The Impact of Clinical Pharmacy Services on the Low-density Lipoprotein Goal Attainment with Lipid Lowering Therapies

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Abstract of thesis entitled (English):

Objective: Coronary heart disease (CHD) is the second leading cause of mortality in Hong Kong. It is well established that low-density lipoprotein cholesterol (LDL-C) plays an important role in the development of CHD and the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) guidelines have recommended more stringent control of LDL-C. Evidence has demonstrated that the development of pharmacist-managed lipid clinics is successful in achieving the ATP III LDL-C goal for the prevention of CHD, resulting in reduced mortality and cardiovascular events. In Hong Kong, the availability of pharmacist-managed clinics is still in its early stage of infancy. The objective of this study was to assess the benefits of the implementation of a clinical pharmacy service (CPS) to assist in dyslipidaemic management.

Methodology: This was a 24-months prospective controlled trial conducted at the lipid clinic of a public hospital in Hong Kong. Three hundred patients were recruited into the study (150 in intervention group, 150 in control group). In the intervention group, apart from routine physician care, a clinical pharmacist assessed LDL-C levels and provided recommendations in accordance to the ATP III guidelines. Medication compliance and the proper use of drugs were assessed. Education on healthy lifestyles was reinforced. Monthly telephone follow-ups were made to check on progress of patients. In the control group, patients received usual medical care with no pharmacist intervention.

Results: In the intervention group, 58.7% patients achieved LDL-C goals compared with 45.3% in the control group ($p < 0.05$). The intervention group achieved 26.4%, 17.4%, and 30.0% mean reduction in LDL-C, TC and TG levels, respectively, compared with 12.6%, 6.6%, and 11.5% in the control group ($p < 0.05$). The odds ratio of achieving LDL-C treatment goal was greater for patients with age 45 – 65 years (odds ratio = 2.574, 95% CI,

1.322 – 5.012). Subjects with familial hyperlipidaemia, high CHD risk factors, and diabetes mellitus would require more aggressive lipid-lowering therapy. The overall compliance with medication in the intervention group was 77.5% at baseline which improved to 79.8% at the end of study following pharmacist intervention ($p < 0.001$). Patients in both groups (92.6% in intervention group, 90.1% in control group) felt that having a CPS was beneficial for their dyslipidaemic management. Physicians at the lipid clinic gave a positive impression of the CPS and valued the potential benefits of the clinical pharmacist in managing dyslipidaemia.

Conclusion: The study demonstrated that pharmacists could assist in dyslipidaemic management by providing drug education and healthy lifestyle advice to patients, together with the assessment of lipid profiles and drug compliance. The results also showed the benefits of CPS which paves way for further development of such services in other problematic areas like hypertension and diabetes mellitus.

Abstract of thesis entitled (Chinese):

目標: 冠狀動脈心臟病是香港人第二大導致死亡原因。根據大家已確立的認識，血中低密度脂蛋白膽固醇引致患上冠心臟病扮演重要的角色。而美國全國膽固醇教育課程對成年人高血膽固醇的治療之第三次的報告建議加強血中低密度脂蛋白膽固醇嚴格的調控。證據顯示發展藥劑師駐守的治療血脂之診所能有效地達到國際報告所提出的治療目標來預防冠心病，進而降低死亡率及病發率。在香港，開設註冊藥劑師駐守的診所仍處於發展初期。本研究目是調查及評估實施臨床藥劑師參與跟進之診所對治療血膽固醇過高症之成效。

方法: 本研究計畫是在香港的公立醫院治療血脂之診所進行了爲期二十四個月前瞻性研究， 招募了 300 名患有高膽固醇的病人 (150 人參與接受藥劑師跟進服務組別， 150 人參與對照組別)。在接受臨床藥劑師跟進服務中，他們除了接受醫生常規診治外， 藥劑師會爲他們評估壞膽固醇的含量及根據指引提供專業建議。並且對病人服藥的遵從性及病人正當服藥方法作出評估。 加強教育病人奉行健康的生活方式。 透過電話方式，每個月向病人定期緊密監察。在對照組中， 病人在沒有藥劑師參與跟進下，只獲得醫生常規診治。

研究結果: 在接受藥劑師跟進服務組別中，百分之五十八點七病人的血中低密度脂蛋白膽固醇值達到國際報告所提出的治療目標，相對之下，對照組病人則爲百分之四十五點三達到目標 ($p < 0.05$)。 接受藥劑師跟進服務組別之低密度膽固醇、總膽固醇及甘油三酯分別平均降低了百分之二十六點四、百分之十七點四以及百分之三十，與對照組之相比，分別是百分之十二點六，百分之六點六以及百分之十一點五（$p < 0.05$）。血中低密度脂蛋白膽固醇治療的目標危險對比值 (odd ratios, OR) 相對高之病人爲四十五至六十五歲病人(OR = 2.574, 95% 信心水準[CI]，1.322 –

5.012)。遺傳性高脂肪病、高風險之冠狀動脈心臟病危險因素及糖尿病之病人需要接受嚴緊降血脂治療法。在實驗組別中，總服藥的遵從性由基線百分之七十七點五到計畫完成時達至百分之七十九點八。兩組病人(實驗組別爲百分之九十二點六，對照組爲百分之九十點一) 均認爲藥劑師跟進服務能改善治療血膽固醇過高之處理。血脂診所的醫生對臨床藥劑師跟進服務給予正面的印象及對藥劑師參與血脂治療的潛在益處作出評價。

結論: 本研究顯示透過藥劑師病人提供藥物教育及給予健康生活方式之意見，同時透過評估各膽固醇指標和服藥的遵從性來控制高血脂水平。結果顯示臨床藥劑師跟進服務之益處可擴展應用於類似醫療服務上如高血壓及糖尿病。

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I am deeply thankful to my supervisor Prof. Vivian WY Lee, for her guidance and support during my postgraduate years at The Chinese University of Hong Kong. She has given me invaluable advice and encouragement which has led me through my study smoothly.

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My sincere thanks also go to everyone of the School of Pharmacy, particularly to Ms. Carrie Chau who has assisted me in translating the Chinese version of the abstract for me.

Finally, I would like to send my warmest love to my family, my husband and my lovely baby son for always being there for me.

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List of Abbreviations

ADA	American Diabetes Association
AFCAPS	Air Force/Texas Coronary Atherosclerosis Prevention Study
AHA	American Heart Association
ALLHAT	Antihypertensive and Lipid-lowering to Prevent Heart Attack Trial
ALLHAT-LLT	Antihypertensive and Lipid-lowering to Prevent Heart Attack Trial – Lipid Lowering Trial
AMI	Acute myocardial infarction
ARR	Absolute risk reduction
ASCOT	Anglo-Scandinavian Cardiac Outcomes Trial
ASCOT-LLA	Anglo-Scandinavian Cardiac Outcomes Trial – Lipid Lowering Arm
ATP	Adult Treatment Panel
BMI	Body mass index
CABG	Coronary artery bypass grafting
CAD	Coronary artery disease
CARE	Cholesterol and Recurrent Events Study
CER	Control event rate
CHD	Coronary heart disease
CI	Confidence interval
CIMT	Carotid intima-media thickness
CK	Creatine kinase
CMS	Central Medical System
CPS	Clinical pharmacy service
CVD	Cardiovascular disease
DCCT	Diabetes Control and Complications Trial
DoH	Department of Health
EER	Experimental event rate
e-PR	Electronic Patient Records
GISSI	Italian Group for the Study of Streptokinase in Myocardial Infarction
GOPC	General outpatient clinic
HbA1C	Haemoglobin A1C
HDL-C	High-density lipoprotein cholesterol
HKSAR	Hong Kong Special Administrative Region
HMG CoA	3-Hydroxy-3-methylglutaryl coenzyme A
HPS	Heart Protection Study

IDL-C	Intermediate-density lipoprotein cholesterol
JBS	Joint British Societies'
L-TAP	Lipid Treatment Assessment Project
LDL-C	Low-density lipoprotein cholesterol
LIPID	Long-term Intervention with Pravastatin in Ischaemic Disease Trial
METEOR	Measuring Effects on Intima-Media Thickness: an Evaluation of Rosuvastatin
MI	Myocardial infarction
NCEP	National Cholesterol Education Program
NHS	National Health Service
NICE	National Institute for Health and Clinical Excellence
NNT	Number needed to treat
NSF	National Service Framework
OR	Odds ratio
OTC	Over-the-counter
PROSPER	Prospective Study of Pravastatin in the Elderly at Risk
PROVE IT	Pravastatin or Atorvastatin Evaluation and Infection Trial
PWH	Prince of Wales Hospital
RCT	Randomized controlled trial
4S	Scandinavian Simvastatin Survival Study
SMS	Sending Messaging System
SPSS	Statistical Package for Social Sciences
TC	Total cholesterol
TG	Triglyceride
TIMI 22	Thrombolysis in Myocardial Infarction 22
TLC	Therapeutic lifestyle changes
UK	United Kingdom
UKPDS	United Kingdom Prospective Diabetes Study
ULN	Upper limit of normal
VLDL-C	Very low-density lipoprotein cholesterol
WHO	World Health Organization
WOSCOPS	West of Scotland Coronary Prevention Study

List of Publications and Presentations related to Thesis

Lee VWY, **Chung JS**, Tomlinson B, Lee KKC. Rate of low-density lipoprotein (LDL) goal attainment with lipid lowering therapies at a lipid clinic in a public hospital of Hong Kong – Possible role of a clinical pharmacy service. (Presented at the ISPOR Eleventh Annual International Meeting). Value in Health. 2006; 9(3): A129.

Lee VWY, **Chung JS**, Ng SL, Lee KKC, Tomlinson B. The impact of clinical pharmacy services (CPS) on the low-density lipoprotein (LDL) goal attainment with lipid lowering therapies. (Presented at the 41st American Society of Health-system Pharmacy Clinical Meeting and Exhibition).

Lee VWY & **Chung JST**. Clinical pharmacy services reduce risk of coronary heart disease. (Presented at The Chinese University of Hong Kong Press Conference. The School of Public Health, Prince of Wales Hospital, Seminar Room 2 & 3. 13 December 2007). The Chinese University of Hong Kong Newsletter. 4 January 2008; Issue 310: 4. Available at: www.cuhk.edu.hk/iso/newsleter/.

Chung JST, Ng SL, Lee KKC, Tomlinson B, Lee VWY. The role of pharmacist in dyslipidaemic management in Hong Kong. Journal of Clinical Pharmacy and Therapeutics. 2008 (*in progress*)

Contributions related to Thesis

Based on the results from this study, the pharmacy manager of the Prince of Wales Hospital has kindly agreed that their pharmacy department would continue to sustain the clinical pharmacy service at the outpatient lipid clinic.

The following items used in this study would be contributed to their service:

- Protocol of study
- Data collection form
- Patient education leaflet
- Pharmacist-physician communication sheet
- Telephone checklist.

Chapter 1. Introduction

1.1 Introduction of the Thesis

In countries where clinical pharmacy services (CPS) are available, studies have shown that the development of pharmacist-managed lipid clinics have been successful in achieving the National Cholesterol Education Program (NCEP) low-density lipoprotein cholesterol (LDL-C) goals for the prevention of coronary heart disease (CHD). Despite this, the development of CPS in Hong Kong is still in its early infancy and few studies on the impact of such services have been carried out. Coronary heart disease is the second leading cause of death among adults in Hong Kong and dyslipidaemia is now considered to be a major modifiable risk factor for developing CHD. Based on the positive results from studies conducted in other countries which demonstrated the benefits of CPS in the management of dyslipidaemia, setting up a CPS in the lipid clinic in Hong Kong would help to improve the care of dyslipidaemic patients. In this study, the main objective was to assess the impact of a CPS on achieving the recommended LDL goals proposed by the NCEP, and to assess the potential value of having a CPS in Hong Kong.

This thesis is based on a study of 300 dyslipidaemic Chinese patients in the outpatient lipid clinic of the Prince of Wales Hospital (PWH) in Hong Kong. Patients were assigned into two groups. In the intervention group, a CPS was set up where patients received educational visits conducted by a clinical pharmacist. Patients in the control groups were only seen by the

physicians. At the end of the study, the two groups were compared to assess the outcomes of their LDL-C goal attainment.

A brief description of CHD and the related risk factors for the development of the disease is described in Chapter 1. Dyslipidaemia and its management including both lifestyle modifications and lipid-lowering drug therapy are also discussed. The current NCEP ATP III guidelines for the desirable LDL-C goal attainment are reviewed. Studies on successful CPS set up in other countries are discussed briefly with examples.

Chapter 2 details the methodology of the study including the background setting, the inclusion and exclusion criterion of the recruited subjects, and the outcome measures of the study. Calculation for the sample size required in this study is discussed and the methods of statistical analysis used are explained.

In Chapter 3, the results of the study are analyzed and presented.

The findings from the study and their implications are further discussed in Chapter 4.

Finally, the conclusion of this study is discussed in Chapter 5.

1.2 Review on Coronary Heart Disease

1.2.1 Definition of Coronary Heart Disease

Coronary heart disease, also known as coronary artery disease (CAD) is a progressive disease, involving the narrowing or blockage of the coronary arteries by atheroma (Scott 1999). Atheroma is the degeneration of the walls of the arteries due to the formation in them of fatty plaques and scar tissue. As a result, the heart muscle does not gain adequate blood supply, leading to angina, coronary thrombosis or heart attack, heart failure and/or sudden death.

Symptoms generally develop in the latter stages, so CHD can be present for many years before a diagnosis is made. The most common symptoms of CHD include palpitations, dizziness, weakness, irregular heartbeat, chest pain, shortness of breath, jaw pain, back pain, or arm pain, especially on the left side. These symptoms can occur either at rest or during exercise or activity. The most serious sign of CHD is abrupt, unexpected cardiac arrest.

1.2.2 Risk Factors for the development of Coronary Heart Disease

Many factors directly or indirectly affect the development of the atherosclerotic plaque that underlies CHD. Cardiovascular risk factors can be classified as modifiable and non-modifiable [Table 1.1]. Non-modifiable risk

factors are factors that cannot be altered whereas modifiable risk factors are those that can be addressed through lifestyle changes and drug therapies.

Table 1.1. Risk Factors for Coronary Heart Disease

Non-Modifiable Risk Factors	**Modifiable Risk Factors**
Age	Smoking
Gender	Dyslipidaemia
Ethnicity	Hypertension
Family history of cardiovascular diseases	Diabetes
Previous cardiovascular events	Obesity
	Physical inactivity

Source: Williams *et al* (2003a)

Understanding the risk factors associated with the development of CHD is important in order to help reduce mortality and morbidity of the disease. It also helps identify strategies for both primary and secondary prevention of CHD. Primary prevention can be defined as using measures to reduce the risk of cardiovascular events in people without CHD but who are at high risk of developing it (Williams *et al* 2003a). Secondary prevention is defined as the prevention of the progression of a disease in symptomatic patients (Stevens *et al* 2002).

According to two separate studies carried out by Khot *et al* (2003) and Greenland *et al* (2003), the majority of CHD cases can be attributed to the presence of one of the four conventional and modifiable risk factors. These include smoking, diabetes, hypertension and dyslipidaemia.

Khot *et al* (2003) analyzed data from 122,458 patients who were enrolled in 14 international randomized clinical trials of CHD conducted during the previous decade. The cohort included 76,716 with ST-elevation myocardial infarction (MI), 35,527 with unstable angina/non-ST-elevation MI, and 10,215 undergoing percutaneous coronary intervention. The main outcome measures were the prevalence of each of the conventional risk factors listed above. The results showed that at least one of the four conventional risk factors was present in 84.6% of women and 80.6% of men with CHD.

In the study carried out by Greenland *et al* (2003), researchers assessed data from a total of 386,915 subjects enrolled in three prospective cohort studies with a follow-up period of 21 to 30 years. The main outcome measures were fatal CHD in the overall population and the occurrence of nonfatal MI in a sub-group of patients who were enrolled in the Framingham Heart Study. This data was then compared against exposure to major CHD risk factors, defined as total cholesterol of at least 6.22 mmol/L, systolic blood pressure of at least 140 mmHg, diastolic pressure of at least 90 mmHg, smoking and diabetes. The results revealed that for fatal CHD, exposure to at least one clinically elevated major risk factor ranged from 87% to 100%.

A number of these studies on established risk factors for CHD have been focused predominantly on the Western populations. However, the

Singapore Cardiovascular Cohort Study (2001) conducted by Lee and his colleagues demonstrated that hypertension, cigarette smoking, diabetes, and dyslipidaemia were also the major risk factors for CHD in Chinese, Malay and Asian Indian males. In a study carried out in Hong Kong Chinese, Lam *et al* (2002) showed that smoking was a strong risk factor for the development of CHD. Having low high-density lipoprotein cholesterol (HDL-C) and high triglyceride (TG) levels were also important risk factors in Hong Kong Chinese with CHD.

Furthermore, the most recently revised NCEP ATP III guidelines (2004) have placed a significant emphasis on more stringent management of the major risk factors that contribute to the development of CHD. Major risk factors include smoking, hypertension, low HDL-C, a family history of premature CHD and age (men $\geq$ 45 years and women $\geq$ 55 years). Coronary heart disease include history of acute MI, evidence of silent MI or myocardial ischaemia, history of unstable angina and stable angina pectoris, and history of coronary procedures. The revised guidelines also introduced the concept of 'CHD equivalents' which include conditions that require the same vigilance used in patients with CHD (Safeer & Ugalat 2002). Coronary heart disease equivalents include peripheral arterial diseases, abdominal aortic aneurysm, carotid artery disease and diabetes mellitus.

Epidemiological data from case-control studies in men (Rosenberg *et al* 1985) and in women (Rosenberg *et al* 1990) showed that the relative risks for CHD associated with current smoking in men and in women were 2.9 and 3.6 respectively. When these smokers took up smoking cessation between two and three years, the relative risk for CHD fell to the same level as that of those who had never smoked for both men and women.

MacMahon and Rodgers (1993) described that the effects of blood pressure reduction is beneficial in reducing the likelihood of developing CHD in patients who have hypertension. From the pooled analysis carried out by the investigators, they showed that this benefit was particularly significant in patients who were over 60 years of age where adequate hypertension treatment helped to reduce the incidence of CHD by about 19%. Their findings showed that the impact of hypertension treatment on the incidence of CHD in middle-aged patients was not significant though the overall mortality was reduced by about 15%. The authors described that this difference in CHD incidence reduction between the two age-group patients could be due to the fact that the risk of CHD is greater in elderly hypertensive patients compared to those who are middle-aged. Nevertheless, from the standpoint of reducing CHD risks, hypertension should be treated in all age-group of patients diagnosed with the condition.

Diabetes mellitus significantly increases the risk of cardiovascular disease (CVD) and CHD. The Diabetes Control and Complications Trial (DCCT Research Group 1993) for type 1 diabetes demonstrated that an intensive treatment program that included multiple daily doses of insulin and frequent blood glucose monitoring could significantly decrease haemoglobin A1C (HbA1C) levels and result in more than 50% reduction in microvascular events. Long-term follow-up results of the DCCT have also shown that intensive glycaemic control reduced the long-term incidence of CVD in people with type 1 diabetes (DCCT Research Group 2005). The authors described that intensive treatment reduced the risk of any CVD event by 42% and the risk of nonfatal MI, stroke, or death from CVD by 57%.

The United Kingdom Prospective Diabetes Study (UKPDS Group 1998) in type 2 diabetics showed that intensive glycaemic control with sulphonylureas or insulin reduced HbA1C by 0.9% over 10 years compared with conventional diet therapy alone. This also resulted in a 25% reduction in microvascular disease, a 33% decrease in microalbuminuria, and a 21% decrease in retinopathy progression. However, the UKPDS trial did not demonstrate a statistically significant reduction in marcovascular endpoints associated with improved glycaemic control. This suggested that macrovascular disease prevention in diabetic patients would require treatment of other cardiovascular risk factors in addition to hyperglycaemia.

It is therefore possible to reduce the epidemic of CHD by focusing on these four conventional risk factors and lifestyle behaviours, and devise strategies to prevent or treat these chronic risk factors in both primary and secondary prevention of the disease. In practice, many of these risk factors are interrelated and the management of CHD is therefore multifactorial. For the purpose of this study, dyslipidaemia was the main risk factor that was investigated where measures were sought to reduce this risk in patients with dyslipidaemia.

1.2.3 Worldwide Figures for Coronary Heart Disease

Coronary heart disease is one of the most common CVDs which are becoming a major health burden in developing countries. According to the World Health Report (WHO 2003a), 17.5 million people died from CVDs in the year 2005, representing 30% of all global mortalities. Over 80% of heart disease deaths took place in low and middle-income countries. Of the 17.5 million deaths from CVDs, around 7.6 million were due to CHD, 5.7 million were due to cerebrovascular diseases, and the remaining were related to hypertension and other heart conditions. The World Health Organization (WHO) estimates that by the year 2015, nearly 20 million people will die from CVDs, making it the leading cause of death in developing countries.

Coronary heart disease is the most important preventable CVD and its epidemiology has been well studied (Nishtar 2002). In fact, all major preventable CVDs are linked by common risk factors and can therefore be managed through a common strategy.

1.2.4 Coronary Heart Disease in Asia Pacific

The Asia Pacific region currently accounts for approximately half the global burden of CVDs (Murray *et al* 1997a). This proportion is expected to continue to increase despite the various CHD preventive strategies that have been employed in this region (Murray *et al* 1997b).

With the unprecedented economic development in these countries, the population in Asia Pacific has had major changes in their lifestyles over the last decade. Coronary heart disease in the Asia Pacific region appears to be increasing in parallel with the westernization of diet and lifestyle (Woo *et al* 1998, Zhou *et al* 2003). The increase in CHD prevalence and mortality is believed to be due in part to increasing life expectancy and in part to increasing levels of CHD risk factors (Ritchie *et al* 2001).

Janus *et al* (1996) described that the degree of economic development varies in each country. It is advanced in Japan, Korea, Taiwan, Hong Kong and Singapore. In China, Philippines, Malaysia, Thailand, Indonesia and India, the economy is rapidly changing. Khor (2001) described that by the year 2020,

CVDs are expected to account for seven out of every 10 deaths in these countries compared with less than half this value today. As a proportion of total deaths from all-causes, CVD in the Asia Pacific region ranges from less than 20% in countries like Thailand, Philippines and Indonesia to between 20 and 30% in urban China, Hong Kong, Japan, Korea and Malaysia. Countries such as New Zealand, Australia and Singapore have relatively high rates that exceed 30 to 35%.

The most economically developed country in this region is Singapore and figures have shown very high CHD mortality rate, with more than 150 deaths per 100,000 among its population (Khor 2001). This has significant implications and provides a warning to the other countries in Asia Pacific that an 'epidemic' of CHD may surge. The effects are likely to be similar to those observed in Western countries. In order to address this, the implementation of appropriate strategies for CHD prevention needs to be developed across the Asia Pacific region (Janus *et al* 1996).

1.2.5 Coronary Heart Disease in Hong Kong

In Hong Kong, CHD is a major health issue and has been the second leading cause of death since the 1960s [Table 1.2]. According to the statistics from the Hong Kong Special Administrative Region (HKSAR) Department of Health (Website: Department of Health, Hong Kong), heart disease accounted

for more than 60,000 hospital admissions in the year 2000 and nearly 5,000 deaths in the year 2002. Among these figures, CHD constituted a major proportion of this mortality, making up 67.6% of CVD deaths. In the year 2005, these figures have increased and approximately 11 persons died from CHD per day.

Table 1.2. Leading causes of death in Hong Kong, 2005

Ranking	Number of Deaths	Percentage (%)
1. Malignant neoplasms	12,310	32.1
2. Cardiovascular diseases	5,568	14.4
3. Pneumonia	4,291	11.1
4. Cerebrovascular diseases	3,434	8.9
5. Chronic lower respiratory diseases	2,261	5.8
All other causes	10,514	27.2
All causes	38,678	

Source: HKSAR Department of Health Statistics (2007)

Coronary heart disease is a cause of disability that has both direct and indirect cost implications to the health system in Hong Kong. The most significant manifestation of CHD is acute myocardial infarction (AMI). This is the death of a segment of the cardiac muscle following the interruption of the blood supply to this region and the patient experiences a 'heart attack' (Walker 1999). The management of patients with AMI is costly. In a study conducted by Lee *et al* (2005), the researchers evaluated that the average annual medical cost for AMI management in the year 2000 was nearly HKD73,000 per patient. In addition, the length of hospitalization, the types of investigational tests and procedures carried out would all further increase the

total annual cost per patient with AMI, depending on the complexity of the disease.

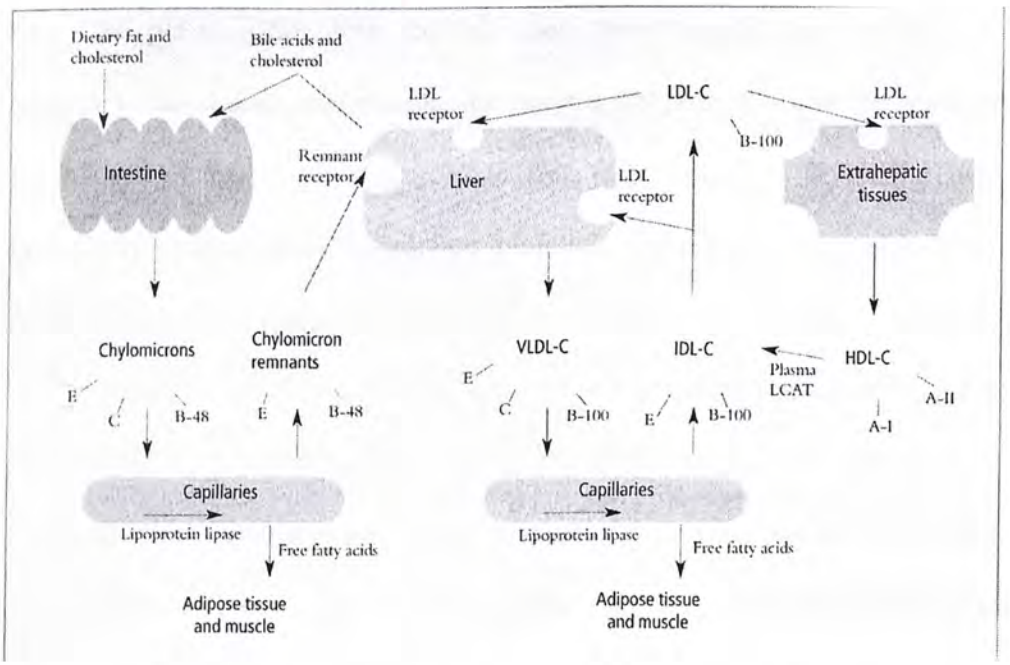
The prevalence of CHD and its mortality in Hong Kong are approaching a level that requires focused attention. Fu (2001) described that the prevalence of CHD in Hong Kong increased from 38.6% in the year 1972 to 59.4% in the year 1992. Despite the wealth of clinical trial evidence and national guidelines recommendations which support aggressive management of the disease, CHD continues to be a major killer in Hong Kong. The primary and secondary prevention of CHD has therefore become the emphasis of healthcare teams dealing with cardiovascular medicine. One strategy to help prevent CHD is to improve the management of dyslipidaemia which, as discussed in Section 1.2.2, is one of the significant risk factors for CHD development.

1.3 Dyslipidaemia

1.3.1 Lipid Transport and Lipoprotein Metabolism

A summary of normal lipid transport and plasma lipoprotein metabolism is shown in Figure 1.1 (Gross and Reese 2005, Walker 1999).

Figure 1.1. Lipoprotein transport and metabolism in the plasma



Very low-density lipoprotein cholesterol (VLDL-C), Intermediate-density lipoprotein cholesterol (IDL-C), Low-density lipoprotein cholesterol (LDL-C), High-density lipoprotein cholesterol (HDL-C), A-I, A-II, B-48, B-100, C and E are apoproteins.
Source: Gross and Reese (2005), Walker (1999)

The major lipids in plasma include cholesterol, triglycerides (TG) and phospholipids. These are transported in the plasma in the form of lipoproteins. There are six main classes of lipoproteins – chylomicrons, chylomicron remnants, very low-density lipoprotein cholesterol (VLDL-C), intermediate-density lipoprotein cholesterol (IDL-C), low-density lipoprotein cholesterol

(LDL-C) and high-density lipoprotein cholesterol (HDL-C). The lipoproteins have a protein component known as apoproteins which are associated with the transport of lipids (Walker 1999).

Dietary cholesterol and TG are absorbed from the intestine and transported in intestinal lymph vessels in the form of chylomicrons which enter the plasma. As these chylomicrons pass through the capillaries of adipose tissue and skeletal muscle, the enzyme lipoprotein lipase catalyses the breakdown of TG in chylomicrons to free fatty acids and glycerol. These breakdown products then diffuse into the fat cells of adipose tissue and muscle cells. The chylomicron remnants are taken up by the liver. Very low-density lipoprotein cholesterol is formed in the liver and contains TG, cholesterol and phospholipids. Intermediate-density lipoprotein cholesterol is formed from VLDL-C by the removal of a large amount of TG, resulting in an increase concentration of both cholesterol and phospholipids. Low-density lipoprotein cholesterol is made from IDL-C by removing all TG. High-density lipoprotein cholesterol is formed in the liver and synthesized in the intestinal epithelium. This contains a high concentration of protein but smaller concentrations of cholesterol and phospholipids (Gross and Reese 2005, Walker 1999).

1.3.2 Definition and Classification of Dyslipidaemia

Dyslipidaemia is a disruption in the amount of lipids in the blood (Walker 1999). Most dyslipidaemias are hyperlipidaemia and this can be interpreted as raised blood cholesterol '*hypercholesterolaemia*', raised blood triglycerides '*hypertriglyceridaemia*', or both '*mixed hyperlipidaemia*' (Williams *et al* 2003b). Hyperlipidaemia can also be classified according to the Frederickson/World Health Organization classification which groups '*hyperlipoproteinaemias*' into six types: I, IIa, IIb, III, IV and V [Table 1.3] (Gross and Reese 2005).

Table 1.3. Frederickson/WHO classification of hyperlipidaemias with examples of primary and secondary causes

Type	Lipoprotein Raised	Primary Causes	Secondary Causes
I	Chylomicrons	Lipoprotein lipase deficiency, apoprotein C-II deficiency	Systemic lupus (rare)
IIa	LDL-C	Familial hypercholesterolaemia	Hypothyroidism, nephrotic syndrome
IIb	LDL-C and VLDL-C	Familial combined hyperlipidaemia	Nephrotic syndrome, diabetes, anorexia nervosa
III	Chylomicrons remnants and IDL-C	Familial type III hyperlipidaemia	Nephrotic syndrome, diabetes, obesity
IV	VLDL-C	Familial combined hyperlipidaemia, familial hypertriglyceridaemia	Diabetes, chronic renal disease
V	Chylomicrons and VLDL-C	Familial combined hyperlipidaemia, apoprotein C-II deficiency	Alcohol, beta-blockers, diuretics

Low-density lipoprotein cholesterol (LDL-C), Very low-density lipoprotein cholesterol (VLDL-C), Intermediate-density lipoprotein cholesterol (IDL-C)
Source: Gross and Reese (2005)

Furthermore, hyperlipidaemia can also be described as primary as a result of a genetic defect, or secondary as a result of a disease or drug therapy. One form of primary hyperlipidaemia is known as heterozygous or homozygous familial hypercholesterolaemia (Walker 1999). In the heterozygous group, patients have a deficiency of LDL receptors that play a major role in the catabolism of LDL, whereas the homozygous group is associated with an absence of LDL receptors and is extremely rare. Patients with both types of familial hypercholesterolaemia are at a high risk of developing CHD.

1.3.3 Coronary Heart Disease and Dyslipidaemia

Cholesterol levels in many Asian countries are rising. Zhang *et al* (2003) showed that there is a strong association between cholesterol levels and the risk of CHD among populations from the Asia Pacific region which includes Hong Kong.

Cholesterol, especially LDL-C, plays an important role in the development of atherosclerotic plaques within the coronary arteries. Atherogenesis progresses as LDL-C accumulates in the inner wall of the arteries. This attracts monocytes and T-cells to the affected area where the monocytes ingest LDL-C and become foam cells. These foam cells cluster together and form fatty streaks. Smooth muscle cells migrate to the affected

wall of the coronary arteries and synthesize proteins which become fibrous plaques. With time, these plaque caps increase in volume and restrict blood flow through the affected arteries, causing CHD (Davies *et al* 1991, Ross and Agius 1992).

The relationship of plasma cholesterol to CHD has been established in the Framingham study and dyslipidaemia is now considered to be a major modifiable risk factor for developing CHD (Colquhoun 2000). Improving lipid status has been clearly demonstrated to reduce the morbidity and mortality associated with lipid disorders (Lipsy 2003). Large scale intervention studies have shown that reducing LDL-C levels can significantly reduce the risk of cardiovascular mortality, adverse cardiovascular events, and the requirement for revascularization procedures (Jacobson 2001).

Brewer (2004) stated that a 1 mg/dL (approximately 0.026 mmol/L) decrease in LDL-C reduces CHD risk by 1%. Similarly, a sustained reduction in total cholesterol of 1% (approximately 0.06 mmol/L) is also associated with a 2 to 3% reduction in the risk of CHD [Table 1.4] (Holme 1993).

High-density lipoprotein cholesterol is a powerful and independent predictor of CHD. High-density lipoprotein cholesterol is often considered to be the 'good' anti-atherogenic lipoprotein (Brewer 2004). High-density lipoprotein cholesterol transports cholesterol from the peripheral tissues to the

liver and plays a major role in maintaining cholesterol homeostatsis in the body (Walker 1999). A low level of HDL-C has been shown to be associated with a higher risk of CHD (Assmann *et al* 1996). The American Heart Association (AHA) supports the view that increasing HDL-C levels can have a more powerful effect on cardiovascular event reduction than LDL-C lowering (Alsheikh-Ali *et al* 2004). Based on epidemiological studies and recent clinical trial data, a 1 mg/dL (approximately 0.026 mmol/L) increase in HDL-C reduces CHD risk by approximately 3% [Table 1.4] (Brewer 2004).

Table 1.4. Risk reduction of coronary heart disease with lipid level changes

Type of Lipid	Lipid Level Changes	Risk Reduction of Coronary Heart Disease
Low-density lipoprotein cholesterol	↓ 0.026 mmol/L	↓ 1 %
Total cholesterol	↓ 0.06 mmol/L	↓ 2 to 3 %
High-density lipoprotein cholesterol	↑ 0.026 mmol/L	↓ 3 %

Source: Holme (1993), Brewer (2004)

1.3.4 Lifestyle Modifications for the Management of Dyslipidaemia

Effective screening, treatment, and follow-up of patients with elevated serum lipid levels are important because of the strong correlation between dyslipidaemia and CHD (Fox and Jones 2001). Therapeutic lifestyle change is an integral part of CHD risk reduction for any patients with lifestyle-related risk factors, and is recommended by the NCEP ATP III guidelines (2001).

Changes in lifestyle for the management of dyslipidaemia include dietary modifications, undertaking more physical exercise, reducing body weight and smoking cessation. A combination of complete smoking cessation, having a body mass index (BMI) of no more than 22 and a mean cholesterol level of 2.3 mmol/L has been estimated to halve the 12-year risk of CHD in both men and women (WHO 2002). Weight loss, smoking cessation, and a dietary reduction of saturated fat have been associated with an increase in HDL-C levels (Williams and Stevens 2003b).

1.3.4.1 Dietary Measures

Diet should be considered as an essential part of the management of dyslipidaemia. Patients should increase their fruit and vegetable intake and reduce their saturated fat intake (Williams and Stevens 2003b). The AHA and the NCEP developed the Step I and Step II diets to reduce the risk of CVD by reducing high blood cholesterol levels.

The AHA Step I diet restricted total fat to no more than 30% of total calories, saturated fat to no more than 10% of total calories, and cholesterol to less than 300mg per day. It was intended as the starting point for patients who had high cholesterol levels (AHA 2000). The AHA Step II diet restricted saturated fat to less than 7% and cholesterol to less than 200mg per day. This was intended for individuals who were already at the Step I goals or for

patients with a high-risk cholesterol level (240 mg/dL) or who had had a heart attack (AHA 2000). An overview of both the Step I and Step II diets are shown in Table 1.5.

Table 1.5. American Heart Association Step I & Step II Diets

	Recommended Intake as Percent of Total Calories	
Nutrient*	**Step I Diet**	**Step II Diet**
Total Fat	30% or less	30% or less
Saturated	7 – 10%	Less than 7%
Polysaturated	Up to 10%	Up to 10%
Monosaturated	Up to 15%	Up to 15%
Carbohydrate	55% or more	55% or more
Protein	Approximately 15%	Approximately 15%
Cholesterol	Less than 300mg per day	Less than 200mg per day
Total Calories	To achieve and maintain desired weight	To achieve and maintain desired weight

**Calories from alcohol not included*

Source: American Heart Association (2000)

Tang *et al* (1998) showed that individualizing dietary advice for reducing cholesterol concentration is modestly effective. A reduction in blood cholesterol concentration of no more than 3% was achieved in patients prescribed dietary advice equivalent to the AHA Step I diet. The more intensive diets, equivalent to the AHA Step II diet, achieved a reduction of approximately 6% in total cholesterol.

With the release of the latest NCEP ATP III guidelines (2001) for the management of cholesterol, the AHA has revised their dietary guidelines accordingly. The new guidelines (AHA 2006) are built upon the Step I diet, with an emphasis on a diet low in saturated fat and trans-fat, and rich in fruits, vegetables, whole grains, fat-free and low-fat diary products, and lean meat, fish and poultry.

The NCEP ATP III (2001) continues to recommend the Step I diet for the general public. For people at higher risk, they should adopt the Therapeutic Lifestyle Changes (TLC) diet [Table 1.6]. These high-risk individuals include those with high LDL-C levels or other lipid disorders, patients with CHD or other CVD, and patients with diabetes mellitus, insulin resistance or metabolic syndrome.

Table 1.6. Therapeutic Lifestyle Changes (TLC) Diet

Component	Recommendation
LDL-raising nutrients	
*Saturated fats**	Less than 7% or total calories
Dietary Cholesterol	Less than 200mg per day
Therapeutic options for LDL-lowering	
Plant stenols or sterols	2 grams per day
Increased viscous soluble fiber	10 – 25 grams per day
Total calories (energy)	Adjust total calories intake to maintain desirable body weight or to prevent weight gain
Physical activity	Include enough moderate exercise to expend at least kcal per day

**Trans fatty acids also raise LDL and should be kept at a low intake*

Source: American Heart Association (2006)

In patients taking lipid-lowering medications, dietary modifications also helps to achieve additional lipid-lowering effect which enhances the therapeutic effects of drug therapy (Denke 2002).

1.3.4.2 Cigarette Smoking

Smoking is associated with increased levels of plasma cholesterol concentration along with decreased levels of HDL-C, increased platelet aggregation and fibrinogen levels, inappropriate stimulation of the sympathetic nervous system, endothelial dysfunction, and altered oestrogen metabolism, all of which contribute to atherosclerotic plaque formation (Ohlsen and Rogers 2004, Williams *et al* 2003a).

There is a strong correlation between cigarette smoking and the risk of MI. The risk is two to four times greater in heavy smokers who smoke at least 20 cigarettes a day, than non-smokers (Williams *et al* 2003a). In men aged 18 to 60 years, the mean total cholesterol level increased by 0.0085 mmol/L for each cigarette smoked. In women aged 31 to 50 years, the mean total cholesterol level increased by 0.0124 mmol/L for each cigarette smoked per day (Muscat *et al* 1991). Patients who are smokers should be encouraged to be on smoking cessation programs.

1.3.4.3 Physical Activity

The World Health Report (WHO 2003b) described that more than 60% of adults worldwide do not engage in sufficient levels of physical activity that are beneficial to their health. The report also specified that physical inactivity is more prevalent among women, the elderly, individuals from low socio-economic groups, and the disabled. Sallis *et al* (1992) listed 10 of the most common reasons for adults not adopting physically active lifestyles [Table 1.7].

Table 1.7. Most common reasons for adults not being physically inactive

	Reasons for being physically inactive
1.	Do not have enough time to exercise
2.	Find it inconvenient to exercise
3.	Lack of self-motivation
4.	Do not find exercise enjoyable
5.	Find exercise boring
6.	Lack of confidence in their ability to be physically active
7.	Fear being injured or have been injured recently
8.	Lack self-management skills, such as ability to set personal goals, monitor progress, or reward progress toward such goal.
9.	Lack encouragement, support, or companionship from family and friends
10.	Do not have parks, sidewalks, or safe and pleasant walking paths convenient to their homes or offices.

Source: Sallis and Hovell (1990), Sallis *et al* (1992)

Patients should be encouraged to take up regular physical activity since being physically active protects against CVD. Wannamethee *et al* (1998) demonstrated that taking up light and moderate amounts of physical activity in patients with a history of CVD was associated with a significant reduction in risk of all-cause mortality. Regular exercise of at least three 20 minutes sessions each week helps to reduce TG and LDL-C levels and raise HDL-C

(Ohlsen *et al* 2004). The longer one exercises, the greater the benefits. Kodama *et al* (2007) demonstrated that two hours of exercise a week raised serum levels of HDL-C, thus protecting the heart. The authors found that a 10-minute prolongation of exercise per session was associated with an approximately 1.4 mg/dL (0.036 mmol/L) increase in HDL-C level. Exercise can be moderate activity such as brisk walking, vacuuming, gardening, or any other activity that causes small increases in breathing or heart rate. More vigorous activity can be in the form of running, cycling, swimming, aerobics and other activities that causes large increases in breathing and heart rate (Morrato *et al* 2003).

1.3.4.4 Weight Control

Apart from maintaining a healthy lifestyle through regular exercise, increased physical activity can also shed excess weight in obese patients. It is estimated that 400 million adults worldwide are obese and 1.6 billion people are overweight (WHO 2006). The prevalence of overweight and obesity is commonly assessed by using body mass index (BMI). Body mass index is defined as the weight in kilograms divided by the square of the height in metres (kg/m^2). According to the WHO, a BMI over 25 kg/m^2 is defined as overweight, and a BMI of over 30 kg/m^2 as obese.

Report from the WHO (2006) showed that the intake of foods high in fats and sweeteners is increasing throughout the developing world and the average daily calorie consumption has increased globally. Diets have moved from being plant-based to high-fat, energy-dense animal-based diets. Lobstein *et al* (2004) described that obesity is also becoming a problem in children and young people in industrialized nations. The researchers stated that around 155 million children worldwide are overweight, with 30 to 45 million children being obese. Among these figures, approximately 22 million children under five are estimated to be overweight worldwide. This increase incidence of child obesity is of special concern and is already epidemic in some countries, for instance, in the United States, where the number of overweight children has doubled and the number of overweight adolescents has trebled since the year 1980 (WHO 2006).

The Framingham Heart Study (1991) has consistently shown that increasing degrees of obesity are accompanied by higher rates of CHD. Wood *et al* (1998) described that being overweight is associated with raised blood pressure, raised blood cholesterol, glucose intolerance, non-insulin dependent diabetes and low levels of physical activity. Hypertension and diabetes mellitus are both significant risk factors for CVD.

Anderson (2003) recommended that obese patients should reduce their weight to a BMI of 25 kg/m^2 or less, unless contraindicated. Recent studies

have suggested that different ethnic groups vary in body fat percentage and BMI, which therefore affects the recommended validity of the BMI cut-off point for obesity (Deurenberg-Yap *et al* 2000). The WHO Expert Consultation (2004) reviewed that Asian populations have different associations between BMI, percentage of body fat, and health risks when compared to the Western populations. The consultation concluded that the proportion of Asians with a high risk of CVD is substantial at BMIs lower than the existing global cut-off point for overweight (BMI > or = 25 kg/m^2) set by the WHO. The cut-off point for observed risk varied from 22 kg/m^2 to 25 kg/m^2 in different Asian populations.

Though Hong Kong has a lower prevalence rate of overweight and obesity than those seen in other countries, the prevalence of overweight in Hong Kong has increased from 25% to 40% in the period 1989 to 1998, and the obesity prevalence has increased from 3.5% to 9% (Woo and Sung 2001). The researchers have also shown that these figures are increasing every year, prompting clinicians that overweight and obesity needs more attention. This problem is not only found in adults but also in children. From 1993 to 2004, childhood obesity has increased from 8.9% to 14.2% for girls, and 11.3% to 20.6% in boys (Wen and Hui 2007).

He *et al* (2001) showed that Hong Kong Chinese have a higher body fat percentage for a given BMI than the Caucasian population which

explained why health risks associated with obesity occurred at a lower BMI in Hong Kong Chinese. A study on obesity and cardiovascular risk factors in Hong Kong Chinese also supported using lower BMI in this population to define obesity and its associated health risks rather than using the criteria established from Caucasians who generally have larger body frames (Lee *et al* 2002). The researchers propose that body fat and fat distribution at a BMI of 23 kg/m^2 in Asians can be considered to be similar to those in Caucasians at a BMI of 25 kg/m^2 (Gallagher 2004). Based on these data, obese Hong Kong Chinese patients should therefore reduce their weight to a BMI of 23 kg/m^2 or less, unless contraindicated.

The risk of death due to CHD and other CVDs in men (Shaper *et al* 1997) and women (Manson *et al* 1995) increases progressively with a rise in BMI from around 20 kg/m^2. Reduction of weight is therefore important in obese patients with CHD. A reduction in BMI helps raise HDL-C and lower LDL-C and TG levels. Lemanski (2005) described that a weight reduction of approximately 9.1kg may decrease LDL-C level by 0.26 mmol/L and increase HDL-C level up to 0.16 mmol/L. The lipid-lowering effect achieved by dietary modifications alone can also be doubled by a 2.3kg loss in body weight (Denke 2002).

1.3.5 Lipid-lowering Drug Therapy for Dyslipidaemia

While non-drug management such as diet alone can be effective in reducing cardiovascular risk, in most individuals at risk, pharmacological measures are also required to achieve the target lipid profiles. Lipid-lowering drug therapy is indicated for reducing cardiovascular risk in both primary and secondary prevention of CHD. Patients with a history of occlusive CVD or at increased risk due to comorbidities like diabetes or other combinations of risk factors is now considered to be a candidate for lipid-lowering therapy (Armitage 2004). Patients with genetic disorders resulting in higher plasma cholesterol levels also require more aggressive treatment using lipid-lowering medications.

A number of different classes of lipid-lowering agents are available worldwide – bile acid sequestrants, ezetimibe, fibrates, statins and nicotinic acid group [Table 1.8]. Each type of agent lowers lipid levels by a different mechanism. As a result, the different types of drugs have different side effects and may affect lipid levels differently [Table 1.9].

Table 1.8. Classes of lipid-lowering agents

Class of Lipid-lowering Agent	Drugs Available	Mechanism of Action
Bile acid sequestrants	Colestipol Cholestyramine Colesvelam	Binds bile acids in the intestine, causing the acids to be excreted rather than used to make bile and causing the liver to remove more LDL-C from the bloodstream to make bile.
Fibrate	Bezafibrate Cirofibrate Fenofibrate Gemfibrozil	Increases the breakdown of lipids and speeds the removal of VLDL from the bloodstream and may decrease VLDL production by the liver.
Ezetimibe	Ezetimibe	Inhibits the intestinal absorption of cholesterol.
Nicotinic acid group	Acipimox Nicotinic acid	Decrease the production rate of VLDL which is used to synthesize LDL.
Statins	Atorvastatin Fluvastatin Lovastatin Pravastatin Rosuvastatin Simvastatin	Blocks the synthesis of cholesterol by inhibiting HMG-CoA reductase and increases the removal of LDL from the bloodstream.

Source: Levy (1999)

Table 1.9. Effect of drug therapy on cholesterol subtypes

Cholesterol Subtype	Approximate effect of drug therapy				
	Statin	**Bile Acid Sequestrants**	**Fibrate**	**Ezetimibe**	**Nicotinic Acid**
Total cholesterol	↓15 – 40 %			↓15 %	
Low-density lipoprotein	↓20 – 60 %	↓15 – 30 %	↓10 – 15 %	↓18%	↓20 – 30 %
High-density lipoprotein	↑5 – 15 %	↑5 %	↑5 – 20 %		↑15 – 35 %
Triglyceride	↓10 – 40 %		↓20 – 50 %		↓20 – 50 %

Source: Armitage and Bowman (2006), Williams (2005)

Overall, statin therapy remains the mainstay of lipid-lowering drug therapy for most dyslipidaemic patients. In some cases, a combination of two or more agents may be required in order to reach the recommended lipid management goals in more aggressive treatment.

1.3.5.1 Statins

Statins have been widely prescribed for the treatment of dyslipidaemia over the past decade. These agents partially block the conversion of 3-hydroxy-3-methylglutaryl coenzyme A (HMG CoA) to mevalonic acid. This is an important regulatory step occurring in the process of cholesterol biosynthesis within the liver. As a result, cholesterol levels fall on initiation and remain suppressed as long as the patient continues to take the medicine (Armitage 2004).

Statins reduce LDL-C as well as TG and total serum cholesterol levels. LDL-C is reduced by 25 to 60% and TG is reduced by 5 to 30%. In addition, statins increase levels of HDL-C by 3 to 15% and this has cardiovascular protective effects (Williams 2005). Grundy et al (2004) described that the current available statins at doses used in landmark trials can lower LDL-C levels by 30% to 40% from baseline, which translates into a similar percentage reduction in CHD risk over a 5-year period [Table 1.10].

Table 1.10. Doses of currently available statins required to attain a 30% to 40% reduction in LDL-C levels

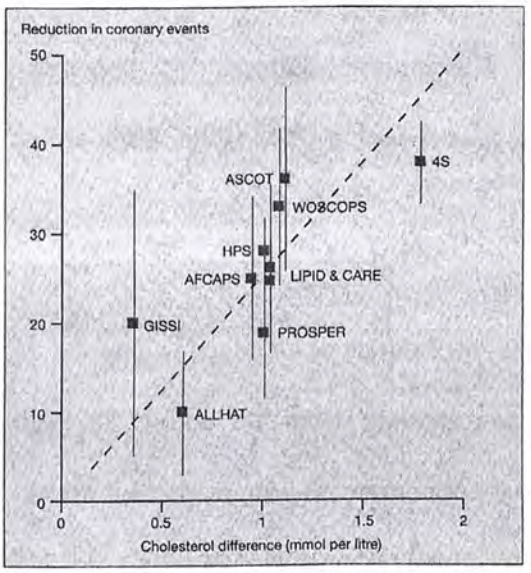
Drug	Dose (mg/dose)	LDL-C Reduction %
Atorvastatin	10*	39
Fluvastatin	40 – 80	25 – 35
Lovastatin	40*	31
Pravastatin	40*	34
Rosuvastatin	5 – 10	39 – 45
Simvastatin	20 – 40*	35 - 41

* For every doubling of the stated dose, an approximate 6% decrease in LDL-C level can be obtained

Source: Grundy et al (2004)

Clinical trials of statins show reductions in coronary and cardiovascular events that are roughly proportional to the average cholesterol difference achieved during the trial, consistent with a log-linear relationship between cholesterol level and risk [Figure 1.2] (Armitage and Bowman 2006).

Figure 1.2. Results of statin clinical trial demonstrate a direct relationship between cholesterol reduction and reduced risk of coronary events



Air Force/Texas Coronary Atherosclerosis Prevention Study (AFCAPS), Antihypertensive and Lipid-lowering to Prevent Heart Attack Trial (ALLHAT), Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT), Cholesterol and Recurrent Events Study (CARE), Italian Group for the Study of Streptokinase in Myocardial Infarction (GISSI), Heart Protection Study (HPS), Long-term Intervention with Pravastatin in Ischaemic Disease Trial (LIPID), Prospective Study of Pravastatin in the Elderly at Risk (PROSPER), Scandinavian Simvastatin Survival Study (4S), West of Scotland Coronary Prevention Study (WOSCOPS)
Source: Armitage and Bowman (2006)

A meta-analysis of the primary and secondary prevention studies of statins concluded that statins reduce the risk of CHD mortality by 25%. In addition, statins have been shown to reduce the risk of MI, stroke, unstable ischaemic episodes and the need for revascularization procedures. More intensive cholesterol lowering with these agents will produce greater benefits, reducing the risk of further CVD in high risk group patients (Ross *et al* 1999). In the Measuring Effects on Intima-Media Thickness: an Evaluation of Rosuvastatin (METEOR) trial, the investigators showed that rosuvastatin reduced LDL-C levels by 48.8% and increased HDL-C levels by 8.0%

compared with baseline concentrations (Crouse *et al* 2007). The METEOR trial also showed that rosuvastatin significantly slowed the progression of atherosclerosis as assessed by carotid intima-media thickness (CIMT) measurements in middle-aged adults with a low Framingham risk score of below 10%.

With the large amount of trial data to support the use of statins, statins have become the drug of choice for most patients requiring cholesterol-lowering treatment. Statin therapy is now recommended for both primary and secondary prevention of CHD. Secondary prevention for patients with established CHD, including those with post-MI, following coronary artery bypass grafting (CABG) or post-percutaneous coronary intervention or with other manifestations of stable or unstable coronary artery disease such as angina. Primary prevention targets patients with a 30% or greater risk of a cardiovascular event over the next 10 years (Williams and Stevens 2003b).

Statins generally appear safe and well tolerated at the standard doses. Common side effects include nausea, diarrhoea, constipation, insomnia and rash. The most concerned adverse effect of statins is myopathy but this is rare. Myopathy or myositis is defined as muscle pain or weakness with a raised creatine kinase (CK) of more than 10 times the upper limit of normal (ULN). It can lead to rhabdomyolysis when the CK level is greater than 10,000IU per litre and this is a life-threatening condition. However, this is rare and the incidence is less than 0.1% (Armitage 2004, Williams and Stevens 2003b).

Patients on statins should be advised to report promptly any unexplained muscle pain, tenderness and weakness. They should also be advised to take stains after 6pm to achieve peak serum drug levels during the night, when maximal cholesterol synthesis occurs (Kreisberg and Oberman 2003).

1.3.5.2 Bile Acid Sequestrants

Bile acid sequestrants are also known as resins. They act by binding bile acids in the small intestine and reducing the enterohepatic circulation of cholesterol. These agents have been used to lower cholesterol levels for at least 30 years (Armitage and Bowman 2006).

Bile acid sequestrants primarily reduce LDL-C levels by 15 to 30% and an increase HDL-C levels by up to 5% (Williams 2005). However, these drugs have a tendency to increase TG levels and must therefore be avoided in patients with hypertriglyceridaemia or mixed hyperlipidaemia with significantly raised TG levels.

The Lipid Research Clinics Coronary Primary Prevention Study (1984) demonstrated that bile acid sequestrants can reduce cardiac events and atherosclerotic progression. They are useful in treating patients with isolated raised LDL-C levels or as an add-on to other drug classes which have failed to achieve therapeutic targets when given alone. However, bile acid sequestrants

are poorly tolerated and can cause constipation, heartburn and flatulence which limit their use.

1.3.5.3 Fibrates

Fibrates were widely prescribed in the 1980s and 90s but their use have gradually fallen as evidence to support the role of statins have grown. Clofibrate, the parent compound and the first fibrate to be prescribed, has now been replaced by the newer analogues. Of these newer drugs, gemfibrozil has been shown to have clear benefit on cardiovascular events in The Veteran Affairs High-Density Lipoprotein Intervention Trial (Rubins 1999).

Fibrates primarily act against triglyceride-rich VLDLs through activation of lipoprotein lipase. The primary effect of fibrates is a reduction in TG levels by 20 to 50% and an increase in HDL levels by 10 to 15% has been shown (Williams 2003b). The effect on LDL-C is less predictable where levels may increase or decrease.

Fibrates are indicated for the treatment of isolated hypertriglycerideaemia or for the treatment of mixed hyperlipidaemia in combination with a statin. Fibrates in general are well tolerated though some patients may experience diarrhoea, nausea and bloating. More serious adverse effects include myopathy and hepatitis but these are rare with monotherapy.

When fibrates and statins are used together, the risk of liver and muscle toxicity is increased and so more frequent close monitoring is needed. The combined use of the two drugs is usually confined to selected patients managed in specialist lipid clinics.

1.3.5.4 Ezetimibe

Ezetimibe represents a new class of drug and is a potent and specific inhibitor of dietary and biliary cholesterol absorption. When administered alone, ezetimibe can reduce total cholesterol by about 15% and LDL-C levels by up to 18%, with little impact on TG and HDL-C. When combined with statin therapy, it can produce an additional 20% reduction in LDL-C levels over and above that of statin monotherapy, with a reduction in TG levels of about 9% and a small increase in HDL-C of about 3% (Williams 2005).

Ezetimibe is useful in those patients who require further LDL-lowering than a statin can produce, and in those who are intolerant of statins. The administration of ezetimibe and fibrates together is not recommended since the safety of this combination therapy has not been well established. Side effects with ezetimibe are rare though diarrhoea, abdominal pain and headache have been reported.

1.3.5.5 Nicotinic Acid Group

Nicotinic acid has been used since the 1970s where the Coronary Drug Project (1975) showed a reduction in recurrent MI in patients treated with the drug. The exact mechanism of nicotinic acid is not fully understood. However, it is believed that nicotinic acid inhibits the release of free fatty acids from the adipose tissue. This therefore reduces the amount available to the liver for the production of plasma TG, VLDL and LDL-C. As a result, nicotinic acid lowers both TG and LDL-C levels and increases the level of HDL-C (Armitage and Bowman 2006).

Despite its effectiveness, the use of nicotinic acid has been limited by its poor side effect profile which includes prostaglandin-mediated flushing of the face and neck, dizziness and palpitations.

A long-acting formulation of nicotinic acid has been recently available and its side effects are better tolerated. With maximal dosing, nicotinic acid can reduce LDL-C levels by 20% and TG levels by 50%. High density lipoprotein cholesterol levels can also be increased by 35% (Williams 2005).

Nicotinic acid is useful for patients with mixed hyperlipidaemia, raised LDL-C levels, raised TG levels, and low HDL-C levels.

1.4 International Guidelines for Dyslipidaemic Management

1.4.1 National Service Framework for Coronary Heart Disease (UK)

The Department of Health (DoH) of the United Kingdom (UK) developed the National Service Framework (NSF) for Coronary Heart Disease in March 2000 to address the burden of heart disease to the country. Coronary heart disease is the leading cause of death in England, killing over 111,000 people in 1998, including more than 41,000 under the age of 75 years (DoH 2000). As a result, the prevention of CHD has become a top government priority. The DoH of the UK has set a target of reducing the death rate from heart disease, stroke and related conditions by 40% in those aged under 75 years by the year 2010 (DoH 2000).

The NSF guidelines for the prevention of coronary heart disease cover strategy development and interventions to promote CHD-related healthier lifestyles (DoH 2000). These include smoking, nutrition, physical activity and weight management. The secondary prevention of CHD is also a fundamental part of the published NSF and specific targets for both total cholesterol and LDL-C levels for patients with or without diagnosed CHD have been issued.

The government also recognized the value of an integrated multi-disciplinary approach when managing CHD. Its NSF guidelines have emphasized the importance of effective communication and collaboration between the different health care organization and staff.

1.4.1.1 National Service Framework Lipid-lowering Goals

The National Service Framework for CHD have laid out the lipid goals that patients should achieve based on the large body of evidence that has demonstrated that cholesterol reduction reduces the risk of CVD. The Heart Protection Study (2002), PROVE-IT study (Cannon *et al* 2004), and the ASCOT-LLA trial (Sever *et al* 2003) have all shown that intensive lowering of LDL-C and total cholesterol concentrations proved beneficial in reducing the risk of CHD.

The authors of the National Service Framework for CHD recommend the following lipid goal guidance (DoH 2000):

- Patients with diagnosed CHD or other occlusive arterial disease. Statins and dietary advice to lower serum cholesterol concentrations either to less than 5 mmol/L or by 25%, and LDL-C to below 3 mmol/L or by 30% (whichever is greater);

- Patients without diagnosed CHD or other occlusive arterial disease with a CHD event risk greater than 30% over ten years. Add statins to lower serum cholesterol concentrations either to less than 5 mmol/L or by 25%, and LDL-C to below 3 mmol/L or by 30% (whichever is greater).

1.4.1.2 The Joint British Societies' Guidelines

The HEART UK (2006) suggested that the National Service Framework for CHD should review these lipid-lowering targets and commented that these recommendations should be superseded by the recent Joint British Societies' (JBS) guidelines.

The latest JBS2 guidelines (2005) consider the risk of developing atherosclerotic cardiovascular disease rather than coronary heart disease alone. This includes acute coronary syndromes, stable angina, cerebrovascular disease and any other arterial atherosclerosis. The aim of the new guidelines is to promote a consistent, multidisciplinary approach to risk factor management in patients with, and those at high risk of developing CVD, by managing overall risk, rather than single risk factors.

The new JBS2 guidelines have placed more stringent lipid goal targets for both total cholesterol and LDL-C as follows:

- Total cholesterol to less than 4 mmol/L or a 25% reduction whichever is lower;

- LDL cholesterol to less than 2 mmol/L or a 30% reduction whichever is lower.

The National Institute for Health and Clinical Excellence (NICE) is developing a set of guidelines on lipid management for the primary and secondary prevention of cardiovascular disease and the report is expected to be out by January 2008. These new recommendations by the JBS2 will be considered in the new guideline, especially for patients who are at high risk of developing CVD. In the meantime, the current NSF targets remain to be the national policy in the UK until the new recommendations by NICE are published.

1.4.1.3 Achievement of the NSF Lipid Profile Targets

Hobbs and Southworth (2005) showed that despite the detailed guidelines provided by the NSF for CHD, patients still fail to meet their recommended lipid-lowering goals. From a small study conducted by Evans and his colleagues (2004), they showed that the majority of general practices in England found implementing the NSF recommendations into operation difficult. The authors described that potential contributing factors to treatment failure included physician reluctance to initiate treatment or to up-titrate drugs, and patient reluctance to maintain therapy.

1.4.2 National Cholesterol Education Program (United States)

1.4.2.1 The Third Report of the National Cholesterol Education Program

In the United States, the NCEP ATP II and III has issued robust guidelines on the treatment of lipid disorders based on the remarkable clinical outcomes from a series of large randomized controlled trials (RCTs) of statin therapy conducted in the past few years (Grundy *et al* 2004). Five major clinical trials of statin therapy for cholesterol management with clinical endpoints have confirmed the benefits of LDL-C reduction in reducing cholesterol events in broad populations including the elderly. The trials are the Heart Protection Study (HPS), the Prospective Study of Pravastatin in the Elderly at Risk (PROSPER), the Antihypertensive and Lipid-lowering to Prevent Heart Attack Trial – Lipid-Lowering Trial (ALLHAT-LLT), the Anglo-Scandinavian Cardiac Outcomes Trial – Lipid-Lowering Arm (ASCOT-LLA), and the Pravastatin or Atorvastatin Evaluation and Infection – Thrombolysis in Myocardial Infarction 22 (PROVE IT-TIMI 22) trial.

1.4.2.2 Review of Clinical Trials

The HPS (2002) randomized more than 20,000 high risk patients with total cholesterol 135 mg/dL (approximately 3.51 mmol/L) or greater to receive simvastatin 40mg daily or placebo. The mean baseline LDL-C was 131 mg/dL (approximately 3.41 mmol/L) and the mean follow-up was 5 years. Simvastatin treatment significantly reduced clinical event rates at 5 years, including a 13% reduction in the primary endpoint of all-cause mortality and a

27% reduction in major coronary events which included nonfatal MI or coronary death. The HPS demonstrated the clinical benefit of lowering LDL-C levels with simvastatin therapy regardless of the baseline LDL-C. Cholesterol lowering with statin therapy was also efficacious in patients whose LDL-C levels were already at the goals recommended by the NCEP ATP III guidelines. In addition, the benefit was observed in older patients and in patients with diabetes.

The PROSPER trial (Shepherd *et al.* 2002) randomized 5804 high risk patients, aged between 70 and 82 years, to receive pravastatin 40mg daily or placebo. At a mean follow-up of 3 years, the composite primary endpoint of CHD death, nonfatal MI, and fatal or nonfatal stroke was significantly reduced by 15% with pravastatin. There was also a 25% reduction in transient ischaemic attacks.

The ALLHAT-LLT (2002) randomized more than 10,000 high risk patients aged 55 years or older to receive nonblinded treatment with pravastatin 40mg daily or usual care. The participants had LDL-C levels ranging from 120 to 189 mg/dL (approximately 3.12 to 4.91 mmol/L), or had LDL-C levels between 100 and 129 mg/dL (approximately 2.6 to 3.35 mmol/L) with known CHD. During the 5-year trial, a large proportion of patients randomized to usual care began statin therapy. The ALLHAT study was the first major statin trial not to show a benefit on clinical events with

statin therapy. CHD events were only significantly reduced in the African-American subgroup with pravastatin therapy. The investigators of the study speculated that the failure to detect a significant reduction in risk in hypertensive patients treated with pravastatin may be due to the small total cholesterol differential between the two treatment groups.

In the ASCOT-LLA study (Sever *et al* 2003), more than 10,000 hypertensive patients with total cholesterol of 250 mg/dL (approximately 6.5 mmol/L) or less were randomized to received atorvastatin 10mg daily or placebo. The lipid-lowering arm of the trial was stopped before the projected 5-year follow-up because of the clear clinical benefit with atorvastatin. A 36% reduction in primary endpoint of nonfatal MI or CHD death was observed. The authors of the study indicated that LDL lowering with atorvastatin therapy had considerable potential to reduce risk for CHD in primary prevention in patients with multiple CVD risk factors.

In the PROVE-IT trial (Cannon *et al* 2004), more than 4,000 patients with acute coronary syndrome and total cholesterol of 240 mg/dL (approximately 6.24 mmol/L) or less, and 200 mg/dL (approximately 5.2 mmol/L) in patients on lipid therapy, were randomized to receive intensive therapy with atorvastatin 80mg daily or moderate therapy with pravastatin 40mg daily. The primary endpoint of the trial was death, MI, unstable angina requiring hospitalization, revascularization after 30 days, and stroke. At the

end of the 2-year study, intensive therapy reduced LDL-C levels to 62 mg/dL (approximately 1.61 mmol/L) and reduced the composite primary endpoint by 16% compared with moderate therapy, which reduced LDL-C levels to 95 mg/dL (approximately 2.47 mmol/L).

1.4.2.3 Low-Density Lipoprotein Cholesterol Goal Targets

Coronary heart disease risk can be estimated using tools such as the Joint British Societies' cardiac risk assessor computer program or coronary risk prediction chart, the revised Sheffield table and the New Zealand guidelines. Calculating CHD risk with these tools takes into account the common associated CHD risk factors which have been described previously in Section 1.2.2. These include hypertension, smoking, TC:HDL-C ratio, diabetes, age and gender. All three risk assessment tools use the Framingham risk equation to determine the risk of a cardiac event. Similarly, the NCEP ATP III guidelines (2001) use the Framingham risk equation to assess the 10-year CHD risk. The guidelines also recommend that initial CHD risk assessment should be carried out with lipid screening every five years in patients over 20 years of age.

More than 99% of the subjects involved in the Framingham study were of European descent and a number of studies have suggested that the Framingham functions may not be appropriate for assessing the 10-year CHD

risk in other ethnic groups. Liu et al (2004) evaluated the performance of the Framingham CHD risk functions in Chinese subjects and their results demonstrated that the original Framingham functions overestimated the risk of CHD in the Chinese population. The investigators concluded that it is better to overestimate rather than underestimate the CHD risk and the Framingham model is still useful for assessing the risk of CHD in the Chinese population. Hence, the Framingham 10-year CHD risk assessment tool was used in our study.

The most recently revised NCEP ATP III guidelines (Grundy *et al* 2004) have placed a significant emphasis on more stringent LDL-C goal attainment in accordance to the calculated 10-year CHD risk of the individual. Based on the data from clinical trials of statin therapy, the authors of the NCEP ATP III report recommend the following:

- High risk patients have CHD or CHD risk equivalents or multiple risk factors that confer a 10-year risk for CHD of more than 20%. A LDL-C level of 2.6 mmol/L is the minimal goal of treatment for these patients, and a LDL-C goal of below 1.8 mmol/L is the optimal goal;

- Patients with a moderately high CHD risk are those with two or more major cardiac risk factors or a 10-year CHD risk of 10 to 20%. The

LDL-C goal remains below 3.4 mmol/L, but a goal of below 2.6 mmol/L should be considered a therapeutic option;

- Moderate risk patients have two or more cardiac risk factors and a 10-year CHD risk of less than 10%. A LDL-C goal of below 3.4 mmol/L is recommended;

- Low risk patients have zero to one cardiac risk factor and as their 10-year CHD risk is very low, a LDL-C goal of below 4.1 mmol/L is considered the target.

1.4.2.4 Compliance with the NCEP ATP III Guidelines

Despite all the evidence and guidelines available, patients still fail to meet the LDL-C targets. Published trials have shown that compliance with the NCEP guidelines for the secondary prevention of CHD and atherosclerotic disease has been poor (Siskind *et al* 2000). Multiple surveys assessing physician compliance with the ATP III guidelines have found only 11% to 25% patients with CHD were at the recommended LDL-C goal (Aliyu *et al* 2004). Olson *et al* (2005) has also stressed the existence of a significant gap between evidence-based treatment guidelines and routine clinical practice in the management of dyslipidaemia.

One of the reasons for the poor compliance with the current NCEP ATP III guidelines is the more stringent recommendations for optimal LDL-C levels. With the more aggressive treatment ATP III guidelines, the cholesterol treatment gap is likely to widen further. The recommended level of LDL-C for optimal CHD risk reduction has decreased markedly in the revised guidelines, particularly for high-risk patients, where the LDL-C level target has dropped from $\leq$2.6 mmol/L to $\leq$1.8 mmol/L (Grundy *et al* 2004). These changes in treatment guidelines have increased the risk of failure in achieving optimal ATP III LDL-C levels. Many cross-sectional studies have shown that only 40% of high-risk patients are achieving LDL-C levels of below 1.8 mmol/L (Leibovitz *et al* 2005).

Other factors responsible for patients not receiving adequate treatment include a lack of focus on asymptomatic diseases, time and reimbursement constraints, inadequate training, a reluctance to prescribe aggressive treatment regimens, and poor communication among healthcare professionals (Ito 2003).

Poor patient compliance with lipid-lowering medications is one of the most important factors affecting the implementation of the NCEP ATP III guidelines. The reasons for poor compliance vary but generally include a lack of patient's knowledge of their condition, the risk factors associated with dyslipidaemia, and the fear of the side effects associated with their drugs (Maenpaa *et al* 1991).

The cost of medications and the formulary choice of lipid-lowering therapy of the health management organization could be a barrier. Pearson *et al* (2000) described that this could be a possible explanation for the low LDL-C goal attainment, even when the physicians are aware of the NCEP ATP III treatment guidelines.

It is therefore important to develop programs that can enhance the implementation of the NCEP ATP III guidelines. Patients on lipid-lowering therapy need to remain compliant to their treatment and structured measures are built to ensure effective monitoring and follow-up of these patients in order to improve their LDL-C and other cholesterol levels. One study suggested that involving a clinical pharmacist in the treatment of patients in dyslipidaemia may represent one way to bridge the treatment gap, especially in patients who are at high risks for CHD (Cross & Franks 2005). Bozovich *et al* (2000) also demonstrated the potential benefits of a pharmacist-managed lipid clinic in achieving the NCEP goals and improving the drug adherence of patients with their lipid-lowering therapy.

1.4.3 Dyslipidaemic Guidelines for Study

The NCEP ATP III guidelines 2001 were adopted in this study based on the reference guidelines used at the outpatient lipid clinic of the Prince of Wales Hospital (PWH) where the study was conducted. In this study, a LDL-C goal attainment of 2.6 mmol/L will be the minimal goal in high-risk patients and a LDL-C goal attainment of 3.4 mmol/L in patients who are at moderate high CHD risk.

1.5 Clinical Pharmacy Services

1.5.1 The Healthcare System in Hong Kong

The Hong Kong healthcare system has undergone few functional changes since the 1960s. Unlike other countries such as the United Kingdom where an integrated healthcare system across all primary, secondary and tertiary levels is developed through its National Health Service (NHS) Plan, the healthcare system in Hong Kong remains public hospital-led and compartmentalized, with limited communication between the secondary and tertiary levels, and the primary and outpatient levels. With the rising expectations from the public regarding the quality of the healthcare system that they are receiving, Hong Kong needs to reform its healthcare setting to meet the demands of its community. A new healthcare system is also required to meet the growing ageing population, the improved socioeconomic status of the population and access to new expensive medical technologies (Yip and Hsiao 2004).

In November 1997, the Hong Kong government commissioned a team from Harvard to evaluate the performance and propose reforms to improve the healthcare system of Hong Kong. This Harvard Report, '*Improving Hong Kong's Health Care System: Why and For Whom?*' was released in April 1999 (Hsiao *et al* 1999).

The Harvard Report recommended the development of a community-based healthcare system that integrates prevention, outpatient, inpatient, community and other social services. In other words, this system will coordinate the public and private sectors together. The report also emphasized the importance of using a multidisciplinary team approach to help improve the healthcare system for patients. This team should involve all the major healthcare professions which include pharmacists who are considered to be one of the key players (Hsiao *et al* 1999).

Under the current healthcare system, the Harvard Report identified that patients often lack knowledge and information on the quality of the care that they receive. With the population living longer and suffering more from chronic diseases such as CVD, cancer and diabetes, pharmacists can play a key role in educating patients on how to manage their condition. New medications are emerging and pharmacists are considered to be experts on drugs. This provides opportunities for pharmacists who can help promote patient education on their medications and conduct regular assessment and monitoring to help prevent any adverse drug reactions and other drug-related problems. Pharmacists can also help to build the primary and secondary interface through close working collaboration between hospital pharmacists and community pharmacists as well as hospital doctors and general practitioners. The recommendations provided by the Harvard Report have

encouraged the development of clinical pharmacy services (CPS) in Hong Kong.

1.5.2 Clinical Pharmacy Services in Hong Kong

In the community, most family doctors train their clinic assistants to dispense medicines without the presence of a pharmacist. Community pharmacists in Hong Kong therefore mainly sell over-the-counter medications. Patients rarely visit a pharmacist to present a prescription for dispensing. This practice is common with several other countries in Asia like Singapore, Malaysia and Thailand, where the process of prescribing and dispensing of medicines has not been separated (Mason 2001).

In the hospitals, the major role of pharmacists is the supply of medicines from dispensaries. However, this is gradually changing. Clinical pharmacists are now taking on a more active role in the multidisciplinary team. Patients are also being educated to understand the potential value that pharmacists can provide through CPS.

As CPSs are developing in Hong Kong, opportunities are arising where pharmacist can be more involved in patient-focussed activities in a clinical setting. Such services can be used as a valuable resource and be integrated into disease management programs. Clinical pharmacists are

encouraged to enhance their pharmaceutical services. The aim is to optimize drug therapies by achieving the desired targets and outcomes. At the same time, pharmacists can help minimize any adverse drug reactions and drug interactions that may affect patient compliance. A number of studies have demonstrated the value of CPS where pharmacists play a key part of the multidisciplinary healthcare team.

1.5.3 Examples of successful Clinical Pharmacy Services

1.5.3.1 Hypertension Clinic

A pharmacist-managed hypertension clinic showed that pharmaceutical care improved blood pressure control and resulted in more patients with hypertension reaching their blood pressure goal when compared with traditional health care from a primary care physician in a prospective, controlled study (Vivian 2002).

In Borenstein *et al* (2003), it also showed that an evidence-based, systematic approach using physician-pharmacist comanagement for patients with uncontrolled hypertension resulted in improved blood pressure control and reduced average visit costs per patient.

1.5.3.2 Diabetes Mellitus Clinic

A randomized controlled trial (RCT) conducted by Choe *et al* (2005) evaluated the effect of case management by a clinical pharmacist on glycaemic control and preventative measures in patients with type II diabetes mellitus. A clinical pharmacist provided evaluation and modification of pharmacotherapy, self-management, diabetes education, and reinforcement of diabetes complications screen processes through clinical visits and telephone follow-ups. Patients in the intervention group who were seen by the clinical pharmacist achieved greater reduction in haemoglobin A1C (HbA1C) levels than those in the control group.

A similar study conducted by Lee and Leung (2003) also demonstrated that a pharmacist-managed compliance clinic for diabetic patients in Hong Kong was also successful in improving glycaemic control and compliance with medications.

Nowak *et al* (2002) carried out a retrospective analysis comparing diabetic patients managed by the pharmacist-managed diabetes clinic and those managed exclusively by their primary care physicians. The results demonstrated that pharmacist-managed diabetes programs achieved better glycaemic control and also better adherence to the American Diabetes Association (ADA) guidelines. The investigators concluded that pharmacists

are in a position to work continuously with a physician to provide this type of care to patients.

1.5.3.3 Smoking Cessation Clinic

Smith *et al* (1995) described that smoking cessation programs offered by community, managed care, and hospital pharmacists showed favourable outcomes and achieved greater long-term smoking cessation rates.

1.5.3.4 Anticoagulation Clinic

In Garabedian-Ruffalo *et al* (1985), it demonstrated that the warfarin anticoagulation clinic staffed by specially trained pharmacists provided improved therapy compared with treatment received by patients before their referral to the clinic. Clinical pharmacists provided patient education, monitored patients for harmorrhagic and thromboembolic complications, and provided advice on warfarin dosage to maintain therapeutic prothrombin times.

1.5.3.5 Haematology-oncology Clinic

Wong and Gray (1999) demonstrated that haematology-oncology clinics provided an excellent opportunity for the development of CPS. The investigators involved a clinical pharmacist in the clinic who carried out chart reviews, pharmacy patient profile reviews, and patient interviews to obtain medication histories. Any drug-related problems were identified and discussed with the physicians. The study also showed that having a clinical pharmacist

can potentially lead to an overall decrease in health care costs and to an improvement of the quality of patient care.

These studies demonstrate the use of pharmacists in a variety of disease management environment, working as part of the multidisciplinary team along with physicians, nurses and other healthcare professionals. These examples of collaborative physician-pharmacist practice models have led to improvements in disease control in patients with hypertension, diabetes and other chronic conditions. The active involvement of pharmacists in these clinical settings also helps to increase patient satisfaction with pharmacist-managed clinical services.

1.5.4 Pharmacist-managed Lipid Clinics

Similarly, CPS can be set up for the management of dyslipidaemia. The development of pharmacist-managed lipid clinics has been shown to be successful in achieving the NCEP LDL-C goals for the prevention of CHD. Olson *et al* (2005) examined the impact of a clinical pharmacy cardiac risk service on lipid screening, control, and treatment outcomes. This was performed by the establishment of a group model health maintenance organization involving a pharmacist working in close collaboration with physicians. The pharmacist assisted with the implementation and long-term management of all evidence-based treatment strategies. Lifestyle modification

with diet and exercise were also emphasized. The results of the study demonstrated that a clinical pharmacist involvement as part of the multidisciplinary team resulted in more patients achieving the lipid goals. Bogden *et al* (1997) concluded that attempts to lower total cholesterol levels and achieve NCEP goals were more successful when combined with programs that included teamwork between physicians and pharmacists. Moreover, the NCEP ATP III (2001) also recommended the use of a multidisciplinary approach to implement its latest guidelines for the prevention of CHD events and the management of dyslipidaemia.

Pharmacists can therefore help reinforce evidence-based treatment guidelines and aid in the implementation of any local clinical guidelines by working in close collaboration with physicians. Other potential benefits of a pharmacist involvement include improving patient's adherence and compliance with their drug therapy by providing advice on lifestyle modifications and medication, as well as monitoring for any possible adverse drug reactions.

1.6 Objectives & General Aims of the Study

1.6.1 Objectives

The objective of this study was to assess the clinical and economic impact of a CPS on achieving the recommended LDL-C goals proposed by the NCEP ATP III guidelines (2001) in a public hospital in Hong Kong.

1.6.2 Study Hypothesis

The hypothesis of this study was that more patients will reach their recommended ATP III LDL-C goals with pharmacist intervention.

1.6.3 General Aims of the Study

The aims of this study included the following:

i. To assess the impact of a CPS on the LDL-C goal attainment in patients with dyslipidaemia;

ii. To assess the impact of a CPS on the patients' adherence and compliance with lipid-lowering therapy before and after the study;

iii. To explore the role of pharmacists in improving the LDL-C goal attainment;

iv. To explore factors associated with LDL-C goal attainment;

v. To explore the time spent and cost-effectiveness of a pharmacist-managed lipid clinic in Hong Kong;

vi. To explore the views of patients and physicians on the development of a CPS in the management of dyslipidaemia.

Chapter 2. Methodology of Study

2.1 Background Setting

This study was a prospective controlled trial, conducted at the medical outpatient lipid clinic of the Prince of Wales Hospital (PWH), a public teaching hospital with 1200 beds providing both primary and secondary health care. Dyslipidaemic patients attend the lipid clinic as outpatients every 16 to 26 weeks for their routine checkups. Two weeks prior to their visits, patients attend the Chemical Pathology Laboratory at PWH to have their lipid profiles and other biochemical tests assessed. These patients were the target group of this study. The study was approved by the Clinical Research Ethics Committee of the Chinese University of Hong Kong.

2.2 Subject Selection and Recruitment Criteria

During the 24-months study period between 17 October 2005 and 17 October 2007, a total of 300 dyslipidaemic patients were recruited from the outpatient lipid clinic at PWH. Demographic characteristics and laboratory data of all patients were obtained from the patients' medical notes and the hospital computer records respectively. This information was documented on the pharmacist data collection form (Appendix I) and the time spent on the documentation process was recorded. All subjects were provided with an information sheet and informed about the protocol and confidential nature of

the study (Appendix II). Written informed consent was obtained from all patients and they were told about their right to withdraw from the study at any time (Appendix III). Recruited subjects were of Chinese origin, aged 18 years or above, male or female, and diagnosed with dyslipidaemia. Subjects on both primary and secondary prevention for CHD were included in the study. Patients who were pregnant, physically or mentally incompetent to give informed consent were excluded from the study.

2.3 Intervention and Control Groups

Patients recruited in the study were assigned to the intervention group and control group using the alternate method on the outpatient lipid clinic patient list.

In the intervention group, apart from routine physician care, patients were followed up by a clinical pharmacist. Subjects in the control group only received routine medical care provided by the lipid clinic physicians with no pharmacist intervention. The physicians were not informed about the group assignment of their patients, and both groups received the same standard medical care.

Educational clinic visits and follow-up of lipid profiles were carried out by the clinical pharmacist for patients assigned to the intervention group.

These visits were scheduled every 16 to 26 weeks on the same day as the routine lipid clinic visits of each patient to meet their convenience. For subjects who were on primary prevention for CHD, the clinical pharmacist assessed the 10-year CHD risk using the Framingham point scores (Appendices IV and V) and the LDL-C goal attainment, in accordance to the NCEP ATP III guidelines. These values were explained to the patients to increase their understanding of their potential cardiovascular risks and the respective LDL-C goals that they should be aiming for.

Each patient was taught about the indication of lipid-lowering drugs, the dose, the appropriate time of administration, and potential adverse drug reactions. Therapeutic lifestyle changes were also reinforced. The importance of drug compliance was emphasized. Table 2.1 categorizes the types of questions asked by the pharmacist at each educational visit. Patients who were non-compliant were provided with pill boxes and were taught how to use these to improve their medication compliance. All patients were given an educational leaflet (Appendix VI) about the management of dyslipidaemia and lipid-lowering drug therapy. If the patient had any other concurrent diseases, the pharmacist provided additional advice on the management of their respective conditions.

Table 2.1. Patient educational visit checklist

Category	Questions
Dyslipidaemia Status	Do you understand what dyslipidaemia is? Do you know what lipid level targets you should be aiming for? What was your lipid level in your last visit?
Drug Therapy	What has your doctor prescribed this medication for? What dose of the medication has your doctor prescribed? How many times during the day has your doctor asked you to take this medication?
Drug Compliance	What times of the day do you take your medications? How do you take your medications? How many times a week do you take miss a dose of your medications? What do you do if you forget to take your medications? Have you stopped taking any medications yourself without your doctor's advice?
Adverse Drug Reactions and Drug Interactions	Have you been told the possible side effects of your medications? Do you buy any over-the-counter products? Do you take any traditional Chinese medicines?
Healthy Lifestyle Behaviours	Do you smoke? Do you drink alcohol? Do you do any exercise every week? What type of diet do you have?

Patients were also given the opportunity to ask the pharmacist questions regarding their drug therapy and were provided with a telephone number to contact the pharmacist if they had further problems after their clinic visits. Any advice given and actions taken by the clinical pharmacist were documented. Any recommendations made to the physicians by the pharmacist were carried out via a physician-pharmacist communication sheet (Appendix

VII). The time spent between the patient and pharmacist at these educational visits was recorded.

Between successive educational clinic visits, monthly telephone follow-up calls were carried out by the clinical pharmacist to patients in the intervention group. This was aimed at assessing the general well being of the patient such as diet and exercises, improve adherence to medications and to identify any problems with their drug regimen. During these calls, a telephone checklist (Appendix VIII) was followed. The pharmacist reminded the patients of their next clinic appointment and prompted the patients to bring all their prescribed medications and any over-the-counter (OTC) medications at their next visit to the clinic. The pharmacist also explained to the patients that any medications that they no longer required could be returned to the pharmacy for proper disposal. The time spent by the clinical pharmacist on conducting these telephone follow-up calls was recorded.

Patient satisfaction about the current medical care in the outpatient lipid clinic was assessed in both the intervention group and control group during their first visit of the study period. This was performed again at the end of the study. Patients in the intervention group were also asked to comment on the educational visits carried out by the clinical pharmacist over the study period. This was obtained by distributing a validated questionnaire (Appendices IX and X) to both groups. Physicians at the lipid clinic were also

asked to comment on the CPS provided via a questionnaire survey at the end of the study (Appendix XI).

2.4 Validation of Survey

The questionnaire surveys for both the intervention and control groups were validated before distributing to the patients for completion. The validation was carried out by asking five patients at the outpatient lipid clinic of PWH to complete the questionnaire. These five patients were not involved in the study. After completing the survey, the same five patients were asked to complete the same questionnaire again one week later. The results obtained on both occasions were then analyzed and compared to observe for any significant differences.

2.5 Data Collection

For both groups of patients, data were obtained from the medical notes and the electronic Patient Records (e-PR) under the Central Medical System (CMS) of the Hospital Authority. Demographics and biochemical tests including lipid profiles were reviewed and served as the baseline levels for comparison at the end of the study. Comorbid medical conditions and both prescribed medications and OTC medications were also identified.

2.6 Outcome Measures

2.6.1 Lipid Value Changes

The main primary outcome of this study was the percentage of patients achieving the NCEP ATP III LDL-C goal attainment at the end of the study in accordance to their CHD risk category. The changes in TC, TG, and HDL-C before and after the study were also evaluated. These primary outcomes were determined and compared in both the intervention group and control group. Factors affecting the LDL-C goal attainment were also assessed.

2.6.2 Compliance Rate with Medications

The level of compliance to prescribed medications was a secondary outcome measure assessed in the intervention group. Patients were considered to be compliant to their medications when their compliance rate was 75% or more. (Lee and Chow 2004) The 'pill-counting' method was used to assess drug compliance. The level of compliance was calculated as follows:

$$\textit{Drug Compliance} = \frac{\textit{(Total number of Follow-up days – No of days with missed doses)}}{\textit{Total number of Follow-up days}} \times 100\%$$

2.6.3 Patient Satisfaction Survey Assessment

Results from the patient satisfaction surveys on the educational visits provided by the clinical pharmacist before and at the end of the study were assessed and compared in the intervention group. This was then compared to the results obtained from the patient satisfaction questionnaire carried out in the control group.

2.6.4 Time spent and Cost of Clinical Pharmacist

The overall time spent by the clinical pharmacist on the documentation process and the activities carried out at the educational visits and telephone follow-up calls for patients in the intervention group were assessed. The cost of the involvement of a clinical pharmacist to maintain this dyslipidaemia management service at the lipid clinic was evaluated based on the average monthly salary of a basic hospital pharmacist.

2.7 Statistical Analysis

2.7.1 Sample Size Calculation

A 90 per cent power (P) of detecting a clinically important difference in LDL-C goal attainment between the two groups at the 5 per cent level of significance (α) was used. The population proportions chosen for the two groups were 0.8 (p_1) and 0.6 (p_2).

Using the below equation (Petrie & Sabin 2000),

$$n = \frac{f(\alpha, P)\,[\,p_1(1-p_1) + p_2(1-p_2)]}{(p_1 - p_2)^2}$$

we have

$$n = \frac{10.5\,[\,0.8(1-0.8) + 0.6(1-0.6)]}{(0.8-0.6)^2}$$

$$= \frac{10.5\,[0.16 + 0.24]}{(0.04)^2}$$

$$= \frac{4.2}{0.04}$$

$$= 105$$

Thus, at least 105 patients would be required in each group. This meant that at least 210 patient would need to be recruited into this study.

2.7.2 Methods of Statistical Analysis

In this study, the statistical analysis was based on the intention-to-treat principle. Statistical analyses were performed using Statistical Package for Social Sciences (SPSS) for Windows, version 13.0 (SPSS Inc., Chicago, Illinois, USA). Demographic data was expressed as mean $\pm$ standard deviation, medians, or proportions where appropriate. Continuous data obtained before and after the study for each subject were analyzed using the two-sided paired *t*-test. Two-sided independent *t*-test was used for continuous data comparing between the two groups. Categorical variables were analyzed by the *Chi*-square test. Odds ratios were calculated to examine the clinical predictors for achieving lipid goals at the end of study. A *p*-value of 0.05 was considered as statistically significant for all tests.

Chapter 3. Results of Study

3.1 Recruitment Details

During the 24-months study period between 17 October 2005 and 17 October 2007, a total of 319 patients were screened for recruitment to this study. Among these subjects, 300 patients were recruited, with 150 patients assigned to the intervention group and 150 patients to the control group. The remaining 19 subjects were excluded for not meeting the entry criteria of the study as discussed in Section 2.2. The mains reasons for excluding these patients are shown in Table 3.1.

Table 3.1. Summary of the reasons for excluding the subjects for recruitment

	Reasons for Exclusion	**Number of Subjects Excluded**
1.	Age below 18 years old	6
2.	Cannot read and/or write to provide written informed consent	7
3.	Mentally incompetent	2
4.	Physically incompetent – blind	2
5.	Lost to follow-up	1
6.	Blood tests not performed at Prince of Wales Hospital	1

Of the 300 patients who were recruited, no subjects were dropped from the study and none were lost to death during the study period.

3.2 Demographic Characteristics of Patients

The demographic characteristics of all patients who completed the study are shown in Table 3.2. No significant differences in any of the characteristics were observed between the intervention group and the control group.

Table 3.2. Demographic Characteristics of all Patients at Baseline

Characteristic	**Intervention Group (n = 150)**		**Control Group (n = 150)**		**P value**
Demographics					
Age (years), mean (SD)	56.2	(10.4)	57.9	(12.9)	*0.211*
Sex (male), n (%)	68	(45.3)	60	(40.0)	*0.352*
Diagnosis of Dyslipidiaemia					
Familial Hyperlipidaemia n (%)	91	(60.7)	94	(62.7)	*0.723*
Time duration (years), mean (SD)	9.8	(3.5)	9.1	(3.7)	*0.427*
Lipid Profile, mean (SD)					
LDL-C, mmol/L	3.53	(1.30)	3.48	(1.35)	*0.741*
HDL-C, mmol/L	1.60	(0.41)	1.63	(0.50)	*0.611*
TC, mmol/L	6.05	(1.41)	5.91	(1.27)	*0.375*
TG, mmol/L	2.20	(1.72)	2.08	(1.24)	*0.463*
Comorbidity, n (%)					
Hypertension	76	(50.7)	78	(52.0)	*0.818*
Diabetes mellitus	40	(26.7)	43	(28.7)	*0.700*
Hypertension & Diabetes mellitus	29	(19.3)	30	(20.0)	*0.885*
Coronary heart disease	9	(6.0)	11	(7.3)	*0.645*
Congestive heart failure	0	(0)	1	(0.7)	*0.318*
Peripheral vascular disease	3	(2.0)	4	(2.7)	*0.703*
Myocardial infarction	1	(0.7)	2	(1.3)	*0.563*
Stroke	4	(2.7)	6	(4.0)	*0.533*
Atrial Fibrillation	2	(1.3)	0	(0)	*0.157*
Cardiac Surgical Intervention	9	(6.0)	10	(6.7)	*0.813*
Thyroid disorder	6	(4.0)	7	(4.7)	*0.778*
Gout	15	(10.0)	12	(8.0)	*0.547*
Other risk factors, n (%)					
Smoker	15	(10.0)	13	(8.7)	*0.693*
Ex-Smoker	20	(14.7)	15	(10.0)	*0.370*
Poor Diet Control	26	(17.3)	23	(15.3)	*0.754*
Lack of Exercise	35	(23.3)	31	(20.7)	*0.579*
Family history of CHD/CVA	30	(20.0)	29	(19.3)	*0.885*
Family history of Dyslipidaemia	86	(57.3)	88	(58.7)	*0.816*
Family history of Hypertension	63	(42.0)	67	(44.7)	*0.643*
Family history of Diabetes Mellitus	35	(23.3)	32	(21.3)	*0.679*

3.3 Drug Therapy of Patients during Study Period

The type of dyslipidaemia treatment that the subjects were prescribed during the study period is presented in Table 3.3. The majority of patients were on one lipid-lowering agent with a few on combination lipid-lowering therapy. Statins were the main choice of lipid-lowering agent indicated for most of the subjects.

Hypertension and diabetes mellitus were the two main co-morbidities found in these patients. As a result, medications for the treatment of these two conditions were also the main concurrent drugs found to be prescribed along with treatment for dyslipidaemia. Hypertension and diabetes mellitus are also significant risk factors for the development of CHD.

Table 3.3. Drug therapy of patients in the Intervention and Control Groups

Drug Therapy Regimen	**Intervention Group (n = 150)**		**Control Group (n = 150)**		**P value**
Patients on mono lipid-lowering therapy, n (%)	141	(94.0)	137	(91.3)	*0.499*
Patients on combination lipid-lowering therapy, n (%)	9	(6.0)	13	(8.7)	*0.377*
Lipid-lowering agents and mean daily dose (MDD)					
Statins	108	(72.0)	115	(76.7)	*0.385*
Atorvastatin, n (%)	9	(6.0)	21	(14.0)	***0.021***
MDD, mg/day	11		28		
Fluvastatin, n (%)	1	(0.7)	2	(1.3)	*0.563*
MDD, mg/day	80		80		
Rosuvastatin, n (%)	73	(48.7)	53	(35.3)	***0.019***
MDD, mg/day	10		11		
Simvastatin, n (%)	25	(16.7)	39	(26.0)	***0.049***
MDD, mg/day	13		22		
Fibrates	24	(16.0)	16	(10.7)	*0.288*
Bezafibrate, n (%)	6	(4.0)	4	(2.7)	*0.522*
MDD, mg/day	343		400		
Gemfibrozil, n (%)	18	(12.0)	12	(8.0)	*0.250*
MDD, mg/day	900		900		
Bile acid sequestrants					
Cholestyramine, n (%)	8	(5.3)	10	(6.7)	*0.628*
MDD, mg/day	6		7		
Ezetimibe					
Ezetimibe, n (%)	4	(2.7)	3	(2.0)	*0.703*
MDD, mg/day	10		10		
Nicotinic acid group					
Nicotinic Acid, n (%)	5	(3.3)	3	(2.0)	*0.475*
MDD, mg/day	950		1000		
Diet alone					
Diet Control, n (%)	11	(7.3)	14	(9.3)	*0.532*
Other concurrent medication, n (%)					
For hypertension	70	(46.7)	73	(48.7)	*0.730*
For diabetes mellitus	33	(22.0)	35	(23.3)	*0.784*
For thyroid disorder	6	(4.0)	4	(2.7)	*0.522*
For gout	13	(8.7)	11	(7.3)	*0.672*
Antiplatelet	14	(9.3)	15	(10.0)	*0.846*
Nitrates	4	(2.7)	3	(2.0)	*0.703*

Table 3.3. Drug therapy of patients in the Intervention and Control Groups – Continued

Drug Therapy Regimen	**Intervention Group (n = 150)**	**Control Group (n = 150)**	**P value**
Over-the counter Medications, *n* (%)			
Simple analgesics	13 (8.7)	10 (6.7)	*0.517*
Antacids	11 (7.3)	8 (5.3)	*0.621*
Vitamin & Mineral Supplements	25 (16.7)	21 (14.0)	*0.523*
Chinese herbal medicines, *n* (%)			
Common colds and flu	7 (4.7)	8 (5.3)	*0.756*
Detoxifying agents	8 (5.3)	6 (4.0)	*0.689*
Minor skin ailments (eczema and allergic dermatitis)	6 (4.0)	5 (3.3)	*0.645*

[#]Number of patients may not sum up to actual total number of patients due to some patients receiving combination therapy.

In terms of drug therapy characteristics between the two groups, no significant differences were found in the majority of cases. Significant differences ($p < 0.05$) were only observed in the number of subjects who were treated with atorvastatin, rosuvastatin and simvastatin.

Atrovastatin, rosuvastatin and simvastatin have different lipid-lowering potency effects. In order to assess whether the significant findings in Table 3.3 for these three drugs would affect the outcomes of this study, the baseline lipid profiles of patients who were on these three drugs were further analyzed [Tables 3.4, 3.5 and 3.6]. No significant differences were observed in LDL-C, HDL-C, TC and TG levels at baseline between the two groups who were on atorvastatin, rosuvastatin and simvastatin.

Thus, the significant difference findings in Table 3.3 should not affect the final results of this study since the only intervention implemented was the development of a CPS in the intervention group and no pharmacist input in the control group.

All patients in both groups were also maintained on the same lipid-lowering therapy throughout the whole study. Any differences observed in the final outcome of this study should therefore be related to the CPS.

Table 3.4. Mean Lipid Concentrations of patients on Atorvastatin at Baseline

Mean Lipid Profile (SD)	**Intervention Group (n = 9)**	**Control Group (n = 21)**	**P value**
LDL-C (mmol/L)	3.40 (1.06)	3.49 (1.69)	*0.819*
HDL-C (mmol/L)	1.54 (0.36)	1.61 (0.53)	*0.713*
TC (mmol/L)	5.76 (1.02)	5.85 (1.57)	*0.771*
TG (mmol/L)	1.99 (1.46)	1.66 (1.00)	*0.505*

Table 3.5. Mean Lipid Concentrations of patients on Rosuvastatin at Baseline

Mean Lipid Profile (SD)	**Intervention Group (n = 73)**	**Control Group (n = 53)**	**P value**
LDL-C (mmol/L)	3.67 (1.62)	3.29 (1.39)	*0.202*
HDL-C (mmol/L)	1.62 (0.38)	1.61 (0.39)	*0.785*
TC (mmol/L)	6.09 (1.63)	5.71 (1.33)	*0.190*
TG (mmol/L)	1.72 (1.08)	1.79 (1.08)	*0.632*

Table 3.6. Mean Lipid Concentrations of patients on Simvastatin at Baseline

Mean Lipid Profile (SD)	**Intervention Group (n = 25)**	**Control Group (n = 39)**	**P value**
LDL-C (mmol/L)	3.40 (0.62)	3.11 (1.10)	*0.186*
HDL-C (mmol/L)	1.68 (0.38)	1.69 (0.35)	*0.947*
TC (mmol/L)	5.76 (0.78)	5.54 (1.03)	*0.360*
TG (mmol/L)	1.69 (1.09)	1.49 (0.85)	*0.429*

3.4 LDL-C Lowering Potency of Statin Doses Prescribed

In this study, 108 patients in the intervention group and 115 patients in the control group were treated with statins as their lipid-lowering therapy [Table 3.3]. As discussed in Table 1.10, statins vary in their lipid-lowering potency according to the doses prescribed and the type of statin prescribed. The relative LDL-C lowering potency of the statin doses prescribed for both the intervention group and control group are presented in Table 3.7. No significant differences were observed between the two groups. When the mean LDL-C lowering potency of statin doses prescribed was compared between the intervention group and control group, no significant differences were observed [Table 3.8]. The statin dosing for the key high-risk group patients found in this study are presented in Tables 3.9 and 3.10.

Table 3.7. Relative LDL-C lowering potency of Statin Doses in the Intervention and Control Groups

Relative LDL-C Lowering Potency of Statin Doses prescribed	**Intervention Group (n = 108) n (%)**	**Control Group (n = 115) n (%)**	**P value**
50 – 59%	3 (2.8)	5 (4.3)	*0.699*
40 – 49%	65 (60.2)	59 (51.3)	*0.184*
30 – 39%	20 (18.5)	33 (28.7)	*0.074*
Below 30%	20 (18.5)	18 (15.7)	*0.566*

Table 3.8. Comparison of Mean Statin LDL-C lowering potency between Intervention and Control Groups

	Intervention Group (n = 108)	**Control Group (n = 115)**	**P value**
Mean Statin LDL-C Lowering Potency % (SD)	42.43 (9.50)	44.67 (8.14)	*0.854*

Table 3.9. Statin Dosing for High-Risk Group Patients in Intervention Group

High-Risk Patients in Intervention Group	**Number of Patients on Statins, *n* (%)**	**Relative LDL-C Lowering Potency of Statin Doses prescribed**	**Number of Patients, *n* (%)**
Diabetic Patients ($n = 40$)	23 (57.5)	50 – 59%	1 (4.3)
		40 – 49%	9 (39.1)
		30 – 39%	7 (30.4)
		Below 30%	6 (26.1)
Hypertensive Patients ($n = 76$)	53 (69.7)	50 – 59%	1 (1.9)
		40 – 49%	9 (17.0)
		30 – 39%	28 (52.8)
		Below 30%	15 (28.3)
Patients with Diabetes & Hypertension ($n = 29$)	16 (55.2)	50 – 59%	1 (6.3)
		40 – 49%	9 (56.3)
		30 – 39%	2 (12.5)
		Below 30%	4 (25.0)
Patients with CHD ($n = 9$)	7 (77.7)	50 – 59%	1 (14.3)
		40 – 49%	3 (42.3)
		30 – 39%	1 (14.3)
		Below 30%	2 (28.6)
Smokers ($n = 15$)	11 (73.3)	50 – 59%	0 (0)
		40 – 49%	5 (45.5)
		30 – 39%	4 (36.4)
		Below 30%	2 (18.2)

Table 3.10. Statin Dosing for High-Risk Group Patients in Control Group

High-Risk Patients in Control Group	**Number of Patients on Statins, *n* (%)**	**Relative LDL-C Lowering Potency of Statin Doses prescribed**	**Number of Patients, *n* (%)**
Diabetic Patients ($n = 43$)	37 (86.0)	50 – 59%	2 (6.1)
		40 – 49%	18 (48.6)
		30 – 39%	8 (24.2)
		Below 30%	9 (24.3)
Hypertensive Patients ($n = 78$)	63 (80.8)	50 – 59%	2 (3.2)
		40 – 49%	13 (20.6)
		30 – 39%	32 (50.8)
		Below 30%	16 (25.4)
Patients with Diabetes & Hypertension ($n = 30$)	23 (76.7)	50 – 59%	2 (8.7)
		40 – 49%	12 (52.2)
		30 – 39%	4 (17.4)
		Below 30%	5 (21.7)
Patients with CHD ($n = 11$)	9 (81.8)	50 – 59%	1 (11.1)
		40 – 49%	3 (33.3)
		30 – 39%	2 (22.2)
		Below 30%	3 (33.3)
Smokers ($n = 13$)	10 (69.2)	50 – 59%	0 (0)
		40 – 49%	4 (40.0)
		30 – 39%	4 (40.0)
		Below 30%	2 (20.0)

3.5 Coronary Heart Disease Risk Category of Patients

Using the NCEP ATP III guidelines (2004) and the Framingham risk equation, the 10-year CHD risk was assessed for each subject who was on primary prevention for CHD in both the intervention group and control group. A summary of the number of patients found in each CHD risk category is given in Table 3.11 No significant differences were observed between the two groups when the numbers of cases found in each CHD risk category were compared.

Table 3.11. CHD Risk category of patients in the Intervention and Control Groups

CHD Risk Category	**Recommended NCEP LDL-C Goal, mmol/L**	**Intervention Group (*n*=150), *n* (%)**	**Control Group (*n* =150), *n* (%)**	**P value**
Low risk: 0-1 risk factor	< 4.1	72 (48.0)	67 (44.7)	*0.564*
Moderate risk: 2+ risk factors (10-year risk < 10%)	< 3.4	15 (10.0)	16 (10.7)	*0.850*
Moderately high risk: 2+ risk factors (10-year risk 10% to 20%)	< 2.6	14 (9.3)	13 (8.7)	*0.841*
High risk: CHD or CHD risk equivalents (10-year risk > 20%)	< 1.8	49 (32.7)	54 (36.0)	*0.545*

3.6 Lipid Profile Changes

For the intervention group, there were significant reductions in LDL-C, TC and TG levels at the end of the study period in comparison to the levels at baseline [Table 3.12]. A significant increase in HDL-C level was also observed at the end of the study.

Table 3.12. Change of Lipid Concentrations in Intervention Group (n = 150)

	Mean (SD) at baseline	**Mean (SD) at end of study**	**Mean difference (SD)**	**Mean % change (SD)**	**P value**
LDL-C (mmol/L)	3.53 (1.30)	2.60 (0.89)	-0.93 (0.07)	-26.35 (0.13)	***< 0.001***
HDL-C (mmol/L)	1.60 (0.41)	1.72 (0.46)	+0.12 (0.02)	+7.50 (0.15)	***< 0.001***
TC (mmol/L)	6.05 (1.41)	5.00 (0.93)	-1.05 (0.09)	-17.36 (0.14)	***< 0.001***
TG (mmol/L)	2.20 (1.72)	1.54 (1.06)	-0.66 (0.07)	-30.00 (0.24)	***< 0.001***

The patients in the control group also showed significant reductions in LDL-C, TC and TG concentrations and a significant increase in HDL-C level [Table 3.13]. However, the magnitude of changes was smaller than those observed in the intervention group.

Table 3.13. Change of Lipid Concentrations in Control Group (n = 150)

	Mean (SD) at baseline	**Mean (SD) at end of study**	**Mean difference (SD)**	**Mean % change (SD)**	**P value**
LDL-C (mmol/L)	3.48 (1.35)	3.04 (1.17)	-0.44 (0.08)	-12.64 (0.44)	***< 0.001***
HDL-C (mmol/L)	1.63 (0.50)	1.69 (0.55)	+0.07 (0.02)	+3.68 (0.11)	***0.001***
TC (mmol/L)	5.91 (1.27)	5.52 (1.26)	-0.39 (0.07)	-6.60 (0.13)	***< 0.001***
TG (mmol/L)	2.08 (1.24)	1.84 (1.57)	-0.24 (0.09)	-11.54 (0.36)	***0.043***

When the mean difference of change in lipid concentrations at the end of the study were compared between the two groups [Table 3.14], significant differences were observed for LDL-C, TC and TG changes ($p < 0.05$).

Table 3.14. Comparison of change of Lipid Concentrations between Intervention and Control Groups

	Mean % Change (SD) in Intervention Group (n = 150)	**Mean % Change (SD) in Control Group (n = 150)**	**P value**
LDL-C (mmol/L)	-26.35 (0.13)	-12.64 (0.44)	***< 0.001***
HDL-C (mmol/L)	+7.50 (0.15)	+3.68 (0.11)	*0.056*
TC (mmol/L)	-17.36 (0.14)	-6.60 (0.13)	***< 0.001***
TG (mmol/L)	-30.00 (0.24)	-11.54 (0.36)	***< 0.001***

3.7 NCEP ATP III LDL-C Goal Attainment

By the end of the study period, 58.7 per cent of the intervention group achieved the recommended NCEP ATP III LDL-C goals in accordance to their CHD risk category compared with 45.3 per cent of the control group ($p < 0.05$). These results are presented in Tables 3.15, 3.16 and 3.17.

Table 3.15. Intervention Group Patients ($n = 150$) at LDL-C goal at Baseline and End of Study

CHD Risk Category	**At LDL-C Goal at Baseline *n* (%)**	**At LDL-C Goal at End of Study *n* (%)**	**P value**
Low risk: 0-1 risk factor *(n = 72)*	58 (80.6)	63 (87.5)	***0.024***
Moderate risk: 2+ risk factors (10-year risk < 10%) *(n = 15)*	8 (53.3)	11 (73.3)	*0.082*
Moderately high risk: 2+ risk factors (10-year risk 10% to 20%) (n = 14)	5 (35.7)	7 (50.0)	*0.165*
High risk: CHD or CHD risk equivalents (10-year risk > 20%) *(n = 49)*	6 (12.2)	7 (14.3)	*0.322*
Overall at LDL-C Goal, *n*(%) *(n = 150)*	77 (51.3)	88 (58.7)	***0.001***

Table 3.16. Control Group Patients (n = 150) at LDL-C goal at Baseline and End of Study

CHD Risk Category	**At LDL-C Goal at Baseline *n* (%)**	**At LDL-C Goal at End of Study *n* (%)**	**P value**
Low risk: 0-1 risk factor *(n = 67)*	50 (74.6)	47 (70.1)	*0.083*
Moderate risk: 2+ risk factors (10-year risk < 10%) *(n = 16)*	12 (75.0)	10 (62.5)	*0.164*
Moderately high risk: 2+ risk factors (10-year risk 10% to 20%) *(n = 13)*	5 (38.5)	4 (30.8)	*0.337*
High risk: CHD or CHD risk equivalents (10-year risk > 20%) *(n = 54)*	7 (13.0)	7 (13.0)	-
Overall at LDL-C Goal, *n*(%) *(n = 150)*	74 (49.3)	68 (45.3)	***0.014***

Table 3.17. Comparison of LDL-C Goal achievement between the two groups at end of study

CHD Risk Category	Intervention Group at LDL-C Goal *n* (%)	Control Group at LDL-C Goal *n* (%)	P value
Low risk: 0-1 risk factor	63 (87.5)	47 (70.1)	***0.013***
Moderate risk: 2+ risk factors (10-year risk < 10%)	11 (73.3)	10 (62.5)	*0.613*
Moderately high risk: 2+ risk factors (10-year risk 10% to 20%)	7 (50.0)	4 (30.8)	*0.223*
High risk: CHD or CHD risk equivalents (10-year risk > 20%)	7 (14.3)	7 (13.0)	*0.847*
Overall at LDL-C Goal, *n*(%)	88 (58.7)	68 (45.3)	***0.021***

At the end of the study period, 62 patients in the intervention group and 82 patients in the control group were not at their recommended ATP III LDL-C levels. The main characteristics of these patients are presented in Table 3.18. The main problematic cases identified include patients with familial hyperlipidaemia, high risks for CHD and diabetic subjects.

Table 3.18. Characteristics of patients who were not at ATP III LDL-C Goal at end of study

Patient Characteristics	**Intervention Group (n = 62)**	**Control Group (n = 82)**	**P value**
Age (years), mean (SD)	43.7 (10.2)	45.8 (9.6)	0.223
Familial Hyperlipidaemia, n (%)	49 (79.0)	64 (78.0)	0.888
Mean Compliance Rate with lipid-lowering drugs, % (SD) {End of Study}	81.2 (5.3)	*Not assessed**	-
Low CHD risk (0 – 1 risk factor), n (%)	9 (14.5)	20 (24.4)	0.135
Moderate CHD risk (2+ risk factors), n (%)	11 (17.7)	15 (18.3)	0.933
High CHD risk (CHD or CHD risk equivalents), n (%)	42 (67.7)	47 (57.3)	0.205
Hypertension	35 (56.5)	43 (52.4)	0.635
Diabetes Mellitus	38 (61.3)	45 (54.9)	0.443
Mean Compliance Rate with all medications, % (SD) {End of Study}	79.5 (7.1)	*Not assessed**	-

*Drug adherence assessment was not evaluated in the control group of the study

3.8 Relationship between Patient Characteristics and LDL-C Goal attainment

The relationship between the final LDL-C goal attainment and the various baseline characteristics of the patients was assessed [Table 3.19]. Where the confidence interval (CI) for the statistic includes a value of 1, it is assumed that the characteristic is not associated with the LDL-C goal attainment at the end of the study. The odds ratio of LDL-C goal attainment at the end of the 24-months study period for patients with age 45 – 65 years lies within a CI range that excludes a value of 1 (odds ratio = 2.574, 95% CI, 1.322 – 5.012). It is therefore assumed that there is an association between LDL-C goal attainment and patient with age 45 – 65 years. The odds ratio of LDL-C goal attainment was not affected by the other patient characteristics noted at baseline. The number of patients with coronary heart disease, peripheral vascular disease, MI, stroke, atrial fibrillation and cardiac surgical intervention was too small to evaluate the odds ratio in these cases.

Table 3.19. Odds Ratio for LDL-C Goal Attainment at the end of study

Characteristic	Intervention Group, *n* (*n* = 88)	Control Group, *n* (*n* = 68)	Odds Ratio	95% CI
Male sex	29	34	0.836	0.440 – 1.589
Age ≤ 45 years	29	34	0.492	0.256 – 1.942
Age between 45 – 65 years	48	21	***2.574***	***1.322 – 5.012***
Age ≥ 65 years	11	13	0.604	0.252 – 1.449
Familial Hyperlipidaemia	42	30	1.765	0.961 – 3.241
Baseline LDL-C ≥ 3.4 mmol/L	23	21	0.792	0.393 – 1.596
Baseline HDL-C ≤ 1.04 mmol/L	17	20	0.575	0.273 – 1.208
Baseline TC ≥ 5.2 mmol/L	16	11	1.152	0.496 – 2.674
Baseline TG ≥ 2.0 mmol/L	20	23	0.575	0.284 – 1.168
Low CHD risk (0-1 risk factor)	63	47	1.126	0.563 – 2.250
Moderate CHD risk (2+ risk factors)	18	14	0.992	0.453 – 2.171
High CHD risk (CHD or CHD risk equivalents)	7	7	0.753	0.251 – 2.260
Hypertension	41	35	0.822	0.436 – 1.550
Diabetes mellitus	2	2	0.767	0.105 – 5.592
Hypertension & Diabetes mellitus	1	2	0.379	0.034 – 4.273
Coronary heart disease	1	1	0.770	0.047 – 12.539
Congestive heart failure*	0	0	-	-
Peripheral vascular disease*	0	0	-	-
Myocardial infarction*	0	0	-	-
Stroke*	0	0	-	-
Atrial Fibrillation*	0	0	-	-
Cardiac Surgical Intervention*	0	0	-	-
Thyroid disorder	3	2	1.165	0.189 – 7.173
Gout	5	6	0.622	0.182 – 2.133

OR = odds ratio; CI = confidence interval
Where the confidence interval for the statistic includes a value of 1, it is assumed that the characteristic is not associated with LDL-C goal attainment at the end of the study.
**Number of patients with these characteristics was too small to evaluate the odds ratio*

Table 3.19. Odds Ratio for LDL-C Goal Attainment at the end of study – Continued

Characteristic	Intervention Group, *n* (*n* = 88)	Control Group, *n* (*n* = 68)	Odds Ratio	95% CI
Smoker	4	6	0.492	0.133 – 1.818
Ex-Smoker	9	7	0.993	0.350 – 2.816
Poor Diet Control	7	10	0.501	0.180 – 1.394
Inadequate Physical Activity	17	14	0.924	0.419 – 2.037
Family history of CHD/CVA	24	15	1.325	0.632 – 2.779
Family history of Dyslipidaemia	53	42	0.937	0.490 – 1.794
Family history of Hypertension	40	32	0.938	0.497 – 1.769
Family history of Diabetes Mellitus	19	16	0.895	0.420 – 1.906

OR = odds ratio; CI = confidence interval
Where the confidence interval for the statistic includes a value of 1, it is assumed that the characteristic is not associated with LDL-C goal attainment at the end of the study.
**Number of patients with these characteristics was too small to evaluate the odds ratio*

3.9 Compliance with Medications

In the intervention group, the overall compliance was 77.5% $\pm$ 9.9% at baseline and this improved to 79.8% $\pm$ 10.0% at the end of study ($p < 0.001$) following pharmacist intervention [Table 3.20]. Based on the definition of medication compliance stated in Section 2.6, there were 83 (56.8%) compliers at baseline and 103 (70.5%) compliers at the end of study ($p < 0.001$). Among the 47 non-compliers at the end of the study, 25 patients (53.2%) were aged less than 45 years old and 9 patients (19.1%) were aged above 75 years old. Eleven of the non-compliers were taking five medications or more. During the study period, no patients returned any unwanted medications to the pharmacist for discarding.

The rate of compliance decreased with the increasing number of medications that the patient had to take. Apart from lipid-lowering drugs, most of these medications were for long-term conditions which included mainly hypertension, diabetes mellitus, thyroid disorder and gout. The reasons for noncompliance found in this study are presented in Table 3.21. In order to overcome these barriers to drug compliance, the clinical pharmacist provided a range of compliance aids to help patients. This is also listed in Table 3.21.

Table 3.20. Change of Medication Compliance following Pharmacist Involvement in Intervention Group (n = 146)*

	Number of Patients, n (%)	**Baseline Mean Compliance Rate, % (SD)**	**End of Study Mean Compliance Rate, % (SD)**	**Mean difference (SD)**	**Mean % change (SD)**	**P value**
1 Drug	50 (33.3)	88.92 (4.63)	91.42 (4.62)	+2.50 (2.27)	+2.81 (2.67)	***< 0.001***
2 Drugs	27 (18.0)	76.61 (2.47)	78.68 (2.26)	+2.07 (2.06)	+2.70 (2.75)	***< 0.001***
3 Drugs	27 (18.0)	75.27 (2.85)	77.57 (2.36)	+2.30 (1.76)	+3.06 (2.39)	***< 0.001***
4Drugs	18 (12.0)	68.69 (2.53)	70.91 (2.52)	+2.22 (2.20)	+3.23 (3.33)	***0.001***
5 Drugs or more	24 (16.0)	64.05 (4.96)	66.22 (4.87)	+2.17(2.37)	+3.39 (3.59)	***< 0.001***
None	4 (2.7)					
Overall Compliance Change (n = 146)*		77.54 (9.93)	79.83 (10.03)	+2.29 (2.09)	+2.95 (2.79)	***< 0.001***

*Four patients were not on any prescribed medications

Table 3.21. Common Reasons for Noncompliance with Medications and Compliance Aids provided by Pharmacist

Problem Category	Reasons for Medication Noncompliance	Types of Compliance Aids
Lifestyle of patient	Busy lifestyles and working schedules with night time shifts.	Provision of pill box. Telephone follow-up reminders. Keeping a timetable or calendar as a reminder. Reorganizing storage of medications at home for easy reminder.
Choice of drug	Did not like taste of drug. Found drug inconvenient to take. Common problem with cholestyramine (Questran ®).	Suggestion of change of medication
Knowledge of drug-specific information	Lack of understanding that medicines should be taken long-term for maximum benefit. Concerned about possible adverse drug reactions and omitted doses, hoping to reduce these possibilities.	Patient information leaflet to improve knowledge on medications. Explanation of the indication of medications and their long-term benefits. Explanation of common adverse drug reactions of medications.
Traditional Chinese medicines	Taking traditional Chinese medicines and omitted doses in case of possible drug interactions with prescribed medicines	Advised patient to take Chinese medicines at least 3 hours prior to or 3 hours after the intake of prescribed medications. Inform doctor that patient is taking traditional Chinese medicines.
Drug therapy regimen	Complex drug regimen with multi-daily dose taking. Patients often commented that they forgot to take midday doses where applicable and left medications at home. Also common problem among diabetic patients.	Use a pill box as a reminder. Carry a small supply of their regular medications when going out. Review drug regimen of patient. Try and simplify drug regimen.
Supply of medications	Ran out of medicines. Did not inform hospital or refer to own doctor for further supply.	Keep a diary or calendar as a reminder when medications would run out. Inform patient's family (with patient's permission) to ensure patient has adequate supply, especially elderly patients with poor memory.

Table 3.21. Common Reasons for Noncompliance with Medications and Compliance Aids provided by Pharmacist - Continued

Problem Category	Reasons for Medication Noncompliance	Types of Compliance Aids
Cognitive function	Poor memory, especially among the elderly.	Keep a diary or calendar as a reminder when to take medications. Inform patient's family (with patient's permission) to supervise patient.
Perceived health	Patient convinced that he was getting better and omitted doses himself.	Counsel patient that medications are indicated for long-term for maximum benefit. Counsel patient not to omit doses without doctor's advice.
Beliefs	Patient felt that he/she is taking too many pills everyday and sometimes omitted doses	Advised patient not to omit doses without doctor's advice. Review medication list.

3.10 Pharmacist Interventions

3.10.1 Range of Pharmacist Interventions

During the 24-months study period, the intervention group was seen by a clinical pharmacist at each follow-up visit to the lipid clinic. The pharmacist also performed monthly telephone calls in between visits to check on the progress of the patients. A range of interventions were carried out by the clinical pharmacist and this is presented in Table 3.22.

Table 3.22. Pharmacist Intervention for Intervention Group (n = 150)

Interventions		**Number of Patients*** *n* (%)	
1	***Lifestyle Modifications***		
	a Healthy dietary advice	150	(100.0)
	b Smoking cessation advice	35	(23.3)
	c Increase exercise	71	(47.3)
	d Reduction of alcohol intake	30	(20.0)
2	***Administration of Medications***		
	a Administration time of medicines	51	(34.0)
	b Dose of medicines to take	33	(22.0)
	c To take with or before food	37	(24.7)
	d Action to take if missed dose	21	(14.0)
3	***Patient Education on Medication***		
	a Indication of medicines	27	(18.0)
	b Possible adverse drug effects	135	(90.0)
	c Action to take if side effects occur	135	(90.0)
	d Inform doctors all medicines currently taking including over-the-counter products, health food products and Chinese medicines.	46	(30.7)
4	***Identification of adverse drug effects & drug interaction***		
	a Adverse drug effects	18	(12.0)
	b Potential drug interactions	11	(7.3)
	Additive induced bleeding effect		
	• Aspirin and Non-steroidal anti-inflammatory drugs	*3*	*(2.0)*
	Reduced drug absorption		
	• Rosuvastatin and Antacid (Gaviscon®)	*2*	*(1.3)*
	• Cholestyramine (Questran ®)and Acarbose	*2*	*(1.3)*
	Enzyme inhibition		
	• Nifedipine and Grapefruit juice	*2*	*(1.3)*
	• Thyroxine and Cimetidine	*1*	*(0.7)*
	• Diltiazem and Simvastatin	*1*	*(0.7)*

Table 3.22. Pharmacist Intervention for Intervention Group (n = 150) – Continued

Interventions		Number of Patients* *n* (%)	
5	***Compliance with medications***		
	a Identification of very poor compliance	42	(28.0)
	b Provision of pill box to aid compliance	14	(9.3)
	c Regular telephone follow-ups reminders	150	(100.0)
	d Provision of patient information leaflets on medication knowledge	150	(100.0)
	e Reinforcement of knowledge on significance of taking prescribed medicines accordingly	60	(40.0)
6	***Dyslipidaemia Management***		
	a Suggestion to increase dose of lipid-lowering therapy	7	(4.7)**
	b Suggestion to change to alternative lipid-lowering therapies	7	(4.7)**
7	***Diabetes Management***		
	a Blood glucose monitoring advice to patients	40	(26.7)
	b Antidiabetic medications advice	35	(23.3)
	c Demonstration on how to use insulin pen	3	(2.0)
8	***Hypertension Management***		
	a Blood pressure monitoring advice to patient	76	(50.1)
	b Antihypertensive medications advice	65	(43.3)
9	***Miscellaneous***		
	a Advice on gout management	15	(10.0)
	b Advice on vitamins and mineral supplements	25	(16.7)
	c Advice on inhaler techniques	3	(2.0)

*Number of patients does not sum up to actual total number of patients as some patients received more than one pharmacist intervention

** Please note that the suggestions made by the pharmacist to increase dose of lipid-lowering therapy and to change to alternative lipid-lowering therapies were not accepted by the physicians or patients. There were two main reasons. Firstly, some physicians explained that the choice of therapy was restricted due to the hospital formulary budget concern of statin therapy. Secondly, patients explained that they were comfortable with the drug therapy that they were currently on and would not like to have their treatment changed. They would prefer to improve their dyslipidaemia via modifying their lifestyle behaviours.

3.10.2 Time spent by Pharmacist

3.10.2.1 Time spent on Documentation

The main documentation activities carried out by the clinical pharmacist in this study included collecting data from the patient medical notes and laboratory parameters from the hospital computer system. The time spent on this process was approximately 20 minutes per patient and 15 minutes per patient respectively. This was carried out for both patients in the intervention group and control group prior to their visit to the lipid clinic.

In the intervention group, the pharmacist also documented any advice provided and interventions made after each educational visit. The time spent on documenting this data was approximately 15 minutes per patient. In between visits, the pharmacist carried out telephone follow-up calls and documented any advice and relevant data. This took approximately 15 minutes per patient.

During the 24-months study period, each patient from both the intervention and control groups visited the lipid clinic a mean 3.34 ± 0.7 times. Each patient in the intervention group received a mean 16.3 ± 3.3 telephone follow-up calls. The average cumulative time spent by the pharmacist on documentation was 205.8 minutes/patient/year. This is equivalent to 3.96 minutes/patient/week.

3.10.2.2 Time spent on Direct Communication with Patients

Overall, the intervention group was seen by the pharmacist a mean 3.34 $\pm$ 0.7 times at the lipid clinic and the average cumulative time spent at these visits was 44.5 minutes/patient/year. On average, each of these educational visits lasted for about 20 minutes per patient.

During the 24-months study period, each patient in the intervention group received a mean 16.3 $\pm$ 3.3 telephone calls from the clinical pharmacist and the average cumulative time spent on these telephone follow-up calls was 108.5 minutes/patient/year. On average, each of the telephone calls lasted for about 10 minutes per patient.

Overall, throughout the study period, the time spent by the clinical pharmacist on carrying out these educational visits at the outpatient lipid clinic and performing telephone follow-up calls was approximately 3.08 minutes/patient/week.

3.10.3 Cost of Clinical Pharmacy Service at the Lipid Clinic

3.10.3.1 Cost of Pharmacist Involvement

Approximately 600 hyperlipidaemic patients are seen at the outpatient lipid clinic of PWH every year. The average monthly salary of a hospital pharmacist is HKD30,000 per month and the average normal working hours is 40 hours per week. This means that the cost of employing a hospital pharmacist is about HKD2.92/minute.

The time spent by the pharmacist on documentation was approximately 3.96 minutes/patient/week. The time spent by the pharmacist at the educational visits and carrying out telephone follow-up calls in this study was approximately 3.08 minutes/patient/week. The total time spent by the pharmacist on both activities was therefore approximately 7.04 minutes/patient/week.

The cost of employing a pharmacist to maintain this CPS would be approximately HKD20.56/patient/week. This is equivalent to HKD88.11/patient/month. On average, 80 hyperlipidaemic patients are seen every month at the outpatient lipid clinic. Thus, it would cost a clinical pharmacist approximately HKD7000/month to view all these patients.

3.10.3.2 Potential Healthcare Cost saving

At the end of the 24-months study period, 88 patients achieved LDL-C goals in the intervention group (n = 150) and 68 patients achieved LDL-C goals in the control group (n = 150).

Using the below equations (Petrie & Sabin 2000),

Control event rate (CER)	= 62/150 = 0.55
Experimental event rate (EER)	= 82/150 = 0.41
Absolute risk reduction (ARR)	= CER – EER = 0.14
Number needed to treat (NNT)	= 1/ARR = 7.14

Hence, the number of patients needed to receive pharmacist intervention at the CPS in order to help one patient attain LDL-C goal would be 7.14 for 24 months. This also means that for every 7.14 patients who receive pharmacist intervention at the CPS, one patient can potentially avoid the risk of developing an AMI.

According to the PWH Pharmacy Department data reported in the year 2004 – 2005, approximately 5,500 patients/year seen at the hospital clinics have dyslipidaemia. As discussed in Section 3.10.3.1, it would cost approximately HKD88.11/patient/month to employ a clinical pharmacist to implement the CPS in the hospital. In order to have a pharmacist to manage

the entire population of 5,500 dyslipidaemic patients who visit the hospital every year, it would therefore cost HKD484,605 per year.

For every 7.14 patients who receive pharmacist intervention at the CPS, one patient can potentially avoid the risk of developing an AMI. Hence, among the 5,500 dyslipidaemic patients, approximately 770 patients can potentially avoid the risk of experiencing an AMI following pharmacist intervention. Lee *et al* (2005) evaluated that the average annual medical cost for AMI management in Hong Kong in the year 2000 was HKD72,720 per patient. The potential cost to treat 770 AMI patients would therefore be HKD55,994,400 per year.

Hence, the potential healthcare expenditure saving of having a CPS to help reduce the risk of dyslipidaemic patients developing an AMI would be approximately HKD50 million.

3.11 Clinical Pharmacy Service Satisfaction Survey

3.11.1 Validation of Survey

Validation of the patient questionnaire showed that there were no significant differences in the responses between the first survey and the second survey that was carried out one week later by the five patients who performed the validation [Table 3.23].

Table 3.23. Validation of Patient Questionnaire (n = 5)

Questions	Week 0 *n* (%)	Week 1 *n* (%)	P value
1. Satisfied with current medical care in lipid clinic			
Strongly Agree	0 (0)	0 (0)	-
Agree	4 (80.0)	4 (80.0)	-
No Comments	1 (20.0)	1 (20.0)	-
Disagree	0 (0)	0 (0)	-
Strongly Disagree	0 (0)	0 (0)	-
2. Understanding of medical condition being diagnosed			
Strongly Agree	0 (0)	0 (0)	-
Agree	5 (100)	5 (100)	-
No Comments	0 (0)	0 (0)	-
Disagree	0 (0)	0 (0)	-
Strongly Disagree	0 (0)	0 (0)	-
3. Explanation of prescribed medicines given by doctors			
Strongly Agree	0 (0)	0 (0)	-
Agree	3 (60.0)	4 (80.0)	*0.374*
No Comments	1 (20.0)	0 (0)	*0.374*
Disagree	1 (20.0)	1 (20.0)	-
Strongly Disagree	0 (0)	0 (0)	-
4. Understanding of indication of medicines			
Strongly Agree	0 (0)	0 (0)	-
Agree	5 (100)	5 (100)	-
No Comments	0 (0)	0 (0)	-
Disagree	0 (0)	0 (0)	-
Strongly Disagree	0 (0)	0 (0)	-
5. Understanding of possible adverse drugs effects of medication			
Strongly Agree	0 (0)	0 (0)	-
Agree	0 (0)	0 (0)	-
No Comments	1 (20.0)	0 (0)	*0.374*
Disagree	4 (80.0)	5 (100)	*0.374*
Strongly Disagree	0 (0)	0 (0)	-
6. Compliance with medications			
Always remember to take medicines as directed	0 (0)	0 (0)	-
Misses a dose once or twice every 3 months	4 (80.0)	4 (80.0)	-
Misses a dose once or twice every 1 month	1 (20.0)	1 (20.0)	-
Misses a dose once or twice every week	0 (0)	0 (0)	-
Does not take medicines at all	0 (0)	0 (0)	-
7. Provision of a Clinical Pharmacy Service at the lipid clinic would be beneficial			
Strongly Agree	0 (0)	0 (0)	-
Agree	4 (80.0)	3 (60.0)	*0.374*
No Comments	1 (20.0)	2 (40.0)	*0.374*
Disagree	0 (0)	0 (0)	-
Strongly Disagree	0 (0)	0 (0)	-

3.11.2 Questionnaire Survey for Intervention and Control Groups

The results of the patient satisfaction survey for the intervention group and the control group are presented in Tables 3.24 and 3.25 respectively.

In the intervention group, more than 90% of patients strongly agreed or agreed that the implementation of a CPS at the lipid clinic would be beneficial in the management of their dyslipidaemia. Patients also agreed that they gained a better understanding in the indications and possible adverse effects of their medications after being counselled by the clinical pharmacist.

Similarly, over 90% of patients in the control group commented that they would welcome the development of a CPS to help improve their dyslipidaemic management. The control group patients also demonstrated a poorer understanding in their medications with regards to the indications and side effects that they should be aware of.

Table 3.24. Patient Satisfaction Survey – Intervention Group (n = 150)

Questions	Baseline *n* (%)	End of Study *n* (%)	P value
1. Satisfied with current medical care in lipid clinic			
Strongly Agree	35 (23.3)	46 (30.7)	***0.001***
Agree	63 (42.0)	81 (54.0)	***<0.001***
No Comments	37 (24.7)	23 (15.3)	***<0.001***
Disagree	15 (10.0)	0 (0)	***<0.001***
Strongly Disagree	0 (0)	0 (0)	-
2. Understanding of medical condition being Diagnosed			
Strongly Agree	16 (10.7)	18 (12.0)	*0.158*
Agree	118 (78.7)	132 (88.0)	***<0.001***
No Comments	9 (6.0)	0 (0)	***0.002***
Disagree	6 (4.0)	0 (0)	***0.014***
Strongly Disagree	1 (0.6)	0 (0)	*0.319*
3. Explanation of prescribed medicines given by Doctors			
Strongly Agree	13 (8.7)	11 (7.3)	*0.158*
Agree	100 (66.7)	102 (68.0)	*0.158*
No Comments	14 (9.3)	11 (7.3)	*0.083*
Disagree	16 (10.7)	18 (12.0)	*0.158*
Strongly Disagree	7 (4.7)	8 (5.3)	*0.319*
4. Understanding of indication of medicines			
Strongly Agree	35 (23.3)	29 (19.3)	***0.014***
Agree	93 (62.0)	121 (80.7)	***<0.001***
No Comments	16 (10.7)	0 (0)	***<0.001***
Disagree	6 (4.0)	0 (0)	***0.014***
Strongly Disagree	0 (0)	0 (0)	-
5. Understanding of possible adverse drugs effects of Medication			
Strongly Agree	4 (2.7)	21 (14.0)	***<0.001***
Agree	19 (12.7)	122 (81.3)	***<0.001***
No Comments	2 (1.3)	3 (2.0)	*0.319*
Disagree	114 (76.0)	4 (2.7)	***<0.001***
Strongly Disagree	11 (7.3)	0 (0)	***0.001***
6. Compliance with medications			
Always remember to take medicines as directed	17 (11.3)	72 (48.0)	***<0.001***
Misses a dose once or twice every 3 months	54 (36.0)	64 (42.7)	***0.001***
Misses a dose once or twice every 1 month	63 (42.0)	11 (7.3)	***<0.001***
Misses a dose once or twice every week	16 (10.7)	3 (2.0)	***<0.001***
Does not take medicines at all	0 (0)	0 (0)	-
7. Provision of a Clinical Pharmacy Service at the lipid clinic would be beneficial			
Strongly Agree	50 (33.3)	61 (40.7)	***0.001***
Agree	89 (59.3)	89 (59.3)	-
No Comments	11 (7.3)	0 (0)	***0.001***
Disagree	0 (0)	0 (0)	-
Strongly Disagree	0 (0)	0 (0)	

Table 3.25. Patient Satisfaction Survey – Control Group (n = 150)

Questions	Baseline *n* (%)	End of Study *n* (%)	P value
1. Satisfied with current medical care in lipid clinic			
Strongly Agree	31 (20.7)	28 (18.7)	*0.083*
Agree	51 (34.0)	62 (41.3)	*0.001*
No Comments	43 (18.7)	41 (27.3)	*0.158*
Disagree	15 (10.0)	18 (12.0)	*0.083*
Strongly Disagree	0 (0)	1 (0.67)	*0.319*
2. Understanding of medical condition being Diagnosed			
Strongly Agree	19 (12.7)	14 (9.3)	*0.025*
Agree	121(80.7)	123 (82.0)	*0.158*
No Comments	7 (4.7)	8 (5.3)	*0.319*
Disagree	3 (2.0)	5 (3.3)	*0.158*
Strongly Disagree	0 (0)	0 (0)	-
3. Explanation of prescribed medicines given by Doctors			
Strongly Agree	10 (6.7)	11 (7.3)	*0.319*
Agree	103 (68.7)	98 (6.5)	*0.025*
No Comments	11 (7.3)	15 (10.0)	*0.045*
Disagree	18 (12.0)	20 (13.3)	*0.158*
Strongly Disagree	8 (5.3)	6 (4.0)	*0.158*
4. Understanding of indication of medicines			
Strongly Agree	32 (21.3)	32 (21.3)	-
Agree	89 (59.3)	90 (60.0)	*0.319*
No Comments	20 (13.3)	18 (12.0)	*0.158*
Disagree	9 (6.0)	10 (6.7)	*0.319*
Strongly Disagree	0 (0)	0 (0)	-
5. Understanding of possible adverse drugs effects of Medication			
Strongly Agree	2 (1.3)	2 (13.3)	-
Agree	15 (10.0)	13 (8.7)	*0.158*
No Comments	5 (3.3)	6 (4.0)	*0.319*
Disagree	120 (80.0)	122 (81.3)	*0.158*
Strongly Disagree	8 (5.3)	7 (4.7)	*0.319*
6. Compliance with medications			
Always remember to take medicines as directed	14 (9.3)	13 (8.7)	*0.319*
Misses a dose once or twice every 3 months	47 (31.3)	50 (33.3)	*0.083*
Misses a dose once or twice every 1 month	70 (46.7)	66 (44.0)	*0.045*
Misses a dose once or twice every week	19 (12.7)	21 (14.0)	*0.158*
Does not take medicines at all	0 (0)	0 (0)	-
7. Provision of a Clinical Pharmacy Service at the lipid clinic would be beneficial			
Strongly Agree	56 (37.3)	55 (36.7)	*0.319*
Agree	86 (57.3)	90 (60.0)	*0.045*
No Comments	8 (5.3)	5 (3.3)	*0.083*
Disagree	0 (0)	0 (0)	-
Strongly Disagree	0 (0)	0 (0)	-

3.11.3 Physician Questionnaire Survey on Clinical Pharmacy Service

Out of the ten questionnaires that were distributed to the physicians in the lipid clinic for completion, 6 responses were received. The results of the physician survey on the clinical pharmacy service that had been developed in this study are shown in Table 3.26. The physicians gave a positive impression of the service and valued the potential benefits of the clinical pharmacist in helping patients to obtain better control of their disease condition.

Table 3.26 Physician Questionnaire Survey (n = 6)

Questions	*n* (%)
1. Impression of Clinical Pharmacy Service	
Excellent	0 (0)
Good	6 (100)
Average	0 (0)
2. Range of services provided by the service	
Excellent	0 (0)
Good	5 (83.3)
Average	1 (16.7)
3. Value of the Physician-Pharmacist Communication Sheet	
Excellent	1 (16.7)
Good	4 (66.7)
Average	1 (16.7)
4. Recommendations provided by the pharmacist	
Excellent	1 (16.7)
Good	5 (83.3)
Average	0 (0)
5. Contact with the pharmacist	
Excellent	1 (16.7)
Good	5 (83.3)
Average	0 (0)
6. The Clinical Pharmacy Service provided for the patients	
Excellent	1 (16.7)
Good	4 (66.7)
Average	1 (16.7)

Chapter 4. Discussion

4.1 Clinical Outcomes of Study

4.1.1 Changes in Lipid Parameters

Although patients in both groups showed a reduction in their lipid parameters (total cholesterol, LDL-C and TG) at the end of the study, the reduction in the intervention group was much more than that found in the control group. In the intervention group, the overall mean reduction was 26.35% for LDL-C, 17.36% for total cholesterol, and 30.00% for TG levels. When this was compared to the control group, the mean reduction in these lipid levels was 2 times more for LDL-C, 3 times more for total cholesterol, and 3 times more for TG levels than that found in the control group.

This demonstrated that under usual physician care (i.e. the control group), there was already a lipid-lowering effect with the current dyslipidaemic management care taking place in the lipid clinic. However, with the involvement of a clinical pharmacist in addition to usual physician care (i.e. the intervention group), this lipid-lowering effect became more pronounced as shown by the difference in mean reduction of the different lipid values before and after the study period as discussed above. This observation could be due to the closer follow-ups provided by the pharmacist via both telephone calls and review of the patient's drug therapy during their clinic visits.

The time spent between the physicians and patients was usually about 10 minutes at each follow-up visit at the lipid clinic. In our study, patients often commented that the amount of time that the physicians spent explaining and discussing the state of their dyslipidaemic condition and prescribed medications was often inadequate. A lack of understanding of these facts by the patients can hinder the adherence to their lipid-lowering therapy. Kiortsis *et al* (2000) described that one of the most predictive factors of compliance with lipid-lowering therapy was the amount of time spent by the physicians with their patients in discussing their cholesterol levels and cardiovascular disease. Physicians often work under very tight schedules, making it difficult to meet all the needs of their patients. Pharmacists can therefore play a key role here, spending more time with patients at the clinic to review their condition whilst working in close collaboration with physicians, helping to manage dyslipidaemic patients together.

In our study, each patient spent approximately 20 minutes with the pharmacist at the lipid clinic during which they received education for drug and non-drug therapy and assessment for adverse effects and adherence with medications and lifestyle changes. This is comparable with the study by Munroe *et al* (1997) where the patients enrolled in their pharmacist-managed program for hypercholesterolaemia spent 15 to 20 minutes with a pharmacist. The results of the patient satisfaction survey carried out in the intervention group showed that following pharmacist counselling, patients gained a better

understanding in both their condition and their prescribed medications, particularly in the indication of their medicines and the possible adverse drug effects that they should be aware of.

4.1.2 Reduction in CHD risk

Brewer (2004) stated that a 0.026 mmol/L reduction in LDL-C level can reduce the risk of CHD by 1%. In our study, a 0.93 mmol/L mean reduction of LDL-C concentration was observed in the intervention group at the end of the study period. This reduction in LDL-C level provided a 35.8% reduction in the risk of CHD. In the control group, a 0.44 mmol/L mean reduction of LDL-C was seen and this related to a 16.9% reduction in CHD risk. Thus, the CHD risk reduction following pharmacist intervention was twice of that observed in the control group.

Holme (1993) also described that a reduction in total cholesterol of 1% (approximately 0.06 mmol/L) provided a 2% reduction in CHD risk. By the end of our study, a 1.05 mmol/L mean reduction of total cholesterol was found in the intervention group. This is therefore associated with a 35.0% reduction in CHD risk. In the control group, a 0.39 mmol/L mean reduction of total cholesterol was observed and this is associated with a 13.0% CHD risk reduction.

These results demonstrated the benefits of CPS in helping to reduce LDL-C, total cholesterol and TG concentrations in dyslipidaemic patients. At the same time, the CHD risk of these patients could also be greatly reduced.

4.1.3 Attainment in NCEP ATP III LDL-C Goals

More patients in the intervention group achieved the NCEP ATP III LDL-C goals when compared to those in the control group at the end of the study period. This was due to the impact of the CPS implemented in the intervention group.

A number of studies conducted in the United States have shown the value of CPS in improving the management of dyslipidaemia (Bozovich *et al* 2000, O'Donnell *et al* 2001). Despite the different healthcare setting in Hong Kong compared to that in the United States, our study demonstrated that pharmacist-managed lipid clinics was also beneficial in improving the NCEP ATP III LDL-C goal attainment in a public hospital in Hong Kong. Lee and Chow (2004) also demonstrated that the involvement of pharmacists had a positive impact on the management of dyslipidaemia in a private community hospital in Hong Kong.

In our study, 58.7% patients in the intervention group achieved the NCEP ATP III LDL-C goals at the end of the study compared to 45.3% patients in the control group. Although more patients in the intervention group reached their LDL-C goal targets, the rate of goal attainment achieved in our study is relatively small when compared to other similar studies (Konzem *et al* 1997, O'Donnell *et al* 2001, Lee and Chow 2004).

In the intervention group, 41.3% patients (n = 62) still did not achieve their recommended LDL-C levels following pharmacist intervention. The Lipid Treatment Assessment Project (L-TAP) showed that as the CHD risk of the patient increased, the likelihood of attaining their recommended LDL-C goals reduced. Patients with the lowest CHD risk (0-1 risk factor) were more likely to be treated to their LDL-C goals 68% of the time. High risk group patients (2+ risk factors) reached their LDL-C goals 37% of the time. Patients with documented CHD attained their LDL-C goal only 18% of the time (Pearson *et al* 2000).

Our study showed similar findings. Among the 62 intervention group patients who did not reach their LDL-C goals, 14.5% patients had the lowest CHD risk category (0-1 risk factor), 17.7% patients belonged to the high risk group (2+ risk factors), and 67.7% patients had documented CHD or CHD risk equivalents. Diabetes mellitus was also noted to be the main CHD risk equivalent factor found among these patients. Diabetes mellitus is known to

be one of the main causes of secondary dyslipidaemia (Walker 1999). These patients would require more potent lipid-lowering therapy and at the same time, adequate control of their blood glucose levels in order to optimize dyslipidaemic treatment.

Further analysis also showed that a major proportion of patients who did not reach their final LDL-C goals in both groups were patients diagnosed with familial hyperlipidaemia. In this study, 91 patients in the intervention group and 94 patients in the control group were documented to have familial hyperlipidaemia. Among the 62 patients in the intervention group who did not attain their recommended ATP III LDL-C level at the end of the study, 49 of them had familial hyperlipidaemia. The mean compliance rate with lipid-lowering drugs of these 49 familial hyperlipidaemic patients was 81.2%. This was satisfactory according to the compliance rate definition used in our study. This showed that despite patients being highly adherent to their treatment, familial hyperlipidaemic patients still had difficulty in achieving the target LDL-C levels, suggesting that more aggressive management needs to be sought for these resistant cases.

4.1.4 Predictors for LDL-C Goal Attainment

The odds of LDL-C goal attainment at the end of the 24-months study period for age 45 – 65 years lies within a CI range that excludes a value of 1 (odds ratio = 2.574, 95% CI, 1.322 – 5.012). It is therefore assumed that there is an association between LDL-C goal attainment and patients with age 45 – 65 years. Patients with this characteristic were more likely to achieve the LDL-C goal in this study.

Kiortsis *et al* (2000) have described that patients below 45 years or over 75 years were found to have poorer drug adherence. Patients below 45 years often lead busy lifestyles and therefore forget to take their medications in order to gain maximum benefits from their prescribed treatment. This group of patients also show a lack of understanding in the long-term health consequences of their dyslipidaemic condition, especially when dyslipidaemia is asymptomatic. Patients above 65 years often have other disease comorbidities in addition to dyslipidaemia, making it more difficult for them to reach their LDL-C goals. Kiortsis *et al* (2000) commented that patients in between these two age groups were more likely to adhere to their prescribed medications. This could explain why patients belonging to the age group, 45 – 75 years old, were more likely to attain their recommended LDL-C level in our study.

Nag *et al* (2007) showed that the odds of LDL-C goal attainment among patients newly diagnosed with CHD or diabetes were more likely among those who were above 65 years old, with a history of hypertension and a history of dyslipidaemia. In another study involving type II diabetic patients, the investigators found that men and patients with a history of hypertension were more likely to have achieved LDL-C goals (Putzer *et al* 2004). The comparison of the clinical predictors for LDL-C goal attainment found in this study to these trials would be unreliable. There are differences in the baseline sample demographics and risk factors, and a major proportion of the patients in our study group also had familial hyperlipidaemia, which makes direct comparison of other similar trials unreliable.

In our study, the number of patients with coronary heart disease, peripheral vascular disease, MI, stroke, atrial fibrillation and cardiac surgical intervention was too small to examine whether these group of patients were more likely to achieve the LDL-C goal attainment. The odds of LDL-C goal attainment were not affected by the other patient characteristics noted at baseline.

4.2 Drug-related Problems

4.2.1 Statin Dosing and LDL-C Lowering Potency

The latest NCEP ATP III guidelines (2004) have placed more emphasis on reaching LDL-C goals, especially for patients who belong to the high and moderately high CHD risk categories. Grundy et al (2004) described that the available statins used in landmark trials such as the HPS trial and the PROVE-IT study, prescribed statins at doses that provided a 30% to 40% reduction in LDL-C levels from baseline. This translates into a similar percentage reduction in CHD risk over a 5-year period.

Among the patients who were prescribed statins in this study, 18.5% patients in the intervention group and 15.7% patients in the control group were on statin doses that only provided a LDL-C lowering potency of below 30% which is not satisfactory. Goals for lipid-lowering drug therapy should be aimed at a 30% to 40% reduction in LDL-C levels. Suggestions were made by the clinical pharmacist to increase the statin doses or to change to a more potent statin for these patients, particularly for those who were at high CHD risks. During the study period, a number of statins such as simvastatin (Zocor®) were still on patent. Physicians explained that the choice of therapy available was restricted due to the hospital formulary budget concern of statin therapy. Pearson *et al* (2000) described that the cost of medications and the formulary choice of lipid-lowering therapy of the health management organization could

be a possible explanation for the low LDL-C goal attainment, even when the physicians are aware of the NCEP ATP III treatment guidelines.

Among the group of patients who were prescribed statins as their lipid-lowering drug therapy, 2.8% subjects in the intervention group and 4.3% subjects in the control group were on statin doses that provided a 50% to 59% reduction in LDL-C levels. Despite this, Grundy et al (2004) have described that LDL-C reductions of greater than 50% often cannot be achieved in practice since many patients do not modify their lifestyle behaviours. The authors described that using cholesterol-lowering drugs alone without lifestyle modifications is incorrect and cannot help to achieve the recommended LDL-C reductions. Patients should be educated that lifestyle changes along with good compliance with their lipid-lowering drugs are both important in order to gain optimal benefits for their dyslipidaemic management.

The main key subgroup of patients who were at high risks of CHD in this study included diabetics, patients with hypertension, patients with known CHD, and smokers. Among the diabetics, 26.1% diabetic patients in the intervention group and 24.3% diabetic patients in the control group received doses of stains that only provided a LDL-C reduction of below 30% from baseline. Among the hypertensive patients, 28.3% subjects in the intervention group and 25.4% subjects in the control group were on statin doses that failed to provide a 30% to 40% LDL-C reduction. Patients who had both diabetes

and hypertension were also noted to be receiving inadequate doses of statins. Among them, 25.0% patients in the intervention group and 21.4% patients in the control group were on statin doses with a LDL-C lowering potency of below 30%. A proportion of patients with known CHD who were prescribed statins as a secondary prevention also failed to receive adequate statin doses. In the intervention group, 28.6% CHD patients and 33.3% CHD patients in the control group were receiving statin doses that provided a LDL-C lowering potency of below 30%. Among the smokers, 18.2% subjects in the intervention group and 20.0% subjects in the control group were not receiving the recommended LDL-lowering potency of statin doses. This showed that despite the NCEP ATP III guidelines (2004), high-risk patients are still being prescribed inadequate doses of statins regardless of their baseline LDL-C levels in clinical practice.

4.2.2 Adherence to Drug Therapy

Dyslipidaemia is an asymptomatic condition and many patients perceive this as a minor disease with little impact on their health consequences. As a result, many patients do not adhere to their prescribed medications in order to obtain optimal LDL-C goals (LaRosa and LaRosa 2000). Andrade *et al* (1995) described that noncompliance with lipid-lowering drugs is a major issue worldwide that needs to be addressed. Likewise, noncompliance to drug therapy is also a problem in Hong Kong. A local survey showed that 30% of

patients with chronic conditions did not adhere with their long-term medications (Chui *et al* 2002).

Good compliance with lipid-lowering therapy is essential in order to maintain optimal LDL-C levels in accordance to the NCEP ATP III guidelines. Adherence to statin therapy of $\geq$ 80% was significantly associated with a lower risk of recurrent MI (Wei and Wang 2002). Another study also revealed that $\geq$ 75% level of adherence to pravastatin provided a substantial reduction in CHD risk in Western populations (Anonymous 1997).

The compliance rate achieved in this study was less than that observed in other similar studies (Lee and Chow 2004). The overall mean compliance rate increased from 77.54% to 79.83% at the end of the study. The compliance rate was also above $\geq$ 75% at both the beginning and end of the study period, which is satisfactory, according to the compliance rate definition used in our study. This shows that drug adherence is not a major issue in this study. These patients have been diagnosed with dyslipidaemia for a mean time of 9 to 10 years and have been taking lipid-lowering drugs during this length of time. As a result, the majority of patients have already established a regular habit of taking their prescribed lipid-lowering drugs accordingly. This suggests that the pharmacist could therefore focus on other lipid-lowering measures for these patients, for instance, healthy lifestyle modifications as recommended by the NCEP ATP III guidelines (2004).

When carrying out the medication compliance assessment in this study, a number of problems were encountered. The method of counting of unconsumed pills was used to assess the adherence to medications in our study. Prior to each educational visit, the clinical pharmacist phoned the patients to remind them to bring along all their unconsumed medications. This method of pill counting is an indirect assessment of adherence and is frequently used for measuring drug adherence (Ross and Hall 1998). However, there are a number of limitations with this method (Pullar *et al* 1989). Patients may fail to return all their remaining drugs or discard them before visiting the clinic. As a result, one would have to assume that patients had taken all their prescribed medications accordingly. On the other hand, patients may bring in all their medications including pills that were prescribed from previous visits, resulting in an inaccurate assessment of adherence.

In our study, a number of patients had the habit of storing all their pills prescribed from their current and previous clinic visits together in one container. This was particularly common among the elderly. The pharmacist had advised the patients to avoid this since it is not good practice. This also made the assessment of their drug adherence inaccurate which could have therefore led to the result of the lower compliance rate found than expected. Old medications should be discarded appropriately and this could be done so by handing any expired or unused medications to the pharmacy. However, in Hong Kong, patients seem to like to keep all their prescribed medications

including both expired drugs and medicines that they no longer need as a 'safe-keeping' purpose. In our study, no patients returned any of their unwanted medicines to the pharmacist.

Apart from the lipid clinic, a number of patients also visited other specialist clinics such as the diabetic clinic and hypertension clinic where they were prescribed their regular medications again, causing a duplication of the medications that they already had. In addition, some patients also obtained further supply of their medications from their private general practitioners. When these patients returned for their educational visits with the pharmacist, they brought back all their prescribed medications obtained from all the clinics that they had visited which led to an inaccurate assessment of their drug adherence. These factors could explain the small improvement observed in the overall compliance rate in our study. The overall mean compliance rate only increased by 2.95% at the end of the study period which was much lower than expected. These results also suggest that there is a problem with our healthcare prescribing system. Measures need to be sought to prevent overprescribing and duplication of prescribed medications for patients.

It is well documented that patient adherence with prescribed medications decreases with the duration of therapy. The greatest decline with drug adherence usually occurs in the first 6 months. The mean drug compliance rate with statins was 79% in the first 3 months and 56% in the

third to sixth months (Benner *et al* 2002). Simons *et al* (1996) also described that only 50% patients continue to take their prescribed lipid-lowering drugs 6 months after the prescription is initiated. This further reduced to 30 to 40% at 12 months. In our study, the mean compliance rate at baseline was 77.5% $\pm$ 9.9% and at the end of the 24-months study period, this increased to 79.8% $\pm$ 10.0%. The final mean compliance rate did not fall below 60% after the 24-months study period as described by Benner *et al* (2002) and Simons *et al* (1996). This could be explained by the regular telephone follow-ups in reminding the patients to complete their prescription and closer monitoring carried out by the pharmacist. The results achieved at the end of the study also showed an improvement in mean compliance rate regardless of the number of medications the patients were taking. The mean compliance rate even improved in patients who were only taking one drug. This shows that regular counselling and review with the pharmacist can help improve and maintain good patient adherence to prescribed therapy over the course of treatment.

Studies have demonstrated that patients who are aged 60 years or above had better drug adherence (Larsen *et al* 2002). Patients who are under 45 or over 75 years old were found to be poorer adherents (Kiortsis *et al* 2000). At the end of our study period, there were 47 patients who still did not achieve $\geq$ 75% mean compliance rate with their medications. Further analysis showed that among these non-compliers, 25 patients (53.2%) were aged less than 45 years old and 9 patients (19.1%) were aged above 75 years old. The

younger group of non-compliers (< 45 years old) were all working. They admitted to not taking their pills as directed and some mentioned that they often forgot taking their medicines due to the busy lifestyles that they led. This suggests that the pharmacist would need to find more innovative ways to remind these patients about good drug adherence. In order to meet their busy schedules, the pharmacist could consider using electronic mails or sending text messages to the patients' mobile phones as a reminder in the future. Some of these patients also showed a lack of understanding of their condition. They felt that dyslipidaemia was a minor disease with little consequences in their long-term health. They did not foresee themselves as having the possibility of developing AMI or other heart diseases. As a result, they did not follow their prescribed therapy accordingly.

4.2.3 Polypharmacy

Polypharmacy can be simply defined as 'prescription of more drugs than is clinically justified'. Some researchers define polypharmacy as taking four, five or more different medications (Reid and Crome 2005).

Polypharmacy is common in older people, particularly those above 70 years old (Reid and Crome 2005). In our study, the patients involved in the intervention group were relatively young with a mean age of 56.2 years old. This explains the relatively small number of patients identified with

polypharmacy (12.0% patients on four drugs and 16.0% patients on five drugs or more). The majority of patients (33.3%) were taking only one drug. Nevertheless, it is still important to monitor for polypharmacy as this can increase the risk of adverse drug reactions and at the same time, reduces the chance of satisfactory compliance. Polypharmacy does not involve only medications prescribed by physicians but also include drugs that patients might have bought OTC, Chinese medicines, and herbal products.

Reid and Crome (2005) described that patients who took more than two daily doses, or more than three different drugs were often found to be poor compliers. Among the non-compliers found at the end of our study, 11 patients were on five drugs or more. The nine 75-years-old non-compliers described previously were also amongst them. These patients were offered pill boxes to help improve their compliance with their medications. The results of the study showed that the provision of pill boxes to these patients did not help to increase their drug adherence as expected. Further discussion between the pharmacist and these patients revealed that they had not been using their pill boxes. They found the pill boxes inconvenient to carry around and some felt that they did not need the help of pill boxes despite the fact that they had been given one. They explained that they accepted the pill boxes when offered because they did not have to pay for one. In order to help patient to accept pill boxes, the pharmacist recommended the choice of using smaller pill boxes where appropriate and other means of compliance aids such as the use of a

drug diary. These advices were also reinforced when carrying out the regular telephone follow-up reminders.

In these non-compliers, the most common comorbidities were hypertension and diabetes mellitus. Most of the drug therapy regimen for hypertension was either once daily dose or twice daily doses. The drug therapy regimen for diabetes mellitus was either once daily, twice daily doses, three times daily doses, or more. Patients who were on three times daily doses or more often forgot to take their midday doses. These complex drug regimens should be reviewed regularly to assess whether they are appropriate for the patients.

Lindley *et al* (1992) explained that one reason for inappropriate polypharmacy is the failure to discontinue medicines that are no longer necessary. Doctors are reluctant to stop medicines that are prescribed by their colleagues, especially if they have limited information about the condition of the patient.

Regular medication review is the key to avoiding polypharmacy and clinical pharmacists can work together with physicians to help prevent 'overprescribing'. Studies in the United States have demonstrated the value of clinical pharmacist intervention to improve inappropriate prescribing in the elderly and patients with polypharmacy (Hanlon *et al* 1996). In the UK, the

NSF for Older People (DoH 2001) has also emphasized the importance of ensuring that the elderly receive appropriate medication review. Conducting a proper medication review is also an opportunity for pharmacists to educate the patient and improve drug compliance.

Apart from reviewing medicines prescribed by doctors, it is also important to check whether patients are taking other drugs. In our study, the pharmacist made specific enquiry about the over-the-counter (OTC) medications and any Chinese herbal products that patients might be taking. Physicians rarely ask their patients these questions and patients frequently will not volunteer this information unless asked specifically. The results of our study showed that 32.7% patients and 14.0% patients were taking OTC products and Chinese herbal medicines respectively in the intervention group. The common OTC products that patients were taking included simple analgesics, antacids, vitamins and mineral supplements. Chinese herbal medicines included products for common colds and flu, detoxifying agents and products for minor skin aliments such as eczema and allergic dermatitis.

4.2.4 Adverse Drug Events and Drug Interactions

The presence of intolerable drug side effects may stop patients from complying with their treatment (Ammassari *et al* 2002). Phansalkar *et al* (2007) described that pharmacists are considered better than other healthcare

professionals at detecting adverse drug events and potential drug interactions. In our study, the pharmacist identified 12.0% potential adverse drug effects and 7.3% potential drug interactions in the intervention group. Among the drug interactions identified, 2.0% involved induced bleeding effect, 2.6% involved reduced drug absorption effect, and 2.7% involved enzyme drug inhibition. From the survey conducted with these patients, 83.3% patients commented that they did not understand the possible adverse drug effects of their medication at the beginning of the study. Inadequate patient education has been suggested to be one of the reasons that can lead to adverse drug events (Schnipper *et al* 2006). Lack of knowledge of adverse drug effects can also hinder patient adherence with their medications. During the educational sessions with the pharmacist, patients were taught about the indications and potential adverse effects of their lipid-lowering therapy including medications that they were taking for other comorbidities. At the end of the study, only 2.7% patients still commented that they did not understand the possible adverse effects of the drugs that they were taking following pharmacist counselling. Schnipper *et al* (2006) described that pharmacist medication review, patient counselling, and telephone follow-up were associated with a lower rate of preventable adverse drug events.

The WHO, the Food and Drug Administration, and the Joint Commission on Accreditation of Healthcare Organizations have all recognized the importance of establishing mechanisms for detecting adverse

drug events and drug interactions in healthcare organizations (Phansalkar *et al* 2007). Similarly, this should also be considered in the healthcare system in Hong Kong. Pharmacists have the expertise to address drug-related problems (Classen *et al* 1991). They can therefore play an important role in adverse drug events surveillance activities, including participations with doctors during their ward rounds and clinic visits with patients.

4.2.5 Patient Busy Lifestyle

Patients commented that the monthly telephone follow-up calls conducted by the pharmacist were much more favourable than having to visit the lipid clinic. The majority of patients explained that they had a busy daily working schedule committed to either to their profession or to their families and childcare. If they had to visit the clinical pharmacist at the lipid clinic on a monthly basis to see the pharmacist, it would be very inconvenient for them. Using the means of telephone calls as a follow-up option was much preferred by these patients and could be just as effective as seeing the patients in person at the clinic.

A recent study conducted in a public hospital in Hong Kong showed that periodic telephone counselling by a pharmacist improved drug compliance, reduced mortality, and reduced the use of healthcare resources in patients receiving polypharmacy (Wu *et al* 2006).The investigators also found

that with regular telephone counselling calls, patients became more aware of their own health and medications.

Other ways of conducting these follow-ups and reminders for good drug adherence could be sought. Text messages and e-mails can be considered and these may be much more welcomed by patients of the younger generation and patients who lead a busy working lifestyle and may find taking phone calls inconvenient. In the UK, Sending Messaging System (SMS) text functionality can now be built into dispensary systems and messages can be sent to patients. This provides a cost-effective way for pharmacists to remind patients to collect prescriptions, to attend clinic appointments and to take their medicines (Anonymous 2006).

4.3 Role of Clinical Pharmacist

The NCEP ATP III guidelines (2001) have placed more emphasis on the importance of patient adherence with lipid-lowering therapy which includes both pharmacotherapy and healthy lifestyle changes. The various interventions recommended by the guidelines represent potential areas for pharmacists to be involved in the care of dyslipidaemia.

4.3.1 Role of Pharmacist

Bottorff (2006) described that pharmacists have numerous opportunities to recognize and recommend treatment for cardiometabolic risk factors and to increase patient compliance by educating patients and healthcare practitioners. In this study, the pharmacist acted as an educator to the patients in the intervention group, teaching them how to follow their prescribed treatment and reinforcing adherence. The educational sessions carried out by the pharmacist included information about dyslipidaemia, cardiovascular risk factors, diet, exercise, and drug-specific counselling including their indications and possible adverse effects to be aware of. Patients also had the benefits of regular communication with the pharmacist who was accessible via a telephone number provided to the patients.

With the rapport built between the pharmacist and the patients, and the rapport built between the pharmacist and the main healthcare professionals

(doctors and nurses), the pharmacist was in a well position, acting as the interface between the patients and their physicians, relaying and reinforcing information between both sides. The involvement of a clinical pharmacist in drug therapy management programs could reinforce the assessment of appropriate drug regimens through discussions between the pharmacist and patient, as well as between the pharmacist and physicians.

Based on the results of our study, the integration of a CPS into the lipid clinic would be beneficial for dyslipidaemic patients in Hong Kong. The pharmacist helped to manage lipid-lowering therapy with significant improvements in lipid parameters and in the number of patients who attained LDL-C treatment goals.

From the surveys conducted in both the intervention group and control group, 92.6% patients and 90.1% patients respectively agreed that having a CPS was favourable and could improve their dyslipidaemic management. The implementation of a CPS was welcomed.

4.3.2 Multidisciplinary Team

Our study showed that lipid values, NCEP ATP III LDL-C goal attainment and CHD risk reduction improved when a pharmacist contributed to the care in dyslipidaemia.

The Harvard Report recommended the use of a multidisciplinary team approach to improve the healthcare system for patients, and pharmacists are considered to be one of the major key players (Hsiao *et al* 1999). Thus, lipid treatment guidelines could be implemented through a multidisciplinary health-delivery system involving pharmacists working in close collaboration with physicians, nurses, dieticians and other healthcare professionals. Teamwork between the physicians and pharmacists is an effective approach to cholesterol reduction (Bogden *et al* 1997).

Multidisciplinary care with an enhanced pharmacist care program can help to improve the management of dyslipidaemia (Tsuyuki *et al* 2002). Through the establishment of pharmacist intervention programs in lipid clinics, pharmacists provided a wide range of functions that included reviewing medical history, monitoring laboratory values, selecting lipid-lowering therapies, and educating patients regarding drug therapies and the importance of compliance (Ito 2003). Bluml *et al* (2000) described that pharmacists can, in collaboration with physicians and patients, identify patients with

dyslipidaemia and support them in their efforts to improve drug compliance and the NCEP ATP III goal attainment.

Despite the recommendations provided by the Harvard Report and data showing the value of pharmacist-managed clinics, little progress has been seen over the last ten years within the healthcare organization of Hong Kong. Pharmacists are underused in physicians' practices. The majority of pharmacists are still dispensary-based with little recognition of their clinical ability and are underutilized as educators to patients. Both hospital clinical pharmacists and community-based pharmacists are readily accessible to patients. Pharmacists have a major role to play not only in the management of dyslipidaemia but also in other chronic conditions. The results from the physician questionnaire survey on the CPS showed that the doctors had a positive impression of pharmacists and valued their help in improving the healthcare of their patients. The establishment of multidisciplinary team care programs should be strongly considered in Hong Kong and their use should be encouraged.

4.3.3 Healthcare Cost Saving

Munroe *et al* (1997) showed that pharmacist involvement in dyslipidaemic management could potentially reduce the overall healthcare expenditures. The findings from this study demonstrated that the implementation of a CPS in the lipid clinic could potentially reduce CHD risk and thus the chances of patients developing an AMI. Lee *et al* (2005) evaluated that the average medical cost for AMI management in Hong Kong is approximately HKD72,720/patient/year. Hong Kong has a current local population of around 7 million. The estimated prevalence rate of CHD is 2.2% and 3% of these patient may experience and AMI. Based on these figures, the total estimated annual medical cost to manage all patients with AMI is approximately HKD340 million.

In order to sustain the CPS, it would cost an average clinical hospital pharmacist approximately HKD1057/patient/year to carry out the activities involved in this study. These include documentation of patient's medical health profile, drug history and laboratory parameters, as well as seeing the patient at the educational visits and following up the patient via monthly telephone calls and recording the data.

Based on the findings from this study, among the 5,500 dyslipidaemic patients seen at the PWH annually, around 770 patients can potentially reduce their risk of developing an AMI following pharmacist intervention at the CPS.

The estimated cost of having a clinical pharmacist to manage 5,500 patients per year is HKD484,605. The estimated cost of treating 770 AMI patients is approximately HKD55,994,400 per year. Having a CPS can potentially provide a healthcare cost saving of around HKD50 million per year at PWH alone. If CPS are developed in all the hospitals of Hong Kong, more patients can potentially have their CHD risks reduced, providing a further healthcare cost saving every year. Ito (2003) described that pharmacist intervention in lipid management programs was highly cost-effective and time efficient and these interventions were also associated with decreases in clinical events.

4.4 Limitations of Study

Several potential limitations have been identified in this study. Firstly, the study was not randomized and the physicians and nurses in the lipid clinic were not blinded to the patients who were involved in this study. Patients in both the intervention and control groups were seen by the same physicians in the lipid clinic. Medical colleagues and nurses were aware of the ongoing CPS that was implemented throughout the study period. The execution of this study may have influenced the physicians and nurses in promoting more attention when reviewing their patients and a change in their routine practice, resulting in a better management of the dyslipidaemic treatment for both the control group and intervention group.

Secondly, this study was carried out at a specialized clinic which managed the care of lipid control, including resistant cases of dyslipidaemia. A majority of these patients had familial hyperlipidaemia (60.7% in intervention group, 62.7% in control group). Familial hyperlipidaemia is an inherited metabolic disorder and these patients often need much more aggressive lipid-lowering therapy than those with normal dyslipidaemia who would respond satisfactorily with standard lipid-lowering treatment. The low LDL-C goal attainment rate found at the end of our study could have been due to the large proportion of familial hyperlipidaemic patients involved. If this study was conducted at another setting, for instance, the general outpatient

clinic (GOPC), the results might show a higher LDL-C goal attainment in patients attending the GOPC.

Thirdly, the clinical pharmacist carried out the questionnaire surveys in both the intervention and control groups. A third party was not involved. This could have therefore led to a bias in the results of the survey.

Fourthly, whilst carrying out this study in the outpatient lipid clinic, a number of environmental restrictions were encountered. The clinical pharmacist carried out the educational visits for the intervention group in the clinic rooms of the outpatient lipid clinic. These clinic rooms were not reserved solely for the pharmacist to conduct the CPS. Patients were seen by the pharmacist prior to seeing their physicians. Depending on the number of physicians working on the clinic day, there were times when all the clinic rooms were occupied and the pharmacist had to either relocate to another area of the lipid clinic or complete the CPS earlier than planned on the day. This was inconvenient for both the clinical pharmacist and for the patients. It would be ideal to have an area assigned or clinic room reserved for the pharmacist to carry out the CPS.

Finally, it was noticed that the timings of the follow-up visits of the patients involved in the study coincided with the festive seasonal period, particularly when their blood samples were taken for lipid profile and other

standard laboratory analysis. On average, patients returned to the lipid clinic for their follow-up visits every 4 to 6 months. This study started in October 2005 and when patients returned for their first follow-up visit, it was just after the Christmas and New Year period, followed by the Chinese New Year. Patients admitted that they had poorer diet control due to the festive season with social events and dinner parties with families and friends. This was reflected in their lipid levels with an increase in LDL-C, total cholesterol and TG concentrations. The second follow-up visits for some patients happened after the Easter holidays where a similar increase in their lipid parameters was seen. Other festive periods included the Dragon Boat festival and Mid-Autumn festival. This might have therefore limited the final potential LDL-C goal attainment in these patients.

4.5 Further Study

Our study demonstrated that clinical pharmacists have a major role to play and have a positive impact on the management of dyslipidaemia in a public hospital in Hong Kong. From the patient satisfaction survey, it also showed that patients welcome the involvement of pharmacists in the management of their condition. It would be worthwhile to continue the CPS in the lipid clinic and observe the long-term impact of pharmacist involvement in dyslipidaemic management. This would also show whether having a CPS in a public hospital in Hong Kong is sustainable or not with the current logistics and available funding.

In Hong Kong, CHD is a form of heart disease that is most common in the ageing population with baseline hypertension, diabetes mellitus and dyslipidaemia. With the development of new and innovative drug therapies to assist in managing cardiometabolic risk factors, this has created many opportunities for pharmacists to evaluate patients' drug regimens and influence lifestyle modification (Bottorff 2006). Apart from lipid control, the present study therefore paves way for the development of CPS in other problematic areas, especially in the management of hypertension and diabetes mellitus. These two conditions have also been identified as the two main co-morbidities among the patients in this study. Both hypertension and diabetes mellitus are well documented to be chronic and complicated morbidities for the development of CHD. They are also modifiable risk factors for CHD

manifestation and pharmacists have an opportunity to work as part of the multidisciplinary team and help improve the care and management of these patients. The success of pharmacist-managed hypertension clinics (Vivian 2002, Borenstein *et al* 2003) and diabetes mellitus clinics (Choe *et al* 2005) in other countries have been discussed. Similarly, CPS in these areas could be set up in Hong Kong.

Apart from specialized outpatient clinics, the integration of CPS could also be considered in general outpatient clinics (GOPC). Many outcome studies have been carried out on the pharmacist-initiated and pharmacist-managed clinics, and results have shown that pharmacists played an invaluable role in improving patient outcomes by finding and solving drug-related problems (Carmichael *et al* 2004). The authors described that the establishment of a model primary care pharmacy service system have provided a high-quality and cost-effective patient care service.

Chapter 5. Conclusion

5.1 Conclusion of Study

Outcomes in dyslipidaemic management can be improved with a clinical pharmacist as a member of the multidisciplinary lipid clinic team. This observation can be due to the closer follow-up provided by the pharmacist via both telephone calls and review of the patient's drug therapy during their clinic visits. The findings from this study supported the role of pharmacists in the management of dyslipidaemia through an integrated health system in a public hospital in Hong Kong.

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Appendices

Appendix I Data collection form

CPS - LDL - _____
Intervention / Control

Pharmaceutical Care Plan

Patient Details

Hospital No.: _____ Male / Female

DOB: _____
Age: _____

Education Level: _____
Occupation: _____

Allergies: _____

Telephone No.: _____

PC/Diagnosis:

HL

Year of Dx: _____

Co-Morbidities & PMH

HT	( )	Stroke	( )	Others:	
DM	( )	AF	( )		
CHD	( )	Cardiac Surgery	( )		
CHF	( )	Thyroid Disorder	( )		
PVD	( )	Gout	( )		
MI	( )				

FH:

HL	( )	Diet	( )		
HT	( )	Exercise	( )	Type: _____	Frequency: _____
DM	( )	Smoker	( )	No. of years: _____	
CHD/CVA	( )	Ex-Smoker	( )	No. of years: _____	
Others:		Alcohol	( )		

SH:

Drug Hx

OTC's	( )
Vitamins	( )
Mineral Supplements	( )
Chinese herbals	( )
Others:	

CPS - LDL - ____ Int / Control

Biochemistry & Haematology Monitoring Chart

Patient's Name:	M/F DOB: Height:

			Dates					
			Baseline	FU 1	FU 2	FU 3	FU 4	FU 5
	Unit	Ref.Range						
Urea & Electrolytes								
Na	mmol/L	135 - 145						
K	mmol/L	3.5 - 5.1						
Creatine	umol/L	62 - 106						
CrCl	ml/min	>60						
Urea	mmol/L	3.4 - 8.9						
Bicarbonate	mmol/L	22 - 30						
Cor.Ca	mmol/L	2.2 - 2.6						
PO4	mmol/L	0.8 - 1.4						
Liver Function Test								
ALT/GPT	IU/L	< 58						
AST	IU/L	10 to 40						
Total ALP	IU/L	M: 85 - 470 F: 45 - 145						
GGT	IU/L	M: < 61 F: < 36						
Alb	g/L	36 - 48						
Total Bil	umol/L	< 15						
Lipid Panel								
LDL	mmol/L	<2.6						
HDL	mmol/L	<1.04 >=1.55						
Total Chol	mmol/L	<5.2						
Total Trigl	mmol/L	< 2.0						
LDL Reference: <2.6; With 2 or more risk factors <3.4; With 0-1 risk factor <4.1. (NCEP JAMA 2001, 285(19): 2486-96)								
Haematology								
Hb	g/dL	13-17						
RBC	/L	4.5-5.5 x 10^{12}						
WCC	/L	3.9-11 x 10^{9}						
Platelets	/L	140-380 x 10^{9}						
MCV	fL	80-96						
ESR		<20mm in 1h						
CRP	MG	0-10						
CK or CPK	units/L	M: 42 - 218 F: 32 - 180						
INR		2.5						
Other Parameters								
Body Wt	kg							
BMI	kg/m^2	18.5 - 25						
Glucose	mmol/l	4.0-6.0						
HbA1C	%	5.1-6.4						
Blood Press	mmHg	120/80						
Pulse	/min							
Serum TSH		0.3-4.2						
Urate	mmol/L	0.19 - 0.43						
CHD Risks								
Risk Category								
CHD 10-year Risk (%)								
LDL Goal								
At Goal?		Y/N						

Appendix II Information sheet on study protocol to patient

The Chinese University of Hong Kong
School of Pharmacy

SUBJECT INFORMATION SHEET

1. **Title of Research Project**
   The impact of Clinical Pharmacy Services (CPS) on the LDL goal attainment with lipid lowering therapies.

2. **Names of Researchers/Position/Institution**

LEE Wing Yan, Vivian	Assistant Professor	
	School of Pharmacy	CUHK
Chung Siu Toye, Jennifer	Master of Philosophy Student	
	School of Pharmacy	CUHK
Lee Kwing Ching, Kenneth	Professor	
	School of Pharmacy	CUHK
TOMLINSON, Brian	Professor	
	Department of Medicine and Therapeutics	
	Faculty of Medicine	CUHK

3. **Purpose of the research**
   I have been invited to participate in a clinical research study to examine the impact of the implementation of a clinical pharmacy service on achieving the target LDL goal in patients who are on lipid lowering agents indicated for hypercholesterolaemia.

4. **Number of Subjects included in the study**
   A total number of 300 patients currently on lipid lowering therapies for hypercholesterolaemia at the outpatient Lipid and Hypertension Clinic of the Prince of Wales Hospital will be invited to participate in this study.

5. **Descriptions of the experiment**
   If I choose to participate in this study, I would have to follow the procedures outlined below:
   i) I would have my medical history recorded and physical examination conducted by a physician. A pharmacist will also review my medical records and provide me with medication advice where appropriate.
   ii) If I am eligible for the study, a single blood sample will be obtained from me at the Prince of Wales Hospital when I come for my medical review in clinic.

6. **Risks, discomforts and inconvenience associated with the research**
   The potential risks of this study include those associated with venipuncture. This includes bruising, pain and inflammation of the injection site. Chance of infection is, however, rare.

7. **Measures to be taken to minimize risks, discomforts and inconvenience**

Venipuncture will be performed by a medical professional to minimize the risks and discomfort caused.

8. **Expected benefits to subjects or others**

The findings of this study will identify:

i) The significance of setting up a clinical pharmacy service in attaining the LDL target in the management of hypercholesterolaemia.

ii) The clinical roles that a pharmacist can provide in optimizing patient's drug therapy.

9. **Payments to subject for participating in the study**

I will not be reimbursed for completion of the study.

10. **Confidentiality of information collected**

I will not be identified in any reports on this study. The records will be kept confidential in compliance with local law.

11. **Inquiries**

Professor Vivian WY LEE is more than willing to answer any of your inquiries regarding the above study. You may reach her at 2609-6860, School of Pharmacy, The Chinese University of Hong Kong.

12. **Voluntary nature of participation**

My participation in this project is voluntary. I may refuse to participate in or withdraw from the study anytime as I wish.

香港中文大學藥劑學院受試者須知

1. 研究項目

在臨床藥劑服務上對於低密度脂蛋白目標達到與減低脂質下治療的效果與影響

2. 項目研究首者/職位/機構

李詠恩	助理教授	香港中文大學藥劑學院
鍾熊小黛	哲學碩士學生	香港中文大學藥劑學院
李炯前	教授	香港中文大學藥劑學院
Tomlinson, Brian	教授	香港中文大學內科及藥物治療學系

3. 研究目的

我已被邀請參與是次計劃。此計劃目的是爲探討在臨床的藥劑學服務上對於低密度脂蛋白目標達到與減低脂質下治療以及病人進行降高膽固醇藥的效果與影響

4. 受試者之數目

此計劃爲沙田威爾斯親王醫院心血管學科門診應邀約見 300 名病患者參與對降低低密度脂蛋白指標在高膽固醇處理研究。

5. 研究內容

假若我選擇參與是次的研究, 我願意遵從以下的指示:

i) 開始時，研究人員將爲病者記錄病歷及由醫生爲病者作身體檢查。

ii) 如果本人附合研究條件，院方將抽取一血液樣本作詳細測試。

6. 實驗中可能產生之不適和不良反應

此計劃可能會產生之不良反應爲因抽取血液而引致的瘀傷、疼痛、針口發炎和機會較微的感染。

7. 在實驗中產生之不適和不良反應時的補救措施

靜脈穿抽血將由經過訓練者負責，以減低不良反應和不適。

8. 醫療上的得益

此計劃希望

i) 找出新的醫學模式及能建立臨床的配藥學服務而獲得對降低低密度脂蛋白指標在

高膽固醇處理

ii) 從而提昇藥物對病者的作用及減低不良反應以及對改善藥物質素的關係與地位。

9. 對受試者的報酬

我不會有任何形式的報酬。

10. 私隱及保密

我的身份將不會在此計劃報告發表。有關的研究資料及個人資料將被保密且受香港法保障。

11. 查詢有關本研究的詳情

本項目之研究者隨時樂意爲受試者解答有關本研究的問題。

請聯絡: 李詠恩教授 (香港中文大學藥劑學院；電話：2609-6860)

12. 參與研究的自願性

我的參與爲自願性。我可以拒絕或在任何時間退出此計劃。

Appendix III Patient consent form for study

INFORMED CONSENT FORM

STUDY TITLE: The impact of Clinical Pharmacy Services (CPS) on the LDL goal attainment with lipid lowering therapies

研究項目: 在臨床的藥劑學服務上對於低密度脂蛋白目標達到與減低脂質下治療的效果與影響

I_____, HK ID No. _____
ADDRESS: _____

hereby, would like to state that I have read the subject information sheet and have been fully explained the nature, purpose, procedure and possible risks of this study by the investigator concerned. I fully understand what is involved in this study and therefore consent to participate in it. I also understand that I have the right to withdraw from the study anytime as I wish.

志願者

本人_____,香港身份證號碼: _____
居住地址: _____

僅此聲明我已參閱過 受試者須知 並完全理解研究者向本人解釋之有關是項研究之性質, 目的, 程序及可能發生的問題。本人亦明白我享有隨時退出是項研究之權利。

Signature of Volunteer　　Signature of Witness
志願者簽署: _____　　見證人簽署: _____

Date　　Date
日期: _____　　日期: _____

INVESTIGATOR
研究者

I, hereby, would like to state that I have fully explained the nature, purpose, procedure and possible risks of this study to the above signed.
本人僅此聲明我已將有關是項研究之性質, 目的, 程序及可能發生的問題向志願者作了詳盡之解釋。

Signature of Investigator　　Date
研究者簽署: _____　　日期: _____

Appendix IV Framingham risk scoring system for male
(Source: Safeer and Ugalat 2002)

	20-34 years	35-39 years	40-44 years	45-49 years	50-54 years	55-59 years	60-64 years	65-69 years	70-74 years	75-79 years
Age	-9	-4	0	3	6	8	10	11	12	13
Total Cholesterol level mg/dL(mmol/L)										
<160 (4.15)	0		0		0		0		0	
160-199 (4.15-5.14)	4		3		2		1		0	
200-239 (5.15-6.18)	7		5		3		1		0	
240-179 (6.20-7.20)	9		6		4		2		1	
≥280 (7.25)	11		8		5		3		1	
Non-smoker	0		0		0		0		0	
Smoker	8		5		3		1		1	

HDL-C level mg/dL (mmol/L)	Points	Systolic Blood Pressure (mmHg)	If untreated	If treated
≥60 (1.55)	-1	<120	0	0
50-59 (1.30-1.53)	0	120-129	0	1
40-49 (1.05-1.27)	1	130-139	1	2
<40 (1.05)	2	140-149	1	2
		≥160	2	3

Point Total	10-year risk (%)	Point Total	10-year risk (%)
<0	<1	8	4
0	1	9	5
1	1	10	6
2	1	11	8
3	1	12	10
4	1	13	12
5	2	14	16
6	2	15	20
7	3	16	25
		≥17	>30

Appendix V Framingham risk scoring system for female
(Source: Safeer and Ugalat 2002)

	20-34 years	35-39 years	40-44 years	45-49 years	50-54 years	55-59 years	60-64 years	65-69 years	70-74 years	75-79 years
Age	-7	-3	0	3	6	8	10	12	14	16
Total Cholesterol level mg/dL(mmol/L)										
<160 (4.15)	0		0		0		0		0	
160-199 (4.15-5.14)	4		3		2		1		1	
200-239 (5.15-6.18)	8		6		4		2		1	
240-179 (6.20-7.20)	11		8		5		3		2	
≥280 (7.25)	13		10		7		4		2	
Non-smoker	0		0		0		0		0	
Smoker	9		7		4		2		1	

HDL-C level mg/dL (mmol/L)	Points	Systolic Blood Pressure (mmHg)	If untreated	If treated
≥60 (1.55)	-1	<120	0	0
50-59 (1.30-1.53)	0	120-129	1	3
40-49 (1.05-1.27)	1	130-139	2	4
<40 (1.05)	2	140-149	3	5
		≥160	4	6

Point Total	10-year risk (%)	Point Total	10-year risk (%)
<9	<1	17	5
9	1	18	6
10	1	19	8
11	1	20	11
12	1	21	14
13	2	22	17
14	2	23	22
15	3	24	27
16	4	≥25	≥30

Knowing my Medicines

What are lipid-lowering drugs for?

These drugs help to reduce the amount of cholesterol and fatty substances called triglycerides in your blood. Cholesterol is vital to the normal functioning of the body, but if levels in the bloodstream are too high, it can be deposited on the artery walls. This forms plaques, which can eventually block the blood vessel, leading to the development of coronary heart disease.

Different types of lipid-lowering drugs are available. Your doctor will prescribe you the most appropriate one to help lower your blood cholesterol.

How should I take my medicines?

You should take your medicines exactly as advised by your doctor or pharmacist. Keep taking your medicines for as long as your doctor has asked you to. If you stop taking your medicines, your cholesterol may rise again.

Can I take lipid-lowering medicines with my other tablets?

There are some medicines that may interact with lipid-lowering medicines. It is important that you tell your doctor or pharmacist any other medical conditions that you have, and all the medicines (both Western & Chinese medicines) that you are taking, including those bought over-the-counter and from health food shops.

What side effects could lipid-lowering medicines have?

The most common side effects are stomach upsets (sickness, stomach pain, constipation, diarrhoea and flatulence), rash, itchiness, headache or indigestion.

Rarely, inflammation of the muscles (myositis) and liver problems have been seen. If you have any unexpected muscle pain, tenderness or weakness, or if your skin or whites of your eyes turn yellow or your urine appears very dark in colour, consult your doctor immediately.

What happens if I miss a dose? What should I do?

If you forget a dose that you should have taken 2 to 4 hours ago and your next dose is not due for at least another 4 hours, then you can take a dose now. Otherwise, just carry on with the next one as normal. Do not take an extra one to make up. Never exceed the maximum number of tablets that you should take within 24 hours.

What should I do if I take too many?

If you take too many tablets by mistake, contact your doctor AS SOON AS POSSIBLE.

How should I store my medicines?

Always keep your medicines out of sight and reach of children. Do not share your medicines with anyone else, it may not suit them.

What else can I do to reduce the risk of developing Coronary Heart Disease?

Eat a healthy diet – try and increase the amount of fruit and vegetables in your diet and reduce the amount of sugar, salt and fat.

Lose weight – being overweight can increase your blood pressure, increase your risk of developing diabetes and increase the risk of developing heart disease.

Exercise – regular exercise for at least three 20-minute sessions each week helps to reduce blood cholesterol. This can be in the form of swimming, cycling, jogging, Chinese-style exercise like Tai Chi Chuan and Qi Gong, or even a brisk walk to shops can help.

Stop smoking – cigarette smoking increases the risk of developing heart disease. The more you smoke, the higher the risk. It is better to stop smoking altogether rather than just cutting down the number of cigarettes you smoke each day.

Always consult your doctor if you have any health problems.
Alternatively you can always seek advice from a pharmacist regarding your medicines.

藥物知多 D

爲甚麼要服食降血脂藥？
降血脂藥幫助減低血液裡的膽固醇和三酸甘油脂。膽固醇對身體的正常運作是很重要的，但如果血液裡的膽固醇含量過高，膽固醇便會容易黏在動脈血管壁上，形成沉積斑塊，最後造成血管的阻塞，引發冠心病。因此，現時有不同種類的降血脂藥。醫生會因應你的情況選擇最合適的藥物來幫助你降低血液膽固醇。

我應如何服食這些藥物？
你應完全遵照醫生或藥劑師的指示服食藥物。若非經醫生指示，請勿停止服用藥物。若擅自停止服用，你的血膽固醇可能會再次升高。

降血脂藥可以和其他藥物同服嗎？
有些藥物會和降血脂藥產生相互作用。告訴你的醫生或藥劑師你有的其他疾病和所有使用的藥物（包括於藥房或健康食品店購買的中、西藥或健康產品）。

降血脂藥有甚麼副作用？
這類藥物較常見的副作用爲腸胃不適（胃部不適、胃痛、便秘、肚瀉、腸胃氣脹），起疹，痕癢，頭痛，消化不良。
較罕見的副作用包括肌肉發炎和肝臟毛病。如果你感到肌肉疼痛、全身發軟或虛弱，皮膚或眼白變黃，或尿液顏色明顯加深，請立即聯絡你的醫生。

如果忘記了服藥會有甚麼後果？應怎麼辦？
如果你忘記的該次藥物二至四小時及下一劑藥物的服用時間不少於四小時，你應即時服藥。否則，你要等待下一次原來的時間服藥。不要自行多服一劑藥物來彌補忘記了服用的藥物。不能服用超過二十四小時內最多可服的份量。

如果我服了太多藥物，應怎麼辦？
若你意外地多服了藥物，請盡快聯絡你的醫生。

我應如何存放我的藥物？
藥物應放在兒童不能看見或觸及的地方。不要和其他人分享藥物，因爲你的藥物未必適用於其他人。

除了服食降血脂藥外，還有甚麼地方我可以做多一點以減少引發冠心病的機會？
健康的飲食習慣 – 嘗試在日常飲食中增加食用纖維水果和蔬菜的份量，及減少糖份、鹽份和脂肪的攝取。
減肥 – 過重會增加你的血壓、引發糖尿病和心臟病的機會。
運動 – 每星期三次以上每次二十分鐘的正確規律運動可幫助降低膽固醇。這些運動包括游泳、踏單車、緩步跑、中國式的運動如太極拳、氣功，甚至逛街都有效。
停止吸煙 – 吸煙可增加患心臟病的機會。你吸煙愈多，患心臟病的機會愈大。完全戒煙比減少每天吸煙數量的效果更好。

如有任何健康問題，請教你的醫生。
有任何關於藥物的問題，請教你的藥劑師。

Appendix VII Physician-pharmacist communication sheet

Physician-pharmacist communication sheet

School of Pharmacy, the Chinese University of Hong Kong

To Doctor: .....

From Clinical Pharmacist: .....

(Pharmacist Contact No: 64735700)

Case Number: .....

Date: .....

Appendix VIII Telephone checklist

Telephone Follow-Up Assessment Form (CPS-LDL-Project)

Patient Name: _____ Patient No.: _____

Pt. Study No.: CPS – LDL - ____ Assessment Date: _____

Checklist	Comments
General Well Being	
❑ How have you been feeling over the last 4 weeks? 1 Very poorly 2 Poor 3 Average 4 Good 5 Very Well	
Medication Pill Box	
❑ Have you been using the pill box? If no, why? ❑ Who fills in the pill box? ❑ Any problems?	
Patient Medicines	
❑ Do you understand what your medicines are indicated for? ❑ What dose of the medication are you taking? ❑ How many times during the day do you take your medicines? ❑ Have you been taking all medicines as instructed? If no, why? ❑ Have you missed any doses in the last 4 weeks? If so, why and what did you do? ❑ Have you bought any medicines yourself (OTC, herbal, Chinese medicines)? ❑ Have you been prescribed any new medicines from other clinic visits or from your own GP? ❑ Have there been any changes to your medicines?	

Side Effects	
❑ Have you felt any discomfort or side-effects from your medicines? ❑ If so, check for any new medicines including OTCs, herbal and Chinese medicines.	
Diet, Exercise & Healthy Lifestyle	
❑ Have you been keeping a low-fat diet? ❑ Have you increased your vegetable and fruit intake? ❑ Have you been doing 20-minute sessions of exercise? ❑ If yes, what type of exercise and how frequent? ❑ If patient is a smoker, has patient tried to cut down smoking?	
Educational Material	
❑ Have you read any of the leaflets provided? ❑ Any questions?	
Others	
Summary of any Actions taken/ Advice given/ Interventions	
Next Assessment Date: _____	

Appendix IX Questionnaire survey provided to Intervention Group

(CPS-LDL-Intervention Group)

Patient Satisfaction Survey of a Clinical Pharmacy Service at the Outpatient Lipid Clinic, Prince of Wales Hospital (PWH)

Please complete the following questionnaire, keeping in mind the medical care you are receiving now. We are interested in your feelings, *good* and *bad* about the medical care you have received. Your feedback will help us identify areas where we can improve our service for you.

How strongly do you AGREE or DISAGREE with each of the following statements?

Circle One Number on Each Line

	Strongly Disagree ☹	Disagree	Uncertain	Agree	Strongly Agree ☺	Not Applicable
1. I am happy with the medical care that I am receiving at the lipid clinic.	1	2	3	4	5	0
2. I understand the medical condition that I have been diagnosed.	1	2	3	4	5	0
3. My doctor always explains to me about my medicines.	1	2	3	4	5	0
4. I am happy to take my medicines.	1	2	3	4	5	0
5. I understand the purpose of my medications and the possible side effects.	1	2	3	4	5	0
6. I always remember to take my medicines as instructed.	1	2	3	4	5	0
7. I try and lead a healthy lifestyle (low-fat diet, no smoking, exercise).	1	2	3	4	5	0
8. After seeing a pharmacist, I understand about my medicines better than before.	1	2	3	4	5	0
9. I find the clinical pharmacy service provided helpful.	1	2	3	4	5	0
10. The time allocated to see the pharmacist was convenient and appropriate.	1	2	3	4	5	0
11. The pharmacist was able to answer my enquiries regarding my pills and condition.	1	2	3	4	5	0
12. I would like to continue seeing a clinical pharmacist during my outpatient visits.	1	2	3	4	5	0

Please add any comments or suggestions below:

_____

_____

_____

On completion, please return this form to the outpatient lipid clinic.

Thank you for your time and help

(CPS-LDL-Intervention Group)

沙田威爾斯親王醫院血脂科門診臨床藥劑學服務
病人滿意程度調查

請根據你現時完成以下問卷。我們希望能夠得知你對現時所得到的醫療服務的評價。我們會參考你寶貴的意見用作改進提供的醫療服務。

你對以下句子的同意／不同意程度有多少？

請於每行圈出一個號碼

	極不同意 ☹	不同意	無意見	同意	極同意 ☺	不適用
1. 我對現時血脂科門診的醫療服務感到滿意。	1	2	3	4	5	0
2. 我明白醫生對我診斷出的病況。	1	2	3	4	5	0
3. 醫生每次都向我解釋給我的藥物。	1	2	3	4	5	0
4. 我樂於服食我的藥物。	1	2	3	4	5	0
5. 我明白我的藥物的效用和可能發生的副作用。	1	2	3	4	5	0
6. 我每次都記得遵照指示依時服藥。	1	2	3	4	5	0
7. 我會嘗試過健康的生活（如低脂飲食，不吸煙的習慣）	1	2	3	4	5	0
8. 見臨床藥劑師之後，我比以前更了解自己服食的藥物。	1	2	3	4	5	0
9. 藥劑師藥物教育服務對我有幫助。	1	2	3	4	5	0
10. 約見臨床藥劑師的時間方便和適合。	1	2	3	4	5	0
11. 藥劑師能解答我對藥物和病況的問題。	1	2	3	4	5	0
12. 我希望於門診時繼續見臨床藥劑師。	1	2	3	4	5	0
13. 當有需要時，我很容易找到臨床藥劑師查詢。	1	2	3	4	5	0

請在以下空位寫上其他評語或建議：

_____

_____

_____

完成後，請將問卷交回心血管學科門診。

謝謝你的幫助！

Appendix X Questionnaire survey provided to Control Group

(CPS-LDL-Control Group)

Patient Satisfaction Survey of a Clinical Pharmacy Service at the Outpatient Lipid Clinic, Prince of Wales Hospital (PWH)

Please complete the following questionnaire, keeping in mind the medical care you are receiving now. We are interested in your feelings, *good* and *bad* about the medical care you have received. Your feedback will help us identify areas where we can improve our service for you.

How strongly do you AGREE or DISAGREE with each of the following statements?

Circle One Number on Each Line

	Strongly Disagree ☹	Disagree	Uncertain	Agree	Strongly Agree ☺	Not Applicable
1. I am happy with the medical care that I am receiving at the lipid clinic.	1	2	3	4	5	0
2. I understand the medical condition that I have been diagnosed.	1	2	3	4	5	0
3. My doctor always explains to me about my medicines.	1	2	3	4	5	0
4. I am happy to take my medicines.	1	2	3	4	5	0
5. I understand the purpose of my medications and the possible side effects.	1	2	3	4	5	0
6. I always remember to take my medicines as instructed.	1	2	3	4	5	0
7. I try and lead a healthy lifestyle (low-fat diet, no smoking, exercise).	1	2	3	4	5	0
8. If a clinical pharmacy service was available, I will be happy to participate.	1	2	3	4	5	0
9. A pharmacist will help me understand my medicines better.	1	2	3	4	5	0
10. I would like to obtain advice from a pharmacist besides my doctor.	1	2	3	4	5	0
11. A pharmacist can answer my questions regarding my pills and condition.	1	2	3	4	5	0
12. I would be happy to see a clinical pharmacist during my outpatient visits.	1	2	3	4	5	0

Please add any comments or suggestions below:

_____

_____

_____

On completion, please return this form to the outpatient lipid clinic.

Thank you for your time and help

(CPS-LDL-Control Group)

沙田威爾斯親王醫院血脂科門診臨床藥劑學服務
病人滿意程度調查

請根據你現時完成以下問卷。我們希望能夠得知你對現時所得到的醫療服務的評價。我們會參考你寶貴的意見用作改進提供的醫療服務。

你對以下句子的同意／不同意程度有多少？

請於每行圈出一個號碼

		極不同意 ☹	不同意	無意見	同意	極同意 ☺	不適用
1.	我對現時血脂科門診的醫療服務感到滿意。	1	2	3	4	5	0
2.	我明白醫生所診斷我的病況。	1	2	3	4	5	0
3.	醫生每次都向我解釋給我的藥物。	1	2	3	4	5	0
4.	我樂於服食醫生給我的藥物。	1	2	3	4	5	0
5.	我明白我的藥物的效用和可能發生的副作用。	1	2	3	4	5	0
6.	我每次都記得遵照指示依時服藥。	1	2	3	4	5	0
7.	我會嘗試過健康的生活（如低脂飲食，不吸煙的習慣）	1	2	3	4	5	0
8.	如有藥劑師藥物教育服務，我會樂意參加。	1	2	3	4	5	0
9.	藥劑師將會令我更了解自己服食的藥物。	1	2	3	4	5	0
10.	除了醫生的勸告，我還希望得到藥劑師的建議。	1	2	3	4	5	0
11.	藥劑師可以解答我對藥物和病況的問題。	1	2	3	4	5	0
12.	我希望於門診時見臨床藥劑師。	1	2	3	4	5	0

請在以下空位寫上其他評語或建議：

_____

_____

_____

完成後，請將問卷交回心血管學科門診。

謝謝你的幫助！

Appendix XI Questionnaire survey provided to Physicians

Physician Satisfaction Questionnaire on the Clinical Pharmacy Service at the Outpatient Lipid Clinic, Prince of Wales Hospital

Dear Doctors,

We would kindly appreciate if you could spend a few minutes to complete this questionnaire in order for us to assess the quality of the clinical pharmacy service (CPS) that we have been providing as part of our project at the Outpatient Lipid Clinic over the past 12 months. Your comments will be deeply valued. Thank you.

Kind Regards
The School of Pharmacy, CUHK.

Physician Name (Optional): _____ **Phone (Optional):** _____

4 = Excellent 3 = Good 2 = Average 1 = Below Average NA = Not Applicable

Please rate the following:

1. Your initial impression of our CPS at the Lipid Clinic:
   4 3 2 1 NA

2. The range of services provided by the CPS:
   4 3 2 1 NA

3. The value of the Physician-Pharmacist Communication Sheet:
   4 3 2 1 NA

4. The recommendations provided by the pharmacist on the Physician-Pharmacist Communication Sheet:
   4 3 2 1 NA

5. Your contact with our pharmacists and other members of the CPS team:
   4 3 2 1 NA

6. The CPS that we have provided for your patients:
   4 3 2 1 NA

7. To the best of your knowledge, please rate your patients' experience with us:
   4 3 2 1 NA

8. Would you like to see CPS being developed at the Lipid Clinic and in other clinical settings? (Please tick)
   ☐ Yes ☐ No
   If Yes, what other settings would you have in mind?
   _____
   _____

9. Please add any comments or suggestions
   _____
   _____
   _____

On completion, please return to the outpatient lipid clinic.
Thank you for your time.