

1.0 INTRODUCTION.

1.1 Purpose of the study and problems investigated.

In 1996 a study conducted at the Johannesburg Hospital concluded that the management of type 2 diabetics at the diabetes clinics was largely confined to the control of hyperglycaemia. Despite increased awareness of the risk factors for coronary artery disease (CAD), these risk factors were being largely ignored in the diabetic patients.¹

Atherosclerosis, particularly CAD, remains the most important cause of morbidity and mortality in patients with type 2 diabetes mellitus.² Intensive glycaemic control reduces microvascular complications as shown in the United Kingdom Prospective Diabetes Study (UKPDS); however its effect on macrovascular disease remains less clear. Risk factors for macrovascular disease in diabetic individuals include obesity, hypertension, dyslipidaemia, reduced physical activity and cigarette smoking.³ The Society for Endocrinology, Metabolism and Diabetes of South Africa (SEMDSA) published guidelines for Type 2 Diabetes care in 2003. These guidelines have clear recommendations for glycaemic control, blood pressure and lipid goals as well as aspirin recommendations.⁴ Obesity is also emerging as a major public health problem and has been recognised by World Health Organization (WHO) as a disease with significant morbidity.⁵

Current comprehensive management of type 2 diabetes mellitus patients should include not only good glycaemic control but also achievement of recommended blood pressure and lipid goals as provided in the SEMDSA guidelines. The purpose of this research report was to provide answers to questions proposed in the study objectives of the research protocol. The following were addressed in this research report:

1.1.1 To determine the extent of glycaemic control in the diabetics at our diabetes clinics as recommended by SEMDSA guidelines.

1.1.2 To determine the number of type 2 diabetics who have co-morbid hypertension and how many of those are reaching the targets recommended by SEMDSA guidelines.

1.1.3 To determine the number of diabetics who are at lipid goals proposed by the SEMDSA guidelines.

1.1.4 To determine the prevalence of obesity in diabetics at our diabetes clinics using the World Health Organization (WHO) definition of obesity.

1.1.5 To compare the findings with those of previous study conducted in 1996. The white patients of the current sample were used to compare the results with those of the 1996 study in order to avoid ethnicity as a confounding factor.

1.2 Validation of the problem.

SEMDSA website provides prevalence data of type 2 diabetes mellitus based on available publications to be approximately 5%-8% for African urban, 4%-8% for African rural, 3% for European and 13% for Indian population groups.⁶ Infectious diseases are currently the leading cause of death in Southern Africa but cardiovascular disease is a close second. Increasing urbanization as well as adoption of the unhealthy lifestyle is likely to result in further increase in the prevalence of cardiovascular disease.⁷

Type 2 diabetes mellitus represents the most common form of diabetes. Individuals with type 2 diabetes have a higher prevalence of metabolic abnormalities, including central obesity, hypertension, and a typical dyslipidaemia that is characterized by high

triglycerides and low high-density lipoprotein cholesterol. This combination of metabolic derangements is associated with a marked increase in the risk of atherosclerotic disease.⁸ Type 2 diabetes is a major worldwide cause of morbidity and mortality. Over the last decade a fundamental change of the principles of the management of type 2 diabetes has occurred. Driven by a large number of multicentre randomized clinical trials documenting improved outcomes associated with not only good glucose control, but also blood pressure and lipid management, as well as anti-platelet therapy, local guidelines have been established for comprehensive treatment of the diabetic patients (SEMDSA guidelines).⁴

The risk of heart disease and stroke is two to four times higher for people with diabetes. Based on twenty years of surveillance, the Framingham Study found a two- to threefold increased risk of clinical atherosclerotic disease in those with diabetes compared with non-diabetic patients.⁹ “Diabetes causes one death every 10 seconds and one amputation every 30 seconds worldwide, and is a major cause of adult onset blindness, cardiovascular disease, and renal failure.”¹⁰ Diabetic patients without previous myocardial infarction have as high a risk of myocardial infarction as non-diabetic patients with a previous myocardial infarction.¹¹ In the United States 70% of diabetics die of heart disease and stroke and at the present time the morbidity and mortality associated with diabetes is astounding. As cardiovascular disease is the ultimate cause of death in the overwhelming majority of patients with diabetes, blood pressure, lipid, anti-platelet therapy and avoidance of smoking are critical components of care. Substantial reduction in cardiovascular mortality could be achieved with aggressive treatment of hypertension, dyslipidaemia, smoking cessation and daily low-dose aspirin for most patients.¹²

The United Kingdom Prospective Diabetes Study demonstrated that lowering blood pressure significantly reduces strokes, diabetes-related deaths, heart failure and microvascular complications in patients with type 2 diabetes¹³ Hypertension affects 20%-60% of individuals with diabetes and the prevalence of hypertension is 1,5 - 3 times higher in diabetic than non-diabetic age-matched groups. The greatest reduction in cardiovascular mortality occurs when a diastolic blood pressure of ~80 mmHg or less is achieved¹⁴

The European Guideline on Cardiovascular Disease Prevention was adopted by the South African Heart Association in February 2000. Patients with type 2 diabetes are considered high risk and an LDL-cholesterol of less than 2,5 mmol/l is recommended for these patients.¹⁵ National Cholesterol Education Program Adult Treatment Panel III Guidelines not only support the notion that diabetics should be considered a coronary heart disease risk equivalent and that therapy should aim for an LDL-cholesterol of less than 2,6 mmol/l but also, based on the Heart Protection Study (HPS) and Pravastatin or Atorvastatin Evaluation and Infection-Thrombolysis in Myocardial Infarction 22 (PROVE IT) study, suggest that even lower LDL-cholesterol targets (less than 1,8 mmol/L) may be appropriate.¹⁶ Lipid management has also been shown to decrease macrovascular disease and mortality in patients with type 2 diabetes.¹⁷

In summary cardiovascular disease is a significant cause of illness, disability, and death among individuals with type 2 diabetes mellitus. The macrovascular complications of

diabetes account for more than 70% of all deaths. “Cardiovascular disease events are four times more common in diabetics, occur at younger age, and have a much greater case-fatality rate.”¹⁸ However, in spite of evidence that aggressive risk factor reduction lowers the risk of macrovascular complications in patients with diabetes; the vast majority of patients do not achieve recommended goals for HbA1c, blood pressure and lipid profiles.¹⁹

1.3 Preview of the organization of the research report.

The remainder of the introductory chapters in this research report concentrates on the review of previous investigations of the problems proposed in this study.

The central chapters that follow present the findings of this study and include a brief description of the methods used to collect and analyze the data. The findings are addressed one at a time following the order of study objectives proposed in the research protocol.

Tables with data collected in the study are included in the appendices, and references are made to figures that serve to present the material in a clear and orderly fashion.

The concluding chapters summarize the findings of this study emphasizing the important conclusions of the whole study. Limitations of the study and questions that arose during the study, but the answers to which are beyond the limits of this research report, are put forward in these chapters. References, Appendix A containing proposed patient visit sheet, Appendix B containing ethics approval documentation and Appendix C which includes tables with data collected in the study, a copy of the patient data sheet, patient information sheet, consent form and a letter for the diabetic clinic sister, complete this research report in the given order.

1.4 Review of current literature.

1.4.1 Comprehensive management of non-insulin dependent diabetes mellitus.

In 1996 Raal et al, 'revisited' the diabetic clinic at the Johannesburg Hospital. The study was a follow up to the 1974 study that showed an unacceptably high prevalence of obesity and hyperlipidaemia at the diabetes clinic at the Johannesburg Hospital and it was concluded that the management of type 2 diabetes was largely confined to the control of hyperglycaemia.²⁰ In the 1996 study eighty-two patients (39 males and 43 females) were tested. The objectives of this research report were to ascertain whether the established risk factors for coronary artery disease were being identified and appropriately managed. The patients were thirty-five years and older with a mean age of sixty and on average had diabetes for 6,2 years. Despite increased awareness of the risk factors for the coronary artery disease these factors had been largely ignored. Thus the conclusion of the 1996 study was that the management of patients at our diabetes clinics was still largely confined to the control of hyperglycaemia.

1.4.2 AUDIT study. Evidence of global under-treatment of dyslipidaemia in patients with type 2 diabetes mellitus.

The Analysis and Understanding of Diabetes and Dyslipidaemia: Improving Treatment (AUDIT) study was a cross-sectional survey involving 2,043 diabetes specialists in fifty countries.²¹ The study investigated the attitudes of physicians specializing in the treatment of patients with type 2 diabetes mellitus towards the management of dyslipidaemia and other cardiovascular risk factors in these patients. The study also confirmed under-treatment of cardiovascular risk factors in type 2 diabetic patients and "showed a worrisome treatment gap between screening for dyslipidaemia and intensive lipid control in patients with type 2 diabetes, especially for those without diagnosed cardiovascular

disease”. Type 2 diabetes was not widely regarded as a coronary heart disease risk equivalent.

1.4.3 Poor control of risk factors for vascular disease among U.S adults with previously diagnosed diabetes.

A study done in United States in order to examine 1999-2000 national data on control of risk factors for vascular disease among civilian U.S population with previously diagnosed diabetes confirmed that even though the control of blood glucose, blood pressure and cholesterol levels is proven to reduce the risk of vascular disease among individuals with diabetes mellitus, further public health efforts are needed to control these risk factors.²²

1.4.4 Glucose, lipid, and blood pressure control in Australian adults with type 2- diabetes.

AusDiab was a national population-based survey of the general population. Of 11, 247 participants, 439 had previously diagnosed type 2 diabetes. The percentage of participant failing to achieve the accepted national clinical targets recommended for diabetes management in place at the time of the survey were determined. Only half of the population met the individual glycemic, lipid, and blood pressure targets recommended at the time of the survey, and approximately one in seven met all three targets. The observations reported in the AusDiab study indicate that the “opportunities for cardiovascular disease risk reduction are missed, as a significant number of type 2 diabetics were not meeting targets for both blood pressure and cholesterol.”²³

1.4.5 “Trends in lipid management among U.S patients with coronary artery disease.”

The objective of this study was to examine lipid management trends for coronary artery disease patients with and without diabetes in order to determine whether those with diabetes are beginning to receive aggressive lipid management consistent with their elevated risk. Outpatient medical records were used from 47, 813 coronary artery disease patients between 1996 and 1998. The study showed that, despite evidence that patients with diabetes have a greater risk for cardiovascular events than coronary artery disease patients without diabetes, there is persistent under-treatment of hyperlipidaemia among coronary artery disease patients with diabetes in relation to those without diabetes. Patients with diabetes were 26% less likely to have a lipid profile and 17% less likely to receive a lipid lowering medication than their non-diabetic counterparts. The limitations of this study include potential for incomplete medical information and patient compliance, as the data was collected via chart review. The results may also not be relevant to the entire U.S. population, taking into consideration that, as indicated in the study, only medical practitioners with high-volume use of medication were invited to participate.²⁴

1.4.6 ADA and ACC Survey Finds Awareness of Link between diabetes, heart disease and stroke critically lacking.

A recent survey of 2,008 people in United States with diabetes revealed that 68% were not aware of their increased risk for heart disease and stroke- the leading cause of death in people with diabetes. The American Diabetes Association (ADA) and American College of Cardiology (ACC) commissioned this survey.²⁵

1.4.7 Heart Protection Study (HPS)

The recently completed HPS enrolled 5963 UK patients (age 40-80 years) with diabetes and 14573 with occlusive arterial disease (but no diabetes). The patients were randomly allocated to receive 40 mg simvastatin daily or matching placebo. Both among the participants who presented with diabetes and among those who did not, there were highly significant reductions of about 25% in the first event rate for major coronary events, for strokes, and for revascularisations.^{26, 27} The conclusions of the HPS were that cholesterol lowering with statin therapy can produce substantial reductions in the risk of heart attacks, strokes, and revascularization in people with diabetes.

1.4.8 Multi-factorial Intervention and Cardiovascular Disease in patients with type 2 diabetes.

Steno-2 Study was a randomized, open, parallel trial conducted in Denmark. In this study target driven, long term, intensified intervention aimed at multiple risk factors in patients with type 2 diabetes and microalbuminuria was compared with conventional treatment. Eighty patients were randomly assigned to receive conventional treatment for multiple risk factors and the remaining eighty patients were randomly assigned to undergo intensive multi-factorial intervention. The macrovascular study ended in December 2001 after eight years of follow up. The mean age of patients was 55,1 years. A total of 118 cardiovascular events occurred during follow up. There were 85 events among 35 patients in the conventional-therapy group, as compared with 33 events among 19 patients in the intensive-therapy group. Diabetic nephropathy developed in 31 patients in the conventional group and 16 in the intensive group. Retinopathy developed in 51 and 38 patients in the conventional and intensive therapy group respectively. Taken together, these data suggest that a “long-term, targeted, intensive intervention involving multiple risk factors reduces

the risk of both cardiovascular and microvascular events by about 50 percent” among patients with type 2 diabetes and microalbuminuria.²⁸

1.4.9 Diabetes guidelines: what really happens in practice.

In the 2006 November issue of the South African Medical Journal, Doctor Farham emphasizes that even though most countries have well-established guidelines for the management of diabetes, the gap between recommendations and practice is wider than is desired in a significant number of patients.²⁹

1.4.10 Diabetes guidelines: easier to preach than practice?

This study was a retrospective audit of outpatient management of type 1 and type 2 diabetes mellitus patients in Australia. Ninety-six patients with type 1 diabetes and five hundred and nine patients with type 2 diabetes were included. Main outcome measures included body mass index, treatment of glycaemia, blood pressure and serum lipids. Looking at the patients with type 2 diabetes only, the study showed that only 30% of patients had glycated haemoglobin (HbA1c) less than 7%, 71% of patients were treated with anti-hypertensive therapy and, of these patients, only 24% had blood pressure less than 130/80 mmHg. About 50% of type 2 diabetics were on lipid-lowering therapy and only 60% had LDL-cholesterol less than 2,6 mmol/l. Thus treatment targets were not being met in a large number of type 2 diabetics.³⁰

1.4.11 Dyslipidaemia in diabetes- an approach to therapeutic intervention.

This review emphasised that although the diagnosis of diabetes is confirmed on blood-glucose levels and anti-diabetic treatment is usually aimed at reducing glucose levels, the major contributor to mortality in diabetics is, in fact, cardiovascular disease.

Macrovascular disease or atherosclerosis, accounts for at least 70% of all mortality in diabetic patients. About 75% of this atherosclerotic diabetic mortality is the consequence of coronary artery disease, the remaining 25% results from the combination of the cerebrovascular disease, peripheral vascular disease or both. Lipid disturbances are common in diabetic subjects, and probably contribute to the high incidence of vascular disease in these patients. Dyslipidaemia should therefore be looked for, and treated, in every diabetic patient. Important conclusions from this review include that type 2 diabetes is not solely a disorder of carbohydrate metabolism but a component of “insulin resistance” syndrome- a cluster of metabolic disorders including impaired glucose tolerance, hypertension, abdominal obesity and dyslipidaemia. It is important to treat all the risk factors as the treatment of hyperglycaemia per se have had little impact on the morbidity and the mortality from macrovascular disease in diabetes.³¹

1.4.12 The Collaborative Atorvastatin Diabetes Study (CARDS).

CARDS study included 2838 patients aged 40-75 years in 132 centres in the UK and Ireland. The patients were randomized to placebo or 10 mg of atorvastatin daily. The patients had no documented history of cardiovascular disease, LDL-cholesterol of 4,14 mmol/l or lower and at least one of the following: retinopathy, albuminuria, smoking or hypertension. The primary end point was time to first occurrence of an acute coronary heart disease event, coronary revascularization or stroke. The findings of this randomized trial showed that acute heart disease events were reduced by 36%, coronary revascularizations by 31%, rate of stroke by 48% and mortality by 27%.³²

1.1.13 4S: Scandinavian Simvastatin Survival Study.

The 4S study was a double-blind, randomized, placebo-controlled clinical trial carried out in 94 clinical centers in Denmark, Finland, Iceland, Norway, and Sweden. The study included men and women aged 35-70 years with previous myocardial infarction or angina pectoris. Of the 4,444 randomized patients, 202 were diabetic (97 randomized to placebo and 105 to simvastatin). The reductions in risk in diabetic patients were 55% for major CHD events, and 37% for any atherosclerotic event.^{33, 34}

1.1.14 ACCORD: Action to Control Cardiovascular Risk in Diabetes Study.

ACCORD represents the largest global study to date in the effort to minimize cardiovascular events in patients with diabetes. This randomized, multi-centre, double blind 2×2 factorial study has enrolled 10,251 patients with type 2 diabetes mellitus. The trial is designed to test the effects on major CVD events of intensive glycaemic control, of treatment to increase HDL-cholesterol and decrease triglycerides, and of intensive blood pressure control. Primary outcome measure for the trial is the first occurrence of a major cardiovascular disease event, specifically non-fatal myocardial infarction, non-fatal stroke, or cardiovascular death. Participants will be treated and followed for 4-8 years at 77 clinical sites administratively located within 7 Clinical Centre Networks in the United States and Canada. Follow up is scheduled to end in June 2009, with the primary results announced in early 2010.³⁵

1.1.15 Multiple Risk Factor Intervention Trial.

The objective of this study was to assess predictors of CVD mortality among men with and without diabetes mellitus and to assess the independent effect of diabetes on the risk of CVD death. Participants were screened from 1973 to 1975 and followed up for 12 years.

Participants were 347,978 men aged 35-57 years, screened in 20 centres in the United States. For men with and without diabetes mellitus, serum cholesterol, blood pressure and cigarette smoking were significant predictors of CVD mortality. For diabetic men the absolute excess risk was progressively greater than for non-diabetic men with higher risk factor levels. Diabetes raises the risk of cardiovascular disease by a factor of $\sim 2,5-3,0$.^{36, 37}

1.1.16 Effects of intensive blood pressure lowering and low dose aspirin in patients with hypertension: principal results of the Hypertension Optimal Treatment (HOT) randomized trial.

This trial included 18,790 patients from 26 countries, aged 50-80 years (mean 61,5 years) with hypertension and diastolic blood pressure between 100 mmHg and 115 mmHg (mean 105 mmHg). In the study sample 6264 patients were randomly assigned to the target pressure less or equal to 90 mmHg, 6264 to less or equal to 85 mmHg, and 6262 to less or equal to 80 mmHg. Felodipine (long acting calcium channel blocker) was given as a baseline therapy with addition of other agents, according to five step regimen. In addition 9399 patients were randomly assigned 75 mg/day acetylsalicylic acid and 9391 patients were assigned placebo. The lowest incidence of major cardiovascular events occurred at mean achieved diastolic blood pressure of 82, 6 mmHg. In patients with diabetes mellitus there was a 51% reduction in major cardiovascular events in the target group with diastolic blood pressure less or equal to 80 mmHg compared with target group with diastolic blood pressure less or equal to 90 mmHg ($p= 0,005$). Acetylsalicylic acid reduced major cardiovascular events by 15% and myocardial infarction by 36%, with no effect on stroke.^{38, 39}

1.1.17 Anglo-Scandinavian Cardiac Outcomes Trial-Lipid Lowering Arm (ASCOT-LLA).

This study aimed to establish the benefits of lowering cholesterol in diabetic patients with well controlled blood pressure and average to below-average cholesterol concentrations, but without established coronary disease.⁴⁰ In the lipid-lowering arm of the ASCOT, 10,305 hypertensive patients with no history of coronary heart disease but at least three cardiovascular risk factors were randomly assigned to receive 10 mg of atorvastatin daily or placebo. Effects on total cardiovascular outcomes in 2,532 patients who had type 2 diabetes at randomization were compared. Median follow up was 3,3 years. Overall, 90% of diabetic participants were white and 76% male, with a mean age of 64 years. Among diabetic participants in the atorvastatin group, total cholesterol and LDL-cholesterol at the end of the study were lower than in the placebo group by 0,9 mmol/l. Compared with placebo, atorvastatin significantly lowered the incidence of total cardiovascular events and procedures among the diabetic group by 23% ($p = 0,036$).

2. CENTRAL CHAPTERS: CURRENT STUDY RESULTS.

2.1 Sources of data and methods.

2.1.1 Sources of data.

The data in this clinical audit was collected from the three academic hospitals (Johannesburg Hospital, Baragwanath and Helen Joseph Hospital) that are part of the University of the Witwatersrand Academic Complex. The sample of 150 patients, which was the minimum number required in order to obtain statistical significance, was calculated with the assistance of a statistician. Inclusion criteria included subject age 35 years and older with a diagnosis of type 2 diabetes on diet, oral agents, insulin (Protaphane) or combination thereof, as treatment. Males and females of all ethnic groups were included in the sample. The end point was marked by the collection of 150 patients. Ethics approval was obtained from the Human Research Ethics Committee of the University of the Witwatersrand (protocol number M060807 - Appendix B).

2.1.2 Methods.

The sister in charge on a given day was provided with a letter stating the aims of the study and invitation to participate. The sister was requested to randomly pick ten patient files. If the patients met the inclusion criteria and were willing to participate they were referred to the doctor in charge of the study. Patients were each provided with a patient information sheet. The aims of the study were explained to each patient and it was emphasised that there were no risks associated with the study. If the patients were willing to participate thereafter they were required to sign a written consent in the presence of a witness.

Patient data sheet were collected. Patients were each allocated a study number. The following data was collected on a patient data sheet:

2.1.2.1 Demographic data: hospital involved, age of the patient, gender of the patient

2.1.2.2 Diabetes and CVD related data: duration of diabetes, presence of other cardiovascular risk factors (coronary artery disease, cerebrovascular disease, peripheral vascular disease, hypertension, family history of premature cardiovascular disease, hyperlipidaemia, exercise, smoking and alcohol intake), and presence of other co-morbid illnesses.

2.1.2.3 Treatment of diabetes and co-morbid diseases, specifically looking at diabetic treatment, aspirin usage, lipid-lowering therapy, anti-hypertensive therapy and other agents.

2.1.2.4 Measurements: waist circumference (cm), height (m), weight (kg), BMI (weight/height²), blood pressure (mmHg).

2.1.2.5 Blood results: fasting lipograms and glycated haemoglobin.

2.1.2.6 Measurements:

Blood pressure measurements were done in triplicate by a single observer using an automatic device after the patient has been resting supine for at least five minutes. The patient was in a sitting position with a back supported, arm bared and resting on the surface at the heart level. The patient was requested not to smoke or consume caffeine-containing beverages in the previous 30 minutes and the appropriate cuff size was used (12 cm for a normal arm and 15 cm for an arm with a mid-upper circumference of ≥ 33 cm). These measurements were done in accordance with the recommendations provided in the South African Hypertension Guidelines 2006.⁴¹ Society for Endocrinology, Metabolism and Diabetes of South Africa (SEMDSA) recommendations for blood pressure goals were

used. Systolic blood pressure of < 130 mmHg and Diastolic blood pressure < 80 mmHg are the recommended targets provided dipstick proteinuria is absent.

Height was measured with a tape measure and recorded in metres. The person was requested to stand barefoot with his/her back against the wall. The feet were held together with the heels placed firmly on the ground and touching the wall. All hats, hair combs, hair bands, clips or pins were removed prior to the measurements. These measurements were done according to the recommendations in the guidelines for the prevention and management of overweight and obesity in South Africa.⁵

Weight was measured with a standard, calibrated scale. The scale was placed on a firm, flat surface. Patients were requested to remove any heavy outer clothing and were barefoot. The individuals standing on the scale were requested not to hold on to the wall or any other support. These measurements were also in accordance with the recommendations of the South African obesity guidelines.

Waist circumference was measured with the individual standing in the upright position, in a horizontal plane mid-way between the superior iliac crest and the rib cage in the mid-axillary line, at the end of normal expiration. Heavy outer clothing and binding garments were removed in order to achieve an accurate measurement. These standards conform to South African obesity guidelines. The IDF consensus worldwide definition of the

metabolic syndrome was used as a gold standard with central obesity being defined as waist circumference greater or equal to 94 cm in males and 80 cm in females.⁴²

Body Mass Index was calculated using the following: $BMI = \text{Weight (kg)} / \text{Height (m)}^2$.

World Health Organization classification of overweight and obesity (based on the BMI)

was used: Underweight	BMI	<18, 5	kg/m ²
Normal weight	BMI	18, 5 – 24, 9	kg/m ²
Overweight	BMI	25, 0 – 29, 9	kg/m ²
Obese Class I	BMI	30, 0 – 34, 9	kg/m ²
Obese Class II	BMI	35, 0 – 39, 9	kg/m ²
Obese Class III	BMI	≥ 40, 0.	

All of the above measurements were done by the doctor in charge of the study in order to minimize any measurement bias.

2.1.2.7 Blood Results:

Fasting serum lipograms and glycated haemoglobin results were obtained from the 2006 patient records. HbA1c was measured using Tina-Quant Hemoglobin A1c II immunological assay (currently used in the three academic hospitals). In 1996 affinity chromatography was used to calculate the HbA1c. SEMDSA guidelines for type 2 diabetes were used as a gold standard for glycaemic control and lipid goals.⁴

Recommendations for glycaemic control:

HbA1c	< 7 %	optimal
HbA1c	7-8 %	acceptable

HbA1c > 8 % addition action required.

Recommendations for lipid goals:

Total-cholesterol < 5,0 mmol/l

LDL-cholesterol < 2,5 mmol/l

HDL-cholesterol > 1,2 mmol/l

Triglycerides < 1,5 mmol/l.

These are in keeping with SEMDSA guidelines. LDL level of less than 2,5 mmol/l has been adopted from the South African Heart Association guidelines in view of the fact that current literature supports that lower LDL cut-off may be appropriate.^{15,16}

The above results were collected on the patient information sheet and subsequently tabulated in order to aid statistical analysis of the data. Diabetic sister information sheet, patient information sheet, data sheet and consent forms as approved by the Ethics committee are attached at the end of this research report- Appendix C.

2.1.2.8 Statistical analysis of the data.

Data collected on the patient data sheet was tabulated using Microsoft Office Excel 2003.

This data was subsequently analyzed with the assistance of Professor Becker and Paul Nasera (statisticians).

Estimation of the sample size was done assuming that LDL-cholesterol is normally distributed in the population. A significance level of 5%, precision 0,92 and standard

deviation 5,78 was calculated using the 1996 study. The above measurements were subsequently used to calculate a sample size of 150 that would be statistically significant. Descriptive statistics were used to describe and analyze the data. Mean as defined by the sum of all the observations divided by total number of all observations was calculated for age, duration of diabetes, BMI, systolic and diastolic blood pressure, total cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides and HbA1c. The means procedure was calculated separately for the entire sample and for the white patients in the sample. The latter was done to allow direct comparison with the 1996 results and to avoid ethnicity as a confounding factor. Two-sample t-test with equal variances, 99 degrees of freedom and 95% confidence intervals was used to calculate a p-value and thus compare the 1996 results with the current data. In addition to means procedures, percentage of patients meeting the recommended goals for HbA1c, BMI, waist circumference, blood pressure and lipids were calculated. Correlations of serum triglycerides and BMI, serum total cholesterol and BMI, serum HbA1c and total cholesterol as well as serum HbA1c and triglycerides were also analyzed. Additional calculations looking at the percentage of patients following a diabetic diet, smoking trends, lipid-lowering therapy usage in the three hospitals including its relation to achieving lipid targets, exercise trends, and aspirin usage were done. P-value less than 0.05 was regarded as significant.

2.2 Results

2.2.1 Comparison of the current results with the 1996 study.

In 1996 Raal et al. conducted a study at the Johannesburg Hospital. The study included eighty-two type 2 diabetic patients (39 males and 43 females). The mean age was 60 years (± 10.3). In the current study 150 patients were collected from the three academic hospitals (50 patients from each), 19 patients (12,67%) out of 150 were of white ethnic group. In order to avoid ethnicity as a confounding factor, only white patients will be discussed in this part of the research report. It is important to emphasise that sample size of 150, calculated from the 1996 study, is required for statistical significance. The main aim of this study was not to compare current results with the 1996 results but to analyze a statistically significant sample of 150 in 2006. The sub-analysis of the 19 white patients is statistically not significant as means of comparison to the 1996 study and hence the p-values must be interpreted with caution. Mean age of the white patients in the current study was 64 years ($\pm 9,53$). P-value of 0,12 showed no statistical difference between the mean age in 1996 and the current study.

In 1996 affinity chromatography was used to measure HbA1c and subsequently Tina-quant Haemoglobin A1c II immunological assay was adopted making the direct comparison of the 1996 and current results difficult. In view of the fact that it cannot be assumed that there is no statistical difference between the two assays, no direct comparison was made and p-value was not calculated. The mean HbA1c was 9,97% ($\pm 3,11$) in 1996 and in the current study 7,43% ($\pm 1, 60$).

In 1996, mean Body Mass Index (BMI), was $29,8 \text{ kg/m}^2 (\pm 5, 53)$ and in the current study $31,28 \text{ kg/m}^2 (\pm 7,46)$. P-value of 0, 33 showed no statistical difference.

In 1996 mean systolic blood pressure was 143 mmHg ($\pm 21,6$), whereas in the 2006 study 133 mmHg ($\pm 18,59$). Two-sample t-test p-value of 0,077 indicates a marginally significant result. The mean for diastolic blood pressure in 1996 was 82 mmHg ($\pm 12,4$) and in the current study 75 mmHg ($\pm 9,08$). P-value of 0,023 shows a statistically significant improvement.

The analysis of the blood lipograms revealed a mean total cholesterol of $6,29 (\pm 1,34)$ mmol/l in 1996 and $4,73 (\pm 0,97)$ mmol/l in 2006. P-value of less than 0, 0001 is in keeping with a statistically significant result. However it is important to note that SEMDSA guidelines recommend that total cholesterol of < 5 mmol/l should be reached in all diabetic patients and even though some improvement in the management of diabetes associated dyslipidaemia was observed only one patient had total cholesterol of less than 2,6 mmol/l, five between 2,6 and 3,9, eight between 3,9 and 5,2 and five greater than 5,2 mmol/l. The X-axis cut-off values were chosen to match those used in 1996 - Figure 2.2.1. The mean triglyceride level in 1996 was $2,38 \text{ mmol/l} (\pm 1,30)$ and was $1,83 \text{ mmol/l} (\pm 0,93)$ in the current study ($p=0.085$). A significant number of patients were still not reaching the triglyceride target of less than 1,5 mmol/l recommended by SEMDSA (13 patients out of 19) – Figure 2.2.2.

Figure 2.2.1 Distribution of total cholesterol among the white patients of the 2006 study

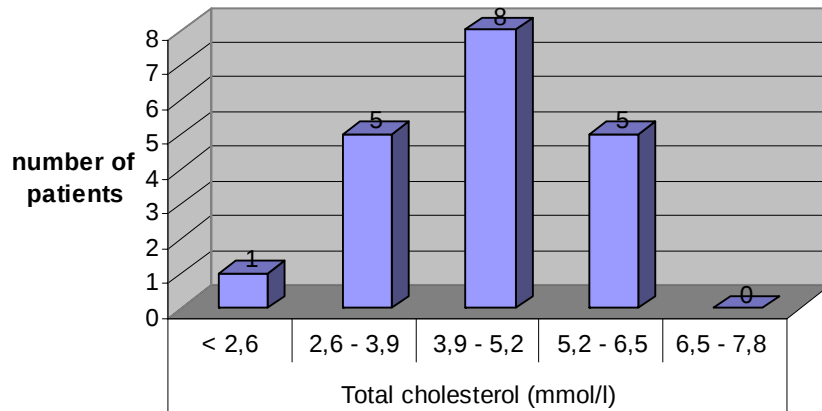
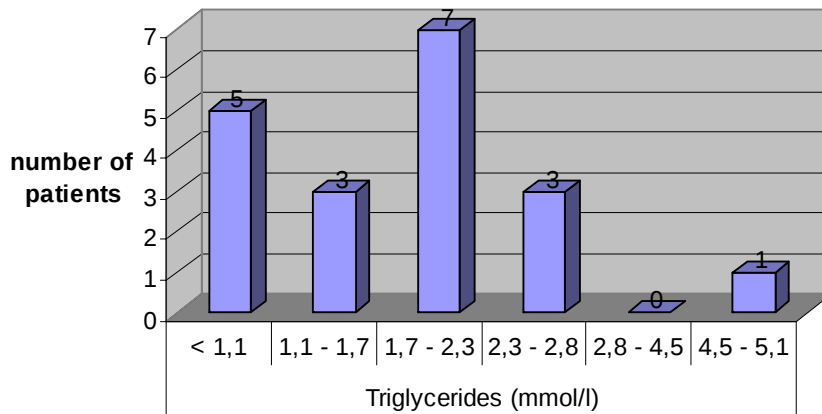


Figure 2.2.2 Distribution of serum triglycerides among the white patients of the 2006 study



High density cholesterol (HDL) targets of greater than 1,2mmol/l are recommended by the current SEMDSA guidelines. In the 1996 study mean HDL was 1,11mmol/ l ($\pm 0,4$) and in 2006 1,17 mmol/l ($\pm 0,32$). P-value of 0,54 indicating no statistically significant improvement.

The low density lipoprotein cholesterol (LDL) mean level was 4,12 mmol/l ($\pm$ 1,25) in 1996 and 2,77 mmol/l ($\pm$ 0,96) in 2006. T-test p-value of 0, 0001 implies a statistically significant improvement but still only seven patients out of 19 (36,84%) had LDL less than 2,5 mmol/l and 12 out of 19 (63,16%) greater or equal to 2,5 mmol/l. Thus despite improvement in the mean LDL levels, a significant number of patients are still not reaching the recommended targets. Table 2.2.1 summarises the results for the white patients in the current sample.

Table 2.2.1 Means procedure-summary of the results for the white patients				
Variable	Label	N	Mean	Std Dev
age	age (years)	19	64.10	9.53
BMI	BMI (kg/m ²)	19	31.28	7.46
SBP	SBP (mmHg)	19	133.42	18.59
DBP	DBP (mmHg)	19	75.00	9.08
cholesterol	TC (mmol/l)	19	4.73	0.97
TGs	TGs (mmol/l)	19	1.83	0.93
HDL	HDL (mmol/l)	19	1.17	0.32
LDL	LDL (mmol/l)	18	2.77	0.96
HBA1c	HBA1c(%)	19	7.43	1.60

In the 1996 study it was demonstrated that even though triglyceride levels tended to increase with an increase in BMI, there was no significant correlation between BMI and triglycerides ($r = 0, 14$) or serum cholesterol ($r = 0, 08$). In the 2006 study no correlation between serum triglycerides and BMI ($r = 0, 07$ $p = 0, 78$) or serum total cholesterol and BMI ($r = -0, 29$ $p = 0, 22$) was noted yet again. In the 1996 study there was also no correlation between glycaemic control as measured by HbA1c and either serum total cholesterol ($r = 0, 08$) or triglycerides ($r = 0, 14$). In 2006 yet again no correlation between HbA1c and either total cholesterol ($r = -0, 14$ $p = 0, 56$) or triglycerides ($r = -0, 07$ $p = 0, 75$) was noted.

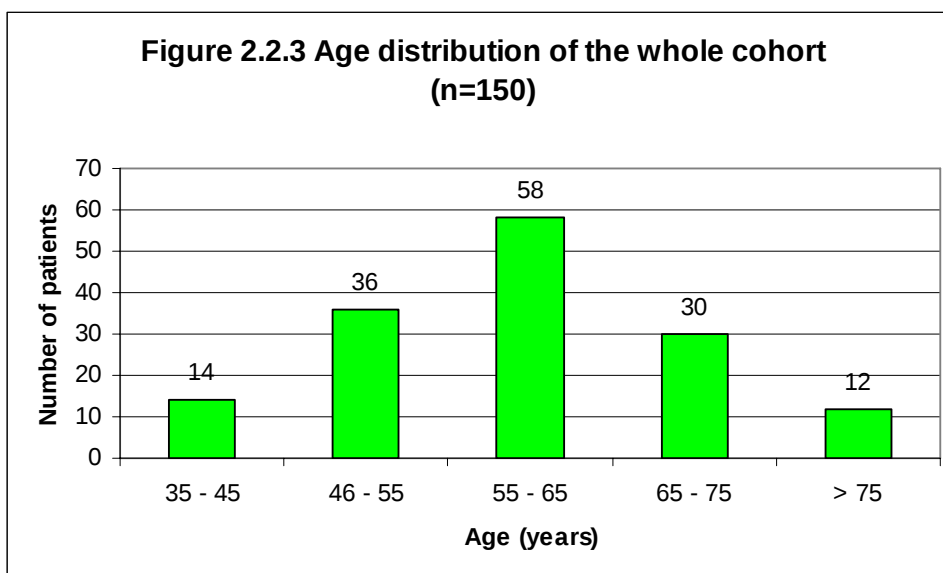
2.2.2 Results for the whole cohort (150 patients).

2.2.2.1 Patient demographic profile.

One hundred and fifty patients were collected from the three hospitals (each hospital contributing one third of the total). The sample included:

- 102 black patients (68%)
- 13 coloured patients (8,7%)
- 16 Indian patients (10,7%)
- 19 white patients (12,7%).

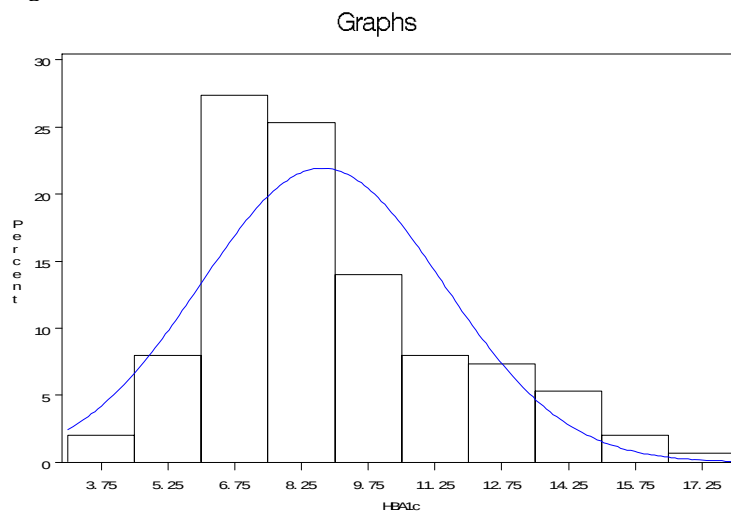
Out of the one hundred and fifty patients, ninety eight were females and fifty two were males. In the sample the mean age was 59,85 years with a standard deviation of 10,77. It is interesting to note that in 1996 study the mean age was 60 years with a standard deviation of 10,3. The age distribution of the whole cohort is shown by Figure 2.2.3.



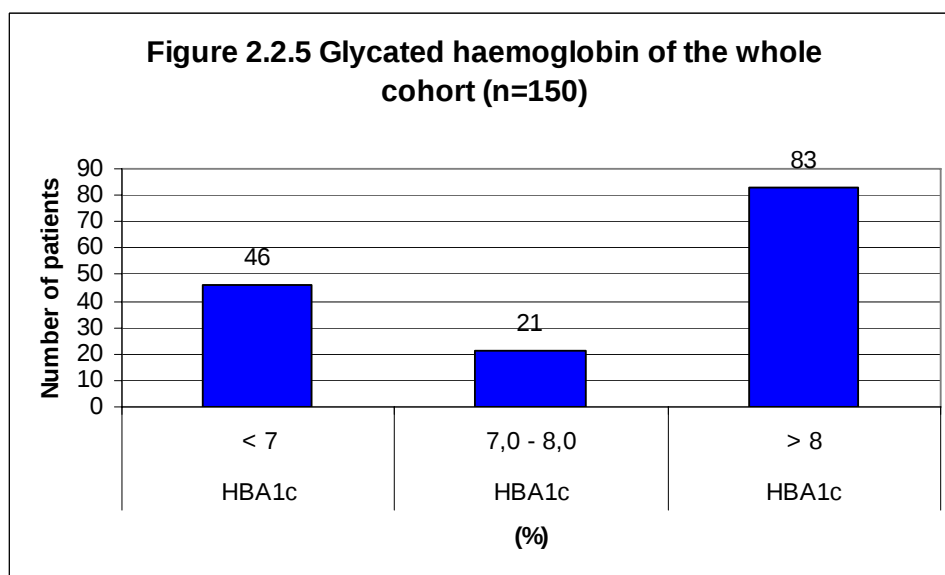
2.2.2.2 Glycaemic control.

In the analysis of the data the range for HbA1c was 3,6% to 16,9%. HbA1c was normally distributed and thus followed a bell shaped curve with a mean of 8,72% and standard deviation of $\pm 2,73$ - Figure 2.2.4.

Figure 2.2.4

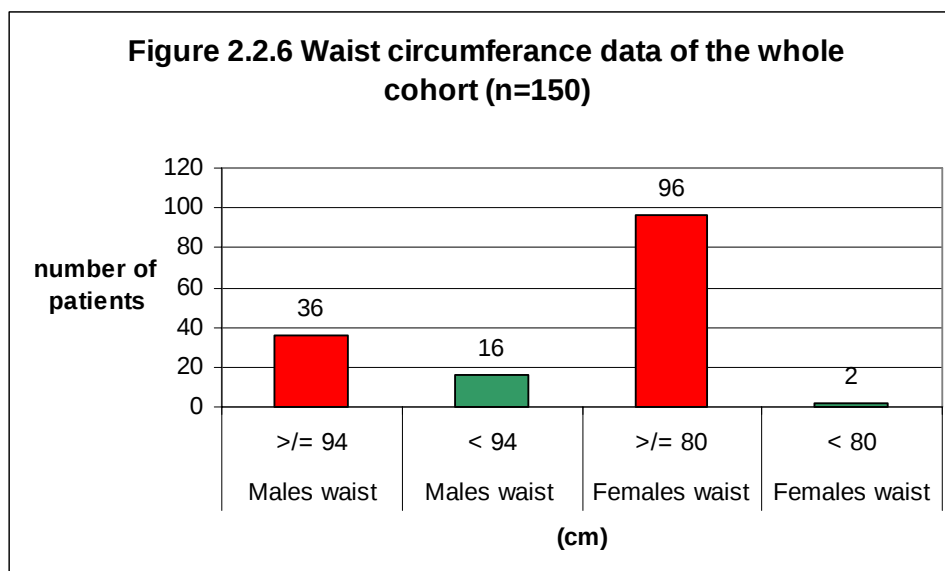


Forty six patients (30,67%) had HbA1c of less than seven. Twenty one patients (14%) had an acceptable HbA1c of seven to eight and eighty three patients (55,33%) had an HbA1c in a range where additional therapy should be implemented ($>8\%$) – Figure 2.2.5



2.2.2.3 Weight, height, BMI and waist circumference.

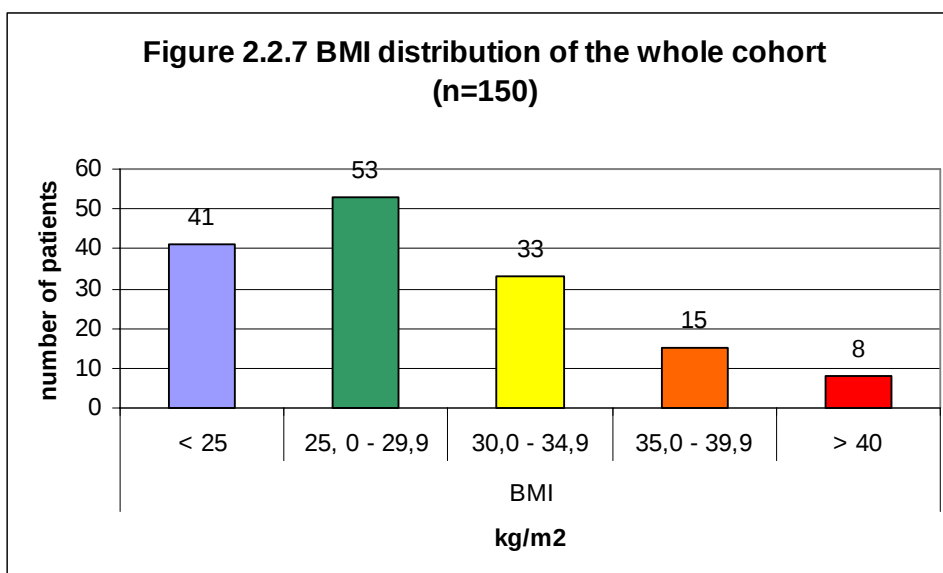
In the sample of 150 patients the range for the waist circumference was 62 cm to 170 cm. Mean waist circumference was 101,18 cm ($\pm 13,51$). In the sample 98 patients were females and only two of them had a waist circumference of less than 80 cm. Thus 98% of diabetic females had a waist circumference that put them in the high risk category. Black patients constituted 68% to the total sample size and since the current waist circumference guidelines are validated only for Indian and European population groups one has to interpret the results with caution. Looking at the males in the sample, out of 52 patients, 36 (69%) had a waist circumference greater or equal to 94 cm. It is thus apparent that only 18 patients out of 150 (12%) had a waist circumference that was below the recommended levels of 80 cm for females and 94 cm for males.



Weight measurements revealed a range of 40 kg to 173 kg and BMI range of 15,81 kg/m² to 61,3 kg/m². The mean height was 113,39 cm ($\pm 78, 51$), weight 80,24 kg ($\pm 18,14$) and BMI 29,19 kg/m² ($\pm 6,56$).

The following list summarizes the BMI results:

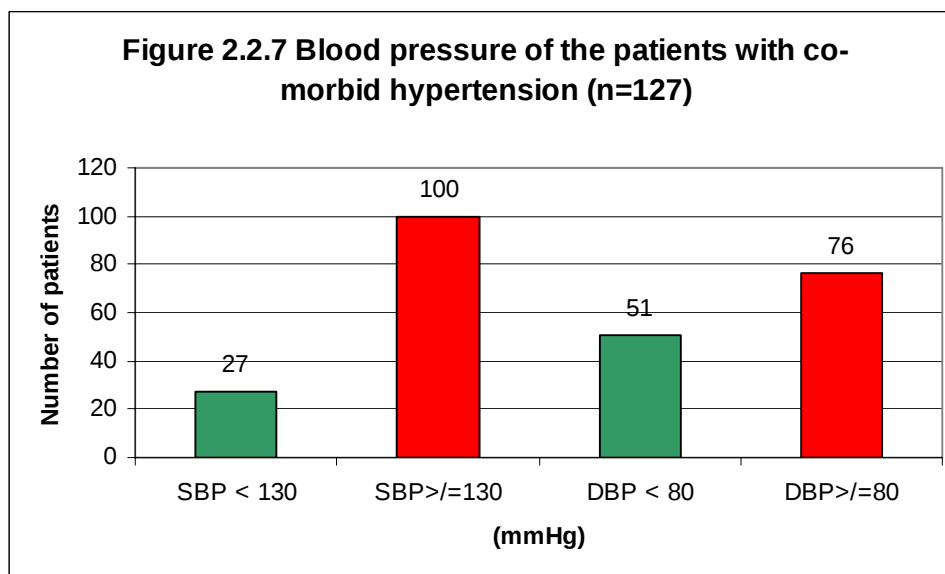
- BMI less than 25 kg/m² was present in 41 patients (27, 33%) normal
- BMI of 25, 0 to 29, 9 kg/m² was present in 53 patients (35, 33%) overweight
- BMI of 30, 0 to 34, 9 kg/m² was present in 33 patients (22, 00%) obese class I
- BMI of 35, 0 to 39, 9 kg/m² was present in 15 patients (10, 00%) obese class II
- BMI of above or equal to 40 kg/m² in 8 patients (5, 33%) obese class III



The above results confirm that obesity is a major problem in type 2 diabetics attending our clinics. Only 41 patients (27,33%) had a BMI within a normal range and 56 patients (37,3%) were obese and 53 (35,3%) were overweight.

2.2.2.4 Control of blood pressure.

In the sample of 150 patients, 127 (84.67%) patients were hypertensive (4- 3.15% newly diagnosed and 123- 96.85% previously known to have hypertension) and 23 (15.33%) patients were normotensive. Out of the 127 patients with hypertension, 100 (78,74%) had Systolic Blood Pressure (SBP) ≥ 130 mmHg and 76 (59,84%) had Diastolic Blood Pressure (DBP) ≥ 80 mmHg. The mean SBP in the hypertensive group was 142, 91 mmHg (SD $\pm 23, 37$) and the mean DBP was 78,24 mmHg (SD $\pm 10,99$).



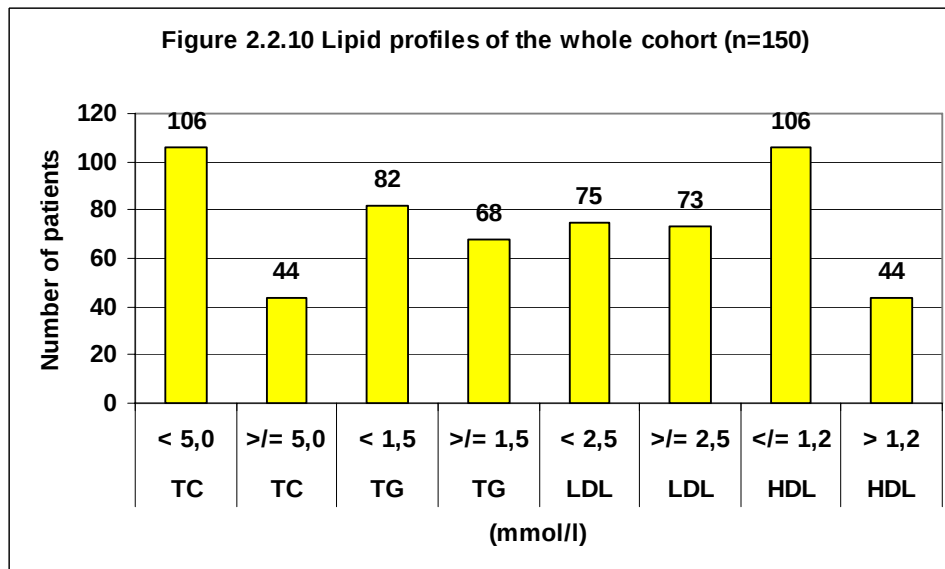
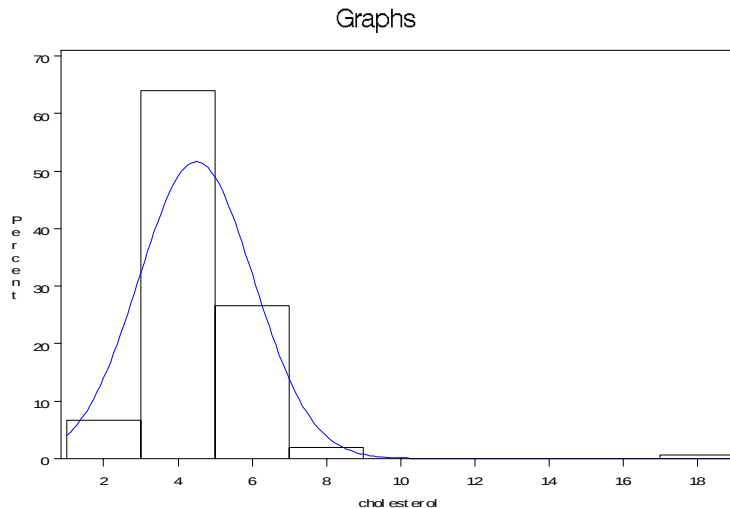
Ten hypertensive patients (7.87%) were not receiving an Angiotensin Converting Enzyme Inhibitor (ACE-I) as part of their therapy despite no obvious contra-indications.

2.2.2.5 Lipid profiles.

The analysis of the data revealed that LDL, HDL, Triglycerides and Total cholesterol were normally distributed in the sample and conformed to a symmetrical, bell-shaped, frequency curve. The range for total cholesterol was 1,8 mmol/l to 17,3 mmol/l. Mean cholesterol

was 4,49 mmol/l ($\pm 1,54$). One hundred and six patients (70, 67%) had total cholesterol of less than 5, 0 mmol/l as recommended by SEMDSA and 44 patients (29, 33%) had total cholesterol of greater or equal to 5, 0 mmol/l.

Figure 2.2.9 Cholesterol distribution.



In the sample of one hundred and fifty patients, triglycerides had a range of 0,1 mmol/l to 6,9 mmol/l and a mean value of 1,56 mmol/l ($\pm 0,93$). Eighty two patients (54,67%) had triglycerides of less than 1,5 mmol/l thus meeting the SEMDSA recommendations and 68 patients (45,33%) had triglycerides of more or equal to 1,5 mmol/l. In the analysis of the

High (HDL) and Low (LDL) density lipoprotein cholesterol the following results were obtained. HDL-cholesterol had a range of 0,2 mmol/l to 2,6 mmol/l. Mean HDL was 1,09 mmol/l ($\pm 0,37$). However only 44 patients (29,33%) were above the recommended HDL level of 1,2 mmol/l and 106 patients (70,66%) had an HDL that was less or equal to 1,2 mmol/l. LDL-cholesterol had a range of 0,3 mmol/l to 6,3 mmol/l. Mean LDL-cholesterol level was 2,59 mmol/l ($\pm 1,03$). Seventy five patients (50,68%) had LDL cholesterol of less than 2,5 mmol/l and seventy three (49,32%) had LDL greater or equal to 2,5 mmol/l -

Figure 2.2.10

LDL was not calculated in 2 patients due to a high triglyceride count.

The following table summarises the mean values for the whole cohort of 150 patients.

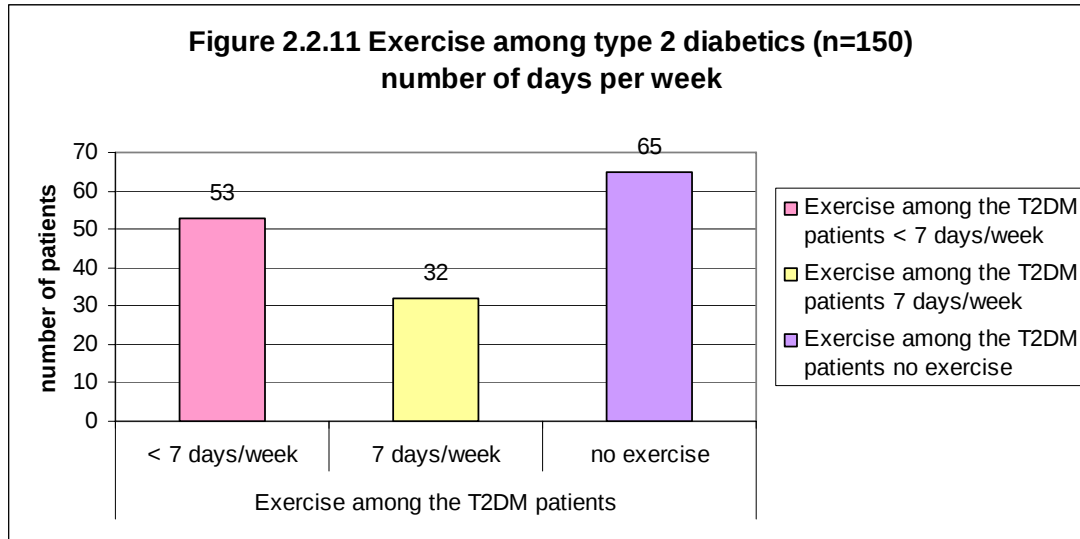
Table 2.2.2 Summary of the means procedure for 150 patients				
Variable	Label		Mean	Std. Dev
age	age (years)		59.85	10.77
waist	waist (cm)		101.18	13.51
height_	height (cm)		113.39	78.51
weight	weight (kg)		80.24	18.14
BMI	BMI (kg/m ²)		29.19	6.56
DBP	DBP (mmHg)		78.24	10.99
SBP	SBP (mmHg)		142.91	23.37
cholesterol	TC (mmol/l)		4.49	1.54
TGs	TGs (mmol/l)		1.56	0.93
HDL	HDL (mmol/l)		1.09	0.37
LDL	LDL (mmol/l)		2.59	1.03
HBA1c	HBA1c (%)		8.72	2.73

2.2.2.6 Other results.

2.2.2.6.1 Exercise among the type 2 diabetic patients.

In the patient questionnaire an enquiry as to the patients exercise routine was made. The patients were asked to estimate how many times per week they were exercising for at least

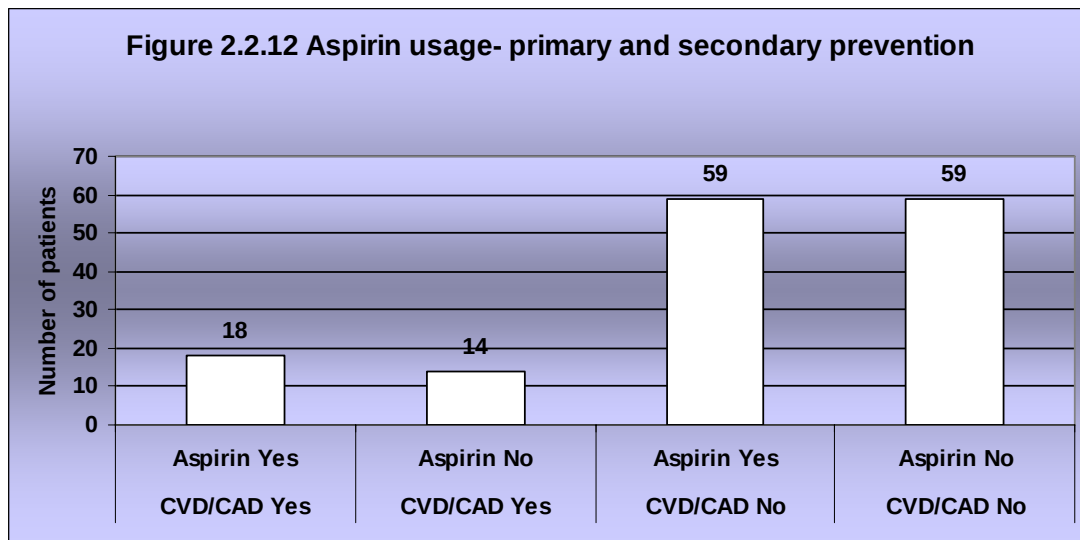
thirty minutes at a time. The following results indicate that our diabetic patients need more education on the importance of regular exercise. Forty three percent of the patients were not exercising at all (65 patients). Thirty two patients were exercising seven days per week (21,3%) and fifty three patients (35,3%) were exercising less than seven days per week.



2.2.2.6.2 Aspirin usage in type 2 diabetic patients attending our clinics.

In the SEMDSA guidelines aspirin is recommended as a secondary prevention strategy in individuals with evidence of macrovascular disease. In addition, aspirin should be considered as a primary prevention strategy in high risk men and women with diabetes. This includes diabetic subjects with the following: a family history of coronary heart disease, cigarette smoking, hypertension, obesity, albuminuria, age >30 years and dyslipidaemia.

In the current study 32 patients (21,3 %) had clinical evidence of large vessel disease and 118 (78,67)% had no evidence of macrovascular complications. In the whole cohort of 150 patients 76 (50,67%) of patients were on aspirin and 74 (49,3%) were not. On more detailed analysis 18 patients (12%) who had documented macrovascular disease were on aspirin and 14 patients (9%) with documented macrovascular disease were not on aspirin. In the whole cohort 59 patients (39,3%) who had no documented macrovascular disease were on aspirin for primary prevention. – Figure 2.2.12.



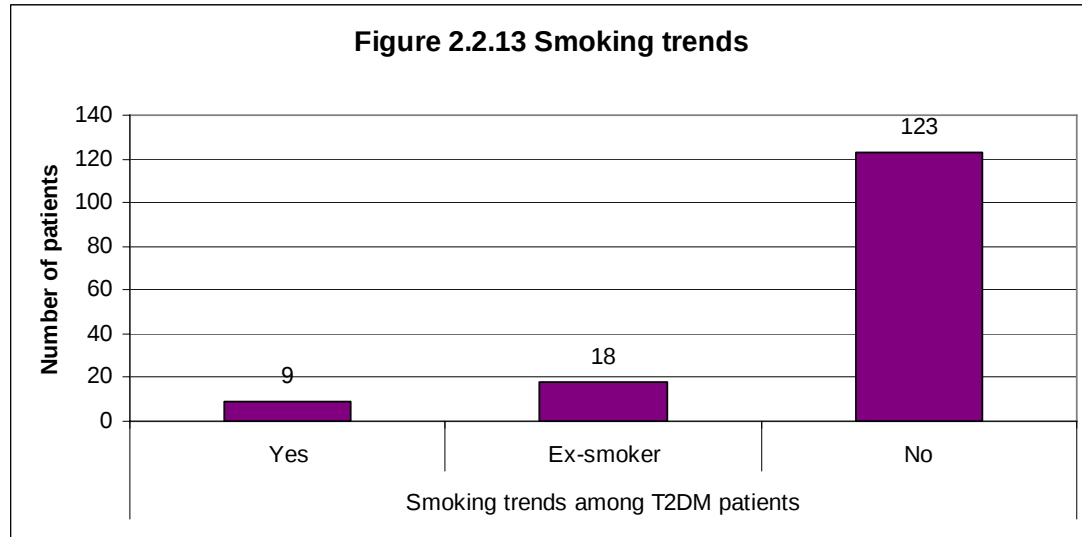
2.2.2.6.3 Adherence to the diabetic diet.

In the analysis of the data only 17 patients (12%) claimed not to be following a diabetic diet. Detailed questioning of those patients revealed that most were not educated about the importance of the diet. A significant number of patients claimed that the diet was culturally unacceptable or not affordable.

2.2.2.6.4 Smoking trends in diabetics at our clinics

123 (82%) of the patients included in the study denied smoking on direct questioning. 9 (6%) of patients were currently smoking and 18 (12%) were ex-smokers – Figure 2.2.13.

In the South African Hypertension guidelines (up dated in 2006), smoking is considered a major cardiovascular risk factor.



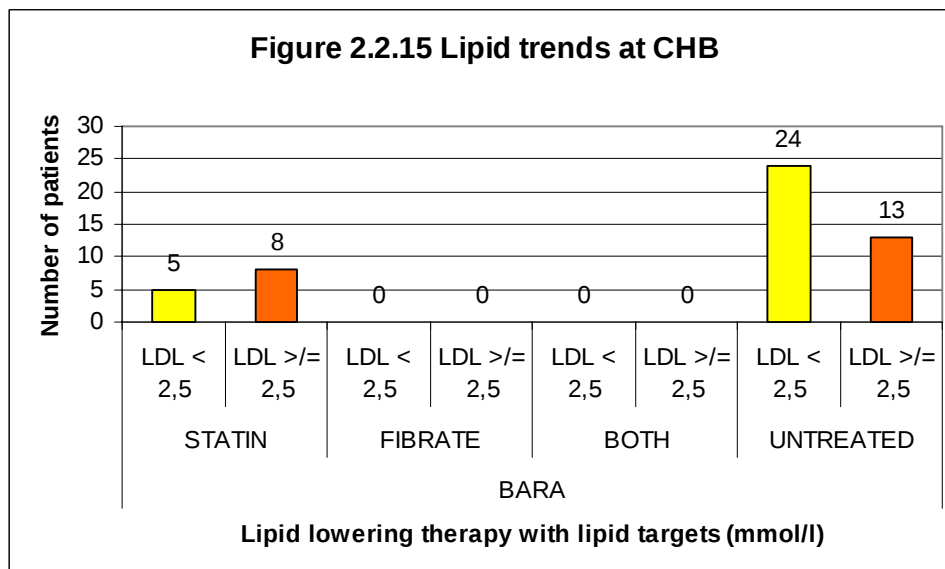
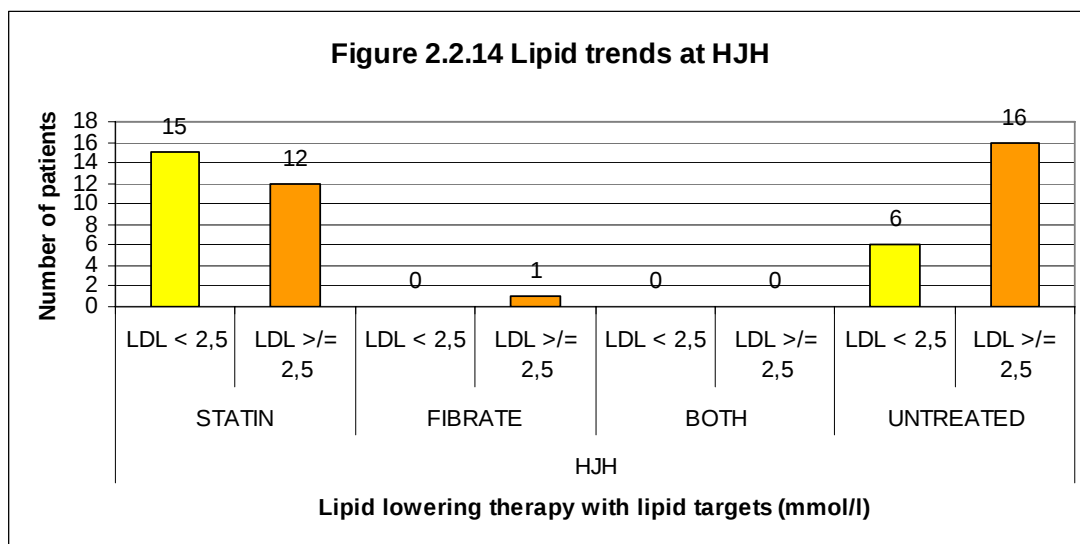
2.2.2.6.5 Lipid management at the three hospitals.

Helen Joseph Hospital contributed fifty patients to the sample of one hundred and fifty.

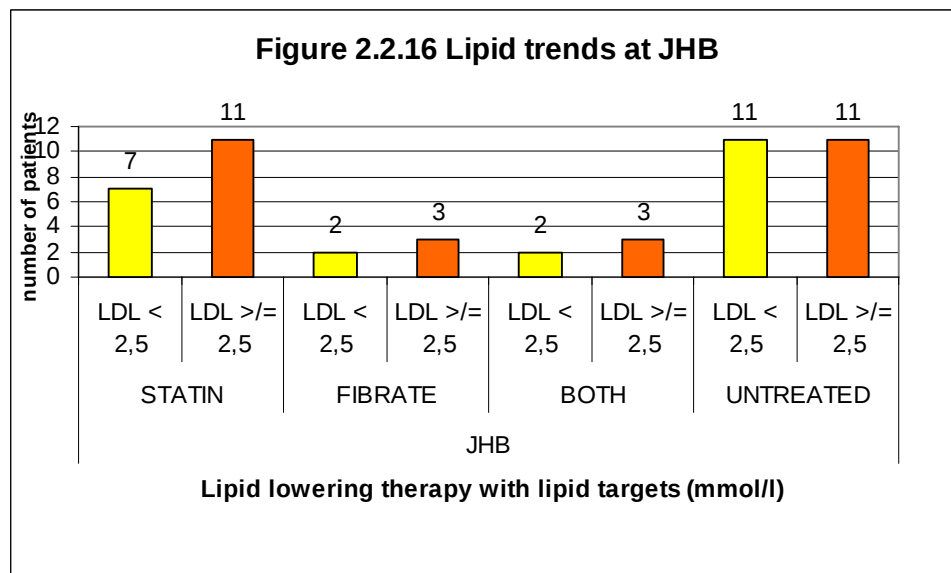
Twenty seven patients were receiving a statin (HMG CoA reductase inhibitor). One patient was on a fibrate only and twenty two patients were receiving no lipid lowering therapy.

Looking at the twenty seven (54%) patients on lipid-lowering therapy with a statin, fifteen (55,6%) had an LDL-cholesterol of less than 2,5 mmol/l and twelve (44,4%) were not at the recommended target. The one (2%) patient on a fibrate was also not at target. Twenty two (44%) patients were not on lipid lowering therapy but sixteen (72,7%) of those had LDL above or equal to 2,5 mmol/l - Figure 2.2.14.

Chris Hani Baragwanath (CHB) contributed one third of the total sample and thirteen (26%) patients were receiving statin therapy whereas thirty seven (74%) were on no lipid lowering therapy. In those receiving statins, eight out of the thirteen (61,5%) were not at the recommended LDL target of less than 2,5 mmol/l. Thirteen patients (35,1%) who were not on any lipid lowering therapy had an LDL-cholesterol above or equal to 2,5 mmol/l. Thus twenty one patients out of fifty (42%) were not achieving the recommended level despite demonstrated benefit of such therapy – Figure 2.2.15

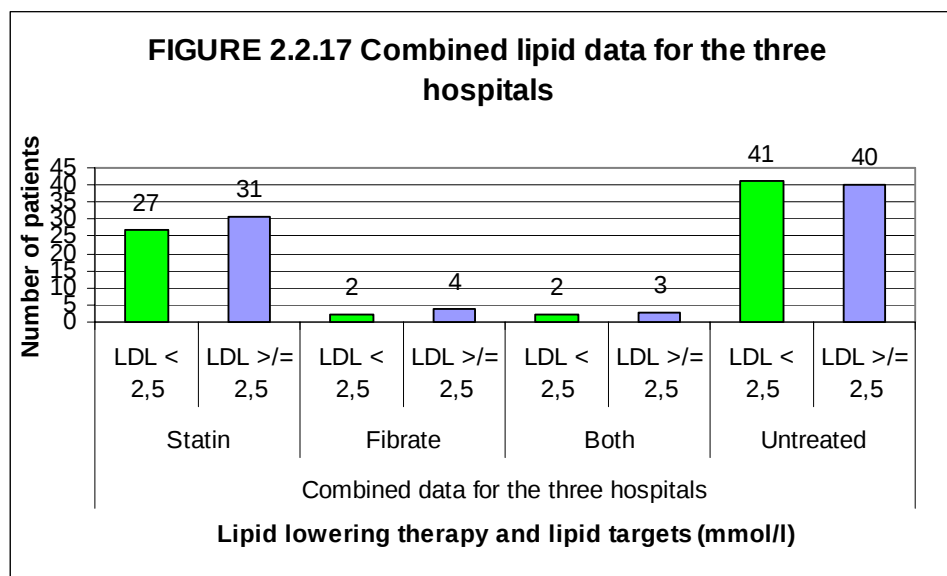


Johannesburg Hospital (JHB) complemented the total sample with fifty patients and the analysis of the results revealed that eighteen patients (36%) were on a statin therapy, five (10%) on a fibrate, five (10%) on both fibrate and a statin, and twenty two (44%) were not on any lipid lowering therapy. Eleven patients out of eighteen (61%) were not achieving the recommended LDL-cholesterol levels despite treatment with a statin. Three patients out of the five (60%) on a fibrate had an LDL above or equal to 2,5 mmol/l and in the five patients on both a fibrate and a statin yet again three (60%) were not reaching the recommended levels. In the twenty two patients on no lipid lowering therapy eleven (50%) had sub-optimal LDL-cholesterol levels. Thus at the Johannesburg hospital twenty eight (56%) patients were not reaching the recommended levels for LDL-cholesterol – Figure 2.2.16



Combined data from the three hospitals thus indicates that out of one hundred and fifty patients fifty eight (38,6%) were on a statin as a mode of lipid lowering therapy. Thirty one (53,4%) of those had an LDL-cholesterol above or equal to the recommended level of 2,5

mmol/l. Six patients (4%) were receiving a fibrate and out of those only two (33%) had an LDL-cholesterol of less than 2,5 mmol/l. Five patients (3,3%) were receiving dual therapy with a statin and a fibrate but three (60%) of those still had an LDL-cholesterol of more than or equal to 2.5 mmol/l. Eighty one (54%) patients were not on any lipid-lowering therapy despite the fact that forty (49,4 %) of those patients had sub-optimal LDL-cholesterol – Figure 2.2.17.



3. CONCLUDING CHAPTER: DISCUSSION

3.1 SUMMARY OF THE FINDINGS

3.1.1 Comparison of the current results with the 1996 study.

Demographic data: the mean age for the patients in the 1996 study was 60 years (± 10 , 3) and for the 2006 study 64 years (± 9 , 53). The sample size for the 1996 study consisted of eighty two white patients who were older than thirty five. In 2006 study nineteen patients out of one hundred and fifty were white and were used for comparison with the 1996 study so as to avoid ethnicity as a confounding factor. There was no statistically significant difference in terms of age between the patients included in the 1996 and 2006 sample.

Glycated haemoglobin: HbA1c showed a statistically significant improvement with a p-value of less than 0,0008, however the mean HbA1c was 7,43 % for the white patients in the 2006 study.

BMI: there was no statistically significant improvement in the BMI ($p = 0,33$).

Blood Pressure: Systolic Blood Pressure showed a marginally significant improvement since the 1996 study ($p = 0,08$) and Diastolic Blood Pressure a statistically significant improvement ($p = 0,02$), however 13 patients out of the 19 white patients in the 2006 study had SBP above or equal to 130 mmHg and 9 patients had DBP above or equal to 80 mmHg.

Lipids: There was a marked improvement in total cholesterol levels that was statistically significant with a p-value of less than 0,0001. This was probably due to increased use of statins as a lipid-lowering therapy. Triglycerides showed marginally significant improvement since the 1996. LDL-cholesterol showed a statistically significant improvement since the 1996 study with a p-value of less than 0,0001. It is important to note that despite improvement only 36,8% of patients had LDL-cholesterol less than 2,5

mmol/l and 63,2% greater than the recommended target. HDL-cholesterol showed no statistically significant change with a p-value of 0,54.

3.1.2 Summary of the results for the entire cohort.

The Society for Endocrinology, Metabolism and Diabetes of South Africa (SEMDSA) publish guidelines for management of type 2-diabetes.⁴ These guidelines give clear recommendations as to the glycaemic, blood pressure and lipid targets in type 2 diabetics. The guidelines also provide us with clear management plan that one should exercise in order to achieve these targets. In addition to glucose, blood pressure and lipid treatment recommendations, the guidelines also emphasize aspirin and the importance of patient education and nutritional counselling. The guidelines were last up dated in 2003 but a regular review of recommendations is undertaken as appropriate support from clinical trials emerges.

The Adult Treatment Panel III of the National Cholesterol Education Program (NCEP ATP III) regards diabetes as a coronary heart disease risk equivalent.¹⁶ These guidelines are evidence-based. Prevalence and incidence of coronary heart disease is increased in patients with type 2 diabetes mellitus and diabetes is associated with a two to four fold increase in the risk of developing coronary artery disease (CAD). Clinical, angiographic and follow-up data of 2253 patients in Italy was analysed between 1983 and 1992 by Natali et al. Abnormal coronary arteries were found more commonly in diabetics ($p < 0,0001$) and lumen stenosis was more frequent even after adjustment for measured cardiovascular risk factors. “Within the diabetic group, the only variable that was independently associated

with increased atherosclerosis score was serum cholesterol, whereas plasma glucose concentration, disease duration and type of treatment were not correlated with the severity of coronary atherosclerosis”.⁴³ Diabetes was associated with excess death from cardiac cause. This excess was similar to, and independent of, that carried by the presence of prior myocardial infarction in the whole population.⁴⁴ Patients with diabetes mellitus and coronary artery disease have rates of death which are approximately 45% over seven years and 75% over ten years. “Approximately 50% of diabetic patients die five years after myocardial infarction, double the rate found in non-diabetic patients”.^{45, 46} The increased risk of restenosis after coronary-based intervention is well established in diabetic patients and exaggerated intimal hyperplasia was shown to be the cause in a study done by Koronowski et al.⁴⁷ The diffuse nature and severity of atherosclerosis in patients with diabetes necessitates aggressive use of established therapies to minimize cardiovascular risk. Target driven, intensive intervention directed at multiple risk factors can markedly reduce the risk of cardiovascular events, as well as microvascular events in patients with type 2 diabetes mellitus. The Steno-2 study (point 1.4.8 page 9) showed that target driven, long term, intensified intervention aimed at multiple risk factors in patients with type 2 diabetes and microalbuminuria reduced the risk of cardiovascular and microvascular events by approximately 50%. Comprehensive management of cardiovascular risk factors was further emphasised in a recent Lancet review from 2005.⁴⁸

The World Health Organization (WHO) has recognized obesity as a disease with morbidity and mortality comparable to that of hypertension. Moreover, it has previously been argued that obesity is less “harmful” in black women than in other groups. However it is now

recognized that obesity as measured by a BMI greater than thirty, is associated with increased risk of many health problems in all populations. The term “healthy” obesity may therefore no longer be appropriate. Weight loss usually reduces the physical, metabolic and psychological hazards facing overweight and obese individuals. Five to ten percent sustainable weight loss results in reduction of many of the risk factors associated with obesity. Death associated with all causes, as well as diabetes and cancer may be reduced by one-half to one-third. Systolic blood pressure may fall by 10-20 mmHg, fasting blood glucose may be reduced by up to 50%, total-cholesterol, LDL-cholesterol and triglycerides may also be reduced thus indicating the great benefit of regular exercise and weight loss. While BMI provides a guide for appropriate weight for height, it does not take into account the effects of distribution of body fat. The amount of intra-abdominal fat is a better predictor of cardiovascular risk, diabetes and other endocrine abnormalities than BMI and waist circumference measurements have been shown to be a good indicator of intra-abdominal fat in adults. The recognition of the importance of the waist circumference measurements has led to the development new International Diabetes Federation (IDF) definition of the metabolic syndrome which recognizes central or abdominal obesity as a necessary requirement.

Despite the recognition of obesity as a disease with significant morbidity and mortality, this study indicates that obesity remains a big problem in our setting. The mean BMI for the 150 patients was $29,19 \text{ kg/m}^2 (\pm 6,56)$, thirty seven percent of patients had BMI above thirty (obese range) and thirty five percent had a BMI in a pre-obese range of 25-29,9. Only twenty seven percent of the patients had a BMI in a normal range thus giving a

disturbing figure of seventy two percent of the patients being in the overweight and obese range. To highlight just how big a problem obesity is, the results also show that ninety eight percent of South African females in the study cohort had a waist circumference above the current recommended 80 cm. Sixty nine percent of males had waist above 94 cm. However one has to be very cautious with the current recommended IDF definition of metabolic syndrome. The figures proposed in the worldwide definition of metabolic syndrome are a guide for people of European and Indian descent. They have not been validated for use in African populations. These statistically worrying figures may have to be adjusted in the near future with the development of new guidelines that are appropriate to all the population groups in South Africa.

Hypertension guidelines published in 2006 clearly indicate that strict blood pressure control is recommended for all type two diabetics. South African guidelines recognize diabetes as a major risk factor. This means that even stage one hypertension (SBP 140-149 and DBP 90-99 mmHg) puts a diabetic patient in a moderate risk group and stage three hypertension (SBP>180 and DBP>110 mmHg) in a very high added risk. The benefit of tight blood pressure control is evidence based. The HOT trial (page 13 point 1.1.16) showed that in patients with diabetes there was 51% reduction in major cardiovascular events in the group obtaining a diastolic blood pressure of less than 80 mmHg. The UKPDS and Heart Outcomes Prevention Evaluation (HOPE) also showed that blood pressure reduction reduces the risk of stroke and heart attack among people with diabetes. Despite the recommendations, out of the one hundred and twenty seven diabetic patients who had co-morbid hypertension in the study cohort, one hundred (78,74%) had systolic

blood pressure above or equal to 130 mmHg and seventy six (59,84%) had diastolic blood pressure above or equal to 80 mmHg. Mean SBP was 142,91 mmHg ($\pm$ 23,37) and mean DBP was 78,24mmHg ($\pm$ 10,99).

Angiotensin converting enzyme inhibitors (ACE-I) are recommended for all type 2-diabetics with hypertension, microalbuminuria or co-existing cardiovascular disease.⁴⁹ The latter statement is evidence based. The HOPE trial, European trial on reduction of cardiac events with Perindopril in stable coronary artery disease (EUROPA) and the Perindopril sub-study in coronary artery disease and diabetes (PERSUADE) randomized trials have all demonstrated that ACE-I prevent cardiovascular events in patients with established cardiovascular disease but no left ventricular dysfunction.⁵⁰ The PERSUADE trial looked at 1, 502 subjects with diabetes at the time of entry into EUROPA study. This study showed that patients with diabetes and cardiovascular disease had similar relative risk reduction on primary and secondary end points but greater absolute risk reduction and a more favourable “number needed to treat” profile (40 vs. 27). The HOPE study which included diabetics with at least one cardiovascular risk factor (hypertension, previous cardiovascular event, microalbuminuria) showed a 25% relative risk reduction in the combined primary end points of myocardial infarction, stroke and cardiovascular death. In the current cohort of one hundred and twenty seven hypertensive diabetics ten patients were not receiving ACE-I therapy despite no contra-indications. This data was not analysed in relation to ethnicity. The mean number of antihypertensive agents used in the management of the hypertensive group was not analysed.

In the above paragraphs the importance of addressing BMI, waist circumference and blood pressure were emphasized. Lipid management and the importance of reaching recommended targets has also been demonstrated in a large number of randomized clinical trials. Since the publication of ATP III, five major trials of statin therapy with clinical endpoints have been published. These trials support inclusion of patients with diabetes in the high-risk category and confirm the benefit of LDL-lowering therapy in these patients. In high risk patients the recommended LDL goal is less than 2,6 mmol/l in SEMDSA and less than 2,5 mmol/l in South African Heart Association guidelines but in very high risk patients, LDL goals of less than 1,8 mmol/l is being proposed as a therapeutic option.¹⁶

The findings of HPS (page 9 point 1.4.7) that cholesterol lowering produces substantial reduction in the risk of heart attack and stroke among people with diabetes has important implications for avoidance of the macrovascular complications of diabetes. In the current study, mean cholesterol was 4,49 mmol/l ($\pm$ 1,54) and 29,33% of patients had total cholesterol above the recommended target of above 5 mmol/l. Triglyceride levels were elevated to above 1,5 mmol/l in 45,3% of the diabetics and LDL-cholesterol was above or equal to 2,5 mmol/l in 49,32 % of the patients. The concern is also that of the patients who were not on lipid lowering therapy forty patients out of eighty one (49,38%) had LDL cholesterol above or equal to 2,5 mmol/l. These results indicate that the SEMDSA guidelines recommended targets are still not being met in a significant number of patients. The exact reasons for such poor lipid management were not the primary end point of this research and would require further study. Lastly it is also important to note that even though the benefits of exercise cannot be emphasized enough forty percent of the diabetics did not exercise at all. Significant number of patients complained that they did not have time to exercise.

In summary one can appreciate that management of diabetic patients at our clinics is sub-optimal. Evidence based support of comprehensive management of diabetic patients has important implications for avoidance of the macrovascular complications of diabetes. In particular, these results support efforts to screen for and effectively manage macrovascular risk factors other than hyperglycaemia in people with diabetes. “The CARDS study provides a strong rationale for treating dyslipidaemia in individuals with diabetes as aggressively as those without diabetes who had myocardial infarction”.⁵¹ Increased awareness of cardiovascular risk factors resulted in the development of new guidelines but has not translated to better care of our patients. With increasing prevalence of diabetes this problem is likely to escalate. It is important to recognize that knowing the guidelines but failing to implement them in clinical practice is of no benefit to the patient. “The ongoing evolution of the South African society, linked with increased westernization of much of the population, suggests that macrovascular disease may increase further in the next decade”.⁵² It is important to remember that prognosis in diabetes is highly dependent on the presence of cardiovascular disease. The UKPDS study showed that the most important risk factor for fatal and non fatal myocardial infarction was high LDL cholesterol, followed by diastolic blood pressure, smoking, low HDL cholesterol and lastly HbA1c. As several modifiable cardiovascular risk factors are present in the majority of patients with type 2 diabetes and because they predict cardiovascular disease, there is a great potential to reduce the burden of macrovascular complications in type 2 diabetic patients.

3.2 UNANSWERED QUESTIONS

Interesting findings have emerged in the course of the study which will require further study but are beyond the limits of this research report. These findings are included in this

chapter in an attempt to stimulate further research that may improve management of our type 2 diabetic patients.

3.2.1 Aspirin

SEMDSA guidelines recommend that aspirin, as a secondary prevention, should be used in patients with evidence of large vessel disease. Aspirin is also recommended as a primary prevention in high-risk patients with a family history of coronary artery disease, smoking, hypertension, obesity, albuminuria, age over thirty years or dyslipidaemia. In the current study records and questionnaires were used to look for evidence of large vessel disease and out of the forty nine percent of the patients who were not on aspirin nine percent had evidence of large vessel disease. As aspirin usage was not a primary objective of this study a more detailed analysis of the evidence for large vessel disease and reasons for those patients who were not on aspirin for not receiving such therapy would be important. Thirty nine percent of patients with no evidence of large vessel disease were on aspirin and it would be important to assess if all of those patients were high risk patients as recommended by SEMDSA.

3.2.2 IDF definition of metabolic syndrome.

As mentioned in a previous chapter the current waist circumference targets may not be applicable to all the ethnic groups and with the development of new guidelines it would be important to review the results of this study.

3.2.3 Reasons for sub-optimal management.

It would be important to interview the physicians working at the diabetic clinics in an attempt to establish the reasons why guidelines are not being followed. The problem of inadequate time, patient numbers and inadequate staff has been identified in this research report but the reasons are still not entirely clear.

3.3 CONCLUSION AND RECOMMENDATIONS.

The global figure of people with diabetes is set to rise from the current estimate of 150 million to 220 million in 2010, and 300 million in 2025.⁵³ The Global Partnership for Effective Diabetes Management, a multidisciplinary group from leading institutions and diabetes organizations worldwide, has developed ten key recommendations to aid physicians overcome the barriers to effective glucose management.⁵⁴ Similar guidelines to better management of cardiovascular risk factors in all type 2 diabetics would be important in order to reduce the macrovascular complications of diabetes.

The improved knowledge of the cardiovascular risk factor identification and management has not translated to better diabetic care. Significant number of patients are not reaching the recommended blood pressure, lipid, BMI, waist circumference and glycaemic targets. With the rise in obesity and diabetes the macrovascular complications are likely to contribute even more to health care burden and morbidity and mortality associated with diabetes. It would be important to conduct studies that look at the unanswered issues as recommended in the previous chapter. In the mean time emphasis should be placed on education of the doctors working in the diabetic clinics to encourage them to adhere to

current SEMDSA guidelines in order to improve the management of the patients at our clinics. Two tertiary care diabetes clinics at Kalafong Hospital in Pretoria underwent a quasi-experimental controlled before-and –after study. The aim of this study was to determine if a physician education programme and a structured consultation schedule would improve the quality of diabetes patient care in a diabetic clinic. The introduction of physician education programme and structured consultation schedule improved the quality of care delivered at the clinics.⁵⁵ Positive outcome of this study should encourage implementation of such programme at all diabetes clinics.

The 4S and HPS have shown that effective reduction of serum total and LDL-cholesterol levels in type 2 diabetic patients with established coronary artery disease results in marked reduction in the risk of recurrent coronary event. More recently, the CARDS study strengthened the evidence for more widespread use of statin therapy in diabetes, and that lipids should receive at least as much attention as glucose and blood pressure control, even if LDL-cholesterol is not markedly elevated. The HOT randomized trial showed a 51% reduction in major cardiovascular events and emphasized the importance of good blood pressure control in type 2 diabetic patients. The Steno-2 study and Multiple Risk Factor Intervention trial further emphasize the importance of rigorous sustained intervention in people with diabetes to control blood pressure and lower serum cholesterol. In conclusion, the evidence for comprehensive management of type diabetic patients is there, but the management of patients at our diabetic clinics is still unfortunately mainly orientated towards glycaemic control and other cardiovascular risk factors are still being largely ignored. Diabetes mellitus has reached epidemic proportions. The estimates for the year

2000 and projections for 2030 indicate that the “diabetes epidemic will continue even if levels of obesity remain constant”.⁵⁶ Growing prevalence of overweight and obesity have joined underweight, malnutrition and infectious diseases as a major health problems threatening the developing world.⁵⁷ Primary prevention of CVD in patients with diabetes should not be neglected on the basis that a smaller body of clinical trial data addresses this issue.⁵⁸ Patients with diabetes are at increased risk of macrovascular complications and furthermore, large number of patients with diabetes do not survive their first event, or if they do survive, their mortality over the subsequent months to years is generally greater than that of the general population. Intensive treatment of all modifiable risk factors (hyperglycaemia, body weight, blood pressure, LDL and HDL cholesterol as well as smoking) is supported by recently published trials.⁵⁹

I would like to propose a patient visit sheet that should be implemented at our diabetes clinics to assist the doctors in providing comprehensive care to all the type 2 diabetics – Appendix A. This patient visit sheet should be designed on the basis of current SEMDSA recommendations and should be up dated as the new evidence arises. The implementation of this patient visit sheet will be discussed with the heads of the diabetes clinics at the respective hospitals with the approval of this research report.

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