised control trial (n=5), Studies including stroke (n=3) assessed adherence aids (n=2), drug related problems (n=4), guideline optimization (n=2), assessed a clinic (n=2), other health practitioners (n=2), risk factor reduction (n=3), not cardiac (n=4), no pharmacists (n=3), optimisation of medicine (n=2), article in Spanish (n= 5), article in Japanese (n=1), use of the medication and not adherence (n=2), no clear randomisation (n=1). Only full texts of randomised controlled trials were included in this review.

Process of data extraction

A table of details of each intervention was developed and it included a full description of the nature of each intervention and its duration. The interventions were compared for differences and similarities and then the main categories were established. They were categorised according to the mode of delivery. A further table was developed for adherence measures then similar measures were grouped. Further variables assessed were arranged in tables to enable analysis. These included setting, patient groups, outcome measures and study design (Please refer to appendix 5-9).

Figure 2.1 Study selection chart

Databases searched	No of articles
Pub Med	174
PubMed central UK	13
Cochrane library	619
Google scholar	1850
Cinhal plus	230
Psyc Info	414
International - Pharmaceutical Abstracts	0
Embase	795
Total	4095 articles



2.4-Results

The 42 studies that met the inclusion criteria were conducted in different countries USA (18 articles), UK (3), Australia (3), Canada (4), UAE (2), Netherland (2), Belgium (2), Thailand (2), Northern Ireland (1), Portugal (1), Brazil (1), Spain (1), Jordan (1) and China (1).

Study Design

All the 42 trials included in this review were randomised controlled trials 27 trials randomised patients into intervention and control groups (Lee *et al,* 2006), (Bouvy *et al,* 2003),(Morgado *et al,* 2011) , (Yunsheng *et al,* 2010),(Carter et al, 2008), (Mazroui *et al,* 2009),(Hunt *etal*,2007), (Holland *et al*, 2007), (Peterson *et al*, 2004), (Murray *et al*, 2007), (Phumipamorn *et al,* 2008), (Sookaneknun *et al,* 2004), (Taylor *et al,* 2003), (Jaffray *et al*, 2007), (Odegard *et al* ,2005), (Mehos *et al,* 2000) ,(Park *et al,* 1996) ,(Obreli-Neto *et al,* 2011), (Lopez *et al*, 2006), (Faulkner *et al*, 2000) ,(Calvert *et al,* 2012), (Zhao *et al,* 2012) , (Planas *et al,* 2009), (Eussen *et al*, 2010), (Jarab *et al*,2012),(Alsabbagh *et al,* 2012), (Ho *et al*,2014). Six trials randomised pharmacies to avoid contamination between the intervention and control groups (Zillich *et al,* 2005) ,(Svarstad *et al,* 2009), (Aslani *et al,* 2010), (Lau et al, 2010), (Blenkinsopp *et al,* 2000), (Mehuys, 2011). Two trials randomised at clinic level to minimize contamination at physician level (Carter et al, 2008),(Carter et al, 2009). Moreover, two trials (Villeneuve *et al,* 2010), (Heisler *et al,* 2012) randomized clusters. Villeneuve *et al*, 2010 randomised clusters including both physicians and community pharmacists. Heisler *et al*, 2012 conducted a cluster randomised effectiveness study in which primary care teams within sites were randomised. On the other hand one trial (Vrijens *et al*, 2006) randomized two districts in Belgium into usual care and a supportive intervention program and one trial (Edworthy *et al,* 2007) randomised cardiologists and accordingly assigned patients to either arm.

Finally, three trials were designed as prospective randomised controlled pilot studies (Gwadry-Sridhar *et al,* 2005), (Varma *et al,* 1999), (Evans *et al,* 2010); all the three trials randomised patients.

Patient/Disease groups

Of the 42 trials that met the inclusion criteria 17 were conducted in patients with hypertension (Lee *et al,* 2006), (Morgado *et al,* 2011) ,(Carter et al, 2008), (Hunt et al, 2008), (Zillich *et al,* 2005) ,(Svarstad *et al,* 2009),(Lau et al, 2010) (Sookaneknun *et al,* 2004) ,(Taylor *et al,* 2003), (Blenkinsopp *et al,* 2000) ,(Mehos *et al,* 2000) ,(Park *et al,* 1996) ,(Obreli-Neto *et al,* 2011) ,(Calvert *et al,* 2012) ,(Carter *et al,* 2009), (Zhao *et al,* 2012) ,(Planas *et al,* 2009), 10 in patients with diabetes (Mazroui *et al,* 2009), (Phumipamorn *et al,* 2008) ,(Taylor *et al,* 2003), (Odegard *et al* ,2005), (Mehuys, 2011) , (Obreli-Neto *et al,* 2011), (Planas *et al,* 2009), (Evans *et al,* 2010), (Heisler *et al,*2012),(Jarab *etal,*2012), 7 in patients with dyslipidemia (Lee *et al,* 2006), (Villeneuve *et al* , 2010), (Aslani *et al,* 2010) ,(Vrijens *et al,* 2006),(Taylor *et al,* 2003), (Evans *et al,* 2010) , (Eussen *et al,* 2010) , 7 in patients with heart failure (Bouvy *et al,* 2003),(Holland *et al,* 2007),(Sadik, 2005),(Gwadry-Sridhar *et al,* 2005),(Murray *et al,* 2007),(Varma *et al,* 1999), (Lopez *et al,* 2006) and 9 in patients with coronary heart disease (Yunsheng *et al,* 2010),(Peterson *et al,* 2004), (Jaffray *et al,* 2007,(Edworthy *et al,* 2007), (Faulkner *et al,* 2000), (Calvert , 2012), (Evans *et al,* 2010),(Alsabbagh *et al,* 2012),(Ho *et al,* 2014). One trial (Lee *et al,* 2006) studied patients with hypertension and dyslipidemia; another trial (Taylor *et al,* 2003) studied patients with hypertension, dyslipidemia, diabetes and patients on anticoagulation therapy. Furthermore, two trials (obreli-Neto *et al,* 2011), (Planas *et al,* 2009) included patients with hypertension and diabetes and finally, one trial (Evans *et al,* 2010) studied patient populations for primary and secondary prevention (hypertension, diabetes, dyslipidemia and coronary heart disease).

Overview of goals of interventions and primary/secondary outcomes

In 19 trials (Lee *et al,* 2006), (Bouvy *et al,* 2003), (Yunsheng *et al,* 2010), (Sadik, 2005), (Peterson *et al,* 2004), (Gwadry-Sridhar *et al,* 2005), (Murray *et al,* 2007), (Aslani et *al,* 2010) ,(Lau *et al,* 2010), (Vrijens *et al,* 2006), (Blenkinsopp *et al,* 2000), (Obreli-Neto *et al,* 2011), (Calvert *et al,* 2012), (Zhao *et al,* 2012), (Planas *et al,* 2009), (Eussen *et al,* 2010), (Alsabbagh *et al,* 2012), (Ho *et al,*2014),(Faulkner *et al,* 2000) the aim of the intervention was to enhance adherence to cardiovascular medication and adherence was the primary outcome. The remaining interventions measured adherence as a secondary outcome; the primary aims being to improve blood pressure control and management of hypertension (Morgado *et al,* 2011), (Carter et al, 2008), (Hunt et al, 2008), (Zillich *et al,* 2005),(Svarstad *et al,* 2009), (Sookaneknun *et al,* 2004) ,(Mehos *et al,* 2000), (Park *et al,* 1996) ,(Carter *et al,* 2009),(Planas *et al,* 2009), (Heisler *et al,*2012), to improve glycaemic control and quality of care for diabetic patients (Mazroui *et al,* 2009), (Phumipamorn *et al,* 2008), (Odegard *et al* ,2005), (Mehuys, 2011), (Jarab *etal,*2012) and to improve clinical outcomes in heart failure patients (Holland *et al,* 2007), (Sadik, 2005) ,(Varma *et al,* 1999), (Lopez *et al,* 2006). Other secondary outcomes included reduction in multiple cardiovascular risk factors (Taylor *et al,* 2003), (Evans *et al,* 2010), to improve use of guidelines for secondary prevention medication in patients with CHD (Jaffray *et al,* 2007), (Edworthy *et al,* 2007) and the achievement of target lipid levels and lipid control (Villeneuve *et al,* 2010).

Setting

In fifteen studies the principal setting for the intervention was a community pharmacy (Bouvy *et al,* 2003), (Zillich *et al,* 2005), (Villeneuve *et al* , 2010), (Murray *et al,* 2007), (Svarstad *et al,* 2009), (Aslani *et al,* 2010), (Lau et al, 2010), ,(Vrijens *et al,* 2006), (Sookaneknun *et al,* 2004), (Jaffray *et al,* 2007), (Blenkinsopp *et al,* 2000), (Park *et al,* 1996) ,(Mehuys, 2011), (Planas *et al,* 2009), (Eussen *et al,* 2010); in 14 studies the interventions were in hospital (Lee *et al,* 2006), (Morgado *et al,* 2011),

(Yunsheng *et al,* 2010), (Mazroui *et al,* 2009), (Sadik, 2005), (Gwadry-Sridhar *et al,* 2005), (Phumipamorn *et al,* 2008), (Edworthy *et al,* 2007), (Varma *et al,* 1999), (Lopez *et al,* 2006) ,(Zhao *et al,* 2012),(Faulkner *et al,* 2000) ,(Alsabbagh *et al,* 2012), (Ho *et al*,2014) and in 9 studies (Carter *et al,* 2009), (Hunt *etal*,2007) ,(Taylor *et al,* 2003), (Odegard *et al* ,2005) ,(Mehos *et al,* 2000), (Obreli-Neto *et al,* 2011), (Carter *et al,* 2008), (Evans *et al,* 2010), (Heisler *et al,* 2012) the setting was a clinic or primary care practice. In two trials (Holland *et al,* 2007), (Peterson *et al,* 2004) the intervention setting was the patient's home and in one trial (Calvert *et al,* 2012) the intervention was delivered in a hospital and community pharmacist setting.

2.5-Details of the intervention

In accordance with the eligibility criteria, all interventions were conducted by a pharmacist. All interventions were complex and included multiple components. However, they are described here according to the principal component of the intervention. Categorization followed the studied trials' description of their interventions and also the researcher's own judgment. Interventions were classified into categories these included: patient education by pharmacist, collaborative care, communication between primary and secondary care, combined interventions and use of electronic devices.

Patient education

Education by a pharmacist was delivered face to face, by telephone or by a home visit.

Face-to-face patient education

Pharmacists provided education face to face with a patient in 21 trials. This followed a pre-specified structure in seven trials (Lee *et al*, 2006), (Bouvy *et al* , 2003), (Morgado *et al*, 2010), (Mazroui *et al* , 2009) (Blenkinsopp *et al* , 2000), (Varma *et al*, 1999), (Eussen *et al*, 2010). In addition, the consultation focused on the disease and prescribed medications (Lee *et al* , 2006), (Al Mazroui *et al* , 2009), (Sadik *et al*, 2005), (Alsani *et al*, 2010), (Murray *et al*, 2007), (Mehuys *et al*, 2011), (Taylor *et al*, 2003), (Phumipamorn *et al*, 2008) , (Varma *et al*, 1999), (Odegard *et al*, 2005), (Park *et al*, 1996), (Planas *et al*, 2009) , (Evans *et al*, 2010). Patient education also included discussions on medication-related problems (Aslani *et al*, 2010) , (Sookaneknun *et al*, 2004), (Odegard *et al*, 2005), (Planas *et al*, 2009), lifestyle changes (Morgado *et al* , 2010), (Phumipamorn *et al*, 2008) , (Sookaneknun *et al*, 2004), (Taylor *et al*, 2003), (Jaffray *et al*, 2007), (Mehuys *et al*, 2011), (Planas *et al*, 2009), (Evans *et al*, 2010) and reinforcement of adherence (Bouvy *et al* , 2003), (Morgado *et al* , 2010), (Sookaneknun *et al*, 2004), (Jaffray *et al*, 2007), (Blenkinsopp *et al* , 2000), (Eussen *et al*, 2010).

Patient education by telephone contact

Telephone counselling was the principal intervention in four trials, three of which (Yunsheng *et al*, 2010), (Jarab *et al*, 2012), (Faulkner *et al*, 2000) included an initial inpatient consultation by a pharmacist regarding the patient's medications, prior to discharge. This was followed by structured telephone counselling by the pharmacist to reinforce the information. In the fourth trial (Alsabbagh *et al*, 2012) there was no inpatient consultation prior to the telephone calls. All subjects in the intervention group received education and counselling on medication adherence. The next call took place within 1–2 weeks or when needed to support medication adherence.

Home visits by pharmacists

In two trials (Holland *et al*, 2007), (Peterson *et al*, 2004) the intervention was delivered in home visits by a pharmacist. These included education on the disease, lifestyle issues and compliance with therapy. Recommendations were also made to physicians and local pharmacies for adherence aids.

Motivational interviews

In one trial (Heisler *et al*, 2012) adherence counselling and medication management was delivered by clinical pharmacists trained in behavioural counselling approaches (motivational interviewing). Details of training, application and implementation were provided to ensure principles of motivational interviews were followed. A 'road map' was provided for the pharmacists and there was also an assessment to check reliability of the technique. However, the aim in this study was to improve blood pressure control by intensifying medication and improving adherence. In this study adherence was a secondary outcome, the primary outcome measure being systolic blood pressure. The primary care teams (primary care providers; physicians, pharmacists and nurses) were randomised to evaluate the real-world effectiveness of pharmacy-team interactions rather than just the efficacy of pharmacist interactions with patients. Two further trials (Lau *et al*, 2010), (Jarab *et al*, 2012) mentioned motivational interviewing, but gave no details on how this component was implemented as part of the intervention and no assurance of the reliability of the technique.

Collaboration between healthcare professionals

Collaborative care

In seven trials (Carter *et al*, 2008), (Hunt *et al*, 2008), (Villeneuve *et al*, 2010), (Gwadry-Sridhar *et al*, 2005), (Edworthy *et al*, 2007), (Obreli- Neto *et al*, 2011), (Carter *et al*, 2009) the intervention involved collaboration between pharmacists and physicians or nurses, in a multidisciplinary approach. Five (Carter *et al*, 2008), (Hunt *et al*, 2008), (Villeneuve *et al*, 2010), (Obreli- Neto *et al*, 2011), (Carter *et al*, 2009) of these trials, addressed suboptimal regimens and poor adherence to medication through these collaborations. The other two trials (Gwadry-Sridhar *et al*, 2005), (Edworthy *et al*, 2007) included joint intensive multidisciplinary team programmes that provided counselling on medications, videos and printed material to promote adherence.

Communication between primary and secondary care

One trial (Calvert *et al*, 2012) evaluated the effect of facilitated communication between hospital and community pharmacists on medication adherence. The intervention group received enhanced in-hospital counselling, communication of discharge medications to community pharmacists and physicians, and ongoing assessment of adherence by community pharmacists.

Combined intervention

One trial (Ho *et al*, 2014) described as a multifaceted intervention that lasted for 1 year following discharge, comprised the following: pharmacist-led medication reconciliation 7–10 days after discharge and at 1 month via an in-person clinic visit or telephone call; pharmacists provided the patient's primary care clinician and/or cardiologist with their contact details for questions or clarifications; and two types of voice messaging (educational and medication refill reminder calls). The medication refill calls were synchronised to when a medication refill was due.

In a second trial (Lau *et al*, 2010) the participants received a number of interventions from the pharmacist which included the following: patient education and motivational interviewing; electronic blood pressure home monitors; home medicine review, dose administration aid and patient medication profile; refill reminders by SMS, telephone or mail.

Use of electronic devices

Four trials (Zilich *et al*, 2005), (Virijens *et al*, 2006), (Svarstad *et al*, 2009),(Mehos *et al*, 2000) used electronic devices as the main intervention. In two trials (Zilich *et al*, 2005) , (Mehos *et al*, 2000) patients were provided with a fully automated self blood pressure monitor and were told to perform two blood pressure measurements each morning. In one trial (Svarstad *et al*, 2009) patients were given a toolkit which included a blood pressure tracker and a pedometer. In another trial (Virijens *et al*, 2006) patients were instructed on how to use a Medication Event Monitoring System (MEMS; medication bottles that contain a microelectronic chip that registers the date and time of every bottle opening). Patients and a pharmacist jointly reviewed the electronically compiled dosing history, educational reminders and a beep card that reminded the patient of the dosing time.

Additional components

Additional components to the above interventions included written information (Zillich *et al*, 2005) (Faulkner *et al*, 2000), (Heisler *et al*,2012), (Morgado *et al*, 2011),(Svarstad *et al*, 2009), (Sookaneknun *et al*, 2004), (Taylor *et al*, 2003), (Blenkinsopp *et al*, 2000),(Mehos *et al*, 2000) ,(Park *et al*, 1996), (Evans *et al*, 2010), (Mazroui *et al*, 2009), (Phumipamorn *et al*, 2008), (Holland *et al*, 2007), (Sadik, 2005), (Murray *et al*, 2007), (Varma *et al*, 1999), (Yunsheng *et al*, 2010), (Jaffray *et al*, 2007), (Jarab *et al*,2012),

,providing patients with a diary, (Sookaneknun *et al,* 2004),(Sadik, 2005), (Varma *et al,* 1999) a pocket medication card (Calvert *et al,* 2012), educational material (Heisler *et al*,2012),(Calvert *et al,* 2012),education regarding the disease (Zillich *et al,* 2005),(Hunt *etal*,2007), (Mehos *et al,* 2000) educational group activities, (Obreli-Neto *et al,* 2011) recommending lifestyle change, (Villeneuve *et al* , 2010), recommendations to physicians, (Zillich *et al,* 2005), (Carter et al, 2008), (Svarstad *et al,* 2009), (Carter *et al,* 2009), (Yunsheng *et al,* 2010), (Edworthy *et al*, 2007), telephone calls (Blenkinsopp *et al,* 2000),(Mehos *et al,* 2000), (Carter *et al,* 2009), (Evans *et al,* 2010), (Odegard *et al* ,2005), (Lopez *et al,* 2006), home visits, (Sookaneknun *et al,* 2004) home medicine review (Lau *et al,* 2010), pill box (Zillich *et al,* 2005), (Svarstad *et al,* 2009), (Yunsheng *et al,* 2010), (Calvert , 2012), (Ho *et al,* 2014) blisters, (Lee *et al,* 2006) electronic blood pressure home monitoring, (Heisler *et al*,2012), (Lau et al, 2010) and visual props and media videos (Gwadry-Sridhar *et al,* 2005), (Edworthy *et al*, 2007).

Intervention duration

The interventions were delivered on a weekly basis (Zillich *et al,* 2005), (Faulkner *et al,* 2000), (Heisler *et al,* 2012), (Odegard *et al,* 2005), (Jarab *et al,* 2012), (Holland *et al,* 2007), (Yunsheng *et al,* 2010), (Calvert *et al,* 2012),(Alsabbagh *et al,* 2012) , monthly basis (Obreli-Neto *et al,* 2011), (Lee *et al,* 2006),(Morgado *et al,* 2011), (Carter *et al,* 2008),(Sookaneknun *et al,* 2004), (Blenkinsopp *et al,* 2000), (Mehos *et al,* 2000), (Park *et al,* 1996),(Carter *et al,* 2009), (Zhao *et al,* 2012), (Planas *et al,* 2009), (Evans *et al,* 2010), (Al Mazroui *et al,* 2009), (Phumipamorn *et al,* 2008), (Villeneuve *et al,* 2010), (Aslani *et al,* 2010), (Virjens *et al,* 2006), (Eussen *et al,* 2010), (Bouvy *et al,* 2003), (Murray *et al,* 2007), (Varma *et al,* 1999), (Lopez *et al,* 2006), (Peterson *et al,* 2004), (Edworthy *et al,* 2007), (Ho *et al,* 2014), at each prescription refill (Svarstad *et al,* 2009),(Mehuys *et al,* 2011), (Sadik *et al,* 2005), arranged during the physician visit (Taylor et al, 2003), (Planas *et al,* 2009), according to pharmacist-determined patient need (Hunt *et al,* 2008), (Jaffray *et al,* 2007) or once over 2 days (Gwadry-Sridhar *et al,* 2005).

2.6-Assessment of outcomes

Measurement of adherence

Diverse indirect measures of adherence were used in the trials. These included prescription refills, MEMS, pill counts and self reported adherence scaled questionnaires: Medication Adherence Report Scale and Morisky Scale. Patients' self-reported adherence alone or in combination with other methods of measurement was widely used in the 42 trials. Thirty-two trials measured adherence by a single approach and 10 trials combined two adherence measures please refer to (Table 2.1 below). To distinguish adherence from non-adherence, consumption or refilling 80% of the prescribed medication doses was the widely accepted threshold among the trials (Obreli-Neto *et al,* 2011),(Faulkner *et al,* 2000),(Heisler *et al,* 2012), (Lee *etal,* 2006),(Sookaneknun et al, 2004),(Taylor *et al,* 2003),(Park *et al,* 1996),(Evans *et al,* 2010),(Villeneuve *et al,* 2010),(Bouvy *et al,* 2003), (Gwadry-Sridhar *et al* , 2005),(Varma *et al,* 1999).

Table 2.1 Measurement of adherence

Indirect measures of adherence; from the 42 trials 32 trials measured adherence by a single adherence measure, 10 trials combined two adherence measures.

Single adherence measurement	Number of trials
Refill data	Ten trials (Heisler *et al,* 2012), (Mehos *et al,* 2000), (Planas *et al,* 2009), (Evans *et al,* 2010), (Villeneuve *et al,* 2010), (Eussen *et al,* 2010), (Yunsheng *et al,* 2010),(Alsabbagh *et al,* 2012), (Ho *et al,* 2014), (Sookaneknun *et al,* 2004)
Self report questionnaires	Seven trials(Taylor et al, 2003),(Almazroui *et al,* 2009), (Odegard *et al,* 2005), (Sadik *et al,* 2005),(Peterson *et al,* 2004), (Jaffray *et al,* 2007), (Edworthy *et al,* 2007)
Morisky scaled questionnaire	Six trials (Zillich *et al,* 2005),(Morgado *et al,* 2011), (Hunt *et al,* 2008), (Carter *et al,* 2009), (Zhao *et al,* 2012), (Jarab *et al,* 2012)
Pill counts	Five trials (Lee *et al,* 2006), (Park *et al,* 1996),(Carter *et al,* 2008),(Phumipamorn *et al,* 2008), (Lopez *et al,* 2006)
MEMS (Medication Event Monitoring System)	Two trials (Virjens *et al,* 2006), (Bouvy *et al,* 2003)
The Horne's Medication Adherence	Two trials(Holland *et al,* 2007), (Aslani *et al,* 2010)

Report Scale (MARS)	
Combination of adherence measurement	
Refill data combined with self reported questionnaires	Four trials (Svarstad *et al*, 2009), (Mehuys *et al*, 2011), (Murray *et al*, 2007), (Varma *et al*, 1999)
Refill data combined with the Morisky scale	Two trials (Obreli-Neto *et al*, 2011), (Calvert *et al*, 2012)
Refill data combined with MEMS	One trial (Gwadry-Sridhar *et al*, 2005)
Refill data combined with MARS	One trial (Blenkinsopp *et al*, 2000)
Refill data combined with pill counts	One trial (Faulkner *et al*, 2000)
Morisky Scale in addition to two scales originally developed in Australia the Tools for Adherence Behaviour Screening (TABS) and the medication refill data (MedsIndex score).	One trial (Lau *et al*, 2010)
For the Morisky scale, Morgado *et al*, 2010, Carter *et al*, 2009 and Calvert *et al*, 2012 used a 5 item scale derived from the 4 item scale. Hunt *et al*, 2008, Zilich *et al*, 2005, Zhao *et al*, 2012, Lau *et al*, 2010 and Jarab *et al*, 2012 all used the 4 item scale. Moreover, Obreli-Neto, 2011 used the 4 item Morisky -Green test translated into Portuguese.	

Impact of interventions on adherence

The review aimed to assess the effect of pharmacist service intervention on adherence. Twenty six trials (Lee *et al*, 2006), (Morgado *et al*, 2011) ,(Carter et al, 2008), (Zillich *et al*, 2005) ,(Svarstad *et al*, 2009), (Lau et al, 2010) ,(Sookaneknun *et al*, 2004) ,(Taylor *et al*, 2003), (Blenkinsopp *et al*, 2000) ,(Park *et al*, 1996) ,(Obreli-Neto *et al*, 2011), (Calvert *et al*, 2012), (Zhao *et al*, 2012), (Mazroui *et al*, 2009), (Phumipamorn *et al*, 2008),(Vrijens *et al*, 2006) ,(Eussen *et al*, 2010) , (Bouvy *et al*, 2003), (Sadik, 2005),(Murray *et al*, 2007),(Varma *et al*, 1999), (Lopez *et al*, 2006) (Edworthy *et al*, 2007), (Faulkner *et al*, 2000),(Jarab *et al*, 2012),(Ho *et al*,2014) showed a statistically significant improvement in adherence to cardiovascular medication. Across the 42 studies a statistically significant improvement in adherence of up to 35% was reported. The results indicate that face-to-face patient education by a pharmacist improved adherence in 15/21 studies, suggesting education could have a significant effect on adherence (refer to Table 2.2 below).

Electronic devices showed success in enhancing adherence in three of four studies. These included the integration of a home automatic blood pressure monitor, the use of electronic reminders (beep card) and an electronic blood pressure tracker. In all these trials pharmacists also provided tailored educational services and patient follow-up. One study (Heisler *et al*, 2012) examined the use of motivational interviews by pharmacists, although it did not show significant results. Details on the training of the pharmacists and the delivery and content of motivational interviews were provided. The authors report that high rates of treatment intensification and medication changes occurred in the control group, leading to improvements in the studied outcomes among the controls.

Telephone calls with patient education and advice improved adherence in two of the four trials that examined this type of intervention. Two other trials (Lau *et al*, 2010), (Ho *et al*, 2014) tested a combination of interventions to improve adherence, which also included medication refill reminders by telephone, and showed significant results. Three of the seven interventions that evaluated a collaborative care approach to improve adherence had statistically significant results. One trial (Calvert *et al*, 2012) examined the impact of communication between hospital and community pharmacies and showed significant results on adherence. Home visits by pharmacists did not show significant results in improving adherence to cardiovascular medication. In one trial (Holland *et al*, 2007) some possible reasons were provided by the authors. These reasons include; that the intervention was brief and/or may have been too late in the disease course to evoke a change in behaviour. Also the pharmacists were not specialists in the disease studied.

Table 2.2 Interventions and their mode of delivery

Intervention	Trials	Result on adherence	Result on outcomes
1-Patient education by pharmacist	Lee *et al* , 2006, Bouvy *et al* , 2003, Morgado *et al* , 2010, Al Mazroui *et al* , 2009, Sadik *et al*, 2005, Alsani *et al* , 2010, Murray *et al*, 2007, Mehuys *et al*, 2011, Taylor *et al* , 2003, Jaffray *et al*, 2007, Blenkinsopp *et al* , 2000, Sookaneknun *et al* , 2004, Phumipamorn *et al*, 2008 , Varma *et al*, 1999, Odegard *et al*, 2005, Park *et al*, 1996, Lopez *et al*, 2006, Zhao *et al* , 2011, Planas *et al*, 2009 , Evans *et al*, 2010, Eussen *et al*, 2010	15 trials (21) significant	16 trials (21) significant
2-Telephone contact	Yunsheng *et al*, 2010, Faulkner *et al*, 2000, Jarab *et al*, 2012, Alsabbagh *et al*, 2012	2(4) trials significant	2 (3) trials significant
3-Use of electronic device	Zilich *et al* , 2005 (SMBP), Svarstad *et al* , 2009 (pedometer, blood pressure tracker), Virijens *et al*, 2006* (Beep card), Mehos *et al* , 2000 (SMBP)	3(4) trials significant	3 (3) trials significant
4-Home visit	Holland *et al*, 2007, Peterson *et al* , 2004	0 (2) trials non significant	1 (2) trials significant
5-Collaborative care	Carter *et al* , 2008, Hunt *et al* , 2008, Villeneuve *et al*, 2010, Gwadry-Sridhar *et al* , 2005, Edworthy *et al*, 2007, Obreli Neto *et al* , 2011, Carter *et al* , 2009.	3(7) trials significant	4 (7) trials significant
6-Motivational interviews	Heisler *et al*, 2012	1(1) trials non significant	0 (1) trials non significant
7Communica ti-on between primary and secondary care	Calvert *et al*, 2012*	1(1) trials significant	0 (0) trials
Combined interventions	Ho *et al*, 2014 , Lau *et al*, 2010	2(2) trials significant	1(2) trials significant
	Notes *Trials that did not evaluate clinical outcomes. Statistical significance at *P* value 0.05. SBPM: self blood pressure monitor.	Total 26/42 trials	Total 27/ 39trials

Effectiveness of interventions on outcomes of cardiovascular diseases

Studied outcomes included blood pressure control, haemoglobin A1c and/or fasting plasma glucose, lipid profiles and low-density lipoprotein cholesterol. Other outcomes were reduction in 10-year Framingham risk score, costs and quality of life, in addition to rehospitalisation, mortality and patient satisfaction with pharmacy services. Thirty nine trials evaluated the effect of pharmacy service interventions on outcomes of the diseases. Twenty seven trials had statistically significant results. The diseases studied in primary prevention were hypertension, diabetes and dyslipidemia. From the 17 studies that studied hypertension 16/17 (Lee *et al,* 2006), (Morgado *et al,* 2011) ,(Carter et al, 2008), (Hunt et al, 2008), (Zillich *et al,* 2005) ,(Svarstad *et al,* 2009), (Lau et al, 2010) (Sookaneknun *et al,* 2004) ,(Taylor *et al,* 2003), (Blenkinsopp *et al,* 2000) ,(Mehos *et al,* 2000) ,(Park *et al,* 1996) ,(Obreli-Neto *et al,* 2011),(Calvert *et al,* 2012) ,(Carter *et al,* 2009), (Zhao *et al,* 2012),(Planas *et al,* 2009) showed significant results and improvement in cardiovascular risk factors. For patients with diabetes 6/10 studies (Mazroui *et al,* 2009), (Taylor *et al,* 2003), (Mehuys, 2011) , (Obreli-Neto *et al,* 2011), (Planas *et al,* 2009), (Jarab et al, 2012) improved glycaemia control. Of the 6 studies in patients with dyslipidemia four (Lee *et al,* 2006), (Aslani *et al,* 2010) ,(Taylor *et al,* 2003) , (Eussen *et al,* 2010) showed improved lipid profiles (Please refer to table 2.2 above).

The diseases studied in secondary prevention were heart failure and coronary heart disease. In heart failure 4/7 trials reported significant results (Sadik, 2005), (Murray *et al,* 2007),(Varma *et al*, 1999), (Lopez *et al,* 2006) in improving clinical outcomes (mortality, rehospitalisation and quality of life). In CHD, two of the eight trials (Peterson *et al,* 2004), (Faulkner *et al,* 2000) achieved significant results on clinical outcomes.

2.7-Evaluation of the interventions

To assess the strength of the evidence a number of checklists for critical appraisal of randomised control trials are available. These include Critical Appraisal Skills Programme (CASP) and The Scottish Intercollegiate Guidelines Network checklist (SIGN). The SIGN 2012 checklist was selected to appraise the trials in this review because it was found easy to follow and served as a useful tool to evaluate the methodology of the trials. Overall, the follow up period in the trials ranged from 3 months (Zillich *et al,* 2005) to 36 months (Obreli-Neto *et al,* 2011); however, in the majority of the studies the follow up period was either 6 months or 12 months.

Regarding the sample size this ranged from a small sample size of 30 patients (Faulkner *et al,* 2000) to a large sample size of 4100 patients (Heisler *et al,* 2012). For randomisation; computer generated random sequence was the most common method of randomisation and was used by 15 trials (Lee *et al,* 2006), (Morgado *et al,* 2011), (Bouvy *et al,* 2003), (Hunt *etal,*2007) ,(Holland *et al,* 2007), (Peterson *et al,* 2004), (Murray *et al,* 2007), (Svarstad *et al,* 2009), (Jaffray *et al,* 2007), (Lopez *et al,* 2006), (Faulkner *et al,* 2000), (Calvert , 2012), (Zhao *et al,* 2012) , (Planas *et al,* 2009), (Eussen *et al,* 2010). A table of random numbers was used in 5 trials (Carter et al, 2008), (Mehuys, 2011), (Carter et al, 2009), (Heisler *et al,* 2012), (Evans *et al,* 2010) and a randomised block design in 6 trials (Zillich *et al,* 2005), (Villeneuve *et al,* 2010),(Ho *et al,* 2013),(Gwadry-Sridhar *et al,* 2005), (Odegard *et al* ,2005),(Alsabbagh *et al,* 2012). In 3 trials the randomisation was not clear (Aslani *et al,* 2010), (Taylor *et al,* 2003),(Park *et al,* 1996). Other randomisation methods used among the trials included randomisation by a statistician (Yunsheng *et al,* 2010), restricted randomisation (Mazroui *et al,* 2009), minimisation method (Sadik, 2005),(Varma *et al,* 1999),(Jarab *et al,* 2012), sealed opaque envelope technique (Lau *et al,* 2010), drawing a number from a container (Phumipamorn *et al,* 2008), simple randomisation (Sookaneknun *et al,* 2004), cluster randomisation (Blenkinsopp *et al,* 2000), coin flip (Edworthy *et al,* 2007),

deck of cards (Mehos *et al,* 2000) , stratified random sampling(Obreli-Neto *et al,* 2011) and an open label study randomisation of two districts (Vrijens *et al,* 2006). Thus according to SIGN checklist for RCTs in 5/42 (Lau *et al,* 2010), (Edworthy *et al,* 2007), (Phumipamorn *et al,* 2008), (Mehos *et al,* 2000), (Sookaneknun *et al,* 2004) trials the randomisation method was poor and in 3/42 trials the randomisation method was not specified (Aslani *et al,* 2010), (Taylor *et al,* 2003), (Park *et al,* 1996). Regarding an adequate concealment method in the 42 trials included in the review, only 11 trials reported the allocation concealment (Lee *et al,* 2006), (Morgado *et al,* 2011), (Holland *et al,* 2007),(Gwadry-Sridhar *et al,* 2005), (Murray *et al,* 2007),(Lau *et al,* 2010) ,(Calvert , 2012), (Zhao *et al,* 2012), (Evans *et al,* 2010), (Heisler *et al,* 2012), (Ho *et al,* 2014). Concealment was not clear in the remaining 31 trials. According to SIGN guidelines this could lead to an overestimation of the effect of the intervention in the trials, where concealment was not clearly mentioned.

Due to the nature of the intervention blinding was not possible in 5 trials (Lee *et al,* 2006), (Zillich *et al,* 2005), (Vrijens *et al,* 2006), (Evans *et al,* 2010),(Alsabbagh *et al,* 2012), 3 trials were single blinded (Hunt *etal,*2007) ,(Park *et al,* 1996), (Lopez *et al,* 2006), blinding was not clear in 19 trials (Bouvy *et al,* 2003), (Yunsheng *et al,* 2010), (Mazroui *et al,* 2009), (Holland *et al,* 2007), (Villeneuve *et al* , 2010), (Aslani *et al,* 2010), (Sookaneknun *et al,* 2004) ,(Taylor *et al,* 2003), (Edworthy *et al,* 2007), (Varma *et al,* 1999), (Odegard *et al* ,2005), (Mehos *et al,* 2000), (Mehuys, 2011), (Faulkner *et al,* 2000), (Zhao *et al,* 2012), (Planas *et al,* 2009), (Heisler *et al,*2012),(Ho *et al,* 2013),(Jarab *et al,* 2012). Blinding included outcome assessors in 7 trials (Sadik, 2005), (Gwadry-Sridhar *et al,* 2005), (Svarstad *et al,* 2009), (Jaffray *et al,* 2007), (Blenkinsopp *et al,* 2000), (Carter et al, 2009), (Eussen *et al,* 2010) , researchers in 3 trials (Carter et al, 2008), (Lau *et al,* 2010), (Obreli-Neto *et al,* 2011), general practitioners in 2 trials (Peterson *et al,* 2004), (Blenkinsopp *et al,* 2000), also in 2 trials pharmacists (Gwadry-Sridhar *et al,* 2005), (Calvert *et al,* 2012), physicians (Gwadry-Sridhar *et al,* 2005), (Phumipamorn *et al,* 2008) and nurses (Phumipamorn *et al,* 2008), (Morgado *et al,* 2011)

and interviewers in one trial (Murray *et al*, 2007). The trials that reported blinding were all single blinded, there were no double blinded or even triple blinded trials. The higher the level of blinding the lower the risk of bias in the study; therefore, a low risk of bias cannot be ruled out among the trials included in this review. In 17 trials (Lee *et al*, 2006), (Morgado *et al*, 2011), (Carter et al, 2008), (Hunt *etal*,2007), (Holland *et al*, 2007), (Gwadry-Sridhar *et al*, 2005), (Svarstad *et al*, 2009), (Vrijens *et al*, 2006), (Sookaneknun *et al*, 2004), (Jaffray *et al*, 2007), (Edworthy *et al*, 2007),(Park *et al*, 1996), (Mehuys, 2011), (Faulkner *et al*, 2000), (Carter et al, 2009), (Heisler *et al*,2012), (Evans *et al*, 2010) all patients were included in the final analysis (intention-to-treat analysis); intention-to-treat was not clear in 5 trials (Mazroui *et al*, 2009), (Zillich *et al*, 2005), (Sadik, 2005), (Peterson *et al*, 2004), (Lopez *et al*, 2006). The results were adjusted in one trial (Villeneuve *et a*, 2010), a sensitivity analysis was used in another (Murray *et al*, 2007) and generalised estimating equations in a third (Odegard *et al, 2005*). All patients were included in the final analysis for the remaining of the 42 trials. Therefore, for less than half of the trials in this review analysis was not on an 'intention to treat' basis.

According to SIGN guidelines 2012 the number of patients that drop out of a study should give concern if this very high. Conventionally, a 20% drop out rate is regarded as acceptable. When examining patient withdrawal rates; dropout rates among the 42 trials ranged from a low dropout rate below 10% in 21 trials (Lee *et al*, 2006), (Morgado *et al*, 2011), (Carter et al, 2008), (Mazroui *et al*, 2009), (Zillich *et al*, 2005), (Holland *et al*, 2007) ,(Sadik, 2005), (Svarstad *et al*, 2009), (Lau et al, 2010) ,(Sookaneknun *et al*, 2004) , (Blenkinsopp *et al*, 2000), (Zhao *et al*, 2012), (Phumipamorn *et al*, 2008) ,(Mehuys, 2011) , (Obreli-Neto *et al*, 2011), (Villeneuve *et al* , 2010),(Vrijens *et al*, 2006), (Jaffray *et al*, 2007),(Edworthy *et al*, 2007),(Ho *et al*, 2014),(Jarab *et al*, 2012).

An acceptable below 20% dropout rate in 14 trials (Taylor *et al*, 2003), (Mehos *et al*, 2000) ,(Park *et al*, 1996), (Planas *et al*, 2009), (Evans *et al*, 2010) (Odegard *et al* ,2005), (Heisler *et al*,2012) , (Eussen *et al*, 2010),(Gwadry-Sridhar *et al*, 2005),(Murray *et al*, 2007), (Lopez *et al*, 2006) (Yunsheng *et al*, 2010),(Peterson *et al*, 2004), (Calvert , 2012) and a high dropout rate above 20% in 6 trials (Bouvy *et al*, 2003), (Hunt *etal*,2007), (Aslani *et al*, 2010), (Varma *et al*, 1999) ,(Planas *et al*, 2009),(Alsabbagh *et al*, 2012). In one trial (Faulkner *et al*, 2000) no patients were lost to follow-up.

Limitations reported by the trials included; confined population and /or trial setting (Lee *et al*, 2006), (Carter et al, 2008),(Carter *et al*, 2009), (Mazroui *et al*, 2009), (Phumipamorn *et al*, 2008) ,(Taylor *et al*, 2003), (Obreli-Neto *et al*, 2011), (Taylor *et al*, 2003),(Sadik, 2005),(Murray *et al*, 2007), (Yunsheng *et al*, 2010), (Evans *et al*, 2010), high patient withdrawal rate and/or limited sample size (Bouvy *et al*, 2003), (Hunt *etal*,2007), (Gwadry-Sridhar *et al*, 2005), (Aslani *et al*, 2010) (Lopez *et al*, 2006), (Faulkner *et al*, 2000), (Calvert , 2012) ,(Planas *et al*, 2009), contamination (Morgado *et al*, 2011), (Sookaneknun *et al*, 2004) ,(Edworthy *et al*, 2007), (Odegard *et al* ,2005), (Park *et al*, 1996), (Eussen *et al*, 2010) , selection bias (Zillich *et al*, 2005) , (Lau et al, 2010), (Blenkinsopp *et al*, 2000) ,(Planas *et al*, 2009), (Heisler *et al*,2012),(Villeneuve *et al*, 2010), ((Vrijens *et al*, 2006) ,(Varma *et al*, 1999), (Jaffray *et al*, 2007), no true control (Zillich *et al*, 2005),(Peterson *et al*, 2004),(Svarstad *et al*, 2009) and measurement of outcomes (Peterson *et al*, 2004), (Mehuys, 2011),(Zhao *et al*, 2012).

The overall assessment of the trials' was performed by rating the methodological quality following the criteria mentioned above. This showed how well each study was done to minimise the risk of bias or confounding. All or most of the criteria were fulfilled in 13 trials (Lee *et al,* 2006), (Morgado *et al,* 2011) ,(Carter et al, 2008),(Svarstad *et al,* 2009), (Lau et al, 2010) (Blenkinsopp *et al,* 2000) , (Heisler *et al,*2012), (Eussen *et al,* 2010) ,(Holland *et al,* 2007),(Gwadry-Sridhar *et al,* 2005),(Murray *et al,* 2007), (Jaffray *et al,* 2007),(Ho et al, 2014). In 21 trials, either not all of the criteria were fulfilled or they were not adequately described, but it is considered that this would be unlikely to alter the conclusions of these trials (Hunt et al, 2008), (Zillich *et al,* 2005) ,(Park *et al,* 1996) ,(Obreli-Neto *et al,* 2011) , (Calvert *et al,* 2012) ,(Carter *et al,* 2009), (Zhao *et al,* 2012) , (Evans *et al,* 2010), (Mazroui *et al,* 2009), (Phumipamorn *et al,* 2008) ,(Odegard *et al* ,2005), (Mehuys *et al,* 2011) , (Villeneuve *et al* , 2010), (Vrijens *et al,* 2006), (Bouvy *et al,* 2003), (Sadik *et al,* 2005), (Varma *et al,* 1999), (Lopez *et al,* 2006) (Yunsheng *et al,* 2010),(Edworthy *et al,* 2007),(Alsabbagh *et al,* 2012). In 8 trials, few criteria were fulfilled, and this may impact on the conclusions (Peterson *et al,* 2004), (Aslani *et al,* 2010), (Sookaneknun *et al,* 2004) ,(Taylor *et al,* 2003), (Mehos *et al,* 2000), (Faulkner *et al,* 2000),(Planas *et al,* 2009), (Jarab *et al,* 2012). Thus, for this review, based on SIGN guidelines applied to forty two trials; eight trials were thought to have an altered conclusion because only few criteria were fulfilled (refer to Appendix 10). Therefore, it is unlikely that, different conclusions would have been found or that different recommendations would have emerged from this review.

2.8- Discussion

This review aimed to assess the effect of pharmacist-led interventions on adherence to cardiovascular medications. Forty two studies were identified, of which 26 had a statistically significant and positive impact on adherence. Interpretation was complex due to the heterogeneity and multiplicity of the components.

Furthermore, it is important to distinguish between the types of non-adherence (intentional, unintentional) because research has shown the underlying causes of these two types of non adherence are very different and this is important in designing appropriate interventions (Clifford *et al,* 2010). Thus the difference in the effect of these interventions could depend on the patients' beliefs and intentions with medication taking. Therefore, interventions such as use of electronic devices as reminders and prompts could target and be effective in patients with unintentional non-adherence (Furniss *et al,* 2014), whilst interventions involving patient education and counselling may be more effective in patients who are intentionally non adherent. The results show that face-to-face patient counselling by a pharmacist and electronic interventions could be effective in improving adherence. However, these interventions also involved other components. Evidence from studies of other diseases revealed that in-person pharmacist and electronic interventions significantly improved adherence to medication (Velligan *et al,* 2013), (Hiligsmann *et al,* 2013). Motivational strategies are increasingly used in healthcare to promote behaviour change due to the need to focus on addressing the rising prevalence of chronic disease. Motivational strategies and behavioural support have also been shown to enhance adherence to medication (Schroeder, 2005), (Viswanathan *et al,* 2012). In this review only one trial studied the use of motivational interviews, by pharmacists, to improve adherence and outcomes and showed no significant results. Furthermore, two trials (Lau *et al,* 2010), (Jarab *et al,* 2012) mentioned the use of motivational interviews in counselling session by the pharmacist, but did not give further details on the reliability of the technique.

In their reviews, Thompson *et al*, 2011 and Dalem *et al*, 2012 addressed the fact that behavioural interventions are effective in improving adherence. However, they did not focus on the pharmacists' role. For this reason, further evidence is needed to establish if and how motivational counselling in the pharmacy setting can lead to improvements in adherence. A telephone call or a reminder by a pharmacist has been found to be an effective approach to improve medication adherence in other diseases and chronic

conditions (Barber *et al*, 2004), (Elliot *et al*, 2008), (Al-Jumah, 2012), (Wu *et al*, 2006). Services in the UK delivered by community pharmacists and include face to face patient education and telephone encounters, such as the New Medicine Service, provide strong evidence that a pharmacist-led approach, focusing on patients' problems and concern can significantly improve adherence in particular with newly prescribed medicines (Elliot *et al*, 2014). Furthermore, a recent UK randomised control trial (Lyons *et al*, 2016) of a pharmacist-led telephone based intervention showed statistically significant results on improving adherence $P = 0.01$. This intervention was designed to improve medication adherence, in patients with diabetes and/or hyperlipidaemia, using a mail-order pharmacy. The intervention involved two telephone pharmacist consultations 4-6 weeks apart, a written summary of the discussion with the patient and a medicines reminder chart; both posted to patients' after first encounter. The authors report that although a mail-order context has some unique characteristics, the intervention is transferable to different settings and pharmacists, due to parallels with existing large successful, national services such as the NMS (Lyons *et al*, 2016).

In the review by Cutrona *et al*, 2010 which reviewed studies focusing on cardiovascular diseases, phone calls showed low success (38%). In our review, four of six trials that evaluated this method had statistically significant results. Therefore, the use of telephone calls and SMS to improve adherence could be an effective approach. Interventions involving home visits by pharmacists have reported increased adherence to prescribed drugs in an older population (Lowe *et al*, 2000), (Al-Rashed *et al*, 2002). Other studies, in contrast, which included a domiciliary assessment by a community pharmacist, have found no effect on adherence (Nazareth *et al*, 2001). Studies in this review were not sufficient to provide evident conclusions. Although interventions in a hospital setting had more significant results, four of these trials were conducted in military hospitals (Lee *et al*, 2006),(Zhao *et al*, 2012),(Al Mazroui *et al*, 2009),(Ho *et al*, 2014) in which financial barriers to adherence are removed and patients' attendance of appointments is

high. Therefore, the results of these studies had limited generalisability and external validity. In the review by Cutrona *et al*, 2010 the results demonstrate that in-person interventions at hospital discharge were more effective (67%) than clinic interventions (47%) and in-person pharmacist interventions were effective when held in a pharmacy (83%) and less effective in clinics (38%). Patients' self-reported adherence alone or in combination with other methods of measurement were widely used in the 42 trials. This is as recommended by the National Institute of Health and Care Excellence 2009 guidelines, which identified that while other types of measures are useful for clinical trials of new drugs; self-report is an appropriate tool for clinical practice. A threshold of 80% to determine adherence from non adherence was accepted among the trials. This finding is similar to other observational studies measuring adherence (Chapman *et al*, 2005), (Blackburn *et al*, 2005), (Pittman *et al*, 2011), (Bramely *et al*, 2006).

A study by Wu *et al*, 2009 showed a positive relationship between level of medication adherence and event-free survival in patients with heart failure. The study found that patients who take 88% of their prescribed medication doses and on 88% of days take the correct dose experienced longer event-free survival than patients who were less adherent. Moreover, in an article by Ho *et al*, 2009 the authors reported an analysis that suggests that there continues to be reductions in clinical outcomes with adherence levels beyond 80% (eg, 80–100%), which suggests that the optimal level of adherence may be higher than current cutoffs. While 80% is generally accepted, there are a few studies which examine levels of adherence against outcomes over a period of time. 'Can the interventions, in the reviewed studies, be adapted to clinical practice?' 'What would be features of an intervention to improve adherence?' These questions should be addressed with caution. The interventions were complex and time intensive as concluded in previous reviews (Evans *et al*, 2011). In addition, a wide variety of approaches have been employed in the pharmacy interventions. The interventions were conducted in different countries with diverse health systems which made comparison difficult. Factors that could contribute to non-adherence for example living environments,

access to health care, financial resources, costs of medication would differ across settings. Thus interventions targeting non-adherence should also differ reflecting these factors. All the interventions included a range of multiple components underlining a belief that a single focus is less likely to be effective. Electronic devices did improve adherence, however, there is the possibility of the Hawthorne effect. Face-to-face patient education by a pharmacist and possibly telephone counselling can be effective. This review has several limitations. There was a marked difference between the studies in their methodology, adherence measurement and duration of follow-up. Studies were included from 1990 to 2013. Definition of adherence was different in the studies conducted in the 1990s from those conducted in the 2000s. Moreover, some trials only published their methodology; therefore these trials were excluded because no results were available. Descriptive, observational studies and studies published in other languages were also not included. The strengths of the review were that only randomised control trials were included and that interventions were examined in different settings, with a focus on pharmacist interventions only.

2.9-Conclusions

Evidence-based data for pharmacy services remain weak, but studies have shown that pharmacists can have an impact through patient education and telephone counselling. Behavioural interventions delivered by pharmacists could have a positive effect but further evidence is needed. Self-reported adherence was the most widely used measure. The acceptable threshold remains at 80% among the cardiac population. Personal contact or counselling by a pharmacist can be an effective method in enhancing adherence, but the frequency of contact to make the intervention more adaptable to practice needs further examination. Finally, more research is needed to evaluate the continuity of care in primary and secondary settings and to promote links between hospital, community pharmacists and other healthcare professionals.

End of Chapter Two

Chapter Three

Pharmacy services and pharmacy roles

Chapter three will discuss a literature search; to determine effective roles of community pharmacists in the UK and whether a community pharmacy intervention could be incorporated into these services. This was important before designing an intervention for a study, to establish feasibility and workability.

3.1-Introduction

Over the past four decades there has been a movement for pharmacy practice away from its original focus on dispensing toward focus on patient care. The role of the pharmacist has advanced from that of a compounder and supplier of pharmaceutical products towards that of a provider of services and information and ultimately that of a provider of patient care (WHO, 2006). The new approach has been given the name pharmaceutical care. The most generally accepted definition of this new approach is:
"Pharmaceutical care is the responsible provision of drug therapy for the purpose of achieving definite outcomes that improve a patient's quality of life"(Hepler and Strand, 1990).

In adopting this definition in 1998, the International Pharmaceutical Federation (FIP) added one significant amendment: "*achieving definite outcomes that improve or maintain a patient's quality of life*" (WHO, 2006). There is a worldwide increasing recognition that community pharmacy can make a significant contribution to public health (Pharmacy and Public Health Forum report 2014). This activity has its origins in the traditional advisory role of the pharmacist, which declined following the establishment of the National Health Service (NHS) in 1948, but has more recently been promoted following ministerial intervention since 1981 (Anderson 2007).

These so-called pharmacy "extended roles" can be seen as a return to the "traditional" role of the community pharmacist before the introduction of the welfare state, and an attempt to draw the pharmacist out of the dispensary and back in touch with the public.

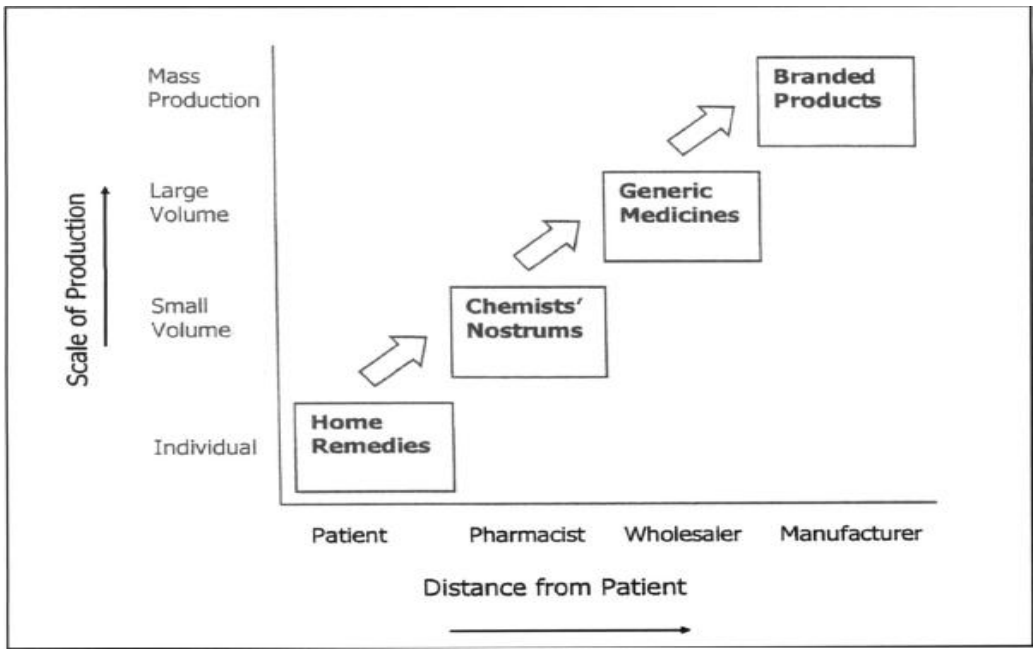
"Pharmacists should move from behind the counter and start serving the public by providing care instead of pills only. There is no future in the mere act of dispensing. That activity can and will be taken over by the internet, machines, and/or hardly trained technicians. The fact that pharmacists have an academic training and act as health care professionals puts a burden upon them to better serve the community than they currently do." (Storpirts, 2012)

The role of the pharmacist and the retail of medicines

The role of the pharmacist was transformed alongside the transformation in the retailing of medicines. The pharmacist changed from being the maker and supplier of medicines, to the supplier of manufactured medicines with information about their use. The twenty first century already shows the signs of providing equally radical change (Anderson 2007). When the scale of production of medicines evolved from individual compounding to industrial mass production, the distance between pharmacist and patient contact increased, as shown in figure 3.1:

Figure 3.1 The shift from patient to manufacturer (Anderson 2008)

Adapted from Anderson S. (2008) From "Bespoke" to "Off-the-Peg": Community Pharmacists and the Retailing of Medicines in Great Britain 1900 to 1970 Pharmacy in History, Vol. 50, No. 2, pp. 43-69



At the beginning of the twentieth century it was still common for families to rely heavily on home remedies made to their own formula. People would present scraps of paper to the local chemist asking for a few pennies' worth of particular ingredients. The core of the chemist business was counter prescribing through the formulation of the Nostrums (the chemists' secret remedies). These Nostrums continued into the 1960's and largely disappeared in 1970s. Machinery to mass-produce medicines was developed in the later decades of the nineteenth century. Following the mass-marketing of the sulphonamides in the late 1930s the possibility of mass-producing large numbers of effective drugs became a reality (Anderson, 2008). By the 1950s and 1960s wholesalers had developed more compact products. By the 1970s the number of prescriptions for liquid medicines had greatly declined and the vast majority of drugs being prescribed were then available as solid dose medicines for oral use, mainly tablets and capsules (Anderson 2008).

Table 3.1 key events in the historical development of community pharmacy and public health (Anderson, 2007)

Table adapted from Anderson S. (2007) Community pharmacy and public health in Great Britian1936 to 2006:how a phoenix rose from the ashes *J Epidemiol Community Health* ;61:844–848.

Year	Policy context	Pharmacy initiative	Implications for pharmacy
1948	Introduction of NHS		Community pharmacists become invisible
1970		Conference on role of pharmacist in health promotion 1978 working party on future of community Pharmacy	Health education an important role
1981	Ministerial statement at British Pharmaceutical Conference		Future of community pharmacy in doubt
1982 **1986**		Ask your pharmacist campaign Pharmacy: a report to the Nuffield Foundation Launch of Health in the High Street	Raised public awareness of the role of pharmacist Pharmacy considered capable of further development. First national distribution of health education leaflets through pharmacies
1987	Promoting better health	Programme for improving primary care	Support for pharmacies to display health education and promotion material
1989		Pharmacy Healthcare re launched	First government funding for pharmacy health promotion scheme

1990	Acheson Report on public health		
1991		Barnet Health Scheme launched	Training to develop pharmacists' knowledge and skills in health promotion
1992	Health of the Nation	Pharmaceutical care report	Proposes range of extended roles for pharmacists
1996		Pharmacy In A New Age	Health promotion considered second most important role to be expanded
1998	Our Healthier Nation	Related to England only	Led to review of pharmacy-related evidence
2001	Chief Medical Officer's report on public health workforce		Identifies different roles in public health for different members of the workforce
2002	The Right Medicine	Agenda for modernising and strengthening the role of pharmacists to deliver improved services to the public and patients	Significant developments in community based pharmaceutical care, and in the role of pharmacists and pharmacies across Scotland
2003	A Vision for Pharmacy in the New NHS		
2004	Choosing health white paper	Programme for improving public health	Substantial reference to pharmacy
2005	Choosing health through Pharmacy	Resolution by Council of Royal Pharmaceutical Society	Pharmacy's public health role to be increased still Further
2006	Our health, Our care, Our say: a new direction for community services		Highlighted that community pharmacies in the UK are easily accessible and their location in the heart to deliver public

			health initiatives
2008	The Department of Health report white paper Pharmacy in England Building on Strengths Delivering the Future		Set out the government's programme for a 21st-century pharmaceutical service
2010	The Department of Health White Paper Healthy lives, Healthy People	Emphasised on the role of Healthy Living Pharmacies (HLPs)	Outlined a radical shift in tackling public health challenges
2011		The Pharmacy and Public Health Forum was established	The development, implementation and evaluation of public health practice for pharmacy
2013	Nuffield trust report Now Or Never Shaping pharmacy for The future	A commission on future models of pharmacy care	Visions for pharmacy, new models of practice, future role of pharmacy in English NHS
2014	Five Year Forward View for NHS England	The new models of health care including the new model of primary care	Pharmacy to be integrated in local care providers' networks
2014	Nuffield trust report Now more Than ever.	An independent assessment of progress made in implementing the recommendations of Now or Never report	A call to integrate pharmacy fully into the models outlined in the 'Five Year Forward View'
2015	The future of primary care: creating teams for tomorrow.	Pharmacists to work in GP practices as well as the traditional role of the pharmacist operating from premises in the community.	Wider use should be made of community pharmacists and pharmacy support staff in managing minor illness and advising people about optimising their medicines.

Identification of the role of pharmacy in public health

With the introduction of NHS the workload of most community pharmacists increased. In 1937, 65 million doctors' prescriptions were dispensed from 13 000 pharmacies; by 1950, the figure had reached nearly 250 million. Most prescriptions needed to be made up individually, and many pharmacists spent much of the working day dispensing, in contrast to, the 1930s where the pharmacists spent most of the time dealing with customers and providing advice (Anderson 2007), (FIP, 2012). The Vaughan Intervention in 1981 addressed the possibility of the future of community pharmacy in public health with a focus on pharmacist role as experts in medicines. Its draft advertisements carried the slogan ''ask your pharmacist: you'll get the help you need'' with the recognition that community pharmaceutical services are essential part of primary health care (Anderson 2007). Furthermore, in 1986 *Pharmacy: a report to the Nuffield Foundation* was published; of its 96 recommendations 26 were related to community pharmacy. With a positive tone it aimed to establish full use of pharmacy contribution to healthcare. The 1980's witnessed further developments in the role of pharmacy in public health after the publication of the Black report and the government programme *Promoting better health* in 1987 (Anderson 2007). Pharmacies displayed health education and promotion materials in addition to the distribution of health education leaflets (Anderson, 2007).

In the 1990's pharmacy public health roles became more defined and included public health areas such as smoking cessation, contraception, prevention of heart disease and drug abuse. One significant development was the Barnet High Street Health Scheme in 1991 that included structured training for pharmacists in public health and received publicity in both pharmaceutical and national media. Furthermore, important publications were produced promoting improvements to health through pharmacy, these included publication of the Government's public health white paper *Our healthier nation* in 1998 (Anderson 2007).

This paper defined the application of pharmaceutical public health and reports commissioned through the Pharmacy Health Link (PHLink) (Public Health report- NPA, 2013). At the beginning of the new millennium, further government support was given to the pharmacy's role in public health. In April 2005, the Department of Health published *Choosing health through pharmacy* by introducing specialists in pharmaceutical public health (Anderson 2007). These specialists provided a link between pharmacy practice and the public. At this stage it became important for community pharmacists to become part of a wider public health workforce and demonstrate that its members can become specialist advisors in public health (Anderson 2007). The Department of Health report white paper *Pharmacy in England Building on Strengths – Delivering the Future*, in 2008 set out the government's programme for a 21st-century pharmaceutical service (Anderson 2007). It builds on *A Vision for Pharmacy in the New NHS* launched in July 2003 and *Our health, our care, our say: a new direction for community services*, published in January 2006 (Anderson 2007). This paper highlighted that community pharmacies in the UK are easily accessible and their location in the heart of the community provides them with the opportunity to deliver public health initiatives. In addition, many pharmacies have long opening hours to meet patients' and consumers' need. Since 2005, over 400 new pharmacies were approved to open to the public, for at least 100 hours per week.

Furthermore, the Department of Health report white paper *Pharmacy in England Building on Strengths – Delivering the Future* addressed the new contractual framework for community pharmacy that was revised in 2005 and placed services into three levels or tiers: essential (dispensing and repeat dispensing, healthy life style advice disposal of medicine), advanced (Medicines Usage Reviews (MURs) a review of patient's medicines to promote adherence) and local enhanced services (smoking cessation, nicotine replacement therapy, supervised methadone administration, emergency hormonal contraception, and minor ailment schemes).

Several examples of pharmacy public health initiatives were presented in the Department of Health report white paper *Pharmacy in England Building on Strengths – Delivering the Future* (Anderson 2007); for example; Heart MOT Service in Birmingham (a NHS health check) in which community pharmacies were commissioned to provide opportunistic testing services for vascular disease. In 2010 the Department of Health published the white paper *Healthy Lives, Healthy People*. The paper outlined a radical shift in tackling public health challenges including smoking, drug and alcohol treatment services and NHS Health Checks for men and women aged 40-74. The paper emphasized the potential role of Healthy Living Pharmacies (HLPs). The HLPs were developed in Portsmouth to make a real difference to the health of people, initially 10 pharmacies were awarded HLP status. These HLP's delivered a range of high quality services such as reducing smoking, weight management, emergency hormonal contraception, chlamydia screening, advice on alcohol and reviews of the use of medicines. They proactively promoted a healthy living culture and worked closely with local GPs and other health and social care professionals. In 2011 there were at least 100 Healthy Living Pharmacies in England and by April 2013 this number has risen to 508. (PSNC, 2014). By May 2014 the number of HLPs across England had grown to over 800 and attracted interest from other areas of the UK and across the world (Pharmacy and Public Health Forum report, 2014).

In 2014 an evaluation of the Healthy Living Pharmacy concept was undertaken by Public Health England (Pharmacy and Public Health Forum report, 2014). Public Health England conducted a survey of 1,034 members of the public. Ninety eight percent of people surveyed stated that they would recommend the HLP service to others and 81% reported that the service they received was excellent. In addition to this survey, a contractor survey (Brown *et al,* 2014) also reported that public health services delivered through HLPs were effective and potentially cost effective. Ninety one percent of contractors said becoming an HLP was a worthwhile investment and 80% said their staff became more productive (Brown *et al,* 2014).

The survey of contractors also identified several obstacles to HLP development. These included managing the increased workload, raising awareness of clients and other healthcare professionals of the services available, and remuneration for the service. In addition to public health pharmacy services delivered by Healthy Living Pharmacies, community pharmacists also deliver services to support medicines optimisation for patients with long term conditions.

3.2- Pharmacy services and contribution areas to patient care

Services that support medicines use for people with long term conditions include Medicines Use Reviews (MURs) and the New Medicines Service (NMS). In this chapter these services were researched because of their potential to accommodate the behavioural intervention identified for this study.

Medication usage review (MUR) in community pharmacy

Medicines Use Reviews were introduced in the UK in 2005. The purpose of a MUR is to improve patients' knowledge and use of drugs. Medicines Use Reviews aim to support appropriate medicines use by patients, identify side effects and drug interactions, and reduce waste. A MUR service is for patients on multiple medicines for long term conditions and can be carried out every 12 months. Pharmacists receive a payment of £28 per MUR and each pharmacy can undertake a maximum of 400 reviews per year (PSNC, 2015). In England the potential annual NHS investment in the service is about £112 million (PSNC, 2015). An interventional MUR can also be carried out if pharmacist identifies a significant problem. A number of research projects and evaluations have quantified MUR activity and sought to understand factors which influence uptake of MURs, by both patient and pharmacist/pharmacy (Bradley *et al.,* 2008), (Mc Donald *et al.,* 2010).

Studies evaluating targeted MUR services, focusing on a particular disease, have reported improved clinical outcomes (Bradley *et al.,* 2008), (Mc Donald *et al.,* 2010). They have also highlighted the need to develop strategies to encourage uptake/delivery of MURs to patients who need them the most, the need for quality assurance of MURs, improving communication between pharmacists and GPs and improving GP enthusiasm for community pharmacy MUR services (Hinchliffe *et al,* 2011).

Medicine Usage Reviews in the UK are usually conducted in the community pharmacy consultation room. However, in some cases they can be conducted at care homes (PSNC, 2015). MURs are usually delivered as a face to face consultation. Medicines use reviews are also carried out in several European countries. In Sweden MURs can be carried out in nursing homes, hospitals and some healthcare centres. In Finland comprehensive MURs started in 2005 and included an interview with the patient, preferably at the patient's home. The MUR in Finland includes assessment of medication through discussion with the patient, the physician and the homecare nurse (PGEU Ref: 10.10.14E002). In the Netherlands Pharmaceutical Home Counselling and Clinical Medication review are new approaches that are in a developing and researching phase. Pharmacists together with doctors review the medication of a patient and discuss the therapy plan with the patient. The pharmacist is paid 150 euros per consultation. The consultation includes exploring medication related problems and exploring medication taking skills based on the patient's actual use and experiences. In Portugal the Pharmacy Association developed a model for a national pharmacy-based 'brown bag' campaign. This campaign includes a medication review that targets patients aged 65 and over, in response to the health problems around a growing aged population, this was launched in 2007.

In Spain, The General Council of Pharmacists has carried out a programme of home care for elderly people. This included a medication review by interview with the patient and carer (PGEU Ref: 10.10.14E002).

Table 3.2 Medication review services in different countries

Country	Pharmacy medication review service (medication reconciliation and patient education)
UK	Medication Usage Reviews
Canada	Medschecks in Ontario
America	Medication Therapy Management
Australia	Home Medicines Reviews
Sweden	MURs in nursing homes, hospitals and healthcare centres
Finland	Comprehensive MUR
Belgium	MUR elderly patients
Netherlands	Pharmaceutical Home Counselling and Clinical Medication review
Portugal	Pharmacy-based brown bag campaign
Spain	Home MUR

The New Medicine Service

Research to support the New Medicine Service development involved work at UCL School of Pharmacy led by Professor Nick Barber. This included a survey (Barber *et al*, 2004) which involved 258 patients above 75 years and commenced on medication for stroke, CHD, asthma, diabetes or rheumatoid arthritis. The patients were followed up by a semi-structured telephone interview and a postal questionnaire at 10 days and 4 weeks.

At follow up one-third of the patients reported non-adherence to their new medicine and two-thirds had a medication related problem (MRP), concerns or need for further information. The study (Barber *et al*, 2004) showed that a significant proportion of patients newly started on a chronic medication quickly become non-adherent, often intentionally. Conclusions from this study were that patients need more support when starting on new medication for a chronic condition and that new services may be required to provide this (Barber *et al*, 2004). Further evidence included a randomised control trial (Clifford *et al*, 2006) which assessed the effects of pharmacists giving advice to meet patients' needs after starting a new medicine for a chronic condition. The pharmacists used a patient centred approach and gave advice to support patients' individual needs. In this study (Clifford *et al*, 2006) five hundred patients were randomised to intervention and control groups. At 4-week follow-up, non-adherence was significantly lower in the intervention group compared to control (9% vs. 16%, P= 0.032). The number of patients reporting medicine-related problems was significantly lower in the intervention group compared to the control (23% vs. 34%, P = 0.021). Intervention group patients also had more positive beliefs about their new medicine. Furthermore the intervention was also found to be cost effective (Elliot *et al*, 2008). This work led to the development and introduction of the New Medicine Service (NMS).

The NMS is a national service based in community pharmacies. The New Medicines Service provides opportunities for community pharmacists to widen their professional activity as experts in medicine and support patients with long term conditions. It aims to support patients to maximise the benefits of the medications prescribed. The New Medicine Service (NMS) was implemented on the 1st of October 2011 and was initially funded by the National Health System until 2013. The NMS provides support with medicines adherence for patients being treated for four conditions/therapy areas (1) asthma/ chronic obstructive pulmonary disease (COPD), (2) Type 2 diabetes, (3)

Antiplatelet/anticoagulant therapy,(4) Hypertension. To be eligible for the service the patient has to have been prescribed a medicine for one of the four conditions mentioned above for the first time. The NMS provides support for adherence in the first two months of the medicine being prescribed. The NMS is to support people in understanding why they need to take new medicines and prepare them for any adverse effects they may experience. The NMS has three stages to the service: patient engagement, intervention and follow up. Part of the importance of the NMS is that when a hospital initiates a new medicine for a patient being discharged, the hospital pharmacist can make a referral into the New Medicine Service. This provides reassurance that any information they provide to patients is reinforced by community pharmacy colleagues. This may improve therapeutic outcomes and decrease hospital readmission. Following its implementation, the Department of Health commissioned an evaluation of the service in 2012, to help determine if it should continue to be funded by the NHS. A research team led by the University of Nottingham, in collaboration with University College London, were awarded a grant to carry out the evaluation. The evaluation included a randomised controlled trial.

How the NMS trial was conducted

Community pharmacies in the East Midlands, South Yorkshire and London were recruited to take part in the study. A total of 61 pharmacies participated, although four withdrew after study initiation. Pharmacists recruited patients when they presented at the pharmacy with a prescription for a new medicine. After accepting the invitation to take part, the patients were randomised to receive either current practice (n=253) or the new medicines service (n=251). Current practice was the normal supply and advice associated with presentation of a prescription for a new medicine for a long-term condition which did not exclude any patients from contacting the pharmacist or another healthcare professional if they wished.

The primary outcome of the study was patients' adherence to their medicine. Secondary outcomes included patients' understanding of their medicines (Beliefs About Medicines Questionnaire (BMQ)), health status and healthcare costs. These data were gathered in self-completion postal questionnaires and a healthcare resource use self-completed diary (Elliot *et al*, 2015). Qualitative research was also conducted to assess how well the service was received by patients and healthcare professionals. Interviews were carried out with patients, pharmacists and GPs to characterise facilitators and barriers to service uptake, informed by individual and organisational perspectives. Thus the qualitative work explored operational dimensions of NMS to deepen and explain the technology appraisal (The Pharmaceutical Journal, 2014) (Elliot *et al*, 2014).

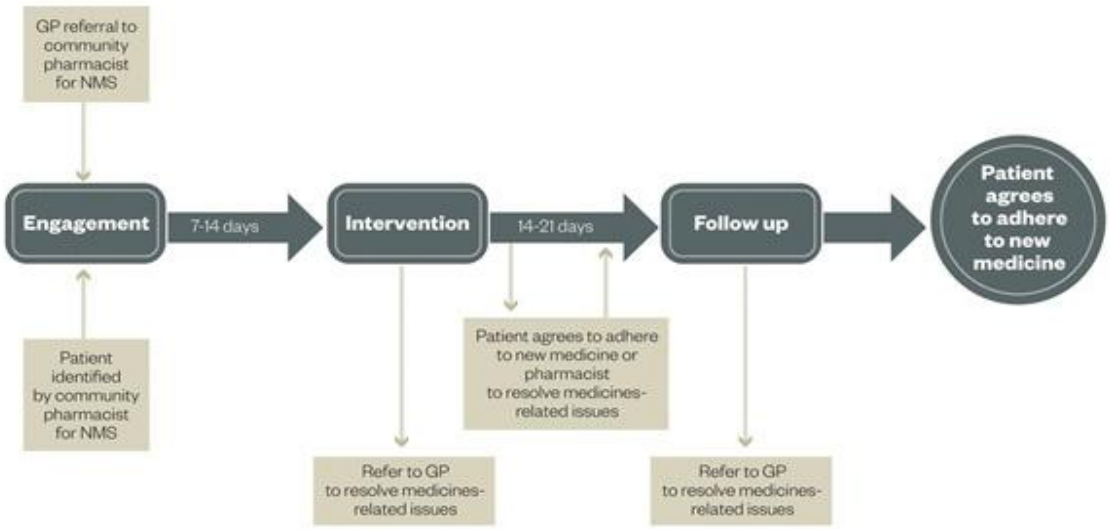
Findings from the randomised control trial to evaluate the NMS

Adherence to medication was assessed after ten weeks. Adherence to treatment was 64.9% in the current practice group and 74.7% in the NMS group (95% confidence interval 1.09–2.58; P=0.018) including patients who switched medicines after advice from their healthcare professional. When the analysis was restricted to patients who continued with the same medication, 60.5% were adhering to their medicine in the current practice group, compared with 70.7% in the NMS group (95% CI 1.06–2.62; P=0.027). An economic evaluation was conducted and suggested that in the long term, it is likely that NMS will deliver better outcomes at overall reduced costs. The cost to the NHS is less for NMS patients because their economic model predicts that these patients will have fewer adverse events and so will make fewer contacts with the health service than patients who did not receive the service. The study was not designed to show differences in use of NHS services during the ten weeks that it was conducted, but rather to model outcomes in the future based on adherence. However, during the ten weeks of the study, it was found that patients visited their GP fewer times and so delivering the NMS was cheaper.

The NMS report also recommended allowing access to patients' records, which could help facilitate the advice given to patients and also suggested benefits of GPs and pharmacists working closely together (Elliot *et al*, 2014).

Figure 3.2 New medicines service intervention

Adapted from -Elliott R, Boyd M, Waring J *et al.* (2014) Understanding and appraising the new medicines service in the NHS in England. Available from: http://www.nottingham.ac.uk/~pazmjb/nms/downloads/report/files/assets/basic-html/index.html#1 (accessed 14 August 2014) Citation: The Pharmaceutical Journal, 23/30, Vol 293, No 7824/5



Regarding continuity of this service, the NMS is included in the recently announced pharmacy contract funding settlement between the Pharmaceutical Services Negotiating Committee (PSNC) and NHS England. It was expected that the settlement would be a multi-year deal, the agreement is for 2014/2015, but the importance of the service has been acknowledged. Pharmacists are paid between £20 and £28 for each completed NMS they provide depending on the total number of patients who receive the service in the month (PSNC). Furthermore, of 11 495 community pharmacies in England, 10 553 (91.2%) had claimed for at least one NMS episode by January 2014 (Elliot *et al*, 2015).

Other pharmacy services in the UK

While reviewing the literature for pharmacy services in the UK several other services and roles were identified. However, some of these roles are still in their early stages of development and may not tackle long term illnesses. Examples include community pharmacy management of minor illnesses and Self Care pharmacy. These services will be discussed briefly.

Community Pharmacy Management of Minor Illness

A new campaign was approved by the Royal Pharmaceutical Society and English Pharmacy Board in 2014 to help with the increasing number of patients presenting in the A&E departments. This involved placing pharmacists within A&E departments to assist people arriving with medicines supply issues, and also referring patients to community pharmacies to deal with common ailments. The evidence behind this proposal included University of Aberdeen Minor Aliment MINA study. This service targets four conditions: musculoskeletal pain, eye discomfort, upper respiratory tract-related and gastro-intestinal disturbance. The MINA study showed that lower costs were associated with the management of these diseases in pharmacies compared with the other settings, and thus provides further evidence of the suitability of pharmacies to manage these conditions. Moreover, health professionals and patients need to be confident in the ability of pharmacists and their staff to manage minor ailments. Government policy is promoting community pharmacy as the preferred setting for the management of minor ailments.

There is evidence from other countries where similar policies have been introduced, that patient behaviour has changed and demand on high cost settings has declined (MINA Study, 2014).

Self Care pharmacy

This is not a new concept; people manage a large proportion of their ailments without consulting either a doctor or pharmacist. Yet pharmacists can play a key role in helping people to make informed self-care choices (WHO, 1996). In 2014, Self Care of patients was developed through UK community pharmacy services. A 'call to action' by the North East London Local Pharmaceutical Committee (NELLPC) has been promoted with a focus on improving patient outcomes. Definition of self care as defined by the Department of Health "the care taken by individuals towards their own health and well-being-including the care extended to the family and the community". The conditions targeted by Self Care pharmacy plans are long term conditions including COPD, asthma, heart disease, arthritis, diabetes and bipolar disorder. The potential impact of self care programmes on these conditions is supported by evidence from systematic reviews. Potential far reaching benefits to the NHS through self care pharmacy could involve improved quality of consultations, reduction in number of GP visits and outpatient visits, reduction in the number of hospital admissions and improved medicines use. The pharmacists delivering self care plans are trained in motivational interviewing and health coaching (which is a process that facilitates healthy, sustainable behaviour change by challenging clients to listen to their 'inner wisdom', identify their values and transform their goals into action). The Self Care service has been commissioned by Newham Clinical Commissioning Group (CCG) and allows pharmacists and patients to develop a joint care plan. Hospitals or GPs will refer patients to a participating pharmacy of their choice, where a self-care plan will be created. Three follow up sessions are then arranged over a 12 week period to empower behaviour change in patients to improve their health and wellbeing outcomes.

Expressions of interest were obtained from pharmacy contractors who wished to participate in the service with the plan for the service to go live in 2015. Self Care Pharmacy at NELLPC has received commissioning of £1.25 million to take the service forward. A question could be raised here regarding whether the intervention designed for this thesis could be incorporated into Self Care pharmacy service. Although Self Care pharmacy service targets heart disease, patients could also be referred to this service from hospitals and pharmacists' in the Self Care pharmacy programme are trained on behavioural skills (motivational interviewing and health coaching), Self Care pharmacy was in its very early stages of development when the design of the intervention for this study took place. Moreover, the primary outcome to be studied in this thesis is adherence to cardiovascular medication. Therefore, it was concluded that the intervention of the study matches criteria required for the New Medicine Service and also could go under a MUR service. Thus, the intervention for this study was designed to be incorporated into existing community pharmacy services such as the NMS and MUR service. This will be further discussed in chapter four of this thesis.

3.3-Barriers to community pharmacy services

It was important to explore barriers to pharmacy services to increase the understanding of the uptake of the intervention (pharmacy service) by patients and also to identify barriers that could prevent pharmacies/pharmacists from delivering these clinical services if appointed to the study. Community pharmacy has become recognized as an easily accessible source of advice in primary healthcare due to pharmacies long opening hours and easy access without an appointment. Pharmacists are believed to be competent and well trained health professionals and there are high expectations on how community pharmacies can be used (Saramunee *et al,* 2014).

Nevertheless, there is evidence behind the underutilisation of novel pharmacy services and that international uptake of such services has been disappointing (Gidman *et al,* 2012). Several studies have aimed to further examine barriers to the uptake of pharmacy services and identify factors affecting service use.

Barriers identified from the literature include:

Pharmacy accommodation and the pharmacy environment

Privacy is clearly an issue; patients could be unaware of existing consultation rooms. In addition, some patients think consultation rooms in pharmacies are used only for drug misuse clients (Saramunee *et al,* 2014). This increases the unwillingness of pharmacy clients to engage in private discussion regarding health without privacy. Certain public health services for example health checks for screening programs and 'flu vaccinations require hand washing facilities and secure internet access (Mc Naughton *et al,* 2011). Indeed 75% of community pharmacies in England are providing MUR services for which a consultation area is a minimum requirement, thus pharmacists may expect that the public would be aware of them (Saramunee *et al,* 2014). However, there still remains a huge variability between pharmacies in the appropriateness of their accommodation. Pharmacy accommodation has been identified as a main barrier in other parts of the UK, e.g advice on prevention of HIV/hepatitis in pharmacies in Scotland and in other countries, e.g. in Sweden, provision of advice on health promotion. Moreover, nearly two thirds of pharmacists in a survey in Canada felt that having a designated space in the pharmacy was very important in facilitating smoking cessation practice, whilst nearly half of participants in a study in Thailand (43%) thought the pharmacy setting was a barrier to smoking cessation counselling (Eades *et al,* 2011).

Secure internet and confidentiality

Pharmacies need to have secure internet connections to allow them to transfer patient identifiable data to other health providers' databases. Many pharmacies in England do not have the full access to the NHS network which is required for the efficient and secure transfer of information between pharmacy and general medical practices. Confidentiality standards and the degree of access permitted to staff within a pharmacy team remain important issues (Mc Naughton et al, 2011). The issue of confidentiality and concerns about other personal information remaining confidential has also been raised in other studies on barriers to pharmacy services use (Saramunee *et al*, 2014) (Gidman *et al*, 2012). This is an important aspect to be considered for the design of an intervention in community pharmacy, because there is a need to transfer patient discharge data from the hospital to community pharmacies.

Access to patient data

Clinical medication reviews can be optimised if pharmacists have full access to patients' medical records. When such access is not completely available this can minimise potential of pharmacists' interventions to improve adherence and resolve medication related problems. This barrier has been recognised and also the need to release full professional potential to improve patient outcomes. In the UK initiatives such as Electronic Prescribing have enabled prescribers, such as GPs and practice nurses, to send prescriptions electronically to a pharmacy of the patient's choice. This makes the prescribing and dispensing process more efficient and convenient for patients and staff. Moreover, recently it has been announced that community pharmacists across England will be given the opportunity to access patients' Summary Care Record (SCR), with the patient's consent, to support their care and treatment. This will allow pharmacists to support patients with better informed and tailored care.

Pharmacists' time

High dispensary work load is a barrier that is highlighted in many studies due to increasing prescriptions. This has been reported to cause stress on pharmacists and even a desire to leave pharmacy as a profession. This also has a negative impact on the interest and ability of pharmacists to deliver clinical services (Saramunee *et al*, 2014). In a review on pharmacy services (Eades *et al*, 2011) lack of time was identified as a main barrier to providing advice on prevention of HIV/hepatitis by pharmacists and support staff in Scotland. Time was also a barrier to providing smoking cessation counselling in the USA. Thus time is considered a crucial barrier to service delivery. Recent moves toward large dispensing factories, internet pharmacies and robotics may not be universally welcomed; but these together with trained accuracy checking technicians could free up pharmacists' time for other services (Saramunee *et al*, 2014).

Training

A need for training has been identified in a number of surveys on different public health services. Training is essential to develop confident and competent staff (pharmacists and pharmacy technicians). Training has been reported as an essential need in different studies; over half of pharmacists in a study in Scotland reported that attaining additional pharmaceutical public health knowledge was a priority for their practice and also felt that lack of training was a main difficulty in providing advice on prevention of diseases such as HIV and hepatitis. Moreover, pharmacists in a study in New Zealand felt that training was a barrier to providing alcohol screening (Eades *et al*, 2011). Several studies have also noted that pharmacists need further training in communication; counselling and motivational skills and that these should be included early in undergraduate pharmacy courses, with an aim, at improving professionalism (Saramunee *et al*, 2014) (Mc Naughton *et al*, 2011). Thus, training can positively affect pharmacists' attitudes and behaviours in relation to health promotion and provision of advice with medicines.

Therefore, it can be concluded that for an intervention to be feasible it would be important to offer training to the pharmacists that take part.

Lack of General Practitioners (GPs) support

There is evidence that GPs do not support pharmacy public health services, which has been an issue with MUR service (Saramunee *et al,* 2014). Uptake of community pharmacy services is likely to improve if endorsed by GPs and integrated with other primary care services. Collaboration at a primary care level is required for signposting, referring into existing systems, avoiding duplication and enabling individuals to select their preferred public health service provider (Saramunee *et al,* 2014). Research in UK demonstrates that GPs in general favour the concept of community pharmacists helping patients understand their medicines, but have subsequently been disappointed with the MUR service. Major problems include inappropriate clinical recommendations, provision to less suitable patients (example: patients with few medicines and no clear medicines related problems) and the MUR service not being integrated with other healthcare provision. However, where therapy changes are recommended to prescribers following MURs, at least half appear to be implemented (Saramunee *et al,* 2014). Furthermore, evidence shows that community pharmacists often feel that their professional competence is underestimated by their medical colleagues. Also community pharmacists and doctors very often lack opportunities to meet in person and discuss various aspects of patient care (PGEU Statement on Role of Pharmacist in Self-Care R: 10.10.14E 002). In 2015, the English Pharmacy Board launched a campaign to integrate community pharmacists into GP practices. This will enable community pharmacists to work more closely with GPs and other healthcare professionals in primary care. In this proposed role, the pharmacist would handle medicines-related issues in general practice, liaising with providers such as hospitals and care homes to reduce errors, review medication and address poly pharmacy (Robinson, 2015).

This took place through a new £15million scheme to fund, recruit and employ clinical pharmacists in GP surgeries launched by NHS England. The scheme will involve a three year initiative. This will give patients the additional support of an expert pharmacist in their GP surgery (NHS England, 2015). Some of the examples of the benefits patients can expect from pharmacists would include extra help to manage long-term conditions, specific advice for those with multiple medications and better access to health checks. Pharmacists can be employed directly by general practices to help patients, while also easing GP workload and improving communication between general practice, hospitals and community pharmacists. The scheme will focus on areas of greatest need where GPs are under greatest pressure, and aims to build on the success of GP practices already employing pharmacists in patient-facing roles (NHS England, 2015).

To summarise, barriers to implementing clinical services run by community pharmacists in the UK can be summarised into (Boyd *et al*, 2013): (1) insufficient integration into patient pathways, (2) poorly developed relationships between GPs and pharmacists, (3) lack of access to information and (4) lack of willingness of pharmacists to provide the service. In order to implement pharmacist-led interventions there is a need to ensure that pharmacists have adequate information about health of the patient and medication. There is also a need to support collaboration between community pharmacists, GPs and other health professionals by a range of interventions, from integrated remuneration systems to personal contacts, solutions that promote greater mutual respect and professional trust (PGEU Statement on Role of Pharmacist in Self-Care R: 10.10.14E 002).

Remuneration for pharmacy services

Implementation of pharmacy services are costly and time consuming. In particular in smaller pharmacies and in rural areas pharmacy services may be difficult to implement without financial support. It is important to ensure that pharmacists receive remuneration for the service and that it does not imply additional costs to pharmacy for undertaking these services. A review of remunerated pharmacy clinical care services (Houle *et al*, 2014) described 60 remunerable pharmacist clinical care services across North America, Europe, Australia and New Zealand. Remunerated services included medication reviews, chronic disease management, prescription adaptations, emergency hormonal contraception counselling, smoking cessation counselling and minor ailment programs. The review (Houle *et al*, 2014) recommended that although lack of remuneration is a commonly expressed barrier preventing pharmacists from providing more clinical care services, the mere presence of a remuneration scheme is insufficient to ensure uptake in practice. For example, some programmes report very low numbers of participating pharmacies and others report a high initial expression of interest but short persistence or very low patient enrolment over time. Therefore, when designing and evaluating programs commonly reported barriers to uptake should be examined. These include insufficient remuneration for services offered, burdensome paperwork and complicated claims submission processes.

The review (Houle *et al*, 2014) also concluded from pharmacist opinion surveys that pharmacists consider the fees for their services to be insufficient considering the time required to provide the patient care. Therefore, front- line pharmacists should be invited to payers' discussions and processes should be piloted prior to rollout to identify administrative issues early. Finally, remuneration models for clinical care services should consider pharmacies' changing business models from primarily dispensing based revenues to a blend of dispensing and patient care reimbursement income (Houle *et al*, 2014).

The table below lists remuneration programmes in the UK. The intervention for our study can be claimed for when delivered through a MUR or NMS service. Both these services are funded by the NHS as illustrated below:

Table 3.3-Pharmacy remuneration programs in the United Kingdom (Houle *et al*, 2014)

Table adapted from- Houle K. D., Grindrod K A., Chatterley T. *et al.* (2014) Paying pharmacists for patient care: A systematic review of remunerated pharmacy clinical care services *Can Pharm J (Ott)*; 147:209-232.

Program	Year started	Location	Payer
Starting Fresh and Smoke Free Pharmacy Services	2008	Scotland	National Health Service Greater Glasgow and Clyde
Community Pharmacy Heart Failure Service	2005	Scotland	National Health Service Scotland
Medicines Use Reviews	2005-2008	Scotland, England and Wales	National Health Service
Discharge Medicines Review Service	NA	Wales	National Health Service Wales
Minor Ailments Scheme	2005	England	National Health Service
	2009	Northern Ireland	Health and Social Care in Northern Ireland
Appliance Use Review	NA	England	National Health Service
New Medicines Service	2011	England	National Health Service
Emergency hormonal contraception program	NA	Wales and Scotland	Bridgend Local Health Group

There is also a need to understand different stakeholders' views on services provided by community pharmacies:

3.4-Pharmacists' and stakeholders views on pharmacy services

It was essential to research stake holders' views regarding pharmacy services. This is to establish the feasibility and the uptake of an intervention when delivered at a community pharmacy level. Below are views from the literature examining patients' views and pharmacists' views regarding community pharmacy clinical services.

What are consumers' (patients') views?

The UK policy and pharmacists' professional organisations have emphasised the potential of community pharmacists to extend their roles in patient care services. Nevertheless, the general public's views are important to be understood for the successful uptake of these services. Evidence shows a generally wide satisfaction of consumers with health advice and services given by pharmacists (Anderson *et al*, 2004) (Eades *et al,* 2011), but a deeper understanding of patients' views is advocated. Numerous studies have examined patient's views on the services provided by pharmacists and found that patients' consider pharmacists to be primarily involved in medicine supply and as drug experts rather than experts on health and illness. Awareness of the pharmacist's extended role is generally low therefore, services may be underutilised (Gidman *et al,* 2012) (Anderson *et al*, 2004). Many pharmacy users do not expect to be offered clinical services by pharmacists. Also patients are often reluctant to trust pharmacists to deliver unfamiliar services particularly those perceived to be 'high risk' and would rather trust pharmacists with low risk illnesses and OTC medicines. Thus, confidence in pharmacists providing public health services is low (Eades *et al,* 2011).

Some patients perceive that trusting pharmacy services could, even seriously threaten their health and that high risk illness should be preferably managed by a physician (Gidman *et al,* 2012). For example health screening results by pharmacists could not result in prescribed treatment or be recorded in medical records. A concern relating to the commercial context and retail environment of community pharmacy also has a negative effect on consumers' views, leading to doubts regarding the commercial motives of pharmacists in providing health services (Mc Naughton et al, 2011) (Gidman *et al,* 2012). In the UK, individuals register with one GP based in a practice. Therefore, the patient becomes familiar with one GP, or a limited number of GPs. This relationship between GP and patient allows rapport to develop, which leads to trust. Pharmacists on the other hand take a more separated role in the dispensary hence, limiting public interaction. Moreover, hierarchies in healthcare also play a role in patients' perceptions of pharmacy services. Thus GPs are viewed as established authority figures, who are seen to 'tell the pharmacist what to do' (Gidman *et al*, 2012). Patients' perceive that uptake of certain health services at pharmacies are a waste of time because these services are existent at GP surgeries and that NHS services should be free. Finally, community pharmacy services need to be integrated with other primary care services. Currently, it seems that role expansion gives rise to duplication of tasks because health professionals' roles are not complementary, or could appear as competitive (Mc Naughton et al, 2011). This is likely to increase costs rather than reduce them. Policymakers should be aware that, without considerable changes to systems or institutional aspects of service delivery, it is improbable that the public will trust pharmacists to deliver unfamiliar services (Gidman *et al,* 2012).

What are pharmacists' views?

In order to understand and assist the behaviour changes associated with providing health services in community pharmacy, it is important to establish the beliefs of pharmacists

regarding this role. A review of pharmacists' perceptions of pharmacy services found that although pharmacists valued the health improvement role, they are more comfortable with medicine related health improvement work (Anderson *et al*, 2004). Other studies show that pharmacists' perceive their potential role in health promotion and prevention as very significant but recognise a wide gap between ideal and actual levels of involvement (Laliberté *et al*, 2012). Other issues include concerns pharmacists have of being intrusive, and believe that they need more support to provide public health services. Moreover, pharmacists fear the lack of demand and expectation of a negative reaction from customers (Eades *et al*, 2011).

Different qualitative studies through interviews and focus groups have demonstrated that most pharmacists are confident in their competence to provide health services, viewing their ability to deliver as being limited mainly by workload and lack of time (Saramunee *et al*, 2014), (Anderson *et al*, 2004). The majority of pharmacists in a survey in Scotland agreed (63%) or strongly agreed (16%) that public health is important to their practice and a little over half agreed (48%) or strongly agreed (8%) that they were public health practitioners. Pharmacists and support staff taking part in focus groups in Sweden on the whole welcomed their role as a health promoter. However, it was noted that not all pharmacists and support staff felt this way and preferred to develop activities in areas in which they received their basic training (Eades *et al*, 2011). In order to improve the health services provided in community pharmacy, training must aim to improve pharmacists' confidence in providing these services. Confident, well trained pharmacists could be able to offer health services more proactively which is likely to have a positive impact on customer attitudes and health (Eades *et al*, 2011).

End of Chapter Three

The three previous chapters serve as a valid base of information to design a study. Chapter one confirmed the need for further research regarding management of cardiovascular disease. This chapter demonstrated that cardiovascular disease constitutes 30% of all cause mortality globally and burdens from this disease are still escalating; unless proper measures of primary and secondary prevention strategies are addressed. This chapter included evidence of the effect of non adherence to medication on outcomes of cardiovascular diseases, showing that promoting adherence to lifesaving medicines after cardiac diseases, is an important area to research and remains challenging. Therefore, from chapter one it became apparent that a study tackling adherence to secondary prevention medication would be pertinent to health care needs. Evidence from chapter one showed that one of the strategies to tackle non adherence to cardiac medication could be pharmacy care.

Chapter two reviewed previous evidence and examined this strategy through a systematic review of forty two randomised controlled trials. The review concluded that pharmacy services could serve as an effective strategy to improve adherence. Twenty six out of the 42 reviewed trials had statistically significant effects on improving adherence to cardiovascular medication. Conclusions drawn from this review included; a behavioural intervention (motivational interviewing) to improve adherence to cardiovascular diseases is an area that requires further investigation and face to face and telephone pharmacist consultations could be effective methods in improving adherence to cardiac medication. The systematic review in chapter two also showed that further research to improve adherence to medication in patients with acute coronary syndromes is needed. From chapters one and two the disease to be studied and the primary and secondary outcomes for the design of a new study were supported.

Methods to deliver a pharmacy intervention were researched in chapter three that examined existing UK pharmacy services. Chapter three; highlighted potential pharmacy services (MURs and NMS) into which an intervention could possibly be incorporated. Chapter three also examined issues such as the beliefs of consumers and pharmacists regarding community pharmacy services and roles. Therefore, it became apparent that

the disease to be studied is acute coronary syndromes and also the primary outcome to be researched is adherence to secondary prevention medication. In addition the strategy to tackle adherence would be pharmacy care and this might be achieved by designing an intervention incorporated into existing UK pharmacy services, conducted by community pharmacists, through collaborations with hospital pharmacists and GP surgeries. Chapter four will discuss the methodology that led to the design and development of such an intervention.

Chapter Four

Methodology of a Feasibility Pilot Controlled Trial

4.1-Field work

Preliminary field work that led to the study design and methodology April 2012

Preliminary field work was undertaken by the researcher. This involved personal communication with relevant individuals and observations at recruitment sites. Discussion took place between the researchers' at UCL School of Pharmacy (UCLSOP) and consultant pharmacist from the London Chest Hospital regarding the target population to be studied (patients with acute coronary syndromes). The consultant pharmacist confirmed findings from the literature, which demonstrate that patients' who stop their medications after a PCI (especially antiplatelets) risk having a re-infarction (a second myocardial infarction) and may need to be readmitted to the hospital. This had been previously recognised by the hospital and lead to the design of an antiplatelet booklet by the pharmacy department. This booklet is offered to every patient prior discharge. In addition, each patient is counselled by a hospital pharmacist. Therefore, designing a study to enhance adherence to these lifesaving medications would be crucial and of benefit for these patients. The time to reinforce information to patients was also discussed. The consultant pharmacist highlighted that information regarding the medication and the disease is mostly needed after discharge, once the patient is in the community. Therefore, it became evident that the intervention would be best if delivered by community pharmacists. Discussions also included; the competency of community pharmacists to uptake such an intervention and also if further training on secondary prevention medication after a myocardial infarction would be important.

The research team at UCLSOP were also informed by the consultant pharmacist that 30% of patients who suffer a myocardial infarction and are admitted to the LCH are from ethnic minorities, in particular South Asians. The concept 'ethnic minority' refers to many different ethnic groups of extreme heterogeneity. This concept is used for groups that share minority status in their country of residence due to ethnicity, place of birth, language, religion, citizenship and other cultural differences. Members of these groups are considered to practice different cultural norms and values from the majority culture

and often a different mother tongue (Scheppers *et al*, 2006). The UK contains a culturally diverse population with ethnic minorities accounting for almost 8% of the population, in the 2001 census. The largest ethnic minority includes Indians, followed by Pakistanis, mixed ethnic backgrounds, Black Caribbean, Black Africans and Bangladeshis. In addition, there is about 500,000 ethnic Middle Eastern living in the UK (Patient.co.uk). Cardiovascular disease is high in all ethnic groups as well as in the general population. However, it is the South Asians who have the highest prevalence of coronary heart disease. South Asian refers to a heterogeneous population, with important differences in diet, culture, and lifestyle among different South Asian populations and religions. Multiple studies of migrant South Asian populations have, however, confirmed a 3- to 5-fold increase in the risk for myocardial infarction and cardiovascular death as compared with other ethnic groups (Gupta, 2006). In an analysis of age-standardized coronary heart disease (CHD) mortality in Canada over a 15-year period, South Asians had the highest CHD mortality compared with individuals of Chinese and European descent. In addition, South Asians are prone to developing CHD at a younger age, often before the age of 40 years in men (Gupta, 2006). Therefore, there is a need to look closer at this particular ethnic group. In addition, very few people from ethnic minority groups attend cardiac rehabilitation programs. Furthermore, there has been little research on cardiovascular medication compliance among ethnic minorities, despite the relatively high prevalence of cardiovascular conditions in these groups (Carter and Taylor, 2003) and a large proportion of research is performed in the UK that presently does not include enough ethnic minority patients, and patients from South Asian backgrounds meaning that results may not necessarily correlate to patients from ethnic groups (patient.co.uk). The LCH is located in an area with a high ethnic minority population and as discussed above, further research in this patient population would be essential. This helped determine the decision regarding the choice of the study site. Moreover, three observational visits to cardiac centres were arranged for the researcher. One to the Chest Hospital Barts and London NHS trust, the second to the cardiac services at the Heart Hospital and a third to the cardiac unit at Imperial College Healthcare NHS trust. These visits were arranged to gain knowledge of hospital pharmacy system in the UK and also observe usual care by hospital pharmacists. During the visit to the Heart Hospital, the

lead pharmacist provided contact details of other cardiac centres' an email was sent to these other centres to discuss the viability of participating in the study (Guys and Thomas, Kings College Brompton, St. George, Imperial, Royal Free). Response was received from the contacted centres. However, it became clear that the study would need to commence (patient recruitment) in a single hospital site because recruitment would be undertaken by a single researcher and that the intervention would be more beneficial if conducted in community pharmacies not in the hospitals.

Other discussions between the researchers at UCLSOP included the type of the intervention. Background literature had revealed that a behavioural approach may be effective in improving adherence. This led to a consultation with a psychologist at the school. This was to further understand motivational interviewing as an approach to enhance adherence to medication and if motivational interviewing could be delivered by a community pharmacist. Training on motivational interviewing was also considered. At this time only few studies involving a pharmacist using motivational interviewing could be found. This supported the idea that further research in this field would be beneficial. Moreover, motivational interviewing had only recently been introduced into the undergraduate curriculum at UCLSOP. Discussions and background research also led to the idea that the intervention would be designed as a randomised control trial, where the intervention group would receive a consultation involving a motivational interview session and the control would receive usual pharmacy care both in the hospital and community. However, due to the complexity of conducting a randomised control trial it was decided to be conducted as a feasibility/pilot study and to develop a methodology that can in the future be adapted to design a larger randomised control trial.

After deciding the recruitment site the aim was to gain support of the community pharmacies and to perceive the interest to take part in the study. A meeting was organised with the secretary at North East London Local Pharmaceutical Committee (NELLPC). The meeting provided information regarding community pharmacies in six

London Boroughs (Tower Hamlets, Waltham Forest, Redbridge, Barking, Havering and Hackney), this included 306 pharmacies. These pharmacies would be invited to participate in the study. Further discussions involved services provided by community pharmacies Medication Use Reviews and The New Medicine Service, especially because hospital patient referral into community pharmacies could take place through the NMS. It was reinforced through the meeting that the intervention could be incorporated into a counselling session of a community pharmacist, also that this could be an opportunity to establish continuity of care that can extend from the hospital to the community pharmacy. Further discussions included reimbursement for the pharmacy services and training for community pharmacists. The NELLPC agreed to support this new study. This support would include; help with recruitment of pharmacies and also collaboration for the training sessions. NELLPC agreed that the study and training sessions could serve as continuous professional development for the community pharmacists and also be an opportunity to introduce new counselling skills such as motivational interviewing.

After approval for the intervention to be conducted in community pharmacies it became important to map the post codes of patients' admitted to the London Chest Hospital. This is to ascertain if the admitted patients lived in the six London Boroughs. Mapping revealed that the majority of the admissions were from around the area of the hospital. Furthermore, to develop the research protocol that would involve motivational interviewing skills. A meeting with an expert clinical psychologist from the University of Buckingham was arranged. This meeting was to determine the compatibility of the protocol with motivational interviewing techniques. The psychologist provided references and constructive input into the protocol. Clinical observation in a UK community pharmacy was also arranged for the researcher to observe Medication Use Reviews (MURs) and the New Medicine Service (NMS). Conclusions drawn from stake holders included; difficulties arise when implementing the NMS especially regarding patient follow up for the second consultation. Patients do not attend the second NMS consultation regularly; therefore it is often conducted by telephone. This was discussed with the psychologist. This is to determine if a motivational interview session could be

conducted by telephone. It was concluded from previous evidence that the intervention can be delivered by telephone (Teeter and Kavookjian, 2014). Finally, a meeting took place with the clinical psychologist at Buckingham to discuss arrangement for community pharmacists training. After the discussions above, numerous risks to the study should be taken into consideration, these could have an impact on the workability of the study.

Risks and contingency

There are several risks to the study these include recruitment risks; not achieving the target sample size, recruitment by hospital pharmacists could lead to loss of patients inside the hospital and further loss of patients during the follow up.

Risks at community pharmacy level; not all patients attending the counselling sessions at the community pharmacies or the patients' discharge letters are not forwarded to the community pharmacies. Participation risks; not a sufficient number of community pharmacies willing to participate in the study, the number of community pharmacists interested in motivational interviewing training and are willing to deliver the intervention.

Risks when delivering the intervention; motivational interviewing is a new counselling method; to what extent will the pharmacist follow motivational interviewing techniques? Therefore, issues with reliability. Risks of data loss not all patients return the adherence and BMQ questionnaires.

With these risks considered, the methodology of the study was developed as a feasibility study examining aspects of delivery and workability. The study examined feasibility at a community pharmacy level (for both recruitment and delivery of an intervention), feasibility at the hospital site (for patient recruitment); feasibility at patient level (uptake of an intervention) and finally feasibility regarding data collection (researcher).

Aims and objectives of the research study

Aim: To investigate if a pharmacy care intervention involving motivational interviews and referral to community pharmacy services in coronary heart disease patients could improve adherence to secondary prevention medication.

Specific objectives are:

- Establish the viability and impact of an intervention after patient's discharge from hospital, on adherence to cardiovascular medication.
- Investigate whether such an intervention is practical and feasible to deliver in UK community pharmacies.
- Examine how communication between healthcare professionals' community and hospital pharmacists, at the interface between primary and secondary care can improve medication reconciliation for patient after a coronary event.

4.2-Methodology

Study design

This was a feasibility study, set up as a pilot clinical trial study to examine potential impact of an intervention. It included an integral process evaluation to examine operational aspects from perspectives of all stakeholders. CONSORT guidelines are used widely to ensure robust reporting of clinical trials. Whilst this feasibility/ pilot study did not conform to all aspects of trial methodology, CONSORT can be used to illustrate the relevant issues in the design and methodology.

Figure 4.1CONSORT checklist for RCT protocols: applied to this study:

Section And topic	Description
Title	Randomized control trial not in title (this would not be an accurate description).
Introduction	Scientific background and explanation of rationale was provided.
Methods participants	Eligibility criteria for participants and the settings and locations where the data were collected were all specified.
Interventions	Precise details of the interventions intended for each group and how and when they were actually administered were provided.
Objectives	Specific objectives and hypotheses were stated.
Outcomes	Primary outcome -self report adherence with coronary artery disease medication, using a validated self-report instrument Validated scales-Morisky scale, BMQ. Secondary outcomes- B.P, LDL-C, beliefs about medicines, measures of the feasibility study including costs and pharmacist time were specified.
Sample size	How the sample size was determined was reported, however, this was a feasibility pilot study so did not follow a calculation based on anticipated change in the primary outcome measure.
Randomization - Sequence generation	Pharmacies were randomized into intervention and control groups. Randomization was by using a table of random numbers. However, simple randomization of the entire sample was not possible.
Randomization - Allocation concealment	Concealment of randomization from the researchers until intervention was assigned.

Randomization - Implementation	Randomization was by an independent statistician at UCL School of Pharmacy.
Blinding (masking)	The researcher was blinded during the data collection and analysis. It was not possible to blind the community pharmacists delivering the intervention or the hospital pharmacists and the patients due to the nature of the intervention.
Statistical methods and analysis	Independent T tests, Chi-square test. Analysis followed an intention-to-treat analysis.

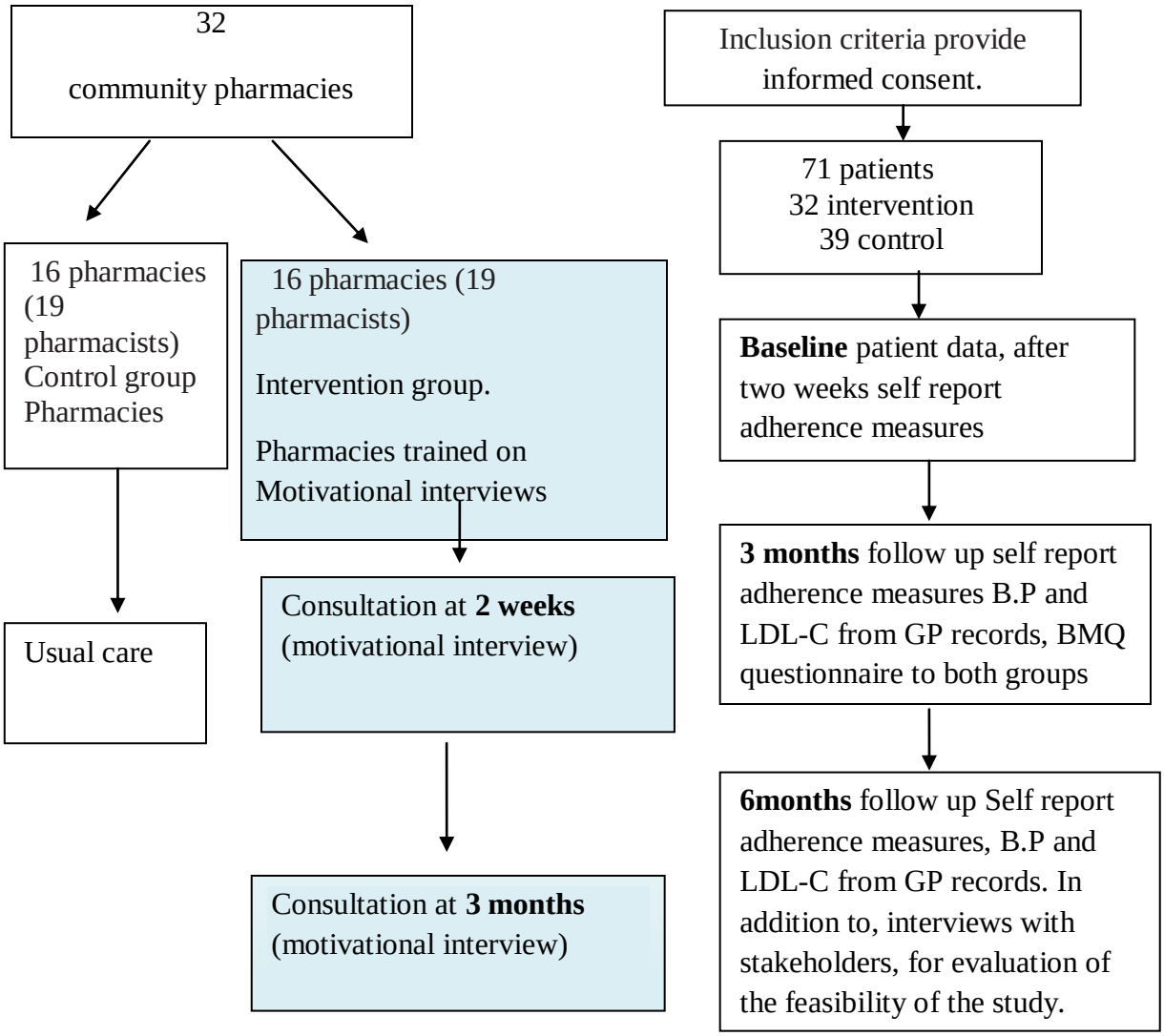
In the evaluation of health care interventions randomised control trials (RCTs) are considered as the "gold standard". Employing an experimental design with adherence to the RCT principles enables an evaluation in which the impact can be attributed to the intervention, rather than known or unknown extraneous factors (Geoffrey and Harding, 2015). However, while seen as a gold standard it is not always possible to achieve due to the fact of being expensive, especially if conducted across different locations/sites. However, if a smaller number of sites were to be included this could limit the generalizability of the findings; in addition, blinding in an RCT is not always possible (Geoffrey and Harding, 2015). Other possible limitations could involve sources of bias such as selection bias, allocation bias, intervention bias, outcome bias and withdrawal bias. This study was designed as a prospective controlled feasibility/pilot, intervention study. Although the study was not designed as a RCT but as a feasibility study, it had a control group and methods of randomisation were employed.

The key features in the design of an RCT involves the following; two arms; intervention and control, to assess differences in treatment outcomes, randomisation to avoid systematic differences between the two arms, blinding of the research team to avoid bias in data collection /analysis, blinding of the participants to avoid placebo or research effects, assurance of the fidelity to the protocol regarding intervention delivery, choosing robust outcome measures and employing a systematic approach to data collection (Geoffrey and Harding, 2015).

In this study randomisation was at pharmacy level, the pharmacies, after enrolment, were allocated into two groups' intervention and control to avoid contamination. Contamination could arise if patients in the control group attended intervention pharmacies. Randomisation was achieved by an independent statistician at UCLSOP (LW) and concealed from the research team to avoid selection bias. Blinding procedures were employed. These included blinding of the researcher for data collection and analysis. However, it was not possible to blind community pharmacists, hospital pharmacists or the participants. The primary outcome measure was adherence to cardiovascular medication and the secondary outcomes included blood pressure and LDL-C. These outcomes were selected after reviewing previous literature with a similar methodology to reduce outcome choice bias. A protocol was designed and followed closely to reduce intervention bias. In addition, an intention-to-treat analysis (ITT) in which all patients assigned to one of the treatments regardless of whether or not they completed or received the intervention was undertaken to avoid withdrawal bias.

A systematic approach to the collection of data was used. Furthermore, measures regarding the feasibility of a randomised control trial were achieved through interviews and questionnaires with all stake holders. It was decided by the research team that the intervention should be delivered at 2 points of time, 2 weeks and 3 months. This is because evidence has shown that adherence to medication decreases with time and therefore, reinforcement of the importance of adherence to cardiac medication could be of benefit at these timings. It was as also determined that follow up of patients would be 6 months because the study is a pilot study. Moreover, data collection would coincide with these timings. Please refer to the figures 4.2, 4.3 below regarding the study design.

Figure 4.2 Study design



The diagram below (Figure 4.3) illustrates the steps of the overall methodology of the study.

The first diagram (4.3a) outlines:

1-recruitment of community pharmacies and pharmacists

2-training of community pharmacists

3-pharmacists deliver the intervention

The second section (4.3b) illustrates:

1-recruitment of patients at the LCH

2-enrollment of patients into the study

3-allocation to pharmacies

4-patients receive the intervention

It also outlines:

1-recruitment of GPs

2-patient follow up by research pharmacist

3-data collection by research pharmacist and finally data analysis and results

Figure 4. 3a Overall methodology design

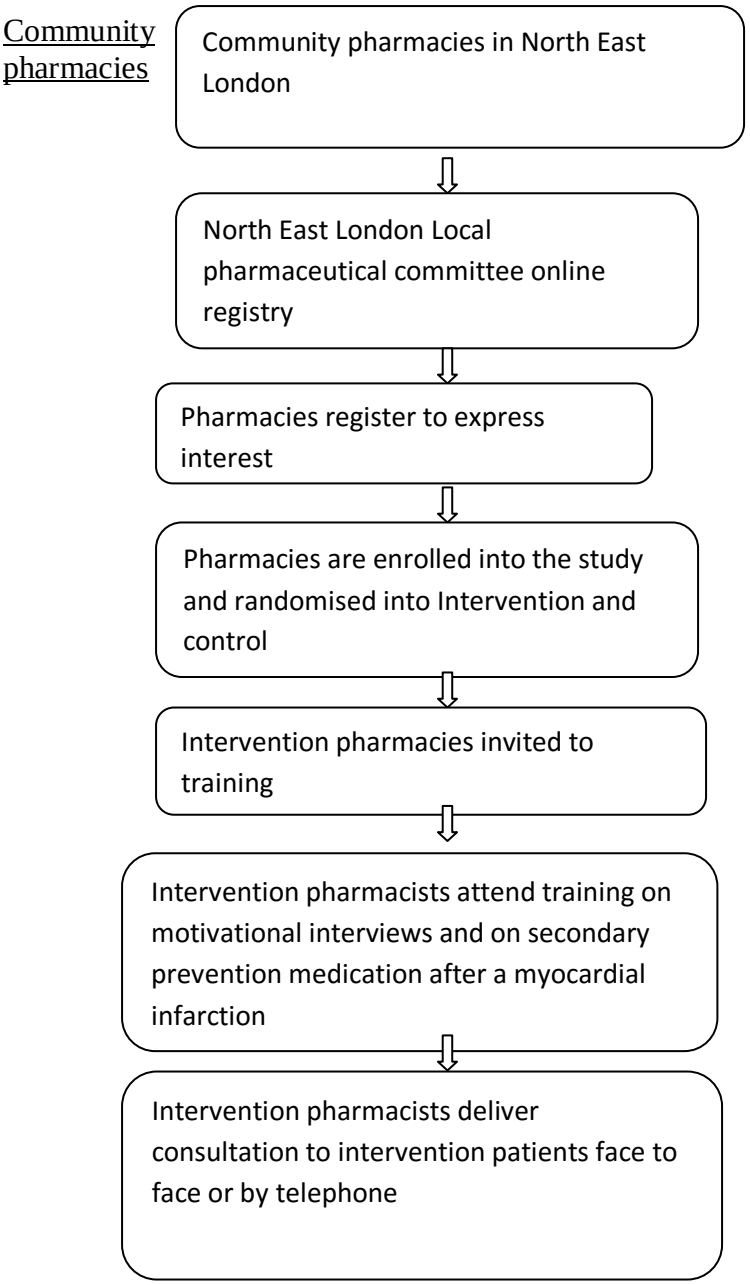
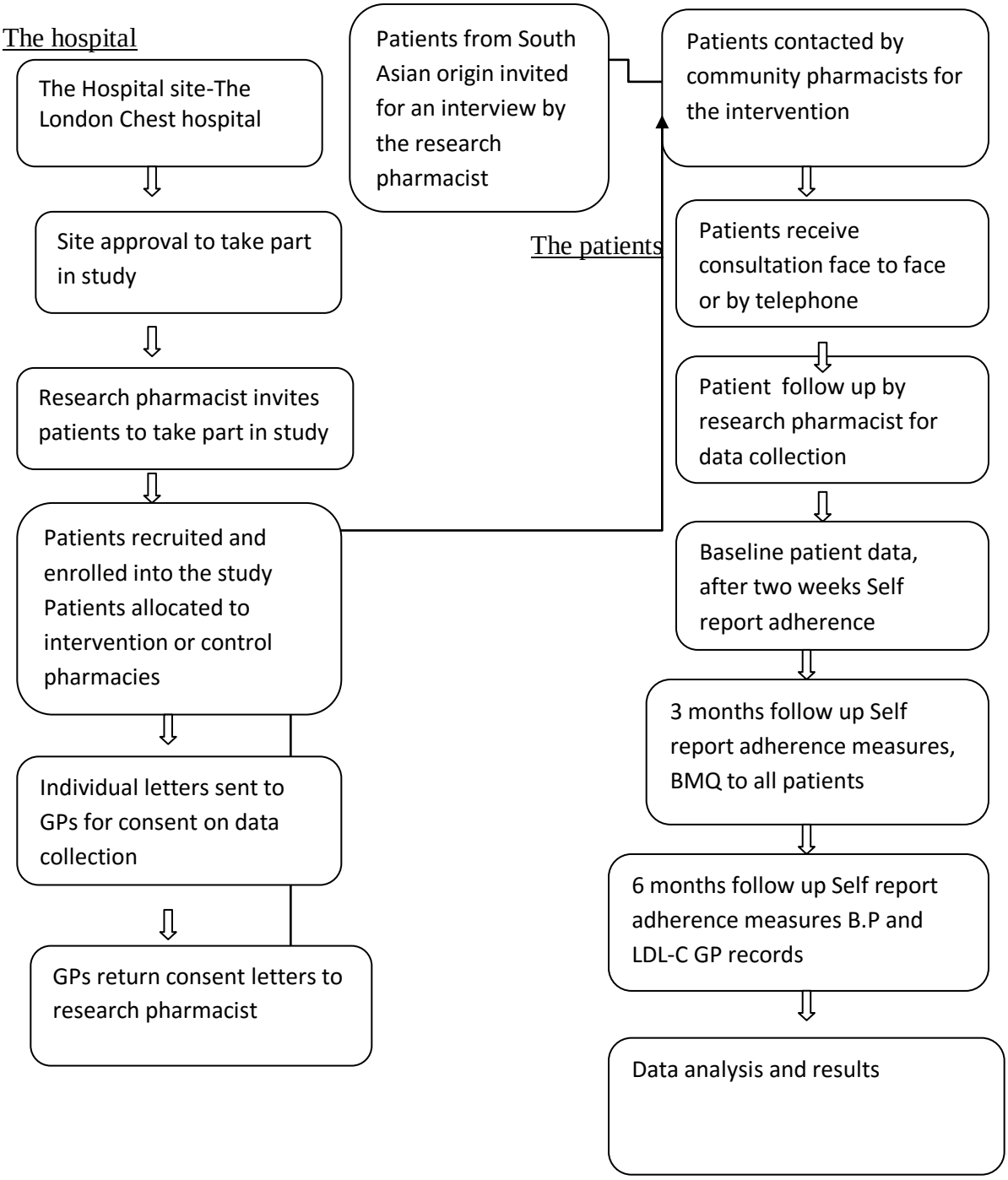


Figure 4.3b


The hospital
The Hospital site-The London Chest hospital
Site approval to take part in study
Research pharmacist invites patients to take part in study
Patients recruited and enrolled into the study Patients allocated to intervention or control pharmacies
Individual letters sent to GPs for consent on data collection
GPs return consent letters to research pharmacist
Patients from South Asian origin invited for an interview by the research pharmacist
The patients
Patients contacted by community pharmacists for the intervention
Patients receive consultation face to face or by telephone
Patient follow up by research pharmacist for data collection
Baseline patient data, after two weeks Self report adherence
3 months follow up Self report adherence measures, BMQ to all patients
6 months follow up Self report adherence measures B.P and LDL-C GP records
Data analysis and results

Study population

This included coronary heart disease patients with a discharge diagnosis of acute coronary syndrome (ACS). Patients discharged from the London Chest Hospital if eligible were enrolled into the study.

Sampling strategy

Study site

The London Chest Hospital (LCH) in Bethnal Green was chosen as the study site. The London Chest Hospital was selected as the study site due to the following facts (1) a large cardiac centre, a large number of patient admissions, a large number of pharmacy staff (2) the pharmacy staff are specialised in cardiovascular diseases (3) the site had established links with community pharmacies surrounding the hospital through the Local Pharmaceutical Committee (4) around 30% of patients are from an ethnic minority background (5) the location of the hospital is in Tower Hamlets that has the fifth highest premature mortality rate from CHD in the country (NHS, 2011). The London Chest hospital is part of Barts and the London, one of Britain's leading healthcare providers. *Bethnal Green* is a district in East London and is *part* of the London Borough of *Tower Hamlets*. The borough has a population of 220,000 which includes one of the highest ethnic minority populations in the capital. The London Chest Hospital was founded in 1848 to offer treatment to the people of the City and east London similar to that offered by the Brompton Hospital (founded in 1841) to patients in west London. Tuberculosis (TB) was a major endemic killing disease at that time, accounting for 20% of all deaths. In 1970 the hospital became one of the pioneers in the investigation and treatment of coronary artery disease. New drug therapy particularly streptomycin, led to a dramatic decline in the incidence of TB, this coincided with the development of heart valve surgery at the LCH. In 2006 the London Chest Hospital launched an award-winning emergency Heart Attack Centre and in 2012 the London Chest Hospital became part of Barts Health NHS Trust. The trust serves a population of 2.5 million in east London and beyond.

A single site was chosen because recruitment was to be undertaken by a single researcher and also due to lack of resources and time for a multicentre trial.

Pharmacies

The primary care pharmacies were the pharmacies in North East London that are located around the London Chest Hospital. These pharmacies already had established links with the London Chest Hospital through the NELLPC. The links were due to their location around the hospital and also the hospital pharmacists at the LCH on certain occasions, conduct training courses for the community pharmacists by collaborating with the NELLPC. Pharmacies in six London Boroughs were invited by the Local Pharmaceutical Committee to participate in the study. Mapping LCH previous patients' postcodes gave an indication of the area where patients normally reside and helped confirm the location areas for the pharmacies. These pharmacies were invited to participate in the study. It was found that the areas were located around the hospital.

Patients

The patients who were invited to participate in the study were those who had been admitted to the London Chest Hospital and had a coronary event. Patients, who live in London, and regularly refill their prescriptions from the pharmacies recruited into the study. The patients included in the study would be adults. Most heart attack victims are middle-aged or older. The average age for a first attack is 66 for men and 70 for women. Only 4% to 10% of all heart attacks occur before age 45 (Harvard, 2009). The patients included in the study would have experienced a coronary event and been discharged on secondary prevention medication, the medications that the study is examining for adherence. Patients were excluded if they did not live in the area where the pharmacies that deliver the intervention were located; this was to avoid the burden of extra travelling.

However, patients prior to recruitment were asked which pharmacy they normally use and if it was within the study area sites they would be considered for eligibility. Patients with other diseases or complications were not included due to the need of extra management plans, surgical or medical, which were beyond the scope of this study. Patients living in care homes were also not included because the primary outcome is adherence and this could lead to bias if the patient is not in control of the medication routine. Patients unable to understand English were not included because the intervention was to be delivered by pharmacists in English.

4.3-Eligibility criteria

The inclusion criteria were as follows:

- Age > 18-yr-old.
- Both Male/female.
- Patients admitted for acute coronary syndromes; angina, NSTEMI/unstable angina, STEMI.
- Patients included are from high risk group (hypertension, diabetes, hyperlipidemia), as well as patient from low risk group.
- Patients medically treated for secondary prevention of coronary artery diseases and discharged on (aspirin, clopidogrel, beta-blockers, or calcium channel blockers, ACE-inhibitors or ARBs, and statins).
- Patients living in /or around East London and willing to refill their prescriptions in the pharmacies involved in the study.

Exclusion criteria:

- Congenital heart disease.
- Complications of myocardial infarction: Arrhythmias, Severe Congestive Heart Failure, Tamponade/Thromboembolic disorder, Rupture (Ventricle, septum, papillary muscle), Aneurysm (Ventricle), Pericarditis, Infection.
- Patients who do not live in/or around East London and do not regularly refill prescriptions in the pharmacies involved in the study.
- Patients who do not live independently (living or nursing home residence).
- Patients with less than one year survival rate.
- Patients unable to understand oral and written English.

4.4-Sample size

Calculation of the sample size in this study did not follow a calculation based on anticipated change in the primary outcome measure. Commonly calculation of a sample size in a randomised control trial would follow the assumption that; a RCT has two comparison groups and that both groups have the same size of subjects; thus sample size calculation will depend on the anticipated difference in the primary outcome measure. However, because this study was not designed as a full randomised trial but as a pilot feasibility study, such a calculation was not considered.

For this pilot study there were certain factors to be considered for the sample size calculation these included; the hospital patient load, the number of eligible patients, number of patients that could decline to participate and number of patients who do not understand English. The hospital patients' load was 1500-2000 patients per year. When we apply a minimum load of 1500 patient per year; an estimated 125 patients per month could be recruited, if we recruit 5-6 patients per a working day. However, since there are only 22 working days per calendar month and taking into account the factors mentioned above. Therefore, we anticipated that if we recruit 1-2 patients per day we can achieve around 200 patients in 4-5 months. Given these factors the enrolment target was set at 200 patients, 100 patients in each group. This sample size was considered sufficient to achieve the study's objectives as a feasibility pilot study.

In addition, previous literature was reviewed to determine the sample size. For instance, a similar study by Obreli-Neto *et al*, 2011 recruited 200 patients and reported a 33 per cent increase in adherence with a margin error of 5 per cent and confidence interval 95 per cent. Furthermore, it was found that the sample size of 200 patients was in line with previous successful trials. These trials aimed at enhancing adherence to cardiovascular medications and recruited and followed-up around 200 patients: Lee *et al*, 2006 increased adherence by 35.5%, Morgado *et al*, 2010 increased adherence by 22.3%, Sadik *et al*, 2005 increased number of compliant patients from 33 to 85 patients and Blenkinsopp *et al*, 2000 increased adherence by 10.6%. Thus a sample size of 200 was chosen.

4.5-Sampling procedures

Study site

The research department and the hospital pharmacists at the LCH were informed about the study, in order to facilitate operational aspects. The researcher was issued with an honorary contract and a letter of access to enable recruitment. Patients were recruited from two wards at the London Chest Hospital: CCU ward and Reviere ward. Patients' recruitment packages after being approved by ethics were printed and piloted to ensure that they would be easy to follow.

Pharmacies

The pharmacies approached were the pharmacies located in North East London and represented by NELLPC. The study was advertised on the NELLPC website with a link to express interest. The pharmacists were also informed that they could contact the researcher directly by email; this is if they had any queries regarding the study before registering interest. After expressing interest the pharmacies were sent individual letters with further details explaining the study. Pharmacists were asked to register their interest to take part in the study by using the link below: please use the link below to complete a form to express your interest. A reminder email was sent to eligible pharmacies for recruitment by the link below.

https://docs.google.com/forms/d/1YZaIoR9kbh_MCxp73qCqoXTULcnro_mEK_Nw2wIBaYU/viewform?sid=657d857b01219bc3&token=SMgNEz4BAAA.eSvWkHQcEo5KdSKHqaTCw.L-JwuMWDD398r2qjKO6cGA .

Patients

Patients were identified from the hospital admission lists and from the lists provided by the research department at the LCH. There were several lists that could be reviewed by the research pharmacist.

These lists included the nurse list, the doctor list, in addition to the admission list. However, it was agreed with the research department at the LCH, that the research pharmacist would review both the research department list and the hospital admission list to avoid recruiting patients on more than one study simultaneously. The research pharmacist then reviewed the patient's hospital chart to outline if the patient matched the inclusion criteria. The research pharmacist could approach the hospital pharmacist to confirm the diagnosis and also approached the patients to confirm the pharmacy used. The patient's address (postcode) and general practitioner details were also identified from the hospital chart.

Randomisation

A list of the pharmacies included in the study was forwarded to an independent statistician at UCL-School of Pharmacy. Randomisation was performed by using a table of random numbers. Randomisation was at pharmacy level to avoid contamination of the controls (Please refer to chapter 5 results for full details on randomisation).

Blinding

In this study the research pharmacist was blind regarding the group allocations for the analysis of the data. This was to reduce bias and increase fidelity. The General Practitioners (GPs) clinics, from where data regarding B.P and LDL-C were collected, were also blind, unless referral of a patient by a community pharmacist took place. Blinding of the hospital pharmacists was not possible. This is because the hospital pharmacists assisted the researcher with sending the discharge summary of the intervention patients from the hospital to the community pharmacists. Furthermore, it was not possible to blind the community pharmacists delivering the intervention or the patients due to the nature of the intervention. The patients attended a face to face intervention in the pharmacy therefore, blinding is not applicable.

4.6- Recruitment of Pharmacies

Role of the research pharmacist

The research pharmacist served as the coordinator for the study. Duties involved liaison with community pharmacists, patients and GPs. Further duties included writing the research protocol along with the patient invitation letters and consent forms; applying for ethical approval, data collection and analysis and also coordinating the training sessions for the pharmacists. The researcher carried out recruitment of patients at the hospital site. The research pharmacist was also responsible for forwarding the intervention group patients' discharge summary from the hospital to the community pharmacy that the patient used. The research pharmacist contacted the community pharmacist by telephone and e-mail to provide the contact details of patients in the intervention group.

Role of hospital Pharmacist

The hospital pharmacist helped the research pharmacist by facilitating operational aspects of recruitment at the hospital site. Other duties included counselling the patients before hospital discharge, liaison with the hospital research team and also the doctors and nurses on the wards. In addition, the hospital pharmacist assisted and supported the research pharmacist during the recruitment process. This was by confirming eligibility regarding the diagnosis of the patient, access to admission lists and patient recruitment wards. Other support included training on how to use the hospital computer system and help with baseline data collection.

The community pharmacies

The community pharmacists needed to be willing to attend further training on both motivational interviewing and secondary prevention medication. Also the pharmacists received and reviewed the patient discharge summary, contacted the patient, contacted the patient's GP if needed. The community pharmacists delivered a face to face or telephone consultation and also followed up patients. As listed below in the inclusion criteria, the community pharmacists also had to accommodate the intervention into a MUR or NMS session and followed these services' criteria and documentation. Pharmacies in six London Boroughs were invited to participate in the study with the following post codes "E1-4, E6-7, E10-18, RM1, 2, 3, 5-14, IG1-3, IG5-8, IG10, IG11, N1, N16, N17, N 21" (Appendix 12).

Pharmacies were recruited with the following inclusion criteria: (1) pharmacies had pharmacists willing to counsel patients and interested in attending further training organised by UCL School of Pharmacy in collaboration with The University of Buckingham and the LPC, (2) pharmacies have a consultation area in which patients can be counselled and have a telephone (land line or mobile), (3) the pharmacists were familiar and knowledgeable with the New Medicine Service and MUR, have contacts or were willing to contact general practitioners and were willing to contact patients to invite for a consultation in the study.

4.7- The intervention and intervention development

The consultation chart (a pro forma to guide the interview consultations between the community pharmacists and patients) was developed by an expert psychologist trained in motivational interviews (KF) from Buckingham University. The psychologist designed and delivered the training workshops to the community pharmacists and wrote with the research pharmacist the consultation road map that would be used by the community pharmacists.

Development of the intervention

The intervention was designed to include a behavioural intervention that involved a motivational interviewing session and to be integrated into existing pharmacy services NMS or a MUR. The aim of the consultation was to identify the key issues that the pharmacist could assist the patients with and allow patients to express their concerns and beliefs regarding the medication. The design of the intervention was developed based on conclusions from the systematic review that was written before designing the study (Chapter 2) and by reviewing previous literature. The search for previous literature including pharmacy interventions, using motivational interviews to improve adherence to cardiovascular diseases resulted in finding only few studies. These studies either had not published their results yet or had no significant results on adherence. The consultation chart was developed by referring to a previous randomised control trial in hypertensive patients Ogedegbe *et al*, 2007, although the intervention was not delivered by pharmacists, but the study showed statistically significant results on adherence to medication and was relevant to the study's methodology. In Ogedegbe *et al*, 2007 trained research assistants used motivational interviewing to potentially improve adherence. Difference in adherence between the intervention and control group in this trial was 14% (P=0.027). The motivational interviewing consultation chart included skills of "Express empathy, develop discrepancy, role with resistance, support self efficacy" (Bisono *et al*, 2006).

The sessions were designed to develop a partnership between the pharmacist with the patient and exchange information to facilitate an informed decision. Furthermore both the pharmacist and the patient would negotiate behaviour and reach an agreement. This would be to access motivation and elicit commitment to change behaviour "in this case adherence to life saving medication". The key methods of a motivational interview include:

- Asking open questions for example "After your Heart Attack can you tell me how you are managing with your medication?"
- Using affirmations for example "Thanks for coming in today."
- Listening reflectively to the patient in a way that the pharmacist is still guiding the session but chooses what to reflect to.
- Summary statements can be used to tie patients' statements together, collect and link ideas and even sum up the consultation.

The pharmacist could refer to NICE clinical guideline for myocardial infarction, during the consultation session if needed. Furthermore, for adherence the pharmacist could also refer to the NICE 2009 guidelines strategies to support medication adherence. The consultation was claimed for under the New Medicine Service (NMS) or under a Medicine Usage Review (MUR). When the patient was eligible for the NMS the pharmacist could also refer to the NMS interview schedule or the MUR guidance if eligible for a MUR. There was an overlap between communication skills for the New Medicine Service that involves a patient-centred approach and the motivational interviewing consultation.

In both the NMS and motivational interviewing the pharmacist starts the consultation by introducing himself/herself, then the pharmacist outlines the purpose of the consultation. In addition, the pharmacist uses open questions which are essential for the nature of the consultation. In the NMS it is important to ask the right question, use open body language and appropriate facial expressions to allow the patient to tell their story (please see NMS learning programme https://www.cppe.ac.uk/programmes/l/nms-d-02). Regarding listening skills both the NMS and motivational interviewing recommend giving the patient a chance to tell what they already know before giving information. In the NMS the pharmacist usually summarises the key points for closing the consultation, while in motivational interviewing summaries should start early during the session and be used consistently as this is one of the a core recommendations of motivational interviewing, which rely on OARS (Open questions, Affirmations, Reflections, Summaries) technique during the session.

For motivational interviewing patients' motivation and confidence are assessed by scales, which are integral to, and influence the subsequent direction of, the consultation. Furthermore, ambivalence is important to be spotted by listening carefully for change in talk and perspectives; this should be responded to appropriately by elicit-provide-elicit technique (please refer to consultation chart appendix 13). In addition, in motivational interviewing the pharmacist asks permission to ask questions and provide information Finally, in motivational interviewing the pharmacist should always mention successes and appreciate progress by commenting positively on attributes, for example patient values, desires and behaviours, this is to express hope, care and support.

4.8-Training for the pharmacists in the intervention group

Evidence based data has shown that studies of workshops on motivational interviewing lasting between half a day and two days, found improvements in knowledge and skills that last at least for a few months (The Health Foundation, 2011). Therefore, the sessions were designed to be around five hours in duration. The sessions started at 10:00 am and finished at 4:00 pm. Two five hours training sessions on motivational interviewing were delivered to allow pharmacists unable to attend the first session the opportunity to attend and also an additional two hours booster session was included in the schedule for the training. Thus the training session schedule planned for the intervention group pharmacists included:

- Two sessions on motivational interviews (each pharmacist only attended one session).
- One booster session on motivational interviews.
- A two hours training session on secondary prevention medication after a myocardial infarction.

The content of the workshop was developed by the research team. Several meetings took place between the psychologist at Buckingham University and the researcher at UCL School of Pharmacy to develop the training session materials. These included principles of motivational interviewing and also case studies to fit pharmacy practice. The training sessions were developed to be interactive and included different role plays. The sessions were developed as continuous professional development courses which could be combined with practice. The training sessions were designed based on evidence showing that training on motivational interviewing is best if delivered as a workshop rather than self guided study and could include practice sessions, role plays with ongoing supervision of the trainer (The Health Foundation, 2011).

The psychologist delivered the training on motivational interviews in interactive sessions with the pharmacists. Training on secondary prevention medication was based on review and update of current clinical guidelines and also treatments and new medications used after a myocardial infarction. The content was written and delivered by the consultant pharmacist from the LCH. The research pharmacist organised the training sessions. In order to ascertain the preferred days for the training and enable attendance, a survey was sent to the pharmacists. This survey addressed locations and timings for the training sessions "Please for your kind thoughts on where you would like training session to take place? UCL School of Pharmacy Brunswick Square, the County Hotel Woodford Green Essex or the London Chest Hospital Bethnal Green? Also would you prefer it to be on a week day evening or on a Sunday morning?" After responses were received the plan was for the training sessions to be conducted on Sunday mornings. Moreover, the first session would take place at the County Hotel and the rest of the sessions were planned to take place at UCL-School of Pharmacy. This would be feasible under the budget available for the training.

A questionnaire was developed to assess the degree of satisfaction with the training on motivational interviews (please refer to results chapter 5). This was given to the pharmacists at the end of each training session. This helped provide information regarding the thoughts and ideas of the pharmacists on motivational interviewing as a new concept of counselling and communication skill. Intervention pharmacists were also given the consultation chart at the final training session. This chart was used during the pharmacy consultations. The chart was laminated as a hard copy and the intervention pharmacists were asked to keep the laminated copy in the consultation room of the pharmacy please refer to (Chart in Appendix 13).

4.9-Delivery of the intervention

The intervention group

The intervention patients on discharge received usual care by a hospital pharmacist. This consisted of a review of medications use, counselling on secondary prevention and any other additional prescribed medication, an antiplatelet leaflet and referral to cardiac rehabilitation. The researcher contacted each pharmacist to confirm that the patient's details were received and if contact between the patient and pharmacist occurred. The researcher also provided the patients with the pharmacist contact details along with the pharmacies locations. The intervention group patients were also contacted by the community pharmacist to invite for a consultation in the pharmacy. The researcher after each patient's discharge forwarded the discharge summary by email to the community pharmacist. This summary included the disease diagnosis, recommendations to the GPs for further management and the medications the patient were stabilised and discharged on. Only patients in the intervention group had their discharge summaries forwarded to the community pharmacist.

The intervention group consultation

Community pharmacy consultation around 2 weeks (Consultation Chart in appendices)

The consultation was designed to be in the pharmacy; a face to face consultation or by telephone for 15-20 minutes which includes: a motivational interview session, the pharmacists should incorporate the key motivational interview skills acquired from the training in their consultation and refer to the laminated copies of the consultation chart.

Follow up after 3 months

The second consultation was based on the same principles and had a structure similar to that of the first session. However, patients were encouraged to contact their pharmacists before 3 months had elapsed if any further support was needed.

The Control Group

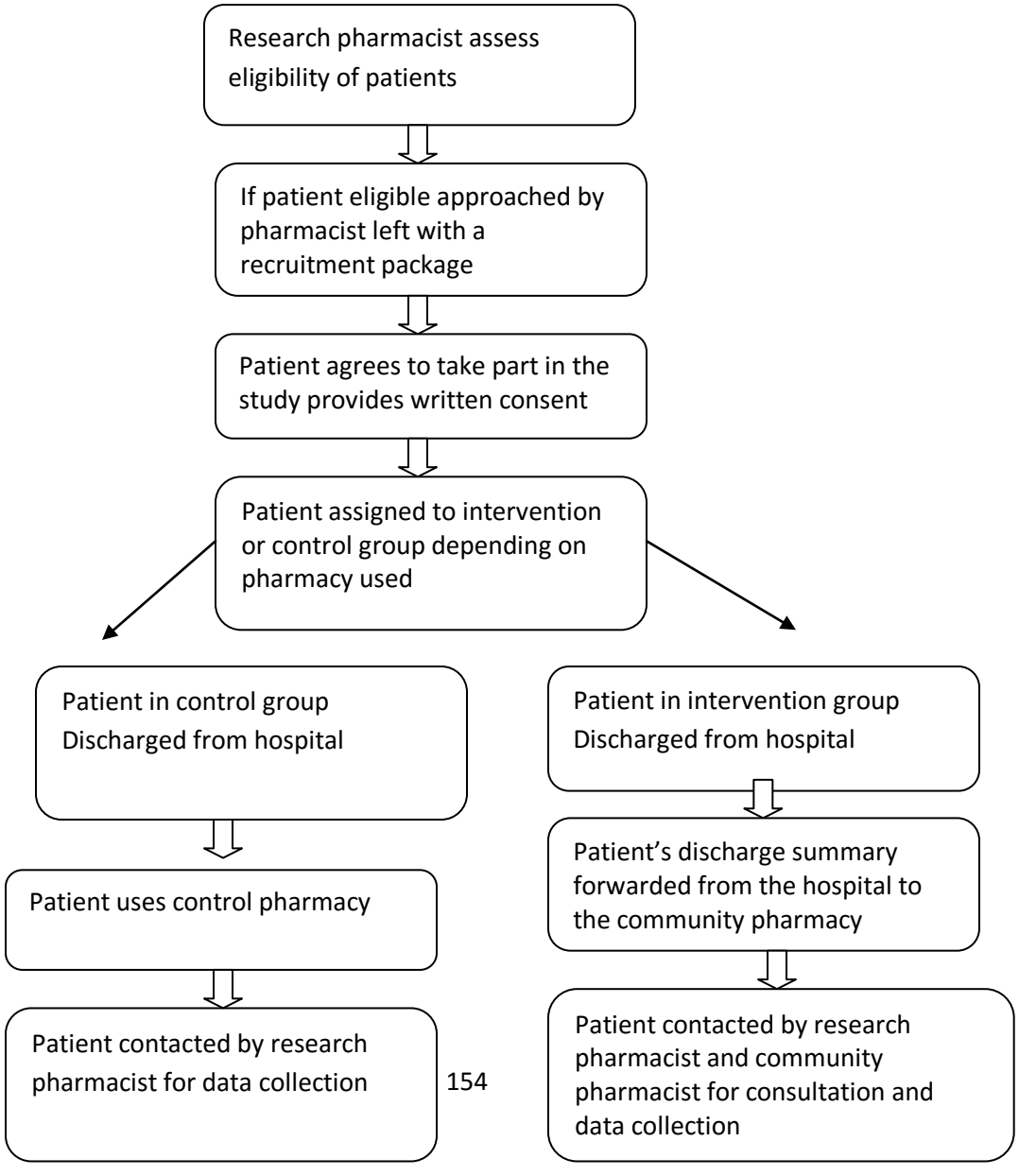
The control patients on discharge received usual care by a hospital pharmacist. This consisted of a review of medications use, counselling on secondary prevention and any other additional prescribed medication, an antiplatelet leaflet and referral to cardiac rehabilitation.

4.10-Patient recruitment

The research pharmacist gave a presentation about the study at the LCH. This was important so that other healthcare professionals (hospital pharmacists, nurses and other medical staff) were informed about the study, to facilitate the recruitment process. It was agreed with the research department at the LCH that the research pharmacist would report to the department each morning for a list of patients eligible for other studies. These patients were not to be approached, to avoid recruiting patients on more than one study at the same time. The research pharmacist received training, through an online training course at the LCH, regarding ethics and on how to approach/ talk to patients during recruitment. Recruitment took place in two wards at the LCH "CCU ward" and "Riviere ward". The research pharmacist confirmed the patient's eligibility. Then the patient was approached by the researcher who explained the study and showed the patient the pharmacies' location on a map especially designed for the study. A recruitment package (this package contained information about the study and also consent forms) was left with the patient and the research pharmacist returned at a later time to obtain written consent. If the patient was interested in taking part in the study he/she would sign a written consent form and be enrolled into the study.

The research pharmacist recorded the following from the patients' charts; patient details (age, ethnicity, diagnosis) and also contact details, regular pharmacy, GP details and a discharge summary. After recruitment patients were allocated into groups according to the primary care pharmacy that they usually refill their prescriptions from. Patients who refill their prescriptions from one of the trained pharmacy sites were assigned to the intervention group. Patients who regularly refill their prescription in the pharmacies that did not take part in the training but agreed to be control pharmacies were assigned to the control group.

Figure 4.4 Patient recruitment at the hospital



4.11-Outcome Measures

The primary outcome measure was self report adherence with coronary artery disease medication. The Morisky Medication Adherence Scale plus one self report question, adapted from Gehi *et al*, 2007, were used to assess adherence. Secondary outcome measures were blood pressure and LDL-C. These data were retrospectively collected at baseline from patients' hospital charts and at 3 months and 6 months from GP practices with patient and GP consent. Other outcomes were the Beliefs about Medicines Questionnaire (BMQ) to assess patients' beliefs regarding their medicines, cost of the intervention and pharmacist consultation time. Measures regarding the feasibility of the study were also collected. These measures included feasibility of conducting the study, feasibility of the intervention and also feasibility regarding the evaluation of the study. These were collected by surveys, questionnaires and interviews with all stakeholders.

Primary outcome measures

The reason for selecting adherence as the primary outcome is because adherence is a determinant of clinical outcomes of cardiovascular diseases. Non adherence is a growing concern to clinicians and healthcare systems because of mounting evidence that it is prevalent and associated with adverse outcomes and higher costs of care (Ho *et al*, 2009). Therefore, adherence is an area that requires further research. Moreover, for this study the intervention could be incorporated into a NMS consultation, where adherence is a primary outcome. The reason that clinical outcomes were not selected as primary outcomes was because the study is designed as a pilot feasibility study and collecting clinical outcomes as primary outcomes would need extra resources.

Adherence measure - Rationale behind choosing self report questionnaires

In a review by Garfield *et al*, 2012 the authors list several characteristics of a measure of adherence "The measure should be rooted in a theory that allows interventions to be tailored towards different types of non-adherence; it would also need be able to be used repeatedly to track patients' adherence over time and in response to interventions; it should, ideally, be brief and acceptable to patients and be able to be used across a range of clinical conditions and it would need to be able to be completed by or in conjunction with carers where necessary." However, the authors were unable to find an adherence measure which met all the above criteria (Garfield *et al*, 2012). Adherence in this study was evaluated by using two self reported measures; a scaled questionnaire the Morisky scale and a single self report one question. In this research design it is not possible to use other adherence measures, for example direct methods cannot be used because the trial is not evaluating a single medication and the method can be invasive. Pill counts were not chosen for this research, because the medication is not arranged in blisters but in their original containers and alteration by patients can occur (pill dumping). Electronic medication monitors MEMS although accurate however, they are expensive and need return visits to download the information from medication vials and this trial did not have external funding to provide patients with MEMS. Furthermore, prescription refills although objective and easy to perform also require a closed pharmacy system. The trial has a prospective design and prescription refills could be best used for retrospective designs. Therefore, the use of self report questionnaires is more suitable to measure adherence for this study design The National Collaborating Centre for Primary Care (NCCPC) 2009 guidelines stated that self-report is the most available method for reporting adherence in a clinical context.

In looking at the advantages and disadvantages of self report in routine clinical practice and to recommend how it should be used by practitioners, the NCCPC guidelines have provided the following evidence based statements; self-reporting is the most simple and inexpensive method of measuring adherence, self-reporting is quick and easy to administer avoiding the use of sophisticated methodology or equipment, self-reporting methods which are validated can feasibly be used in clinical settings. Self-reporting can identify those who are non adherent. It is most likely those reporting non adherence are being truthful, self-reporting can gather social, situational and behavioural factors including revealing patterns of medicine use and what leads to non-compliance.

In addition, there are some disadvantages of self report, as discussed in chapter 1. Self-reporting has the problem of over-estimating adherence; inaccurate self-reporting can be caused by recall bias, social desirability bias and errors in self-observation. Taking these advantages and disadvantages into account self-reported adherence measurements were used for this study, these included:

1- The Morisky scale

Self reported adherence measurement the Morisky scale was used to measure adherence in this study. It has been widely used in trials evaluating adherence to cardiovascular medication (Morgado *et al*, 2010, Carter *et al*, 2009, Calvert *et al*, 2012). Morisky *et al*, 1986 developed a 4-item scaled questionnaire to assess adherence with antihypertensive treatment. It is composed of 4 yes/no questions about past medication use patterns and is thus quick and simple to use during drug history interviews. The scale has been used for many different diseases such as hypertension, hyperlipidemia, asthma and HIV. This version of the original scale became known as the Morisky Medication Adherence Scale (MMAS-4). The MMAS-4 has been cited almost 1000 times since its publication in 1986 and modified extensively by others. It has also been translated and used in many languages. In 2008, Morisky published an updated version the MMAS-8 which has a higher reliability and higher sensitivity and specificity than the MMAS-4. .

The MMAS-8 has also been translated into different languages. In 2008 Morisky *et al*, examined and tested the concurrent and predictive validity of this structured, self-reported medication adherence measure in patients with hypertension. Morisky *et al*, 2008 reported that from a total of 1367 patients whom participated in the study the eight-item medication adherence scale was reliable ($\alpha = 0.83$) and significantly associated with blood pressure control ($P<0.05$). The sensitivity of the measure for identifying low versus higher adherers was estimated to be 93%, and the specificity was 53%. The medication adherence measure seemed to be reliable with good concurrent and predictive validity in primarily low income, minority patients with hypertension, and might function as a screening tool in outpatient settings with different patient groups (Morisky *et al*, 2008).

A systematic review by Garfield *et al,* 2011 identified 58 measures of adherence. The review found that while validation data were presented in support of the vast majority of self reported measures (54/58) under study, data for a relatively small number of measures was presented for reliability (16/58) and time to complete (3/58). The review also found that few of the measures were able to distinguish between different types of non-adherence and the authors report that this limits their ability to be used effectively in the continuous improvement of targeted adherence enhancing interventions. Garfield *et al,* 2011 found that the Morisky scale is reported as having low internal reliability in half the papers that assessed it and as having acceptable internal reliability in the other half papers. Furthermore, The Morisky 8 item scale has been previously validated in over 1,000 patients with hypertension but not with other conditions (Garfield *et al,* 2012). In the Morisky 8 item, six of the eight items address general adherence rather than over a specific time scale and items two and five address adherence over a fortnight and a day respectively (Garfield *et al,* 2012).

In other studies the Morisky scale has been shown not to be associated with the clinical outcome or sensitive to poor adherence (Dunbar-Jacob *et al*, 2012). In the 8-item Morisky Medication Adherence Scale, the first seven items are Yes/No responses while the last item is a 5-point Likert response. The additional items focus on medication-taking behaviours, especially related to underuse, such as forgetfulness, so barriers to adherence can be identified more clearly. Moreover, the MMAS ranks the degree of adherence instead of defining an absolute cut off for adherence (Lam and Fresco, 2015). Unlike analyzed scales that have a recommended cut off value; patients that took 80% or more of their medicines, as ascertained by an objective measure, for example, MEMS, are reported as adherent, and those who took less than this cut off value are reported as non-adherent (Lam and Fresco, 2015). Despite the strengths and weaknesses the Morisky scale was chosen to be used in this study because it has been widely used and has been validated in a large sample. However, because a perfect measure does not exist, for this research a multi-measure approach was employed.

2-*Self report one question*

In the Heart and Soul Study Gehi *et al*, 2007 followed 1015 outpatients with established coronary heart disease. The patients were asked a single question "In the past month, how often did you take your medications as the doctor prescribed?" Non adherence was defined as taking medications as prescribed 75% of the time or less, (8.2%) reported non adherence to their medications, and 146 (14.4%) developed cardiovascular events. Non adherent participants were more likely than adherent participants to develop cardiovascular events during 3.9 years of follow-up (22.9% vs 13.8%, *P*=.03). The study concluded that in outpatients with stable coronary heart disease, self-reported medication non adherence is associated with a greater than 2-fold increased rate of subsequent cardiovascular events. A single question about medication adherence may be a simple and effective method to identify patients at higher risk for adverse cardiovascular events.

The reason behind choosing this one self report question is that it was used in patients with coronary heart diseases, in a large population more than 1000 patients. In addition, it is very simple to use. Possible responses to this one question were: "All of the time" (100%), "Nearly all of the time" (90%), "Most of the time" (75%), "About half the time" (50%), or "Less than half the time" (<50%). Modification to the single question used by Gehi *et al*, 2007 was used. This was derived from a scale used to measure adherence in clinical trials for patients with HIV. This modified scale has been widely used in HIV clinical trials, as recommended by the Outcomes Committee of the AIDS Clinical Trials Group (ACTG) who promotes the use of this scale in other projects (please refer to Appendix 14).

Secondary outcome measures

Blood pressure and LDL-C

These outcomes were selected as secondary outcomes because both high blood pressure and high cholesterol level are established risk factors for coronary heart disease. In addition, blood pressure (BP) and low-density lipoprotein cholesterol (LDL-C), can serve as biomarkers of the efficacy of pharmacotherapy to lead to optimal cardiovascular health outcomes. The relationship between BP and LDL-C control and clinical outcomes has also been established through both epidemiological and clinical treatment trials (Lee *et al*, 2006) and also these markers have been employed in trials studying adherence to secondary prevention medication of a similar methodology to our study. These outcomes were recorded at baseline from the patients' hospital data and then retrospectively from the GP practices by the research pharmacist, by fax and telephone after obtaining patient consent. It was not possible to provide patients with home blood pressure and LDL-C monitors or to measure these outcomes by the participating pharmacists because pharmacies could vary in provision of these services.

Blood pressure was classified before the study according to the British Hypertension Society guidelines 2011 into hypertension systolic blood pressure>= 140-159 mmHg and diastolic blood pressure of >= 90-99 mmHg. In addition the Joint British Societies recommend cholesterol limits for people who have, or are at risk of, coronary heart disease: total cholesterol - less than 4.0mmol/l and LDL cholesterol - less than 2.0mmol/l.

The Beliefs about Medicines Questionnaire (BMQ)

The BMQ was used to assess patient's belief about the medication. The BMQ could serve as useful tool to examine a relationship between beliefs about medications and self-reported medication adherence. Previous literature has shown patients' beliefs about treatment influence treatment engagement and adherence (Horne *et al*, 2013). Furthermore, this relationship has been studied in previous trials (Gatti *et al*, 2009) (Sjolander *et al*, 2013) where patients who reported better adherence have expressed positive beliefs regarding the necessity of their medicines. In this study we sought to examine this relationship with the hypothesis that patients' beliefs about medicines could be associated with adherence. The BMQ is a valid and reliable scale; it has been validated for use across a range of different diseases including renal, cardiac, diabetes, asthma, psychiatric and general medical illnesses (Horne and Weinman, 1999). The scale comprises two main sections, the BMQ specific and BMQ general. The BMQ specific is comprised of two subscales, which are BMQ necessity and BMQ concerns. The BMQ general also originally comprised of two subscales which are BMQ harm and BMQ overuse. A third subscale, which is BMQ benefit, was later added to BMQ general. In this research only the BMQ specific will be used to assess participants' beliefs about their medication.

The authors report moderate to high internal consistencies of BMQ specific scale (Horne *et al*, 1999). The reported Cronbach's alphas were; BMQ necessity= 0.55-0.86 and BMQ concerns = 0.63-0.80, depending on the specific diseases. Two week test-retest of the BMQ among asthmatic group indicated reliability of its various subscales (BMQ concerns r=0.76 and BMQ necessity r= 0.77). Discriminant and criterion validity were also established for the scale; correlations were obtained between BMQ concerns scores and self-reported medication adherence as well as between BMQ subscale scores and other measure of illness and medication beliefs.

Table 4.1 The Beliefs about Medicines Questionnaire- Specific

BMQ Specific (Necessity sub scale)
My life would be impossible without my medicines
Without my medicines I would be very ill
My health at present, depends on my medicines
My medicines protect me from becoming worse
My health in the future will depend on my medicines
BMQ Specific (Concerns subscale)
I sometimes worry about the long term effects of my medicines
Having to take my medicine worries me
I sometimes worry about becoming too dependent on my medicines
My medicine disrupts my life
My medicines are a mystery to me

Using the BMQ scale, participants are asked to rate their agreement with the specific statements using a 5 point likert scale (1= strongly disagree, 2= disagree, 3= uncertain, 4= agree and 5 =strongly agree). The scores of each subscale are computed from the sum of all items within that particular subscale and range from 5-25 for both subscales BMQ necessity and BMQ concerns. The necessity-concerns differential can be computed by subtracting the total BMQ concerns subscale score from the total BMQ necessity subscale score. A positive differential score indicates that the participants perceive the benefits of their medication to outweigh the risks, in contrast negative differential score indicates that participants perceive the risk of taking their medication outweigh their benefits. The differential scores range from -20 to 20.

Cost of the study

There were several costs associated with conducting this feasibility study. These included training of the community pharmacists on motivational interviews. The costs of the training sessions including room booking, material printed, time required for the training, delivery of the training by a psychologist and reimbursement for the pharmacists' time. These were recorded by the research pharmacist. Furthermore, cost of the community pharmacist intervention in terms of time and material spent on counselling patients. The community pharmacists were asked to record the time they spent in contacting and counselling patients, also if they were able to fit the session under a NMS or MUR and how many sessions could one pharmacy manage per day, to establish if an intervention can be accommodated into a daily schedule of a community pharmacy.

4.12-Liaison with the general practitioners (GPs)

The research pharmacist used the data recorded at baseline (patient's postcode and GP practice) to contact the patients' GPs. Each Patient's general practitioner was sent by mail an individual letter by the research pharmacist, explaining briefly the study along with a copy of the patient's consent form. The GPs provided written consent on providing the results of blood pressure measurements and LDL-C levels during the timeline of the study. The GP surgeries who did not return the consent forms were contacted by telephone by the research assistant and faxed a copy of the invitation letter and the patient's consent form. The GPs agreed to fax the patients' results and be part of the study.

4.13-Process evaluation

The process evaluation will enable an assessment of the feasibility of the intervention in practice and examine the types of settings, situations or circumstances in which an intervention is more or less likely to be effective. If the intervention is not demonstrated to have a significant impact, the process evaluation may be helpful in establishing why it was not successful, e.g. if it is due to difficulties in implementation rather than its inherent inefficacy. This will assess the implementation and operation of the intervention, its workability in settings and secondary or perceived impacts.

For this study this will include: (1) recruitment and training of the community pharmacists which can be established from pharmacists' response rates (expression of interest); (2) attendance at the training sessions and feedback from pharmacists regarding the training; (3) feasibility of the delivery of the intervention in a community pharmacy setting (community pharmacists' feedback on patient contact and invitation to the consultation, attendance of patients to the pharmacy, patients' receiving the consultation by telephone, the benefit of receiving a hospital discharge summary and the possibility of incorporation of the consultation under a NMS/MUR service); (4) for GP enrolment the study process evaluation will include GPs' response rate through GP letters returned, workability and feasibility of provision of data from GP surgeries for the secondary outcomes; (5) in the hospital measures such as patients' willingness to participate in the study, recruitment rates will need to be established and finally; (6) patient feedback on the pharmacy intervention in terms of time, benefit and acceptability. Measures regarding the feasibility of the study are summarised in the table below

Table 4.2 Measures regarding the feasibility of the study

Measures would include:

Hospital Pharmacists:

1- **Number of hospital pharmacists willing to take part in the trial.**
2- **Time spent in sending a discharge letter to the community pharmacists and time spent in contacting community pharmacists.**
3- **Hospital pharmacists drop out during the study.**

Community pharmacists:

1- **Number of pharmacies and pharmacist willing to take part in the study.**
2- **Number of community pharmacists willing to take part in the training and time spent on training.**
3- **Time spent by the community pharmacist in counselling patients in the two sessions.**
4- **Time spent by community pharmacist in contacting the patient and patient follow up.**
5- **Community pharmacists drop out during the study.**

Patients:

1- **Number of eligible patients.**
2- **Number of patients contacted by the community pharmacists.**
3- **Number of patients attending the first and second visit to the community pharmacies.**
4- **Number of patients counselled for the NMS or MUR**

Instruments for evaluation of the feasibility study

Instruments for evaluation of the feasibility study involved interviews, questionnaires and email surveys with all stakeholders' pharmacists and patients and also a log book and record of important numbers and events during the management and operation of the trial. This log book was kept by the researcher.

Semi structured interviews were conducted with hospital pharmacists, community pharmacists and patients. A semi-structured interview is a method of research used in the social sciences. While a structured interview has formalized, limited set questions, a semi-structured interview is flexible, allowing new questions to be brought up during the interview as a result of what the interviewee says. The interviewer in a semi-structured interview generally has a framework of themes to be explored. Interviews were conducted to evaluate operational aspects of the trial and assess workability; in addition to understand the stakeholders' points of view regarding the feasibility of this study. This included for the hospital pharmacists the feasibility of conducting a study in the hospital, for the community pharmacists all aspects of the training, the consultation and operation in the pharmacy and for patients' views regarding any potential benefits and uptake of the intervention.

Table 4.3 Questions for interviews with stakeholders

Questions for hospital pharmacist

- **Please can you tell me your thoughts regarding patient recruitment and data collection, also regarding extra time needed for this?**
- **Please can you tell me your thoughts regarding a copy of the patients discharge summary to be sent to the community pharmacy? Do you think this is vital for continuity of patient care?**
- **Please can you tell me your thoughts regarding patient care services available in community pharmacies and how useful they are for patients?**

Questions for community pharmacists

- **Can you please tell me what you felt went well in the study, and what problems did you experience?**

Training

- **Can you kindly tell me your view of the training in regards to location, timing, convenience and length /duration?**
- **How helpful, did you feel the training was adequate?, can you kindly provide any comments on particular aspects of the training, what was helpful, what was difficult?**

Delivery of the intervention

- **To what extent do you feel you were able to adhere to motivational interviewing techniques in the consultation?**

- **Can you please tell me your view on the use and value of motivational interviewing to support patients?**

Identifying patients and making arrangements for the consultation

- **Please can you inform me about how much time was required for identifying patients and arranging for the consultation? Did you find that time?**
- **How much time did you need to conduct the consultation?**
- **How much time did you require for arranging the second consultation?**
- **How much time did you require to conduct the second consultation?**
- **Please can you describe what went well? And what problems did you experience?**
- **Can you kindly tell me what kind of impact did the consultation have on operation of pharmacy or other pharmacy staff or customers?**

Questions for patients:

- **What is your perceived value of the consultation, how satisfied are you with it?**
- **Was the consultation convenient regarding the time and the pharmacy location?**
- **So can you please describe the experience that you had with the pharmacy?**
- **Was the consultation with the pharmacist helpful, can you tell me about it?**
- **Was there anything that was not convenient?**
- **So do you think it was beneficial in providing information about what the medicines are?**

The questions were first piloted before the conduction of the interviews to assure feasibility. The interviews were audio taped with the permission of the pharmacists and patients and notes were also taken. The interviews were then further transcribed, coded and analysed.

Evaluation was conducted to demonstrate if the designed methodology of this pilot study could be later adapted to design a larger trial. Also to identify weaknesses and problems in the operation of the study that could be avoided for future design of a larger study. Moreover, to highlight any strengths in the design and methodology of this pilot study that helped facilitate operation.

Assessment of the fidelity the intervention

A scaled one question recommended by the psychologist at UCL School of Pharmacy was used, to assess the fidelity of the motivational interviewing techniques during the community pharmacy consultations. Pharmacists were asked to quantify adherence to the protocol and also to what extent they used motivational interviewing, in their consultations with the patients. This was part of process evaluation and was achieved by using the following scale question: "From a scale of 1-5 with 1 being the lowest and 5 the highest, how much did you adhere to the protocol and use motivational interviewing in your consultation?"

4.14-Data collection

Data collection for primary and secondary outcomes was carried out at the hospital and also at UCL School of Pharmacy by the researcher and research assistant. The feasibility study was designed as a prospective study therefore; a schedule (timetable) was designed for the patients to be recruited and for follow up. Patients recruited on the study would receive the intervention and also have their data collected at different timings depending on the time they were enrolled into the study. Data in this study were collected by telephone and also by post.

Data collection of self-report questionnaires

The researcher contacted the patients by telephone to fill the Morisky questionnaire and also the one self-report question. At recruitment, the researcher explained to the patients in the intervention group that they would be contacted by a community pharmacist for the intervention and by the research pharmacist for data collection to avoid confusion. The research pharmacist was provided with a mobile phone dedicated for data collection. If a patient did not answer, a voice message was left on the answering machine and the researcher would contact the patient at a more convenient time.

Data collection of the Belief about Medicines Questionnaire

This included a postal questionnaire sent by the research pharmacist by mail to both groups of patients, to evaluate the effect of the intervention on patients' beliefs regarding the medication. A prepaid envelope was also included so that the patients could return their response.

Data collection of secondary outcomes

Patients' baseline data regarding LDL-C and blood pressure were collected by the research pharmacist at the LCH. The data collected at the hospital included the initial LDL-C and blood pressure reading on admission. Other baseline data collected from the hospital included gender, age, diagnosis, ethnicity, post code and GP practice. The research assistant contacted the GPs to collect data regarding LDL-C and blood pressure. Initially it was agreed to collect the data by telephone but the method was changed to faxing the data to ensure accuracy and also confidentiality of the data collected. The research pharmacist employed the UCL School of Pharmacy fax form and faxed the patient's consent form to the GPs.

Timings of data collection

Data was collected at baseline from the hospital, at 2 weeks for the self report questionnaires, at 3months for the BMQ-Scale and at 3 and 6 months for self report questionnaires, blood pressure and LDL-C.

4.15-Data processing and analysis

Data processing

The researcher kept a record of the study's process. This included number of eligible patients, number of patients recruited each day and number of discharge summaries sent to pharmacies also patient attendance to pharmacy consultations and all aspects of the operation of the study. Furthermore, the researcher filed each patient's consent form along with a discharge summary and data sheet. The patient data sheet included GP contact details, ethnicity and patient's address and contact details.

Folders were developed for both patients in the intervention group and control group. Each patient was allocated a trial number. Data regarding adherence to secondary prevention medication and also data including blood pressure and LDL- C were filed under each patient's trial number. This resulted in each patient's file to include the following: a file number, a discharge summary, a patient data sheet, a signed consent form, Morisky adherence sheet at three points of time baseline, 3months, 6 months, Belief regarding Medicines questionnaire sheet, GP faxed results sheet at two points of time 3 months and 6 months. Folders for data from interviews and questionnaires with stakeholders were also created by the researcher.

Data analyses

Data were analysed by using the Statistical Package for the Social Sciences (SPSS) version 22 for windows. In accordance with accepted practice for clinical trials an 'intention to treat' approach was followed, in which all patients recruited to the study were included in the analyses irrespective of whether they received the full intervention or remained in the study until completion.

An independent T-test was used to compare difference in adherence between the intervention group and control group at baseline, 3 months and 6 months. Significance was set at 5 percent level. The independent t-test is an inferential statistical test that determines whether there is a statistically significant difference between the means in two unrelated groups. In this sample there were two groups' intervention and control unrelated to each other. In addition, an independent T-test was used to compare difference in blood pressure and LDL-C between the intervention group and control group at baseline, 3 months and 6 months, significance was set at 5 percent level. A chi-square test was used to test if there was a relationship between beliefs regarding the medicines and adherence significance was also set at 5 percent level. Furthermore, data from interviews and questionnaires with stakeholders were analysed by labelling and coding all of the data to enable identification of similarities and differences. In addition, content analysis was applied to make sense of the data collected and highlight important messages, features and findings.

4.16-Ethical consideration

Ethical approval was sought by the researchers from The National Research Ethics Service NRES Committee North west –Preston through the IRAS integrated research application process. A favourable opinion was granted from the committee on the 28th of March 2013 before starting the study, R&D approval was also obtained from the Joint Research Management Office Queen Mary Innovation Centre at Barts Health NHS trust and from R&D office at University College of London. (Refer to the ethics approval letters in the appendices). During recruitment the patients were informed that their participation would be voluntary and that they could withdraw from the study at any time they choose without an explanation. The patients enrolled on the study needed to sign a written consent and also consent for data collection from GPs. Eligible patients were provided with a recruitment package. The package described the study and the data that would be collected.

The patients were informed how their data would be used, analyzed and that the data would be anonymous and unidentified. Patients were given a trial number after enrolment to ensure confidentiality. Patients were only referred to through the trial number. For data protection a locked cabinet in the hospital was allocated by the pharmacy team to store patients' consent forms and other data regarding GP surgery and contact details. The patient's discharge summary to the community pharmacies, was forwarded electronically through the secure hospital pharmacy computers. The hospital computers were password protected and the passwords were changed periodically. The record of the research daily activities was kept in the hospital and stored in the locked cabinet.

The community pharmacists stored the information regarding the consultation with the patient based on MURs and NMS record keeping and data requirements. Patient data was treated as strictly confidential. In case a significant problem was identified by the community pharmacist conducting the intervention, the pharmacist would refer the patient back to the GP or the prescriber, if the referral was urgent then the referral would be by telephone and further documented.

Further research data (Morisky questionnaire, BMQ questionnaire) were collected by the research pharmacist from the patients. The data was stored at UCL School of Pharmacy in a designated cabinet and locked. The school computers were password protected and only accessible to the research team, passwords were changed on a regular basis. The data would be stored for more than five years and destroyed by UCL School of Pharmacy at the end of this period.

4.17-Reliability of the results

The research pharmacist and research team followed the study protocol closely. The research pharmacist conducted interviews with stakeholders by telephone and the interviews were audio recorded. The research pharmacist also followed the interview structure closely to reduce bias. The researcher reviewed and revisited the transcripts several times for new codes. Furthermore, 10% of the interviews were checked by the supervisor for reliability. The motivational interviewing consultation designed for the intervention was written by the psychologist from Buckingham University and was also reviewed by the psychologist at UCLSOP to ensure compatibility with motivational interviewing techniques and to increase reliability. The community pharmacists adhered and tried to be consistent with the protocol of the intervention. Furthermore, the community pharmacists were asked to rate their use of motivational interviews with the patients by a scaled questionnaire designed by the psychologist to evaluate reliability.

4.18-Validity of the results

This study used Methodological triangulation which involves using more than one method to gather data. Triangulation will help bring the results together and enhance the validity. The study employed both interviews and questionnaires and used both quantitative and qualitative measures. Two quantitative measures of adherence were used; a validated scale for adherence measurement the Morisky scale and a one self-report question. This was to increase the validity of results for the primary outcome which is adherence to the cardiovascular medication. The study also used the BMQ questionnaire which is a valid and reliable scale. The BMQ has been validated across a range of different diseases.

Additionally, the study was designed with a control group and had a randomisation design, which could lessen external validity problems. However, generalizability will still need to be tested in a larger study and with different regions and pharmacy settings. Furthermore, the results were reviewed and checked by the supervisor and also by an independent statistician at UCLSOP to ensure that the tests applied were accurate and relevant to the studied outcomes. The results of the study were compared with other similar previous studies on cardiovascular diseases and adherence to medication as a check of validity.

The methods of evaluation selected for this study each have their strengths and weaknesses for example interviews could serve as a good measure of attitudes of respondents, also can provide in-depth information, allow good interpretive validity and have a quick turnaround for instances in telephone interviews. However, if conducted face to face could be expensive and time-consuming and possibly involve reactive and investigator effects. Moreover, questionnaires are considered practical and cost effective to use, also the results of questionnaires can be quickly and easily quantified by the researcher, although it is argued that questionnaires can be inadequate to understand some forms of information such as changes of emotions, behaviours and feelings. Therefore, for this study a mixed approach for evaluation was employed involving validated scales, interviews, questionnaires, records of study operation and conversations with all involved stakeholders; in order to be able to produce valid and reliable data from this pilot feasibility study.

End of Chapter Four

Chapter Five

Results of a Feasibility Pilot Controlled Trial

This chapter will demonstrate results of the feasibility study. It will include results on recruitment rates of pharmacies, GPs and patients, response rates of patients/attrition, characteristics of respondents and results showing comparison of intervention and control. The chapter will also show results on the impact of intervention, primary and secondary outcomes, and measures regarding the feasibility and acceptability of the randomised control trial and from perspective of stake holders' pharmacists and patients.

5.1-Results on recruitment rates of pharmacies, patients and GPs

Feasibility of recruitment of community pharmacies

Pharmacists were contacted by North East London LPC and asked to register their interest to take part in the study. Twelve pharmacies expressed initial response after one week. After two weeks a further ten pharmacies showed interest. A final email was forwarded to eligible pharmacies and recruitment of pharmacies by the LPC registry was closed on the 8th of May 2013. The total number of pharmacies who showed interest to participate in the project at that time was 22, these pharmacies included in total 26 pharmacists. Further pharmacies were invited to take part in the study, after discussions between the researchers raising concern that the number of pharmacies may not be sufficient to meet the patients' sample size. A talk by the researcher regarding the study was given during a pharmacy meeting that was also organised by the LPC. This led to a further 20 pharmacies (24 pharmacists) expressing interest. Therefore, the total number of pharmacies was increased from 22 to 42 and the total number of pharmacists expressing interest was 50. From the 42 pharmacies that expressed interest to be part of the study 32 pharmacies fulfilled the inclusion criteria and were allocated into intervention 16 pharmacies (19 Pharmacists) and control 16 pharmacies (19 Pharmacists) this is discussed in the section below. These pharmacies were marked on a map for North East London.

Allocation of pharmacies to intervention and control groups

Simple randomisation of the entire sample was not possible because dates of training sessions had to be set in advance. Thus procedures were adopted to ensure comparability of the intervention and control groups for this feasibility/pilot study. Pharmacy recruitment was all done through NELLPC. Pharmacists informed of study by two different routes. Firstly, by email 22 pharmacies responded that they wished to take part. These were randomised to intervention and control by an independent statistician at the UCL School of Pharmacy. This process was concealed from the researcher and the research team and was performed at pharmacy level to avoid contamination of controls. To achieve sufficient numbers a second group were invited to participate during a professional meeting and 10 pharmacies met the inclusion criteria. Therefore, pharmacists wishing to take part and able to attend the pre-determined dates of the training were allocated to the intervention group. The control group was a matched sample drawn from remaining pharmacists who expressed a wish to take part.

Pharmacies allocation and recruitment

Figure 5.1 The first recruited tranche of pharmacies and their randomisation

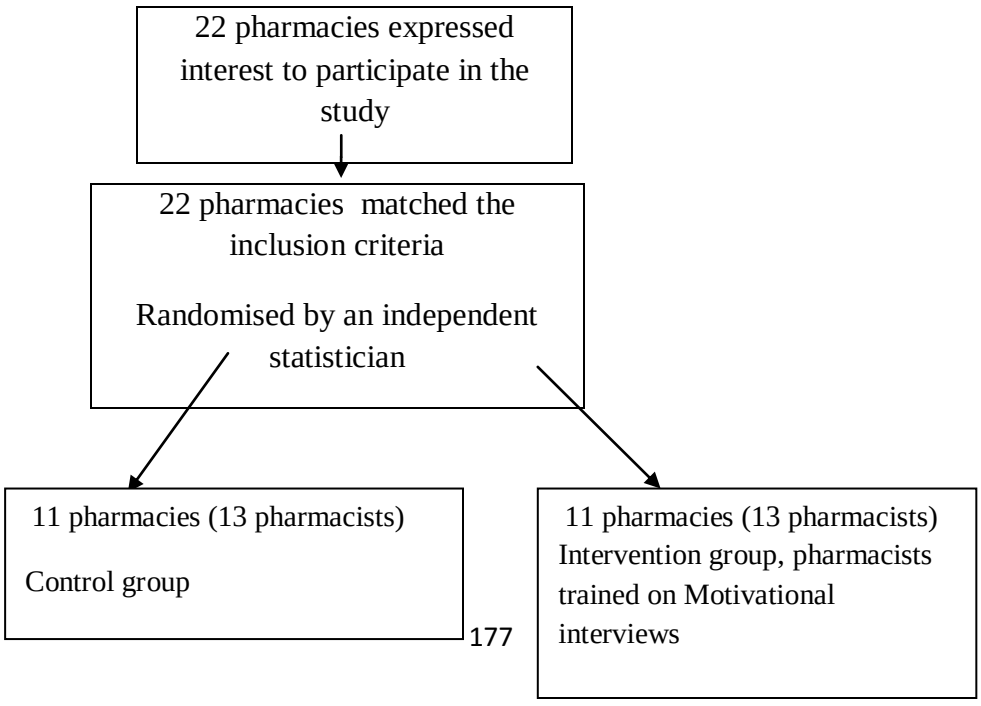


Figure 5.2 The second recruited tranche of pharmacies

Further pharmacies were invited to participate in the study after a decision made by the research team to increase the number of pharmacies:

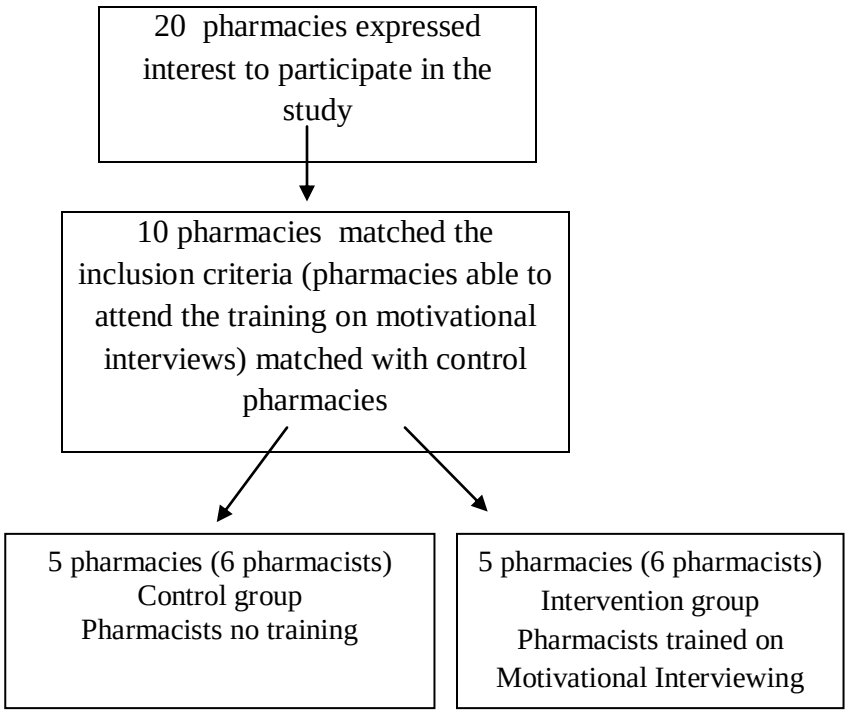
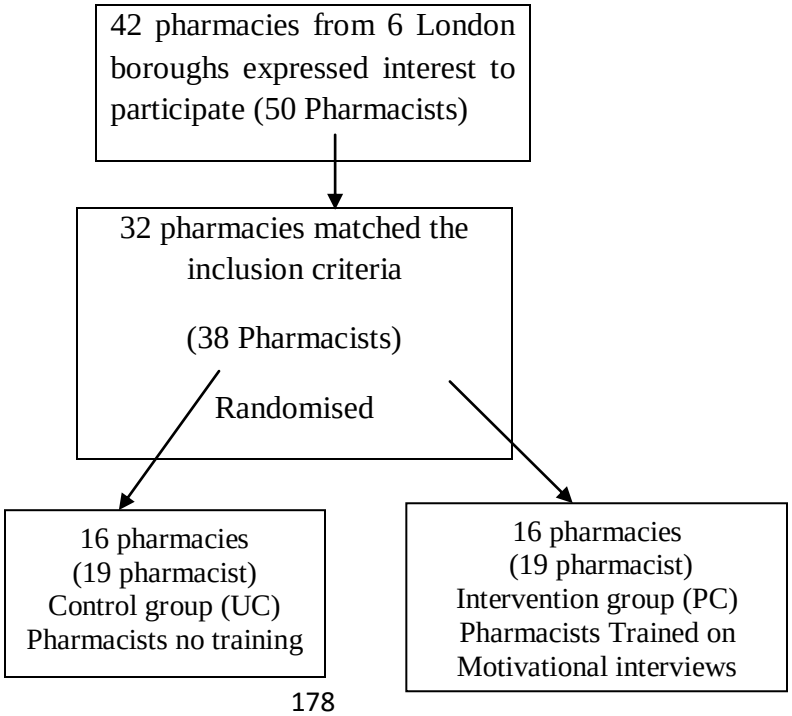


Figure 5.3 The total number of pharmacies included in the study and their allocation



Feasibility of the training of community pharmacists

Email invitations were sent to the intervention group pharmacists to attend the training. The training sessions were conducted according to the schedule outlined in the methodology of the study these included:

- Two sessions on motivational interviews.
- One booster session on motivational interviews plus a training session on secondary prevention medication.

Eleven pharmacists attended the training that took place on the 23rd of June 2013. A second training session took place at the UCL-School of Pharmacy on the 4th of August 2013, nine pharmacists attended the training. A further training session took place on the 8th of September 2013; this included a booster training on motivational interviews along with training on secondary prevention medication organised by the London Chest Hospital. On the 8th of September 2013 10/19 pharmacists attended the booster training. All 19 intervention pharmacists received at least 5 hour training on motivational interviewing please see chart below (attendance of intervention pharmacist at the training sessions). However, not all pharmacists received the booster training or the training on secondary prevention medication. The given course material was sent by email and mail to the pharmacists unable to attend the booster session or training on secondary prevention medication.

Locations of the training sessions

The first training session took place at the County Hotel in North East London. The second training session took place at UCL School of Pharmacy in central London. The third and final session which included a booster training on motivational interviews also took place at UCL School of pharmacy. Each training session was 5 hours in length except for the booster session that was 2 hours. The locations were determined depending on the study's available funds for room booking, training materials and catering and also the participants' preference.

Figure 5.4 Chart Attendance of intervention pharmacist at the training sessions

The training sessions were scheduled to be delivered on Sundays, due to work commitments of the pharmacists during the working days of the week. Intervention group pharmacists were eager to attend and learn the new skills. Below are some of the emails sent to the researcher by the intervention group pharmacists after the invitation to the training.

"I am very enthusiastic about the opportunity you are creating and am pleased that it seems pharmacy is moving in the right direction. Well done to you. I would like to ask when exactly the training will take place and how and when we will be informed."

Regards G.S , B. Pharmacy

"Thanks for the invite to study. Definitely interested, would you know roughly when the two days training is?

CK. W., W. Pharmacy

Certain difficulties were faced during the organisation of the training sessions. These included agreement between the pharmacists on the date of the training, therefore more than one day was organised. This also had an impact on the psychologist's time, having to deliver the training more than once. The location of the training had an effect on the number of pharmacists that could attend, due to the fact that most of the pharmacists worked in North East London and the preferred location was to be around this London area. Not all pharmacists were keen to travel beyond this area. Before deciding the dates and locations, an email survey was sent to the 13 pharmacists (first tranche of recruited pharmacists) in the intervention group to ask about preferred locations and days for the training sessions on motivational interviews. The majority of pharmacists agreed that Sunday was a good day for the training. Most pharmacists agreed that the county hotel would be more convenient because the pharmacies that they work at are located around the county hotel. Some pharmacists still did not mind that it was at UCL School of Pharmacy.

"*Yes at UCL it is convenient yea it is fine, it isn't too difficult to get to.*"

Few pharmacists disagreed *"The School of Pharmacy is time consuming."*

Other pharmacists did not mind the location of the training.

"I do not mind UCL or county Hotel as long as there is free parking that will be wonderful."

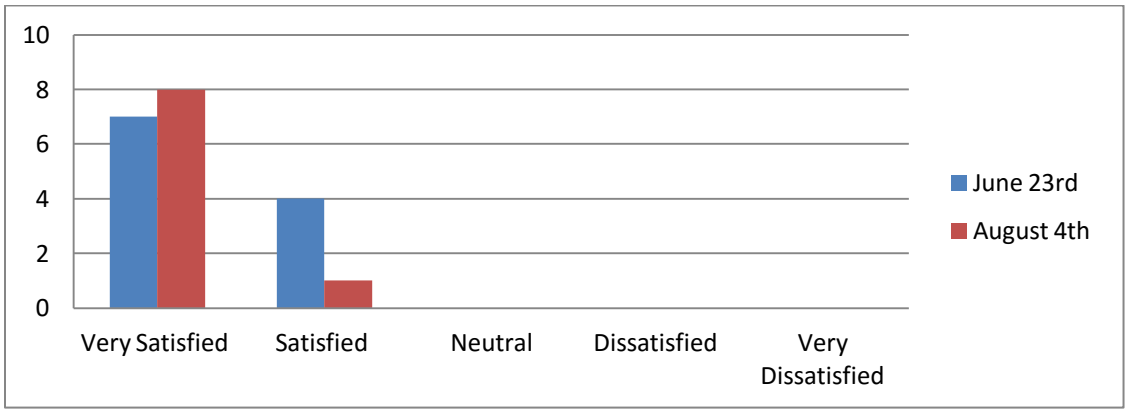
A certificate of attendance was organised by UCL School of Pharmacy for the pharmacists that attended the training, this was given to the pharmacists after they completed the training (please refer to certificate in Appendix 15).

Evaluation of the training

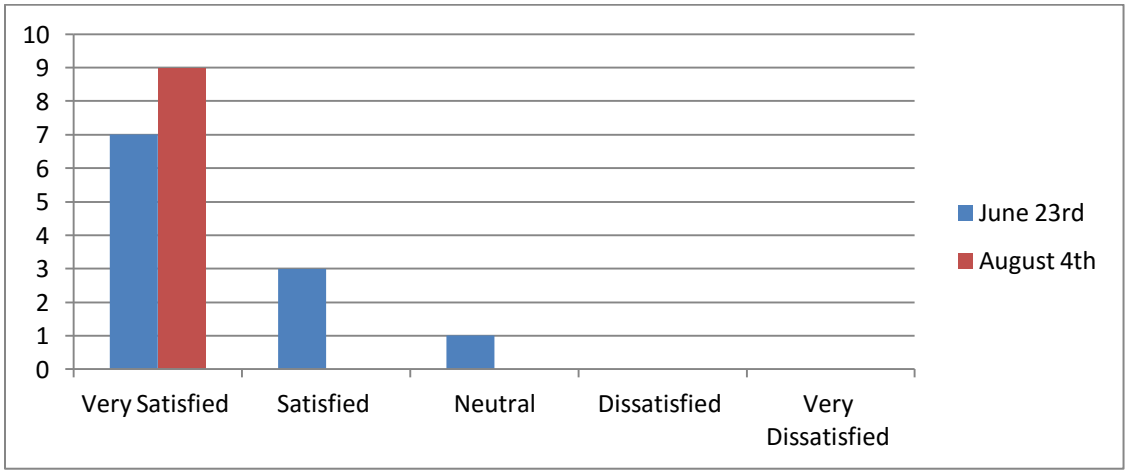
A questionnaire was developed to assess the degree of pharmacists' satisfaction with the training on motivational interviews (please also refer to questionnaire in Appendix 16). This was filled by the pharmacists at the end of each training session.

Figure 5.5 Evaluation of the questionnaire for the course on motivational interviews 23rd June and August 4th 2013

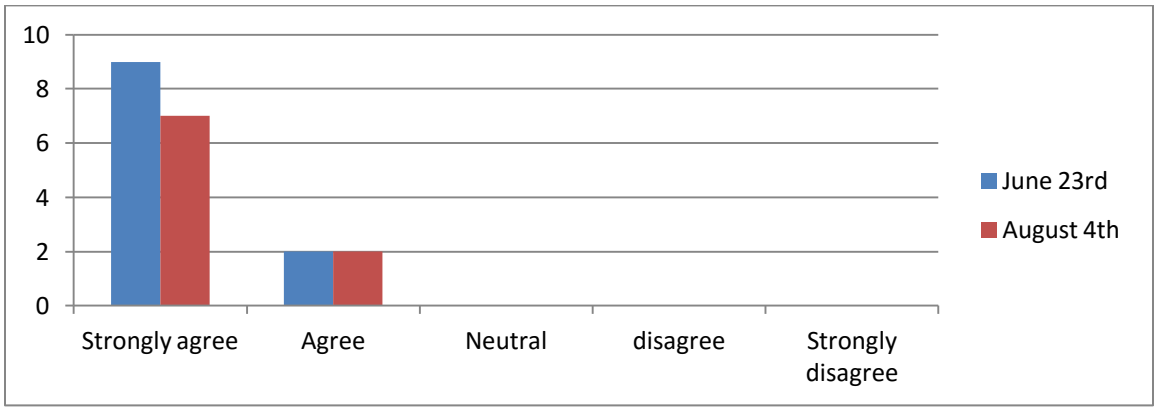
1- How satisfied are you with the course content (range and depth)?



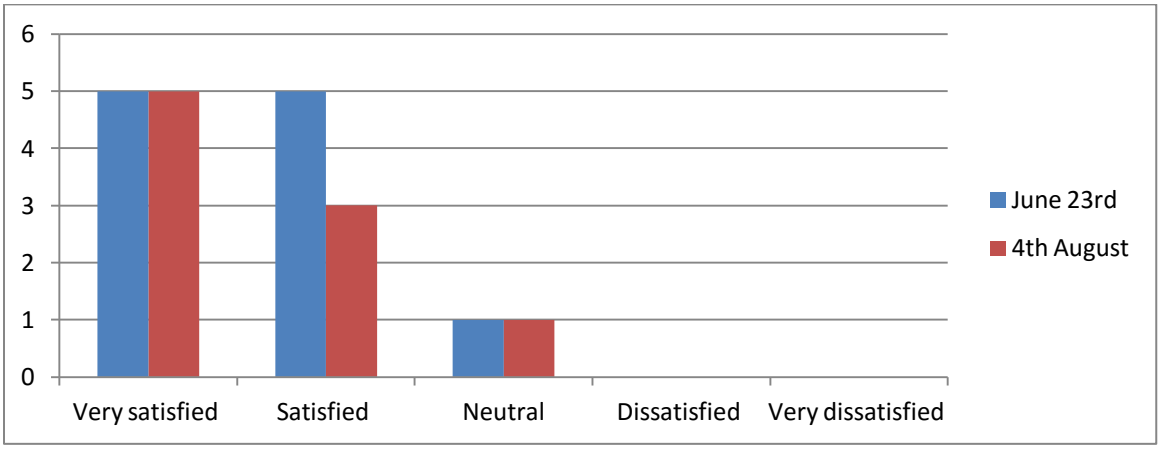
2- How satisfied are you with the delivery and teaching methods?



3- Did this course succeed in enhancing your consultation skills as a health care practitioner?



4- How satisfied are you with the length and time of the course?



Results from the questionnaire above; show that the majority of intervention group pharmacists were either very satisfied or satisfied with the motivational interviewing course content, delivery, time and length and also teaching methods. The majority of pharmacists also either strongly agreed or agreed that the course managed to enhance their consultation skills as healthcare professionals.

Below are the intervention group community pharmacists' comments on the training. These results are from the evaluation questionnaire:

- *This actually should be incorporated into the pharmacy curriculum.*
- *Very enlightening in new ways of improving patient outcomes through motivational interviews consultation.*
- *Very positive learning from a specialist outside pharmacy we communicate every day I now know how badly we do it.*
- *I plan to attend further training if possible it would be helpful to my practice.*
- *Very interactive many thanks.*
- *Well done, constructive, very informational.*
- *Although do not like group work in this case it was very helpful.*
- *Very informative thank you very much.*
- *Very informative and well structured, some great new ways to motivate patients without putting any pressure on them and putting the ball in their court.*

Assessment of community pharmacists motivational interviewing skills after the training

The psychologist evaluated the uptake of motivational interviewing skills by the pharmacists in the course of the training. However, for a future larger study scales such as the Motivational Interviewing Treatment Integrity (MITI 3.1) scale (Moyers et al, 2005), using recorded role-play activities that occur one week after the training has been received, would be recommended. The MITI is an instrument designed to measure the degree to which a practitioner is interacting with a client in a way that is consistent with motivational interviewing. To use the MITI, trained raters observe or listen to a 20 minute interaction. Validated scales such as the MITI can also provide feedback that can be used to increase clinical skills in the practice of motivational interviewing.

Interviews with community pharmacists

The researcher invited the intervention group community pharmacists for a telephone interview to study their views regarding the training, the operation and delivery of the consultations at the pharmacy and also the use of motivational interviewing in the intervention. Four pharmacists agreed and were interviewed.

Pharmacists' views regarding the training

In the interviews some pharmacists reported that the motivational interviewing skills that they learned from the training sessions, needed to be applied to their practice in the pharmacy to be sustained as a skill.

"Sustained application of motivational interview techniques will be the real test." "Ability to mature after learning is fantastic putting the knowledge to work."

Other pharmacists agreed that they were able to learn the skills during the training sessions and could apply to practice.

"I think during the training day I was able to learn the skills, so it was easy to learn in a couple of days that I went to so yes."

Few pharmacists thought that they needed more sessions and time to learn motivational interviews. *"A lot to take in could be better if sessions were done over a few weeks." "A refresher session will be good" "May be a bit long but informative"*.

The pharmacists also reported that the role plays practiced during the training course were very helpful and enabled them to learn the skills of motivational interviewing.

"Because we did the hand out role play that stayed in mind so you recall what you were doing then"

In addition some of the pharmacists agreed that motivational interviewing would be a useful skill to learn earlier at university level.

"I think it is a really relevant skill to have and it would be good to know about it earlier on, at university"

Pharmacists' years of graduation and thus ages differed. This had an effect on the uptake of the skills some pharmacists had adopted certain techniques in counselling due to long experience with patients and faced difficulties in changing these techniques.

"You have not to lose attention because you tend to go back to old practice that is hard isn't it?"

"It was all fine but I noticed during the motivational interviewing course the age range of the pharmacists that were there, I think I was the only one below the 30 mark and if you do not get it totally then I do not think there will be a right amount of change."

"Yes if I could have started it earlier and became more natural, than having to change a little bit from what I was doing."

It was observed and reported to the researcher by the psychologist during the training sessions that younger pharmacists accepted and adapted the new skills of motivational interviewing more easily.

Making arrangements with patients for the consultation

The intervention patients were referred from the LCH to the pharmacies for the consultation. The community pharmacists reported in the interviews that they contacted the patient and if the patient agreed to attend the consultation a convenient time was agreed between both the pharmacist and the patient.

"We decided on a time convenient to him and me so it was on a Saturday which was fine."

Patients who did not attend a face to face consultation were contacted by telephone and the pharmacists reported that they were able to engage the patient by telephone.

"My own patients were not involved in my group, I had a patient who uses a different pharmacy, but I still managed to engage patient on phone".

Furthermore, if a patient did not respond an additional call was arranged by the community pharmacist. Pharmacists also reported that contacting the patients did not have a negative impact on the operation of the pharmacy.

"Patients did not contact the pharmacy, I had to contact them."

"Effect on operation of pharmacy in terms of time and resources, minimal"

"No it doesn't have an effect on the operation of the pharmacy"

Community pharmacists agreed that the integration of motivational interviews in services such as a MUR or NMS did not add extra timing on the consultation or the operation of the pharmacy.

"I do try to keep the consultation short as possible but it has had an effect before but motivational interviewing has not changed that."

"In a busy pharmacy, coming out of a consultation can be stressful for the team. At times there can be a lot of prescriptions waiting to be checked. This is regardless of which techniques you use."

"The shops floor keeps on running as it is, me being in the consultation room does not make any difference."

The community pharmacists reported that they delivered the consultations between 15-20 minutes. This is similar to the time pharmacists spend on a pharmacy consultation without using motivational interviews.

"I try to make it about 10-15 minutes, but it depends on how many medication people are on."

"We decided, because he had a parking place so he could not be for long, so we decided yea 20 minutes and we stuck to that target we tried and covered everything in that time."

"*I just need to prioritise what needs to be done first and knowing that I will be away for at least 10 minutes and they do not interrupt me."*

"No the time not really it takes the same I just combine it together so it probably has not changed the time too much."

Thus the interviews show that the time to deliver the intervention with an incorporated motivational interview; did not differ from the time needed to deliver existing pharmacy sessions such as MURs and NMS.

Views regarding the consultation also varied between the pharmacies depending on the number of available supporting staff that worked in the pharmacy and how busy the pharmacy usually is.

"*The team needs to be trained up and the staff need to know what they are doing, so I do not have to sit physically and watch what they are doing, so they do all the dispensing and if they need anything they refer to me."*

Integration of the intervention into a MUR or NMS session

The pharmacists reported that it was not always possible to fit the intervention sessions under a MUR or NMS.

"I couldn't fit under MUR or NMS I did not claim for the session"

However, some reported that it was easier to fit under a NMS session and this was mostly because the patients were referred from the hospital and were on first time new medications such as antiplatelets.

"Patient was on Ticagrelor as a new medicine, I put it under an NMS",

Some pharmacists contacted the patients without claiming for the sessions. *"Perhaps more details on NMS/MUR integration. I did not claim for the session"*

The pharmacists reported that such queries should have been addressed earlier during the protocol design and the need to provide a clear protocol supported by rules and regulations from the LPC.

"I think some consultation should have been done with the LPC to see how NMS, MUR would impact on the intended study, and whether these would be paid."

Motivational interviewing in the intervention

In the interviews the community pharmacists expressed that motivational interviews were important for the patients and a useful tool to enhance adherence.

"It allows you to extract more information out of the patients, rather than directing them to a closed answer."

"Motivational interviewing works tremendously well for some patients such as the patients who had a life changing event."

"It encourages people a bit more to see what they can do and what is holding them back and then they can say for themselves."

"Motivational interviewing is a useful tool for pharmacists in motivating patients to get adherence and meds optimisation."

One pharmacist reported that it made the patients feel that they were cared about by a health care professional

"You can feel from the patient that you are not only doing it for money but you are doing it because you care about them."

Another pharmacist reported that motivational interviewing is a useful tool but depends on the patient receiving the consultation.

"Motivational interviewing will work tremendously well for some patients such as the patients who had a life changing event. It will be a tool used with some patients, but it does depend on their desire to change." This statement could be related to causes of non-adherence that could influence the patient's behaviour. Causes of non-adherence could be internal or external. For internal causes these could involve conscious decisions regarding the medicines, but could also include forgetfulness and misunderstandings about medicines. Other internal causes of non adherence can be related to mood and anxiety (Horne, 2005). While external causes involve ease of medicine use, the dose regime, in addition to social factors and prescription costs (Horne, 2005).

It was also reported by the pharmacists that motivational interviewing in their consultation made the consultations more structured and helped in interacting with patients.

"When using motivational interviewing when you are speaking to a patient your consultation becomes much more structured, yes I do think it is a useful skill it does help you to interact with patients and get them more on board."

The pharmacists also expressed in interviews that motivational interviewing is a useful skill to learn and differs from their traditional counselling technique.

"When using motivational interviewing a lot of information can be retrieved and it is different from what we were practicing traditionally."

"When you are using motivational interviews you realise that it is not the simple yes and no from the patients and it is telling the patient how you admit to help"

Moreover, keeping a laminated copy of the consultation chart, available in the pharmacy was important to use on need and pharmacists reported that they referred to it during their consultation.

"I still have my cards and I can look back at them the ones you sent in the post. They are useful I have not used the mapping sheet but I have used all the questions"

"Yes it was useful to refer to the chart and refresh your way of counselling."

Importance of a discharge summary for the consultation

Community pharmacists believed that the discharge summary that was sent by the research pharmacist from the hospital was very useful and important for the consultation.

"The discharge summary is vital/ paramount for discharge patients especially if new medications are added or medications changed on admission."

"Discharge summary is extremely important. Can be hard to work out what medication the patient is on. Hospitals do not refer patients to see their pharmacist."

Number of patients referred to pharmacies

The number of patients referred to the intervention pharmacies depended on pharmacy location and the recruited patients' postcodes. Most pharmacies had either one or two patients. However, one pharmacy that was closest to the hospital had 7 patients and three pharmacies had no patients referred to them (Please refer to Appendix 17)

The table below contains information recorded by the researcher summarising established measures regarding the feasibility of the study in regards to community pharmacies.

Table 5.1 Established measures regarding the feasibility of the study in regards to community pharmacies

Community pharmacists	
1-Number of pharmacies and pharmacist willing to take part in the study.	Pharmacies 42 Pharmacists 50
2-Number of community pharmacists willing to take part in the training and time spent on training.	Pharmacies 32 Pharmacists 38 Time spent on training 5-9 hours
3-Time spent by the community pharmacist in counselling patients in the two sessions.	15-20 minute/ patient
4-Time spent by community pharmacist in contacting the patient and patient follow up.	15 minutes/patient
5-Community pharmacists drop out during the study.	1 community pharmacist dropped out of the study

Results show that from the number of community pharmacies willing to take part one can conclude that recruitment of community pharmacists in studies of such nature could be feasible. In this study this was achieved by collaboration with NELLPC. In addition, community pharmacist dropout was minimal.

Due to the incorporation of the consultation into existing services (MUR, NMS) extra time for the consultation was not needed. A typical review MUR will take between 10 and 20 minutes this is also usual for a NMS session. Thus the consultation time was considered by pharmacists to be practical.

Assessment of the delivery (fidelity) of the intervention

Fidelity regarding the delivery of the intervention was assessed by using a scaled one question. Pharmacists were asked to quantify adherence to the protocol and also to what extent they used motivational interviewing, in their consultations with the patients. The outcome showed a positive score of 3.8 from 5. Community pharmacists survey results (Scale question) "From a scale of 1-5 with 1 being the lowest and 5 the highest, how much did you adhere to the protocol and use motivational interviewing in your consultation? How long was your consultation?"

Table 5.2 Community pharmacists survey results

Pharmacist 1	Score 2	20 minutes
Pharmacist 2	Score 3	15 minutes
Pharmacist 3	Score 4	15 minutes
Pharmacist 4	Score 5	10 minutes
Pharmacist 5	Score 5	15-20 minutes
Pharmacist 6	Score 4	15 minutes
Pharmacist 7	Score 4	10-15 minutes

This result is in line with the results from the interviews with pharmacist. Pharmacists' responses varied from using motivational interviewing quite a lot to using just small things taken from the motivational interviewing protocol.

Feasibility of the study from perspectives of hospital pharmacists'

The researcher conducted interviews with five hospital pharmacists. These interviews were face to face and took place at the hospital. The interviews were to determine the pharmacists' thoughts, regarding the feasibility of conducting a prospective study, patient recruitment at the hospital. The interviews were also to determine the pharmacists' views on continuity of care across the primary and secondary care interface and on existing community pharmacy services.

Feasibility of conducting a prospective study

Hospital pharmacists expressed that they are overloaded and conducting recruitment as a prospective study could be challenging in regards to time and workload. However, hospital pharmacists reported that if additional staff were employed and if allowed extra time recruitment might be feasible. The hospital pharmacists mentioned in the interviews that recruitment would depend on the nature of the study and the expected outcome.

"Hospital pharmacists are overloaded, cannot commit 100% could do recruitment if given more time."

"Feasible, depends on the study and how involved if retrospective easier and less pressure prospective is different more pressure and depends on how much data and how long."

Pharmacists' views on continuity of care

The hospital pharmacists' supported the idea of sending a discharge summary to the patient's community pharmacist. Hospital pharmacists reported that this could reduce medicine wastage, improve communication between primary and secondary care and support existing community services such as MURs and NMS. Discharge letters in current practice are sent to patient's GP by the ward clerk and also sent to community pharmacists on need for dosette boxes only.

Hospital pharmacists expressed that regular practice of sending a discharge letter with the patient to take to the community pharmacist is a vital recommendation and could be achieved.

"Very important, decreases medication wastage, currently used for dosette boxes, can be sent by staff but easier to give to patients to take to community pharmacist."

"Definitely community pharmacists should be getting more information. The letter could be sent directly from the hospital, ideal option is to give to the patient then also to post the letter".

Hospital pharmacists' views on community pharmacy services

The interviews revealed that hospital pharmacists do not have sufficient information regarding services offered in community pharmacies such as MURs and NMS. The interviews demonstrated that hospital pharmacists need more information, especially regarding the NMS and also how vital this service can be to patient care and in supporting patients in regards to adherence. Sufficient information regarding community pharmacy services, could determine patient referral into these services, after hospital discharge and eventually increase uptake by patients who are in essential need of support in primary care.

"MUR's are very important, for patients on long term medicines, monitoring outside the hospital is important, I do not know much about the NMS, I know it is a new service."

"Useful at some aspects, counselling before the patient leaves the hospital should be enough; I do not know how good the community pharmacist could pick up stuff to be viewed. I do not know much about these services.

The table below contains information recorded by the researcher summarising established measures regarding the feasibility of the study in regards to hospital pharmacists. The table illustrates how hospital pharmacists although had increased workload, made time to assist the researcher with patient recruitment, but were unable to fully undertake the recruitment process. Therefore, patient recruitment took place by the researcher. For a larger study it would be recommended to employ research assistants for patient recruitment. Moreover, as shown in the table, time was needed to send the patient discharge summary to the community pharmacists. This time would have been reduced if an existing system similar to sending the summary to the GPs was readily available.

Table 5.3 Feasibility of the study in regards to hospital pharmacists

Hospital pharmacists	
1-Number of hospital pharmacists willing to take part in the trial.	Hospital pharmacists did not recruit patients. Recruitment was undertaken by the research pharmacist. However, number of hospital pharmacists who provided support and assistance to the research pharmacist was 5.

2-Time spent in sending a discharge letter to the community pharmacists and time spent in contacting community pharmacists.	For each patient the discharge summary was printed at the hospital then scanned and emailed to the community pharmacist. The community pharmacist was then contacted and informed. For each patient 30 minutes was needed. Total time for 32 intervention arm patients 16 hours. This was done on different days depending on patient discharge.
3-Hospital pharmacists drop out during the study.	This is not applicable.

Results on patient recruitment

Recruitment was for 4 months. Patient recruitment commenced on the 15th of October 2013 and was discontinued on the 10th of February 2014. Patients were recruited from two wards at the London Chest Hospital; CCU ward and Reviere ward. Before commencing with patient recruitment, a pilot for recruitment was conducted, during the pilot three patients were found to be eligible from the CCU ward. The recruitment package was left with the patients to read and then give their thoughts and opinions regarding enrolment into the study. The three patients reported that the patient information sheet was easy to follow and understand. All three patients were willing to take part in the study and willing to attend the consultation at the pharmacy. These patients were not recruited into the study.

The research pharmacist reviewed patient's charts in the two wards where recruitment took place. Once patient eligibility was confirmed the patient was approached by the researcher, who explained the study briefly and showed the pharmacies' locations on a map. The patients were given a recruitment package. The research pharmacist returned at later time to obtain written consent from the patient. If the patient expressed interest he/she was recruited into the study. Patients differed in their response and acceptability to be recruited. Some patients were keen on taking part and other patients were simply not interested in being part of a study. Explaining the study as a service to be provided after hospital discharge and an opportunity for further follow up by a pharmacist could have encouraged some patients to participate. The research pharmacist had to be cautious as not to disturb patients, some patients were severely tired and ill after the heart attack. In addition, there were certain times when patients could not be approached such as lunch time and protected time that is designated for patient rest.

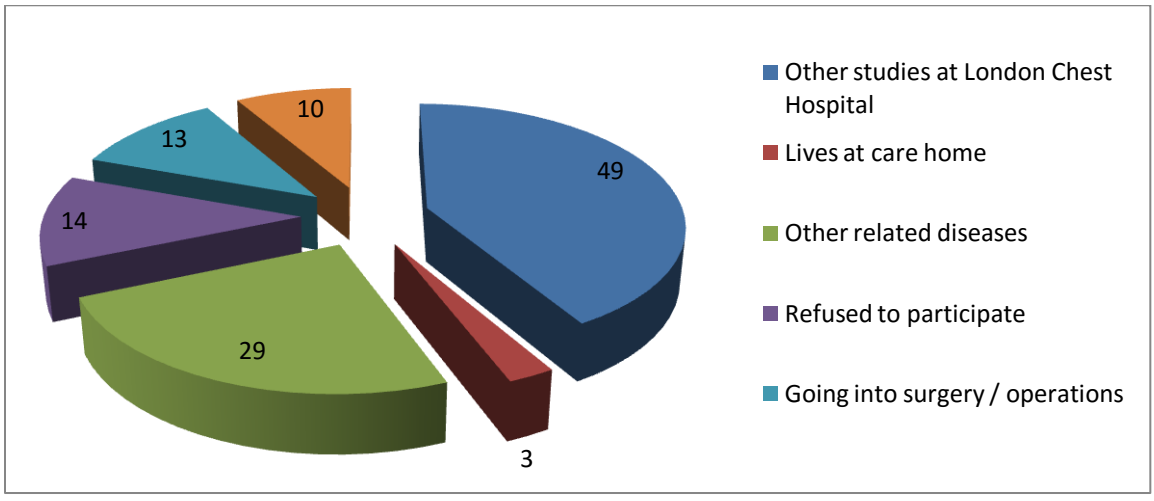
Two hundred and thirty three patients were assessed for eligibility. On average it was possible to recruit 2- 3 patients per day excluding the days where there were no eligible patients. Recruitment was undertaken by one researcher, a sample size of 71 patients was reached. The decision to stop recruitment was due to time constraints. Patients were excluded if they did not meet the inclusion criteria as shown in the table and chart below.

Table 5.4 Patients excluded from the study

Other studies at London Chest Hospital	49	Eligible
Lives at care home	3	Did not meet the inclusion criteria
Other related diseases	29	Did not meet the inclusion criteria
Refused to participate	14	Eligible but refused
Going into surgery / operations	13	Did not meet the inclusion criteria
Diagnosis changed	10	Did not meet the inclusion criteria
Has mental illness/problems	11	Did not meet the inclusion criteria
Does not speak English	13	Did not meet the inclusion criteria
Lives outside pharmacy areas	20	Did not meet the inclusion criteria
Patients consented to participated in the study	71	Eligible
Total	233	

Thus from 233 patients, 49 were eligible, 14 refused to participate, 170 did not match eligibility criteria and 71 patients were eligible and enrolled into the study.

Figure 5.6 Patients excluded from the study



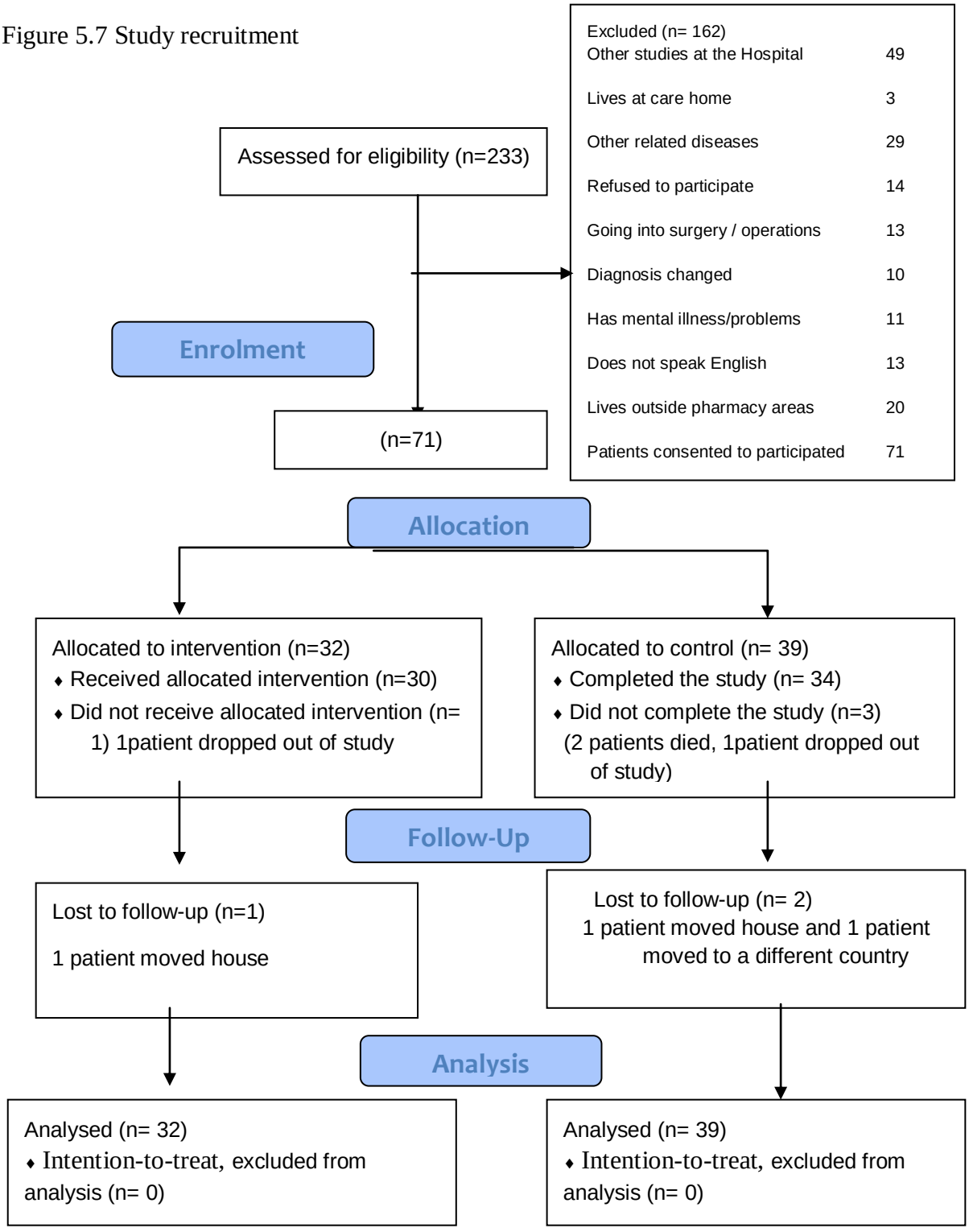
Challenges at the hospital during patient recruitment

A number of challenges occurred during the recruitment of patients; these included the following; (1) several research projects took place at the LCH at the same time recruitment was ongoing for this project. Therefore, recruitment would not start before 10 am until a list of patients (not to approach) was issued to prevent recruiting a patient into two studies at the same time, (2) protected time took place between 12:00 pm and 2:00 pm, during this time patients could not be approached because they would have time to eat, rest, sleep or have a visit from a family member, (3) due to the workload at the LCH eligible patients' charts were not always available (used by other health care team) during the time available for recruitment which could have also led to missing out some potential eligible patients, (4) patients after a coronary event stay for approximately two days in the hospital. After leaving the recruitment package with the patient for 24 hours some of the patients would be discharged or transferred to other wards before making the decision to be enrolled in the study, (5) the research pharmacist was at the recruitment site 3 days per week, which is 12 days per month this sums up to approximately 48 days. Further challenges at the hospital included; the forwarding of the discharge summary. Patients in the intervention group had their discharge summaries sent to the community pharmacist. It was difficult to forward the summary to the community pharmacies as there was no system at the hospital to forward the summary directly. In contrast there was existing developed software to send the summary to the patient's GP.

5.2- Patients' response rates/attrition

Seventy one patients were enrolled in the study; 32 in the intervention group and 39 in the control group. Sixty four patients completed the study, two patients died, 2 patients dropped out of the study 2 patients moved houses and could not be located and 1 patient moved to a different country. From the 32 patients in the intervention group 30 patients were in contact with pharmacist and completed the study as shown in the consort diagram below:

Figure 5.7 Study recruitment



Patients' perceived value of the consultation

The researcher conducted telephone interviews with coronary heart disease patients in the intervention group, after they received consultations from the community pharmacists. The patients invited to an interview were randomly selected by the researcher from the list of intervention patients. Four patients agreed to be interviewed regarding their thoughts and experiences of the community pharmacy service intervention. Below are results of these interviews.

Patient satisfaction with the consultation

Patients reported in interviews that they were very satisfied with the consultation. They found it reassuring to be able to talk to a pharmacist face to face or on the telephone regarding their medicines and disease.

"Yes I was very satisfied with it, I think it is a very good idea because we could discuss things and problems and everything so it definitely has value."

"I found it reassuring, that I could talk to somebody and have any questions answered."
"It has been very good to have someone on the other end of the phone."

Information from the consultation

The patients reported that being in contact with a pharmacist was very helpful after the heart attack. They reported in the interviews that the pharmacists were able to explain about the medicines and answer any questions they had. Furthermore, the patients mentioned that the fact that the consultations were delivered by a pharmacist was beneficial, because pharmacists have knowledge about medicine and some patients faced problems such as side effects and adapting to a routine with the medicine after discharge, especially when having to take more than one medicine.

"It was helpful because it takes a long while thinking about what the tablets are?"

"I was having problems with clopidogrel and that it was making me sleepy and we did discuss that and things like the blister pack"

"He explained all the medicines to me and everything and I told him how I was feeling because I was feeling really ill with them you know"

Some patients also reported that the fact that the consultation was offered by a pharmacist was convenient, because community pharmacists are easy to reach and easier to contact.

"Yes to have someone who you are confident is familiar with your situation and is an expert in the drugs you are taking to give you that extra support."

"Definitely, absolutely it is advice and it is so beneficial and it does provide information, if there are any problems or questions I need to ask about medication or doses then I can ask and get that answer easily so yes."

The patients mentioned that they felt that they were able to build rapport with the pharmacists' in the consultations.

"It is not like yes let's get this over with, no you have a nice person who has a genuine concern and when you feel you got empathy from a healthcare professional it makes you feel like you are not in the urge or on your own"

"When it first initially happened and I got more concerned about the medication, I mean when it first happened this was like a welcoming sign to have someone you have seen and you are going through a lot and someone actually following you up so you can put the connection. It helped me yes."

In the interviews the patients' expressed that the consultations saved them time, they did not have to book an appointment with a GP or go to another pharmacy for information, also some patients looked forward to the consultation with the pharmacist and could get problems solved.

"Because speaking in general if you have to go to a GP or book an appointment we do not have to do that. I can talk to the pharmacist in a private situation"

"You see a different GP every time and the cardiologist I have seen him once."

The patients mentioned that the contact by a pharmacist helped with adherence to the cardiac medication. They described the pharmacy contacts as promotes to adhere further to the medicines. Also that the pharmacy consultations helped some patients get their medicines arranged in blisters or dosette boxes that was also useful for adherence.

"I think it did help like when the pharmacist says are you taking your medicines? it is like a reminder so I keep them out there by the kettle so I see them first thing in the morning, so I take them, I think just that little promote you know is an additional help and keeps me on my toes."

"Things like the blister pack it helped me find a pharmacy that did it for me."

"You are all checking us on the medication if they have been missed and the impact of the medication"

Timing of the consultations

Patients reported that the timings of the consultation with a pharmacist at the pharmacy or on the telephone were all convenient. Patients who attended face to face appointments had prearranged booking times with the pharmacist and patients contacted by telephone also reported that the telephone timings were all convenient.

"Well we got there and I think in the beginning he was busy, so we waited for a while but it wasn't too long, then we went into a little room and my wife was with me."

"You have all been quite good because I have spoken three, four times now and he has been very polite and asked if it is ok to speak even if I am at work. It has been very very good I have had no problems with timings."

"Yes the timings was ok it was fine", "I am retired so the timing is ok for me it is fine"

Problems and unhelpful aspects of the consultation

The patients did not find anything inconvenient or not useful with the consultations, they described it as a positive experience.

"In what you are all doing now no I cannot see anything not useful at all, no not at all no."

"Like I said it was a positive experience, so there isn't anything not useful"

Advantages from the consultations

The patients reported that being in continuous contact with a pharmacist made them feel secure after a life changing event. The patients also thought that the pharmacy consultation was a good service and should be offered to all patients after a heart attack. Patients thought that the service especially if delivered by telephone would be of benefit to elderly patients and carers or family members.

"Yes it is certainly a useful service, especially for older people yes because older people are perhaps a little bit more confused, or for a family member if it was an older person it would be of assistance."

"I definitely think it would be great if it could be rolled out across the board really for every patient."

"It makes you feel like you have not just been forgotten about, you know it is a major thing that has happened a life changing event, and you are not just forgotten and put aside no someone is calling following you up, asking questions, I think it is a good thing and idea.

One patient mentioned that it was the best thing the NHS had thought of.

"I think that this is one of the best ideas the NHS has come up with."

Another patient also mentioned that it was the only consistent service after her heart attack.

"I think in the actual fact it is the only service following my heart attack that has been a consistent follow up."

Information in the table below was recorded by the researcher and summarises established measures regarding the feasibility of the study in regards to patients.

Table 5.5 Feasibility of the study in regards to patients

Patients	
Number of eligible patients.	233 patients
Number of patients enrolled in the study.	71 patients
Number of patients in the intervention group and eligible for a pharmacy consultation.	32 patients
Number of patients contacted by the community pharmacists.	30 patients
Number of patients attending the first and second visit to the community pharmacies.	9 patients attended consultations 21 patients contacted by telephone

The results on the number of patients willing to participate and the uptake of the intervention by the patients demonstrate that the intervention was workable for patients. The interviews also show that there was a high level of patient satisfaction with the consultations and that the pharmacists succeeded in engaging the patients and building rapport.

Results on liaison with the general practitioners (GPs)

The research pharmacist used the data recorded at baseline (patient's postcode and GP practice) to contact the patients' GPs. Patients' general practitioners were sent by mail individual letters explaining briefly the study along with a copy of the patients' consent forms. The GPs provided written consent on providing the results of blood pressure measurements and LDL-C levels during the timeline of the study. The number of GP consent letters returned to the researcher at UCL-School of Pharmacy was 50 consent letters from 71. The remaining 21 GP surgeries that did not return consent letters were contacted by telephone and were faxed the patient's consent letter. Baseline data for blood pressure and LDL-C results were collected by the research pharmacist from the hospital database. Furthermore, these results were collected from GPs at 3 months and 6 months.

Challenges with data collection from general practitioners surgeries

Several challenges were faced during data collection from GPs these included;

(1) *Reliability of data*

Collecting patient data by telephone from receptionists was difficult. It was apparent that some receptionists did not understand which tests were being asked for, particularly regarding LDL -C. It was also not always clear to the receptionists when the most recent tests had been taken. In some cases nurses were available to give information, but not always. Therefore, a decision was made to fax the results. Once the decision was moved to faxing forms for GPs to fill in; data collection improved. However, forms were mostly hand written and not always easy to read.

(2) *Tests not performed*

Not all patients were tested either for BP or bloods at the designated times. It was often reported that patients had not had any further tests.

(3) *Late start*

Due to the delayed start and the initial issues with receptionists providing data, the first wave of results were not fully collected until the end of the first phase. This meant that the GPs were being asked for second test results within a couple of weeks of providing the first results. Obviously in some cases there was no new data and there was not a definitive more than 4 week period between data collection points. It is therefore crucial that the data is collected in line with the data collection schedule and that in cases of delay the schedule is amended accordingly.

(4) *Patients stopped using regular GP*

Five patients stopped using their regular surgery and changed their surgery practice this was overcome by contacting the patients and enquiring regarding the address of their new practices. However this had an effect on the time for data collection.

(5) Three patients' charts at the hospital did not have the patients' GP contact recorded.

(6) One GP physician wrote a letter to the research pharmacist explaining that it was difficult to be part of the study because of workload at the surgery (letter can be found in Appendix 18) and suggested to recruit a nurse at the GP practice to commit to the study for data collection.

Due to all the listed obstacles above only one third of patients had full results on clinical outcomes blood pressure and LDL-C. For a larger study it would be recommended that all tests are performed at agreed times. It also could be better if data were to be collected from GPs electronically to improve accuracy. Thus in a larger study it might be important to recruit nurses at GP surgeries to undertake and facilitate data collection of such clinical outcomes.

5.3-Results on outcomes

Characteristics of respondents and comparison of intervention and control

Seventy one patients were recruited into the study from the London Chest Hospital:

Patients' sex

From 71 patients 54 patients were males and 17 patients were females: This result is typical with acute coronary syndrome statistics; where a man to women ratio is approximately 2:1 in the same age group (Mozaffarian *et al.*, 2015).

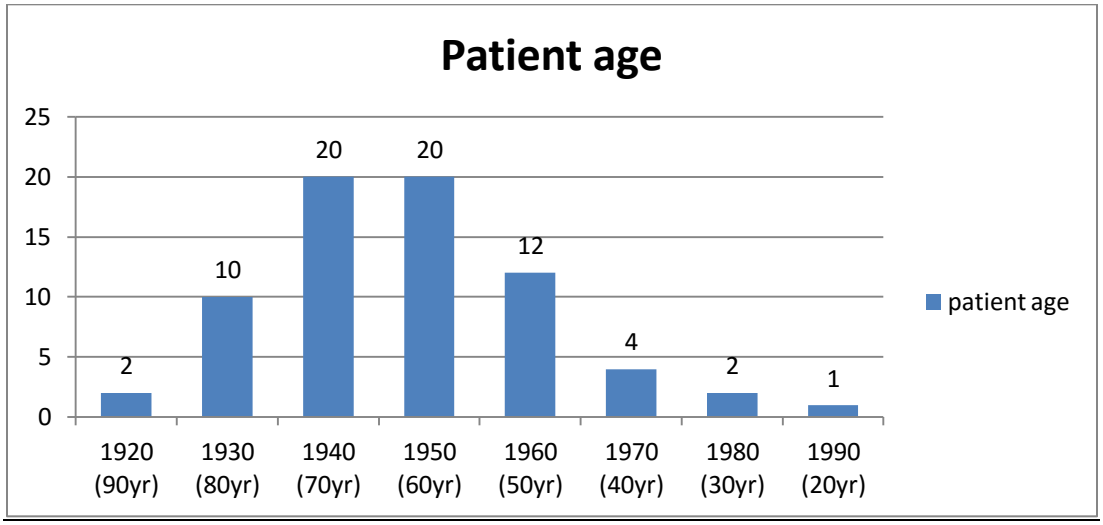
Diagnosis- type of acute coronary syndrome

From 71 patients 51 patients had a ST-Elevation Myocardial Infarction (STEMI), and 20 patients had a Non ST- Elevation Myocardial Infarction (NSTEMI).

Age

The majority of patients were in their sixties and seventies this result is also typical with acute coronary syndrome (Mozaffarian *et al.*, 2015).

Figure 5.8 Patient age

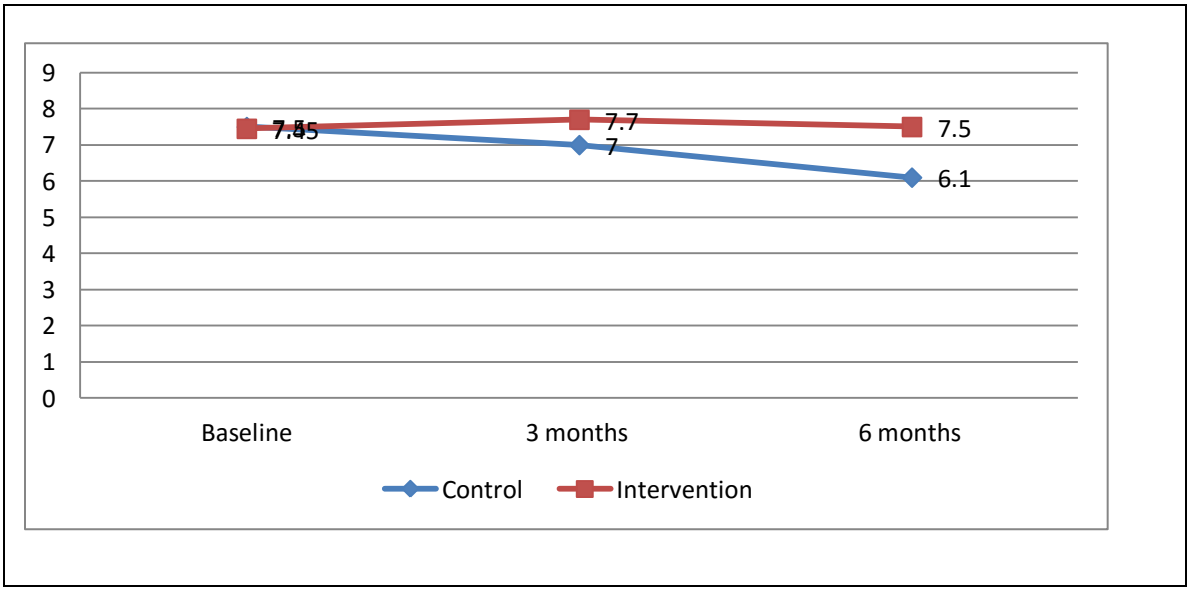


5.4- Impact of intervention results on primary and secondary outcomes

Results on adherence to secondary prevention medication

To evaluate adherence two measures were applied The Morisky MMAS-8 scale and a modified one question by Gehi *et al*, 2007. The Morisky MMAS-8 scale was used to evaluate adherence to the secondary prevention medication. The questionnaire was collected at 2 weeks after hospital discharge, three months and six months, the following results were found using the Independent T-test. At baseline there was no significant difference in adherence between the intervention group (Mean=7.45, SD=0.79) and the control group (Mean=7.5, SD=0.93) t (66) = -0.19 (*P*=0.85). At 3 months, there was a statistically significant improvement in adherence in the intervention group (Mean= 7.7, SD=0.56) compared with the control group (Mean= 7.0, SD=1.81), on the Morisky scale (t (44) = 2.4, *P*=0.026). This corresponded to a mean difference between the groups of 0.78 points [95% CI 0.14-1.42]. At 6 months, there was a statistically significant improvement in adherence in the intervention group (Mean=7.5, SD=1.47) compared with the control group (Mean =6.1, SD=2.09), on the Morisky scale (t (55) =2.9, *P*=0.004). This corresponded to a mean difference of 1.37 points [95% CI 0.45- 2.28] please refer to the graph below:

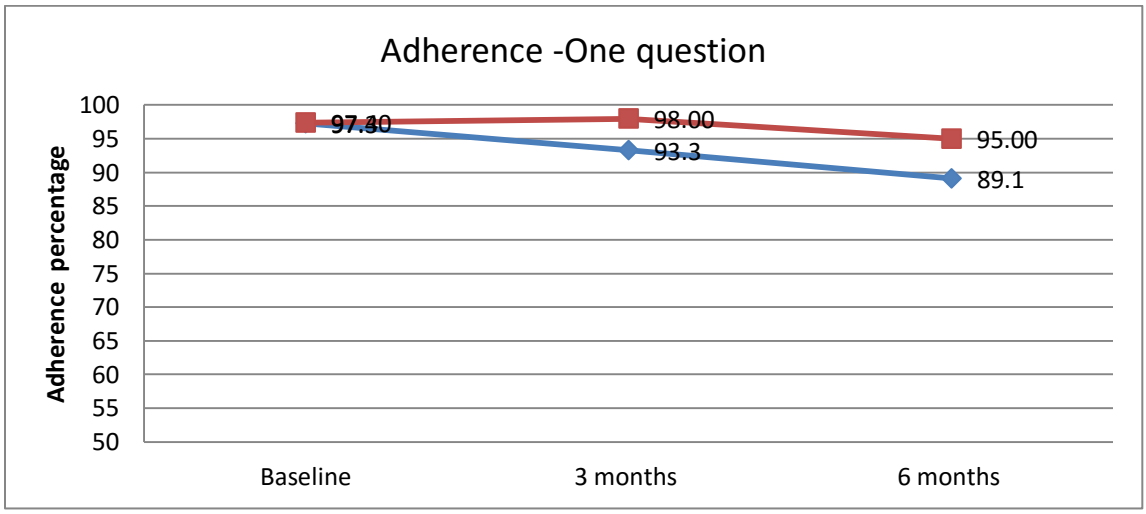
Figure 5.9 Result on adherence by Morisky scale



Measurement of adherence by Self report one Question

Self report one question by Gehi *et al*, 2007 was used to measure adherence. This question was modified from a scale used to measure adherence in clinical trials for patients with HIV. The one question was filled by patients at baseline, 3 months and at 6 months. At baseline there was no significant difference in adherence between the intervention group (M=97.4, SD=5.5) and the control group (M=97.3 SD=8.6) t (66) =0.023 (*P*=0.98), at 3 months there was no statistically significant difference in adherence between the intervention group (M= 98, SD=3.3) and control group (M= 93.2, SD=18) t (65) =1.68 (*P*=0.09) and no statistically significant difference at 6 months between the intervention group (M=95, SD=17.9) and control group (M=89.1, SD=23.7) t(62)= 1.22 (*P*=0.2). An improvement in adherence with the one question was observed in the intervention group at 3 months and 6months when compared to the control group but did not reach statistical significance as shown in the figure below:

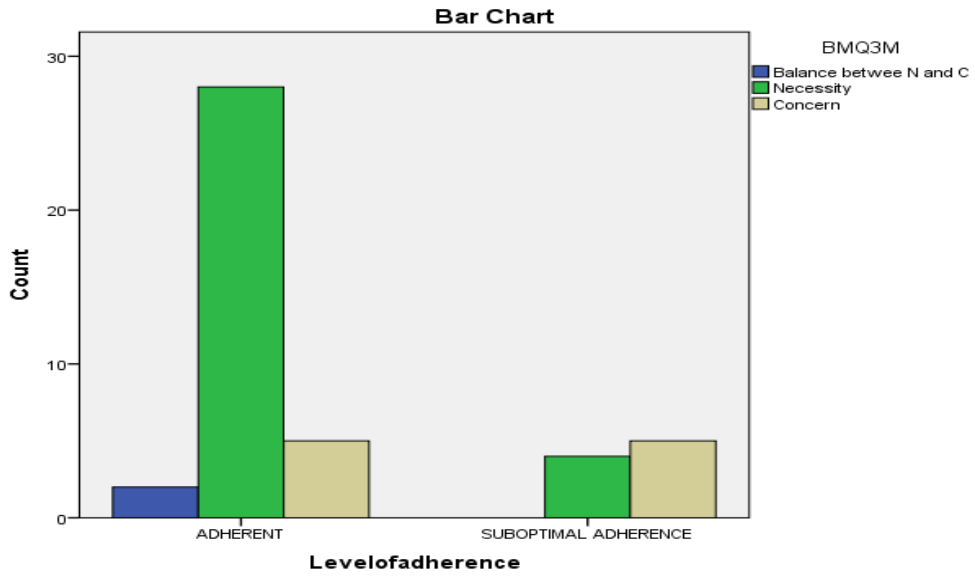
Figure 5.10 Result on adherence with self report one question



Beliefs regarding the medication

Forty four patients from seventy one returned by mail the BMQ specific questionnaire. A chi square test was used to investigate if there was a relationship between adherence to secondary prevention medication and patients' beliefs regarding their medicines. There was a statistically significant relationship between the level of adherence and the beliefs regarding medicines, X^2 (2, N=44) = 7.124, P=0.028. Patients who reported better adherence showed positive beliefs regarding the necessity of their medicines. Please refer to the chart below. The chart demonstrates results for 44 patients in two groups' adherent patients (Morisky score moderate 6-8, Morisky score high =8) and patients with suboptimal adherence (Morisky score < 6). In the adherent group (28) patients perceived the necessity of their medication, a lesser number of patients (5) had concerns regarding medication taking and even a lesser number (2) their concerns were equal to the necessity of their medication. In the suboptimal group a greater number of patients (5) had concerns regarding medication taking and a lesser number (4) perceived the necessity of the medications.

Figure 5.11 Result on beliefs regarding medicine



N=Necessity, C=Concern

Blood pressure results

Blood pressure classified according to the British Hypertension Society guidelines 2011 into hypertension systolic blood pressure>= 140-159 mmHg and diastolic blood pressure of >= 90-99 mmHg. Blood pressure was measured at baseline, 3 months and 6 months. Around two-thirds of patients in both groups did not have a follow-up evaluation from their GPs. Thus at 3 and 6 months there was no statistically significant difference between the two groups for both systolic, diastolic blood pressure and LDL-C.

Table 5.6 Result on systolic blood pressure in mmHg

	Intervention	Control	*P* value
Baseline	132	124	0.4
3 months	127	121	0.3
6 months	132	129	0.6

An independent-samples t-test was conducted to compare the means of systolic blood pressure between the intervention group and the control group.

At baseline: there was no statistically significant difference between intervention group in systolic blood pressure at baseline (M=132.8, SD 27) and the control group (M= 124.8, SD= 26) t (22) = 0.68 *P*=0.4.

At 3 months: there was no statistically significant difference between the intervention group (M=127, SD= 20) and the control group (M= 121, SD=20) t(28) = 0.87, *P*=0.3.

At 6 months there was no statistically significant result between the intervention group (M=132, SD= 11) and the control group (M=129, SD= 12) t(11)=0.4, *P*=0.6.

The results show that systolic blood pressure in the intervention group at 3 months decreased by 5 mmHg and at 6 months returned to the same as baseline, if compared to the control group in which systolic blood pressure decreased by 3 mmHg at 3 months but increased by 5mmHg at 6 months as shown in the figure below.

Figure 5.12 Systolic blood pressure results in mmHg

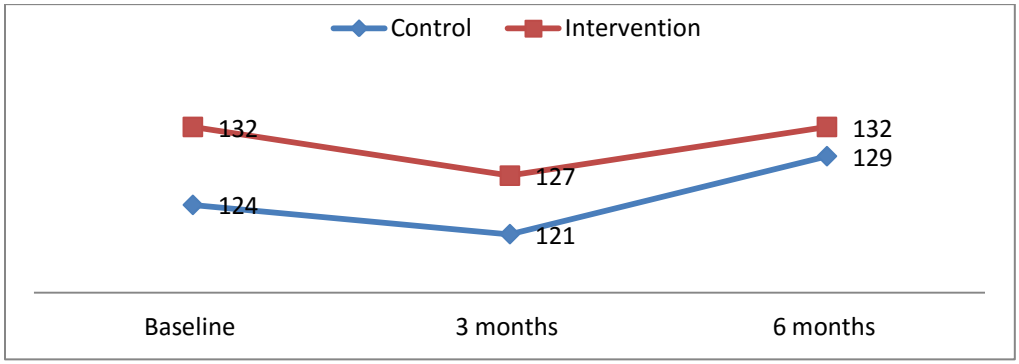


Table 5.7 Result on diastolic blood pressure in mmHg

	Intervention	Control	*P* value
Baseline	74	73	0.8
3 months	73	72	0.84
6 months	68	75	0.2

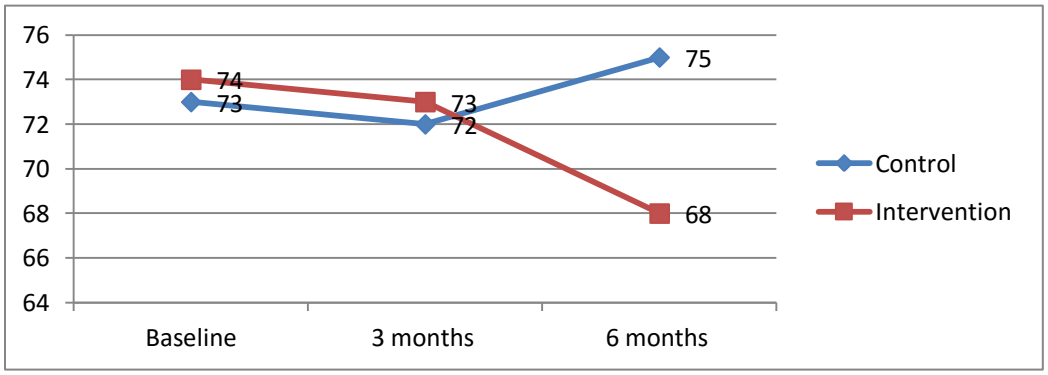
An independent-samples t-test was conducted to compare the means of diastolic blood pressure between the intervention group and the control group. There was no statistically significant difference between intervention group in diastolic blood pressure at baseline (M= 74, SD=7.2) and the control group (M=73, SD= 11) t (20) = 0.15, *P*=0.8. The study was not powered to show an effect on clinical outcomes; however, the difference in blood pressure between the intervention and control at 3 months could reflect adherence but would need to be tested in a further larger study.

At 3 months there was no statistically significant difference between the intervention group (M=73, SD= 11.5) and the control group (M=72, SD= 9.9) t(24) =1.92 , *P*=0.84.

At 6 months there was no statistically significant result between the intervention group (M=68, SD= 11.7) and the control group (M=75, SD=4.8) t (9) =-1.26, *P*=0.2.

However, at six months the diastolic blood pressure in the intervention group decreased by 6mmHg from baseline if compared with the control group in which diastolic blood pressure increased by 2 mmHg from baseline as shown in the figure below:

Figure 5.13 Diastolic blood pressure results in mmHg



The results on both systolic and diastolic blood pressure were not statistically significant but at 3 and 6 months the changes in blood pressure observed could be clinically important especially as controlling high blood pressure for secondary prevention is important for patients after a coronary event. The reduction in blood pressure in the intervention group could also be an indicator of adherence to medication, because blood pressure can serve as a biomarker of the efficacy of pharmacotherapy.

Low Density Lipoprotein-Cholesterol in mmole/l

Joint British Societies recommend cholesterol limits for people who have, or are at risk of coronary heart disease: total cholesterol - less than 4.0mmol/l and LDL cholesterol - less than 2.0mmol/l. LDL-C was measured at baseline, 3 months and 6 months.

Table 5.8 Result on LDL-C in mmole/l

	Intervention	Control	*P* value
Baseline	2.75	2.79	0.9
3 months	2.65	2.67	0.9
6 months	1.8	2.59	0.4

An independent-samples t-test was conducted to compare the means of LDL-C between the intervention group and the control group. There was no statistically significant difference between intervention group in LDL-C at baseline (M=2.75, SD= 1.05) and the control group (M=2.79, SD=1.4) t (24) = -0.079, *P*=0.9.

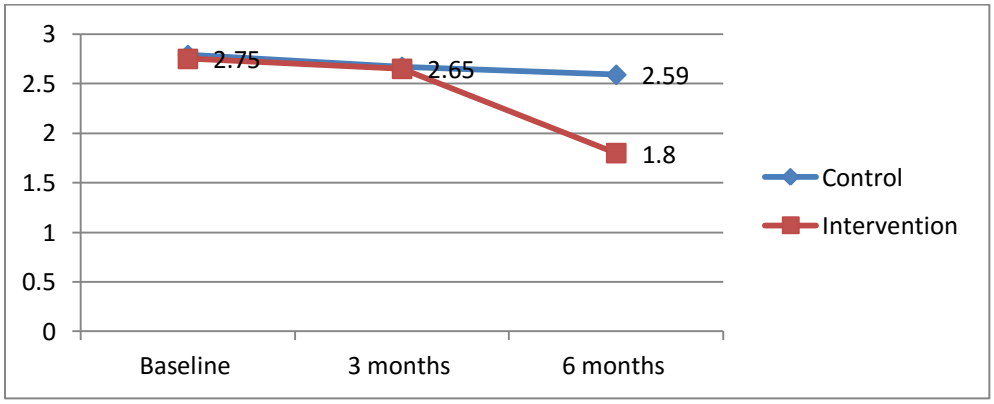
At 3 months there was no statistically significant difference between the intervention group (M= 2.65, SD= 1.17) and the control group (M= 2.67, SD= 1.21) t(24) =-0.039, *P*=0.9.

At 6 months there was no statistically significant result between the intervention group (M=1.8, SD=0.4) and the control group (M= 2.59, SD= 1.8) t(4) =-0.746, *P*=0.4.

There was a 0.79 mmole/l difference in LDL-C at six months between the intervention group and control group as shown in the figure below. The result on LDL-C should be addressed with caution due to the small sample size, missing data and statistical non significance. However, high total cholesterol and LDL-C are established risk factors for myocardial infarction, NICE 2014 guideline recommends using high dose statin such as

atorvastatin 80 mg for treatment in people with CVD for secondary prevention. Therapy should be started as soon as possible after the diagnosis and the aim is that LDL-C should not be above 1.8 mmol/L; with an even lower target of 1.3mmol/L. Thus the result although statistically not significant could be of clinical importance to the patients. However, cannot be attributed to the intervention. The reduction in LDL-C in the intervention group could also be an indication of adherence to statins.

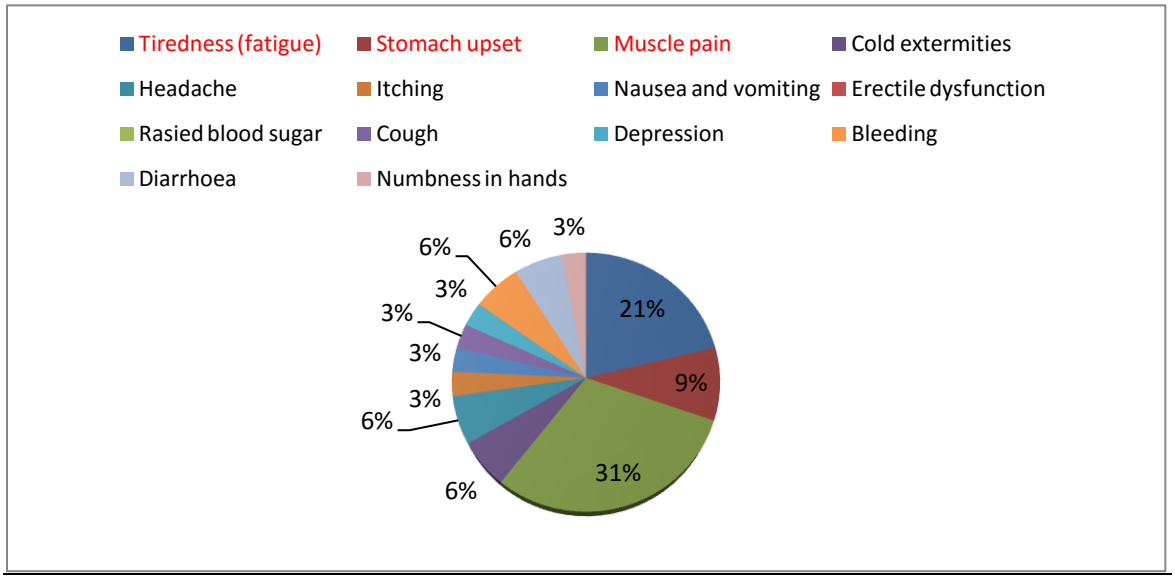
Figure 5.14 Results on LDL-C in mmole/l



Side effects

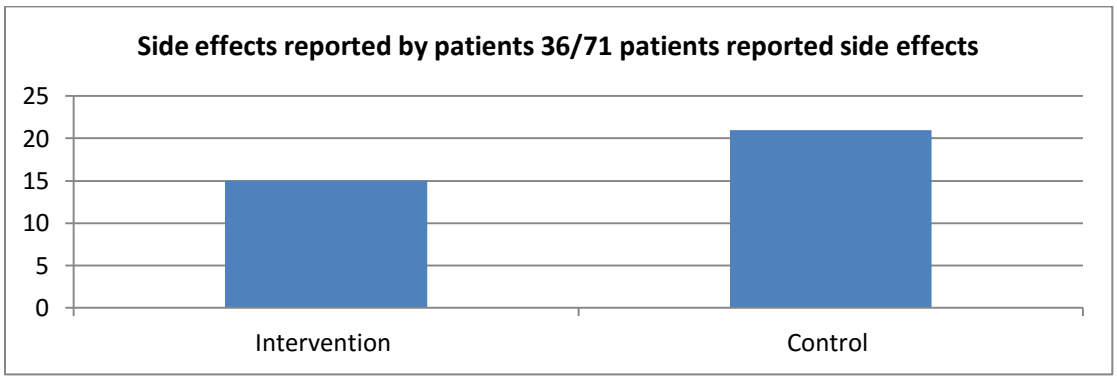
Recording the side effects reported by the patients' were not an objective in this feasibility study. However, the World Health Organisation lists side effects as potential reasons for non adherence to medication. Therefore, patients' experiences of side effects could have had an effect on medication taking and adherence. The side effects reported by the patients included the following: diarrhoea, nose bleeds, bleeding in urine, erectile dysfunction, cough, fatigue, back pain, muscle pain, indigestion, stomach pain, depression (feeling low), cold extremities, itching, rash, cough, headaches and numbness. The most reported side effects included muscle pain, stomach upset and tiredness.

Figure 5.15 Side effects experienced by patients



More patients in the control group reported that they experienced side effects than the patients in the intervention group; from the 71 patients' 21 patients in the control group reported side effects compared to 15 patients in the intervention group. This might have had an effect on medication taking behaviour and adherence in the control group compared to the intervention group please refer to chart below. However, the result was statistically not significant P=0.56.

Figure 5.16 Difference in side effects between intervention and control



Costs for the study

The study was designed as a pilot feasibility study and the intervention was incorporated into remunerated services at community pharmacies. Therefore, costs would be predicted to be minimal. However, there were some necessary costs for the feasibility of the study. These included training costs on motivational interviews and also pharmacists were reimbursed for their time in the study.

Total costs of this pilot study are listed below

- Intervention pharmacists attended 5-7 hours of training on motivational interviews and 2 hour training on secondary prevention medication after a myocardial infarction. The cost of the training for all three sessions:
  Psychologist training fees £1095
  Materials £500
  Rooms, catering £540
- Community pharmacists (intervention group only) reimbursement for training and participation £150/pharmacist paid in two instalments £75 each.
  19 pharmacists x 150= £2850
- Research assistant costs for data collection from GPs £500
  Total for all costs = £5485.

In addition, other costs included cost of a researcher (study coordinator), hospital pharmacists' time and other non-remunerated costs.

For a larger study these costs should be taken into consideration and funding will need to be secured. For this study these costs were covered by the Harold and Marjorie Moss Charitable Trust scholarship. This charity supports pharmacy research and was applied for and gained by the researcher at the beginning of the study.

The table below summarises overall conclusions regarding feasibility of the study and feasibility of the pharmacy intervention:

Table 5.9 Overall conclusions regarding feasibility of the study

Feasibility of the study				
Event	Conclusion	Comment	Problems	Recommendation for larger study
Pharmacy recruitment	Feasible	Was achieved by collaboration with LPC.	Caused problems with randomisation.	-Simple randomisation of overall sample. -Recruit by only one method.
Training	Feasible	Pharmacists attended and committed to the study.	-More than one training session had to be organised. -Some pharmacists did not attend the booster or training on secondary prevention medication. -Pharmacists not assessed on skills at the end of training.	-Arrange more than one training session. -Ensure all pharmacists receive the full training sessions. -Organise online training. -Assess pharmacists on skills using valid scales.
Hospital pharmacists recruitment	Not feasible	Hospital pharmacists can assist with study but not undertake full commitment to study duties.	Overloaded	Recruit research assistants to operate study including patient recruitment and administrative work. -arrange a system at hospital for communication between hospital and community pharmacists.
Patient recruitment	Feasible	Undertaken by researcher.	-Other ongoing research projects.	-Arrange study with research department at

			-Matching patients with recruited pharmacies. -Patients not sure which pharmacy to use after discharge.	hospital. - Organisation of recruitment time. -More than one researcher or research assistant at study site. - Promote study at site, awareness of study by other professionals (Doctors, nurses). -Review inclusion criteria, may be recruit only patients after first myocardial infarction. -Recruit a larger number of pharmacies.
Recruitment of GPs	Feasible	GPs provided consent to be part of study.	Problems occurred with data collection not with GP recruitment.	-Send invitation letter by post and also by telephone and fax.
Data collection from pharmacies	Feasible	Undertaken by researcher.	-Not all pharmacists had time to be interviewed. - Researcher had to contact pharmacists several times due to workload at pharmacy.	- Conduct focus groups not interviews.
Data collection from patients	Feasible	Undertaken by researcher, data collection by telephone led to a higher response Patients provided written consent for interviews.	- Needed to contact patients several times.	-Collect data by mixed methods telephone and post.
Data collection from GPs	Not feasible	Undertaken by research assistant.	-Late start due to difficulty collecting data from receptionists.	-Arrange tests to be performed at agreed times for data collection.

			-Tests not available.	-Employ nurses for the study to collect clinical outcomes.
Event	Conclusion	Comment	Problems	Recommendation for larger study
Patient uptake and attendance to consultations	Feasible	Patients interested in study. Patients welcomed the extra support from community pharmacists.	-Patients preferred to receive intervention by telephone. - Less patients attended face to face consultations.	Deliver the intervention entirely by telephone.
Arrangement with pharmacists	Feasible	Researcher acted as a link between patients and community pharmacists.	-Pharmacists had to contact patients more than once. -pharmacists reported that mostly they had to contact patients.	-Provide patients with pharmacy contact details on discharge and encourage patients to contact designated pharmacy. -Provide patients with a referral letter to pharmacy. -Organise number of patients per pharmacy.
Fitting session under MUR, NMS	Not feasible	Not all sessions were reimbursed.	Sessions did not fit under MUR, mostly fitted under NMS.	-Provide clear reimbursement plans. - Collaborate with LPC on rules and regulations of pharmacy services. - Fit consultation sessions under NMS only.
Use of motivational interviews	-	Pharmacy consultations were not recorded.	Variation between pharmacists on using motivational interviewing skills.	-Record and review consultations between pharmacist and patient. -Assess pharmacists on skills early before

				start of consultations.
Operation and delivery in the pharmacy	Feasible	Pharmacists reported in interviews that the consultations did not affect the operation of the pharmacy because incorporated in to existing services.	- Time to contact patients and invite to consultation.	-Need to ensure pharmacists have secure emails and internet connections to allow data transfer. - Explain to patients regarding pharmacy services during hospital stay and encourage patient to contact pharmacy after discharge -Incorporate intervention in existing services at pharmacy level

End of Chapter Five

Chapter Six

Interviews with South Asians in the UK and adherence to cardiovascular medication after Coronary Heart Disease

This chapter describes a small study to gain some insight into South Asian patients regarding their medication and adherence after a coronary event. The consultant pharmacist at the London Chest Hospital informed the research team that around 30% of admitted patients for CHD are from South Asian origin. This was true for the patients' sample recruited into the feasibility study 17/71 patients were from South Asian origin. Fourteen of these patients agreed to be interviewed by the researcher. Thus a sample of South Asian patients' was invited for an interview to study their adherence patterns and beliefs regarding the use of secondary medication after a coronary event.

6.1-Background

Coronary heart disease (CHD) remains the most common cause of death (and premature death) in the UK. There are 94,000 deaths from CHD each year (CHD, Statistics 2010). South Asians living in the UK (people from India, Pakistan, Bangladesh, Sri Lanka and Nepal) have a higher premature death rate from CHD at a younger age, often before the age of 40 years in men (Gupta *et al*, 2006). An explanation for excess deaths from coronary heart disease in South Asians is still not clear. Several theories in previous literature include "migration, disadvantaged socioeconomic status, proatherogenic diet, lack of exercise, high levels of homocysteine and LP(a) lipoprotein, endothelial dysfunction, enhanced plaque and systemic inflammation (Velmurugan and Gupta, 2005).

The use of secondary prevention medication in patients after CHD is vital to maintain optimal heart function and to prevent mortality (Ens *et al*, 2013). Adherence to medication in this patient group is necessary because evidence that non adherence is associated with adverse outcomes (Ho *et al*, 2009). However, there has been little research on adherence to cardiovascular medication among ethnic minorities and patients from South Asian backgrounds, despite the relatively high prevalence of cardiovascular conditions in these groups.

In addition, it is not known whether ethnicity plays a role in medication non adherence (Lai *et al*, 2011). Therefore, there is a need to look closer at this particular ethnic group regarding adherence to medication after a coronary heart disease.

6.2-Objectives

1- Provide an insight into adherence patterns to cardiovascular medication in South Asians after coronary heart diseases.
2- Identify factors that may influence adherence to cardiovascular medication.

6.3-Methods

Design

Interviews with South Asian patients, discharged from a London Heart Attack Centre (London Chest Hospital), after a coronary heart disease event were conducted. After 3 months of discharge and receiving secondary prevention cardiovascular medicines, patients were invited to participate in a telephone interview. This is to study their adherence to cardiac medication. Ethical approval for the interviews was gained from National Research Ethics Service Committee North West –Preston, also from the R &D Joint Research Management Office Queen Mary Innovation Centre and the R&D office University College of London.

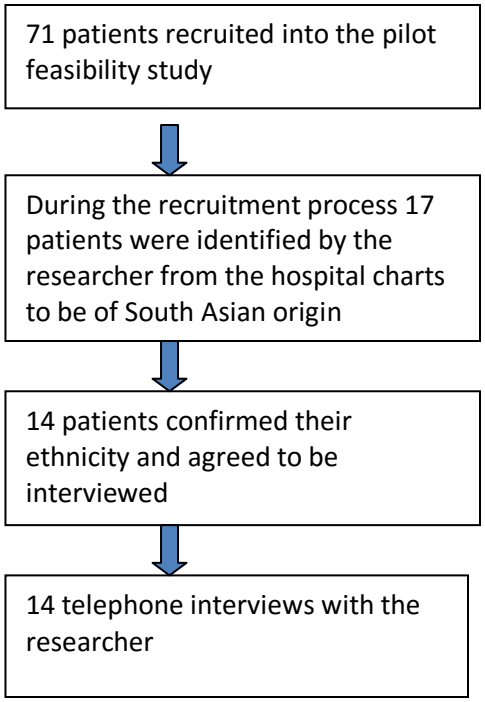
Study setting

The study was undertaken in collaboration with a London Heart Attack Centre in a district in East London UK.

Sampling and recruitment

Patients, who were eligible and had signed written consent to be part of the feasibility study, would be approached before discharge from the hospital by the researcher. This is to confirm if they would be interested in being interviewed by telephone regarding their medicines. The research pharmacist reviewed the patients' hospital charts to confirm eligibility for an interview. Patients were eligible if they had a coronary event ST elevation myocardial infarction or non ST elevation myocardial infarction, were prescribed secondary prevention medication, are from South Asian origin and can communicate in English. Seventeen South Asian patients before discharge from the centre were approached and invited to take part in the interviews, with an independent researcher. Fourteen patients provided written consent and took part in the telephone interviews. The three patients who did not take part were simply not interested in being interviewed. South Asian ethnicity was determined from the hospital charts and further confirmed by the patients.

Figure 6.1South Asian patient recruitment



6.4-Data Collection

The Interview

Semi-structured interviews were conducted. The questions were adapted from a previous study Garavalia *et al*, 2009. The reason the questions were adapted from Garavalia *et al*, 2009 was because the interviews in Garavalia *et al*, 2009 were designed to explore coronary heart disease patient's adherence to secondary prevention medication. Garavalia *et al*, 2009 investigated myocardial Infarction patients' perspectives and beliefs regarding their medication and designed their study with a qualitative descriptive methodology; patients were asked to describe their experience with the disease and medication. This study also wanted to explore South Asians' perspectives of their disease and medication to gain some insight regarding adherence after a coronary event. Previous literature has shown that factors that influence medication-taking behaviour in coronary artery disease include perception about coronary artery disease and about the medicines (Rashid *et al*, 2014). In this study we further explore adherence patterns and factors that may influence adherence to medication. Thus the questions were modified and three domains were studied: perception of disease, perception about the medication and factors that influence adherence.

The semi structured interview adapted from Garavalia *et al,* 2009: First can you describe your heart attack that led to your hospitalization? Please can you tell me your beliefs regarding the medications that you have been prescribed and importance of the medicines for your heart disease? Please can you tell me if you are having problems in taking your medication? for example are you using a pill organiser?, are you experiencing side effects? Are you having any problems in forgetting to take your medicines? Can you tell me what your medications are supposed to do? At this point, what do you think about your heart disease or do you think your heart disease is a serious matter? What changes have you made to your lifestyle as a result of your heart disease/attack? How do you think your heart disease affects your life or may change your future?

Instruments

Apart from the interviews, quantitative measures (measures of adherence and beliefs about medicines) were employed. These were already collected for the main study and included; the Morisky Scale and the Belief about Medicines Questionnaire Specific. The self report 8-Item Morisky Medication Adherence Scale (MMAS-8) was used to assess adherence. The MMAS-8 has a high reliability, sensitivity and specificity. The Belief about Medicines Questionnaire Specific (BMQ-S): The BMQ-S was used to assess patients' beliefs about their medication. It is a valid and reliable scale having been validated for use across a range of different diseases and also cardiac illnesses (Horne and Weinman, 1999). The scale comprises two main sections, the BMQ specific and BMQ general, the BMQ specific is comprised of two subscales, which are BMQ necessity and BMQ concerns. In this research the BMQ specific was used to assess participants' beliefs about their medication.

6.5-Data processing and analysis

All interviews were transcribed verbatim. A framework approach to analysis was undertaken involving the development of an initial coding framework with each domain of interview schedule, informed by literature and themes that emerged from the data. As analysis proceeded this was modified and refined using constant comparison techniques; in which all items of data assigned a particular code, were appraised for similarities and divergences from those already coded. Data from the Morisky and BMQ-scale were also analyzed and linked with the results from the interviews. To ensure reliability of the coding procedure, coding of the transcripts was undertaken by two members of the research team.

6.6-Results

Fourteen interviews were carried out between January 2014 and April 2014. The interviews ranged from 9 – 17 minutes in length. Participants' ages ranged from 32 years to 72 years with 7 patients in their 30's and 40's. Thirteen were male and one only was a female, country of origin of patients included Bangladesh (N=5), Pakistan (N=3) and India (N=6). Themes derived from the results included: importance of medicine, forgetfulness, organized routine, knowledge regarding the medicines, family support, side effects, feeling ill or feeling healthy, rely on health care practitioner, exercise, severity of the disease, life style factors (Asian food and dietary intake), causes of the disease, fatality and socioeconomic status.

Perception of disease

Beliefs regarding the disease feeling ill or feeling healthy

When asked to describe their experience of a heart attack, the majority of the patients described it as being intense unbearable pain, accompanied by tightness, sweating, burning, vomiting, severe indigestion pain. Very few described it as little pain, one patient thought that it was a chest, breathing problem.

"I had a breathing problem heavily too much and now I am walking no breathing problem".

The patient that thought it was a chest problem described feeling healthy after the heart attack and that the breathing problem was resolved. Another patient described it as a vomiting problem.

"No I didn't agree I had a heart attack I was vomiting and everything apart from that I didn't have any pain".

Beliefs of the acute nature of the disease in some older patients affected long term medicine use in patients who showed low adherence.

"Breathing problem is not serious now, I do not know whether I should continue medication or not, they will tell me".

Patients' who believed that the disease was acute showed a lower score on the Morisky scale with time. On the other hand the majority of young patients expressed difficulty in acceptance of having a chronic disease and the need to use medicines on a long term basis.

"I didn't take medicine all my life and then suddenly you have 6 different medicines a day this is the only confusion" ," It is first time I am on medicines I need time to adapt to a routine."

Severity of the disease

Patients' responses differed regarding the severity and seriousness of the heart disease. Some patients described it as been very serious

"Yes of course the disease is serious you could die"

Others thought it was serious before but currently after the event it is not serious

"The disease is not serious at the moment", "Mentally I do not feel it is a serious matter, I have been told that it is serious", some patients were not sure *"it is pretty serious isn't it?"*

Patients who believed the disease was serious scored high on the Morisky scale and had positive beliefs regarding the medicines on the BMQ scale with the belief that the medicines could prevent future cardiac events.

Causes of the disease

Causes of the disease were reported by most of the patients to be due to family history and genetics to a lesser extent due to risk factors (high cholesterol, smoking and not eating healthy).

"My family history my father died only when he was 51 and my brother when he was only 31 and he died he had another heart attack".

Other reported causes included stress, flu and a chest problem. Two patients were not sure of the causes

"I have not got a clue", "I do not know there were no symptoms of anything; I was not getting tired or anything".

This demonstrates that the majority of patients did not perceive the link between risk factors and the disease. Mostly patients believed that the disease was inevitable and running in the family.

Lifestyle factors

Younger patients in this sample were more able to link the importance of healthy lifestyle choices such as regular exercise and healthy eating with the disease.

"I am looking carefully at what I eat and I have cut down my alcohol".

However, older patients lacked understanding of the relationship between lifestyle and disease.

"No before the heart attack I did not do any exercise" "Just walking nothing more because I am an old man".

Fatality

Fatalistic views were reflected in the interviews, and the idea of the will of God and not the individual to determine future health was often reported

"What can you do I mean if God gave you the life whatever he gave you have to live".

In addition, worries of having another heart attack were also raised in more than half of the patients' interviews.

"I am worrying about another heart attack coming", "Now I worry all the time, it could happen any time again".

Compliant patients believed that the medicines were important to prevent a second heart attack. This was reflected in the adherence scores.

Role of medications necessity verses concerns

Importance of medicine

When asked regarding the importance of taking medicines nearly all the patients responded as very important.

"I think they are pretty important that is the reason they gave them to me."

Only few patients were not very sure how important the medicines were to maintain health

"I do not know if they are important or not", "If I go without my medicine I will realise if it is important or not but at the moment I need medicine".

Some patients mentioned that the number of tablets to take or the long duration to take was of concern *"Too much medicine, is it good for you?"*

The patients who reported in the interviews that their medicines were important had positive BMQ scores and scored high on the Morisky adherence scale.

Knowledge regarding the medicines

Half of the patients expressed knowledge about their medicines when asked the question can you please tell me what your medications are supposed to do? On the other hand half reported little knowledge, mostly relying on a family member to gain the knowledge or on a healthcare professional or simply not interested in knowing

"They are for cholesterol and clotting something like that, do not really know."

Patients who did not have knowledge regarding the medicine still reported that they were adherent and also had positive BMQ results.

"Chemist explained but memory not good", "Yes my GP told my son and at the hospital they told my son this is for this and this is for that, but they are important to take", "They are supposed to thin your blood, no I do not know what the others are supposed to do."

Studies in patients with chronic diseases have previously shown that medication adherence can be enhanced if patients are provided with good information about their treatment and that adherence to medication is correlated with knowledge regarding the prescribed medicines (Burge *et al*, 2005). This was not the case in this study.

<u>Factors that influenced adherence</u>

Forgetfulness

Several patients had problems with remembering to take their medications. The patients reported that this was attributed to being on medication for the first time, their young age, or trying to fit the medication into a habit as a daily routine.

"I take the medication all once a day so if I forget I forget the whole lot", "So far no problem with medicine, only one problem I keep forgetting to take."

These patients were young patients and reported that their non adherence was unintentional. They expressed a need to accept the disease and adapt to a new life style and routine that would include medication consumption.

An organized routine

Patients were asked to describe their daily routine of taking their medications. The majority of patients were able to list their medicines and how they take them every day. Ways to remember were reported as use of a pill box, writing on the boxes in native language, arranging them in a bag and making them accessible around the house. The patients reported that it took time to form a habit of taking the medication everyday and that they were trying to organise a daily routine to help with forgetting.

" I remember now, before I had to get used to it but now I am in a routine" "I never had taken medicines before and then suddenly I start taking it in my mind I am not taking medicine but now no I am taking it."

Family support

Family support varied among the patients, support was either offered as help in organizing the medicines, providing the knowledge about the medicines, helping with healthy eating and stress management. The patients' reported that the family support they received helped with their adherence to the medicines.

"My sister and my cousin they are trying to help me, she cooks for me."

"My daughter gives me the medicine and I just take so I remember."

Side effects

The main side effects reported by the patients included muscle pain, coughing, cold extremities, bruising and lethargy. The patients that experienced side effects reported in the interviews that they continued to take their medicines.

"One tablet ramipril tablet I was coughing and the coughing comes and goes every time, I told my GP and now I am on a different medication and I take it every day ", "My feet do feel cold then they do not stay long it is just you know, it is not a major thing I still take my medicine."

"I am bruising very easily and it seems to stay there for a while you know the aspirin, but the GP said that obviously I need to take it so there hasn't been no next steps."

Relying on health care practitioner

More than half of the patients depended on a healthcare practitioner regarding taking medicines and how important they are for the disease.

"The doctor said they are important for my body.", "I do not think about it if doctor says I need it then I need it that's it.", "I have the medicine regularly otherwise the doctor said there will be something wrong without the medicine."

Socioeconomic status

Two patients reported living in low socioeconomic status (bad accommodation, large families, drugs and depressing environments) which affected healthy dietary choices and added further stress and worries to their physical and mental health. Moreover, this was accompanied by depression and had a negative effect on adherence to medicines after a CHD.

"I cannot sleep every night, I am worried and smoking, now I am going to sleep because one children is go sleeping on the floor, you know a little bit of space give it to me because I am worried but I am not happy I do not have enough accommodation.", "I have been living in this hostel for four years and people in this place are too many they are always banging shouting and screaming, I cook my food and if I leave it for ten minutes it is gone from the cooker, I need to get out of this hole."

Cardiac rehabilitation

All the patients had either attended or were committed to attending cardiac rehabilitation, except one patient that thought that cardiac rehabilitation was additional medical treatment for example further injections and procedures.

"No I didn't go to cardiac rehabilitation. If they start putting injections again, I do not want to go through that again."

The patients' that attended cardiac rehabilitation reported that it was very useful and helpful.

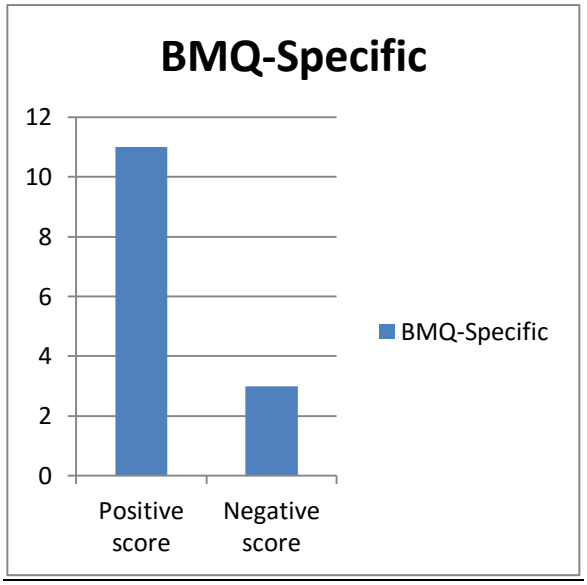
"Yes, I did complete cardiac rehabilitation and they are very impressed with results that came out.", "Yes, I am currently doing the cardiac rehabilitation program and I am very happy with the progress.", "I went to cardiac rehabilitation and I am thinking right now of joining a gym, I have changed the food I eat after cardiac rehabilitation".

Belief about Medicines Questionnaire Specific

Results on the Belief about Medicines Questionnaire Specific (BMQ-S) 11 out of 14 patients scored positive on the BMQ-S and only 3 out of 14 had a negative score. In BMQ-S the fourteen patients' had a mean (+/- SD) necessity score of 21 and a mean (SD) concern score of 15 (Please refer to the figure below). This showed that more patients at three months believed that the benefit of their medicines outweighed their concerns. Patients who had positive BMQ-S scores had a score that was positively correlated with adherence.

Figure 6.2 Results on BMQ-S

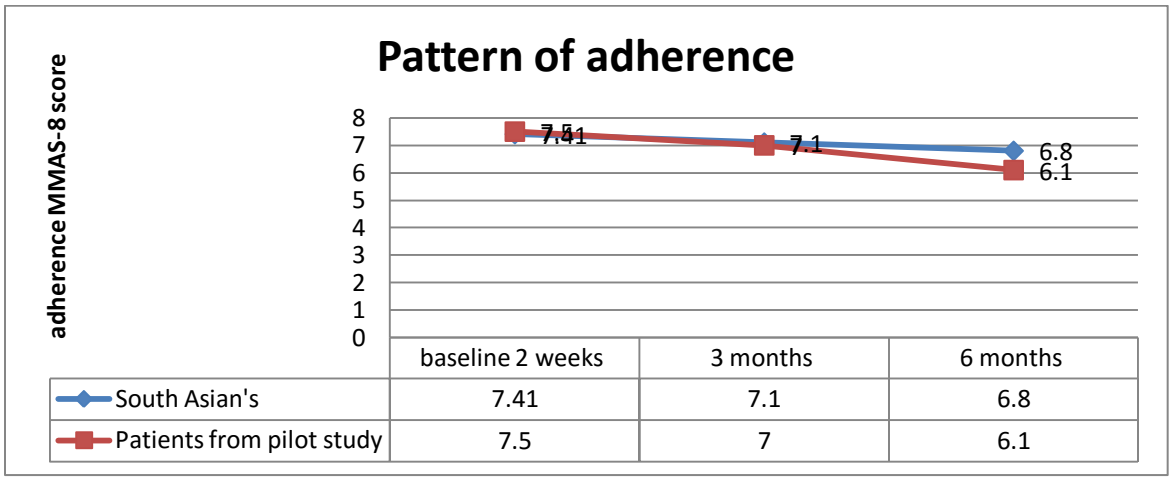
No. of patients	BMQ-S- Necessity sub scale/Concerns Subscale	
1	25/12	Positive score
2	25/10	Positive score
3	*15/20*	*Negative score*
4	25/12	Positive score
5	20/13	Positive score
6	19/14	Positive score
7	20/19	Positive score
8	21/16	Positive score
9	25/19	Positive score
10	*19/20*	*Negative score*
11	21/15	Positive score
12	24/11	Positive score
13	*17/21*	*Negative score*
14	21/15	Positive score
	21/15	*Mean score*



Adherence

On the 8-Item Morisky Medication Adherence Scale (MMAS-8) at baseline the South Asian patients' had a mean (SD) adherence MMAS-8 scale of 7.41 from 8 and this decreased with time to 7.1 and 6.8 at 3 and 6 months respectively. A similar pattern of adherence to medication was observed in the patients from the pilot study that included 71 patients, adherence to medication decreased with time as measured by the MMAS-8 scale of 7.5 and this decreased with time to 7 and 6.1 at 3 and 6 months respectively. Thus there was no evident difference in adherence patterns between the South Asians' and the patients in the pilot study regarding adherence to medication after an acute myocardial infarction as shown in the chart below:

Figure 6.3 Patterns of adherence



Additional factors that could influence adherence

It was also concluded from the interviews that factors that could have influenced adherence in this group of patients included: forgetfulness, depression, taking medication for the first time, not forming a habit or routine for medication taking. Factors such as knowledge and side effects did not seem to have an effect on adherence in this particular group of patients.

6.7-Discussion

The interviews highlight perspectives of members of the South Asian community regarding their disease and medication. The results illustrate that there was a belief in the importance of the medicines after a coronary event among the interviewed South Asian patients. The patients who adhered to the medicines believed that the medicines could prevent future cardiac events. Older patients perceived the disease to be of an acute nature. This affected long term adherence in this sample. In addition, older patients were unable to correlate a link between risk factors such as exercise and diet with cardiovascular diseases.

On the other hand younger patients had difficulty in accepting the disease and this affected their ability to adapt to a routine for medication taking. Coronary heart disease is perceived as a disease of senior citizens, as only 4% to 10% of all myocardial infarctions occur before age 45 (Harvard, 2009). However, South Asian patients more often experience CHD before the age of 40; and in this sample half of the patients were in their 30's and 40's. Furthermore, younger patients in this study were more able than older patients to correlate risk factors with cardiac disease. Both young and old patients reported in the interviews that family history and genetics were the main cause of their disease, also that the disease was inevitable and thus early prevention and further treatment might not have a significant role. Moreover, both young and old patients expressed strong family support with their disease and medication.

A similar pattern of adherence to medication was observed in the South Asian group compared to the patients from the pilot study. Adherence to cardiovascular medication reduced with time in both groups. Thus there was no evident difference in the adherence pattern after a myocardial infarction. Another finding in our study was that the patients rely on health care practitioners for the importance and knowledge of the medicines and also follow doctors' orders and instructions with the belief that health management should be left to qualified health professionals. The interviewed South Asian patients' in this study expressed the importance of attending cardiac rehabilitation and had attended or were scheduled to attend. Previous literature has shown that low-levels of Cardiac rehabilitation participation among South Asian and other ethnic minority groups have been reported in several English-speaking countries including the USA, Canada, the UK and Australia (Beswick *et al.* 2004). This has been attributed to reasons such as exercise, culture and religion, programme access and structure and communication and language (Galdas *et al*, 2011). The sample of patients in this study reported benefits from attending cardiac rehabilitation especially regarding the appropriate diet after myocardial infarction and the nature and amount of exercise they could uptake.

In the UK, the key health policy outlining the national standard for cardiac rehabilitation, the National Service Framework (NSF) for Coronary Heart Disease (DOH, 2000), states that services should be accessible and acceptable to all the people they serve regardless of their ethnicity. This includes ensuring staff and services are able to meet people's needs in ways that are culturally, religiously and linguistically appropriate and providing culturally appropriate advice about healthful lifestyles (British Heart Foundation, 2004). Several UK-based community health projects designed to improve CHD prevention and rehabilitation among South Asian individuals, such as Project Dil in Leicester (Farooqi & Bhavsar 2001), the BRUM study in Birmingham (Jolly *et al.* 2009) and the Khush Dil project in Edinburgh (Mathews *et al*, 2007), offer encouraging directions for healthcare professionals, in the design and delivery of culturally sensitive cardiac rehabilitation services (Galdas *et al*, 2011). Due to the small number of participants in our study a larger qualitative study focusing on South Asian uptake of programmes such as cardiac rehabilitation would be of benefit.

The findings in this study are preliminary however; they can provide an insight on adherence patterns to cardiovascular medication in a South Asian population. The findings should be approached with caution due to the small sample size and the short length of the interviews. Nevertheless, this study showed that increased belief regarding the necessity of the medicines was correlated with positive adherence scores. This finding is in line with other studies with large sample sizes, for example a study that involved 1611 coronary heart disease patients from 35 practices in Ireland found; that a strong belief in the necessity of one's medication and a lower level of concern about one's medication were associated with higher levels of adherence (Byrne *et al*, 2005).

Factors that influenced adherence in our study included: forgetfulness, depression, taking medication for the first time and not forming a habit or routine for medication taking. Factors that were reported not to have an influence on adherence were side effects and knowledge. The factors found in our study fall under the WHO framework for medication adherence that lists reasons for non adherence include younger age, socioeconomic factors, mental health (depression) and side effects (WHO, 2003) and can also be compared to results of a review (Ens *et al*, 2013) that concluded that medication side-effects, knowledge regarding the medicines, cost, forgetfulness and higher frequency of dosing are contributed to non-adherence.

The main side effects reported by the patients included muscle pain, coughing, cold extremities, bruising and lethargy. Although, these were reported by the patients' a sample size of 14 patients is small to assign these side effects, to the general South Asian population. In this study patients who reported side effects still believed that the medicines were important. As mentioned in other studies (Ens et al, 2013) this area needs further examination. Moreover, there are very few studies focusing on beliefs and adherence patterns after coronary heart disease of South Asians in the UK and due to the large South Asian population in the UK, larger studies of this nature are imperative.

The patients expressed in the interviews that they follow doctors' orders and instructions with the belief that health management should be left to qualified health professionals. This has also been concluded in other studies examining health beliefs of UK South Asians' related to lifestyle diseases (Lucas *et al*, 2013). In this study patients unable to understand and communicate in English were not included, this was a restriction to understanding communication barriers between South Asian patients and health care practitioners and how this could reflect on adherence. Other limitations in this study include imbalanced gender mostly male and only one female took part in the interviews, thus the view might not be representative.

Furthermore, telephone interview has drawbacks against face-to-face interview: e.g. not able to build rapport with participants, people might be less likely to talk on the phone, which subsequently did not generate rich data. Despite these limitations, the findings have shed light on the factors that influence adherence patterns to cardiovascular medication in a South Asian population and also the study raises awareness to the fact that larger studies could be beneficial in understanding culture issues around adherence to medication after coronary events.

End of Chapter Six

Chapter Seven

Discussion

Many new medicinal cardiovascular therapies have been introduced in the past half century. There is robust evidence that when appropriately used these reduce morbidity and mortality rates. However, there are continuing challenges relating to prescribing standards and strategies, and to the willingness and/or abilities of medicine users to take drugs in an optimal manner (NICE, 2009). It has been estimated that in the order of 30-50% of medicines prescribed for chronic conditions are not taken as recommended (Barber *et al*, 2004). Chapters One and Two of this thesis demonstrated that medication taking adherence amongst individuals and populations at risk of and living with cardiovascular conditions remains problematic. Although the overall human harm and financial cost attributable to sub-optimal CVD medicines prescribing and use is not well quantified (see below), addressing this issue is important. It is possible that enhanced health outcomes could be achieved via relatively simple measures delivered in community pharmacies and/or by community pharmacists and allied professionals.

Examples of potentially useful interventions range from the systematic use of screening questions addressed to patients who have been recently discharged from hospital care (or who might for other reasons be at raised risk of sub-optimal vascular disease medicines use) through to pharmacists reviewing medication refill/repeat dispensing patterns and taking action to facilitate better medicines taking as and when indicated. As demonstrated by the reported success of the New Medicines Service in England (Elliot *et al*, 2014), other strategies could involve follow-up telephone calls by pharmacists to patients who may be having problems with adherence to new (or established) therapeutic regimens. Whatever the approach taken, it is important to emphasise that non-adherence is not solely 'a patient problem', and does not merely cause the physical wastage of medicines. It can be caused by inadequate supportive care and result in not only avoidable individual and family distress but also adversely impact upon the NHS and other health care systems by needlessly increasing overall demand for services (NICE, 2009).

Against this background the research this thesis describes investigated in the context of post-hospital discharge MI care whether or not a pharmacy led intervention – a central element of which involved the use of motivational interviewing techniques – could be shown to result in beneficial medicines taking behaviour changes. The sections immediately below summarise key aspects of the analysis undertaken and offer relevant interpretations. Issues such as the wider role of techniques such as motivational interviewing in the future development of NHS primary care and the extent of the health gains that could be generated, together with the implications such progress could have for pharmacy practice and policy, are then explored.

7.1 Key Findings

Recruitment and training of the community pharmacists

The project undertaken was a prospective controlled pilot study. As indicated above, its central objective was to investigate the feasibility and impact of a pharmacy care intervention on adherence to medication in the post MI care context, and ultimately on coronary heart disease outcomes. The research undertaken generated a range of positive findings. Recruitment of pharmacies and training was, for example, successful. Many pharmacists were keen to take part, although their involvement was determined not only by their personal motivation but by factors such as the support staff time and financial resources available. Without adequate resourcing pharmacists may not be able to take part in training events and patient care programmes, even when well motivated to do so. In this study community pharmacists in the intervention group were highly committed, and drop-out over the period that research was undertaken was minimal (pharmacist dropout 1/20). The Local Pharmaceutical Committee in North East London played a vital role in recruiting professional participants and in facilitating the delivery of training sessions by providing a venue and communicating the importance of clinical service provision to local community pharmacists.

Those who became involved in the research process reported that, after 2 days of training and one booster session, they felt confident in delivering the study intervention and using motivational interviewing skills. However, some also said that they would have preferred further sessions involving patient and practitioner role playing and additional time for practicing their newly acquired competencies. Such observations may raise questions about pharmacy education and pharmacists' capacities to act as continuously developing health care professionals. These are not explored in depth here, but it is of note that these findings are similar to those of other studies undertaken in the UK and elsewhere amongst a range of practitioner groups. For instance, Van Eijk-Hustings *et al* (2011) worked with diabetes specialist nurses and dieticians to provide intensive training in motivational interviewing via a course involving 3 full days and 2 booster sessions. They reported that *'the spirit of motivational interviewing'* was present after the training sessions, and increased during follow-up periods. Yet in most cases only simple techniques were used and the nurses and dieticians taking part in their investigation said that they needed more support and training in order to apply the more complex aspects of motivational interviewing (Van Eijk-Hustings *et al*, 2011).

Some of the research findings contained in the available literature are not supportive of providing short motivational interviewing training courses. (See, for example, Efraimsson *et al*, 2011, who studied smoking cessation support given by nurses in Sweden.) Yet overall there is evidence that short courses can increase knowledge and change practice, at least for limited periods (Baer *et al*, 2004; Miller *et al*, 2004). The Health Foundation (2011) has argued that the duration of training opportunities is less important than their quality. The latter includes dimensions such as the clarity and effectiveness with which the autonomy respecting principles underpinning motivational interviewing methods are expressed and communicated.

Effective training should ideally include opportunities to practice with 'expert patients' or similar subjects, and to receive informed feedback about performance together with, where needed, ongoing supervision and coaching (The Health Foundation, 2011). In the study reported in this thesis the training course content was delivered by a skilled psychologist who sought to adapt the training given to addressing the needs of post MI patients in the NE London social environment.

There is also evidence that the pre-existing attitudes of professionals can impact on their willingness to learn and apply motivational interviewing techniques (The Health Foundation, 2011). Those most willing to volunteer to take part in training may have a greater affinity with this 'counselling' (or in medical terms 'consultation') style than other professionals. Follow-up interviews undertaken with community pharmacists involved in this research suggested the existence of such preference variations. This raises some concerns about the viability of universalising the changes in pharmacy practice explored here. Yet against this, it is also of note that significant numbers of pharmacists in the control group and from the LPC who did not take part in either research arm requested opportunities for training in motivational interviewing.

Patient recruitment and uptake of the intervention

Recruitment is always likely to be challenging in prospective studies aimed at health protection rather than immediate symptom relief or curing overt disease. Recruitment rates can be influenced by both service user and investigator side factors (Thoma *et al*, 2010). This may be so, for instance, when patients find trial objectives difficult to understand, and/or fear negative outcomes. Related factors can affect investigators if protocol designs are complex and when, for instance, they experience difficulties in obtaining informed consent from patients (Thoma *et al*, 2010).

Many trials do not meet their recruitment targets (Treweek *et al,* 2013). A relatively recent study of 114 UK multicentre trials supported by two of the UK's largest research funding bodies (the Medical Research Council and the NIHR's Health Technology Assessment Programme) found that less than a third achieved their original recruitment goals (n=38; 31%) and that more than half had to be extended (n=65; 53%) (McDonald *et al,* 2006). In this study the researcher involved followed the agreed recruitment strategy closely, and had piloted it before the formal commencement of this phase of her research. Service users were in the main prepared to participate, and some specifically said that they agreed to take part because the intervention involved follow-up by a health care practitioner working in primary care. Even so, the pilot undertaken did not reach its target participant patient population of 200 individuals. This was partly due to time constraints and the fact that patient recruitment was undertaken by just one PhD student researcher. The fact that the recruitment process took place at a single hospital site may have limited the generalisability of the study results to wider populations.

It is in addition of note that the patient sample included not only individuals with a first myocardial infarction but also patients who had suffered a second or subsequent myocardial infarction. Thus the subjects involved differed regarding their knowledge and experience regarding the use of medicines being recommended to them. Those who had experienced a re-infarction may, at least in some cases, have already acquired a negative/less than optimal approach to medicines usage. Sample members may have also varied with regard to their familiarity with the community pharmacies used for repeat dispensing. During the study some patients 'refilled' their prescriptions at a pharmacy other than the agreed intervention pharmacy. Uncertainty regarding which pharmacy to use after discharge was more common amongst patients on 'first time' medications than it was amongst those with earlier experience of taking protective post MI treatments.

Any future study might seek to recruit only patients recovering from a first myocardial infarction, in order to ensure greater consistency in the sample population. However, people experiencing a second or subsequent infarction may be thought to be of special interest in that they might be at raised risk of not using their prescribed medicines to best effect, perhaps because of problems such as low motivation associated with depression stemming from long standing illness or a lack of a sufficiently ordered approach to routinising protective drug use.

The study intervention was successfully delivered in the context of existing pharmacy services. It was performed by community pharmacists via either a face-to-face contact in their consultation rooms or by telephone. The pharmacists taking part reported that conducting consultations did not interfere with their wider pharmacy practice responsibilities and did not require undue amounts of time-consuming documentation completion. Similar findings have been generated by US and other studies in which motivational interviewing has been used alongside traditional pharmacy counselling techniques (Burke *et al,* 2003; Britt *et al,* 2004). A meta-analysis of 72 randomised control trials (Rubak *et al,* 2005) showed that motivational interviewing can be effective even when applied in brief encounters of no more than 15 minutes, and that more than one encounter per patient leads to statistically significant increases in the observed effect size. A US study by Pringle *et al,* 2014 – that included 218 pharmacies – also found that motivational interviewing could be incorporated into pharmacy workflow processes without affecting normal operations.

Fidelity of consultation techniques

The pharmacy consultations undertaken in this pilot study were not audio-recorded to assess their technical fidelity, albeit intervention arm pharmacists consistently reported that they adhered to the intervention protocol. Fidelity was assessed at the end of the study via the use of a scaled question.

Were a full scale study to be conducted it would be recommended that fidelity should be assessed at an early stage, and then at different stages throughout the duration of the research process. This could be achieved by community pharmacists recording (with due permission) all consultations and then by, say, a random 10% of each practitioner's total being reviewed by researchers.

In this research the community pharmacists involved in the intervention arm invited patients to take part in consultations. Some NHS users were contacted more than once. This inevitably involved some additional work. But, as already indicated, those undertaking interviews reported that doing so did not have a negative impact on the operation of their pharmacies and their overall patterns of activity.

Telephone 'versus' face-to-face motivational interviewing interventions

Two thirds of the patients taking part in this study chose to receive the intervention by telephone. Differences in the time, length and nature of the intervention may have occurred when it was given and received by telephone rather than face-to-face. As this project was designed to be a pilot feasibility study it was judged important to offer the intervention by both methods. It is now apparent that telephone consultations were preferred by a majority of patients. Hence for any future larger study delivery via this route would be a recommendation. Regarding whether or not there is a difference in the effectiveness of motivational interviewing delivered via alternative modes, some older evidence suggests that providing interventions by telephone may limit the rapport established and so treatment impact (Soet & Basch, 1997). This might be because providers and recipients are obliged to operate without non-verbal communication cues (Resnicow *et al*, 2002).

However, more recent evidence from reviews and meta-analyses demonstrates that motivational interviewing can be effectively delivered by telephone (Easthall *et al,* 2013; Teeter and Kavookjian, 2014). Teeter and Kavookjian, for example, conducted a systematic review of studies of telephone-based motivational interviewing interventions aimed at improving medication adherence. They included nine articles. The majority (five) of these found that motivational interviewing can be effective in increasing medication adherence when provided by telephone, albeit no studies were found that directly compared the two approaches (ie face-to-face versus telephone). The conclusion offered here is that there is a need for more sophisticated comparative studies looking at possible differences in outcomes achieved through the face-to-face as opposed to telephone applications of motivational interviewing amongst particular sub-populations. However, there is at the same time already adequate evidence that the aggregate effectiveness of telephone based consultations is broadly comparable with that of face-to-face interviews. More research is also needed on the cost-effectiveness of telephone versus the in-person delivery of motivational interviewing (Teeter and Kavookjian, 2014). In relation to this present study there may be instances in which a face-to-face pharmacist consultation on adherence offers advantages, such as when it is useful to examine the consequences of what might be medicine side-effects or observe blister packs (Lee *et al,* 2006). Nevertheless, the research that the English NMS is based upon involved telephone consultations which were shown to be cost effective with regard to enhancing adherence rates (Barber *et al,* 2004; Clifford *et al,* 2006; Elliot *et al,* 2014).

The intervention offered in this study was typically incorporated into an NMS consultation. (The majority of all NMS interventions are delivered by telephone – see Elliot *et al,* 2014.) It is of note that more recent studies that have included assessing pharmacist interventions delivered by telephone also indicate that they can significantly improve medicines taking adherence amongst patients with long term conditions (Lyons *et al,* 2016).

Telephone consultations have in addition proved to be of demonstrable effectiveness when delivered by other health care professionals. For example, around 12% of GP consultations are performed over the phone. This has been judged as useful in delivering many aspects of NHS primary care (Campbell *et al*, 2015). The advantages of conducting pharmacist and other consultations via telephone (and potentially through other IT based routes) may, over and above their relatively modest financial cost, on occasions include the fact that such approaches allow service users a beneficial sense of anonymity and/or control (Teeter and Kavookjian, 2014).

Telephone-provided consultations may help to increase service access for less advantaged populations such as those found in rural localities, and for individuals with restricted access to conventional health care provisions because of problems like poor mobility. The findings of this thesis support the view that a greater proportion of pharmacy services could in future desirably be offered via telephone.

Pharmacists' access to discharge summaries

In the study reported here discharge summaries were forwarded from the hospital pharmacy service provider to community pharmacists in order to facilitate consultations. Independently located pharmacist access to patients' hospital discharge summaries is not (as yet at least) usually available in the UK, or elsewhere in the world. This limits the potential of pharmacists' interventions to improve adherence and resolve medication related problems (PGEU Statement: 10.10.14E 002). However, NHS England has recently announced that it intends to facilitate community pharmacy access to Summary Care Records (SCRs). This present study may be regarded as demonstrating the potential importance of record sharing between community and hospital care providers as a step towards further enhancing the support offered to patients/health service users who wish to better manage their conditions with the help of community pharmacists.

All the main stakeholders whose views were elicited during this research – including hospital based as well as community pharmacists, together with participating GPs and pharmacy service users – expressed support for the supply of discharge summaries to community pharmacies. This finding is in line with evidence from the Royal Pharmaceutical Society (2014). The RPS recently launched a hospital referral to community pharmacy '*Innovators Toolkit*'. This was developed in response to the report "*Now or Never: Shaping Pharmacy for the Future*" (Smith *et al*, 2013). In the Royal Pharmaceutical Society's view hospital referrals to community pharmacies should be made electronically and could become routine practice with five years (i.e. by about 2020). The findings of this thesis can once again be taken to be consistent with the view that significant improvements in the efficiency and effectiveness pharmaceutical care should be possible, given appropriate pharmacy practice developments alongside wider health service reforms.

Bridging the interface between primary and secondary care

The observation that patients have problems with medicines taking as they move between primary and secondary care is by no means new. Research in this area has been ongoing for well over two decades (The Pharmaceutical Journal, 2004). Difficulties that can arise at this interface range from failures to ensure that hospital engendered prescription changes are effectively communicated to GPs and other primary care providers through to different brands of the same drug being prescribed and supplied. This last can, if uncorrected, cause patients to consume unduly high drug doses. Improving communication across institutional and other service boundaries is important. The approach adopted in this study sought to contribute towards this goal and was in line with previous Royal Pharmaceutical Society recommendations, such as those of the 2012 RPS report *"Keeping Patients Safe when they Transfer between Care Providers".*

The latter included a variety of guidelines intended to promote better service co-ordination. The findings of the present study highlighted the importance of such recommendations, while at the same time demonstrating the continuing existence of care co-ordination problems. This was in part illustrated by the fact that less than half of the pharmacists involved in the project did not previously have an *NHS.net* email address, and that referral at discharge into clinical services provided by community pharmacies is not as yet a part of standard hospital discharge care. Following-up patients and optimising their medicine use through community pharmacy interventions after hospital discharge has the potential to improve outcomes and in this study has shown, likely to be welcomed by most patients. Those receiving the pharmacy intervention described here reported high levels of satisfaction. Interviewees said they found it beneficial and reported their appreciation of being able to ask questions about their treatment without the need to book and attend a GP appointment. Service users reported that they felt well supported in the community by pharmacists working as (primary) health care professionals.

Letters were sent to all the GP's of the patients enrolled in the study. They demonstrated their support by consenting to the provision of blood pressure and LDL-C test results. However, in practice numerous problems were encountered during the data collection phase of the research undertaken. For instance, in many instances test results were not available at the agreed time of data collection, and practice receptionists on occasions appeared unfamiliar with the information needed. For a future larger study recruitment of nurses working in GPs' surgeries to help collect and provide data at the appropriate data collection points could help avoid such difficulties.

Pharmacy remuneration

Successful community pharmacy service changes are often dependent on timely and otherwise adequate financial support. This was recognised from the start of the research reported here. It was intended that remuneration for the pharmacy consultation involved should take place via either by a MUR or an NMS payment based approach. In the event a majority of the consultations undertaken were classified as NMS interventions. However, some counselling sessions could not be categorised as either MUR or NMS consultations, and so were not claimed for by the pharmacists/pharmacies who undertook them. Additional costs were also incurred in relation to attending the motivational interview training sessions. These expenses were accommodated via the study's small budget, together with support from the LPC. But the key point to stress here is that without transitional funding arrangements of one sort of another it is likely to prove very difficult – if not impossible – to achieve large scale practice changes in the community pharmacy context, even in the presence of a professional consensus that new ways of working are desirable.

Use of the Beliefs About Medicine Questionnaire (BMQ) to determine pharmacy service users' adherence support requirements

The research undertaken for this thesis found a statistically significant relationship between self-reported adherence levels and subjects' beliefs about medicines at 3 months (P=0.028). Patients who reported better adherence displayed more positive beliefs regarding the necessity of taking their medicines than those with poorer adherence. There are some uncertainties regarding the causal links underpinning these study observations. However, they are consistent with other research undertaken in the UK and elsewhere (Gatti *et al,* 2009; Sjolander *et al,* 2013; Horne *et al,* 2013).

For example, Horne *et al's* 2013 meta-analysis of research published on the application of the Necessity-Concerns framework in the context of medicines taking identified 3,777 studies, of which 94 fulfilled the inclusion criteria applied. It was found that adherence rates were positively associated with positive perceptions of treatment necessity [95% CI (1.569-1.934), $p<0.0001$] and relatively few concerns about unwanted treatment consequences [95% CI (0.450-0.564), $p<0.0001$]. A cross-sectional survey by Clifford *et al* (2008) explored beliefs about medicines using the Necessity-Concerns framework as embodied in the BMQ. It included patients who reported adherence, unintentional non-adherence or intentional non-adherence. These authors found that intentional non-adherers, compared to adherers, had relatively low belief levels regarding the necessity/positive value of taking their medication and relatively high levels of concern about taking it. By contrast, the beliefs of unintentional non-adherers were not significantly different from those of adherers. It was concluded that at the time when they start a new medication for a chronic condition people who become intentional non-adherers are likely to hold beliefs that are significantly different from those of adherers and unintentional non-adherers (Clifford *et al*, 2008). The patients involved in the study central to this thesis were not all on new protective medications for a first myocardial infarction. Even so, Clifford *et al's* work is relevant to its findings, as is the analysis offered by Horne and his colleagues. Both provide evidence that perceptual factors (that is, medicines taking related beliefs and preferences) can influence an individual's motivation to start and continue with treatment.

This study employed a motivational interviewing based pharmacy intervention in an attempt to improve adherence. But not all non-adherence with agreed medicine taking recommendations stems from motivational problems. The evidence available indicates that behavioural interventions utilising motivational interviewing techniques are more likely to benefit individuals displaying intentional non-adherence than they are those classified as unintentional non-adherers (Hugtenburg *et al*, 2013).

The latter are more likely to help to use their medicines as effectively as possible by interventions like medicine taking reminders and allied 'resilience' promoting measures (Furniss *et al*, 2014). The conclusion to be drawn here is therefore that tools such as the BMQ should ideally be used at a relatively early stage to determine individual needs, and that pharmacists should through applying comprehensive consultation and personal judgement skills seek to tailor the help they give in order to optimise adherence rates amongst all sections of the medicines using community.

The importance of this conclusion was recently underlined by the publication of a descriptive prospective observational study of patients surviving myocardial infarctions. This found that unintentional non-adherence is normally the primary form of non-adherence in the year following a myocardial infarction (Molloy *et al*, 2014). Unintentional and intentional non-adherence are not necessarily mutually exclusive – a mixture of these behaviours can exist in individuals. Yet such findings imply that motivational interviewing alone is unlikely to optimise medicine use and its outcomes, and that it should not be simplistically regarded as a non-adherence 'cure-all'. The view taken here is that acquiring motivational interviewing techniques *per se* ought to help professionals such as community pharmacists to address intentional non-adherence as effectively as possible. Further, when intelligently used by comprehensively skilled and empathetic professional practitioners as just one aspect of their overall approach to communicating with patients, motivational interviewing linked interventions should also help people to reflect on the environmental and non-cognitive behavioural barriers to their taking medicines in ways that generate benefit. A duly supportive therapeutic, social and physical environment may in addition motivate patients to find and implement ways of overcoming all such barriers to optimal medicines use, as well as adopting healthier life styles.

7.2 Motivational Interviewing and the Wider Development of NHS Primary Care

Incorporating the above understanding into under-graduate and post-graduate pharmacy education might prove important for the future development of the profession. However, the currently available evidence as to the value of motivational interviewing based pharmacy interventions remains poor (Pringle *et al*, 2014). Notwithstanding the findings of a limited number of other investigations involving pharmacists' use of motivational interviewing (Hedegaard *et al*, 2014) this present study adds new knowledge in that it demonstrates that motivational interviewing techniques can be successfully adopted, adapted and delivered by pharmacists in order to improve medicines taking adherence. There is no evidence showing that any one type of health professionals (such as doctors *versus* nurses, or pharmacists *versus* doctors) is inherently more effective at motivational interviewing than any other (The Health Foundation, 2011). Logically there is no reason why this should be so except in as much that, as with other aspects of health related communication, the effectiveness of interventions can in any given social context be influenced by patient/consumer expectations relating to the competencies, authority and trustworthiness of the communicator. However, such perceptions are plastic and change over time, as norms relating to accepted professional roles evolve.

Having said this, there is presently stronger evidence that medical doctors and nurses can use motivational interviewing to improve adherence in medication taking than is so in the case of pharmacists. (See Smith *et al*, 1997; Kemp *et al*, 1998; Daley *et al*, 1998; Schmaling *et al*, 2001; Rosen *et al*, 2002; Dilorio *et al*, 2003; Miller, 2004; Bisono *et al*, 2006; Thompson et al, 2010; and Rubak *et al*, 2005.) For example, a meta-analysis by Easthall *et al* (2013) included 26 studies that evaluated the use of motivational interviewing and related cognition based behaviour change techniques by doctors and nurses to improve medication adherence. Although the aggregated effect size the authors calculated is relatively modest [0.34 (0.23 to 0.46) $p < 0.001$] this study

offers robust evidence that motivational interviewing can effectively support medicines taking adherence in primary care. It also found that motivational interviewing and other cognitive-based behaviour change techniques are flexible and adaptable to various primary care contexts, and suggested that informed practitioners ought to incorporate them into their consultation skill sets in order to facilitate medication-taking related (and other) behaviour changes (Easthall *et al*, 2013). Despite the continuing lack of pharmacy specific evidence such observations may be therefore taken to justify the introduction of motivational interviewing into pharmacy curriculums for undergraduate and postgraduate pharmacists in the UK and elsewhere (Goggin *et al*, 2010; www.consultationskillsforpharmacy.com/docs/docb.pdf). It may be argued that there is a need for more evidence on the effectiveness of behavioural pharmacy interventions before suggesting an extended formal role for them in areas such as (in England) the provision of the NMS and MURs. But at the same time undue conservatism could harm to community pharmacy at this stage in its development.

7.3 The Scale of the Health Gains Potentially Achievable

It has already been observed that – despite the extensive interest shown in adherence related topics – the amount of 'lost health gain' due to failures to take medicines in ways fully consistent with the available evidence as to achieving optimal outcomes has not been well quantified. This weakness in the evidence base available cannot be corrected here, although it is possible to offer some outline observations relating to the overall scale of the health gains available. In the case of cardiovascular diseases age standardised death rates in England and Wales have more than halved in the last half century. This has in part been due to declines in smoking rates. But there is also good reason to believe that medicines have played an important part despite the fact that non-adherence in CVD medicines taking is common. If rates of appropriate medication usage can be enhanced even better outcomes should in future be achieved.

Evidence supporting this conclusion includes the fact that non-adherence to statins use in the year after hospitalisation for myocardial infarction has been linked to a 12-25% increased relative risk of mortality (Rasmussen *et al*, 2007). Moreover, non-adherence to cardio protective medications (β-blockers, statins, and/or angiotensin-converting enzyme inhibitors) is associated with a 10-40% relative increase in the risk of (cardiovascular) hospitalisation and a 50-80% relative increase in mortality rates (Ho *et al*, 2009).

The pilot feasibility study reported in this thesis was not powered (or of sufficient duration) directly to measure changes in clinical outcomes. Instead a validated measure of self-reported adherence with coronary artery disease medication was employed. Data were also gathered on blood pressure and LDL-C levels, along with the BMQ based analysis already reported. As described earlier, after six months self-reported medication adherence amongst those receiving motivational support from community pharmacist was 17 per cent greater than that recorded by control patients. This compares to a recent US study (Palacio *et al*, 2014) that found that a phone-based motivational interview improved adherence in the case of antiplatelet medicines usage by 14% ($p < 0.01$). The effect observed during the present study was also similar in magnitude to the reported effect of automated text messaging used to prompt adherence to cardiovascular preventive treatment (Wald *et al*, 2014). Some other research has failed to find similar benefits in relation to the treatment of people who have experienced strokes and other forms of vascular disease (Hedegaard *et al*, 2014; Ostbring *et al*, 2014). Nevertheless, it is concluded here that there is mounting reason to believe that greater use of well-targeted motivational interventions by community pharmacists could prove to be of substantive value in today's environment. It is also possible if not probable that combinations of different types of approach to enhancing medication taking in high risk patient groups would have even greater effects.

Nevertheless, it remains true that the current evidence base relating to the utility of pharmacy led interventions in this field is inadequate. Some authors have suggested that investing in high risk therapeutic situations like post myocardial infarction care should contribute cost effectively to improving health outcomes (Peterson *et al,* 2004; Lee *et al,* 2006; Morgado *et al,* 2010; Aslani *et al,* 2010). Yet studies like the one reported here have to date failed to demonstrate statistically significant results in relation to proxy clinical outcomes such as reduced blood pressure and LDL-C levels (See Ho *et al*, 2013; Yunsheng *et al*, 2010; and Jaffray *et al*, 2007). A relatively recent review by Cai *et al* (2013) concluded that too few pharmacy based trials are available, and that further larger scale quantitative research involving CVD patients should be conducted. The conclusion drawn here is in line with that analysis, albeit it is worth emphasising again that undue caution in relation to seeking to improve pharmaceutical care aimed at promoting better medicines taking could prove damaging not only for pharmacy but also to the public's overall health interests.

The extent of this last possibility is highlighted by the fact that, despite the advances made since the 1960s, vascular disease still causes over 150,000 deaths a year in the UK. Some 40,000 of these are of people aged under 75 years. At the same time over a million people are at any one time living with moderate and severe disabilities caused by events such as MIs and strokes in England alone. Even if it were conservatively estimated that enhanced pharmaceutical care leading to more effective medicines use would decrease the incidence/consequences of such events by only 5 per cent, this could significantly benefit several thousand 'new' patients annually.

7.4 Implications for Pharmacy Policy and Practice

In future, the implementation of plans stemming from the 2014 publication of NHS England's *'Five Year Forward View*' and the ongoing development of initiatives such as the formation of '*Healthy Living Pharmacies'* will create more opportunities for the delivery via community pharmacies of interventions like the one utilised in this research. Even if the pilot model described and evaluated here needs further refinement, it is likely that over time related interventions will emerge and become widely adopted. This is not least because the available evidence indicates that after a life changing event such as a myocardial infarction many patients welcomed the additional primary care support that appropriately skilled community pharmacists are capable of providing. Dispensing and medicines information supply processes will over time become increasingly computerised. Yet simultaneously the effective provision of personal care by pharmacists serving as health professionals is likely to be increasingly prized. In this context the positive responses of GPs involved in this investigation are both welcome and informative.

Some previous research studies have indicated that GPs have typically had negative attitudes towards extending community pharmacists' clinical roles (Saramunee *et al,* 2014). This was, for instance, partly revealed in 2005, when the Royal College of General Practitioners raised concerns about extending the prescribing rights available to pharmacists. Yet the responses of the GPs involved in this study were more positive than such observations imply. Establishing clinical roles for pharmacists working in GP surgeries has been an English Pharmacy Board objective since 2014. It is now being successfully realised. A key implication of the findings of this thesis is that there are also valuable opportunities for independently located community pharmacists to take play more active parts in clinical (including urgent as well as long term) care provision, working as constructive partners with GPs and primary care professionals like practice and community nurses.

Evidence such as that generated by the 2010 PINCER evaluation (Avery *et al,* 2010) and the 2012 PRACtICe study (Avery *et al,* 2012) has established that pharmacists can play critically important parts in reducing the occurrence and mitigating consequences of prescribing errors, and in more generally improving the quality of medication regimens. Yet the research findings described here also support the view that pharmacists can usefully act as not only experts on medicines at the pharmaceutical science and pharmacological levels, but as professionals skilled in understanding and facilitating changes in the behaviours of people who can benefit by taking medicines in optimal ways.

The clinical care and patient support roles of pharmacists located in all primary care settings are, it can be claimed, becoming more widely recognised and accepted. The findings of this research indicate that, in addition to recent measures aimed at encouraging the employment of pharmacists in GP surgeries, innovative approaches to developing community pharmacy contributions to the wellbeing of seriously ill patients in need of better overall care demand further investigation. Recent Government announcements to the effect that pharmacists across England will, with appropriate patient consent, soon be able to access patients' Summary Care Records (SCRs) can be taken to be an endorsement of this conclusion. One recent report (HSCIC report, 2015) found that 85% of the pharmacists interviewed during its preparation agreed or strongly agreed that SCR access reduced the need for them to contact GPs before making clinically relevant decisions. It underlined the fact that pharmacist access to SCRs can help doctors and their patients to avoid prescribing errors and the harm they may, if uncorrected, cause.

The Royal Pharmaceutical Society has argued that practice developments such as those involving motivational interviewing based intervention evaluated will help pharmacists, together with the people they serve, improve medicines adherence. The RPS (2012) has also called for closer working between secondary and primary care, and suggested that good hospital pharmacy practice could beneficially include recommending community delivered NMS and MUR consultations during discharge processes. Although in this present study interviews with hospital pharmacists revealed that their knowledge regarding community services is often minimal, these observations can once again be taken to indicate that the type of intervention pioneered in this study will over time become incorporated into mainstream hospital and community policy and practice.

A final point to note here is that during the period devoted to designing this study and its core interventional approach several new pharmacy development initiatives were identified. They ranged from the innovative Self Care Pharmacy programme being pioneered by the NE London LPC to the emerging the role of pharmacists in modern hospital A&E departments. In addition, the Scottish 'minor ailments scheme' based on the MINA study (MINA study final report, 2014) has already been shown to reduce inpatient attendance rates at hospital A&E departments. The transfer of responsibility to community pharmacists involved, which permits them to prescribe treatments for patients with a range of common non life-threatening diagnoses, has '*given a confidence boost to the profession'*. This service also provides value for money for the Scottish taxpayer. However, in England no comparable arrangements have yet been agreed. In the case of the Self Care Pharmacies being established in North East London, this new scheme could serve to promote and facilitate the delivery of pharmacy intervention like the one evaluated here. It aims to enhance long term condition treatment quality, in part by providing participating pharmacists with training on both motivational interviewing and health coaching.

Moreover, patients can be enrolled into the Pharmacy Self Care service via hospital referrals. It therefore contains many of the aspects of the intervention developed and piloted for this study.

7.5 Study Strengths and Limitations

The strengths of the research reported in this thesis include the fact that the novel intervention employed utilised well-validated instruments such as the Morisky Scale questionnaire to assess adherence and the BMQ to observe necessity and concern linked beliefs about taking medicines. It is also the case that effective blinding procedures were put in place, and that the project was well supported by pharmacist and other participants.

Its main limitations relate to the small size of the sample recruited and the fact that it was focused on improving care in just one area of North East London, which limits the confidence with which its findings can be generalised. It would in addition be correct to say that using measures of adherence that do not rely on self-reported data would have increased the value of the findings generated, as would have been the capacity to identify varying rates of adherence on a medicine-by-medicine basis. However, within the resources available it is arguable that the approach used was the best affordable.

7.6 Future Research

Although positive, the findings of this pilot study need to be confirmed via a larger, more adequately powered, multicentre randomised controlled trial. A proposal for such a investigation was developed by the research team in partnership with an established Clinical Trial Unit – Priment CTU – and via a series of meetings with potential collaborators.

Institutional partners included The London Chest Hospital, University College London Hospital, Southampton University Hospital and Queen Alexandra Hospital Portsmouth together with the LPCs for North East London, Hampshire and the Isle of Wight, and North Central London. Approval for the study was gained from the consultant cardiac pharmacists at the designated sites. Members of the public were also involved in its design, including patients who had taken part in the feasibility study and other individuals with experience of coronary heart disease. When finalised, the proposal was submitted to the NIHR, but it did not win funding. Subsequent feedback revealed that it was not rejected on scientific grounds. Rather, an indication that behavioural interventions were not prioritised during the relevant round, which means that it might be selected for another call. Details of this proposal, which should arguably be regarded as an integral part of the findings generated by the research reported in this thesis, are provided in Appendix 24.

7.7 Conclusion

Since the end of the 1950s dramatic declines in the levels of mortality caused by the vascular diseases have been achieved in England and the other UK nations and across the more affluent countries more generally. Much of the increase in life expectancy recorded in Britain in the last half century has been attributable to such progress. However, the acute and long term consequences of events such as myocardial infarctions together with strokes still account for about 30 per cent of all deaths in this country, and represent a dominant cause of potentially avoidable disability. More could be done to reduce this burden through the facilitation of healthy life styles and the effective use of medicines (and other forms of health care) aimed at enhancing the primary, secondary and tertiary prevention of cardiovascular conditions and their sequelae.

Since the 1950s there have also been major changes in pharmacy practice, in both the hospital and community settings. In overall terms the main focus of the profession can be said to have shifted away from medicines production and supply towards areas such as promoting the safety and effectiveness of clinical care and achieving better health outcomes. The latter commonly demands combining the skills needed for identifying the most effective pharmacological use of medicines with an ability to understand and influence the behaviours of individuals and communities seeking relief from illness and the preservation of good health. The prospective controlled pilot study described in this thesis brings together these two over-arching themes. Specifically, the research undertaken demonstrates how enhanced pharmaceutical care, which in part involves pharmacists using motivational interviewing and allied psychological techniques to support changes in health determining behaviours, can help to further improve health outcomes relating to using medicines for (secondary) preventive care purposes amongst patients recovering from acute coronary events.

Over simplified approaches, which lack due appreciation of the fact that problems such as failing to adhere to agreed pharmaceutical treatment programmes are complex and cannot be resolved only by altering patients' motivational levels, should be avoided. Future NHS pharmacists will need comprehensive consultation and service users support skills to match their expertise in the traditional pharmaceutical sciences. Further, being able to successfully move more towards assuring the optimisation of medicines use in the cardiovascular and other chronic disease contexts will demand the organisation of larger multicentre randomised controlled trials. But the additional knowledge generated by this study provides evidence of the likely value of such efforts, and the design of further research projects could and should be informed by the findings of the work reported here.

As the development of increasingly effective medicines and treatment regimens for maintaining vascular health and stopping the progression of disabling and life threatening conditions continues, achieving optimal outcomes for both individuals and communities will require continuing investment in areas such as the promotion of adherence in medicines taking. In some instances this will help limit care costs. But in the final analysis the most vital point to make is that pharmacy as a profession with expertise in not only the biological actions of drugs but in meeting the needs and influencing the behaviours of people who require them has the opportunity to play an even more important part in future individual and public health improvements than it has been able to fill in the past.

The End

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Appendices

Appendices

Appendix 1 Epidemiological transition 3 basic ages by Omran and 4 stages by Olshansky and Ault. Adapted from Gaziano T.A., (2005) Cardiovascular Disease in the Developing World and Its Cost-Effective Management *Circulation*; 112: 3547-3553.

Stage	Description	Life in years	Dominant Form of CVD	Percentage of Deaths Due to CVD	Percentage of the World's Population in this Stage	Regions Affected
Pestilence and famine	Predominance of malnutrition and infectious diseases	35	RHD, cardiomyo-pathy due to infection and malnutrition	5–10	11	Sub-Saharan Africa,parts of all regions excluding high-income regions
Receding pandemics	Improved nutrition and public health leads to increase in chronic diseases, hypertension	50	Rheumatic valvular disease, IHD, hemorrhagic stroke	15–35	38	South Asia, southern East Asia and the Pacific, parts of Latin America and the Caribbean
Degenerative and man-made diseases	Increased fat and caloric intake, widespread tobacco use, chronic disease deaths exceed mortality from infections and malnutrition	60	IHD, stroke (ischemic and hemorrhagic)	>50	35	Europe and Central Asia, northern East Asia and the Pacific, Latin America and the Caribbean, Middle East and North Africa, and urban parts of most low-income regions (especially India)
Delayed degenerative Diseases	CVD and cancer are leading causes of morbidity and mortality; prevention and treatment avoids death and delays onset; age-adjusted CVD declines	>70	IHD, stroke (ischemic and hemorrhagic), CHF	<50	15	High-income countries, parts of Latin America and the Caribbean
RHD indicates rheumatic heart disease; CHF, congestive heart failure.						

Appendix 2 Eastern Mediterranean Region -Cardiovascular Disease-Facts (Alwan, 1997), (Jabbour *et al,* 2012), (Gaziano *et al,* 2011).

Country	Facts
Kuwait	An increasing death rate from coronary heart disease and hypertension, deaths from CVDs, accidents and malignant neoplasms accounts for almost half the general mortality, age adjusted mortality rates 300 per 100,000 population.
Qatar	Diseases of the circulatory system were responsible for 37% of deaths.
Bahrain	Diseases of the circulatory system were reported to be responsible for 30% of Deaths. Coronary heart disease is the predominate type of cardiopathy and the fourth leading cause of hospital admission.
Jordan	CVDs were reported as the leading cause of death in accounting for 44.4% of male and 34.5% of female mortality. Almost half the patients with confirmed CVDs are below the age of 50 yrs and 17% are above the age of 60 yrs.
Cyprus, Egypt, Islamic Republic of Iran, Iraq, Morocco, Oman, Pakistan and Saudi Arabia.	Hypertension (Blood Pressure > 140/90) has been reported to affect more than 20% of adults. A survey in Egypt showed that 26% of adult Egyptians suffer from hypertension. Similarly in Oman 26.3% of adults suffer from Hypertension. Egypt, Yemen and Iraq- have high rates of age-adjusted mortality rates 500 per 100,000 population.

Appendix 3 Coronary heart disease/cardiovascular disease primary risk calculators and risk prediction charts

ETHRISK® calculator based on Framingham data which may be appropriate for British black and ethnic minority groups

There are increasing numbers of alternative risk prediction scores, particularly focused on specific groups, e.g. people with diabetes, ethnic populations.

- ASSIGN: developed in Scotland and includes an index of deprivation and also family history (Woodward *et al*, 2007).
- Reynolds Risk Score: provides a greater accuracy for assessment of cardiovascular risk in women (Ridker *et al*, 2007).
- UK Prospective Diabetes Study (UKPDS) Risk Engine for people with type 2 diabetes :
    - Provides risk estimates and 95% confidence intervals, in individuals with type 2 diabetes not known to have heart disease, for:
        - Nonfatal and fatal coronary heart disease.
        - Nonfatal and fatal stroke.
    - These can be calculated for any given duration of type 2 diabetes based on current age, sex, ethnicity, smoking status, presence or absence of atrial fibrillation and levels of HbA1c, systolic blood pressure, total cholesterol and HDL cholesterol.
- INDANA (INdividual Data ANalysis of Antihypertensive drug intervention) risk calculator: focuses on patients with raised blood pressure.
- Other risk calculators include the older Sheffield Table for Primary Prevention of Cardiovascular Disease, the New Zealand tables and tables proposed by the European Society of Cardiology.

A number of risk prediction charts are available for assessment of cardiovascular risk factors the charts are intended to allow the introduction of the total risk stratification approach for management of cardiovascular disease.

Examples of these charts -WHO/ISH cardiovascular risk prediction charts provides specific information on countries in each WHO sub region.

The charts have been generated from the best available data, using a modelling approach with age, sex, smoking, blood pressure, blood cholesterol, and presence of diabetes as clinical entry points for overall management of cardiovascular risk.

Separate charts have been developed for assessment of cardiovascular risk in patients with type 2 diabetes. There are also charts when there is absence of cholesterol measurement.

-Joint British Societies' cardiovascular disease (CVD) risk prediction chart.

The charts exist for non diabetic and diabetic men and women.

-The American Heart Association used Framingham risk factor data to prepare charts for estimating CHD risk.

- Risk charts derived from the SCORE risk estimation system that offers direct estimation of total fatal cardiovascular risk in a format suited to the constraints of clinical practice.

Appendix 4 adapted from Osterberg, 2005 summary of measures of adherence

Osterberg L and Blaschke T., (2005), Adherence to medication. *N Engl J Med*; 353: 487–497.

Test	Advantages	Disadvantages
Direct methods		
Directly observed therapy	Most accurate	Patients can hide pills in the mouth and then discard them; impractical for routine use
Measurement of the level of medicine or metabolite in blood	Objective	Variations in metabolism and "white-coat adherence" can give a false impression of adherence; expensive
Measurement of the biologic marker in blood	Objective; in clinical trials, can also be used to measure placebo	Requires expensive quantitative assays and collection of bodily fluids
Indirect methods		
Patient questionnaires, patient self-reports	Simple; inexpensive; the most useful method in the clinical setting	Susceptible to error with increases in time between visits; results are easily distorted by the patient
Pill counts	Objective, quantifiable, and easy to perform	Data easily altered by the patient (e.g., pill dumping)
Rates of prescription refills	Objective; easy to obtain data	A prescription refill is not equivalent to ingestion of medication; requires a closed pharmacy system
Assessment of the patient's clinical response	Simple; generally easy to perform	Factors other than medication adherence can affect clinical response
Electronic medication monitors	Precise; results are easily quantified; tracks patterns of taking medication	Expensive; requires return visits and downloading data from medication vials
Measurement of physiologic markers (e.g., heart rate in patients taking beta-blockers)	Often easy to perform	Marker may be absent for other reasons (e.g., increased metabolism, poor absorption, lack of response)
Patient diaries	Help to correct for poor recall	Easily altered by the patient
When the patient is a child, questionnaire for caregiver or teacher	Simple; objective	Susceptible to distortion

Appendix 5 Intervention setting

Intervention setting	The studies	Result on adherence
Hospital (14)	Lee *et al*,2006 , Morgado *et al* , 2010 , Al Mazroui *et al* , 2009, Sadik *et al* , 2005, Gwadry-Sridhar *et al* , 2005, Phumipamorn *et al*, 2008, Edworthy *et al*, 2009, Lopez *et al* , 2006, Zhao *et al* , 2011, Faulkner *et al* , 2000 , Varma *et al*, 1999, Jarab *et al*, 2012, Ho *etal*, 2014, Alsabbagh *et al*, 2012	12 (14) Significant
Community pharmacy (15)	Bouvy *et al*, 2003, Zilich *et al* , 2005, Villeneuve *et al*, 2010, Murray *et al* , 2007, Svarstad *et al*, 2009, Aslani *et al*, 2010, Lau *et al* , 2010, Vrijens *et al* , 2006, Sookaneknun *et al* , 2004, Jaffray *et al* , 2007, Blenkinsopp, 2000, Park *et al* , 1996, Mehuys *et al* , 2011, Planas *et al* , 2009, Eussen *et al* , 2010.	10 (15) Significant
Both hospital and community pharmacy (1)	Calvert *et al*, 2012.	1(1) Significant
Clinic or primary care practice (9)	Carter *et al* , 2008, Hunt *et al* , 2008, Taylor *et al* , 2003 , Odegard *et al* , 2005, Mehos *et al* , 2000, Obreli-Neto *et al* , 2011, Carter *et al* , 2009, Evans *et al* , 2010, Heisler *et al* , 2012.	3 (9) Significant
Home visit (2)	Holland *et al*, 2007, Peterson *et al*, 2004.	0 (2) Non significant

Appendix 6 Interventions and their mode of delivery

Intervention	Trials	Result on adherence
1-Patient education by pharmacist	Lee *et al* , 2006, Bouvy *et al* , 2003, Morgado *et al* , 2010, Al Mazroui *et al* , 2009, Sadik *et al*, 2005, Alsani *et al* , 2010, Murray *et al*, 2007, Mehuys *et al*, 2011, Taylor *et al* , 2003, Jaffray *et al*, 2007, Blenkinsopp *et al* , 2000, Sookaneknun *et al* , 2004, Phumipamorn *et al*, 2008 , Varma *et al*, 1999, Odegard *et al*, 2005, Park *et al*, 1996, Lopez *et al*, 2006, Zhao *et al* , 2011, Planas *et al*, 2009 , Evans *et al*, 2010, Eussen *et al*, 2010	15(21) significant
2-Telephone contact	Yunsheng *et al*, 2010, Faulkner *et al*, 2000, Jarab *et al*, 2012, Alsabbagh *et al*, 2012	2(4) significant
3-Use of electronic device	Zilich *et al* , 2005 (SMBP), Svarstad *et al* , 2009 (pedometer, blood pressure tracker), Virijens *et al*, 2006 (Beep card), Mehos *et al*, 2000 (SMBP)	3(4) significant

4-Home visit	Holland *et al*, 2007, Peterson *et al* , 2004	0 (2) non significant
5-Collaborative care	Carter *et al* , 2008, Hunt *et al* , 2008, Villeneuve *et al* , 2010, Gwadry-Sridhar *et al* , 2005, Edworthy *et al*, 2007, Obreli Neto *et al*, 2011 , Carter *et al*, 2009.	3(7) significant
6-Motivational interviews	Heisler *et al*, 2012.	1(1) non significant
7-Communication between primary and secondary care	Calvert *et al*, 2012.	1(1) significant
8-Combined interventions	Ho et al, 2013, Lau *et al*, 2010.	2(2) significant

Appendix 7 Main Intervention

Trial	Intervention	Trial	Intervention	Trial	Intervention
1-Lee *et al* , 2006 **FAME Trial**	Patient education Every 2 months. and blisters (continued provision)	6-Al Mazroui *et al* , 2009	physician recommendations, Patient education, Written information, monthly hospital visits	11- Peterson *et al* , 2004	Home visits monthly Patient education
2-Bouvy *et al* , 2003	Patient education Base line interview, monthly follow up.	7-Hunt *et al* , 2008	Collaborative care pharmacist and physician, Patient education.	12- Villeneuve *et al* , 2010	Collaborate care of pharmacists and physicians, 3 visits, an additional visit if needed patient education
3-Morgado *et al* , 2010	Patient education 3 visits baseline, 3 and 6 months, written material, recommendations	8-Zillich *et al* , 2005	SBPM (Electronic),4 visits face to face within 3 months, Patient education physician recommendations Adherence aids Written material	13-Gwadry-Sridhar *et al* , 2005	A multidisciplinary team (nurse, hospital pharmacist, educator) 2.5 hour

					intervention with Four specific multifaceted components were oral, written, visual props and media videos. Delivered over 2 days
4- Yunsheng *et al* , 2010 **telephone contact**	Patient education at baseline, telephone calls 2 weeks, 1,3,6,9 months Written information and pillbox. Recommendations physicians and nurses.	9- Holland *et al* , 2007	Home visits, GP recommendations, adherence aids, written information	14- Murray *et al* , 2007 In patients with low health literacy and limited resources.	Patient education baseline interview verbal, written and pictures. Contact physician and nurses on need.
5- Carter *et al* , 2008	Collaborative care pharmacist and physician, baseline interview 4 visits adherence aids, telephone contacts on need.	10-Sadik *et al* , 2005	Patient education, written material, diary cards physician recommendations, visits for medication refills.	15- Svarstad *et al* , 2009	Written material, Electronic blood pressure tracker. Pedometer, pill boxes. Patient education during regular 6 visits

Main Intervention

Trial	Intervention	Trial	Intervention	Trial	Intervention
16- Alsani *et al* , 2010	Patient education and the use of a multi-part questionnaire, 4 visits.	21- Taylor *et al* , 2003	Review of the disease and medication for MRP, patient educations, physician recommendations, written materials,	24- Edworthy *et al* , 2007	Patient education. A joint intensive program including

			education on the use of pill boxes, glucometers.		physicians, pharmacists and nurses. Videos and printed material, Telephone contacts.
17- Lau *et al* , 2010	Patient education. Electronic B.P home monitor. Motivational interviewing. Home medicine review , dose administration aid, patient medication profile, Refill reminders by SMS, telephone or mail.	22- Jaffray *et al* , 2007	Patient education. Physician recommendations.	25- Varma *et al*, 1999.	Research pharmacist Physician discussions Patient education in hospital and every 3 months, written information (booklet), diary cards. Community pharmacist Reviewed patients cards and mailed to the researchers.
18- Vrijens *et al* , 2006	Review by patient and pharmacist of each patient's electronically compiled dosing history plus educational reminders, Beep Card.	23- Blenki-nsopp *et al*, 2000.	Patient education (verbal, written) based on a guided questioning, 3 interventions, intervention could be by telephone, referral to GPs	26- Odegard *et al* , 2005.	Baseline interview to develop a diabetes care plan, weekly in person or telephone meetings
19- Phumi p-amorn *et al* , 2008	Pharmacist patient education on diabetes accompanied by its pamphlet, 4 visits.				
20- Sookan e-knun et al 2004	Monthly face to face interviews with patients, physician recommendations, educational leaflets and a diary. Occasional home			27- Mehos *et al* , 2000 SMBP	Written material, pharmacist counseling, electronic blood

	visits.				pressure monitors, 2 unrestricted visits, monthly telephone contacts, Diaries, physician recommend ations.

Main Intervention

28- Park *et al* , 1996	4 visits each 1 month apart, a comprehensive pharmaceutical service. Physician recommendations Verbal counselling, written information.	32- Faulkn- er *et al* , 2000	Weekly telephone contact was made with each patient for 12 weeks.	37- Evans *et al* , 2010	Interview to determine risk factors, booklet, telephone alert to patients, notification to physicians, follow up every 8 weeks by telephone, mail, electronic mail, face to face appointments.
29- Mehuy -s *et al* , 2011	Patient education and couselling at the start of the study and at each prescription refill.	33- Calvert *et al* , 2012	Education on hospital discharge, pocket medication card, list of tips, pill boxes, communication between study pharmacist contacted by telephone community pharmacists, physicians, patients.	38- Heisler *et al* , 2012	Data of patients loaded into a data base, review patients electronic medical record, pharmacist contacted patients a phone or in person encounter, a welcome pack with written information, B.P monitors, motivational interviewing scheme, follow up appointments.
30- Obreli- Neto *et al* , 2011	Individual follow- ups and educational group activities, adherence problem discussions participation of patients in their drug treatment. Suggestions to physicians	34- Carter *et al* , 2009	Collaborative care Majority recommendations to physicians, visits, telephone contact.	39- Eussen *et al* , 2010	5 individual counseling sessions by a pharmacist during a 1-year period. During these sessions, patients received structured education about the importance of medication adherence. Lipid measurements, a wallet card.

	concerning new drug regimens. A visual reminder				
31-Lopez *et al* , 2006	Pharmacist patient education. Telephone calls every month for 6 months and then every 2 months for the remaining 6 months. Written information	35-Zhao *et al* , 2011	Patient education, supervision for side effects, follow up by telephone, recommendations to physician.	40-Alsabb-agh *et al*, 2012	Patients were invited to participate in telephone-based cardiac rehab., regardless of participation in the formal program. Subjects in the intervention group were assessed by the pharmacist and received education andcounseling on medication adherence.
		36-Planas *et al* , 2009	Patients seen on monthly basis, patient education, (individual plan), Physician recommendations	41-Jarab *et al*, 2012	face-to-face objective-directed education from a clinical pharmacist and necessary lifestyle changes, followed by 8 weekly telephone follow-up calls to discuss and review the prescribed treatment plan and to resolve any patient concerns.
				42-Ho *et al*, 2014	(1)pharmacist-led medication reconciliation and tailoring; (2) patient education; (3) collaborative care between pharmacist and a patient's primary care clinician and/or cardiologist; and (4) 2 types of voice messaging (educational and medication refill reminder calls)

Appendix 8- Adherence measurement and threshold

Trial	Adherence measure	Adherence Threshold	Trial	Adherence measure	Adherence Threshold
1-Lee *et al* , 2006	Pill counts	80%	6-Al Mazroui *et al* , 2009	Self-reported adherence.	--------
2-Bouvy *et al* , 2003	MEMS	Two Cutoff values 80% And 95%	7-Hunt *et al* , 2008	A Four validated patient self-reported questions. Morisky	--------
3- Morgado *et al* , 2010	Morisky scale 5 item	------	8-Zillich *et al* , 2005	Self-reported medication adherence was assessed using a validated 4-item questionnaire developed by Morisky	--------
4- Yunsheng *et al* , 2010	Prescription refills, The CMA is the ratio of days supply obtained to total days between refill records.	The trial considered high adherence to be > 90%	9- Holland *et al* , 2007	(medication adherence report scale or MARS; R Horne, personal communication, 2002)	--------
5- Carter *et al* , 2008	Pill counts	---------	10-Sadik *et al* , 2005	Self reported questionnaires	--------

Trial	Adherence measure	Adherence Threshold	Trial	Adherence measure	Adherence Threshold
11- Peterson *et al* , 2004.	Self-reported questionnaire	Compliance was assessed according to the used questionnaire	16-Aslani *et al* , 2010	Brief Medication Questionnaire, Medication Adherence Report Scale (MARS Scale)	----------
12-Villeneuve *et al* , 2010	Proportion of days during the follow up period with coverage by the medication dispensed	>=80%	17-Lau *et al* , 2010	Self-reported Morisky score, Tool for Adherence Behaviour Screening (TABS), Medsindex score (refill data).	< 100 Meds refill data
13-Gwadry-Sridhar *et al* , 2005	pharmacy refill data MEMS	>=80%	18- Vrijens *et al* , 2006	MEMS	--------

14- Murray *et al* , 2007 **Used different measurement of adherence**	Electronic prescription monitors. Refill adherence as the medication possession ratio. Self reported adherence	-------	19- Phumipamorn *et al* , 2008	Pill counts %	--------
15-Svarstad *et al* , 2009	self-reported patient adherence prescription refills	-------	20- Sookaneknun et al , 2004	Adherence was calculated by the number of medicines taken divided by the number supplied multiplied by 100.	>=80% good adherence <= 80% bad adherence.

Trial	Adherence measure	Adherence Threshold	Trial	Adherence measure	Adherence Threshold
21- Taylor *et al* , 2003	Self report obtained by dividing the estimated doses taken by the total number of doses prescribed.	<80%	24- Edworthy *et al* , 2007	Patient reported adherence	------
22-Jaffray *et al* , 2007	Self reported compliance	----------	25-Varma *et al* , 1999	Self reports and Drug use profiles (DUPs) graphic chronologic reviews PMRs continuous patient drug records.	Below 80% under compliance More than 120% over compliance.

23- Blenkinsopp, 2000	Self reported adherence. MARS Prescription refills	From the Mars scale those that scored 34 or 35 were classed as adherent. Those scoring 33 or less as non-adherent.	26- Odegard *et al* , 2005	Self-report medication adherence	----------

Trial	Adherence measure	Adherence Threshold	Trial	Adherence measure	Adherence Threshold
27- Mehos *et al* ,2000	Prescription refill data	----------			
28-Park *et al* , 1996	Pill counts	80%	32-Faulkner *et al* , 2000	Pill and packet counts and refill records	80%
29- Mehuys *et al* , 2011	Prescription refill data. Self report question	----------	33- Calvert *et al* , 2012	Morisky 4 item and prescription refills proportion of days covered (PDC).	PDC >= 75%
30- Obreli-Neto *et al* , 2011	The morisky-Green test translated into Portuguese. And computerized dispensed medication history.	80-115%	34-Carter *et al* , 2009	Morisky scale	----------
31- Lopez *et al* , 2006	Tablet accountability	95%-100%	35-Zhao *et al* , 2012	Morisky scale 1986, 1983	----------
36- Planas *et al* , 2009	Prescription claims data (continuous measure of medication acquisition)	----------	40- Alsabbagh *et al*, 2012	Electronic filling records	70%
37- Evans	Prescription	80%	41-Jarab *et*	Morisky scale	80%

***et al* , 2010**	dispensations (fills)		*al*, 2012		
38-Heisler *et al* , 2012	Pharmacy refill data	>20% gap days	42-Ho *et al*, 2014	Prescription refills	80%
39-Eussen *et al* , 2010	Pharmacy dispensing data. Medication possession ratio (MPR).	MPR of 0.9 or more was defined as adherent			

Appendix 9 Effect of pharmacy care on adherence and outcomes

Study	Trial length no. of patients	Effect on adherence	Effect on outcomes of the diseases
Lee *et al*, 2006 **USA** **FAME study**	14 months 159	35.5% absolute change in adherence p<0.001, persistence was sustained in the pharmacy care group p<0.001	Significant improvements in systolic BP 133.2 mmHg to 129.9mmHg (*P*=.02) and LDL-C 91.7 to 86.8 mg/dl *P*=.001). Significant reductions in systolic BP in the pharmacy care group (−6.9 mm Hg; 95% CI, −10.7 to −3.1 mm Hg) vs the usual care group,(−1.0mmHg; 95%CI, −5.9 to 3.9mmHg; *P*=.04), but no significant between-group differences in LDL-C levels or reductions.
Bouvy *et al*, 2003 **Nether-land**	6 months 152	Intervention group did not use diuretics for 140/7656 days, control group 337/6196 days (relative risk 0.33, 95% CI).	There were no significant differences in rehospitalizations, mortality, or disease-specific quality of life between groups.
Morgado *et al* , 2010 **Portugal**	9 months 197	Medication adherence was 57.6% at baseline in the Intervention Group and 74.5% at the end of the study p=0.012. Difference in low adherence 22.3% Intervention Group vs 43.8% Control Group P=0.0017	Significant lower systolic blood pressure -6.8 mmHg (*P* = 0.006) and diastolic blood pressure -2.9 mmHg (*P* = 0.020) levels were observed in the intervention group
Yunsheng *et al* , 2010 USA	Sep 2000-August 2005. 689	No significant effect 0.88 in the Pharmacy Intervention and 0.90 in the Usual Care p=0.51	At one year, 65% in the Pharmacy Intervention condition and 60% in the Usual Care condition achieved an LDL-C level < 100 mg/dL (*P* = .29) the result was not statistically significant.

Carter *et al* , 2008 **USA**	9 months 179	At baseline medication adherence was significantly better in the control group 89% vs 71% in the Intervention group, after 9 months 92% control and 94% intervention group p=0.396.	The mean adjusted difference in SBP was 8.7 (95% CI: 4.4, 12.9) mm Hg, while the difference in DBP was 5.4 (CI: 2.8, 8.0) mm Hg. BP was controlled in 89.1% of patients in the intervention group and 52.9% in the control group p<0.001 significant result
Al Mazroui *et al* , 2009 **UAE**	12 months 240	Non adherence was decreased from 48.3% at baseline Intervention Group to 21.4%, 49.1% in the Control group to 32.5% p<0.05	Significant reductions (*P* <0.001) in mean values (baseline *vs.* 12 months of HbA1c [8.5% *vs.* 6.9% systolic 131.4 mmHg *vs.* 127.2 mmHg and diastolic blood pressure 85.2 mmHg *vs.* 76.3 mmHg were observed in the intervention group; no significant changes were noted in the control group.
Hunt *et al*, 2008 **USA**	12 months 463	No difference between the groups 67% IG vs 69% Control Group. A small non significant result increase from baseline 61% to 67%in the Intervention Group.	Significantly lower systolic (p = 0.007) and diastolic (p = 0.002) blood pressures compared to control (137/75 mmHg vs. 143/78 mmHg). In addition, 62% of intervention subjects achieved target blood pressure compared to 44% of control subjects (p = 0.003)
Zilich *et al*, 2005 **USA HOME study**	3 months 125	No significant differences at any time between the groups, p=0.38, significant increase in adherence in the High- Intensity group 61.3% at baseline to 87.7% end of the study p=0.004.	From baseline, SBP declined 13.4mmHg in the High-Intensity group and 9.0mmHg in the Low- Intensity group. At the final visit, the difference in SBP/DBP change between the High-Intensity and Low -Intensity group was -4.5/-3.2mmHg (P=.12 for SBP and P=.03 for DBP). Diastolic B.P significant result
Holland *et al*, 2007 **UK**	6 months 293	No evident differences, final adherence scores were marginally higher in the intervention group. P=0.68.	134 admissions occurred in the intervention group compared with 112 in the control group (rate ratio=1.15, 95% confidence interval; P=0.28), 30 intervention patients died compared with 24 controls (P=0.54). The difference was statistically non significant.
Sadik *et al* , 2005 **UAE**	12 months 221	No. of patients with self reported compliance was 85 vs 35 in Intervention Group and Control Group respectively and at baseline was 33 vs 32, P<0.05.	Intervention patients showed significant (*P* <0.05) improvements in a range of summary outcome measures exercise tolerance, forced vital capacity, health related quality of life.
Peterson *et al*, 2004	6 months 94	No significant result Self-reported patient compliance with medication did not change over the course	The reduction over the course of the study in cholesterol levels within the intervention group was statistically significant (4·9 ±0·7 to 4·4 ± 0·6, *P* < 0·005), whereas there was no change within the control group (*P* = 0·26). The reduction in total cholesterol in the intervention group should

		of the study, and total cholesterol levels were not significantly related to self-reported patient compliance either at the baseline ($P > 0{\cdot}50$) or at follow-up ($P > 0{\cdot}30$).	translate to an expected 21% reduction in cardiovascular mortality risk and a 16% reduction in total mortality risk – more than twice the risk reduction achieved in the control group.
Villeneuve *et al*, 2010 **Canada**	12 months 108	Persistence and adherence at 12 months > 80%	No significant clinical impact on lipid control in patients with dyslipidemia.
Gwadry-Sridhar *et al*, 2005 **USA**	12 months or until death. 134	No statistically significant difference in compliance.	A significant effect on knowledge Health related quality of life The composite end points (mortality, hospital readmission, emergency visits) occurred in 60% control, 67% intervention but was not statistically significant.
Murray *et al*, 2007 **USA**	12 months 314	During the 9-month intervention period, medication adherence was 67.9% and 78.8% in the usual care and intervention groups, respectively (95% CI). However, these salutary effects dissipated in the 3-month post intervention follow-up period.10.9% difference in adherence between the intervention and the control group adherence became 66.7% and 70.6%difference 3.9%	Emergency department visits and hospital admissions were 19.4% less annual direct health care costs were lower ($–2960) in the intervention group.
Svarstad *et al*, 2009 **USA TEAM trial**	6 months-one year 576	The intervention group reported lower non adherence (18% vs 29%, p= 0.02).	Had better BP control (55% vs 36%, p 0.001)
Aslani *et al* , 2010	9 months 142	No significant result	Patients significantly lowered their cholesterol levels p<0.01 5.10 mmole/l Intervention Group,4.81 CG end of study 4.63

			Intervention Group and 4.80 Control Group
Lau *et al*, 2010 **HAPPY trial**	6 months 395 completed the study Hidden group 178	It cannot be concluded that the intervention improved adherence in comparison to the control group. On the Morisky scale, the proportions of adherent participants in each group increased significantly over six months but the difference between groups was not statistically significant. Significant result in differences between the intervention and the control group in the tabs adherence score p=0.046, and significant results in the intervention between the control and the intervention group in the Medsindex score p=0.046.	Significant reduction in systolic BP occurred in both groups (PCG: 9.97 mmHg, p<0.001; UCG: 4.61 mmHg, p<0.01) and was significantly greater in the PCG (p=0.02) mean reduction in B.P 10mmHg.
Vrijens *et al*, 2006 Belgium	1 year 392	6.5% increase in post baseline adherence p<0.001 and 13% increase in persistence p=0.002	Did not evaluate outcomes
Phumipa-morn *et al* , 2008 **Thailand**	8months 135 diabetic Muslims	The percent pill count was increased in the study group p= 0.004 (+6.8 vs -2.8) but not in the control.	No significant difference in A1c between the study and control group. P=0.56. Total cholesterol and LDL-C improvements were greater in the study group than the control. P=0.002
Sookane-knun *et al*, 2004 **Thailand**	6 months 235	The treatment group showed significantly better adherence p=0.014 Significantly better adherence increased by 58% to 70%	The study group had significant reduction in systolic and diastolic blood pressure p=0.037, 0.027, respectively.
Taylor *et al*, 2003 **USA**	12months 81	The percentage of patients with medication compliance scores of 80%-100% increased by 15% in the intervention group but	The percentage of patients responding to hypertension, diabetes, dyslipidemia and anticoagulation therapy increased significantly in the intervention group and declined in the control group.

		not in the control, however compliance scores did not differ significantly between the groups.	
Jaffray *et al* , 2007 UK	12 Months 1614	No significant effect on self reported compliance.	No statistical significant differences in outcomes.
Blenkins-opp, 2000[19] UK	6 months 282 180 completed the study	At baseline the percentage of patients who were adherent was very similar in the two groups 52.3% and 51% in the Intervention Group and Control Group respectively post study this increased to 62.9% and 50%, p<0.05.	Patients whose blood pressure was uncontrolled prior to the study were more likely to become controlled in the intervention group (*P*<0.05).
Edworthy *et al*, 2007 Canada	19 months 2643	Adherence in the intervention group was greater than in the control group only for beta-blockers (89% versus 80%; P<0.01) and lipid-lowering agents (83% versus 78%; P<0.05).	Total days in hospital per patient were similar (10.9 days in the usual care group versus 10.2 days in the intervention group; P not significant). Crude mortality was 6.2% and 5.5% in the usual care and intervention groups, respectively, with no significant difference (P=0.15) rehospitalization rates results were not significant. Post hoc analysis an important difference in the number of days in hospital might have been achieved by the program with considerable cost savings p<0.05)
Varma *et al*, 1999 Ireland	12months 83	No significant change in adherence from self reports, from computerized patient drug records an increased number of patients in the intervention group were compliant p=0.039.	Group A patients showed improved exercise capacity, significant improved knowledge of their drug therapy, fewer hospital admissions p=0.006.
Odegard *et al* , 2005 USA	12months 77	Self report medication adherence was not significantly improved by the intervention.	The mean HbA1c did not differ between groups p=0.61, a reduction in HbA1c was noted for both groups over time compared with baseline (p=0.001).
Mehos *et al* , 2000 USA	6 months 41	Mean compliance with antihypertensive therapy was 89% in the control and 82% in the intervention group p=0.29.	Reductions in systolic and diastolic pressures were significantly reduced from baseline in the intervention group (17.0 and 10.5 mm Hg p<0.0001) but not in the control group (7.0 and 3.8 mmHg, p=0.12 and p=0.09)
Park *et al*, 1996 USA	Oct. 1993-May1994. And Oct.1994-	Compliance for visits 2 through 4 showed no difference among the groups , however	Blood pressure control was significantly improved in the study group.

	1995. 64	compliance was greater on visits 2, 3 compared with control 96.7+-4 vs 86.0+- 20.7 p=0.025	
Mehuys *et al*, 2011 Belgium	6 months 288	No evident result: prescription refill rates was very high in both study groups (control group: median = 94.7%; intervention group: median = 99.7%). Moreover, a substantial proportion of patients had adherence rates of more than 100%, even up to 200% . Data were considered unsuitable for further analysis. With respect to the self-reported adherence, both study groups declared themselves to be very adherent to their diabetes medication.	The intervention significantly reduced HbA1c (between-group difference 0.5%, P = 0.009).
Obreli-Neto *et al* , 2011 **Brazil**	36 Months 200	Significant improvement 50.5% of adherent patients at baseline vs 83.5% of adherent patients after 36 months p<0.001no significant changes in the control group.	Significant improvements in the number of patients reaching adequate values for their blood pressure (26.8% at baseline vs. 86.6% after 36-months; P< 0.001), fasting glucose (29.9% at baseline vs. 70.1% after, 36 months; P< 0.001), A1C hemoglobin (3.3% at baseline vs. 63.3% after 36 months; P<0.001
Lopez *et al*, 2006 **Spain**	12 months 134	Difference in compliance between the intervention and control group. 88.2% vs 60.5% at 2 months, 91.1% vs 69% at 6 months and 85% vs 73.9%.	32.9% fewer patients in the intervention group were admitted again *vs*. the control group. The mean days of hospital stay per patient in the control group were 9.6 (SD = 18.5) *vs.* 5.9 (SD = 14.1) in the intervention group
Faulkner *et al*, 2000 **USA**	24 months 30	Compliance was significantly better in the intervention group up to 2 years p<0.05 63% vs 39% and 48% vs 23%.	Lipid profile results were significantly better in the intervention group p<0.05 up to 2 years after start of therapy than in the control group for all parameters except high density lipoprotein.
Calvert *et al* , 2012 **USA**	6 months 143	Self report adherence no difference between intervention and control. Using Proportion of Days Covered adherence to both statins and beta	Did not evaluate outcomes

		blocker there was better adherence in the intervention vs control but result not statistically significant(53%-38% p=0.11). Adherence to β-blockers was statistically Significant (p=0.03) in intervention versus control (71% vs 49%, respectively.	
Carter *et al* , 2009 **USA**	6 months 402	The percentage of patients with poor self-reported medication adherence declined from 18.7 ± 22.0% to 14.7 ± 20.9 in the control group and from 17.3 ± 27.5 to 14.6 ± 25.4% in the intervention group (p=0.602 and p=0.979, respectively).	Mean BP decreased 6.8/4.5 and 20.7/9.7 mm Hg in the control and intervention groups, respectively, (p<0.05), BP was controlled in 29.9% of patients in the control group and 63.9% in the intervention group p<0.001)
Zhao *et al*, 2012 **China**	6 months 278	Significant difference in percentage of patients with low adherence 24.8% intervention group vs 41.7% control group p=0.0014	BP was controlled among significant patients more in Intervention Group (76.4%) than in Control Group (50.6%) (P = 0.0000). Significant lower SBP (-8.5 mmHg, P = 0.0001) and DBP (-4.7 mmHg, P = 0.0013) levels were observed in Intervention Group.
Planas *et al* , 2009 **USA**	9 months 52	Adherence increased by 7% in the intervention group but the result was statistically not significant.	The mean intervention group SBP decreased 17.32 mm Hg, whereas the mean control group SBP level increased 2.73 mm Hg (P = 0.003)
Evans *et al* , 2010 **Canada**	6 months 176	The proportion of patients exhibiting statin adherence of 80% or greater did not significantly differ between groups at study end (73.1%] and 80.0% respectively, p=0.333). However, 85.2% in the follow-up group continued with statin therapy at the end of the study compared with 67.0% in the single-contact group (p=0.005).	Neither the mean reduction in 10-year risk (-2.68 for the follow-up group and -1.25 for the single-contact group, one-tailed p=0.098) nor individual risk factors were significantly different between groups.
Heisler *et al*, 2012	14 months 4100	More effective in increasing medications	The mean SBP decrease from 6 months before to 6 months after the intervention period was approximately 9 mm Hg in

USA		than improving medication adherence.	both arms. Mean SBPs of eligible intervention patients were 2.4 mm Hg lower (P <0.001) immediately after the intervention than those achieved by control patients.
Eussen *et al*, 2010 **Nether-lands**	12 months 1016	Significantly lower rate of discontinuation within 6 months after initiating therapy versus usual care (95% CI). No significant difference between groups was found in discontinuation at 12 months (95% CI). Median Medication Possession Ratio was very high (>99%) in both groups and did not differ between groups.	In the pharmaceutical care patients both mean cholesterol and LDL-C levels declined significantly during the study. A significant negative association between the Medication Possession Ratio and total cholesterol p=0.002
Alsabbagh *et al*, 2012 **Canada**	6 months 95	The mean adherence to all recently initiated cardiovascular medications combined was 88.8% in the intervention group and 89.9% in the usual care group (P = 0 .73).	Did not evaluate outcomes
Jarab *et al*, 2012 **Jordan**	6 months 171	The intervention group compared with the usual care group had small but statistically significant improvements in the secondary measures self-reported medication adherence, and self-care activities.	Patients in the intervention group had a mean reduction of 0.8% in A1c versus a mean increase of 0.1% from baseline in the usual care group (P = 0.019). Between-group differences in changes in the secondary measures of HDL-C and body mass index were not significant.
Ho *et al*, 2014 **USA**	12 months 253	241 (95.3%) completed the study (122 in Intervention and 119 in Usual Care). In the Intervention group, 89.3%of patients were adherent compared with 73.9%in the Usual Care group (P = .003). Mean Proportion of Days Covered was higher in the Intervention group (0.94 vs 0.87; P< .001). A greater proportion of intervention patients were adherent.	There were no statistically significant differences in the proportion of patients who achieved BP and LDL-C level goals.

Appendix 10 Strength of the evidence

Scottish Intercollegiate Guidelines Network checklist for critical appraisal of randomised control trials was used to appraise the trials. The overall assessment of the paper starts by rating the methodological quality of the study, by using the following coding system:

++	All or most of the criteria have been fulfilled. Where they have not been fulfilled the conclusions of the study or review are thought very unlikely to alter.
+	Some of the criteria have been fulfilled. Those criteria that have not been fulfilled or not adequately described are thought unlikely to alter the conclusions.
-	Few or no criteria fulfilled. The conclusions of the study are thought likely or very likely to alter.

Study's author	No. of pat.	Period month	Randomise	Allocation	Blindness	Intention To Treat	Drop outs	Limitation /quality
1-Lee *et al* , 2006	159	6	Computer generated random sequence	Concealed	Not Blinded	All Included	10%	Confined population ++
2-Bouvy *et al* , 2003	152	6	Computer	Not clear	Not clear	Not all Included	61 40%	1. patient death 2.Lost MEMS +
3-Morgado *et al*, 2010	197	9	Computer	Concealed	nurses blinded	All included	7 3%	Contamination ++
4- Yunsheng *et al* , 2010	689	12	Statistician	Not clear	Not clear	Not all included	19%	Enrolled mostly Caucasians +
5- Carter *et al* , 2008	179	9	Table of random numbers	Not clear	Investigator and research nurse	All Included	19 10%	Generalized to Clinics ++
6-Al Mazroui *et al* , 2009	240	12	Restricted	Not clear	Not clear	Not clear	6 2%	Confined population +
7- Hunt *et al* , 2008	463	12	Computer	Not clear	Single	All included	41%	High withdrawal +

8- Zillich *et al* , 2005 HOME study	125	3	Block design	Not clear	Not blinded	Not clear	8 6%	Selection bias No true control +
9-Holland *et al*, 2007	293	6	Computer	Concealed	Not clear	All included	4 1%	No clear placebo ++
10-Sadik *et al* , 2005	221	12	Minimization Method	Not clear	Assessors Blinded	Not reported	13 6%	Confined population +
11- Peterson *et al*, 2004	94	6	Computer	Not clear	GPs	Not reported	13 13%	Outcome measurements -
12- Villeneuve *et al*, 2010 TEAM	225	12	Cluster Stratified Block randomisation	Not clear	Not clear	Adjusted results	6%	Selection bias External validity +
13-Gwadry-Sridhar *et al* , 2005	134	12	Stratified Block Randomisation	concealed	Outcome assessors Community pharmacists and physicians	All included	23 17%	Pilot study, limited sample size. ++
14-Murray *et al* , 2007	314	12	Computer	Concealed	Interviewers	Sensitivity analysis	44 14%	Single pharmacist ++
15- Svarstad *et al* , 2009	576	12	Computer	Not clear	Outcome assessors	All included	5.2%	Not a traditional control group. ++
16- Aslani *et al* , 2010	142	9	Not clear	Not clear	Not clear	Not all included	45 31%	Low recruitment High dropout rate -
17- Lau *et al*, 2010	395	6	Sealed opaque envelope technique	Concealed	Researchers	Not all included	41 10%	Sample bias ++
18-Vrijens *et al* , 2006	392	12	Open label randomised two districts	-------	Not blinded	All included	37 9%	Selection of participants +
19-Phumip-amorn *et al* , 2008	135	8	Drawing a number from a container	Not reported	Physician and nurses	Not all included	5 3%	Confined population +
20-Sookane-	235	6	Simple	Not clear	Not clear	All	8	Patients notes

knun et al , 2004			randomization technique			included	3%	labelled -
21- Taylor *et al* , 2003	81	12	Not clear	Not clear	Not clear	Not all included	12 14%	Limited generlizability -
22-Jaffray *et al* , 2007	1614	12	Computer	Not clear	Assessors blinded	All included	121 7%	selection bias ++
23-Blenkinsopp *et al*, 2000	282	12	Cluster randomisation Sequentially for pharmacists	Not clear	GPs were blinded Assessors blinded	Not all included	20 7%	Patient recruitment ++
24- Edworthy *et al* , 2007	2643	19	Coin flip	Not clear	Not clear	All included	6%	Transfer of care of patients between cardiologists +
25- Varma *et al* , 1999	83	12	Restricted randomisation minimisation Method	Not clear	Not clear	Not all included	34 40%	Patient recruitment +
26- Odegard *et al* , 2005	77	12	Blocks Not clear	Not clear	Not clear	Intention to treat using generalised estimating equations	11 14%	Randomisation within clinics +
27- Mehos *et al*,2000	41	6	Deck of cards	Not clear	Not clear	Not all included	5 12%	Assessment of outcomes -
28-Park *et al*, 1996	64	4	Not clear	Not clear	Single blinded	All included	11 17%	Pharmacists aware of group assignment +
29-Mehuys *et al* , 2011	288	6	Randomization table generated	Not clear	Not clear	All included	8 2%	Outcome measures are unavailable +

30-Obreli-Neto *et al*, 2011	200	36	Stratified random sampling	Not clear	Researchers blinded	Not all included	6 3%	Limited generliz-ability +
31- Lopez *et al* , 2006	134	12	Computer	Not clear	Single Blinded	Not clear	9.7% lost to follow up 42.6% Lost to death	High dropout rate +
32-Faulkner *et al*, 2000	30	24	Computer	Not clear	Not clear	All included	No drop-outs	Small sample size -
33- Calvert *et al*, 2012	143	6	Computer	Concealed	Pharmacists Blinded	Not all included	28 19%	Targeted number of patients was not achieved +
34-Carter *et al*, 2009	402	6	Table of random numbers	Not clear	Assessors Blinded	All included	17%	Generalized to Clinics +
35-Zhao *et al* , 2012	278	6	Computer	Concealed	Not clear	Not all included	7.2%	Pharmacist's experience, Outcome measures +
36-Planas *et al*, 2009	52	9	Computer	Not clear	Not clear	Not all included	36.5%	High withdrawal, Selection bias -
37-Evans *et al* , 2010	176	6	Table of random numbers	Concealed	Not blinded	All included	20 11%	Single centre +
38-Heisler *et al* , 2012	4622	14	Random number generator	Concealed	Not clear	All included	522 11%	Continued improvement in control group. Selection bias ++
39-Eussen *et al*, 2010	1016	12	Computer	Not clear	Assessors blinded	Not all included	117 11%	Contamination of the control with intervention group. ++
40-Ho *et al*, 2014	253	12	Block randomisation	Concealed	Not clear	INT analysis	Less than 10%	++ May not be generalizable

41-Alsabbagh *et al,* 2012	95	9	Block randomisation	Not clear	Open labelled	High withdrawal rate	>20%	Slow recruitment Not blinded +
42-Jaarab *et al,* 2012	171	6	Minimisation	Not clear	Not clear	Not mentioned	8%	Short duration and underpowered -

Appendix 11 List of search terms used in the review

Pubmed Search Terms
("pharmacy"[MeSH Terms] OR "pharmacy"[All Fields] OR "pharmacies"[MeSH Terms] OR "pharmacies"[All Fields]) AND care[All Fields] AND adherence[All Fields] AND ("cardiovascular diseases"[MeSH Terms] OR ("cardiovascular"[All Fields] AND "diseases"[All Fields]) OR "cardiovascular diseases"[All Fields] OR ("cardiovascular"[All Fields] AND "disease"[All Fields]) OR "cardiovascular disease"[All Fields])) AND (("1990/01/01"[PDAT] : "2012/07/20"[PDAT]) AND Randomised Controlled Trial[ptyp]) **adherence[All Fields] AND ("pharmacists"[MeSH Terms] OR "pharmacists"[All Fields]) AND ("hypertension"[MeSH Terms] OR "hypertension"[All Fields])) AND (("1990/01/01"[PDAT] : "2012/07/20"[PDAT]) AND Randomised Controlled Trial[ptyp]) adherence[All Fields] AND ("pharmacists"[MeSH Terms] OR "pharmacists"[All Fields]) AND ("diabetes mellitus"[MeSH Terms] OR ("diabetes"[All Fields] AND "mellitus"[All Fields]) OR "diabetes mellitus"[All Fields] OR "diabetes"[All Fields] OR "diabetes insipidus"[MeSH Terms] OR ("diabetes"[All Fields] AND "insipidus"[All Fields]) OR "diabetes insipidus"[All Fields])) AND (("1990/01/01"[PDAT] : "2012/07/20"[PDAT]) AND Randomised Controlled Trial[ptyp])(adherence[All Fields] AND ("pharmacists"[MeSH Terms] OR "pharmacists"[All Fields]) AND ("hyperlipidaemia"[All Fields] OR "hyperlipidemias"[MeSH Terms] OR "hyperlipidemias"[All Fields] OR "hyperlipidemia"[All Fields] OR "Hyperlipidemia"[All Fields])) AND (("1990/01/01"[PDAT] : "2012/07/20"[PDAT]) AND Randomised Controlled Trial[ptyp])(adherence[All Fields] AND ("pharmacists"[MeSH Terms] OR "pharmacists"[All Fields]) AND ("coronary disease"[MeSH Terms] OR ("coronary"[All Fields] AND "disease"[All Fields]) OR "coronary disease"[All Fields] OR ("coronary"[All Fields] AND "heart"[All Fields] AND "disease"[All Fields]) OR "coronary heart disease"[All Fields] OR "coronary artery disease"[MeSH Terms] OR ("coronary"[All Fields] AND "artery"[All Fields] AND "disease"[All Fields]) OR "coronary artery disease"[All Fields] OR ("coronary"[All Fields] AND "heart"[All Fields] AND "disease"[All Fields]))) AND (("1990/01/01"[PDAT] : "2012/07/20"[PDAT]) AND Randomised Controlled Trial[ptyp])adherence[All Fields] AND ("pharmacists"[MeSH Terms] OR "pharmacists"[All Fields]) AND ("heart failure"[MeSH Terms] OR ("heart"[All Fields] AND "failure"[All Fields]) OR "heart failure"[All Fields])) AND (("1990/01/01"[PDAT] : "2012/07/20"[PDAT]) AND Randomised Controlled Trial[ptyp]) (("pharmacy"[MeSH Terms] OR "pharmacy"[All Fields] OR "pharmacies"[MeSH Terms] OR "pharmacies"[All Fields]) AND care[All Fields] AND ("patient compliance"[MeSH Terms] OR ("patient"[All Fields] AND "compliance"[All Fields]) OR "patient compliance"[All Fields] OR "compliance"[All Fields] OR "compliance"[MeSH Terms]) AND ("cardiovascular diseases"[MeSH Terms] OR ("cardiovascular"[All Fields] AND "diseases"[All Fields]) OR "cardiovascular diseases"[All Fields] OR ("cardiovascular"[All Fields] AND "disease"[All Fields]) OR "cardiovascular disease"[All Fields])) AND (("1990/01/01"[PDAT] : "2012/07/20"[PDAT]) AND Randomised Controlled Trial[ptyp]) ("pharmaceutical services"[MeSH Terms] OR ("pharmaceutical"[All Fields] AND "services"[All Fields]) OR "pharmaceutical services"[All Fields] OR ("pharmaceutical"[All Fields] AND "care"[All Fields]) OR "pharmaceutical care"[All Fields]) AND adherence[All Fields] AND ("cardiovascular diseases"[MeSH Terms] OR ("cardiovascular"[All Fields] AND "diseases"[All Fields]) OR "cardiovascular diseases"[All Fields] OR ("cardiovascular"[All Fields] AND "disease"[All Fields]) OR "cardiovascular disease"[All Fields])) AND (("1990/01/01"[PDAT] : "2012/07/20"[PDAT]) AND "humans"[MeSH Terms] AND Randomised Controlled Trial[ptyp])** **EMBASE search terms: Adherence, Cardiovascular, Cardiovascular disease, Care, Disease, Pharmacy, Pharmacy care, Adherence, RCTs.** **PsycINFO search terms: adherence, cardiovascular disease, disorders, care, disease, pharmacy, treatment compliance.**

Appendix 12 Intervention pharmacies information

Pharmacy Name	Location	Ownership type	Consultation area availability	Information Sources	Pharmacists Qualification
Intervention group pharmacy					
1-	IG1 2RZ Ilford lane	Independent chain pharmacy	Yes	BNF, Drug Tariff, MEP, Martindale, Internet sources	MRPharmS
2-	E18 2PB High Road Woodford	Independent	Yes	NPA member, BNF, Martindale, MEP	MRPharmS
3-	1G3 8TG High Road, Goodmayes	Independent	Yes	BNF, Drug Tariff, MEP, Martindale, Internet sources	PhD MSc. Mpharm
4-	RM8 1YT Green Lane Dagenham	Independent	Yes	BNF, Martindale, MEP	MRPharmS
5-	E10 7AA Leyton Waltham Forest	Large Chain	Yes	BNF, Drug Tariff, MEP, Martindale, Internet sources	MPharm MSc.
6-	RM6 6NL High Road Romford	Large Chain Mulitiple	Yes	BNF Medscape one portal	Certificate in primary care therapeutics
7-	IG11 0LG	Independent chain	Yes	BNF, Drug Tariff, MEP, Martindale, Internet	MPharm MSc.

				sources	
8-	E14 7HG	Independent	Yes	BNF, Drug Tarrif	MPharm
9-	E14 0EA	Independent	Yes	BNF, Drug Tarrif	MPharm
10-	E14 3BT	Independent chain	Yes	BNF, Drug Tariff, MEP, Martindale, Internet sources	MPharm MSc.
11-	RM8 1BJ	Independent	Yes		
12-	IG3 8BS	pharmaram chemists	Yes	bnf martindale stockleys all other normal resources	cppe ongoing basis cpd and other numerous accreditation
13-	E7 8LQ	Independent	Yes	BNF, Drug Tariff	PGDIP, MSc
14-	IG11 7TF	Community	Yes	BNF, Martindale, Internet, Compendium	CVD, Anticoagulation, Medicines Management,Drug Therapeutics
15-	E3 5ES	Independent	Yes	BNF, Martindale, Internet,	MPharm
16-	IG11 7NN	Independent	Yes	BNF Drug Tarrif MEP	MPharm

Appendix 13 Motivational Interviewing Chart

Motivational Interviewing Consultation Schedule:

Adapted from Ogedegbe et al, 2007

1. Introductions: The pharmacist should introduce him/herself to the patient
2. The pharmacist should briefly outline to the patient why they are in the pharmacy and the nature of the consultation (e.g. NMS, etc).

3. Agenda Setting: Ask an open question to find out what the patient wants to get out of their consultation
4. Respond to this using the core MI Skills: OARS (see techniques sheet). The pharmacist should use these consistently during the remainder of the consultation.
    a. Open Questions
    b. Affirmations
    c. Reflections
    d. Summaries

5. Information Gathering: Elicit: What do you know about the medication that you are taking and how you should be taking it?
    a. The pharmacist should respond to this using MI techniques and allow the patient to direct discussion regarding their medication, emotions, behaviours, etc.

6. Assess the patient's motivation and confidence:
    a. When appropriate, ask: On a scale from 1 to 10 (with 10 being the highest), how motivated/interested are you in taking your medication as prescribed?
    b. On a scale from 1 to 10 (with 10 being the highest, how confident are you that you can take your heart attack medication as prescribed?

7. Elicit barriers, concerns and positive self-motivational statements: depending on the patient's responses to the above questions, the pharmacist can follow up with additional questions or OARS techniques:
    a. For high numbers: Can you tell me about why you chose X (number) rather than a lower number, like a 1 or a 2? (eliciting positive motivational statements)

b. For low numbers (ask as appropriate): Can you tell me about why you chose X (number) rather than a higher number like a 9 or 10? What would it take to get you to a 9 or 10?

REMINDER: At all times, allow space for the patient to express their views and respond with OARS.

8. Summaries: The pharmacist should draw together the discussions thus far, summarising the major content for the patient.
9. Elicit: What do you think about all this? Is there something else you want to add?

If necessary, provide information:

10. Ask permission: "Would it be ok if I shared with you some information regarding…"
11. Provide information: Take care to do this in short bursts and to maintain the balance in the consultation, so that the patient talks more than the pharmacist.
12. Elicit: "What do you make of that information?" or similar.

If you need to provide additional information, continue to use the ELICIT-PROVIDE-ELICIT approach (see techniques sheet)

Assess patient's values and goals:

13. Elicit: Can you tell me about some goals you have in life and how your health relates to these?
14. Spot ambivalence: Reflect this
15. Pharmacist should listen carefully for CHANGE TALK and respond appropriately using EARS:
    a. Evoking (open questions)
    b. Affirmations
    c. Reflections
16. Action Mapping: Some patients find it is helpful to write a list about how their medication fits into their life, their goals and their values (offer the patient the Action Mapping Sheet). What do you think about completing this?
    a. If accepted, complete the action mapping sheet with the patient
    b. If rejected, discuss patient goals and values verbally. Pharmacist may offer to make notes for their own memory.

17. Summary: Pharmacist summarises the discussion about goals and values

Next steps:

18. Elicit: "So what do you think you will do…?"
19. Thanks: Pharmacist to thank the patient for their participation and engagement in their consultation
20. Follow-up: Pharmacist to arrange or discuss the 3-month follow-up appointment. Provide the patient with Pharmacy/Pharmacist contact details where appropriate.

3-month follow-up:

1. Review: In our last meeting we spoke about few issues regarding the medication and we highlighted some key points can remind tell me again a little of what we discussed?
2. Worries: Can you tell me about any concerns you have had with your medication since we last met.
    a. Allow patient to outline concerns and reflect upon these.
    b. If necessary, give advice using ELICIT (permission) – INFORM – ELICIT formula (see Action-mapping Sheet).
3. Solution-focused: Some patients have found it useful to review what approaches/solutions/techniques did or did not work for them. What would you think about doing this?
    a. Tell me about what approaches/solutions/techniques you have tried since last time.
    b. Use OARS to respond and elicit more information regarding these.
4. Future-oriented: Having considered how you've taken your medication in the past few weeks, tell me about your plans for your medication and health in the next few months.
    a. If appropriate set new goals, allowing them to be patient-driven.
    b. Use action-mapping sheet if desired.

Motivational Interviewing: Key Techniques Sheet

OARS:

- Open Questions
    - e.g. Tell me about; What do you think about, etc.
    - Avoid closed questions

    - Take care not to ‘stack’ questions or continue questions – allow space for an answer
- Affirmations
    - Mention their successes, appreciate progress, comment positively on attributes (e.g. patient values, desires, behaviours)
    - Express hope, caring and support
- Reflections
    - Simple reflections: Repeat or rephrase using comparable words
    - Complex reflections: Paraphrase what you heard, reflect back the feeling, continue the paragraph
    - Amplified Reflections: Take what you hear, lift it, increasing intensity
    - Keep voice neutral, do not turn into a question by lifting voice
    - Avoid pre-statements (padding!) e.g. so, it seems like, etc.
- Summaries
    - Reflect the content of the discussion over the past few minutes, joining it together
    - Enable deeper thinking by joining together the content of the discussion

Recognise ambivalence:

- Patients’ conflicting positive and negative thoughts on a topic
- Reflect these back
- Reflect their negative thoughts FIRST, then their positive thoughts

Spot Change Talk

- Reflect this back
- Elicit more through open questions
- Affirm

Informing: ELICIT – PROVIDE - ELICIT

- ELICIT (1):
    - Ask what the patient already knows
    - Ask what the patient thinks they should do to proceed
- PROVIDE:
    - Ask for permission to inform
    - E.g. “would you like to know about some other approaches that some people have found useful?” “Would it be ok if I told you some concerns I have about your plan?”
- Resistant patients:
    - Ask if they would like to hear your information now or later

- Prefacing: “There’s something I have to tell you, but I’d really like to know what you think about it.” “This may or may not concern you but…”

- ELICIT (2):
  - Ask open questions: “What do you make of that?” “What does this mean for you?”

Appendix 14 Self report questionnaires

The Morisky 8 Items Tool (MMAS)

©Morisky Medication Adherence Scale (MMAS-8-Item).
This is a generic adherence scale and the name of the health concern can be substituted in each question item. You indicated that you are taking medication for your (identify health concern, such as “high blood pressure”). Individuals have identified several issues regarding their medication-taking behaviour and we are interested in your experiences. There is no right or wrong answer. Please answer each question based on your personal experience with your [health concern] medication.

(Please check your response below)

	No=1	Yes=0
1. Do you sometimes forget to take your [health concern] pills?		
2. People sometimes miss taking their medications for reasons other than forgetting. Thinking over the past two weeks, were there any days when you did not take your [health concern] medicine?		
3. Have you ever cut back or stopped taking your medication without telling your doctor, because you felt worse when you took it?		
4. When you travel or leave home, do you sometimes forget to bring along your [health concern] medication?		
5. Did you take your [health concern] medicine yesterday?		
6. When you feel like your [health concern] is under control, do you sometimes stop taking your medicine?		
7. Taking medication everyday is a real inconvenience for some people. Do you ever feel hassled about sticking to your [health concern] treatment plan?		

8. How often do you have difficulty remembering to take all your medications?

(Please circle your response below)

Never/Rarely……....4

Once in a while……3

Sometimes……....2

Usually……1

All the time……..0

Coding Instructions for the ©Morisky Medication Adherence Scale (8-Item)

You will need to reverse the code response in a positive direction for item number 5 and standardize the code for item 8 (0-4), resulting in a scale from low adherence to high adherence. Item 8 is divided by 4 when calculating a summated score. This procedure standardizes the 5-point Likert scale. The total scale has a range of 0 to 8.0. The eight-item compliance scale had an alpha reliability of 0.83 (n= 1367) among patients diagnosed with essential hypertension attending an outpatient clinic of a large teaching hospital. We have used a 75% completion criterion for establishing eligibility. The median value of all missing items would be substituted for the missing item for individuals meeting the eligibility criterion.

Re-codes:

If Item5 = 0 Item5r = 1 (high adherence)

If Item8=4 Item8r = 1 (highest adherence)

If Item8=3 Item8r = .75 (high adherence)

If Item8=2 Item8r = .50 (moderate adherence)

If Item8=1 Item8r = .25 (low adherence)

If Item8=0 Item8r = 0 (lowest adherence)

Adherence Level	Percent
Low Adherence (< 6)	32.1
Medium Adherence (6 to <8)	52.0
High Adherence (= 8)	15.9

Morisky DE, Ang A, Krousel-Wood M, Ward H. Predictive Validity of a Medication Adherence Measure for Hypertension Control. *Journal of Clinical Hypertension* 2008; 10(5):348-354

Krousel-Wood MA, Islam T, Webber LS, Re RS, Morisky DE, Muntner P. New Medication Adherence Scale Versus Pharmacy Fill Rates in Seniors With Hypertension. *Am J Manag Care* 2009;15(1):59-66.

Morisky DE, DiMatteo MR. Improving the measurement of self-reported medication nonadherence: Final response. J Clin Epidemio 2011; 64:258-263. PMID:21144706

This footnote is required on all tables or figures which present the ©MMAS-8.

Self report question adapted from Gehi *et al*, 2007, QOL-Adherence forms (Brief adherence self-report questionnaire. The AIDS Clinical Trials Group sponsored by the National Institute of Allergy and Infectious Diseases (NIAID).

https//www.fstrf.org/apps/cfmr/apps/common/.../actg/…/910747pp

Please complete the scale below.

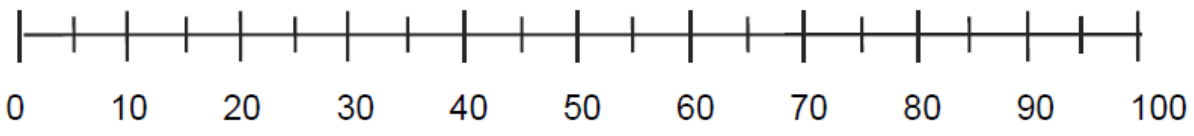
We understand that many people on cardiac medications find it very difficult to take them regularly. We would like to know HOW MUCH of your cardiac medications you have taken DURING THE LAST MONTH.

Please put a cross (x) on the line below at the point showing your best guess about how much of your cardiac medication you have taken in the last month. We would be surprised if this was 100% for most people.

For example: 0% means you have taken none of your cardiac medication.

50% means you have taken half your cardiac medication.

100% means that you have taken every single dose of your cardiac medication in the past month.



Appendix 15 Certificate to community pharmacists for training on motivational interviewing

UCL School of Pharmacy

Presents

Certificate of Attendance

to

Name

For the course in Motivational Interviewing Training for use in pharmaceutical settings to support patient adherence

Date: September 2013
Number of Hours: 6-8hours

....

Dr. Katherine Finlay
University of Buckingham
UCL-School of Pharmacy

Felicity Smith
Professor of Practice and Policy

.....
Hemant Patel
Mr. Hemant Patel
Secretary,North-East London LPC

Appendix 16 Questionnaire to evaluate the course on motivational interviews

Please note that the questionnaire is completely anonymous

Tick as appropriate

1. How satisfied are you with the course content (range and depth)?

Very satisfied	Satisfied	Neutral	Dissatisfied	Very Dissatisfied

2. How satisfied are you with the delivery and teaching methods?

Very satisfied	Satisfied	Neutral	Dissatisfied	Very Dissatisfied

3. Did this course succeed in enhancing your consultation skills as a health care practitioner?

Strongly agree	Agree	Neutral	disagree	Strongly disagree

4. How satisfied are you with the length and time of the course?

Very satisfied	Satisfied	Neutral	Dissatisfied	Very Dissatisfied

5. Do you have any further suggestions or comments regarding the course?

Pharmacist comments:

- This actually should be incorporated into the pharmacy curriculum.
- Sustained application of motivational interview techniques will be the real test.
- A lot to take in could be better if sessions were done over a few weeks.
- Perhaps more details on NMS/MUR integration.
- Very enlightening in new ways of improving patient outcomes through motivational interviews consultation.
- A refresher session will be good.
- Very positive learning from a specialist outside pharmacy we communicate every day I now know how badly we do it.
- I plan to attend further training if possible it would be helpful to my practice.
- Very interactive many thanks.
- Well done, constructive, very informational.
- Extremely rewarding will take away and implement.
- Ability to mature after learning is fantastic putting knowledge to work.
- Although do not like group work in this case it was very helpful.
- Very informative thank you very much.
- May be a bit long but informative.
- Very informative and well structured, some great new ways to motivate patients without putting any pressure on them and putting the ball in their court.

Appendix 17 Pharmacies and patients consultations

Pharmacy	Number of patients	Consultation
1-	2 patients	2 contacted by telephone
2-	7 patients	2 went to pharmacy 4 contacted by telephone, 1 patient lost to follow up.
3-	4 patients	1 went to pharmacy, 1 dropped out of study, 2 contacted by telephone
4-	3 patients	3 contacted by telephone
5-	3 patients	All 3 went to the pharmacy for the consultation
6-	1 patient	1Contacted by telephone
7-	4 patients	1 went 3 contacted by telephone
8-	2 patients	1went to pharmacy, 1 contacted by telephone
9-	1 patient	1Went to pharmacy
10-	1 patient	1Contacted by telephone
11-	1 patient	1Contacted by telephone
12-	No patients	
13-	1 patient	1Contacted by telephone
14-	2patients	2 contacted by telephone
15-	No patients	
16-	No patients	
Total of intervention group 32 Patients, total attended consultation 9 patients and 21 contacted by telephone, 1 patient dropped out of the study, 1 patient lost to follow up.		

Appendix 18 Letter from General Practitioner

Dr Aarron Patel MBBS

Dr Aarron Patel Surgery
Chadwell Heath Health Centre
Ashton Gardens
Chadwell Heath Romford
Essex RM6 6RT

Tel: 020 8918 0580 Fax: 020 8918 0582

13 March 2014
Zahraa Jalal
Centre for Pharmacy Practice
UCL School of Pharmacy
Mezzanine Floor
BMA House
Tavistock Square
London
WC1 H 9JP

Email: zahraa.ali.11.ucl.ac.uk

Dear Zahraa Jalal,

RE:- KD D.O.B. 01/10/1967 ,

Thank you for your letter received on 12 March 2014 requesting GP assistance with data collection regarding blood pressure and LDL-C testing in patients with myocardial infarction.
I would wish to assist you in your valuable research but as a single handed GP with twice the average GP list size to manage it is extremely difficult to support research work in addition to my clinical workload.
However, I am happy to allow a member of your team to collect the required data at our surgery including providing a consultation room for you to undertake blood pressure readings for my patient. Alternatively, I can request my practice nurse to undertake overtime to assist you if you are agreeable to reimburse the costs of employing our practice nurse (at a rate of £20 per hour).
I look forward to hearing from you

Yours sincerely,
Dr Aarron Patel

Appendix 19 Enquiries from pharmacists who expressed interest to take part in the study

Dear Zahraa,
Thank you for your email in relation to the two days of MUR and NMS training.
As a pharmacist myself who would be taking part, I would be grateful if you could confirm the following:
1. Who will be paying for the two days training?
2. At what amount is the payment for?
I look forward to hearing from you shortly, and thank you for your assistance in advance.

Kind Regards, | Director | Britannia Pharmacy
Head Office
21 - 23 Horns Road
Ilford, Essex, IG2 6BN
www.britanniapharmacy.com

Hi Zahraa
I am very enthusiastic about the opportunity you are creating and am pleased that it seems Pharmacy is moving in the right direction. Well done to you. I would like to ask when exactly the training will take place and how and when we will be informed?
Regards
G.S
Britannia Pharmacy

Hi Zahraa
My names is C. P., and I am one of the pharmacists from Britannia Pharmacy, in relation to the two training days, any ideas of when it will take place?
Kind Regards
C. P
Britannia Pharmacy

Dear zahraa. Thanks for the invite to study. Definitely interested, would you know roughly when the two days training is?
CK Wan

Appendix 20 Recruitment letters

General practitioners consent letter Title of research: Feasibility and Potential Impact of Community Pharmacy Care including Motivational Interviews on Adherence to Secondary Prevention Medication in patients with Coronary Heart Diseases

Chief investigator: Professor Felicity Smith Researcher: Zahraa SMA Jalal (PhD student), Principal investigator : Sotiris Antoniou

Dear Doctor,

I am Zahraa SMA Jalal, a PhD student at the UCL-School of Pharmacy. I would like to request your assistance with a study that aims to investigate the potential impact of a pharmacy care intervention involving motivational interviews and referral to the New Medicine Service in coronary heart disease patients on adherence to secondary prevention medication and on outcomes of coronary heart disease.

Despite the importance of secondary prevention, non-adherence rates for myocardial infarction patients are still low for prescribed, evidence-based medicines and the main concern is not with compliance alone but with patients that discontinue medications that can lead to serious consequences. Medications like aspirin and clopidogrel if stopped early can lead to short term consequences for instance rehospitalisation and even increased risk of death.

The intervention aims to increase patients' understanding of their medication by motivating the patients to use their medication to achieve optimal outcomes. This is a pharmacy based study and eligible patients will be identified at discharge from The London Chest Hospital. There will be two groups of patients' intervention group and control group. The intervention will be delivered by community pharmacists and will include two counselling sessions incorporating motivational interviews for which pharmacists will have received training.

To evaluate the outcomes, I would like to ask your assistance and permission to obtain both LDL-C and blood pressure data of patients included in this study. Patients' will have given their consent for this information to be collected a copy of the patient consent form is attached to this letter. For each surgery we estimate that there will be only a small number of patients. The research pharmacist will contact the surgery by telephone or email to ask for the data, the patients' information will be treated as strictly confidential. If you are happy to assist, please sign the consent form and return in the pre-paid envelope provided to the researcher's address below or alternatively if you prefer further information, you can email or phone the researcher.Thank you for your time and I look forward to hearing from you. If you need further information please do not hesitate to contact me:

Zahraa SMA Jalal
Department of Practice and Policy
UCL School of Pharmacy
Mezzanine Floor, Entrance A, BMA House , Tavistock Square, London WC1H 9JP.

General practitioners consent form
Patient Identification Number for this trial:

CONSENT FORM

Title of Project: Feasibility and Potential Impact of Community Pharmacy Care including Motivational Interviews on Adherence to Secondary Prevention Medication in patients with Coronary Heart Diseases

Chief investigator: Professor Felicity Smith Researcher: Zahraa SMA Jalal (PhD student)

Principal Investigator Sotiris Antoniou

Please initial all boxes

I confirm that I have read and understand the General Practitioners consent letter dated 31/01/2013 (version 2) for the above study. ☐

I agree to provide assistance and permission to obtain both LDL-C and blood pressure data of patients included in this study. Patients' will have given their consent for this information to be collected. ☐

Name of General Practitioner	Date	Signature

Please return to researcher's address

Zahraa SMA Jalal
Department of Practice and Policy
UCL School of Pharmacy
Mezzanine Floor, Entrance A, BMA House
Tavistock Square, London WC1H 9JP

Patient invitation letter

Title of research: Feasibility and Potential Impact of Community Pharmacy Care including Motivational Interviews on Adherence to Secondary Prevention Medication in patients with Coronary Heart Diseases

Dear Sir or Madam,

I would like to invite you to participate in a research study that aims to enhance patients' knowledge regarding their disease and medication and as a result their compliance to secondary prevention medication after a heart attack.

Before you decide to take part in the study, it is important that you understand why this study is being done and what it will involve. Thus, please read the Patient Information Sheet carefully and discuss it with others if you wish.

If you are interested to take part in the study, please inform the hospital pharmacist/research pharmacist. If you prefer further information, you can email or phone the researcher or chief investigator.

Kind regards

Researcher (PhD-student)	Chief Investigator
Zahraa SMA Jalal	Professor Felicity Smith
Centre for Pharmacy Practice,	Professor of Practice and Policy
UCL- School of Pharmacy,	UCL-School of Pharmacy
Mezzanine Floor, BMA House,	Department of Practice and Policy
Tavistock Square, London WC1H 9JP	29-39 Brunswick Square, London WC1N 1AX

Principal Investigator
Sotiris Antoniou
Consultant Pharmacist
Pharmacy Department
London Chest Hospital
Barts Heath NHS Trust
Bonner Road
London E2 9JX

Patient Information Sheet

Title of research: Feasibility and Potential Impact of Community Pharmacy Care including Motivational Interviews on Adherence to Secondary Prevention Medication in patients with Coronary Heart Diseases

Who Am I?

I am Zahraa SMA Jalal a PhD student

at the UCL-School of Pharmacy.

What is the purpose of this study?

The study is testing a new way for local pharmacists to help patients who have had a heart attack with their medicines. It is a way of consulting with patients to identify problems, and help achieve the best outcomes. We want to see if this new service is better than what happens at present.

Why have I been chosen?

You are being invited to take part in this study because you live in East London, have had a heart attack that has been treated at the London Chest Hospital and you obtain your medicines from one of the pharmacies taking part in the study.

What will I be asked to do if I take part?

In this study there are two groups of pharmacies. In one group (intervention), the pharmacists have been trained in a new way of supporting patients who have had a heart attack to take their medicines. The other group (control) will provide their services as usual. Pharmacies have chosen to be intervention or control pharmacies by chance. If you collect your medicines from one of the intervention group pharmacies, when you leave hospital you will be given a letter for your local pharmacist, who will then invite you to have a consultation about your medicines on two occasions, the first about 2 weeks after you leave hospital and the second about 3 months later, the consultation will take approximately 20 minutes. If you collect your medicines from a pharmacy in the control group, you will receive care as usual from the hospital and community pharmacy.

To help us evaluate the intervention participants in both groups will be asked to complete 2 questionnaires about the services and using medicines that will take a total of around 10 minutes to complete. The researcher may also call you to ask about how helpful the consultation was.

Do I have to take part?

No, it is up to you to decide. The research pharmacist will go through this leaflet with you, which you can keep. If you agree to take part you will be asked to sign a consent form. You are free to withdraw from the study at any time without giving a reason.

A small number of participants will also be contacted by the researcher for a brief interview, which will take between 10 and 30 minutes, if you are agreeable this will be audio-recorded. The researcher will use anonymised verbatim quotes and the participant is allowed to stop, edit and delete audio recording.

With your permission to help us evaluate the intervention we will also ask your GP for some routine information on your blood pressure and cholesterol, a copy of your consent form will be sent to your GP.

What are the possible advantages of taking part?

We cannot promise that the study will help you, but we hope it will provide information to help us plan services in the future.

What are the possible disadvantages of participating in this study?

There should be no disadvantages to taking part. Whichever group you are in, your pharmacist will provide usual services for you.

Is the study confidential and what will happen to the results of this study?

All the information that you will provide or any other information we may obtain about your medication from your hospital records will be treated strictly confidential. The

What if something goes wrong?

If you have a concern about any aspect of the study, you should ask to speak to the researcher [Zahraa SMA Jalal], project supervisor [Professor Felicity Smith] or consultant pharmacist at The London Chest Hospital [Sotiris Antoniou]. They will do their best to answer your questions. If you remain unhappy and wish to complain, or have any concerns about any aspect of the way you have been approached or treated by members of staff you may have experienced due to your participation in the research, National Health Service or UCL complaints mechanisms are available to you. Please ask your research doctor if you would like more information on this. In the unlikely event that you are harmed by taking

information you provide will be made anonymous by removing your personal details. That means that you will not be identified in any report or publication that is produced about the study. The results of the study will be reported as a part of a thesis and may be published in professional journals. If you would like a copy of the report or papers, please ask the researcher, Zahraa SMA Jalal.

part in this study, compensation may be available. If you suspect that the harm is the result of the Sponsor's (University College London) or the hospital's negligence then you may be able to claim compensation. After discussing with your research doctor, please make the claim in writing to the [Professor Felicity Smith] who is the Chief Investigator for the research and is based at [The UCL-School of Pharmacy, Department of Practice and Policy29-39 Brunswick Square, London WC1N 1AX

Tel: 0207753 5800 Email : f.j.smith@ucl.ac.uk] . The Chief Investigator will then pass the claim to the Sponsor's Insurers, via the Sponsor's office. You may have to bear the costs of the legal action initially, and you should consult a lawyer about this.

Further information and contact details

If you would like to know more about this study, please contact the researcher Zahraa SMA Jalal

Centre for Pharmacy Practice, UCL- School of Pharmacy, Mezzanine Floor, BMA House, Tavistock Square, London WC1H 9JP.

Email:zahraa.ali.11@ucl.ac.uk

Thank you for reading this – please ask any questions if you need to.

CONSENT FORM Patient Identification Number for this trial:

Title of Project: Feasibility and Potential Impact of Community Pharmacy Care including Motivational Interviews on Adherence to Secondary Prevention Medication in patients with Coronary Heart Diseases

Chief investigator: Professor Felicity Smith Researcher: Zahraa SMA Jalal (PhD student) Principal investigator: Sotiris Antoniou

Please initial all boxes

1. I confirm that I have read and understand the patient information sheet dated 31/01/2013 (version 1) 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, without my medical care or legal rights being affected. ☐
3. I give permission to the community pharmacist to contact me and/or to refer me to the GP in case of need. ☐
4. I understand that the study will involve the collection of data regarding my blood pressure and cholesterol results from my GP to help evaluate the intervention. ☐
5. I am aware that I might be contacted by phone by the research pharmacist for an interview and that a request maybe made to audio-record but this is not a requirement. ☐
6. I understand that the researcher will use anonymised verbatim quotes and the participant is allowed to stop, edit and delete audio recording. ☐
7. I am aware that I will be asked to complete 2 questionnaires about the services and using medicines. ☐
8. I agree to take part in the above study. ☐

Name of Participant Date Signature

Name of Person taking consent Date

Appendix 21 BMQ and Adherence results for South Asians sample

Patient No.	Control	Intervention	Result on BMQ	Adherence Baseline, 3months 6months		
2 RN	BMQ 25/10		B/R Positive	8	8	8
40 HG	BMQ 25/19		B/R Positive	8	8	8
1MH		BMQ 25/12	B/R Positive	6.75	8	7
10MB		BMQ 25/12	B/R Positive	7.5	8	7.5
16MP		BMQ 21/15	B/R Positive	8	8	8
42ZQ		BMQ 24/11	B/R Positive	8	8	8
45MV		BMQ 17/21	R/B Negative	5.75	5.75	5.75
57IR		BMQ 20/19	B/R Positive	8	8	8
55MB		BMQ 21/15	B/R Positive	8	8	8
7SA			R/B Negative	5.75	0.7	0
39FM	BMQ 19/10		R/B Negative	7	7	8
15MS		BMQ 19/14	B/R Positive	7	6.75	7
12NB	BMQ 20/13		B/R Positive	8	8	5.5
32NM	BMQ 21/16		B/R Positive	8	8	6.75

Appendix 22 Coding, themes and analysis

	Forgetting	Sufficient knowledge	Insufficient knowledge	Family support	Side effects	Feeling ill	Feeling healthy
1	32				32 muscle pain	32 indigestion	
2			39		39 vomiting		
3	40		40		40 coughing	40 vomiting and sweating	
4			2	2	2 cold feet	2 sweating	
5			55		No side effects	55	
6	7		7			7 tightness	
7	12	12			Bruising	12 tightness	
8	1	1			No side effects	1 chest pain	
9		10		10	No side effects	10 burning pain	
10	42				No side effects	42 vomiting	42
11			15	15 relies on son		15 breathing problem	
12		16			Cold extremities	16 body pain	
13		45				45 sweating	
14			57	57 relies on daughter	No side effects		

	Relying on healthcare practitioners	Cardiac rehabilitation	Asian food	Exercising Before heart attack	Not exercising Before heart attack	Severity of the disease	Non severity of the disease
1		32 yes went ot rehab.		32			32
2	39 if doctor says I have to take it then I have to	39 Yes going				39	
3	40 doctor say take regular	40 yes went to rehab.	spicy and ghee	40 walking			
4	2	2 yes			2		
5	55 if prescribed	Yes 55	Curries	55 walking		55 not sure	
6		No 7		7	7	7 yes	
7	12	12 yes			12 little		
8		1yes	1 greasy		1 no	1 yes	
9		10 yes	10 walking				
10			42	42		42 you can die	
11	15 relies on GP	15 yes	15 junk		15		15
12	16 relies on healthcare practitioner	16yes	16		16		
13		45 yes	45	45			45
14		57 yes	57	57			57

	Importance of the medicine	Problems taking the medicine	Organising the medicine	Not organising the medicine	Taking medication for the first time	Family history of the disease	Eating healthy Diet
1	32 important			32	32	32	32
2	39 important						
3	40 not sure						
4	2 important		2 organise				
5	55 not sure		55 organise				Not sure
6		7 not taking		7			
7	12 important						12
8	1 important		1 once a day				
9	10 v. important		10				
10	42 v.		42				

	important	
11	15 v. important	
12	16 not sure	
13	45 not sure	45
14		57

	Not eating a healthy diet	Causes of the disease	Use of pill box	Worries of another heart attack	Fatality and God	Depression	Socio-economic status
1		32 family history					
2	39	39 eating junk food and cholesterol					
3		40 family history brother, father		40			
4		2 stress		2			
5		55 not sure	Uses pill box				
6		No clue		7			
7	45 alcohol	Stress, family, genetics, high cholesterol		12			
8		1 junk food		1	1		
9	10 before attack	Diet	10 yes	10		10	10
10		Flu 42	42 yes				
11		15 chest problem			15		
12	16 smoked			16			
13				45			
14	Smoker	Smoking			57		57 lack of rest

1262
AJG

Gallagher London

MARKET REFORM CONTRACT

UMR: B1262FI0103012

SCHEDULE

Policy No:	B1262FI0103012
Underwriters:	Syndicate NWL 1218 at Lloyd's
The Insured:	LONDON UNIVERSITIES PURCHASING CONSORTIUM IN RESPECT OF PARTICIPATING MEMBERS AS PER SCHEDULE OF NAMED INSUREDS
Address:	Mezzanine 2, University of London Union, Male Street, London, WC1E 7HY
Business: the	The Undertaking of any **Trial** by or on behalf of the **Insured** in connection with **Insured's** activities.
Broker:	Gallagher London
Period of Insurance:	a) From: 1st August 2012 To: 1st August 2013
Underwriters	b) Any subsequent period for which the Insured shall pay and the shall agree to accept a renewal premium
	Both days at 12.01Local Standard Time at principal address
Limits of Liability:	**APPLICABLE TO EACH NAMED INSURED as per Schedule**
	SECTION 1 No Fault Compensation Policy GBP 10,000,000 each and every claim but limited to GBP 12.500,000 in the annual aggregate
	SECTIONS 2 Clinical Testing Legal Liability Policy GBP 10,000,000 each and every claim but limited to GBP 12,500,000 in the annual aggregate.
	The total liability of the Underwriters shall not exceed GBP 12,500,000 in the annual aggregate.
	The Limits of Liability are inclusive of Deductible.
First Premium:	As per Individual Security Details
Policy Territory:	Section I – Worldwide excluding USA/Canada Section II - Worldwide
Deductible:	GBP 2,500 each and every claim
	other than
	United States of America jurisdiction under Section II where USD25,000 each and every claim shall apply.

Appendix 24

This proposal was informed by a feasibility/ pilot study that has been undertaken by the applicants:

Title of the research proposal
A multicentre randomised controlled trial to evaluate the impact of a motivational interviewing-based community pharmacy intervention to enhance clinical outcomes (LDL-C) to secondary prevention medication in patients with coronary heart disease.

The aim
The aim of the study will be to evaluate the impact of a community pharmacy intervention involving motivational interviews with coronary heart disease patients on adherence to secondary preventive medication and clinical outcomes. The study will also include an integral process evaluation of the feasibility and acceptability across different locations, patient populations and pharmacy settings.

Design
Multi-centre prospective randomised controlled trial of a community pharmacy based intervention for patients discharged from hospital following an acute coronary syndrome (ACS).

Sites and setting
The study will be undertaken in 4 areas in the south of England two parts of London, Portsmouth and Southampton. Involvement of these locations will enable participating of patients from urban and rural areas of differing socio-economic backgrounds. It will involve a number of hospital sites and community pharmacies, so that differences in the organisation and delivery of services and different types of pharmacy can be taken into account.

Target population
Patients discharged from 4 cardiac centres with a first diagnosis of ACS, randomised to intervention and control arms.

Inclusion criteria patients above 18yrs, admitted with ACS, discharged on secondary prevention medication, consent to participation.

Exclusion criteria congenital heart disease, complications of myocardial infarction, do not live independently (nursing or care home), terminal illness, unable to understand English.

Duration
Total duration of trial 4 years (48 months)
Recruitment of pharmacies and training 6 months
Recruitment of patients 10 months
Duration of follow up of patients 12 months
Data collection, follow up, process evaluation, writing reports, dissemination 20 months

The intervention

Patients discharged from four cardiac centres after a first coronary event will receive a telephone consultation involving a motivational interview delivered by a community pharmacist 2 weeks post-discharge and again at 3 and 6 months. The patient's discharge summary will be forwarded from the hospital, by the research assistant, to the community pharmacist. The patient will also be given a copy of the discharge letter. The patients will receive a motivational interviewing consultation of 15-20 minutes, Pharmacists will be provided with a laminated copy of the consultation to use during their consultation with the patient. The community pharmacist should claim the consultation through the New Medicine Service (NMS) (part of their NHS contractual framework). Although the service will be paid for through the NMS, pharmacists will be reimbursed for their time and for taking part in the intervention (Training time and contacting the patients to invite to the intervention).

The consultation

Communication is integral to any practitioner-patient interaction. Motivational interviewing is a patient-centred counselling technique, which aims to evoke behaviour change through the exploration and resolution of ambivalence (Rubak et al, 2005; Miller & Rollnick, 2002). Motivational interviewing aims to facilitate and enhance the patient's intrinsic motivation to change or uptake a behaviour (such as medication adherence) by engaging the patient in an empathetically supportive, collaborative but strategically directed conversation. The consultation will involve a motivational interview session, the pharmacist will incorporate the key motivational interview skills that they learned from the training in their consultation and refer to the consultation chart. Typically, those trained in motivational interviewing use a variety of techniques that can be divided into microskills, strategies and behaviour change techniques of "Express empathy, develop discrepancy, role with resistance, support self efficacy" (Bisono *et al*, 2006). The sessions will aim to develop a partnership between the pharmacist with the patient and exchange information to facilitate an informed decision. Furthermore both the pharmacist and the patient will negotiate behaviour and reach an agreement. The goal is to access motivation and elicit commitment to change behaviour "in this case would be adherence to life saving medication"

Training for pharmacists

Intervention pharmacies will be invited by UCL School of Pharmacy for training on motivational interviewing and the delivery of the intervention. The training will include a two day workshop on motivational interviews and one day training on secondary prevention medication. Training on motivational interviewing will be delivered by an expert psychologist from UCL School of Pharmacy. Training on secondary prevention medication will be delivered by an expert consultant pharmacist from the London Chest Hospital. Trained pharmacists will undergo assessment after completing the training. The pharmacists will be assessed through role plays of the intervention to assure fidelity of motivational interviewing techniques. To test for the success of the training and ensure that the pharmacists who undergo the training have sufficient skills to deliver the intervention, the Motivational Interviewing Treatment Integrity (MITI 3.1) scale will be used (Moyers et al, 2005) using recorded role-play activities that occur one week after the training has

been received. The MITI is an instrument designed to measure the degree to which a practitioner is interacting with a client in a way that is consistent with motivational interviewing. To use the MITI, trained raters observe or listen to a 20 minute interaction. Pharmacists will also be asked to complete a self-report instrument to assess their knowledge and confidence in their new skills.

Training venue and facilitators

Training will take place at all the cardiac centres' areas at the following locations UCL-School of Pharmacy, University of Portsmouth and University of Southampton. The universities will be contacted in advance to arrange the training location and convenient times. The training will run for two months every 2 weeks at a different location, it is estimated that each training session will accommodate around no more than 20 pharmacists per group. It will be delivered by a registered psychologist and trainer in motivational interviewing with over a decade of experience and facilitated by collaborators at the relevant sites. Two training sessions will be held in the London area.

Sampling strategy and procedures

The design of the study will follow CONSORT guidelines for randomised control trials www.**consort-statement**.org and analysis will follow an intention to treat. Randomisation will be performed by an independent statistician at UCL School of Pharmacy. Patient randomisation: patients will be randomly allocated by using a table of random numbers into intervention and control arms. The randomisation will be concealed from the research team. Pharmacies in the intervention areas London, Portsmouth and Southampton will be allocated to intervention and control according to their postcode area and then invited to the training. Analysis will be conducted by an independent researcher. The researcher and the research assistants will be blind to the patients' allocation, it is not possible to blind the patients or the pharmacists delivering the intervention due to the nature of the intervention.

Sample size

To detect a clinically important difference in LDL-C of 0.4mmol/L, and assuming standard deviation of 1.25mmol/L and correlation between baseline and follow up measurements of 0.48 (from feasibility work) the total sample size required is 316 (90% power, 5% significance). Inflating this for clustering by pharmacist: assumed ICC=0.05, average of 3 patients per pharmacist (2 after drop out), 166 pharmacist clusters of 3 patients (total=498 patients) will be required.

Pharmacies

There are around 1282 pharmacies in central and east London, 132 pharmacies in Portsmouth, 114 in Southampton this sum up to a total 1582 Pharmacies

An invitation letter for the study will be sent to the pharmacies through the local Pharmaceutical Committees (LPC). Pharmacies will register their interest online by an online register set up by the LPC's for the trial. It is estimated depending on previous data from pharmacy recruitment in the pilot study, invitations sent to 360 pharmacies resulted in a response rate of 50 pharmacies. Therefore, it could be possible to recruit around 220 pharmacies in this trial. The pharmacies will be allocated to 110 pharmacies intervention and 110 pharmacies control; this will depend on

pharmacy response rate. Approximately each pharmacy will deliver the intervention to 1-2 patient's depending on the sample size. The number of pharmacies and patients included in the study will vary according to the area and city location, it would be anticipated that more pharmacies and patients from the London area will be recruited.

Recruitment procedures

There will be three stages of recruitment:

Recruitment of hospitals: An invitation letter will be sent from UCL School of Pharmacy to the cardiac centres which already been approached and expressed a willingness to participate, and/or are already on-board. The letter will explain the protocol and what is expected to occur during patient recruitment. The letter will also explain the role of the research assistants that will undertake the recruitment and what is needed from the hospital pharmacists to facilitate the process. The hospitals' will sign an agreement contract for the trial with UCL School of Pharmacy and also help arrange honorary contracts for the researchers.

Recruitment of pharmacies/pharmacists: Pharmacies that express interest to take part in the study will be mailed individual letters explaining the study. The pharmacies will be informed that the pharmacy will be allocated to either intervention or control by chance. Invitation to the training will be after randomisation, only intervention pharmacists will be invited to the training. The control group pharmacists will be offered the training after the completion of the intervention.

Recruitment of patients: Recruitment of patients will be by the research assistants. A research assistant will be allocated in each of the cardiac centres. The research assistant will review the patient's hospital chart to assess patient eligibility and postcode. Patients with a first coronary event will then be approached, explained about the trial and then left with a recruitment package to read. The assistant will return at a later time to answer any queries the patient has and a consent form will be signed, if the patient expresses interest to be part of the study. Patients enrolled on other studies will not be included.

Instruments and outcome measures for evaluation of the intervention

Primary outcome: LDL-C and blood pressure (from hospital charts at baseline and from GPs during patient follow up)

Secondary measures

1- Adherence to secondary prevention cardiovascular medications (Antiplatelets, betablockers, ACE inhibitors or ARBs, calcium channel blockers and statins)

2-Rehospitalisation, re-infarction (from hospital charts)

3-Beleif Medicines Questionnaire-Specific (mailed to patients)

4-Concept on subjective wellbeing SWLS scale and PANAS (mailed to patients)

Measures of adherence will be robust (use multiple measures):

- Self-report on a validated scale Morisky self report questionnaire MMAS-8 this will be collected by mail and telephone.
- Prescription refill data from the pharmacies this will enable detection of adherence for the different medicines. A letter will be sent to both control and intervention pharmacies

explaining the study and pharmacies will have to provide consent for collection of refill data that will be collected by the research assistants.

- Repeat prescription requests from GPs, a letter will be sent to both control and intervention patients' GPs explaining the study and the GPs will provide consent for collection of patients' prescription data.

Costs

An economist from Priment CTU will evaluate costs of delivery and costs impact (improved adherence, less morbidity, hosp admissions avoided). The economic evaluation will report the cost-effectiveness of the intervention compared to treatment as usual over 12 months. Life-time costs and quality adjusted life years (QALYs) will be calculated from a previously developed CVD model.

Data collection

Data will be collected by the research team. The research assistants will collect data from participating pharmacists, pharmacies, GPs and patients in control and intervention groups. Data will be collected from the hospitals at baseline and at 6 months and 12 months.

Process evaluation

An integral process evaluation will assess operational aspects with patients, pharmacists, GPs and hospitals, to identify circumstances required for successful implementation. The integral process evaluation will employ quantitative and qualitative methods to ensure a comprehensive evaluation of feasibility, acceptability, perceived impact across all sites and from all perspectives. This will include assessment of:

- No. of eligible patients and response rates
- No. placed with a participating pharmacy
- Measures of uptake by pharmacists
- Attrition rates pharmacists and patients in contact following discharge, successful arrangement of consultation, successful completion of intervention
- The effectiveness of training and fidelity to intervention, especially the employment of motivational interviewing techniques in the delivery of the intervention.

The acceptability/ workability in all and perceived impact from the perspective of all stakeholders which will be examined in semi-structured interviews with representatives of all stakeholders

Operational aspects in the pharmacy

Adherence to protocol; the pharmacists will keep a copy of the consultation in the pharmacy, in the consultation room to refer to during their consultation. The pharmacist will conduct the consultation by telephone in the consultation room. The intervention should aim not to affect the workflow of the pharmacy because it is designed to fit under the New Medicine Service consultation. Interviews with patients that complete the intervention will be conducted to evaluate the perceived value of the consultation. Treatment fidelity to intervention; this will be measured by asking the pharmacists to audio record their consultations with the patients after both patient and pharmacist consent. Pharmacists will conduct consultations with the use of audio equipment and 20 minutes of each consultation will be assessed using the MITI to calculate how motivational interviewing congruent the session was.

Acceptability and perceived impact from all stakeholders: interviews will be conducted with a sample of hospital and community pharmacists, patients (intervention and control).

PPI- public patient involvement -Patients and pharmacists that were part of the pilot study were involved in writing the full protocol for this main study.

Dissemination plan A dissemination strategy for the project will be developed to allow uptake and success of the project.
Stakeholders in this project will include:

- The hospitals (the cardiac centres), Presentations on the project will be given in each cardiac centre to the healthcare professionals to raise the awareness of the project and its objectives this will facilitate recruitment. Leaflets will be designed and included in the patient recruitment package to be given to eligible patients.

- The Local Pharmaceutical Committees (LPC) in each area, attendance at LPC meetings by the researchers

- The pharmacies (Pharmacists)

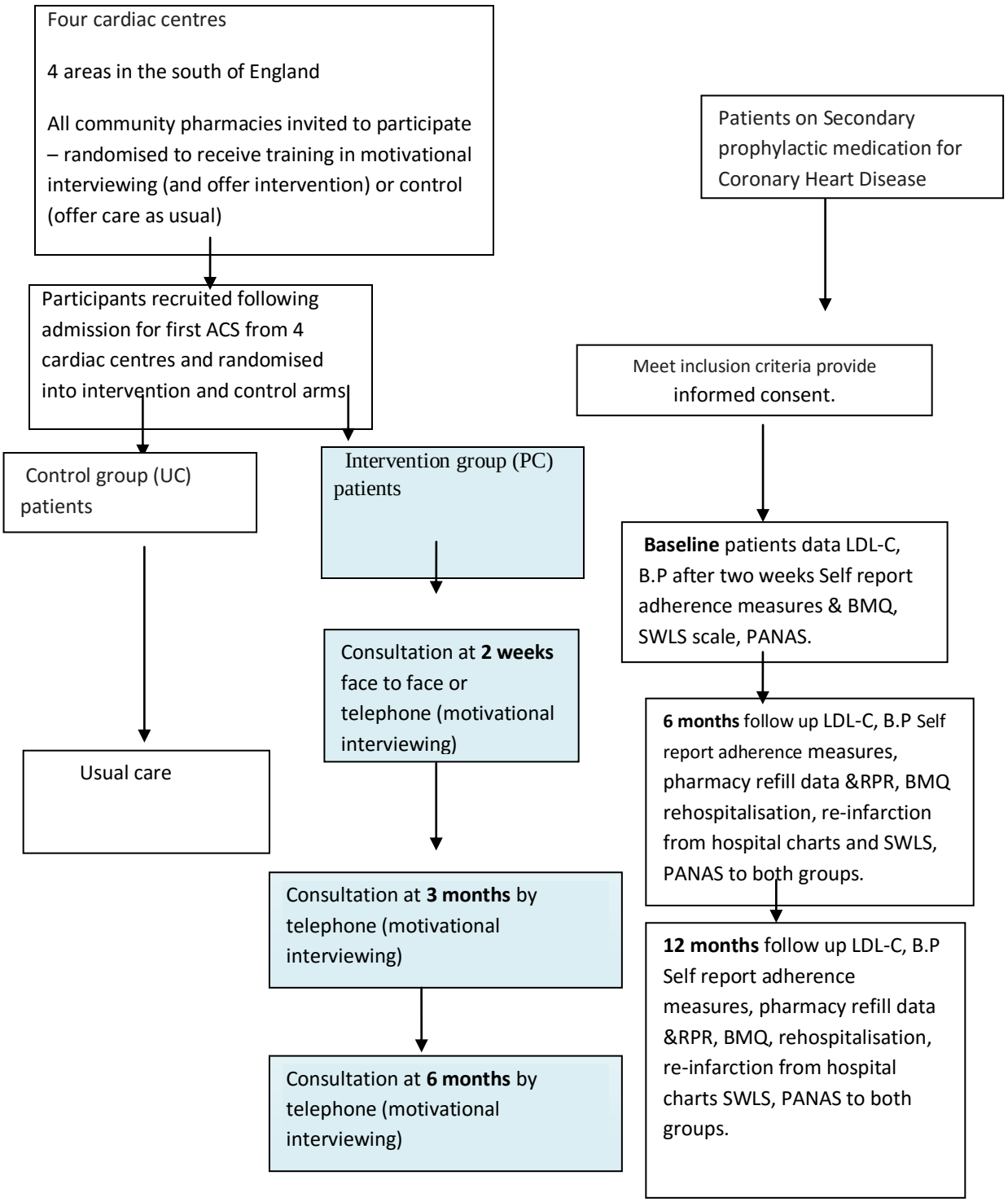
- The patients

A website for the project will be developed to allow all stake holders to be informed.
The trial protocol will be presented in conference presentations and posters.
The trial will be registered on Clinicaltrials.gov.

Costs and justification of costs

- Psychologist and consultant pharmacist training fees for all training sessions
- Materials for the training and training certificates
- Room bookings and catering
- Research team and research assistants' Salaries
- Postdoctoral project manager (Full time employment)
- Research assistants (Full time employment)
- Collaborators
- Economist
- Advisory group expenses
- Travel expenses to sites
- Telephone costs
- Documentation
- Patient Public Involvement costs (travel)
- Community pharmacists (intervention group only) reimbursement for training and participation
- Community pharmacists (control group only) training
- GPs costs nurses to provide patient data at surgeries

Flow chart for the multicentre trial proposal



BMQ: Beliefs Medication Questionnaire SWL: Satisfaction With Life scale, PANAS: positive and negative affect scale, RPR: Repeat prescription requests. http://internal.psychology.illinois.edu/~ediener/SWLS.html, http://www.google.co.uk/url?sa=t&rct=j&q=&esrc=s&source=web&cd=1&ved=0CCgQFjAA&url=http%3A%2F%2Fwww.cnbc.pt%2Fjpmatos%2F28.Watson.pdf&ei=QU6QVJn4DI2LaMGLgvgH&usg=AFQjCNE1zfLunrDdxVxR8cZL7hSf4wtDiQ&sig2=Jc_1rZOuaFnT-HPPNEf_Ug&bvm=bv.81828268,d.d2s

The End