ASSESSMENT OF THE PRESCRIBING PATTERNS OF LIPID LOWERING DRUGS AT THE ADULT UNIVERSITY TEACHING HOSPITAL IN LUSAKA ZAMBIA

By

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Bpharm,DipPharm

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Masters of Clinical Pharmacy

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DECLARATION

I, **Luke L. Biete** hereby declare that the work in this discussion is original except where acknowledgements indicate otherwise.

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APPROVAL

This dissertation of Luke Lundau Biete has been approved as fulfilling the requirements or partial fulfillment of the requirements for the award of Master of Clinical Pharmacy by the University of Zambia

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Examiner 3.…….....

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Date ……..

Chairperson Board of Examiners …….

Signature ……...

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Supervisor …….....

Signature ……..

Date ……..

DEDICATION

This dissertation is dedicated to my lovely wife Nancy Sambwa Biete, my dear son Luke Lundau Biete (Jr.) and my dear daughter Kisu Kashimbi Biete for their encouragement, support and sacrifice during the entire period I stayed away from them doing my studies, my late parents Mr. Biete Zwau and Mrs. Margaret A.M Biete for their wonderful parental guidance, my elder brother Remmy Biete for his unwavering support and encouragement since my early days of schooling and my entire family for their encouragement and support. In a special way, I would want to dedicate this work to the Almighty God for his sustenance and guidance during the period of my studies.

ABSTRACT

Background: Appropriate drug utilization has a huge contribution to global reduction in morbidity and mortality. While thousands of patients have been wrongly prescribed statins, others at high risk of cardiovascular accidents (CVA) have been deprived of treatment. According to the Adult Treatment Panel fourth guidelines (ATP IV), prescription of Lipid Lowering Drugs (LLDs) should not only be based on cholesterol but also on other Atherosclerotic Cardiovascular Disease (ASCVD) risk factors.

Methods: A cross sectional design was applied to 140 files of patients at clinic 5 (medical clinic) of the Adult University Teaching Hospital (Adult UTH) and it aimed to determine whether the prescribing patterns of LLDs were in conformity with the ATP IV guidelines. This sample size was based on a 10% (0.1) estimated prevalence of prescriptions containing LLDs in line with the 2014 WHO country profile on Non-communicable diseases (NCDs) which accounted for 23% death estimates in Zambia out of which 8% were due to CVDs. Based on prescriptions given, files of patients for whom LLDs were prescribed were identified out of which study samples were randomly selected. IBM SPSS version 21.0 was used for statistical analyses.

Results: There were 89(63.6%) female and 51(36.4%) male patient's files reviewed. Hypertension (HTN) was the most frequent risk 126(90%) while CVDs were the most common diagnosis category 93(66%). Among the 140 patients whose files were reviewed, 64(45.5%) were found to be eligible for the LLD therapy while 76(54.3%) were not though the difference was not statistically significant (p-value = 0.31). The most commonly prescribed LLD was atorvastatin 20mg 91(65%) while rosuvastatin 20mg and omega-3 were the least prescribed each representing 1 patient (0.7 %). All 64 eligible patients were prescribed atorvastatin out of whom 10(15.6%) received appropriate dosing while 54(84.4%) received inappropriate dosing (Statistically significant: p-value < 0.001). The chi-square exact test results showed that only diagnosis category and prescribed LLDs were significantly associated with dosing appropriateness among the categorical variables (P-values = 0.02 and < 0.001 respectively) while for continuous variables, lipogram duration was significantly associated with dosing appropriateness(P-value <0.001). The unadjusted odds ratios (OR) showed that patients with CVD diagnosis had on average 13 times increased odds for inappropriate dosing (OR = 13.2, CI = 1.76 – 98.93, p-value = 0.01).

Conclusion: This study suggests that the prescribing patterns were not in conformity with the ATP IV guidelines as they were more inclined to individual CVD risk factors and not the individual patients' overall levels of risk.

Key words: Assessment, Prescribing Patterns, Lipid Lowering Drugs

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ABBREVIATIONS

ACC	-	American college of cardiology
AHA	-	American heart association
ASCVD	-	Atherosclerotic cardiovascular disease
ATP	-	Adult treatment panel
ATP III	-	Adult treatment panel third report
ATP IV	-	Adult treatment panel fourth report
BMI	-	Body mass index
CAD	-	Coronary artery disease
CHD	-	Coronary heart disease
CV	-	Cardiovascular
CVDs	-	Cardiovascular diseases
DM	-	Diabetes mellitus
EAS	-	European atherosclerotic society
ECG	-	Electrocardiogram
ESC	-	European society of cardiology
FDA	-	Food and Drug administration
GP	-	General practitioner
HDL – C	-	High density lipoprotein cholesterol
IHD	-	Ischaemic heart disease
LDL – C	-	Low density lipoprotein cholesterol
LLDs	-	Lipid lowering drugs
LLT	-	Lipid lowering therapy
MI	-	Myocardial infarction
NCDs	-	Non-communicable diseases
NCEP	-	National cholesterol education program
NHANES	-	National health and nutrition examination survey

RCT	-	Randomized control trials
SCORE	-	Systemic Coronary Risk Estimation
TC	-	Total Cholesterol
TG	-	Triglycerides
TLC	-	Therapeutic lifestyle changes
UTH	-	University Teaching Hospital
WHO	-	World Health Organization

DEFINITIONS AND ACRONYMS

Atherosclerosis: a condition where the arteries become narrowed and hardened due to an excessive build up of plaque around the artery wall. The disease disrupts the flow of blood around the body thereby, posing serious cardiovascular complications.

Coronary heart disease: Coronary heart disease (CHD) which sometimes is also described as coronary artery disease (CAD) is a condition in which the vascular supply to the heart is impeded by atheroma (Atherosclerosis of the epicardial vessels), thrombosis or spasms of coronary arteries which may impair the supply of oxygenated blood to the cardiac tissue thereby, causing myocardial ischaemia which if prolonged may cause the death of cardiac muscle cells, i.e. a myocardial infarction (MI).

Dyslipidaemia: elevated total cholesterol (> 4mmol/L), elevated LDL-C (> 2mmol/L), elevated triglycerides (> 1.7mmol/L) levels with a low HDL-C concentration (< 1.0mmol/L in men and < 1.2mmol/L in women) or some combination of these abnormalities.

Ischaemic heart disease (IHD): include all causes of myocardial ischaemia which may present as an acute coronary syndrome (unstable angina, N-STEMI or STEMI, chronic stable exertional angina pectoris and ischaemia without clinical symptoms.

Risk factor: a measurable element or characteristic that is causally associated with an increased rate of a disease that is an independent and significant predictor of the risk of presenting a disease.

CHAPTER ONE
BACKGROUND AND INTRODUCTION

1.1 Introduction

Appropriate drug utilization has a huge contribution to global reduction in morbidity and mortality with its consequent medical, social and economic benefits (Tefera et al., 2002) while on the other hand, inappropriate prescribing is known all over the world as a major problem of health care delivery (Erah et al., 2003).

According to the World Health Organization (WHO), more than half of all medicines are inappropriately prescribed, dispensed or sold (WHO, 2011), with such practices being most prevalent in healthcare settings in the developing world where mechanisms for routine monitoring of medicines use are still in early stages of development (Massele et al., 2015).

It has been reported in the United Kingdom (UK) that thousands of patients may have been wrongly put on statins, a class of lipid lowering drugs (LLDs) while others at high risk of cardiovascular accidents (CVA) have been deprived of treatment following a major National Health Service (NHS) blunder. The errors in the system used by one in three practices meant that patients with little risk of heart diseases may have been needlessly prescribed the LLDs while those in grave danger of CVAs were not offered the medications (Donnelly, 2016).

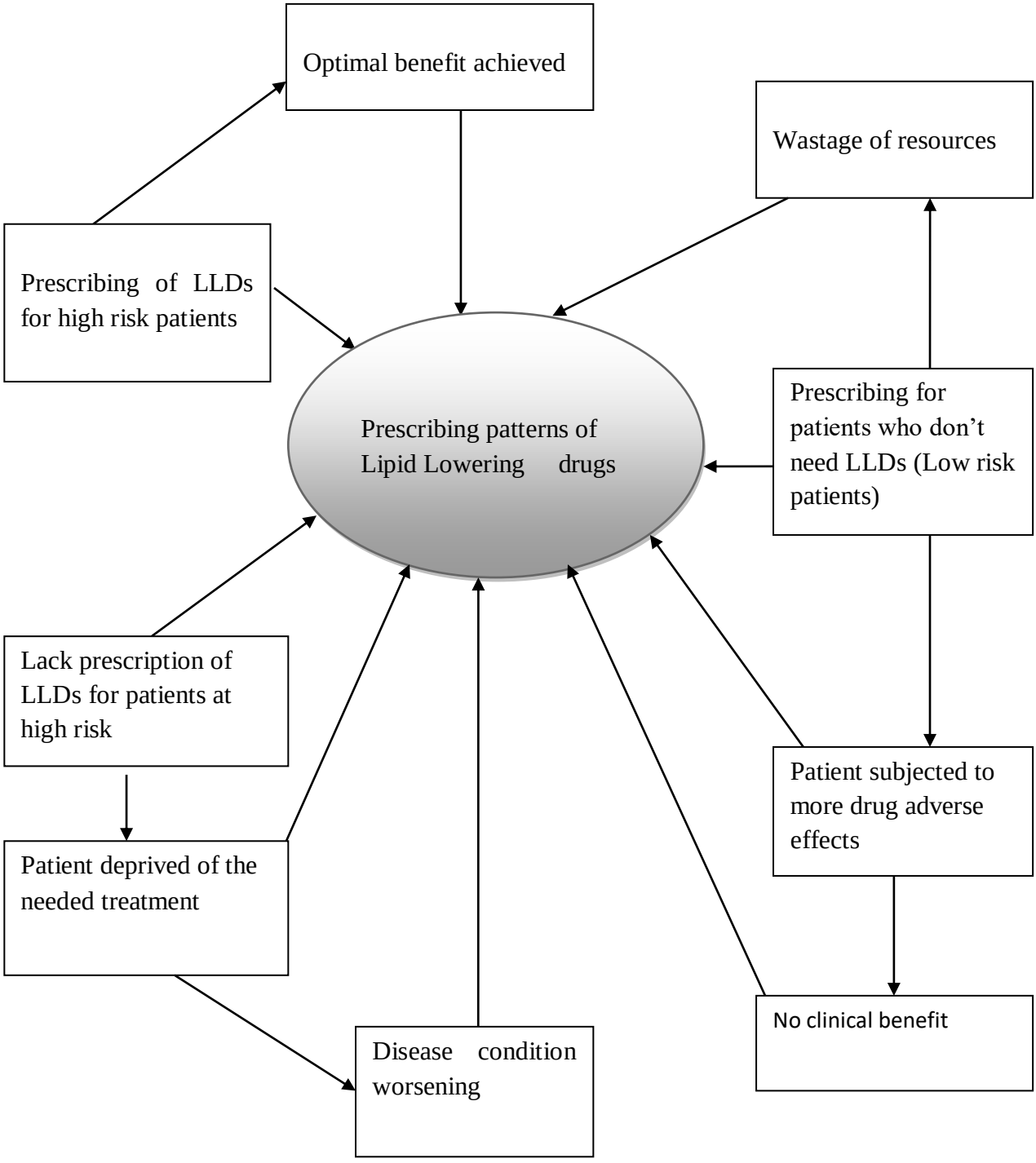
It is established that LLDs are used both in primary and secondary prevention of cardiovascular diseases (CVDs), primary prevention being that which is undertaken in individuals with a high risk of developing CVDs while secondary prevention is undertaken to prevent recurrence of events in those with established CVDs (Martins et al., 2010). If target levels cannot be reached even on maximal doses of LLDs therapy or drug combinations, patients will still benefit from treatment based on the extent to which the dyslipidaemia has been improved as evidence shows that for every mmol/L reduction in LDL-C; there is a 10% reduction in mortality, 20% reduction in all-cause morbidity, 23% reduction in major cardiac events and 17% reduction in stroke (Klug et al, 2012). Further, pleiotropic effects of statins also play a part in CV events prevention through improvement in endothelial function, plaque stabilization, anti-inflammatory effect, anti-coagulative effects, anti-oxidant activity and reduced plasma viscosity (Werner et al., 2002).

The benefit of statins for prevention of cardiovascular (CV) events in type 2 diabetes is established, but a gap exists between guidelines recommendations and clinical practice (Berthold et al., 2009). Another point worthy noting is that while treatment of those with the highest risk level will bring the most desired benefit, treatment of those with low risk of CVDs may just expose them more to adverse drug effects and would not benefit much (Preis et al., 2009).

The ultimate goal of the new cholesterol practice guidelines is to reduce a person's risk of cardiovascular accidents (CVA), stroke and death. Therefore, commencement of LLDs treatment should not just be based on cholesterol alone but it should be considered along with other factors known to make a CVA or stroke more likely (Goff et al., 2013). Further, identifying whether someone already has or is at risk for atherosclerotic cardiovascular disease (ASCVD) and could benefit from treatment is very cardinal and greater emphasis should be placed on the prevention of coronary heart disease (CHD) in patients with multiple risk factors in addition to treatment for secondary prevention as stipulated by fourth guidelines of the Adult Treatment Panel of 2013 (ATP IV, 2013). In these guidelines, patients with low density lipoprotein cholesterol (LDL-C) ≥ 4.92 mmol/L (190 mg/dl), Diabetes and aged 40-75 years with LDL-C between 1.81 – 4.90 mmol/L (70-189 mg/dl), no diabetes but with an estimated 10 year ASCVD risk of ≥7.5 % who are between 40 to 75 years of age with LDL-C between 1.81 – 4.90mmol/L (70-189 mg/dl) qualify to be prescribed LLDs under primary CVDs prevention . On the other hand, patients with known CHD like myocardial infarction (MI), angina, prior stroke, transient ischaemic attack (TIA), peripheral arterial disease and coronary revascularization, combination of risk factors that result in a 10 year risk of atherosclerotic cardiovascular disease (ASVD) events of ≥ 20 %, chronic kidney disease with estimated GFR < 45mls/min/ 1.73m^2 and risk equivalent for CVDs in diabetic patients qualify for secondary CVD prevention.

There is a notable increase in the prescription of LLDs as could be noted from Ndola Teaching Hospital (NTH), another regional referral hospital where anecdotal evidence showed 17% prescription rate. This present study assessed the prescribing patterns of LLDs at the Adult University Teaching Hospital (Adult -UTH) in Lusaka, Zambia to ascertain whether there was adherence to ATP IV guidelines of 2013. The Adult Treatment Panel (ATP) is a panel of experts of the National Cholesterol Education Program (NCEP) whose main goal is to reduce increased CVD rates due to dyslipidaemia by coming up with guidelines which are regularly updated.

1.2 Conceptual framework



1.3 Statement of the problem

If CVDs prevention was practiced as instructed in the guidelines, it would markedly reduce the prevalence of CVDs and so it is not only the prevailing risk factors that are of concern but poor implementation of preventive measures as well (Koseva et al., 2016).

It is one thing to have guidelines in place both on a global or local level and yet another thing to have them implemented e.g. the benefit of statins for prevention of cardiovascular (CV) events in type 2 diabetes is established, but a gap exists between guideline recommendations and clinical practice (Berthold et al., 2009).

There is no data on studies regarding the prescription patterns of LLDs in Zambia. However, there is a notable increase in the prescription of LLDs as could be seen from the anecdotal evidence from Ndola Teaching Hospital (NTH), another regional hospital which showed 17.1% as the prescription rate of LLDs. The scenario at Adult UTH in terms of prescription rate was not established though it could be speculated not to be different from that at NTH, it being a teaching hospital and also the national referral hospital. This notable increase in LLDs prescription could not be substantiated and as such whether patients were getting any desired benefit or not was the question that needed to be answered.

The problem that comes with prescribing LLDs without following guidelines are in two extremes where on one end patients in need of therapy may end up being deprived while on the other end, those not in need may end up being prescribed and thus subjecting them to unnecessary side effects such as athralgias, myopathy, myositis which can lead to rhabdomyolysis, altered liver function test, sexual dysfunction, thrombocytopaenia, visual disturbance, hypersensitivity. Prescribing for patients not in need is further a drain on the resources which are already limited while depriving the patients in need may lead to occurrences of CVDs and other related complications.

The grounds on which prescription of LLDs was based at Adult UTH had not been established, whether on individual risk factors or the individual patients' overall risk as required by the ATP IV guidelines and hence the need for this current study.

1.4 Justification of the study

Many studies on the prescription and use of LLDs have been done mostly in the developed countries while less has been done in the developing countries, the category in which Zambia falls where there is an emerging rise in CVDs and where over three quarters of CVDs deaths have been recorded (WHO fact sheet, 2016). The serious nature of CVDs and their major economic impact, calls for optimal treatment in real world settings to reduce their contribution to the extensive escalating costs of healthcare (Graham et al., 2007).

Drug utilization studies facilitate the rational use of drugs in populations and are very essential for evaluating and analyzing the drug therapy from time to time, to observe the prescribing patterns of physicians, with the aim of validating the use of drugs and minimizing the adverse drug reactions (WHO, 2003).

The study was very significant in that it would help establish what considerations are made by clinicians before prescribing LLDs. Further, this information would be cardinal in helping to streamline the approach to treatment so that high risk patients are targeted as they are the most likely to get the optimal benefit with minimal adverse effects.

The Adult UTH was strategically chosen as a study site because of it being a national referral hospital and also a teaching hospital.

The findings may help physicians to appreciate the need to appropriately prescribe LLDs and avoid treatment of patients who may not need LLDs while on the other hand avoid depriving those patients who may be in need of the LLD treatment. The findings may also be useful to Pharmacists in their usual quest to enforce the rational use of medicines like LLDs so as to effectively manage the patients while dieticians and or nutritionists may be helped to establish programs which will promote healthy diets, it being a significant part of therapeutic lifestyle changes (TLC). Eventually, patients may be able to get the optimal benefit while on the hand be spared from undesired adverse effects.

The finding of this study may eventually help in the formulation and or strengthening of treatment guidelines which will enhance the prudent use of the limited resources available through promotion of appropriate prescription of LLDs.

1.5 Research question

Are the prescribing patterns of lipid lowering drugs at the Adult University Teaching Hospital in Lusaka, Zambia in conformity with the fourth guidelines of the Adult Treatment Panel (ATP IV)?

1.6 General objective

To assess whether the prescribing patterns of lipid lowering drugs at the Adult University Teaching Hospital in Lusaka, Zambia were in conformity with the ATP IV guidelines.

1.7 Specific objectives

i. To identify the cardiovascular risk factors in patients who were prescribed lipid lowering drugs.
ii. To determine the diagnosed conditions which prompted the prescription of lipid lowering drugs.
iii. To ascertain the eligibility of patients for the lipid lowering drugs they were prescribed.
iv. To identify the most prescribed lipid lowering drugs and their doses.

CHAPTER TWO

LITERATURE REVIEW

2.1 Global perspective

Pratyay and colleagues carried out a study in 2012 whose aim was to determine current prescribing patterns of lipid-lowering drugs (LLDs) adopted by physicians in East India. In this prospective, non-interventional, uncontrolled, open chart, pharmaco-epidermiologic study, 200 dyslipidaemic patients were involved. The prescribing pattern of LLDs was recorded along with the serum levels of lipid parameters at the time of initiating LLD therapy. The findings were that males above 40 years were predominantly prescribed LLDs representing 89.5% while advice regarding life style modification was included in only 18% of prescriptions. The ratio of prescribing LLDs for primary and secondary prevention of coronary artery disease (CAD) was 1:1.15 of which the LLDs prescribed were statins and fibrates, representing 80.5% and 14.5% respectively. It was concluded that the prescribing patterns of the LLDs was in accordance with the specific recommendations made for the South Asian Indian populations, as well as with the 2001 third guidelines of the National Cholesterol Education Project (NCEP – III guidelines) (Pratyay et al., 2012). While there are similarities in the study environment between their study and the current study, it should be stressed out that unlike the regional hospital in which they did their study, the present study was undertaken at a national hospital whose findings would serve as a baseline for future studies.

A study was done on prescription cholesterol lowering medication use in adults aged 40 and over in the USA by Qiuping and others. The period which was under consideration was from 2003–2012, and using the National Health and Nutrition Examination Survey (NHANES) data, it was found that there was a significant increase in the percentage of adults in this age group who used a prescription cholesterol-lowering medication. In 2003–2004, one in five adults reported using a prescription cholesterol-lowering medication in the past 30 days. By 2011–2012, that number had risen to one in four adults. In 2011–2012, the majority of adults using a cholesterol-lowering medication reported using a statin alone, representing 83% while 10% used both a statin and a nonstatin and 7% used only a nonstatin. Simvastatin was the most commonly used medication, with 42% of all cholesterol-lowering medication users reporting its use followed by atorvastatin at 20.2%. While use of a prescription cholesterol-lowering medication increased with age, the

use was similar between men and women and race of Hispanic origin groups. On the other hand insurance was found to influence use of prescription cholesterol lowering drugs in that adults aged 40–64 who reported having health insurance or prescription medication coverage were more likely to take prescription cholesterol-lowering medications (Qiuping et al., 2012). The study looked at prescription of cholesterol lowering drugs in a specific age group and how the trends have been changing over time.

In India, Sreedevi and friends carried out a study which focused on prescription pattern of statins in cardiovascular diseases, of which prescriptions were collected from out-patient departments visiting different hospitals of Hyderabad, Andhra Pradesh, India. The prescriptions, which included hypolipidaemic drugs (Statins) were audited and analyzed category-wise, the data having been collected using the World Health Organization (WHO) based prescription auditing proforma. A total of 1000 prescriptions were collected out of which 306 patients on statin therapy like those for treatment of hyperlipidaemia or prophylaxis in stroke, CVDs or other disorders were analyzed and the findings were that more males were prescribed statin therapy, representing 61.5% whereas, females were 38.5%. When it came to the age criteria, the age group on high statin therapy in males was 60-70 yrs (48%) while in females it was 50-60 yrs (39%). Further findings were that statins were prescribed more in CVDs, accounting for 279 patients (91.2%) followed by diabetes which accounted for 199 patients (65%) while they were prescribed the least in those with renal insufficiency. In terms of drugs, atorvastatin was the highest prescribed, it having been prescribed in 261 patients (85.3%) while lovastatin was the least prescribed, it having been prescribed in only 7 patients (2.3%) (Sreedevi et al., 2011).In their study, they identified factors influencing prescription of LLDs and similarly in the current study, this was one of the objectives, the information which is cardinal in validating rational prescription of LLDs.

In UK, a national retrospective cohort study entitled; Patient Factors Influencing the Prescribing of LLDS for Primary Prevention of CVDs in UK General Practice was carried out in 2013. In this study, Wu and others reported that out of 365,718 patients with complete data, 13.8% were prescribed lipid lowering drugs, 28.5% of whom were eligible while 10.1% of those ineligible meaning only 41.7% of those prescribed lipid lowering drugs were eligible. The predictors were similar in eligible and ineligible patients and these results showed that over half of the patients

with CVDs risks who started using LLDs were ineligible for this type of treatment while on the other hand many eligible patients were not prescribed treatment. It was also revealed that prescription of LLDs by General Practitioners (GPs) was found to be influenced by CV risk factors, but calculated CV risk was not the main predictor of prescribing behavior. A conclusion was made that most LLDs for primary prevention were prescribed to ineligible patients and that there was underuse of LLDs in eligible patients (Wu et al., 2013).

In German, Berthold and colleagues undertook a study to identify patient-related factors predicting statin prescription. Patients were stratified according to primary and secondary prevention. The study was cross sectional where the quality of care in 51,640 patients with type 2 diabetes in German diabetes registry was assessed. The findings were that 34% had established atherosclerotic disease out of which 25.5% received a statin. The prescription frequency was significantly higher in the secondary where CHD and peripheral diseases were concurrent representing 38.1% compared to the primary prevention group with 95% confidence (CI) 37.4–38.9% vs. 18.5% with 95% CI 18.0 – 19.0% respectively. In primary prevention the odds for statin prescription increased with estimated cardiovascular risk, indicating that prescription decisions are at least in part based on risk assessment. Positive predictors for statin prescription were secondary prevention, hypertension, former smoking, baseline LDL-cholesterol, and microalbuminuria. It was found that the majority of patients with type 2 diabetes were not receiving statins, with only 25% of them receiving statin prescriptions (Berthold et al., 2009). While prescription of statins is recommended in diabetes type 2 for whose predicting factors Berthold and friends were seeking to identify, the present study looked at the prescribing patterns of all LLDs regardless of the line with all the risk factors and the overall level of risk of patients.

In 2000, Primatesta and Poulter reported the findings of their study called; Lipid concentrations and the use of lipid lowering drugs: evidence from a national cross sectional survey. In this large, nationally representative sample whose objective was to evaluate the prevalence of the use of lipid lowering agents and its relation to serum lipid concentrations in English adults, about 2/3 of participants had a total cholesterol concentration above the “ideal” of 5mmol/l, and despite the high prevalence of CHD in the English population only 2% were taking LLDs. It was further found that only about 10% of adults with dyslipidaemia (total cholesterol ≥6.5 mmol/l) received lipid lowering treatment (LLT) while cholesterol concentrations were only reduced to the current

target of <5 mmol/l in less than 1/3 of people undergoing treatment. Of the 117 participants whose 10 year risk of coronary heart disease was estimated at ≥30% and whose total cholesterol concentration was ≥5 mmol/l, only four were taking LLDs of which none of these had achieved a total cholesterol of <5 mmol/l (Primatesta and Poulter,2000).

In a Portugal population based study carried out in 2003, Alves and Azevedo revealed that the prevalence of hypercholesterolemia in a sample of community dwellers aged 40 - 65 years was 84.9%. Eligibility for drug treatment was observed in 29.8% of subjects, having been higher in men than women. Among medicated individuals, 58.2% had serum cholesterol concentration equal or below the primary target and controlled hypercholesterolemia was more frequent in women. The study also revealed that high prevalence of hypercholesterolaemia in individuals does not always warrant them to be commenced on LLDs therapy as could be seen from the low levels of eligibility (Alves;Azevedo, 2003). Based on their conclusion, the current study sought to establish whether treatment was indeed targeted at the high risk patients who were likely to benefit more from it or was only based on hypercholesterolaemia which Alves and Azevedo argued that it should not be the case.

In 2010, Strandberg reviewed many studies on the use of LLDs by comparing the usual treatment with more intensive statin treatment in coronary artery disease (CAD). In his review, Strandberg concluded that the overall evidence indicates that at least heart failure of ischaemic cause can be prevented or postponed with effective statin therapy. It was also pointed out that in patients with established CAD, more effective cholesterol lowering with statins is associated with fewer heart failure admissions especially among those with milder heart failure at baseline. However, it was concluded that in established heart failure of ischaemic cause, initiation of statin treatment may have prognostic benefit only among those with milder disease. In those with advanced disease or established heart failure of heterogeneous cause, initiation of even effective statin therapy and LDL lowering does not improve prognosis but is not associated with specific adverse effects either. Therefore, discontinuation of ongoing statin treatment is not indicated if heart failure develops when other indications for statin treatment exist and so given experimental and epidemiological data, HDL raising therapies together with statin treatment may offer new possibilities at least for heart failure prevention but this needs to be tested in specific trials

(Strandberg, 2010). This study having been a Meta-analysis, they affirmed the benefit of using LLDs.

2.2 Regional perspective

An interventional study was undertaken to improve the use of LLDs at Brits District Hospital of South Africa in 1999. It came about after the therapeutics committee discovered that simvastatin 20mg and 10mg were taking the third and fourth positions in the drug expenditure list. In this study, Van Deventer and others reported that out of the 147 patients found to be on LLDs 28% were male while 72% were female, all having an average age of 55 years. It was found that no BMIs or genograms indicating family history were included in the files while there was no indication of diet having been discussed, only in 8% of files was the smoking history of the patient recorded while only 30% of the files contained serum cholesterol results that were newer than one year. This means therefore, that there was an irrational use of drugs in the first instance as more patients who were taking the LLDs didn't need them after all (Deventer et al, 1999). Their study was meant to improve the use of LLDs at Brits district hospital.

In South Africa, a cross-sectional observational study called the Dyslipidaemia International Study (DYSIS) was carried out in 2011 which aimed at evaluating lipid goal attainment and thus evaluated the prevalence of dyslipidaemia in statin – treated patients. Out of 1,029 participants, a group of patients at high CV risk was identified and 73.5% of statin-treated patients were found to be at very high risk for CVD. Despite statin therapy, 85.6% of the very high risk group had at least one lipid abnormality, of which a majority had two or more lipid abnormalities, high LDL-C levels having been the most common which was diagnosed in 60.1% of all very high-risk patients. Not surprising, the metabolic syndrome was present in 67.2% of the sample, since its components also contribute to elevated CVD risk. Marked ethnic differences in cardiovascular risk profiles and the primary indication for statin therapy were observed, in that while about half of Asian and mixed-ancestry patients had clinically overt CVDs, the rate in black patients was less than 10%. The major indication for statin therapy in black patients was diabetes, it having been present in 71.2% of patients while family history of premature CVD was very uncommon, it only accounting for 1.8% in black patients. In addition to identifying factors that are associated with dyslipidaemia in statin-treated patients, this study (along with previous DYSIS studies) also highlighted the deficiencies of LLT in clinical practice (Raal et al., 2011). They evaluated the

success of statin therapy one of the LLDs in attaining the lipid goals using a cross sectional observational study and identified the deficiencies in clinical practice. On the other hand, the present study was focused on assessing if at all the initiated treatment had been appropriately commenced in the first place by determining the eligibility to therapy of those who were being treated with LLDs and it also helped to highlight the CVD risks most prevalent in patients at the UTH.

2.3 Local Perspective

While there is paucity of data as regarding the prescribing patterns of LLDs in Zambia, a study carried out by WHO in collaboration with Ministry of Health in 2008 to determine the prevalence rates of the common non communicable diseases (NCDs) and the extent to which they are associated with behavioral and biological factors among Zambians, it was concluded that the tobacco smoking epidemic was in its early stage, as well as for diabetes while hypertension, hypercholesterolaemia, alcohol consumption, and overweight or obese were already at alarming levels (Songolo et al., 2008).The findings by Songolo and others shows the growing trend of hypercholesterolaemia and metabolic syndromes like diabetes and other risk factors which are a vital predisposition to CVDs which shows that the Zambian population has increasingly become predisposed to CVD risks.

Carrying out this study at Adult UTH which is a tertiary and national referral hospital was of great significance, knowing that prescribing of LLDs is one of the most likely steps to be taken in prevention of CVDs apart from lifestyle modification. Further, the present study was very appropriate in helping to determine whether the prescribing patterns of LLDs at the UTH in Lusaka, Zambia were in conformity with the ATP IV guidelines which are formulated by experts from the American College of Cardiology (ACC) and the American Heart Association (AHA) and which are also backed by World Heart Federation (WHF).

CHAPTER THREE

METHODOLOGY

3.1 Study design

The study was designed to be a cross sectional study and was suitable as it was going to reveal the actual prescription patterns of LLDs for that particular period.

3.2 Study setting

- The study was carried out at the Adult UTH in Lusaka which is the largest public tertiary and national referral hospital in Zambia.
- The study was conducted at clinic five 5 which is the out - patient wing under the Department of Internal Medicine.

3.3 Study population

Files of patients who were treated at clinic 5 of the Adult UTH Lusaka, Zambia during the time of data collection for whom some of the drugs prescribed were LLDs.

3.4 Sample size determination

The sample size was found using the following formula: $N = \frac{Z^2P(1-P)}{e^2}$

Where;

N = Sample size required

P = Prevalence of prescriptions containing LLDs - 0.1 (10%) which was estimated prevalence based on the WHO country profile of Non-communicable diseases in 2014 which indicated that in Zambia, death estimates due to NCDs accounted for 23% out of which 8% were death estimates due to CVDs.

Z = Confidence level which at 95 % is 1.96

e = Marginal error which in this case is 0.05 (5 %) and the answer was 138.24

Therefore, sample size was 140files.

NB: The power of estimation was at 80%

3.5 Inclusion criteria

i. Files for Patients being treated as out – patients (clinic 5) at Adult UTH under the department of Internal Medicine.

ii. These files were for patients who were being treated during and at the time of data collection.

iii. These files were for patients who had LLDs as some of their prescribed drugs.

3.6 Exclusion criteria

i. Files which didn't have clear details regarding patient age, BP, medical history and smoking history.

3.7 Sampling method

i. Patient files whose owners had been prescribed LLDs were identified and noted down.

ii. These files had numbers allocated to them and a sampling frame was then compiled.

iii. Thereafter, pieces of paper with corresponding file numbers were picked using a simple random sampling method and the files they represented were picked as the study samples.

3.8 Data collection

i. A researcher's data collection form was used to collect information from patient files.

ii. The information collected included; age, gender, BP, body weight and heights from which the BMI was calculated, social history, medical history(hypertension, diabetes, stroke, cardiac failure, myocardial infarction, angina pectoris), family history (definite MI or sudden death before 55 years in father or other first degree male relative, or before age of 65 years in mother or other first degree female relative), medication history and lipid profile results in cases where the lipid tests had been requested for and done.

iii. Diabetes and hypertension being significant risk factors for CVDs which prompt the prescription of LLDs were identified as shown below.

iv. Patients found to have been prescribed oral hypoglycaemic drugs or insulin or found to have had the fasting blood glucose levels of $\geq$ 7mmol/l ($\geq$ 126 mg/dl) on more than one instance were considered as diabetic.

v. Patients found with BP $\geq$ 140/90 mmHg on more than one instance or found to have been taking anti-hypertensive medication were considered to be hypertensive.

vi. An assessment as to whether a lipid profile test (TC, LDL-C, HDL-C and TG.) was done was conducted and where results were found, they were noted down in the questionnaire.
vii. Apart from the number of risk factors patients were found to have, collected data was further used in the Pooled cohort equation to determine their level of CVDs risk.

3.9 Data analysis

IBM SPSS version 21.0 was used for statistical analysis and to produce some graphical output. All statistical tests were at 5% significance level. Independent samples T-test was used to compare mean values between groups and the Pearson's chi-squared test was used for comparison of proportions between groups. The Fisher's exact test was used when one or more of the cells had an expected frequency of five or less. Some variable categories with less frequency were collapsed together accordingly. Study variables were checked for evidence of co-linearity based on a Spearman correlation coefficient >0.8. The relationship between study variables and prescription of LLDs was examined using logistic regression. The selection for entry into the logistic regression model was considered at level $p<0.20$ or known clinical significance.

3.10 Variables

The research variables focused on the criterion adopted in the fourth guidelines of the Adult Treatment Panel (ATP IV) of 2013, the CVD risks which should not be taken in isolation but rather have all to which an individual patient is exposed to be considered and finally determine one's overall level of CVD risk or the 10 years risk level. Table 1 below shows these variables;

Table 1: Variables

Variable	Definition	Scale of measurement
Age	Age was defined as age of individual patients at the time of data collection	Continuous
Gender	Sex was defined as male and female	Categorical (Dichotomous) 1=male, 2=female
CVDs risk factors	Age	Categorical Men 45 years Women 55 years
	Cigarette smoking	Categorical (Dichotomous) 1= Smoker 2= Non smoker
	Hypertension	Categorical 1= Systolic > 140mmHg 2=Patient taking anti-hypertensive drugs
	Family history of premature CHD (Definite MI or sudden death) of the following; < 55 years in father or other first degree male relative < 65 years in mother or other first degree female relative)	Categorical 1 = with family history 2 = No family history
	Risk equivalents - CHD high risk category conferred with an estimated 10-year risk for a cardiovascular event of more than 20% (ATP III 2004) meaning that their presence will call for commencement of treatment. Diabetes, Metabolic syndrome	Categorical 1=Present 2= absent
	Total cholesterol (TC) and LDL-C	Categorical
Conditions	Conditions for which LLDs were prescribed	Categorical CHD, stroke, heart failure, diabetes, Angina etc
Eligibility	- Adults with clinical ASCVD	Categorical (Dichotomous)

	- Adults with LDL-C ≥4.92mmol/L(190 mg/dL) - Adults 40 to 75 years of age with diabetes - Adults ≥7.5% estimated 10-year risk of ASCVD	1=Eligible 2=Non eligible
Lipid lowering drugs	LLDs prescribed	Nominal Atorvastatin, rosuvastatin, ezetimibe, niacin, gemfibrozil,fenofibrates, omega 3 etc

3.11 Ethical consideration

a). Ethical approval and clearance was given by the ERES Converge Research Ethics Committee. This was after scrutinizing the procedures to be used during research and also that the patients whose files were to be reviewed would not in any way be subjected to risks which could cause concern.

b). Permission to carry out the research study at Adult-UTH was also granted by management and this therefore means that the study was legally conducted at this site.

c). The information obtained was kept confidential and was not used for any other purpose apart from the intended purpose of this research. This was done in order to prevent records of patients from being accessed by individuals who were not supposed to do so.

d). The anonymity of the clinicians who prescribed the LLDs and the patients whose files were reviewed was maintained and this procedure helped to maintain and protect the integrity of both the prescribers and the patients.

3.12 Study limitations

a). There was neither interference nor change with the treatment of the patients whose files were reviewed.

b). The study was only conducted at one institution and so there might be need to extend to other hospitals.

CHAPTER FOUR

RESULTS

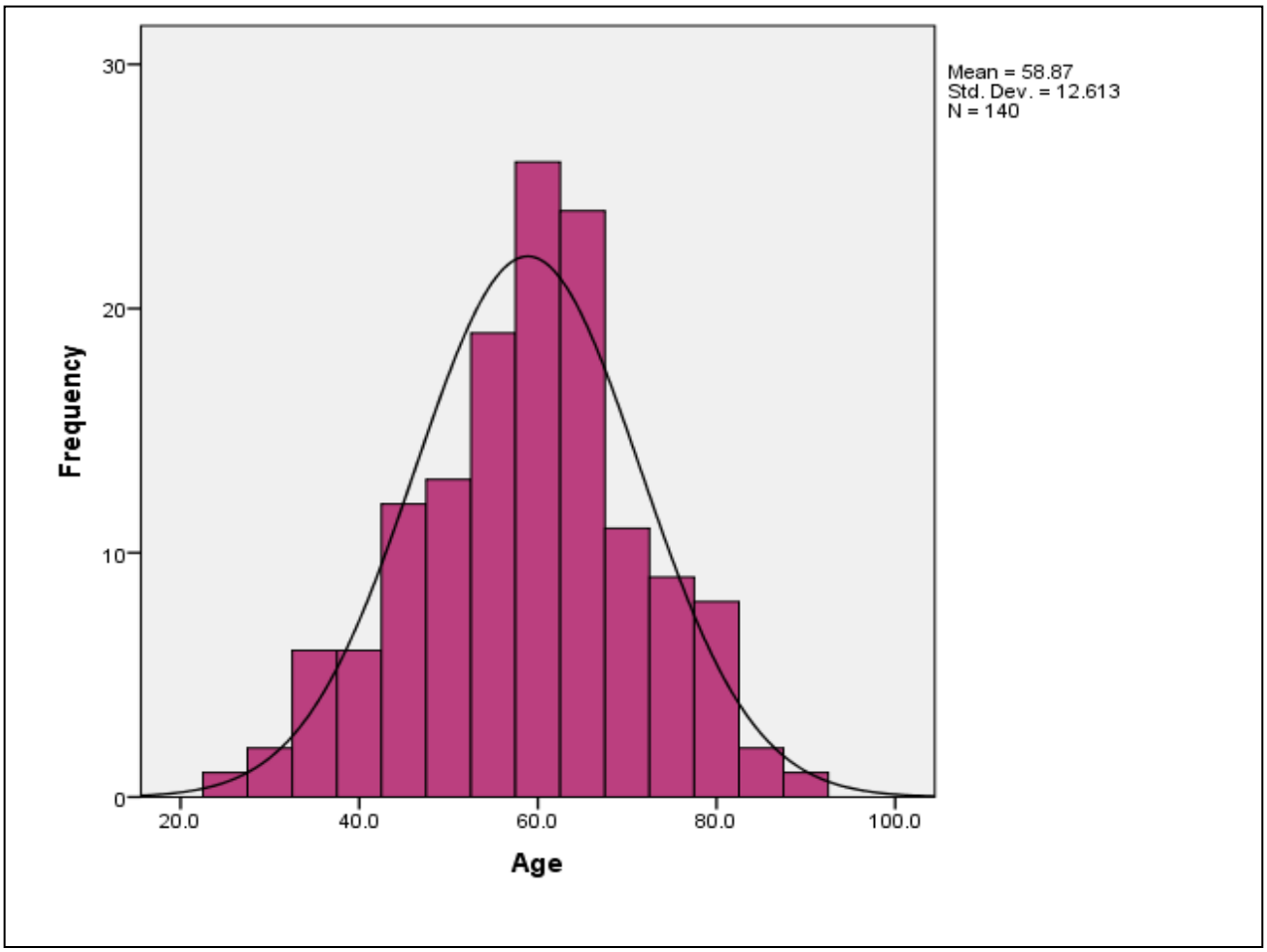
4.1Characteristics of patients who were prescribed LLDs

An overview of the descriptive statistics for the 140 patients is presented in Table 2.

Table 2: Patient summary descriptive summary statistics (n = 140)

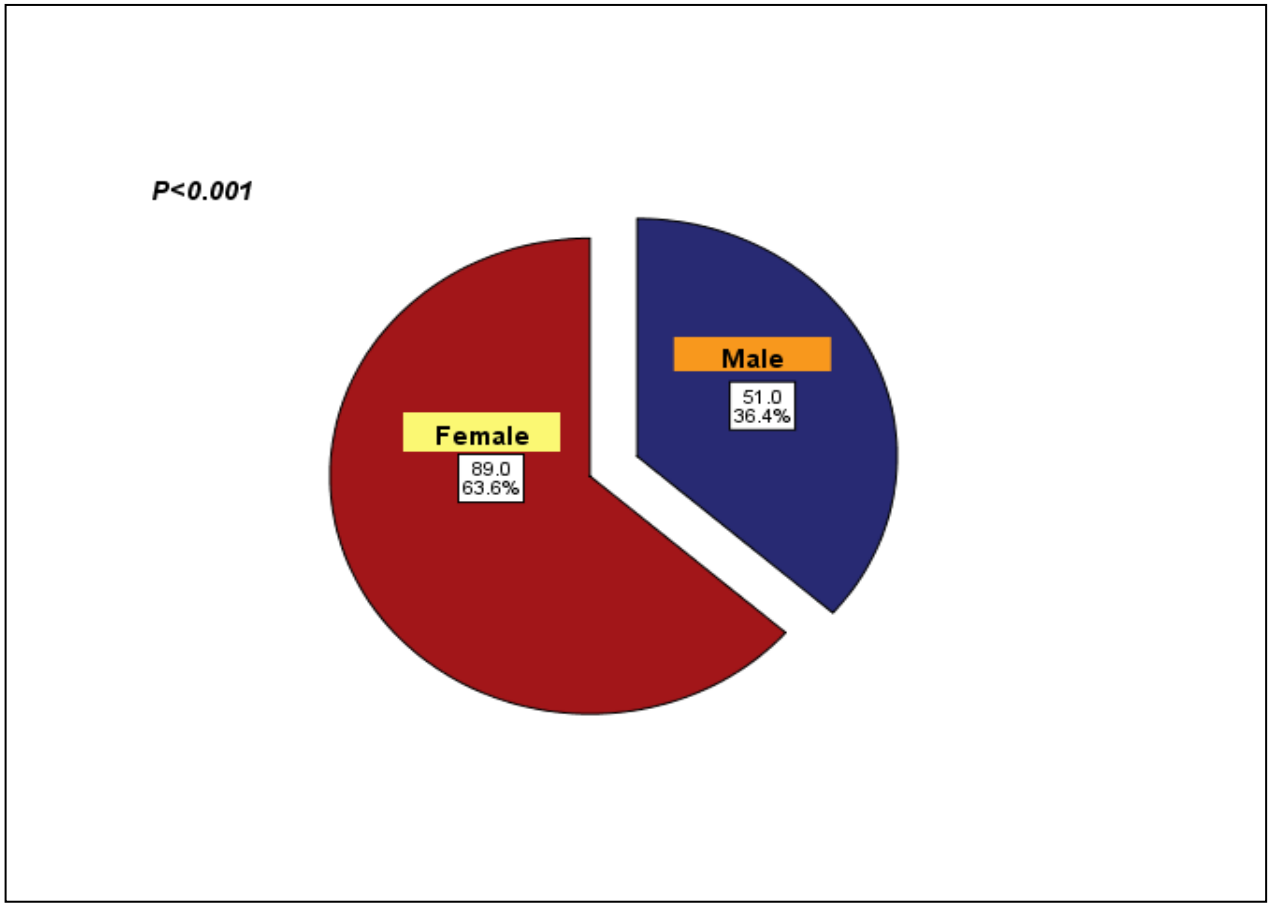
Variable	Frequency (n = 140)	Percentage
Sex		
Male	51	36.4
Female	89	63.6
Age group		
25-44 years	19	13.6
45-74 years	102	72.9
75-92 years	19	13.6
Smoking and alcohol history		
Patients found to be smokers	11	7.9
Patients taking alcohol	24	17.1
Medical history		
Hypertension	125	89.3
Diabetes	39	27.9
Heart Failure	32	22.9
Stroke	47	33.6
IHD (Ischaemic Heart Disease)	13	9.3
Diagnosis category		
CVD	93	66.4
Kidney related	9	6.4
Obesity	35	25
Diabetes	2	1.4
HTN/DM (Hypertension/Diabetes co-morbidity)	32	22.9
Metabolic Syndrome	2	1.4
Prescribed LLDs		
Atorvastatin 10mg	38	27.1
Atorvastatin 20mg	91	65
Atorvastatin 40mg	9	6.4
Rosuvastatin 20mg	1	0.7
Omega 3	1	0.7
Eligibility of patients for the prescribed LLDs		
Patients eligible for the prescribed LLDs	64	45.7
Dosing appropriateness among the eligible patients		
Patients who received appropriate doses	10	7.1

Figure 1. Histogram showing Patients age distribution



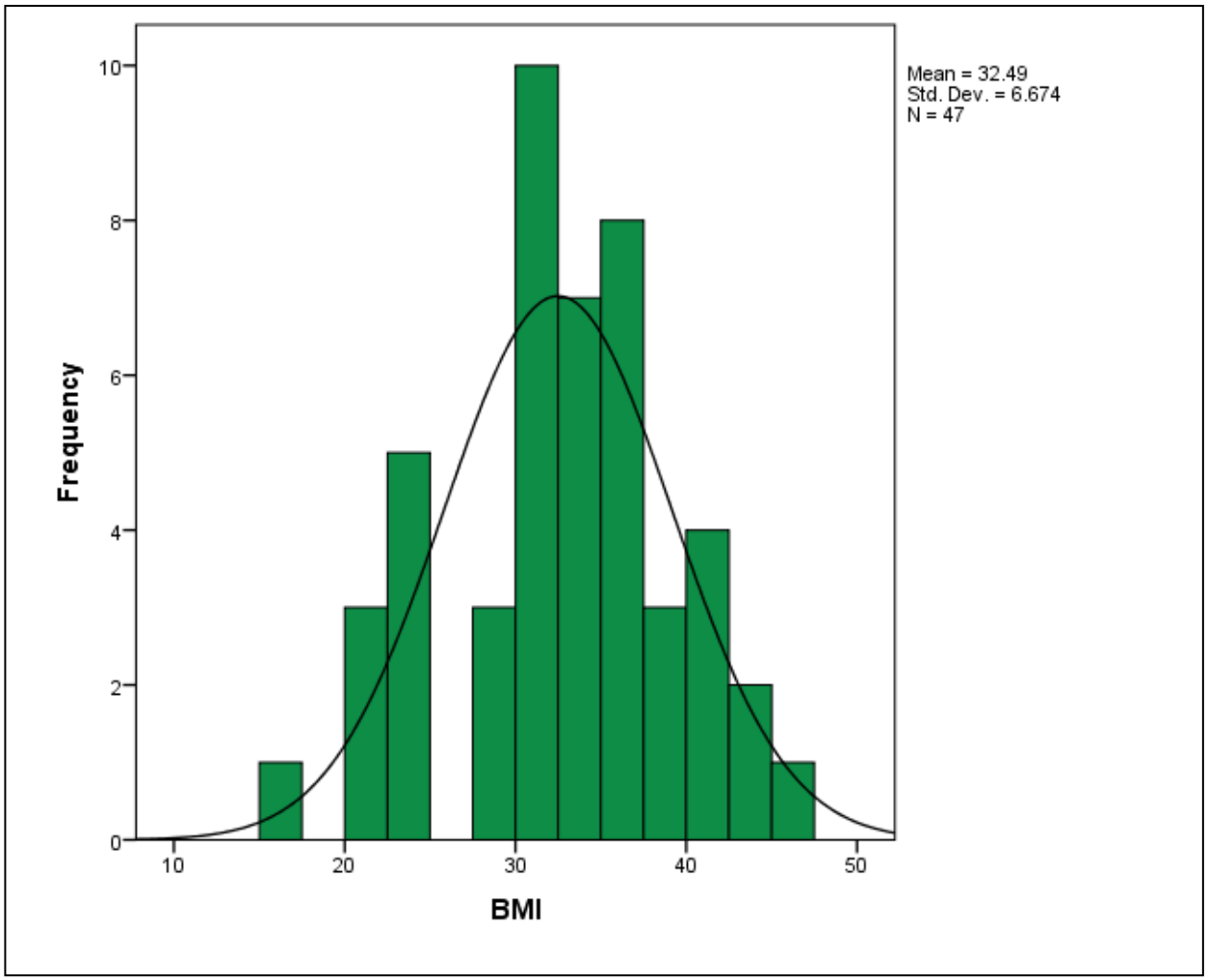
The age of the patients was about normally distributed with mean 58.9 years (SD = 12.61). The minimum patient age was 25 years and maximum 92 years. There were 19 patients (13.6%) aged between 25 – 44 years, 102 patients (72.9%) aged between 45 – 74 years and 19 patients (13.6%) aged 75 years and above.

Figure 2. Pie chart showing Patients gender distribution



There were more female patient files than male patient files reviewed, 89 (63.6%) versus 51 (36.4%) and this proportional difference was significant with p-value < 0.001.

Figure 3. Histogram showing distribution of patient BMI

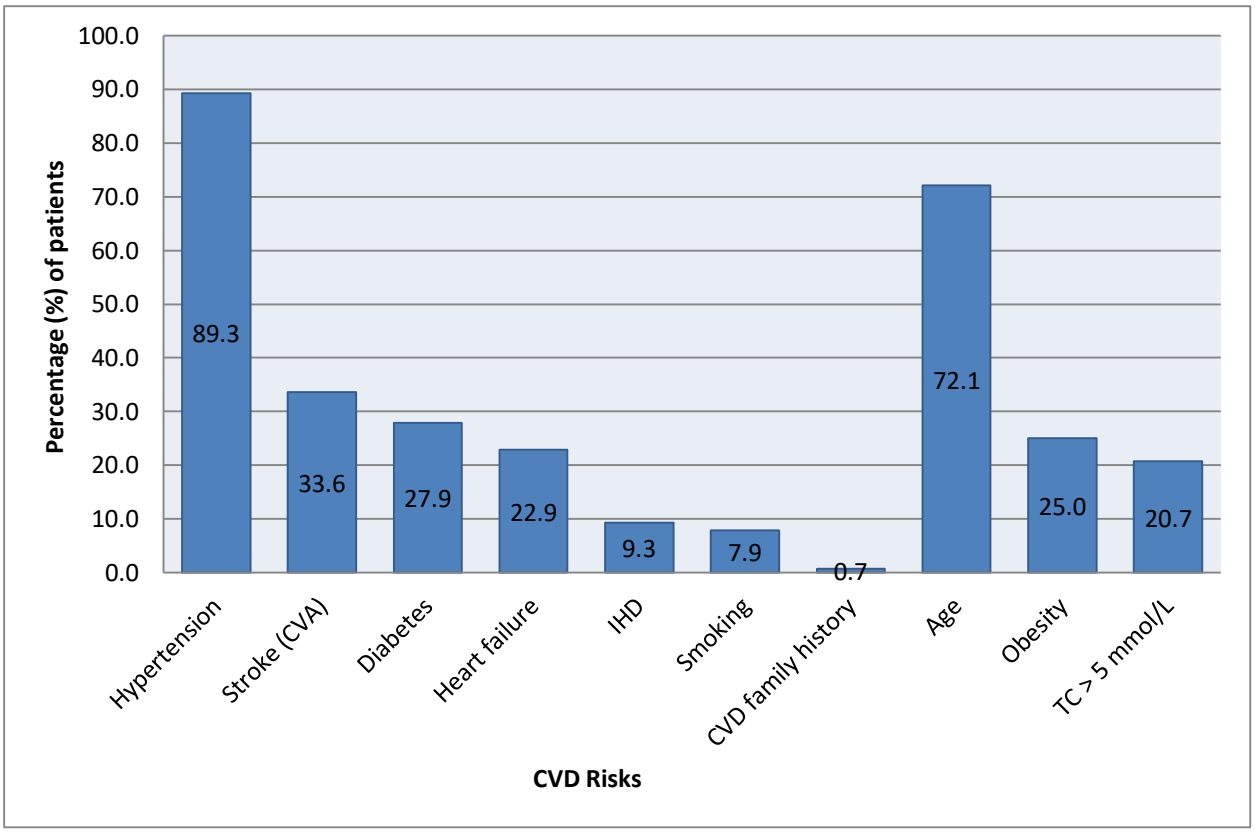


There were 47 patient files with recorded BMI and the mean BMI was 32.5 Kg/m^2 (SD = 6.67) while a greater majority of the patients with recorded BMI were obese.

4.2 Cardiovascular risks among patients for whom LLDs were prescribed

This describes the individual cardiovascular risks that were recorded in individual patients which in a way might have influenced the prescribing of LLDs. Figure 4 shows these individual CVD risks.

Figure 4. Bar chart showing CVD risk factors among the patients

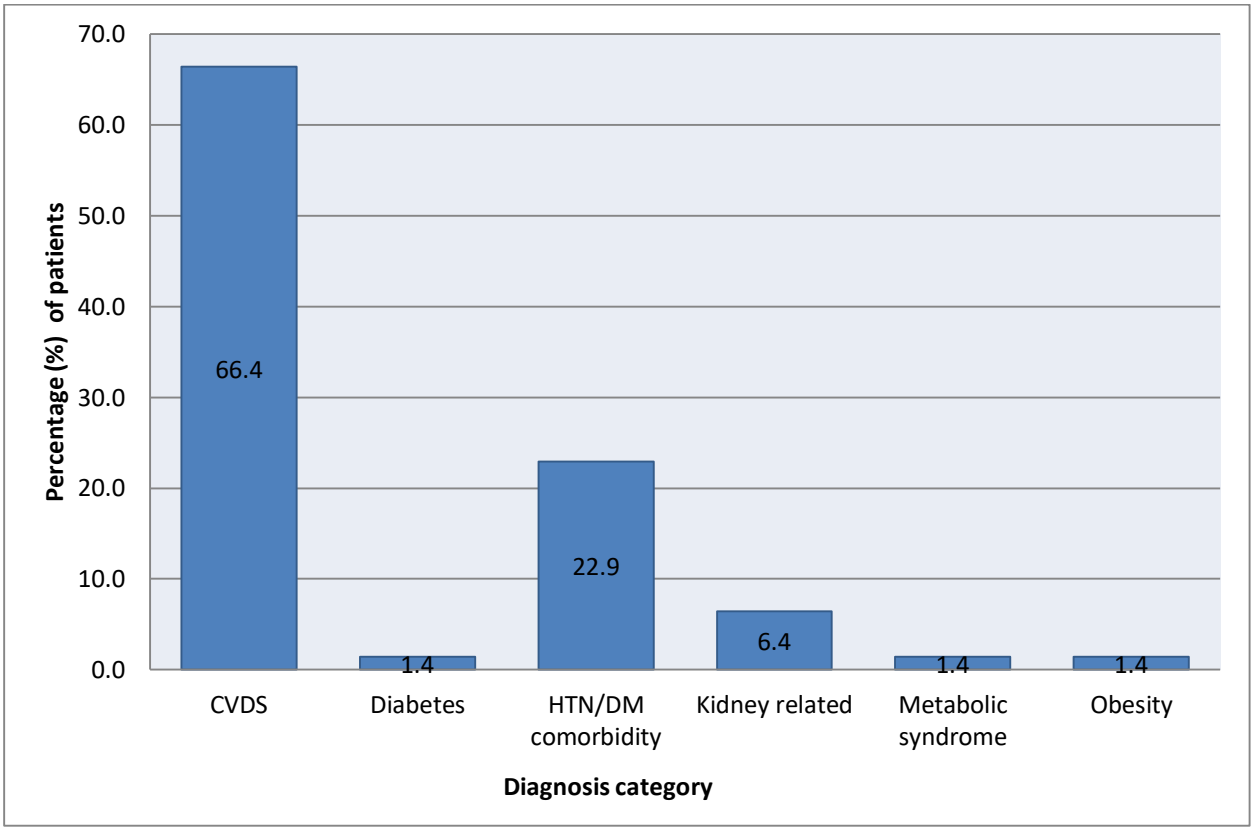


Hypertension was the highest presenting CVD risk having been present in 125 patients (89.3%) followed with age where 101 patients (72.1%) were predisposed to CVDs based on their age. CVD family history was the least frequent risk as only in one patient (0.7%) was it recorded risk.

4.3 Diagnosed conditions in patients for whom LLDs were prescribed

This describes the categories of diagnoses among the patients for whom LLDs were prescribed and this is as shown in Figure 5.

Figure 5. Bar chart showing diagnosis category distribution of the patients

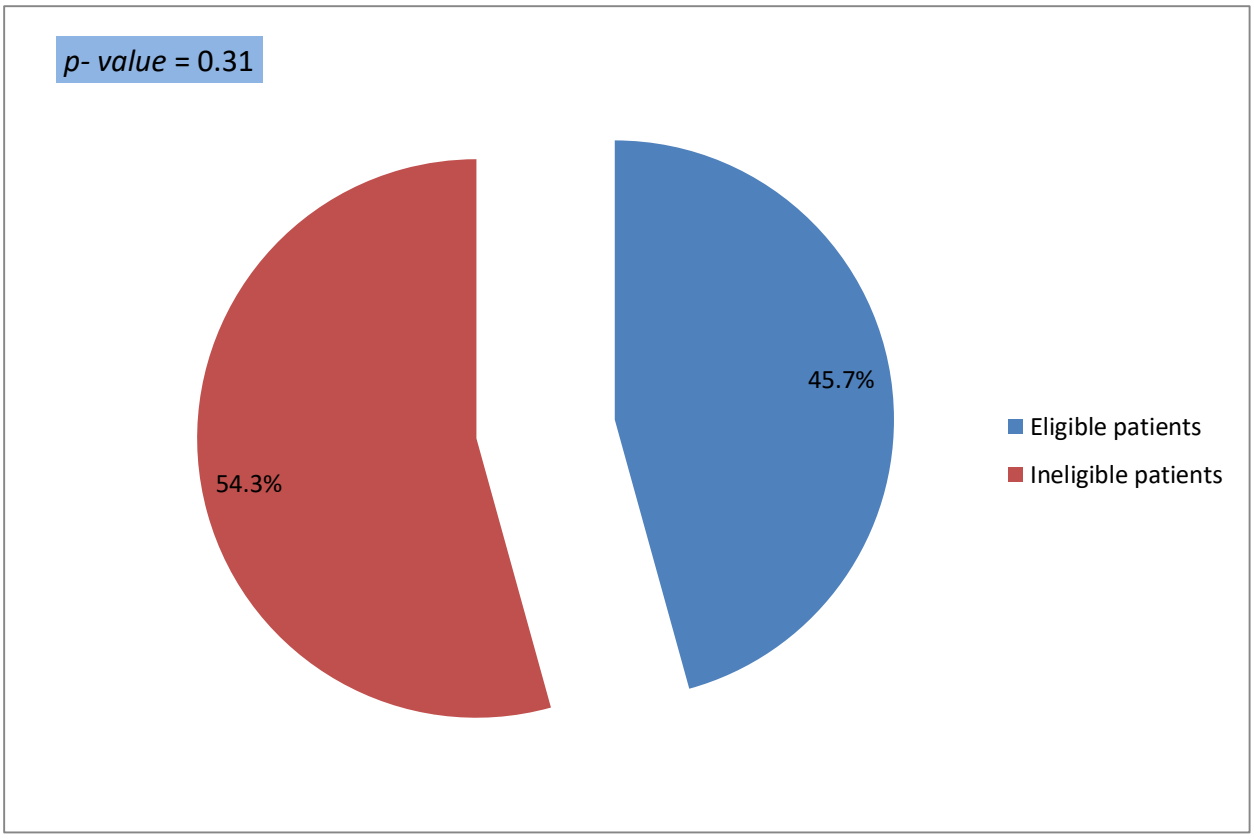


The most common diagnosis category was CVD with 93 patients (66.4%) followed by hypertension/diabetes co-morbidity with 32 patients (22.9%) while 9 patients (6.4%) had kidney related conditions. Diabetes, metabolic syndrome and obesity were the least frequent diagnosis categories each representing 2 patients (1.4%) respectively.

4.4 Eligibility for the prescribed LLDs according to the fourth guidelines of the Adult Treatment Panel (ATP IV) eligibility criteria

The eligibility of patients for the LLDs they were prescribed was determined based on ATP IV guidelines of 2013 as illustrated in appendix E and the outcome is as shown in Figure 6.

Figure 6. Pie chart showing Patients Eligibility for prescribed LLDs

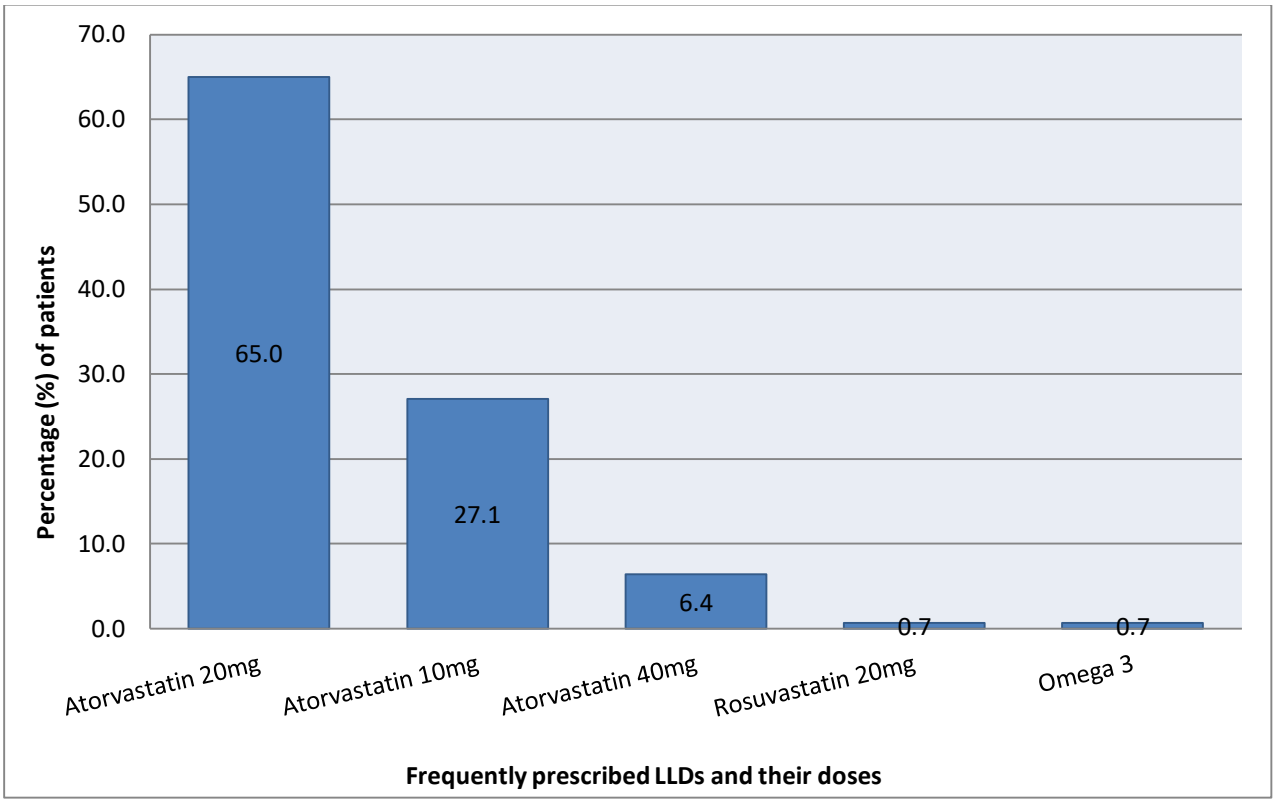


Out of the 140 patient files reviewed, 64 (45.7%) patients were found to be eligible for the LLD therapy they were prescribed while 76 (54.3%) patients were not eligible for the prescribed LLD though this proportional difference was not statistically significant, p-value = 0.31.

4.5 Most commonly prescribed LLDs and their specific doses

This describes the most commonly prescribed LLDs among the 140 patients at the Adult UTH and this is as shown in Figure 7.

Figure 7. Bar chart showing the prescribed LLDs and their actual prescribed doses

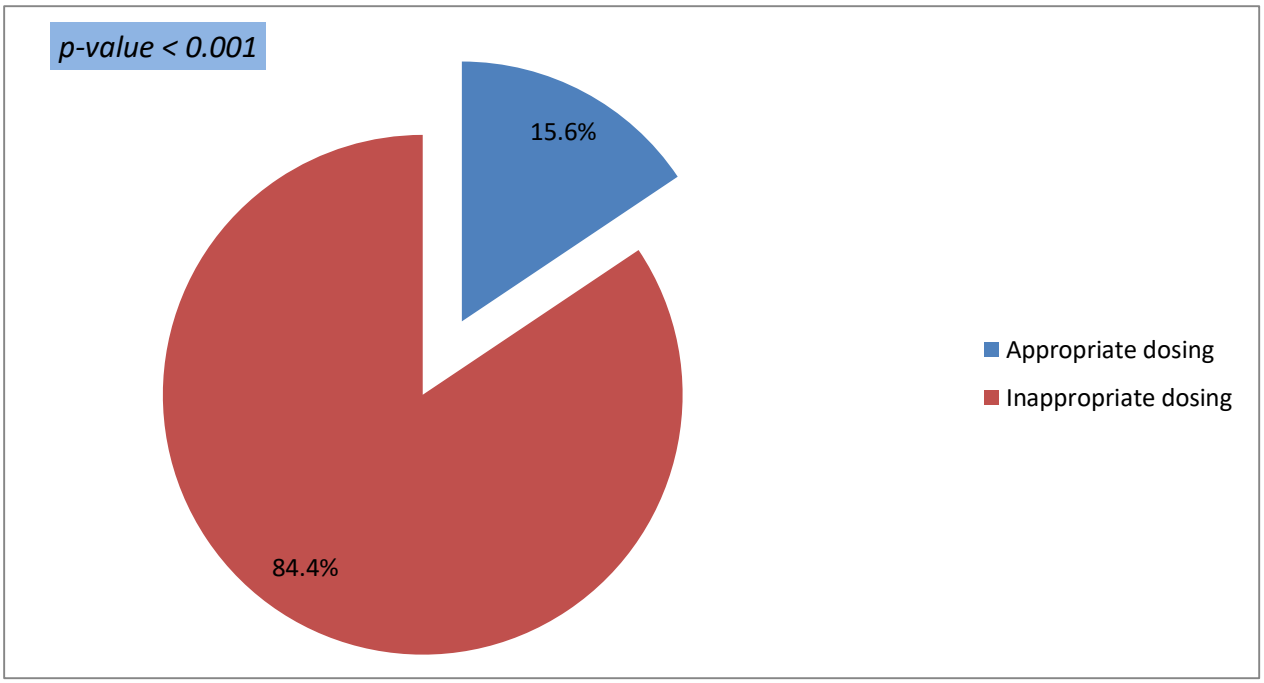


The most commonly prescribed LLD for the sample patients was Atorvastatin 20mg for 91 patients (65%) followed by Atorvastatin 10mg for 38 patients (27.1%) while Atorvastatin 40mg was prescribed in 9 patients (6.4%). Rosuvastatin 20mg and omega 3 were the least prescribed LLDs, each having been prescribed in only one patient (0.7%) respectively.

4.5.1 Appropriateness of dosing among the eligible patients according to the American Heart Association which is also adopted in the ATP IV guidelines (Refer to appendix J)

The appropriateness of dosing was determined only in those patients who were found eligible for the prescribed LLDs and the results were as shown in Figure 8.

Figure 8. Pie chart showing dosing appropriateness for the 64 eligible patients



Among the 64 patients found to have been eligible for the prescribed LLD therapy, 10 (15.6%) received appropriate dosing while 54 (84.4%) received inappropriate dosing and this proportional difference was statistically significant, p-value < 0.001.

4.5.2Bivariate analysis for dosing appropriateness association

Tables 3a and 3b show bivariate analysis results for association with dosing appropriateness. At 5% significance level, only diagnosis category and prescribed the LLDs were significantly associated with dosing appropriateness among the categorical variables, P-values = 0.02 and < 0.001, respectively. This therefore, means that diagnosis category and prescribed LLDs were closely associated to the dosing appropriateness. Among the continuous variables, lipogram duration was significantly associated with dosing appropriateness, p-value <0.001 meaning dosing appropriateness was closely associated with how long ago the lipogram was taken. TC and LDL-C results were marginally associated with dosing appropriateness, p-values = 0.06 and 0.05, respectively meaning TC and LDL-C did not affect the dosing appropriateness that much.

Table 3a. Bivariate analysis for association with dosing appropriateness (categorical variables)

Variable	Inappropriate dosing		Appropriate dosing		P-value
	N	%	n	%	
Sex					
Male	23	42.6%	3	30.0%	0.51
Female	31	57.4%	7	70.0%	
Age group					
25-44 years	5	9.3%	1	10.0%	0.99
45-74 years	49	90.7%	9	90.0%	
BMI category					
Other	45	83.3%	7	70.0%	0.38
Obese	9	16.7%	3	30.0%	
Smoking					
No	33	61.1%	7	70.0%	0.28
Yes	5	9.3%	2	20.0%	
Unrecorded	16	29.6%	1	10.0%	
Alcohol intake					
No	28	51.9%	6	60.0%	0.90
Yes	11	20.4%	2	20.0%	
Unrecorded	15	27.8%	2	20.0%	
Hypertension (HTN)					
No	6	11.1%	1	10.0%	0.99
Yes	48	88.9%	9	90.0%	
DM Medical History					
No	31	57.4%	6	60.0%	0.51

Yes	10	18.5%	3	30.0%	
Unrecorded	13	24.1%	1	10.0%	
HF Medical History					
No	31	57.4%	6	60.0%	0.47
Yes	5	9.3%	2	20.0%	
Unrecorded	18	33.3%	2	20.0%	
Stroke Medical History					
No	11	20.8%	4	50.0%	0.09
Yes	42	79.2%	4	50.0%	
IHD Medical History					
No	24	44.4%	8	80.0%	0.14
Yes	12	22.2%	1	10.0%	
Unrecorded	18	33.3%	1	10.0%	

Table 3a cont'd. Bivariate analysis for association with dosing appropriateness (categorical variables)

Variable	**Inappropriate dosing**		**Appropriate dosing**		**P-value**
	N	%	n	%	
HTN Drug History					
No	5	9.3%	1	10.0%	0.99
Yes	49	90.7%	9	90.0%	
DM Drug History					
No	32	59.3%	6	60.0%	0.50
Yes	9	16.7%	3	30.0%	
Unrecorded	13	24.1%	1	10.0%	
Echo and ECG					
No	12	22.2%	3	30.0%	0.73
Yes	29	53.7%	6	60.0%	
Unrecorded	13	24.1%	1	10.0%	
Diagnosis category					
CVD	44	81.5%	5	50.0%	0.02
HTN/DM	8	14.8%	2	20.0%	
Other	2	3.7%	3	30.0%	
Prescribed LLD					
Atorvastatin 10mg	17	31.5%	1	10.0%	<0.001
Atorvastatin 20mg	37	68.5%	6	60.0%	
Atorvastatin 40mg or other	0	0.0%	3	30.0%	

Table 3b. Bivariate analysis for association with dosing appropriateness (Continuos variables)

Variable	Inappropriate dosing	Appropriate dosing	P-value
Age			
(n, mean, SD)	54, 60.8, 13.12	10, 61.4, 12.07	0.90
BMI			
(n, mean, SD)	11, 31.9, 6.24	3, 36.3, 6.02	0.30
TC			
(n, mean, SD)	19, 5.8, 1.14	7, 4.7, 1.55	0.06
LDLC			
(n, mean, SD)	8, 3.8, 0.45	6, 2.7, 1.02	0.05
HDLC			
(n, mean, SD)	4, 1.2, 0.38	4, 1.3, 0.32	0.80
TG			
(n, median, IQR)	13, 1.5, 0.65	5, 1.0, 0.23	0.12
Lipogram Duration			
(n, mean, SD)	19, 1.4, 0.58	6, 0.8, 0.26	<0.001

4.5.3 Logistic regression analysis predicting dosing inappropriateness

Multivariate logistic regression predicting dosing inappropriateness did not find any independent variables significantly associated with dosing inappropriateness. However, unadjusted odds ratios for stroke medical history indicated that patients with no stroke history had on average 74% reduced odds for inappropriate dosing [Odds Ratio (OR) =0.26, 95% Confidence Interval (CI) = 0.06 – 1.22, P-value = 0.087) but this was not statistically significant (Table 3).

Compared to patients with other diagnosis category, patients with CVD diagnosis had on average 13 times increased odds for inappropriate dosing (OR = 13.2, CI = 1.76 – 98.93, P-value = 0.01) and this was statistically significant meaning patients with CVD diagnosis were 13 more times likely to be prescribed inappropriate doses. Patients with HTN and diabetes co-morbidity had on average 6 times increased odds for inappropriate dosing (OR = 6.0, CI = 0.56 – 63.98, P-value = 0.14) although this was not significant (Table 4).

Compared to patients who were prescribed Atorvastatin 20mg, patients who were prescribed Atorvastatin 10mg had on average 2.8 times increased odds for inappropriate dosing (OR = 2.8, CI = 0.31 – 24.72, P-value = 0.37) but this was not statistically significant (Table 5).

Table 4. Logistic regression predicting dosing inappropriateness for stroke medical history

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.forEXP(B)	
								Lower	Upper
Step 1[a]	Stroke(1)	-1.340	.784	2.920	1	.087	.262	.056	1.218
	Constant	2.351	.523	20.193	1	.000	10.500		

a. Variable(s) entered on step 1: Stroke.

Table 5. Logistic regression predicting dosing inappropriateness for CVD diagnosis

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.forEXP(B)	
								Lower	Upper
Step 1[a]	Diag			6.379	2	.041			
	Diag(CVD)	2.580	1.028	6.304	1	.012	13.200	1.761	98.926
	Diag(HTN/DM)	1.792	1.208	2.201	1	.138	6.000	.563	63.984
	Constant	-.405	.913	.197	1	.657	.667		

a. Variable(s) entered on step 1: Diag.

Table 6. Logistic regression predicting dosing inappropriateness for Atorvastatin 10 & 20 recipients

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.forEXP(B)	
								Lower	Upper
Step 1[a]	Drugs(1)	1.014	1.119	.821	1	.365	2.757	.307	24.719
	Constant	1.819	.440	17.085	1	.000	6.167		

a. Variable(s) entered on step 1: Drugs.

Table 7. Shows Cross Tabulation of Patient condition, Drug and dose appropriateness

DiagCategory * Apprpriate_dosing * Drugs Crosstabulation

Drugs				Apprpriate_dosing		Total
				Yes	No	
Atorv 10	DiagCategory	CVD	Count	0	14	14
			% within DiagCategory	0.0%	100.0%	100.0%
			% within Apprpriate_dosing	0.0%	82.4%	77.8%
		HTN/DM	Count	0	3	3
			% within DiagCategory	0.0%	100.0%	100.0%
			% within Apprpriate_dosing	0.0%	17.6%	16.7%
		Metabolic Syndrome	Count	1	0	1
			% within DiagCategory	100.0%	0.0%	100.0%
			% within Apprpriate_dosing	100.0%	0.0%	5.6%
	Total		Count	1	17	18
			% within DiagCategory	5.6%	94.4%	100.0%
			% within Apprpriate_dosing	100.0%	100.0%	100.0%
Atorv 20	DiagCategory	CVD	Count	2	30	32
			% within DiagCategory	6.3%	93.8%	100.0%
			% within Apprpriate_dosing	33.3%	81.1%	74.4%
		Kidney related	Count	2	1	3
			% within DiagCategory	66.7%	33.3%	100.0%
			% within Apprpriate_dosing	33.3%	2.7%	7.0%
		HTN/DM	Count	2	5	7
			% within DiagCategory	28.6%	71.4%	100.0%
			% within Apprpriate_dosing	33.3%	13.5%	16.3%
		Metabolic Syndrome	Count	0	1	1
			% within DiagCategory	0.0%	100.0%	100.0%
			% within Apprpriate_dosing	0.0%	2.7%	2.3%
	Total		Count	6	37	43
			% within DiagCategory	14.0%	86.0%	100.0%
			% within Apprpriate_dosing	100.0%	100.0%	100.0%
Atorv 40	DiagCategory	CVD	Count	3		3
			% within DiagCategory	100.0%		100.0%
			% within Apprpriate_dosing	100.0%		100.0%
	Total		Count	3		3
			% within DiagCategory	100.0%		100.0%
			% within Apprpriate_dosing	100.0%		100.0%
Total	DiagCategory	CVD	Count	5	44	49
			% within DiagCategory	10.2%	89.8%	100.0%
			% within Apprpriate_dosing	50.0%	81.5%	76.6%
		Kidney related	Count	2	1	3
			% within DiagCategory	66.7%	33.3%	100.0%
			% within Apprpriate_dosing	20.0%	1.9%	4.7%
		HTN/DM	Count	2	8	10
			% within DiagCategory	20.0%	80.0%	100.0%
			% within Apprpriate_dosing	20.0%	14.8%	15.6%
		Metabolic Syndrome	Count	1	1	2
			% within DiagCategory	50.0%	50.0%	100.0%
			% within Apprpriate_dosing	10.0%	1.9%	3.1%
	Total		Count	10	54	64
			% within DiagCategory	15.6%	84.4%	100.0%
			% within Apprpriate_dosing	100.0%	100.0%	100.0%

CHAPTER FIVE

DISCUSSION

The study sought to determine whether the prescribing patterns of LLDs drugs at the UTH was in conformity with the ATP IV guidelines which emphasizes on the need to consider the overall 10 year CVD risk of an individual and not and just individual CVD risks.

5.1Cardiovascular risks among patients for whom LLDs were prescribed

The first objective was to identify the cardiovascular risk factors and the overall levels of risks in patients for whom LLDs were prescribed. The study revealed that hypertension was the most frequent individual CVD risk, representing 89.3% which translated to 125 patients. The findings were different from that of the 2012 study by Raja and colleagues in a tertiary care teaching hospital in Southern India where diabetes with hypertension was found to be the most common disease for which hypolipidaemic drugs were prescribed, representing 37%. This could be due the fact that hypertension is one of the leading risk factors for heart disease and stroke today of which it is estimated that by 2025 there will be 1.56 billion adults living with high blood pressure (WHO, 2016).

There was a variation in the subsequent findings in that while only 27.9% patients had diabetes mellitus (DM) in the present study, Sreedevi and colleagues in 2011 revealed that among the statin prescriptions for CVDs in India, 65% of patients were found to have diabetes mellitus. This could be attributed to India being one of the highest leading countries in prevalence of diabetes, having had 69.2 million people living with diabetes (8.7%) as per 2015 data (WHO,2016) compared to the 3.5% age standardized diabetes prevalence in Zambia (Bailey et al., 2016).

Similar to the UK study where it was revealed that the calculated CV risk was not the main predictor of prescription of LLDs by General Practitioners (GPs) but was influenced by CV risk factors (Wu et al., 2013) , the findings in this present study also revealed that the CV risk score could only be calculated in very few patients in that out of 9 patients (6.4%) who had complete data needed to calculate the 10 year ASCVD risk using the pooled cohort equations, only 4 patients (3.7%) had the higher levels of risk. Inadequate or poor patient history taking could be one of the reasons as to why useful patient details could not be found on the files and thus, making it difficult to calculate the 10 year ASCVD for most of the patients.

5.2 Diagnosed conditions for whom LLDs were prescribed

In its second objective, the study further sought to determine the diagnosed conditions for which the patients were treated and it was revealed that among the diagnosis categories, CVDs were the most common, representing 93 patients (66.4%) followed by hypertension/diabetes co-morbidity with 32 patients (22.9%).The presence of hypertension either alone or as a co morbidity with other conditions in these CVD diagnosis categories could be attributed to the rising of hypertension prevalence and its correlates in Lusaka urban district of Zambia where it was found to be 34.8% (Goma et al., 2011). While diabetes was found to be the major indication for statins in a South African study by Raal and colleagues in 2011 with 71.2% of patients, the findings in the present study revealed that hypertension co morbidity with diabetes was the second most common diagnosis category with 23% of patients. This could be attributed to the fact that up to 75% of adults with diabetes also have hypertension and patients with hypertension alone often show evidence of insulin resistance and thus making the two conditions intertwined which also share a significant overlap in underlying risk factors and complications (CDC,2007).

5.3 Eligibility of patients for the prescribed LLDs

The third specific objective was to investigate the eligibility of patients for the LLDs they were prescribed and the findings were that only 64 patients (45.7%) were found to be eligible while 76 patients (54.3%) were not eligible although the difference was not statistically significant (p value = 0.31). According to the fourth guidelines of the Adult Treatment Panel of 2013 (ATP IV, 2013), patients with low density lipoprotein cholesterol (LDL-C) ≥ 4.92 mmol/L (190 mg/dl), Diabetes in those aged 40-75 years with LDL-C between 1.81 – 4.90 mmol/L(70-189 mg/dl), non diabetes patients aged between 40 to 75 years but with an estimated 10 year atherosclerotic cardiovascular disease (ASCVD) risk of ≥7.5 % and with LDL-C between 1.81 – 4.90mmol/L (70-189 mg/dl) qualify to be prescribed LLDs under primary CVDs prevention while Patients with known CHD like myocardial infarction (MI), angina, prior stroke, transient ischaemic attack (TIA), peripheral arterial disease and coronary revascularization, combination of risk factors that result in a 10 year risk of ASVD events of ≥ 20 %, chronic kidney disease with estimated GFR < 45mls/min/ 1.73m^2 and risk equivalent for CVDs in diabetic patients qualify for secondary CVD prevention.

Among the eligible patients in this current study, there were 43 stroke patients (67.2%), 13 IHD patients (20.3%), 4 patients with a high calculated 10 year ASCVD (6.3%) patients with a high calculated 10 year ASCVD while metabolic syndrome represented 2 patients (3.1%) and similarly diabetes mellitus patients aged above 40 years with the LDL ≥ 1.81 – 4.90mmol/L represented 2 patients (3.1%). On the overall, this picture shows that 56 patients (40%) were eligible under secondary prevention which is aimed at preventing the re-occurrence of the CVDs they had earlier suffered from while 8 patients (5.7%) were eligible under primary prevention because of their pronounced CVD risks. This was comparable to a study in German by Berthold and colleagues in 2009 which revealed that the prescription frequency of statins was significantly higher in the secondary prevention where CHD and peripheral diseases were concurrent representing 38.1% compared to the primary prevention group.

Further, the findings in this present study were comparable to the UK study in 2013 by Wu and friends where 41.7% of patients were found eligible for LLDs. The prescription patterns in this present study were at variance with the evidence based practice like the ATP IV guidelines which stresses the need to base LLD drug treatment on an individual's overall risk level, the practice which has been shown to be both less expensive and more effective which eventually might be expected to free up resources for other competing priorities, especially in developing countries than guidelines which depend on arbitrary criteria such as the ability to pay or on blanket preventive strategies (Gaziano, 2005).

Further, while total cholesterol was ≥ 5 mmol/L in 29 patients (20.7%), the calculated 10 year ASCVD based on the results taken within the last immediate 12 months and the other risk factors revealed that only 4 patients (2.9%) had the higher (10 year risk levels ≥7.5%)and thus, they were considered to be among those eligible for the LLD therapy. Taking total cholesterol ≥ 5mmol/L and other individual risks without gauging the patients' overall CVD risk could be one major reason which led to the prescription of LLDs for patients who were actually not eligible, representing 76 patients (54.3%).

On the other hand, there was a variation with the findings in a Portuguese study which showed a lower eligibility for LLDs which was at 29.8% (Alvez: Azevedo, 2003). This could be due to the

differences in the study setting in that while the present study was done at a single institution, theirs was a population based study.

5.4 Most commonly prescribed LLDs and their specific doses

The fourth and last objective was to identify the most prescribed LLDs and their doses. The findings were that statins were the most prescribed LLDs, representing 139 patients (99.3%) while only one patient (0.7%) was on a non statin LLD. Atorvastatin was the most prescribed statin with 20mg having been the most frequently prescribed dose with 91 patients (65%), followed by the 10mg dose which was prescribed for 38 patients (27.1%) while the 40mg dose was the least prescribed atorvastatin dose, having been prescribed in only 9 patients (6.4%). Rosuvastatin another statin drug was only prescribed in one patient (0.7%) and similarly, Omega 3 the only non statin LLD was only prescribed in one patient (0.7%).

The findings of atorvastatin having been the most prescribed LLD in the present study was comparable to an Indian study where Sreedevi and others reported in 2011 that atorvastatin was also the highest prescribed LLD, it having been prescribed in 85.3% patients. On the other hand there was a variation with the findings of the USA study in which Qiuping and colleagues reported in 2012 that Simvastatin was the most commonly used medication, with 42% of all cholesterol-lowering medication users reporting its use followed by atorvastatin at 20.2% and unlike the current study where patients were only prescribed a single group of drugs, it was revealed in the USA study that the majority of adults using a cholesterol-lowering medication reported using a statin alone 83% , followed by the 10% of patients who used both a statin and a non-statin while the 7% used only a non-statin.

In the period under review including the immediate past twelve months, simvastatin was found to have been more readily available at the Adult - UTH pharmacy than any other LLD (UTH Pharmacy records, 2016). With this in mind, the prescribing patterns in terms of drugs of choice in this present study could be said to have been influenced by the prescribers own preferences of drugs and probably on their clinical experience. Furthermore, when compared to atorvastatin, simvastatin is said to cause more adverse events like the serious myopathies especially the higher doses (FDA, 2011) and so this also could be one other reason why prescribers preferred atorvastain.

5.4.1 Appropriateness of dosing among the eligible patients

The appropriateness of dosing was only assessed among the 64 eligible patients and the findings were that only 10 patients (15.6%) received appropriate doses while 54 patients (84.4%) received inappropriate doses. According to ATP IV guidelines of 2013, patients with ASCVD like stroke and IHD are supposed to be prescribed high intensity statin therapy like rosuvastatin 20 – 40mg or atorvastatin 40 - 80mg with the aim of achieving LDL-C reduction by 50% as shown in appendix J. However, in this study only one patient (0.7%) among the stroke patients was prescribed the required high intensity statin therapy doses while none of the IHD patients were prescribed the required high intensity therapy. On the other hand, the appropriateness of prescribing atorvastatin 20mg and 10mg based on the 10 year ASCVD risk, 10mg for one metabolic syndrome patient and 20mg for one diabetes mellitus patient was also based on the recommendations of the guidelines which states that such patients should be treated with moderate intensity statin therapy with the aim of reducing LDL-C by 30 to 49% with drugs like atorvastatin 10 - 20mg, rosuvastatin 5 -10mg, simvastatin 20 – 40mg, pravastatin 40 - 80 mg, lovastatin 40mg.

The bivariate analysis results for association with dosing appropriateness at 5% significance level showed that only diagnosis category and prescribed LLD drug were significantly associated with dosing appropriateness among the categorical variables, P-values = 0.02 and < 0.001, respectively while among the continuous variables, lipogram duration was significantly associated with dosing appropriateness, P-value <0.001. TC and LDLC results were marginally associated with dosing appropriateness, P-values = 0.06 and 0.05, respectively. The unadjusted odds ratios for stroke medical history indicated that patients with no stroke history had on average 74% reduced odds for inappropriate dosing [Odds Ratio (OR) =0.26, 95% Confidence Interval (CI) = 0.06 – 1.22, P-value = 0.087) but this was not statistically significant. Compared to patients with other diagnosis category, patients with CVD diagnosis had on average 13 times increased odds for inappropriate dosing (OR = 13.2, CI = 1.76 – 98.93, P-value = 0.01) and this was statistically significant while Patients with HTN and diabetes co-morbidity had on average 6 times increased odds for inappropriate dosing (OR = 6.0, CI = 0.56 – 63.98, P-value = 0.14) although this was not significant (Table 4).

The high levels of inappropriate dosing among the eligible patients could be attributed to the lack of establishing the overall CVD risk in patients and hence making it difficult to gauge appropriate doses. The other reason could be the non availability of the local guidelines which are supposed to serve as the closest reference while not embracing the international guidelines like the ATP IV could be another reason.

CHAPTER SIX
CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

This study showed that hypertension was the most frequent individual CVD risk among those found to have been prescribed LLDs while CVDs in general were the most frequent diagnosis category. Further, the study showed that more patients were taking LLDs which actually they didn't even need as could be seen from the low levels of eligibility (45.7%). Atorvastatin was the most prescribed LLD while inappropriate dosing was high among the eligible patients (84.4%). This study suggests that the prescribing patterns were not in conformity with the ATP IV guidelines. This is because the prescribing patterns were found to be more inclined to individual CVD risk factors and not the overall levels of individual patient's risks as provided for by the ATP IV guidelines which emphasizes on the need to put in consideration of all the CVD risks and where possible, gauge patients' 10 year ASCVD risk level before initiating LLD therapy.

6.2 Recommendations

This covers the focus areas that should be taken from this study to help uphold the standard prescribing practice of LLDs which should help optimise therapeutic outcome. On the other hand, this part will also give guide on the suggested future studies to cover areas which this present study did not cover. The following are the recommendations;

i. There is need to always consider all the CVD risks and overall individual patient's levels of CVD risks and thereafter, decide whether they would benefit from high intensity, moderate intensity or mild intensity of LLD therapy.

ii. There will be need to have periodical clinical sensitization on the current guidelines like in this case the ATP IV guidelines on the prescription of LLDs so as to ensure that only eligible patients are prescribed LLDs so that they get the optimal desired benefit.

iii. There is need to formulate local guidelines in that while there is a growing trend of cardiovascular diseases, there are currently no local guidelines on the prescription of LLDs.

iv. The extent to which the level of qualification or experience of the prescriber affects the prescription patterns of LLDs remains speculated while the extent to which the availability, side effects and the cost of LLDs influence the prescription of LLDs and related doses need to be established. Further, the effectiveness of LLD therapy in achieving the required reduction percentages of LDL-C may need to be ascertained and so additional studies may be needed

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APPENDICES

Appendix A: Detailed table of patient summary descriptive statistics (categorical variables, n = 140)

Variable	Frequency (n = 140)	Percentage
Sex		
Male	51	36.4
Female	89	63.6
Age group		
25-44 years	19	13.6
45-74 years	102	72.9
75-92 years	19	13.6
BMI category		
Underweight	1	0.7
Normal	8	5.7
Overweight	3	2.1
Obese	35	25
Unrecorded	93	66.4
Smoking		
No	100	71.4
Yes	11	7.9
Unrecorded	29	20.7
Alcohol intake		
No	88	62.9
Yes	24	17.1
Unrecorded	28	20
Hypertension (HTN)		
No	15	10.7
Yes	125	89.3
Diabetes Medical History		
No	81	57.9
Yes	39	27.9
Heart Failure Medical History		
No	76	54.3
Yes	32	22.9
Unrecorded	32	22.9
Stroke Medical History		
No	79	56.4
Yes	47	33.6
Unrecorded	14	10

Continued - Patient summary descriptive statistics (categorical variables, n = 140)

Variable	Frequency (n = 140)	Percentage
IHD Medical History		
No	96	68.6
Yes	13	9.3
Unrecorded	31	22.1
Patients on anti – hypertensive medication		
No	14	10
Yes	126	90
Patients on anti – diabetic medication		
No	81	57.9
Yes	40	28.6
Unrecorded	19	13.6
Echoa and ECG		
No	39	27.9
Yes	76	54.3
Unrecorded	25	17.9
Cardiac_enzymes		
No	105	75
Yes	3	2.1
Unrecorded	32	22.9
Diagnosis category		
CVD	93	66.4
Kidney related	9	6.4
Obesity	2	1.4
Diabetes	2	1.4
HTN/DM	32	22.9
Metabolic Syndrome	2	1.4
Prescribed LLDs		
Atorvastatin 10mg	38	27.1
Atorvastatin 20mg	91	65
Atorvastatin 40mg	9	6.4
Rosuvastatin 20mg	1	0.7
Omega 3	1	0.7
Eligibility for prescribed LLDs		
No	76	54.3
Yes	64	45.7
Appropriate dosing among the eligible patients		
No	54	38.6
Yes	10	7.1
Not Eligible	76	54.3

Patient summary descriptive statistics (continuous variables)

Variable	Summary statistics
Age	
(n, mean, SD)	140, 58.9, 12.61
BMI	
(n, mean, SD)	47, 32.5, 6.67
TC	
(n, mean, SD)	56, 5.5, 1.24
LDLC	
(n, mean, SD)	20, 3.4, 0.81
HDLC	
(n, mean, SD)	13, 1.2, 0.30
TG	
(n, median, IQR)	32, 1.2, 0.66
Lipogram Duration	
(n, mean, SD)	55, 1.2, 0.76
Serum glucose	
(n, mean, SD)	8, 5.7, 1.24

Appendix B: Data collection form

Data form Number: .....

1. Name of Lipid lowering drug prescribed and dose: …….....

2. DEMOGRAPHIC DETAILS

a). Sex: Male ☐ Female ☐

(Tick in the appropriate box)

b). Age (years) .....

c) BP (mmHg) .....

d). Body weight (Kg) ..... Height (Mtrs) ..... Waist circumference .....

e). BMI (Kg/m^2) ..... (To be calculated using the standard formula)

3. SOCIAL DETAILS

a). Was the patient a Cigarette smoker?

Yes ☐ No ☐ (Tick in the appropriate box)

b) If the patient was a non smoker but has history of smoking, state possible the period that has passed from the time they last smoked.

.....

e). Was the patient taking alcohol?

Yes ☐ No ☐ (Tick in the appropriate box)

4. MEDICAL HISTORY

Did the patient suffer or have a history of having suffered from any of the following conditions?

(Tick in the appropriate box)

a). Hypertension Yes ☐ No ☐

b). Diabetes Yes ☐ No ☐

c). Cardiac failure Yes ☐ No ☐

d). Stroke Yes ☐ No ☐

e). IHD (STEMI or N-STEMI, Angina etc) Yes ☐ No ☐

If yes, State which one …….

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5. DRUG HISTORY

Was the patient taking drugs for any of the following conditions? (Tick in the appropriate box)

a). Hypertension Yes ☐ No ☐

b). Diabetes Yes ☐ No ☐

---

6. FAMILY HISTORY

a). Was there found any history CVDs or sudden death in the patient's family caused by stroke, heart failure, MI or other CVDs?

Yes ☐ No ☐ (Tick in the appropriate box)

b) If the answer to question 6 (a) was yes, what relationship was there between the patient and the person who died.....

---

7. LABORATORY DATA

Indicate details of the following laboratory findings if they were requested for during treatment.

a). Lipid profile:

Total cholesterol ..... LDL – C .....

HDL – C ..... Triglycerides .....

(Readings to be recorded using the unit of mmol/L)

b). Date when the test was done …….....

c). Serum glucose Fasting blood glucose (mmol/L).....

Appendix C: Major CVDs Risk Factors

The majority of CVDs risk factors can be controlled, treated or modified while some cannot be controlled (World heart federation 2012) and thus, they are classified either as modifiable or non-modifiable in nature. In the ATP III report, the National Cholesterol Education Program (NCEP) compiled the following as the major CVD risk factors:

- Age (men, 45 years; women, 55 years)
- Cigarette smoking
- Hypertension (blood pressure ≥ 140/90 mmHg or patient is on antihypertensive medications)
- Family history of premature CHD: (definite MI or sudden death before 55 years in father or other first degree male relative, or before age of 65 years in mother or other first degree female relative)
- Low high-density lipoprotein (HDL) cholesterol level (<40 mg/dL (1.04 mmol/L) in men, <50 mg/dL (1.30 mmol/L) in women). HDL cholesterol ≥ 60 mg/dl (1.55 mmol/L) counts as a negative risk factor and so its presence removes one risk factor from the total count.
- Risk equivalents - CHD "risk equivalents," are defined as another high risk category conferred with an estimated 10-year risk for a cardiovascular event of more than 20% (ATP III 2004) meaning that their presence will call for commencement of treatment. Diabetes and metabolic syndrome are common examples of the risk equivalents as explained below;

Diabetes -It has been established that individuals having plasma glucose value of 7.0mmol/L (126mg/dl) or higher have atherogenic dyslipidaemia (Verges 1999) and additionally, diabetes type 2 is associated with 2 to 3 fold increase in the likelihood of developing CVD (Fox et al 2004).

Metabolic syndrome – is characterized by the abdominal obesity, atherogenic dyslipidaemia, increased blood pressure, insulin resistance (with or without glucose intolerance) and pro thrombotic or pro-inflammatory states.

Other examples of risk equivalents are non-coronary atherosclerotic disease, such as peripheral vascular and carotid disease, and abdominal aortic aneurysm, diabetes mellitus and multiple CHD risk factors.

Appendix D: Risk Factors (WHF 2012 AND ATP III 2004)

MODIFIABLE RISK FACTORS	NON – MODIFIABLE RISK FACTORS
Hypertension – BP > 140/90mmHg is one of the important causes of premature death worldwide and is the leading cause of CVD	**Age** – CVD becomes increasingly common with advancing age because of the subtle physiological changes that occur when one gets older even in the absence of disease (45 years for men and 55 years for women)
Tobacco use – Smoking is estimated to cause nearly 10 % of all CVDs. Within two years of quitting, the risk of CHD is substantially reduced and within 15 years the risk of CVD returns to that of non smoker.	**Gender** – A man is at greater risk of heart disease than pre-menopausal woman. Once past the menopause, a woman's risk is similar to man's. however, risk of stroke is similar for men and women
Diabetes fasting – having plasma glucose value of 7.0mmol/L (126mg/dl) or higher. It is considered as a risk equivalent and is associated with a 2 to 3 fold increase in the likelihood of developing CVD (Fox et al 2004)	**Family history** – coronary heart disease e.g. definite MI or sudden death e.g from stroke before 55 years in father or other first degree male relative or before age of 65 years in mother or other first degree female relative
Physical inactivity – Insufficient of physical can be defined as less than five times 30 minutes of moderate activity per week or less than three times 20 minutes of vigorous activity per week or equivalent	
Unhealthy diet –high intakes of saturated fat, trans-fats, salt and low intakes of fruits, vegetables and fish are linked to CVD risk	
Dyslipidaemia – raised blood cholesterol increases the risk of heart disease and stroke. Low high-density lipoprotein (HDL) cholesterol level (<40 mg/dL in men, <50 mg/dL in women). HDL cholesterol ≥ 60 mg/dl counts as a negative risk factor and so its presence removes one risk factor from the total count.	
Overweight and obesity – strongly related to major CVD risk factors such as hypertension, glucose intolerance, type 2 diabetes and dyslipidaemia	

Appendix E: Fourth Guidelines of the Adult Treatment Panel (ATP IV) of 2013

The national Cholesterol Education program is managed by a division of the National institutes of Health called the National Heart, Lung and blood Institute whose main goal is to reduce increased CVDs rates due to dyslipidaemia by coming up with guidelines. These guidelines are written and regularly updated by a panel of experts called the Adult Treatment Panel [ATP]and have been supported by other organizations, including the American Heart Association (AHA), American College of Cardiology (ACC), American Diabetes Association (ADA), American Association of Clinical Endocrinologists (AACE), and American College of Physicians (ACP) ,

The ATP IV guidelines of 2013 is a comprehensive guideline for evidence –based treatment of blood cholesterol to reduce ASCVD risk which represent a change from ATP III guidelines of 2004 and below are the guidelines regarding what should be considered before commencing LLDs;

Primary prevention of CVDs

1. LDL-C ≥ 4.92 mmol/L (190 mg/dl).
2. Diabetes and aged 40-75 years with LDL-C between 1.81 – 4.90 mmol/L(70-189 mg/dl).
3. No diabetes and estimated 10 year ASCVD risk of ≥7.5 % who are between 40 to 75 years of age with LDL-C between 1.81 – 4.90mmol/L (70-189 mg/dl)

Secondary prevention of CVDs

1. Patients with known CHD i.e. myocardial infarction (MI), angina, prior stroke, transient ischaemic attack (TIA), peripheral arterial disease and coronary revascularization.
2. Combination of risk factors that result in a 10 year risk of atherosclerotic cardiovascular disease (ASVD) events of ≥ 20 %.
3. Chronic kidney disease with estimated GFR < 45mls/min/ 1.73m^2.
4. Risk equivalent for CVDs in diabetic patients.

Appendix F: Four Statin Benefit Groups - (Extract of ATP IV Guidelines Update, 2013)

Four 'Statin Benefit Groups' have been identified that have the potential to reduce the risk of atherosclerotic cardiovascular disease. The benefit of therapy has been found to clearly exceed the potential for adverse effects in adults. The four groups are as follows:

1. Individuals with clinical ASCVD (Secondary prevention): Clinical ASCVD Atherosclerotic Cardiovascular Disease is defined by the inclusion criteria for the secondary prevention statin RCTs (acute coronary syndromes, or a history of MI, stable or unstable angina, coronary or other arterial revascularization, stroke, TIA, or peripheral arterial disease presumed to be of atherosclerotic origin).

2. Individuals with primary elevations of LDL-C $\geq$ 4.92mmol/L (190 mg/dL)

3. Individuals 40 to 75 years of age with diabetes and LDL-C levels of 1.81 – 4.90 mmol/L(70-189 mg/dL). For the primary prevention of ASCVD in individuals with diabetes (diabetes mellitus type-1 and type-2), estimated 10-year ASCVD risk can also be used to guide the intensity of statin therapy.

4. Individuals without clinical ASCVD or diabetes who are 40 to 75 years of age with LDL-C 70- 189 mg/dL and an estimated 10-year ASCVD risk of 7.5% or higher. Data has shown that statins used for primary prevention have substantial ASCVD risk reduction benefits across the range of LDL-C levels of1.81 – 4.90 mmol/L(70-189 mg/dL).

Appendix G: The New Pooled Cohort Equations

This tool estimates the 10-year and lifetime risks for atherosclerotic cardiovascular disease (ASCVD) which is defined as coronary death or nonfatal myocardial infarction, or fatal or nonfatal stroke.

Age:	☐ Years
Gender:	◯ Female ◯ Male
Race	☐ White ☐ Black Americans ☐ Others
Total cholesterol:	☐ mmol/L
HDL cholesterol:	☐ mmol/L
Smoker:	◯ Yes ◯ No
Diabetes:	◯ Yes ◯ No
Systolic blood pressure:	☐ mmHg
Diabetes	◯ Yes ◯ No

Calculate risk:

The risk score is used to calculate a 10 year risk score and one's levels of risk is determined, the fact which together with the number of risk factors help to categorize patients as to whether they are high risk, moderately high risk, moderate risk or low risk. Risk equivalents and confirmed CHD are categorized as high risk.

Estimates of 10-year risk for atherosclerotic cardiovascular disease (ASCVD) are valid for ages 40 through 79. Estimates of lifetime risk for ASCVD are provided for adults 20 through 59 years of age.

For decision as to whether a patient qualified for LLDs, the ATP IV guidelines of 2004 was used and for this information, refer to appendix E.

NB: This assessment tool should not be used alone as a guide for patient care but should be used together with the practitioners clinical judgment.

Appendix H: European Society of Cardiology (ESC) Guidelines of 2016 with risk estimation based the SCORE (systemic coronary risk estimation) risk charts

RISK CATEGORY AND TREATMENT APPROACH	PRESENTING SYMPTOMS OR CONDITIONS
Very high risk Drug treatment is more frequently required in this category of patients	Subjects with any of the following: • Documented CVD, clinical or unequivocal on imaging. Documented clinical CVD includes; previous AMI, ACS, coronary revascularization and other arterial revascularization procedures, stroke and TIA, aortic aneurysm and PAD. Une-quivocally documented CVD on imaging includes; plaque on coronary angiography or carotid ultrasound. It does NOT include some increase in continuous imaging parameters such as intima–media thickness of the carotid artery. • DM with target organ damage such as proteinuria or with a major risk factor such as smoking or marked hypercholesterolaemia or marked hypertension. • Severe CKD (GFR <30 mL/min/1.73 m2). • A calculated SCORE ≥10%.
High risk These qualify for intensive lifestyle advice and may be candidates for drug treatment.	Subjects with: • Markedly elevated single risk factors, in particular cholesterol >8 mmol/L (>310 mg/dL)(e.g. in familial hypercholesterolaemia) or BP ≥180/110 mmHg. • Most other people with DM (with the exception of young people with type 1 DM and without major risk factors that may beat low or moderate risk). • Moderate CKD (GFR 30–59 mL/min/1.73 m2). • A calculated SCORE ≥5% and <10%.
Moderate risk These should be offered lifestyle advice to maintain their low- to moderate-risk status.	SCORE is ≥1% and <5% at 10 years. Many middle aged subjects belong to this category.
Low risk	SCORE <1%.

- Statin therapy is recommended as a first-line agent and should be the highest tolerated dose to reach goal.

Appendix I: Approximate Average Lipid Changes By Statin Dosage (Maron et al., circulation 2000)

Statin (mg/day)						Lipid Change (%)		
Rosuvastatin*	**Atorvastatin**	**Simvastatin**	**Lovastatin**	**Pravastatin**	**Fluvastatin**	**LDL-C†**	**HDL-C**	**TG**
		10	20	20	40	−22	4-8	−10-15
	10	20	40	40	80	−27	4-8	−10-20
	20	40	80			−32	4-8	−15-25
	40	80				−37	4-8	−20-30
	80					−42	4-8	−25-35
5						−38	10	−32
10						−45	11	−7
20						−48	5	−20
40						−56	7	−25

*Rosuvastatin (Crestor) package insert compared with placebo.

†The addition of ezetimibe, 10 mg, to any of these statins will reduce LDL-C by another 12% to 15%.

Appendix J: Intensity of statin Therapy According to the Expert panel (American Heart Association)

High - Intensity Statin Therapy	**Moderate-Intensity Statin Therapy**	**Low Intensity Statin Therapy**
Daily dose lowers LDL-C on average, by approximately ≥ 50%	Daily dose lowers LDL-C on average, by approximately 30 % to < 50%	Daily dose lowers LDL-C on average, by 30 %
Atorvastatin 40 – 80mg Rosuvastatin 20 - 40 mg	Atorvastatin 10 - 20 mg Rosuvastatin 5- 10mg Simvastatin 20 – 40mg Pravastatin 40- 80 mg Lovastatin 40mg Fluvastatin XL 40mg bid Pitavastatin 2 – 4 mg	Simvastatin 10mg Pravastatin 10 – 20mg Lovastatin 20mg Fluvastatin 20 - 40mg Pitavastatin1 mg

- Individual responses to statin therapy varied in the RCTs and should be expected to vary in clinical practice. These might be a biological basis for less than average response
- Evidence from one1RCT only: down-titration if unable to tolerate atorvastatin 80mg.
- Although simvastatin 80mg was evaluated in RCTs, initiation of simvastatin 80mg or titration to 80mg is not recommended by the Food and Drug administration (FDA) due to the increased risk of myopathy, including rhabdomyolysis.