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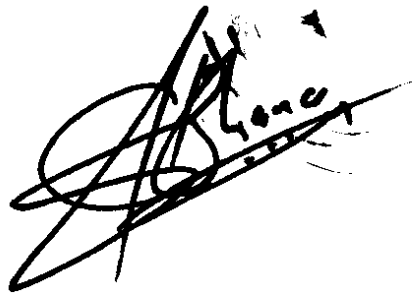
TO COMPARE CONTROL IN THE SAME INSULIN-REQUIRING TYPE-2 DIABETIC PATIENTS IN A CLINIC BEFORE AND AFTER THE IMPLEMENTATION OF SPECIALIST-SUPERVISED CARE

Sindeepkumar Amrathal Bhana

A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in fulfilment of the requirements for the degree of Master of Medicine in the branch of Internal Medicine, Johannesburg, 2014

DECLARATION

I, Sindeepkumar Amrathal Bhana declare that this research report is my own work. It is being submitted for the degree of Master of Medicine in the branch of Internal Medicine in the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other university.



30th October 2014

I dedicate this work to my loving parents Amrat and Sushila for having made numerous sacrifices so as to afford me a good education. Research requires time and I want to thank my wife and sons for allowing me to steal valuable family time to finish this work.

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- Dr. N. Govind for her advice and input in the structure of this MMed
- Dr. B. Pauly and Ms I. Nemudzivadhi for helping me develop this database over the last 8 years
- Prof. Huddle for his mentorship over the last 20 years and the support in changing the Chris Hani Baragwanath Academic Hospital's diabetes services
- Prof. Shires for agreeing to be my supervisor and for the support in my academic career as an endocrinologist.

PUBLICATIONS AND PRESENTATIONS ARISING FROM THIS PROJECT

Oral presentation:

Bhana, S., Huddle, K., Shires, R. To compare control in the same insulin-requiring Type-2 diabetic patients in a clinic before and after the implementation of specialist supervised care. The Society for Endocrinology, Metabolism and Diabetes of South Africa Congress. Johannesburg, April 2013

ABSTRACT

Title: To compare control in a group of insulin-requiring Type-2 diabetic patients before and after the implementation of specialist-supervised care.

Objective: To evaluate and compare any differences in control, i.e. $HbA1_C$, total cholesterol, BP and BMI in a single group of Type-2 diabetes patients during two time periods, i.e. before and after specialist-supervised care. In addition, to describe differences in the use of anti-platelet and statin therapy for primary cardiovascular prophylaxis**.**

Methods: Patients were recruited from the Diabetes Clinic at Chris Hani Baragwanath Academic Hospital (CHBAH) and the audits of two separate time periods were conducted. The first audit recorded standard of care delivered by registrars from January 2005 to December 2007. The second audit recorded care after the introduction of specialist-supervised care from September 2009 to September 2012. The patients were all insulin-requiring and were required to be seen for at least 24 months during both audit periods. The first recorded $HbA1_C$ in (i) 2005 and (ii) from September 2009 triggered the inception of a patient's assessment periods. Data for at least 80% of parameters had to be available for a patient to be included in the audit.

Results: This study showed significant differences using ANCOVA comparing final values for each audit after adjustment for their respective baseline values in respect of $HbA1_C$ ($p<0.000$), SBP ($p<0.012$) and BMI ($p<0.001$) after the implementation of an endocrinologist-supervised clinic. The percentage of patients reaching guideline targets, and the use of aspirin and statins, improved as well.

Conclusion: This study showed a difference in the level of care delivered by the endocrinologist-supervised clinic as opposed to one which was led by registrars.

However, other factors may have contributed to the outcomes, most notably that the consultation time with each patient was longer after the introduction of expert supervision in 2009.

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NOMENCLATURE

American Diabetes Association	ADA
Blood Pressure	BP
Body Mass Index	BMI
Cardiovascular Disease	CVD
Chris Hani Baragwanath Academic Hospital	CHBAH
Collaborative Atorvastatin Diabetes Study	CARDS
Confidence Interval	CI
Diabetes Control and Complication Trial	DCCT
Diana Princess of Wales Hospital	DPWH
Diastolic Blood Pressure	DBP
Difference	Diff
Endocrinologist / Diabetologist Supervised Clinic	ESC
Glycated Haemoglobin	$HbA1_C$
Height	ht
Human Immunodeficiency Virus	HIV
International Diabetes Federation	IDF
Justification for the Use of Statins in Primary Prevention: An Intervention Trial Evaluating Rosuvastatin	JUPITER
King Abdulaziz Medical City	KAMC
Low Density Lipoprotein	LDL
Myocardial Infarction	MI
National Health Laboratory Services	NHLS
National Institutes for Health Care Excellence	NICE
Oral Hypoglycaemic Agents	OHA

Purchasing Power Parity	PPP
Registrar-driven Type 2 Diabetes Clinic	RDC
Society for Endocrinology, Metabolism and Diabetes of South Africa	SEMDSA
South Africa	SA
Standard Deviation	SD
Standard Error of Mean	SEM
Study Period 1	SP1
Study Period 2	SP2
Systolic Blood Pressure	SBP
Total Cholesterol	TC
United Kingdom Prospective Diabetes Study	UKPDS
United States of America	USA
Weight	wt

CHAPTER 1

1.0 BACKGROUND LITERATURE ANALYSIS AND CRITIQUE

Type-2 diabetes is a multifactorial disease with a strong polygenic and environmental component, notably obesity. Obesity is thought to be the primary cause of Type-2 diabetes in people who are genetically predisposed to the disease (Rosenbaum et al., 1997). Over the past decade South Africa (SA) has been burdened by a rising prevalence in both communicable and non-communicable diseases. In particular, the prevalence of Type-2 diabetes is rising in both rural and urban areas. The high health and economic burden associated with this disease necessitates an urgent need to implement disease prevention strategies and improve diabetes-care in the population (Mayosi et al., 2009).

Type-2 diabetes mellitus is a metabolic disorder characterized by high blood glucose in the context of insulin resistance and relative insulin deficiency. This is in contrast to Type-1 diabetes mellitus, an autoimmune disease, in which there is an absolute insulin deficiency due to the autoimmune destruction of islet cells in the pancreas. Type-2 diabetes constitutes about 90% of cases, the other 10% being primarily due to Type-1 diabetes mellitus, gestational diabetes and some rare inheritable forms.

1.1 Prevalence of Type-2 diabetes

In the 21st century the prevalence of Type-2 diabetes is approaching epidemic proportions, with a world-wide prevalence estimated to be as high as 8.3% and a further 6.4% having impaired glucose tolerance (IGT) (Bertram et al., 2013). Strikingly, 50% of people remain undiagnosed, with recent figures showing between 77.9% and 80.0% being undiagnosed in Africa's low- and middle-income countries respectively (Bertram et al., 2013). In 2011, 366 million people world-wide were affected by diabetes, compared to approximately 30 million in 1985, a 12 fold increase. The rising prevalence of diabetes

mirrors the increase in the prevalence of obesity (Beckles et al., 2011). Type-2 diabetes is common in both the developed and developing countries (Bertram et al., 2013).

The National Diabetes Fact Sheet reported that the United States of America (USA) now has an estimated 25.8 million Type-2 diabetic patients, 18.8 million of whom are diagnosed, and approximately 7 million undiagnosed. They further report another 79 million people to have pre-diabetes. In the USA 1.9 million new cases are diagnosed per year in people aged 20 and older. It is estimated that by the end of 2030, 552 million people will suffer from Type-2 diabetes world-wide, 80% of whom will be from the low and middle income countries (Murray, 2009, Whiting et al., 2011).

It is estimated that sub-Saharan Africa currently has 12 million Type-2 diabetic patients with a regional prevalence of 3.8% (Figure 1). This is expected to double in the next decade. Within Africa, Southern Africa is estimated to have one of the highest prevalence's of diabetes (Murray, 2009).

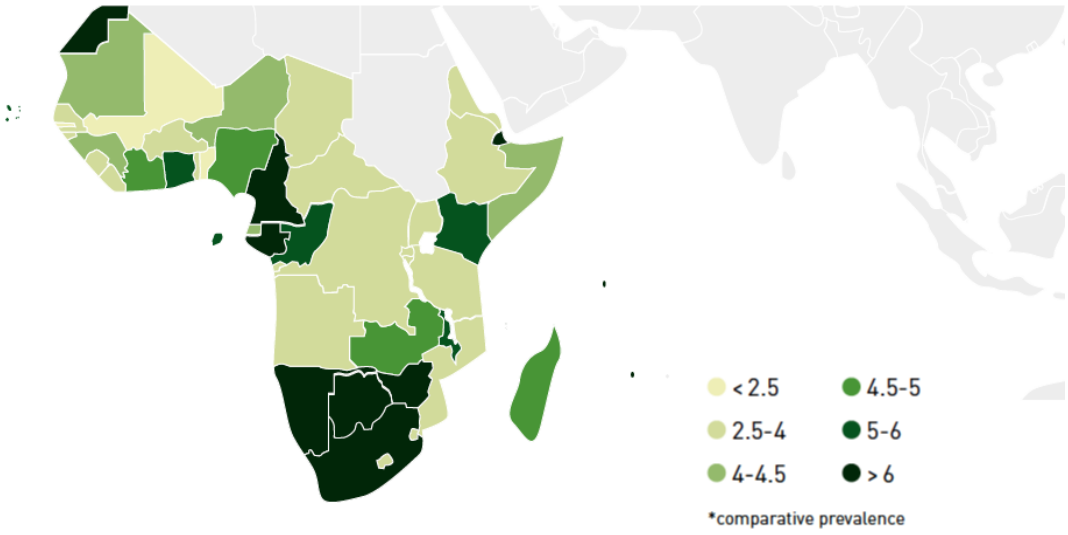


Figure 1 Prevalence rates of Type-2 diabetes in different countries in Africa (Murray, 2009)

In SA, it is estimated that Type-2 diabetes affected 2-3 million people prior to 2006 (Soma and Rheeder, 2006). The estimated prevalence of Type-2 diabetes in SA in 2000 was

5,5% but this had increased to 9% by 2006. As many as 80% of people with diabetes in Southern Africa remain undiagnosed (Bertram et al., 2013, Soma and Rheeder, 2006). The prevalence of diabetes among Black South Africans in Cape Town in 2009 was, 12.1% in males and 13.1% in females respectively (Peer et al., 2012). This was the first study to demonstrate that urban Black South Africans had a significantly higher prevalence of diabetes compared to a decade ago. Erasmus *et al* found a much higher prevalence (28.2%) of Type-2diabetes among the mixed ancestry (coloured) population of the Western Cape (Erasmus et al., 2012). Despite concerted efforts on the part of government and healthcare providers worldwide, this condition remains under-diagnosed (Beckles et al., 2011).

Within SA there are marked differences in the prevalence of Type-2 diabetes between rural and urban populations (Bertram et al., 2013). Of South Africans living with diabetes, 65% reside in urban areas and 35% in rural areas. The higher urban prevalence can be explained by a more unhealthy diet, lack of physical exercise and more sedentary forms of employment. The differences in prevalence of Type-2 diabetes in urban and rural areas in South Africa is shown in Figure 2.

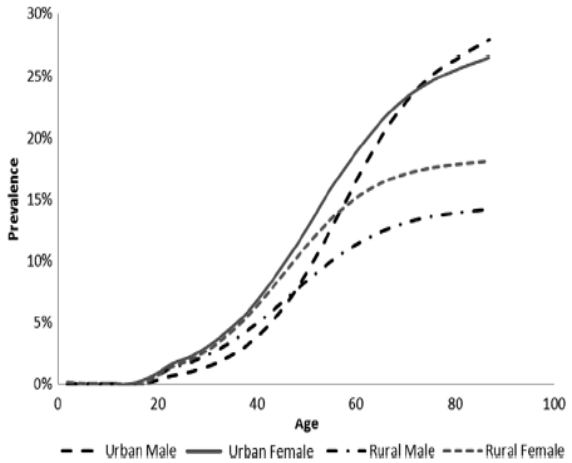


Figure 2. Differences in prevalence of Type-2 diabetes in rural and urban males and females in South Africa (Bertram et al., 2013).

1.2 Aetiology of Type-2 diabetes

The causes of Type-2 diabetes are multi-factorial and include both genetic and environmental elements that affect beta-cell function and insulin sensitivity in muscle, liver, adipose tissue and pancreas. Twin studies suggest a strong genetic contribution for the risk of Type-2 diabetes (Florez et al., 2003). The general risk world-wide is 5-10% and increases to 40% if a first degree relative has Type-2 diabetes (Meigs et al., 2000, Weijnen et al., 2002). The risk is also influenced by race and ethnicity e.g. Pima Indians have a risk of 40 to 50% in adults over the age of 35, Mauritians of Indian origin up to 30%, and South African Indians up to 13% (Knowler et al., 1993, King and Rewers, 1993, Soderberg et al., 2005, Omar et al., 1994).

Genetic susceptibility, however, only accounts for a portion of the risk to developing diabetes. Lifestyle factors, such as lack of physical exercise, obesity, and access to high dense calorie foods contribute to the risk of developing diabetes. Hallal *et.al.* reported that 31.1% of adults are physically inactive world-wide, ranging from 17% in South-East Asia to as high as 43% in the Americas (Hallal et al., 2012).

Insulin resistance is the major determinant of hyperglycaemia, and obesity is probably the most important factor in the development of insulin resistance. The increase in prevalence of Type-2 diabetes in SA parallels the rise in obesity (Figure 3). In South African male adolescents obesity rates have doubled from 1.6% to 3.3%, and 5% to 7.5% in female adolescents from 2002 to 2006 (Reddy et al., 2012). The rates of obesity are lower in rural than in urban youth. One of the reasons to account for the differences in prevalence of obesity between rural versus urban populations is differences in diet. The diets of people living in rural areas tend to be higher in unrefined carbohydrates and fibre,

and lower in saturated fats and sugars, corresponding to the more traditional way of eating (Reddy et al., 2012, Kiawi et al., 2006, Pretorius, 2013).

Pretorius *et al*. stated from their work "With urbanisation their diet has changed to a more westernised diet with a resultant decrease in carbohydrates and fibre and an increase in fat, processed food and salt consumption"(Pretorius, 2013). The poor diet and lack of physical exercise contribute to the increasing rates of obesity. In addition, cultural issues such as the perception that "obesity is a sign of good living", keeps the incidence of obesity high. In the context of hunger and deprivation, obesity confers respect and affluence (Kiawi et al., 2006).

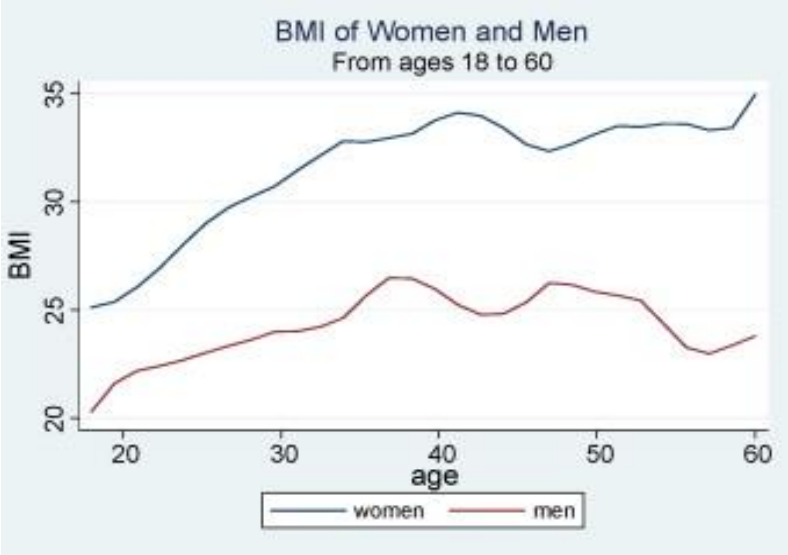


Figure 3. The body mass index of males and females in an urban African township in the Cape Town metropolitan area showing high rates of obesity (BMI>30) (Case and Menendez, 2009)

There is also an association between risk of Type-2 diabetes and environmental factors, such as small particulate air pollution and endocrine disruptors (Remillard and Bunce, 2002, Pearson et al., 2010).

1.3 Chronic complications and mortality

Chronic uncontrolled diabetes is complicated by macro- and micro-vascular disease. Studies suggest that approximately 50% of Type-2 diabetic patients will have macro- or micro-vascular complications at diagnosis and these complications progress with disease duration (UKPDS, 2012). In SA, it is estimated that 115,000 new cases of Type-2 diabetes develop each year, as well as 7,800 cases of visual impairment due to retinopathy and 2,100 patients requiring foot or toe amputations(Bertram et al., 2013).

Table 1. The modelled incidence of Type-2 diabetes and the incidence of retinopathy and amputations in SA (Bertram et al., 2013)

	Diabetes		Retinopathy		Amputation (foot or toe)	
Age group	Male	Female	Male	Female	Male	Female
25–34	7,106	11,853	18	38	0	0
35–44	12,644	17,594	143	213	166	246
45–54	15,419	16,768	493	551	316	386
55–64	10,373	9,238	956	838	246	214
65–74	4,722	4,518	1,260	985	158	140
75+	2,191	3,009	1,182	1,134	94	114
Subtotal all ages	52,455	62,980	4,050	3,760	980	1,100
Total both sex		115,435		7,810		2,080

Mortality data in SA diabetic patients has not been accurately reported. However, diabetes, heart disease and stroke are the next most significant causes of death following that due to the human immunodeficiency virus (HIV) infection (Bradshaw et al., 2003). Data from Statistics South Africa, for 1999-2006, shows a sustained increase in death from diabetes (38%). (see Fig. 4)

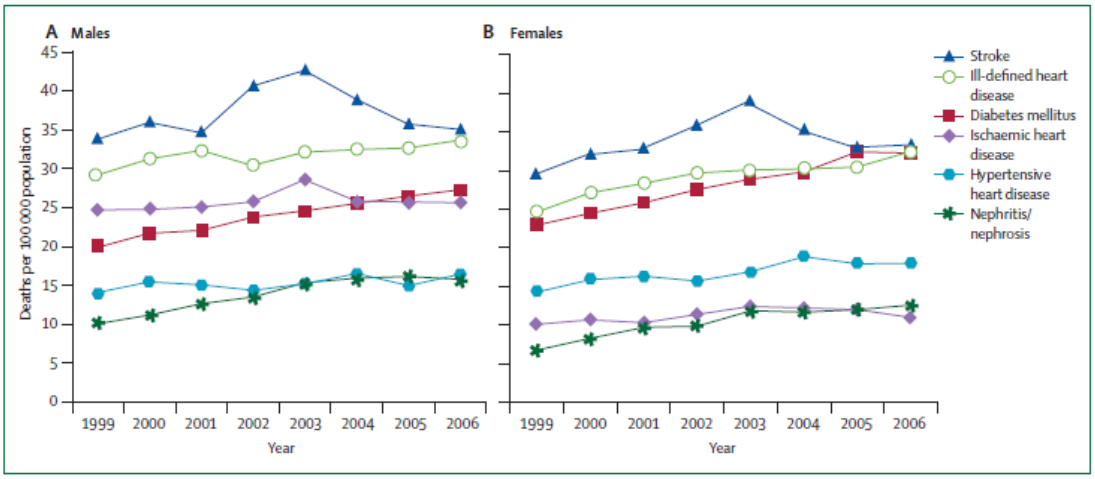


Figure 4. Death rates per 100 000 from certain non-communicable diseases in males and females in South Africa, 1999-2006 (Mayosi et al., 2009).

1.4 Factors influencing the complications of diabetes

Factors influencing the complications of diabetes include duration of disease, glycaemic control, hypertension, dyslipidaemia and smoking (Klein, 1995).

The United Kingdom Prospective Diabetes Study (UKPDS) showed an upward trend in $HbA1_C$ in both conventionally- and intensively- treated groups. Furthermore, there was a correlation between poor glycaemic control and complication rates. The UKPDS also showed a 37% risk reduction of microvascular complication for every percentage point reduction in $HbA1_C$. Good blood pressure (BP) control showed that lowering the pressure to a mean of 144/82mmHg significantly decreased the risk of strokes, diabetes related deaths, heart failure, microvascular complications and visual loss (UKPDS, 1998, Stratton et al., 2000). Parving *et al*. showed that even modest control of hypertension also had a beneficial effect on the rate of decline in glomerular filtration rate (Parving et al., 1983). The myocardial infarction hazard ratio was 0.84 (p=0.052) (in the intensive arm of the UKPDS), with a reduction in 16% for every percentage point reduction in $HbA1_C$. This result was, however, statistically not significant (Holman et al., 2008).

The Heart Protection Study and Collaborative Atorvastatin Diabetes Study (CARDS) showed that diabetic patients benefit from statin use and that this is independent of their baseline levels of low density lipoprotein (LDL) (Collins et al., 2003, Colhoun et al., 2004). Cohen *et al*. have shown in black patients with a PCSK9 mutation that there is a 88% reduction in CVD risk as a result of the low LDL cholesterol (Cohen et al., 2006). This implies that any drop in LDL, irrespective of cause, may also benefit Southern African Black patients who have, to date, not been widely studied in a large primary prevention study.

Bariatric surgery is a good indicator that weight loss lowers glycaemia in Type-2 diabetes and, in the majority of cases, reverses the diabetes (Pories et al., 1995). Thus, weight management is paramount in improving glycaemia and decreasing the rate of complications.

Lastly, anti-platelet therapy has been shown to significantly reduce the first event of coronary heart disease (odds ratio, 0.72 [95% CI, 0.9 to]) and ischaemic stroke in diabetic patients (Hayden et al., 2002). The use of low dose aspirin as primary prophylaxis is well documented (De Berardis et al., 2009).

1.5 Economic impact of Type-2 diabetes

The cost of treatment and morbidity as a result of diabetes mellitus carry an enormous economic burden. Data from the 2011 National Diabetes Fact Sheet showed that in 2007 the total deaths relating to diabetes in the USA were 231,404. The cost of treatment of diabetic patients in the USA, in 2007, was $174 billion, $116 billion for direct medical costs and the balance as indirect costs (i.e. disability and work loss). The health expenditure in 2011 amounted to $465 million which accounted for 11% of the total health budget in the USA (Whiting et al., 2011). The cost burden of diabetes on the South

African economy has as yet not been established, but is likely to be high in keeping with data from other countries. Figure 5 below estimates cost where South Africa has been placed in Group 1. The three groups were determined based on gross national income per capita expressed in purchasing power parity (PPP) for 2005. Group 1 had a PPP ≥$8000 (Kirigia et al., 2009).

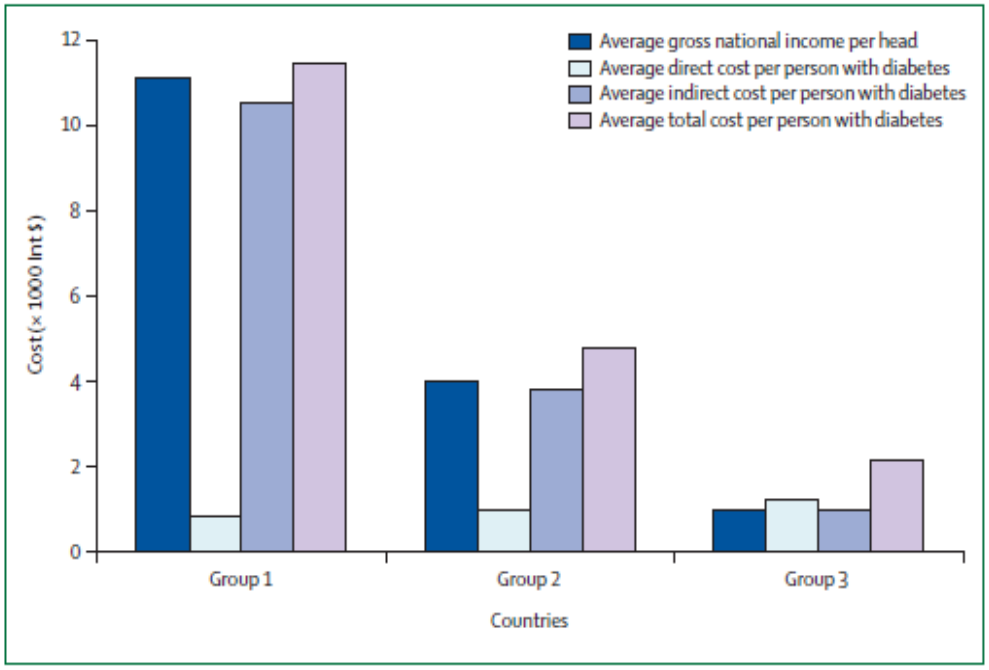


Figure 5 shows the estimated cost where South Africa has been placed in group 1 (Kirigia et al., 2009)

1.6 Diabetes Guidelines

The landmark studies in Type 1 diabetes, the Diabetes Control and Complication Trial (DCCT) and the Stockholm Diabetes Intervention Study; and those in Type-2 diabetes, the UKPDS and the Kumamoto Study, helped to establish glycaemic goals of therapy to improve long-term outcome in Type-1 and Type-2 diabetes (Turner et al., 1998, DCCT-Group, 1993, Reichard et al., 1988, Shichiri et al., 2000). The South African guidelines established by the Society for Endocrinology, Metabolism and Diabetes of South Africa

(SEMDSA) are in line with those of the American Diabetes Association (ADA). The major recommendations are that:

a) $HbA1_C$ be done every 3 to 6 months
b) A dilated-eye examination and urinary microalbumin assessment, annually
c) Foot examination
d) Blood pressure to be lowered to below 130/80mmHg
e) Add statin therapy as primary prophylaxis (SEMDSA, 2010, ADA, 2009)

1.7 Non-specialist versus specialist care in diabetic patients

Audits on the quality of care and cardiovascular risk parameters in diabetics have shown varying degrees of success in reducing complications. An audit on a 100 patients at each of the hospitals, King Abdulaziz Medical City (KAMC) in Riyadh and Diana Princess of Wales Hospital (DPWH) in Grimsby, United Kingdom showed that BP, $HbA1_C$, lipids and urine dipstick were performed in 95%, 89%, 84% and 51% at KAMC and 100%, 85%, 92% and 95% at DPWH. The NICE guidelines targets of systolic blood pressure (SBP), diastolic blood pressure (DBP), $HbA1_C$ and total cholesterol were achieved in 53%, 55%, 18% and 54% at KAMC and in 46%, 39%, 35% and 71% at DPWH (Dirar et al., 2012). British general practitioners reported that only 34% of Type-2 diabetics achieved a $HbA1_C$ of $\leq$7% (Fox et al., 2006). In urban academic centres in the USA, 28% reached a $HbA1_C$ $\leq$7% $HbA1_C$, 32% attained a LDL target below 2.6 mmol/l, and 19.9% achieved a blood pressure below 130/85 mmHg (McFarlane et al., 2002). By contrast, an audit of the General Practice Unit of the University Of Hong Kong showed that 70-80% of their diabetic patients had a $HbA1_C$ $\leq$7. A cross-sectional study of diabetic patients treated by specialists 5 years apart in Malaysia showed that glycaemic control was unsatisfactory in many patients (mean $HbA1_C$ approximately 8%; fasting glucose

approximately 9 mmol/L), with lipids well-controlled but hypertension being poorly controlled. The majority (approximately 71%) of patients in both cohorts were treated with oral hypoglycaemic agents (OHA) and only 24% were on insulin therapy. The conclusion was that the demographic profile, glycaemic control and cardiovascular risk factors were remarkably similar in both their earlier and later cohorts. They concluded that more concerted efforts are needed to increase diabetes awareness and education (Mohamed and Diabcare-Asia Study, 2008).

In a South African study comprising of 300 patients at Kalafong Hospital, physician education programmes and a structured consultation schedule showed an improvement in quality of care in two clinics with similar patient characteristics. The duration of the doctors consultation time increased but the number of annual visits for each diabetic patient was decreased. This study however did not show a significant change in $HbA1_C$ levels (van Zyl and Rheeder, 2004).

In 2009, a cross sectional study of 150 patients from three tertiary hospitals in Gauteng, South Africa was conducted to determine the level of control in patients with Type-2 diabetes. The mean $HbA1_C$ was 8.7%, 25% of patients had SBP $\leq$130mmHg, 16% had DBP $\leq$80mmHg. Fifty one percent of patients were on aspirin. That study did not state whether the patients were on oral therapy alone or OHA plus insulin (Klisiewicz and Raal, 2009).

The above audits show disparate degrees of glycaemic control and other cardiovascular risk parameters among ethnic groups with different levels of health care.

The treatment profile of patients in the above mentioned audits were either patients on OHA alone or OHA with insulin.

An audit measuring parameters of control in the same insulin-requiring diabetic population treated by non-specialist versus specialist-supervised care over two different periods has, to date, not been reported in the literature.

Whether the glycaemic control and other cardiovascular risk parameters in Type-2 diabetic patients differ under non-specialist versus specialist has not, to date, been addressed.

1.8 Care of diabetic patients at the CHBAH

Chris Hani Baragwanath Academic Hospital (CHBAH), is one of the world's largest hospitals with 2888 beds, located in the huge sprawling township of Soweto (estimated population of 1.5 million), which is the largest urban population of Black Africans in Southern Africa. Soweto is, by and large, an economically disadvantaged township.

Prior to September 2009, Type-2 diabetic patients at CHBAH were managed by junior doctors, medical officers and registrars of the Department of Internal Medicine. After September 2009, a change towards specialist care (i.e. diabetologist, medical registrars or fellows under the supervision of an endocrinologist) was initiated. Patients were assessed on average 4-6 times a year, usually by a different doctor at each visit. Diabetic patients not requiring insulin are referred to primary health care facilities (i.e. Soweto Clinics) and only insulin-requiring patients are now treated at the Diabetes Clinic at CHBAH.

1.9 Audits of diabetic files

Unpublished data previously collected by myself at the Diabetes clinic in the years 2005-2007 showed that the average $HbA1_C$ in the 905 patients was 10.28%. The mean known duration of diabetes was 10.27 years. Ninety percent of patients were on insulin. The percentage of patients who had hypertension was 87.7%, of which only 30.5% had SBP <130mmHg, and 47.5% a DBP <80mmHg. The mean, SBP was 143mmHg and DBP

79.5mmHg. Only 53.2% of patients had been on low-dose aspirin (150mg) and 31.0% on a statin for primary prophylaxis of CVD. The local guidelines for Type-2 diabetes management at the time set the following goals:

a) $HbA1_C \leq 7.0\%$
b) BP ≤130/80mmHg
c) Total cholesterol ≤5mmol/l

While there could be many reasons for not achieving the guideline targets, the main reasons were longer duration of diabetes (10.27 years), older population (65.8years), lack of patient education, lack of staff, and inadequate resources. The above data prompted the need to study the differences, if any, in the parameters of control between the clinical care delivered by medical registrars and medical officers versus that under specialist supervision.

1.10 Aims of the study:

1. To perform a second audit of diabetic patients who were managed under supervised specialist care (from September 2009 to September 2012).
2. To compare parameters of control (i.e. $HbA1_C$, BP, Total Cholesterol and BMI) in the two audits i.e. 2005-2007 and after supervised specialist care (2009-2012).
3. To evaluate the use of anti-platelet and statin therapy as primary prophylaxis in the second audit.

CHAPTER 2

2.0 SUBJECTS AND METHODS

2.1 Patients

In 2005, data was collected in 506 patients. These patient were seen from 2005 to 2007, and comprised the first study period, audit 1. In September 2009, 415 of the above - mentioned patients were still attending the diabetes clinic. The second study period, audit 2, spanned September 2009 to September 2012. Only 136 patients had adequate data spanning both study (audit) periods from 2005 to 2012 for data analysis. The remaining 370 patients had missing data, were lost to follow up, were referred to a local primary health care facility because their metabolic parameters were close to target, or in some instances may have died.

Black South African Type-2 diabetic patients requiring insulin +/- OHA and attending the CHBAH diabetic clinic were assessed. Patients who were seen over a 24 month period in both of the audit periods, and who had 80% of parameters available for both audit periods fulfilled these criteria. One hundred and thirty six Type-2 insulin-requiring diabetic patients were included in the study. The patient variables that were assessed in both audits were:

a) $HbA1_C$
b) Blood pressure
c) Non-fasting total cholesterol
d) BMI

Use of antiplatelet and statin therapy, and waist circumference were assessed for the second audit only.

2.2 Methods

2.2.1 $HbA1_C$

Note that the method for measuring $HbA1_C$ changed between the two audits. During the first audit the $HbA1_C$ was measured using the Hitachi 917 machine. During the second audit, two methods were used, the Hitachi 917 and the DCA Vantage machine. The DCA Vantage was introduced in the second quarter of 2011 as a point of care $HbA1_C$ assessment. The National Health Laboratory Service (NHLS) conducted a test to validate the two methods. Forty eight samples were used to assess $HbA1_C$ using both methodologies and a statistical analysis performed. Sixteen samples did not have absolute results using the DCA Vantage method and were not statistically analysed. The remaining 32 samples were analysed by Deming regression and Altman-Bland difference test methods. The regression statistics showed the following: Multiple R= 0.990350691, R^2 = 0.9807944491 with a standard error of 0.423371898. The Y intercept was -0.415 and the slope 1.045984006. This conversion factor was utilized to standardize any variation in the $HbA1_C$ results during the second audit period.

2.2.2 Blood pressure

The blood pressure and pulse were measured electronically by nursing staff over both audit periods. The blood pressure was measured using a Dinamap Pro 100 (Orimax) for the first audit. The hospital tender for the blood pressure machines were subsequently awarded to Welch Allyn, and the Welch Allyn Flexiport TM blood pressure machine was used for the second audit.

2.2.3 Total Cholesterol

The methodology utilised the Roche Hitachi Analyser. This remained the same between the years 2005 and 2012.

2.2.4 Body mass index (BMI)

Height and weight were measured by nursing staff using an electronic scale, which measures both height and weight, during both audit periods. The BMI (wt/ht^2) was calculated for each patient. In the first audit waist circumference was measured by the treating doctor and it was measured by either one of two nursing staff over the second audit period using the same brand of measuring tape.

2.3 Statistics

Values were retrieved from patient records and loaded into a Microsoft Excel spreadsheet for data cleaning and coding. Missing values were retrieved from new files, the laboratory database or archives. If key variables, such as the first $HbA1_C$ of each study period, were not available, the patient was excluded. If 80% of the total variables measured, but always including $HbA1_C$, were available, that patient was included. The data was imported from the Microsoft Excel spreadsheet to a statistical package (e.g. STATA version II) for the purpose of analysis. A descriptive analysis was used to describe the demographic characteristics of the patients. Mean and standard deviation were calculated. Categorical variables such as gender, use of aspirin and statins had their percentages calculated. A paired t-test was used to compare the mean BP, weight, BMI, $HbA1_C$ and total cholesterol at the beginning and end of each audit period, and the mean of the variables between the two audits. Ancova was used to adjust for baseline differences and regression in audit 1 and 2. X^2 (Chi-square test) was used to report the percentage of patients that attained target variables at the end of each audit and McNemar test for paired proportions to ascertain if this difference in proportions is statistically significant or not.

Results were considered significant if the P value was <0.05.

CHAPTER 3

3.0 RESULTS

3.1 Clinical Characteristics

The patients enrolled in this study were of African descent and of the 136 patients with Type 2 diabetes, 94 (69.12%) were female. The mean age of patients was 65.8 years and the mean duration of diabetes was 14.67 ± 7.8 years.

3.2 Audit One

The characteristic of audit one are listed in Table 2.

Table 2. Metabolic Parameters of control in Type-2 diabetic patients over a 24 month follow up period between January 2005 and December 2007 i.e. Audit 1

Variable		**n**	**Start**	**SD**	**min**	**max**	**n**	**End**	**SD**	**min**	**max**
HbA1c	%	131	10.05	2.85	5.5	18.5	132	9.49	2.37	5.7	15.3
SBP	mmHg	125	140.02	24.65	95	202	126	148.89	23.83	105	216
DBP	mmHg	113	78.42	11.90	60	110	121	80.35	11.88	60	114
T Chol	mmol/L	100	4.71	1.24	1.6	9.4	112	4.61	1.21	1.8	9.4
BMI	wt/ht^2	102	32.93	7.19	16.76	52.28	102	33.74	7.49	21.76	55.91
Weight	kg	109	85.60	18.70	50	137.2	108	87.64	19.28	53.6	152.2

n=number; SD=standard deviation; min=minimum value; max=maximum value

3.3 Audit Two

The characteristic of audit two are listed in table 3.

Table 3 Metabolic Parameters of control in Type-2 diabetic patients over a 24 month follow up period between September 2009 and September 2012 i.e. Audit 2

Variable		n	Start	SD	min	max	n	End	SD	min	max
HbA1C	%	132	10.37	2.72	5.6	18.2	134	8.24	1.83	5.3	13.6
SBP	mmHg	122	145.4	21.64	104	224	127	142.43	22.32	90	199
DBP	mmHg	117	82.69	12.09	60	126	124	81.19	10.71	63	116
T Chol	mmol/L	114	4.67	1.54	1.7	11.5	92	4.77	1.49	1.3	9.4
BMI	wt/ht^2	111	34.13	8.03	19.77	67.37	123	34.11	8.00	18.59	62.08
Weight	kg	117	89.61	21.63	53	183.4	129	89.56	21.22	47	169
Waist (F)	cm						78	105.87	13.82	78	155
Waist (M)	cm						35	106.69	16.03	82	168

n=number; SD=standard deviation; min=minimum value; max=maximum value; F=Female; M=Male

3.4 HbA1C

The changes in $HbA1_C$ over a 24 month treatment period for both audits are shown in table 4. In audit one, the paired t-test shows a significant fall ($p<0.0177$) in $HbA1_C$ from baseline (10.08 ± 2.87%) to 24 months (9.47 ± 2.39%). Audit two showed an even larger fall ($p<0.0001$) in $HbA1_C$ from baseline (10.34 ± 2.71%) to 24 months (8.26 ± 1.84). The mean $HbA1_C$ achieved at the end of both audits are shown in table 5. The specialist-supervised study period (audit two) showed a great fall in achieved $HbA1_C$ to 8.22 ± 1.8% (95% CI 7.91 – 8.53; n=131) as compared to audit one 9.48 ± 2.37% (95% CI 9.07 – 9.89; n=131). This difference was significant ($p<0.0001$). When adjusting for baseline values of $HbA1_C$ Ancova shows the difference in the end $HbA1_C$ in both audits to be highly significant (F 32.96, $p<0.0001$) (Table 6). Figure 6 shows the percentage of patients that reached a target $HbA1_C \leq 7\%$, 17.56% at the end of audit one as compared to 29.85% at

the end of audit two. The McNemar test showed this difference to be significant (exact sig (2-tail) 0.017) (Table 7).

Table 4. Paired t-test from the beginning to the end of both 24 month audit periods for: $HbA1_C$ (%); Systolic Blood Pressure (mmHg); Diastolic Blood Pressure (mmHg); Total Cholesterol (mmol/L) and BMI (wt/ht^2)

Audit	Variable*	n	Mean	SD	CI	p value
1	$HbA1_C$ 1	128	10.08	2.87	9.58 – 10.58	0.0177
	$HbA1_C$ 2	128	9.47	2.39	9.05 – 9.89	
	Diff	128	0.61	2.87	0.11 – 1.11	
2	$HbA1_C$ 3	131	10.34	2.71	9.87 – 10.81	0.0001
	$HbA1_C$ 4	131	8.26	1.84	7.94 – 8.58	
	Diff	131	2.1	2.09	1.72 – 2.44	
1	SBP 1	118	139.31	24.15	134.90 – 143.71	0.0023
	SBP 2	118	147.72	23.53	143.43 – 152.01	
	Diff	118	-8.42	29.27	-13.75 – -3.08	
2	SBP 3	115	145.58	21.35	141.64 – 149.53	0.1630
	SBP 4	115	142.57	22.91	138.34 – 146.81	
	Diff	115	3.01	22.98	-1.24 – 7.25	
1	DBP 1	103	78.19	12.21	75.81 – 80.58	0.1326
	DBP 2	103	80.37	11.73	78.08 – 82.66	
	Diff	103	-2.18	14.56	-5.02 – 0.67	
2	DBP 3	107	82.72	11.54	80.51 – 84.93	0.2906
	DBP 4	107	81.42	10.67	79.38 – 83.47	
	Diff	107	1.3	12.65	-1.13 – 3.72	
1	TChol 1	85	4.76	1.27	4.49 – 5.04	0.0729
	TChol 2	85	4.58	1.15	4.33 – 4.82	
	Diff	85	0.19	0.95	-0.02 – 0.39	
2	TChol 3	81	4.86	1.72	4.49 – 5.24	0.497
	TChol 4	81	4.78	1.54	4.44 – 5.12	
	Diff	81	0.08	1.11	-0.16 – 0.33	
1	BMI 1	89	33.05	7.47	31.48 – 34.62	0.0062
	BMI 2	89	34.22	4.59	32.62 – 35.82	
	Diff	89	-1.17	3.92	-2.0 – -0.34	
2	BMI 3	107	34.12	8.12	32.56 – 35.67	0.096
	BMI 4	107	33.78	8.15	32.22 – 35.34	
	Diff	107	0.34	2.08	-0.06 – 0.73	

*In the variable column: 1=beginning of Audit 1; 2=end of Audit 1; 3=beginning of Audit 2; 4=end of Audit 2; n=number; SD=standard deviation; CI=95% confidence interval;

Table 5. Paired t-test of the means achieved at the end of both 24 month audits for: $HbA1_C$ (%); Systolic Blood Pressure (mmHg); Diastolic Blood Pressure (mmHg); Total Cholesterol (mmol/L) and BMI (wt/ht^2)

Audit*	Variable	n	Mean	SD	CI	p value
1	$HbA1_C$ (%)	131	9.48	2.37	9.07 – 9.89	0.0001
2	$HbA1_C$	131	8.22	1.8	7.91 – 8.53	
	Diff	131	1.26	2.26	0.87 – 1.65	
1	SBP (mmHg)	118	148.65	23.93	144.29 – 153.02	0.0197
2	SBP	118	142.56	22.50	138.46 – 146.66	
	Diff	118	6.09	27.99	0.99 – 11.20	
1	DBP (mmHg)	111	80.75	11.99	78.49 – 83.00	0.6301
2	DBP	111	81.42	10.77	79.40 – 83.45	
	Diff	111	-0.68	14.74	-3.45 – 2.10	
1	TChol (mmol/L)	78	4.77	1.31	4.47 – 5.06	0.4513
2	TChol	78	4.88	1.55	4.54 – 5.23	
	Diff	78	-0.12	1.36	-0.42 – 0.19	
1	BMI (wt/ht^2)	100	33.73	7.49	32.25 – 35.22	0.4723
2	BMI	100	33.93	7.96	32.35 – 35.51	
	Diff	100	-0.20	2.70	-0.73 – 0.34	

*In audit column: 1=end of Audit 1; 2=end of Audit 2; n=number; SD=standard deviation; CI=95% confidence interval

Table 6. Stats from ANCOVA comparing final values for each audit after adjustment for the respective baseline values

Audit	Variable	Means	n	SD	SE	F	p value
1	$HbA1_C$ (%)	9.469531	128	2.389760	1.837123	32.9613	0.000000
2	$HbA1_C$	8.259542	131	1.842439			
1	SBP (mmHg)	147.7203	118	23.53281	21.84883	6.4669	0.011647
2	SBP	142.5739	115	22.90524			
1	DBP (mmHg)	80.36893	103	11.72478	10.69454	0.0268	0.870042
2	DBP	81.42056	107	10.66827			
1	Chol (mmol/L)	4.576471	85	1.145555	.9067063	0.9352	0.334945
2	Chol	4.780247	81	1.544378			
1	BMI (wt/ht^2)	34.21645	89	7.591854	3.014020	10.891	0.001151
2	BMI	33.77999	107	8.149179			

1=End value of Audit 1; 2=end value of Audit 2; n=number; SD=standard deviation; SE=standard error; F=Ancova

3.5 Systolic Blood Pressure

The changes in SBP over a 24 month treatment for both audits are shown in table 5. The paired t-test shows a significant rise ($p<0.0023$) in SBP from baseline (139.31 ± 24.15mmHg) to 24 months (147.72 ± 23.53mmHg) in audit one. The SBP was essentially

no different from baseline (145.58 ± 21.35mmHg) to 24 months (142.57 ± 22.91mmHg) in audit two. The mean SBP achieved at the end of both audits are shown in table 5. Audit two showed a greater fall in achieved SBP 142.56 ± 22.5mmHg (95% CI 138.46 – 146.66; n=118) as compared to audit one 148.65 ± 23.93mmHg (95% CI 144.29 – 153.01; n=118). The difference was significant ($p<0.0197$) on paired t-test and after adjusting for baseline differences using Ancova ($F=6.47$, $p<0.012$) (Table 6). The percentage of patients that reached a target SBP <130mmHg was 20.63% at the end of audit one as compared to 29.13% at the end of audit two as shown in figure 7. The McNemar test confirmed this difference to be significant (Table 7).

3.6 BMI

The changes in BMI over a 24 month treatment period for both audits are shown in table 4. The paired t-test shows a significant rise ($p<0.0062$) in BMI from baseline (33.05 ± 7.47kg/m^2) to 24 months (34.22 ± 4.59kg/m^2) in audit one. The BMI was essentially no different from baseline (34.12 ± 8.12kg/m^2) to 24 months (33.78 ± 8.15kg/m^2) in audit two. The mean BMI achieved at the end of both audits are shown in table 5 where the paired t-test showed a non-significant difference ($p<0.47$), however the difference was significant when adjusting for baseline using Ancova ($F=10.89$, $p<0.001$) (Table 6).

3.7 Aspirin Use

One hundred and twenty seven of the 136 patients (93.4%) were on aspirin for primary prophylaxis for CVD at the end of audit two.

3.8 Statin Use

Ninety one of the 136 patients (66.9%) were on a statin at the end of audit two.

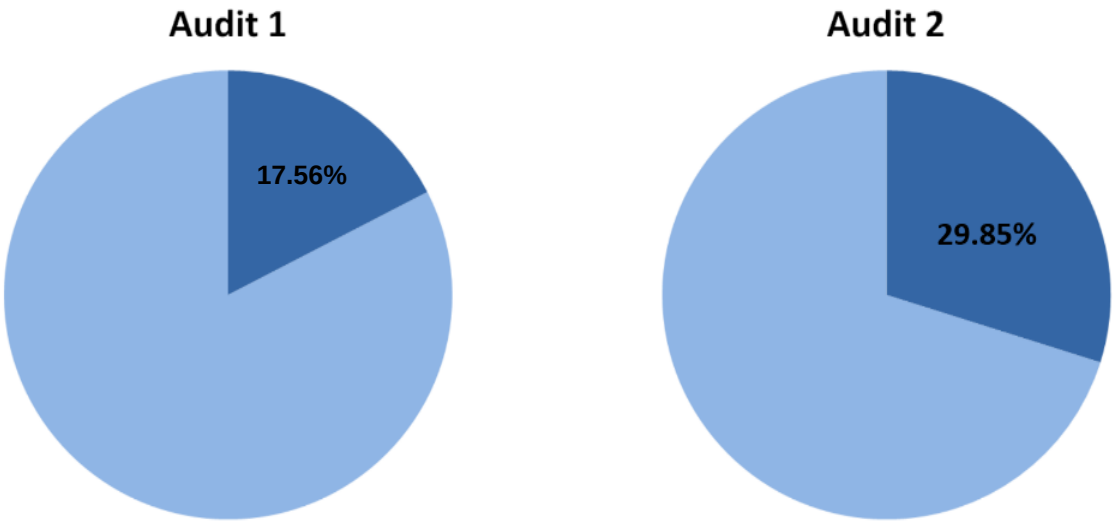


Figure 6. Percentage of patients with target $HbA1_C$ <7.0%

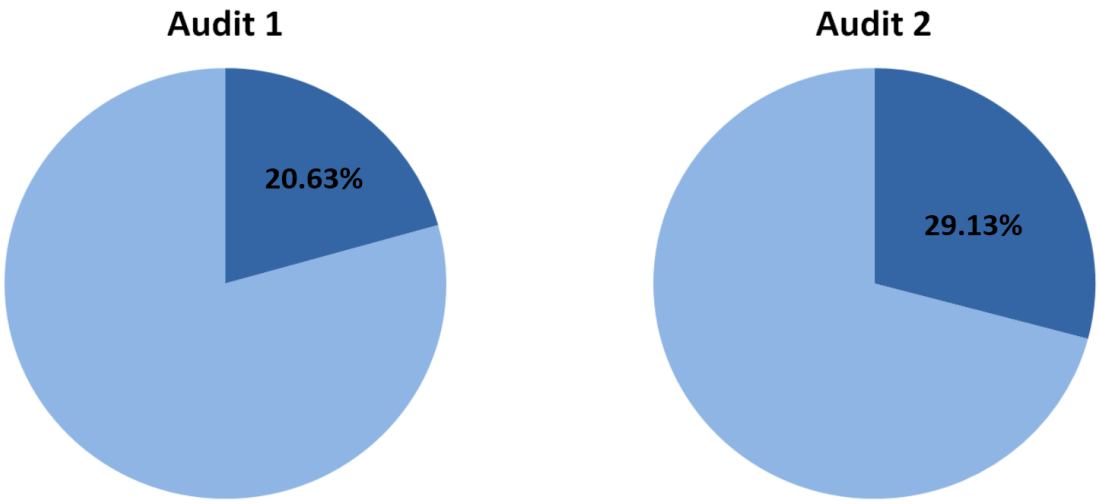


Figure 7. Percentage of patients with target Systolic Blood Pressure <130 (mmHg) achieved at the end of both audits

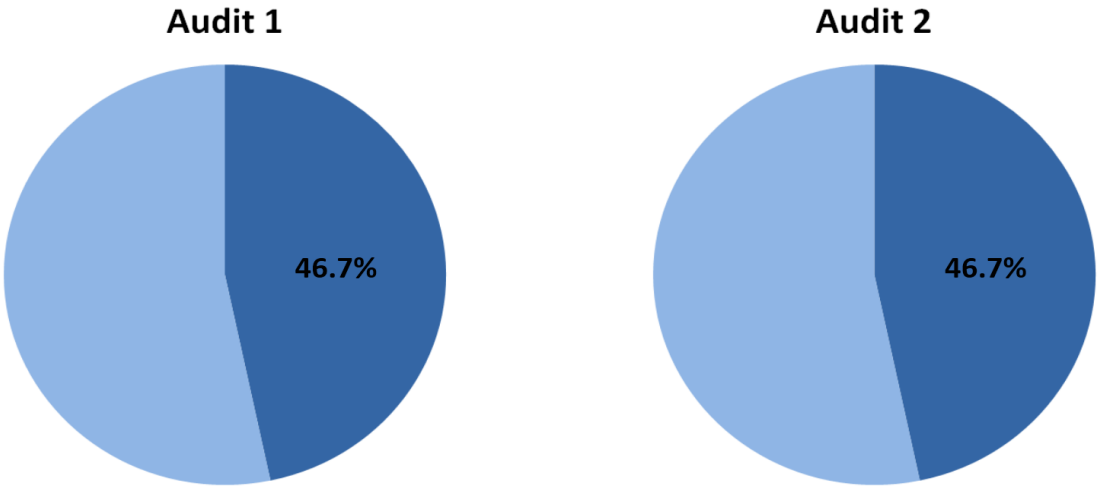


Figure 8. Percentage of patients who achieved target Diastolic Blood Pressure <80 (mmHg) at the end of both audits

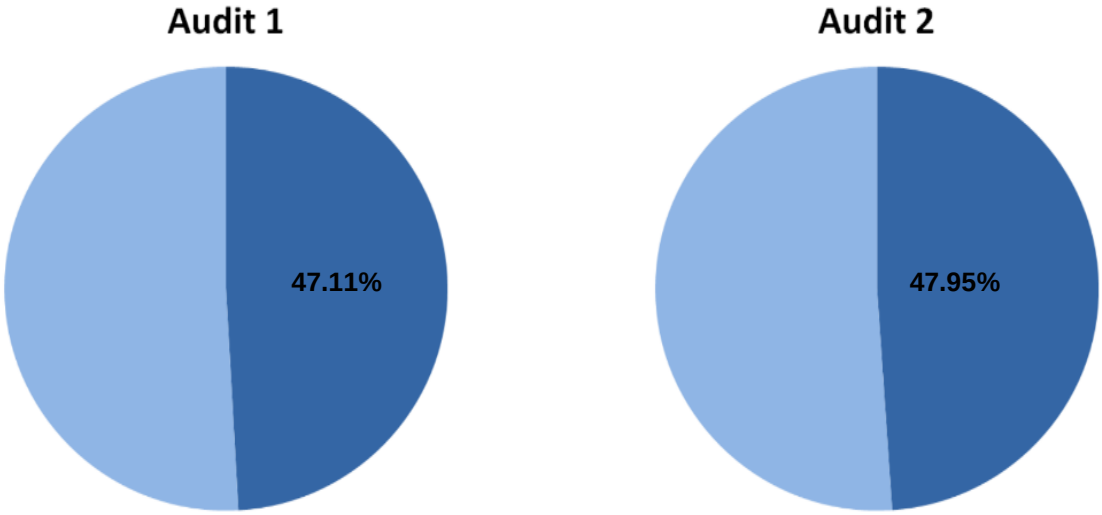


Figure 9. Percentage of patients who achieved a Total Cholesterol <4.5 (mmol/L)

Table 7. McNemar Test comparing the percentage of patients that have reached targets of $HbA1_C$, SBP, DBP and Total Chol. between the end of Audit 1 and 2

	HbA1c 2-4	**SBP 2-4**	**DBP 2-4**	**Chol 2-4**
N	122	118	111	78
Chi-Square[b]		1.531	.024	.593
Asymp. Sig.		.216	.877	.441
Exact Sig. (2-tailed)	.017[c]			

b= Continuity Corrected; c=Binomial distribution used; 2=end of Audit 1; 4=end of Audit 2

CHAPTER 4

4.0 DISCUSSION

4.1 $HbA1_C$

In this audit of patients on combined oral hypoglycaemic agents and insulin therapy, the means of the $HbA1_C$ values in 131 patients at the beginning of Audit 1 and in 132 patients in Audit 2 were 10.05 ± 2.85% and 10.37 ± 2.72%, respectively (Table 2). Our study group was not comparable to most American and European cohorts. The Steno-2 study showed a baseline $HbA1_C$ of 8.4 ± 1.6% in their intensive therapy group (Gaede et al., 2008). The large difference in $HbA1_C$ levels is probably a result of the differences between the two population groups, in that our patient group and that of the Steno-2 study had different demographic profiles. Our patients were somewhat older, with an average age of 65.8 years, as opposed to 55 years in the Steno-2 study. Another variable is that the patient burden per health care provider and available treatments vary between different hospitals and countries. The larger SD in this audit versus that in the Steno study, may be the result of the greater range in duration of the diabetes, and thus reflect a wider variation in residual Beta-cell function, and also, perhaps, disparities in treatment delivered by different healthcare providers in our cohort. The baseline $HbA1_C$ in our cohort was much higher than that reported by the Diabcare Africa study, i.e. 8.7 ± 2.5%, 7.7 ± 2.2%, and 8.1 ± 2.3%, respectively for East, Central and West Africa. This is probably as a result of the patient demographics in the Diabcare Africa cohort (Sobngwi et al., 2012). The mean duration of illness was less, at 8.0 ± 6.0 years in the Diabcare study versus 14.67 ± 7.8 years in our study (Table 2). The mean BMI was also less in the Diabcare at, 27.6 ± 5.6kg/m^2 versus 32.93 ± 7.19 kg/m^2 in our study. Furthermore, 88% of the 2352 patients in the Diabcare cohort were on oral agents alone.

The second objective of this study was to note the changes in mean $HbA1_C$ after a 24 month follow up in each of the audits. In the first audit (where the patients were managed by registrars and medical officers) the difference in $HbA1_C$ was significant with a mean $HbA1_C$ of 10.05 ± 2.85% at the start vs. 9.49 ± 2.37%, at the end (Table 2). The paired t-test in 128 patients showed a difference of 0.61% (Table 4). The second audit had a mean $HbA1_C$ at the start of 10.37 ± 2.72% vs. 8.24 ± 1.83% at the end (Table 3), with the paired t-test demonstrating a difference of 2.12 ± 2.09% (Table 4). Both of these results were highly significant. Whilst the UKPDS study showed that the trend in $HbA1_C$ is upwards in both their conventionally and intensively treated groups, this audit showed a significant improvement despite the longer duration of the diabetes, higher BMI and, presumably, more advanced Beta-cell failure (UKPDS-Group, 1998b). The improvement in the second audit was likely as a result of a longer duration in consultation time (while this was not measured directly, in Audit 1 the registrars managed between 35 and 50 patients in a 4 hour period, whereas in Audit 2, 10 patients were seen during a minimum of 2 hours), the better diabetes care facility and the availability of specialist supervision. Both audit periods had the same diabetes educator cohort and education programme. A dedicated full-time podiatrist was available during Audit 2. Ophthalmologists were also available in a separate section of the hospital for the first audit, whereas for the second audit, a non-mydriatic fundal camera for eye assessment was available at the clinic itself. Both the dedicated availability of a podiatrist and retinal camera may influence complications outcome but would not influence the $HbA1_C$. The differences in $HbA1_C$ at the end of both audits may be due to the improvement in the quality of clinical care delivered by the health care provider.

Another objective was to note the difference in the mean $HbA1_C$ achieved at the end of each treatment period. The mean $HbA1_C$ in 131 patients at the end of Audit 1 and Audit 2 was 9.48 ± 2.37 and 8.22 ± 1.8%, respectively (Table 5). The paired t-test showed a significant difference of 1.26 ± 2.31% ($p \leq 0.0001$). When baseline values for both audits are adjusted for, using Ancova: the difference between the final $HbA1_C$ values between the two audits are still highly significant F= 32.96 and $p<0.0001$ (Table 6). Both the lower $HbA1_C$ and the narrower SD in the latter group reflect a meaningful improvement in level of care over and above the aforementioned reasons for this possible difference.

This result is comparable to the Malaysian study, in which the patients were treated by specialists, where the mean $HbA1_C$ over a five year period remained approximately 8%, the major difference between these studies is that the Malaysian cohort was predominantly treated with oral agents (71%), thus indicating a less advanced (severe) diabetes (Mohamed and Diabcare-Asia Study, 2008).

The percentage of patient that reached a target of 7.0% or lower at the end of Audit 1, as per SEMDSA and ADA guidelines, was 17.56% (23 of 131 patients) (SEMDSA, 2010, ADA, 2009). This increased to 29.85% (40 of 134 patients) at the end of Audit 2. The McNemar test for paired proportions showed this difference to be significant. The binomial distribution was 0.017. These results were achieved in spite of the average duration of illness for each patient now being at least five years longer.

This improvement is in line with the percentage of patients that had achieved a $HbA1_C$ below 7.0% in the British General Practitioners audit of 24%, in the KAMC audit of 35%, 28% in the urban academic centres in the USA, and only 18% in the DPWH audit in Riyadh (Fox et al., 2006, Dirar et al., 2012, McFarlane et al., 2002).

The improvement in glycaemic control of the diabetes may be a result of:

1) The longer consultation time in Audit 2 vs Audit 1 and, consequently, a lesser patient load per doctor.
2) The on-site availability of a senior specialist to assist the non-specialist doctors during Audit 2.
3) The introduction of point-of-care $HbA1_C$ measurements with its inherent advantages which was only introduced late in Audit 2 and is thus less likely to have influenced the fall in $HbA1_C$.

4.2 Blood Pressure

The BP targets, as per SEMDSA and ADA guidelines, for the two Audits was a BP <130/80mmHg (SEMDSA, 2010, ADA, 2009). The patient characteristics in 1148 Type-2 diabetic patients with hypertension in the UKPDS were a mean age of 56 years, BMI of 29kg/m^2, and a BP 160/94mmHg. That study showed that a 10mmHg drop in SBP was much more beneficial than a reduction in $HbA1_C$ from 8% to 7.1% in reducing all macro- and micro- vascular outcomes (UKPDS-Group, 1998a, UKPDS-Group, 1998b). "Tight control" equated to a mean of 144/82mmHg vs "non-tight control", 154/87mmHg. There were benefits seen in stroke i.e. 44% reduction (p=0.013); diabetes related death 32% reduction (p=0.019); diabetes related end-points 24% reduction (p=0.0046); microvascular endpoints of 37% reduction (p=0.0092); and heart failure 56% reduction (p=0.0043). A 21% reduction in myocardial infarction was the only outcome that was not significant (p=0.13).

The mean BP in a Cameroonian cohort of 308 Type-2 diabetic patients was 142.7/83.7mmHg. Compared to the their cohorts' baseline, the mean baseline BP in our cohort was lower. The mean SBP in 125 patients at the start of audit 1 was 140.02 ± 24.65 mmHg and in 113 patients a DBP of 78.42 ± 11.9 mmHg (Table 2). This was in

spite of the higher BMI 32.93 ± 7.19 kgm^2 (Table 2) and longer duration of diabetes in our subjects.

Furthermore, our BP outcome was comparable to the Diabcare Africa Study which had a mean SBP of 139.0 ± 24.0mmHg and a mean DBP of 82.0 ± 13.0mmHg (Sobngwi et al., 2012). The SBP during Audit 1 in our cohort showed a significant worsening (p value of 0.0023, Table 4) over the 24 month period, and is consistent with many studies in Type-2 diabetic patients. Reasons cited for this increase in BP are progression of the underlying disease, progressive increases in weight, and lower levels of activity with age. However, these likely do not apply to our patients as Audit 2 showed an improvement in both SBP and DBP, albeit not statistically significant (Table 4).

When the mean SBPs achieved at the end of each Audit were compared, the paired t-test showed a significant improvement, at the end of Audit 2 vs. the end of Audit 1. The difference was 6.09mmHg ($p \leq 0.0197$) (Table 5). Adjusting for baseline SBP in both audits using Ancova, the difference was still significant, $F=6.467$ and $p<0.012$ (Table 6). The mean DBP achieved at the end of each Audit showed good control but no significant difference was demonstrated (Table 5 and 6). The percentage of patients that achieved a target SBP <130mmHg increased from 20.63% in Audit 1 to 29.13% in Audit 2. This was however not significant when employing the McNemer test (Table 7), but this was better than the 21% achieved in the Diabcare cohort (Sobngwi et al., 2012). The previously mentioned KAMC and DPWH cohorts showed that 53% and 46% of patients reached target SBPs respectively. Both of these studies have demonstrated the need to intensify efforts in achieving better SBP control.

4.3 Total Cholesterol

The CARD study showed that in Type-2 diabetic patients, primary prevention with statins is a viable and cost effective intervention (Colhoun et al., 2004). Whilst no equivalent study has been performed in Southern African Black patients, the SEMDSA guidelines has the same target for total cholesterol as the ADA guidelines, i.e. below 4.5mmol/l, and has recommended statin use as primary prophylaxis (SEMDSA, 2010, ADA, 2009). The mean total cholesterol (TC) at the beginning of Audit 1 was 4.71 ± in 1.24 mmol/l in 100 patients and 4.61 ±1.21 mmol/l in 112 patients at the end of Audit 1. When comparing the difference in the mean in 85 patients from the beginning to the end of Audit 1, the difference was a fall of 0.187 ± 0.95mmol/l, but was not statistically significant (Table 4).

The paired t-test was used to compare the mean TC at the beginning to the end of Audit 2 in 81 patients, the levels were 4.86 ±1.72 mmol/l and 4.78 ±1.54 mmol/l, respectively. The mean difference was 0.084 ± 1.11 mmol/l, which was not statistically significant. (Table 4)

An objective of this study was to assess the difference in the TC achieved at the end of both audits. A total of 78 patients were compared. The mean at the end of Audit 1 was 4.77 ± 1.31mmol/l and at the end of Audit 2 was 4.88 ±1.55 mmol/l. Although the trend in mean TC was worse, the p value (<0.45) was not significant. (Table 5) This was confirmed using Ancova (F=0.935 and p≤0.34). (Table 6)

The percentage of patients that achieved TC below 4.5mmol/l were comparable in both Audits at 47.11% and 47.95%, respectively. (Figure 9) These results were comparable to the Diabcare cohort where the mean was 4.9 ± 1.2mmol/l and KAMC cohort in which

54% reached a target cholesterol of lower than 4.5mmol/l (Sobngwi et al., 2012, Dirar et al., 2012). However, our study population had much lower starting TC levels than the cohorts studied in the UK and Ireland which are considered developed nations (Colhoun et al., 2004). Given that there are currently no restrictions in the use of statins at CHBAH, one would expect that more than 66.4% of our cohort to have been on statins.

4.4 BMI

The concept of BMI originated from the insurance industry in the Netherlands. The SEMDSA, ADA and IDF criteria all use BMI to assess obesity. Normal BMI is 18 to 25 kg/m^2, overweight being 25.1 to 29.99 kg/m^2, obese 30-34.99 kg/m^2, and morbidly obese 35-39.99 kg/m^2 (SEMDSA, 2010, ADA, 2009, IDF, 2009).

The average BMI at the beginning Audit 1 in 102 patients was 32.93 ± 7.19 kg/m^2, and rose to 33.74 ± 7.49 kg/m^2. For Audit 2, 111 patients at the beginning of the period had a BMI of 34.13 ± 8.03 kg/m^2 and at the conclusion of Audit 2 was 34.11 ± 8.00 kg/m^2 in 123 patients. The difference in the mean in Audit 1 was 1.17 ± 3.92 kg/m^2, which was significantly worse with a p value <0.006. The difference in means in Audit 2 was only 0.337 ± 2.08 kg/m^2. However, this fall was minimal and was not significant. ($p< 0.096$). The result was, however, gratifyingly unexpected as most studies have shown a continued increase in weight in all Type-2 diabetic patients other than those being treated with metformin alone.

After adjusting for baseline differences in BMI, Ancova showed a significant worsening between the end results achieved at the end of both audits, the $F=10.891$; $p<0.0012$ (Table 6). Currently, SA has an epidemic in obesity (Swinburn et al., 2011). This may adversely affect the attainment of $HbA1_C$ and BP targets.

4.5 Aspirin Use For Primary Prophylaxis

The use of low dose aspirin for primary prophylaxis in Type-2 diabetes is well documented (De Berardis et al., 2009) and its use in the diabetic clinic at CHBAH has increased markedly from 53.2% in 2005(Audit 1) to 92.7% in 2012 (the end of Audit 2).

4.6 Lipid Lowering Agents for Primary Prophylaxis

In 2005, a mere 31% patients were on a statin, but this increased to 66.67% by 2012. This is still sub-optimal. However, many of our patients have TC levels below 3.5mmol/l and LDC levels below 1.5mmol/l and may not require such interventions. Although the guidelines encourage statin use, these patients often are not prescribed statins. One may deduce from the JUPITER study that achieving lower LDL levels has cardiovascular benefits (Ridker et al., 2009). However, no studies have yet been undertaken in South African Black diabetic patients who generally have low TC and LDL levels.

CHAPTER 5

5.0 CONCLUSION

This study demonstrates that there was a meaningful and beneficial difference in the level of care delivered by doctors working in an endocrinologist/diabetologist supervised clinic (ESC) as compared to a "registrar-driven" Type-2 diabetes clinic (RDC). While both groups achieved a statistically significant improvement in $HbA1_C$, the ESC managed a 2.1 percentage point difference in $HbA1_C$ which was significantly better than in the RDC, which will hopefully translate into a reduction in micro-vascular complications, as in UKPDS.

The percentage of patients reaching a target of $HbA1_C$ of 7% was 29.85% in the ESC as compared to 17.56% in the RDC.

While it has been recognised that patients with Type-2 diabetes often have refractory hypertension with at least 2-3 drugs being required to control the BP, this study showed that SBP improved in the ESC and that more patients achieved a target SBP below 130mmHg and diabolic BP below 80mmHg than the RDC.

Weight remained unchanged during the RDC study period but tended to improve in the ESC. BMI had significantly changed from the end of Audit 1 to 2.

The percentage of patients on aspirin and a statin for primary CVD prophylaxis increased from the beginning of Audit 1 through to the end of Audit 2.

5.1 Future Considerations

This study shows that there are avenues that may need to be explored to improve control. Blood pressure, in particular, remains a tough challenge and future studies in this population group need to explore the use of combination therapies, patient education programmes on dietary strategies, improving physical activity and especially weight

reduction as a means of improving BP and other important parameters that impact on CVD morbidity and mortality.

5.2 Limitation of this study

1) The number of patients studied are relatively small
2) Important CVD biochemical markers and complication have not been evaluated, nor their relationship to $HbA1_C$, BP, BMI, weight, and waist circumference.

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APPENDIX A – Ethics Approval Letter

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

Division of the Deputy Registrar (Research)

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
R14/49 Dr Sindeepkumar A Bhana

CLEARANCE CERTIFICATE	M110825
PROJECT	To Compare Control in the Same Insulin-Requiring Type-2 Diabetic Patients in a Clinic Before and After the Implementation of Specialist-Supervised Care (revised title)
INVESTIGATORS	Dr Sindeepkumar A Bhana
DEPARTMENT	Department of Medicine/Edocrinology
DATE CONSIDERED	26/08/2011
DECISION OF THE COMMITTEE*	Approved unconditionally

Unless otherwise specified this ethical clearance is valid for 5 years and may be renewed upon application.

DATE 31/01/2014 **CHAIRPERSON** .....
(Professor P E Cleaton Jones)

*Guidelines for written 'informed consent' attached where applicable

cc: Supervisor : Professor Roy Shires

DECLARATION OF INVESTIGATOR(S)

To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10004, 10th Floor, Senate House, University.
I/We fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee. **I agree to a completion of a yearly progress report.**

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES