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CARDIOVASCULAR DISEASE RISK PROFILE OF THE SOUTH-AFRICAN MIXED ANCESTRY POPULATION WITH HIGH INCIDENCE OF DIABETES MELLITUS: BASELINE AND THREE YEAR FOLLOW-UP

THESIS SUBMITTED IN FULFILMENT OF THE REQUIREMENT FOR THE AWARD OF THE DEGREE OF DOCTOR OF TECHNOLOGY OF BIOMEDICAL TECHNOLOGY IN THE FACULTY OF HEALTH AND WELLNESS SCIENCES AT THE CAPE PENINSULA UNIVERSITY OF TECHNOLOGY

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SUBMITTED DECEMBER 2013
BELLVILLE
DECLARATION

I, David Jonah Soita hereby declare that the contents of this thesis represent my own unaided work, and that the thesis has not previously been submitted for academic examination towards any qualification. Furthermore, it represents my own opinions and not necessarily those of the Cape Peninsula University of Technology.

Signature…………………………………..Date……………………
ACKNOWLEDGEMENTS

I wish to take a moment and express my appreciation to those that have contributed to the success of this project.

First and foremost, to God for the divine wisdom, guidance, strength and courage to embark on and complete this study.

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This project wouldn’t have been successful without the population of Bellville South, particularly those that participated in the study.

To Cape Peninsula University of Technology (CPUT) for funding the study. Opinions expressed in this thesis and conclusions arrived at, are those of the author, and are not necessarily to be attributed to CPUT.
DEDICATION

To the two girls and boys in my life
Jane, Joan Joel and Jude

With love and gratitude
PUBLICATIONS RESULTING FROM THESIS

The following publications resulted from this thesis:


PRESENTATIONS

Presentations at local and international conferences:

1. Soita, J.D., Hassan, M.S., Matsha, T. & Erasmus, R.T. High prevalence of impaired glucose tolerance and diabetes amongst the middle aged population of Bellville South, Cape Town, South Africa. The 48th Annual Congress of the Federation of South African Societies of Pathology, 19 to 21 July 2008. Cape Town, South Africa.


3. Soita, J.D., Hassan, M.S., Matsha, T. & Erasmus, R.T. High prevalence of impaired glucose tolerance and diabetes amongst the middle aged population of Bellville South, Cape Town, South Africa. International Congress of Pathology, Brazil, 2008.


ABSTRACT

Introduction: Cardiovascular diseases (CVD) have become the leading cause of morbidity and mortality amongst the global population. Originally thought to be a health burden of high income countries, the prevalence is rapidly increasing in developing countries. For example, in 2008, an estimated 17.3 million died from CVD, and 80% of these (13.8 mil) were from low to middle income countries. Epidemiological data on CVD in Africa is scanty and of poor quality and national vital registration is available in only 5% of Africa’s 53 countries. Furthermore, data on CVD risk amongst the South African population and specifically the mixed ancestry community is poorly described. The increasing global population of people with CVD has been largely attributed to increasing rates of determinants and risk factors which include obesity, metabolic syndrome (MetS), type 2 diabetes mellitus (DM) and chronic kidney diseases (CKD). The prevalence of DM in South Africa is known to be on the rise with more affected communities being South African Asians followed by coloureds.

Aims and objectives: The aim of this study was to determine the CVD risk profile of the Bellville South community during a baseline and three year follow-up study, by assessment of known risk factors, MetS, type 2 DM, obesity and CKD.

Methods: Participants for this study were drawn from an urban community of the Bellville South suburb of Cape Town. At baseline (January 2008 and March 2009) 946 individuals aged 16 to 95 participated. All participants received a standardized interview and physical examination during which anthropometric measurements were performed three times and their average used for analysis: weight (kg), height (cm), waist (cm) and hip (cm) circumferences. Body Mass Index (BMI) was calculated as weight per square metre (kg/m²). A blood sample was obtained from all participants after an overnight fast for the determination of biochemical profiles: glucose, glycated haemoglobin, creatinine, total cholesterol, high density lipoprotein cholesterol (HDL-C), triglycerides and low density lipoprotein cholesterol (LDL-C) which was calculated using Friedewald’s formula. Kidney function test was assessed through estimated glomerular filtration rate (eGFR) using the cockcroft-Gault and MDRD equations. Blood pressure was measured according to the World Health Organisation (WHO) guidelines. Participants with no history of doctor diagnosed DM underwent a 75 g oral glucose tolerance test as recommended by the WHO. Metabolic syndrome was determined using JIS, NCEP ATPIII and IDF criteria. The follow-up examination was conducted in 2011 (3 years from
baseline) using similar procedures. A total of 198 participants formed the follow-up cohort whose measurements were compared to those of the baseline. Finally, the prediction and processes/progression of the risk factors were determined.

**Results:** At both baseline and follow-up studies, females had a higher BMI compared to their male counterparts. The crude prevalence of type 2 DM, including the previously diagnosed type 2 DM was 28.59% (age-adjusted = 33.5%, 95%CI: 30.01 – 36.92), and that of undiagnosed type 2 DM was 17.8% (age-adjusted = 12.4%, 95%CI: 9.8 – 14.8). The overall prevalence of CKD was 28.7% (269) and was higher in females (31.4%) compared to 20.2% in males. MetS was present in 46.5% of the participants. Gender-specific prediction for CVD risk calculated using the 30-year CVD interactive risk calculator showed that high CVD risk was present in normoglycaemic and younger subjects (under 35 years). At follow-up, the cumulative incidence of progression in glucose tolerance status was: 16.2% (32 participants including 11 with new-onset diabetes), and increased in a stepwise fashion with the number of components of MetS. Between baseline and 3-year evaluation glomerular filtration rate (eGFR) increased by 8.7 ml/min (95% confidence interval: 6.9-10.7), reflecting variables trajectories across baseline strata of kidney functions.

**Conclusion:** Given the findings of this study and the estimated increases in the determinants and risk factors of CVD in the mixed ancestry population of South Africa this trend may continue to worsen if current trajectories do not change.
GLOSSARY

The following definitions are obtained from the free medical dictionary (http://www.thefreedictionary.com)

**Anthropometric** - It is the measurement of body size, weight and proportion

**Adipose tissue** - These are special fat containing cells

**Alcohol** - An intoxicating chemical substance formed by action of natural or added yeast on sugar grapes during fermentation. It is expressed as percentage of volume or weight

**BMI** - Body Mass Index is a method used to measure whether a person is overweight or obese. It is calculated as weight (kg) divided by height (m) squared

**Cardiovascular** - Pertaining to the Heart and blood vessels

**Coloured** - A Race of mixed ancestry in South Africa

**Cholesterol** - A fatty substance produced by the body and also taken in with food, Excessive amounts heighten the risk for heart diseases

**Developing Countries** - A nation where the average income is much lower compared to the highly industrialized and developed ones

**Dyslipidaemia** - Abnormal blood fat levels

**Ethnic** - A group of people sharing a common origin

**Fasting Glucose** - A blood test done to determine the blood sugar level in a fasting state (not eaten for 8-12 hours)

**Fat** - Animal tissue containing glycerol and fatty acids

**Fat Diet** - Are food products containing fatty acids. E.g. fried foods, meat pies, full cream, milk, high fat butter and fatty meat products

**Glucose** - A simple sugar that is the body’s main source of energy. When absorbed into the blood stream, it requires insulin so as to provide energy to the body cells

**Gluconeogenesis** - Biochemical process in which glucose is synthesized from non-carbohydrate sources such as amino acids so as to meet the needs of the body during starvation. It occurs in the liver and kidneys

**HbA1c** - The ratio of glycosylated haemoglobin in relation to the total hemoglobin in circulation

**Hyperglycemia** - Excessive blood glucose concentrations, a sign that diabetes is not well controlled

**Hypertension** - Raised blood pressure
**Impaired Glucose Tolerance**- A condition associated with elevated blood sugar after a meal but not meeting the criteria for diabetes. It precedes the onset of diabetes

**Industrialized Countries**- Countries of middle/high income also called developed countries such as USA, UK, Japan etc.

**Insulin**- A hormone secreted by the pancreas and helps to regulate carbohydrate metabolism

**Insulin resistance**- A condition in which the body does not respond normally to the action of insulin

**Lipolysis**- Process by which lipids particularly triglycerides in fat are broken down into fatty acids

**Metabolism**- The physical and chemical processes by which substances are produced or broken down into energy or products for the uses of the body

**Obesity**- A condition of being extremely over weight, with a BMI of over 30

**OGTT**- Oral glucose tolerance test- is a test of the body's ability to utilize carbohydrate. It is performed by giving a standard dose of glucose solution and measuring the blood for glucose after two hours

**Urban**- An urban area refers to town or city and is characterized by dense population usually not less than 2000 people per kilometer

**Venous Blood**- Blood obtained from the veins but not the pulmonary vein

**CrCl** (Creatinine clearance)-is the volume of blood plasma that is cleared of creatinine per unit time

**GFR** (Glomerular Filtration Rate)-Is a test used to check how well the kidneys are working, it specifically estimates how much blood passes through the glomeruli each minute.

**LDL** (Low dense lipoproteins)-one of the five major groups of lipoproteins (Loosely referred to as bad cholesterol)

**HDL** (High Dense Lipoproteins) - one of the five major groups of lipoproteins (Also referred to as good cholesterol)

**MDRD** (Modification of diet in renal disease) - Is a formula/equation used in GFR estimation using 4-variables: serum creatinine, age, ethnicity, and gender.
## LIST OF ABBREVIATIONS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>ADA</td>
<td>American Diabetes Association</td>
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<tr>
<td>CAD</td>
<td>Coronary Artery Disease</td>
</tr>
<tr>
<td>CDC</td>
<td>Centre for Disease Control</td>
</tr>
<tr>
<td>CKD</td>
<td>Chronic kidney disease</td>
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<tr>
<td>CVD</td>
<td>Cardiovascular disease</td>
</tr>
<tr>
<td>DM</td>
<td>Diabetes Mellitus</td>
</tr>
<tr>
<td>HDL</td>
<td>Cholesterol- High Density Lipoprotein Cholesterol</td>
</tr>
<tr>
<td>IFG</td>
<td>Impaired fasting glucose</td>
</tr>
<tr>
<td>IGT</td>
<td>Impaired glucose tolerance</td>
</tr>
<tr>
<td>LDL</td>
<td>Cholesterol- Low Density Lipoprotein- Cholesterol</td>
</tr>
<tr>
<td>MI</td>
<td>Myocardial Infarction</td>
</tr>
<tr>
<td>NCDs</td>
<td>Non Communicable Diseases</td>
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<tr>
<td>WHO</td>
<td>World Health Organization</td>
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<tr>
<td>OGTT</td>
<td>Oral Glucose Tolerance Test</td>
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<tr>
<td>MetS</td>
<td>Metabolic syndrome</td>
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<tr>
<td>JIS</td>
<td>Joint Interim Statement</td>
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<tr>
<td>IDF</td>
<td>International diabetes Federation</td>
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<tr>
<td>GFR</td>
<td>Glomerular Filtration Rate</td>
</tr>
<tr>
<td>CrCl</td>
<td>Creatinine clearance</td>
</tr>
<tr>
<td>MDRD</td>
<td>Modification of diet in Renal Disease</td>
</tr>
<tr>
<td>NCEP ATP III</td>
<td>National Cholesterol Education Program Adult Treatment Panel III</td>
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</tbody>
</table>
TABLE OF CONTENTS

DECLARATION...........................................................................................................................................ii

ACKNOWLEDGEMENTS...............................................................................................................................iii

DEDICATION................................................................................................................................................iv

LIST OF PUBLICATIONS...............................................................................................................................v

PRESENTATIONS..........................................................................................................................................vi

ABSTRACT..................................................................................................................................................vii-viii

GLOSSARY................................................................................................................................................ix-x

ABBREVIATIONS..........................................................................................................................................xi

Preface and thesis outline..............................................................................................................................xx-xxi

CHAPTER ONE: LITERATURE REVIEW
1. Introduction .................................................................................................................................................1

1.2 Definition of Cardiovascular disease....................................................................................................1

1.3 Epidemiology of cardiovascular disease............................................................................................2

1.3.1 Cardiovascular disease in South Africa..........................................................................................3

1.4 Forms of cardiovascular disease...........................................................................................................4

1.4.1 Aneurysm.........................................................................................................................................4

1.4.2 Angina...............................................................................................................................................4

1.4.3 Atherosclerosis..............................................................................................................................5

1.4.4 Cerebral vascular accident..............................................................................................................6

1.4.5 Cerebral vascular disease...............................................................................................................6

1.4.6 Congestive cardiac failure..............................................................................................................7
1.4.7 Coronary artery disease
1.4.8 Myocardial infarction
1.4.9 Peripheral artery disease

1.5 Classification of cardiovascular disease risk factors
1.5.1 Non-modifiable risk factors
1.5.1.1 Age
1.5.1.2 Gender
1.5.1.3 Ethnicity

1.5.2 Modifiable risk factors
1.5.2.1 Dyslipidaemia
1.5.2.2 Smoking
1.5.2.2.1 The effect of nicotine on endothelial tissue
1.5.2.3 Obesity
1.5.2.3.1 Obesity in South Africa
1.5.2.3.2 Physical inactivity and obesity
1.5.2.3.3 Dietary lifestyle and obesity
1.5.2.3.4 Obesity and Cardiovascular disease

1.5.2.4 Hypertension
1.5.2.4.1 Effects of hypertension on the cardiovascular system

1.5.2.5 Chronic kidney disease
1.5.2.5.1 Epidemiology of chronic kidney disease
1.5.2.5.2 Chronic kidney disease and risk of cardiovascular
1.6 Diabetes mellitus

1.6.1 Diabetes mellitus in South Africa

1.6.2 Association between diabetes and cardiovascular disease

1.6.2.1 Pathological mechanisms linking diabetes to cardiovascular disease

1.6.3 Natural history of diabetes mellitus

1.6.4 Conversion of glycaemic status

1.6.4.1 Components of metabolic syndrome

1.6.4.2 Haemoglobin A1C

1.6.5 Cardiovascular disease intervention measures

1.6.5.1 Behavioural risk factors of cardiovascular disease and other non-communicable diseases

1.6.5.2 Physiological and metabolic risk factors of cardiovascular disease and other non-communicable disease

1.6.5.3 Challenges encountered in cardiovascular disease prevention

1.7 Cardiovascular disease risk assessment models

1.8 Social economic impact of cardiovascular disease and diabetes mellitus

1.8.1 Direct cost

1.8.2 Indirect effects

1.9 Rationale of the study

1.10 Aim of the study

1.10.1 Objectives of the study
CHAPTER TWO MATERIALS AND METHODS

2.1 Introduction ..................................................................................................................................................31

2.2 Ethical statement ...........................................................................................................................................31

2.3 Study setting and population ........................................................................................................................31

2.4 Criteria for inclusion into the study ................................................................................................................32

2.4.1 Exclusion criteria ......................................................................................................................................32

2.5 Research design for the baseline and follow-up evaluations ...........................................................................32

2.5.1 Selection of participant's .........................................................................................................................33

2.6 Pre-participation instructions .........................................................................................................................34

2.7 Data collection ..............................................................................................................................................34

2.8 Clinical measurements ................................................................................................................................35

2.8.1 Anthropometric measurements ...............................................................................................................35

2.8.1.1 Weight ..................................................................................................................................................35

2.8.1.2 Height ..................................................................................................................................................36

2.8.1.3 Waist circumference ............................................................................................................................36

2.8.1.4 Hip circumference .................................................................................................................................36

2.8.1.5 Calculation of BMI ..............................................................................................................................36

2.8.2 Physiological measurements .....................................................................................................................37

2.8.2.1 Blood pressure ..................................................................................................................................37

2.8.2.2 Administration oral glucose test .........................................................................................................37

2.8.3 Biochemical analyses ................................................................................................................................38

2.8.4 Metabolic syndrome scoring .....................................................................................................................39
2.8.5 Progression and risk measurement ................................................................. 40
2.9 Labelling of samples ......................................................................................... 40
2.10 Transportation of samples ............................................................................. 40
2.11 Data management .......................................................................................... 40
2.12 Statistical analysis ......................................................................................... 41

CHAPTER THREE: RESULTS

3.1 Introduction ..................................................................................................... 42
3.2 Baseline results ............................................................................................... 42
  3.2.1 Diabetes mellitus and metabolic syndrome ................................................. 42
3.3 Chronic kidney disease .................................................................................... 46
  3.3.1 Determinants of chronic kidney disease .................................................... 48
3.4 The 30-year cardiovascular disease risk profile ............................................... 49
3.5 At 3-year follow-up ......................................................................................... 54
  3.5.1 Changes in glucose tolerance status ......................................................... 54
3.6 Chronic kidney disease progression ............................................................... 57

CHAPTER FOUR: DISCUSSION

4.1 Cardiovascular risk at baseline ...................................................................... 62
  4.1.1 Diabetes mellitus ........................................................................................ 62
  4.1.2 Metabolic syndrome ................................................................................... 63
  4.1.3 Thirty (30) year cardiovascular risk profile .............................................. 64
4.1.4 Chronic kidney disease...........................................................................65

4.1.5 Cardiovascular disease at 3 year follow-up........................................66
  4.1.5.1 Diabetes mellitus ............................................................................66
  4.1.5.2 Chronic kidney disease.................................................................68

CHAPTER FIVE: CONCLUSION........................................................................70

CHAPTER SIX: LIMITATIONS.......................................................................72

CHAPTER SEVEN: RECOMMENDATIONS..................................................74

CHAPTER EIGHT: REFERENCES...................................................................76

APPENDICES

Appendix A: Ethics approval letter..............................................................100
Appendix B: Application for change of topic...............................................101
Appendix C: Letter of invitation to participate............................................102
Appendix D: Information sheet.................................................................103
Appendix E: Consent form.........................................................................106
Appendix F: Questionnaire.........................................................................110
Appendix G: Phlebotomy protocol..............................................................119
Appendix H: Method, equipment and reference values for biochemical tests..122

xvii
Appendix I: Other social marketing procedures ......................................................... 123
Appendix J: Quality control measures ...................................................................... 125

LIST OF FIGURES

Figure 1: Distribution of cardiovascular disease mortality rates ................................. 2
Figure 2: Interclass correlation between BMI and Lipid dependent equation full CVD outcome ............................................................................................................. 50
Figure 3: Cardiovascular disease risk score for men and women in relation to their age ..................................................................................................................... 53
Figure 4: Diabetes mellitus were most common in participants in whom eGFR was deteriorated (69.5%) ..................................................................................... 59

LIST OF TABLES

Table 1: Body weight and obesity classification ......................................................... 13
Table 2: Classification of glucose tolerance status ..................................................... 38
Table 3 Criteria for classification of Metabolic syndrome ......................................... 39
Table 4: Characteristics of 819 participants, stratified by gender ............................. 43
Table 5: Age-specific frequency of undiagnosed type 2 diabetes mellitus according to the WHO criterion among the mixed ancestry population of South Africa ................. 44
Table 6: Prevalence of metabolic syndrome and components of metabolic syndrome by gender ......................................................................................................... 45
Table 7: Glycaemic status and age-specific prevalence of metabolic syndrome according to the JIS definition among the mixed ancestry population of South Africa .................................................................................................................... 46
Table 8: Chronic kidney disease stages according to the NKF-KDOQI, using Modification of Diet in Renal Disease Glomerular Filtration Rate estimations and CKD-EPI estimation

Table 9: Characteristics of participants, stratified by the presence of CKD (stages 3 to 5)

Table 10: Multivariable adjusted odd ratios (and 95% confidence intervals) for the determinants of CKD stage 3-5

Table 11: Characteristics of cohort, stratified by gender

Table 12: Cardiovascular disease risk factors used in the equation in different age groups

Table 13: CVD risk stratified by BMI and glycaemic status

Table 14: The characteristics of participants at baseline and follow up

Table 15: Comparison of individuals that progressed to those with normoglycaemia

Table 16: Baseline characteristics by status for chronic kidney disease during follow-up

Table 17: Predictors of changes in multinomial logistic regressions (age and sex adjusted)

Table 18: Predictors of changes in multinomial logistic regressions (multivariable adjusted)
PREFACE

The present study is of longitudinal design focusing on cardiovascular disease (CVD) in South African Mixed Ancestry adults. The CVD risk factors included are diabetes mellitus (DM), metabolic syndrome (MetS), obesity and chronic kidney diseases (CKD). The thesis outline is provided here under.

Chapter 1

Provides a brief insight on CVD and its contributing factors, presenting an overview of what is currently known from studies conducted globally. The relative contribution of environmental factors such as socio-economic status, sedentary lifestyle including physical inactivity, consumption of high-calorie food and urbanization are also discussed. The frame-work below gives a summary of some of the cardiovascular disease risk factors discussed in chapter 1.

![Diagram of cardiovascular disease risk factors]

**Predisposing risk factors for CVDs**

- **Non-modifiable risk factors**
  - Age
  - Gender
  - Ethnicity
  - Dyslipidaemia
  - Hypertension
- **Modifiable risk factors**
  - Smoking
  - CKD
  - Obesity
  - DM

Chapter 2

Describes a detailed study design, materials and methods used in the study.

Chapter 3

Findings obtained from the study are organised and described in detail in this chapter.

Chapter 4

Provides an integrated discussion of the study findings.
Chapter 5
This chapter gives a brief conclusion of the study.

Chapter 6
Provides limitations of the study

Chapter 7
Recommendations for further studies are suggested in this chapter.

Chapter 8
Referrences for all chapters appear in this chapter.
CHAPTER ONE

LITERATURE REVIEW

1. Introduction

In the recent past, chronic diseases including CVD have become the leading cause of morbidity and mortality amongst the global population (Institute of Medicine, 2010). It is reported that by 2005, global mortality statistics due to CVD related causes (mainly coronary heart disease, stroke, and rheumatic heart disease) had risen from 14.4 million in 1990 to 17.5 million. Over 80 percent of these deaths are documented to have occurred in low and middle income countries. It is further estimated that there will be nearly 20 million deaths in 2015 due to CVD, accounting for 30 percent of all deaths worldwide (WHO, 2010; Yusuf et al., 2004). This evidence clearly shows that CVDs and NCDs in general are an emerging and evolving public health issue even within low income countries which should not be ignored in preference to communicable diseases. Attributable to the rise in CVDs is the global prevalence of obesity known to have reached epidemic proportions, type 2 diabetes mellitus, hypertension and the rise in CKD cases.

1.2 Definition of Cardiovascular disease (CVD)

Cardiovascular diseases are a group of ailments that affect the cardiovascular system. The cardiovascular system is comprised of the heart as the pump with arteries, veins, arterioles, venules and capillaries as conduits for transporting the blood (Zaret et al., 1998). Cardiovascular diseases are increasingly common worldwide, and disproportionately affect people in developing countries (WHO, 2012). Furthermore, within developing countries such as South Africa, the CVD risk factors are increasingly common among disadvantaged or previously disadvantaged populations who were thought to be at lower risk of such conditions (Sliwa et al., 2008). For example, hypertension, a condition that was rarely observed in non-Western populations in the 1940s has emerged as the most common cause of heart failure in Africa (Opie, 2006). Research shows that the aetiology of CVD is multifactorial and is influenced by both environmental and genetic factors (Hu et al., 2011). The increase in CVD has been attributed to the adoption of Western lifestyle and diet with a parallel increase in obesity, DM and hypertension (Hu, 2011). Evidence from systematic studies suggests that CVD risks that were almost unprecedented in non-Caucasian South Africans are now apparent.
in both rural and urban adult populations (Tollman et al., 2008; Alberts et al., 2005; Peltzer, 2002; Van Rooyen et al., 2000 & Tibazarwa et al., 2009).

1.3 Epidemiology of cardiovascular disease

Cardiovascular disease is one of the diseases under the classification of Non Communicable Diseases (NCDs). Many nations globally, especially those that are classified as middle income have observed a change in disease patterns from poverty associated infectious diseases to lifestyle associated NCDs (Jayawardena et al., 2012). This shift in epidemiological transition which is mainly triggered by industrialization and subsequent urbanization has resulted into a rise in non-communicable diseases and CVD (WHO, 2010). On the other hand, high income countries such as USA are beginning to see decreasing rates of CVD (Figure 1).

![Global distribution of CVD mortality rates in males & females](image)

**Figure 1.** Distribution of cardiovascular disease mortality rates (Mendis et al., 2011)
1.3.1 Cardiovascular Disease in South Africa

Nearly two decades post-independence, South Africa is undergoing a health transition with a high burden of non-communicable diseases (MRC report 2006). South Africa is one of the countries found in the Sub-Sahara region, with majority of its population of black South Africans (Statistics South Africa, 2011). With the exception of South Africa which has undergone rapid industrialization in the past decades, most of the countries in this region are low income and so classified as developing. The majority of the population in this region is mainly rural based (WHO, 2010). As is the case with other developing countries therefore, the observed rise in the prevalence of CVD in South Africa can be attributed to change in lifestyle patterns where individuals consume unhealthy diets with little or no physical activity resulting into obesity and dyslipidaemia (Tibazarwa et al., 2009). One of the few studies conducted in South Africa to profile CVD is the Heart of Soweto, in Johannesburg. Soweto is a predominantly black township in an urban setting within Johannesburg. A big proportion of its participants had previously been diagnosed with CVD, with 62% newly diagnosed (Sliwa et al., 2008). The interpretation of their data showed a high prevalence in CVD risk factors within the study population. In a separate study conducted by Alberts et al., (2005), an increased prevalence of CVD risk factors was observed in the rural black population of Limpopo. Findings from their study highlight the rise in CVD risk factors, even amongst the rural communities.

Numerous studies have shown that DM and obesity are known CVD risk factors (Berry 2007). Generally, there is scarcity of data on CVDs in South Africa except for that provided by local studies. For example, the 10 year follow-up studies by Motala et al., (2003) on the prevalence of DM amongst South Africans of Indian descent found a high prevalence of DM and other cardio metabolic risk factors in this group. Similarly, in a study conducted on South Africans of the mixed ancestry residents in a peri-urban setting, Levitt et al., (1999) also found a high incidence of DM and overweight. These comparisons therefore highlight the fact that there may not be a very big margin in the prevalence of CVD risk factors in all strata of South African populations whether urban or rural.
1.4 Forms of cardiovascular disease

Cardiovascular diseases are least explored in South Africa. The only studies conducted thus far are on Angina (Hemingway et al., 2008), Cerebral vascular Accident (Connor et al., 2007). There are various forms of CVD, and can be classified as follow:

1.4.1 Aneurysm

Aneurysm is an ancient Greek word meaning dilation. It refers to the localized permanent blood-filled bulge or ballooning of a blood vessel due to weakening caused by disease. Aneurysms commonly occur in arteries supplying the base of the brain, but might also affect the main heart vessels such as the aorta. As the size of the aneurysm increases, so too does the risk of rapture which can result into severe haemorrhage and other complications or even death depending on the site of rapture (Zaret et al., 1998).

The aetiology of aneurysms has previously been studied. For example, Krex et al., (2001) mentioned that besides genetic factors, presence of other cardiovascular risk factors such as smoking and hypertension may contribute to the occurrence of aneurysm. They further mentioned that trauma, infections and tumours could also predispose subjects to occurrence of this condition.

There is no clear data on the epidemiology of aneurysm. However, available information shows varying statistics depending on the design of the study. For example, review of literature till 1996 from autopsy studies revealed a prevalence of between 0.4 to 4.1%. Generally, about 2 million Germans and 6 million Americans are assumed to have cerebral aneurysms (Krex et al., 2001), but adds that other regions could have higher prevalence rates.

1.4.2 Angina

Angina pectoris is a severe chest pain experienced by an individual, primarily due to ischaemia or lack of blood supply which results into reduced oxygen to the cardiac (heart) muscle (Hemingway et al., 2008). Another source defines angina as “pain that comes on with exertion causing the person to stop or slow down and goes away within 10 minutes. The pain is located over the sternum, or in both the left chest and the arm” (Mannheimer et al., 2002; Anderson et al., 2007). Angina occurs as a result of inadequate coronary blood supply to the cardiac
muscle. Coronary artery disease occurs as a result of atherosclerosis, which results in arterial thickening, hence affecting blood supply (Mannheimer et al., 2002).

The prevalence of angina varies widely from country to country. According to a systematic review of 31 countries by Hemingway et al., (2008), the prevalence ranged between 0.7 to 14%. The report shows that females have a higher incidence of up to 15.1% compared to males with up to 5.7%. These variations were observed across all regions.

**1.4.3 Atherosclerosis**

Atherosclerosis is a condition in which an artery wall thickens as a result of a build-up of fatty materials such as cholesterol (Falk, 2006). Cholesterol has been perceived by some as a poison. It is a vital compound that is essential only in small quantities for the functioning of the human body. According to Zaret et al., (1998), cholesterol serves the following three main functions in human beings;

1) It is used to manufacture steroid or cortisone-like hormones, including sex hormones by some glands.
2) It facilitates production of bile acids by the liver, which are essential to the digestion of fats;
3) And, most importantly, it is the main component of cell membranes and structures; a kind of building block for body tissues without which mammalian life would not be possible.
4) Useful in fighting infection
5) Helps in making vitamin D

Cholesterol becomes a problem when the level in the blood is much, or has deposits of it in the wrong places. For example, coronary heart disease results when cholesterol is deposited inside the walls of the heart's coronary arteries Coronary arteries are the main suppliers of blood and oxygen to the heart's own muscle tissue (myocardium). These deposits form fatty, toughened blockages called plaques, a process referred to as atherosclerosis (Falk, 2006). Cholesterol can also be deposited within arteries elsewhere in the body, where it may contribute to the incidence of stroke (from blocked arteries in the brain) and peripheral vascular disease (from arterial blockage in the legs).
In the context of CVD, cholesterol plays a vital role in either reducing or increasing the risk of CVD, depending on the type. For example, elevated levels of HDL-cholesterol are known to confer a protective effect against DM and CVD, while that of LDL-cholesterol heightens the risk (Howard 2000; Barter 2007). Studies have demonstrated that individuals with long standing DM have thickened carotid arteries due to deposits of fatty streaks of plaques with elevated LDL cholesterol, which increases the risk of CVD (Lorenz et al., 2006; McNeill et al., 2004).

1.4.4 Cerebral vascular accident / stroke

Cerebral vascular accident which is also commonly called as stroke is a neurological condition of “rapidly developing signs of focal (or global) disturbance of cerebral function, leading to death or lasting for over 24 hours, with no other obvious cause other than vascular (Zaret et al., 1998). Cerebral infarction due to atherosclerosis has been attributed to play a role in the development of stroke (Lee 2005). Cerebral vascular accident or stroke has become an increasingly prevalent form of CVD in South Africa (Connor et al., 2007). It is known to result from longstanding and uncontrolled or poorly managed hypertension. For example, a study conducted to establish the prevalence of stroke survivors in the north eastern South Africa found 103 stroke subjects out of 982 who had responded positively to the screening questions from a population of 42,378 individuals who had been invited into the study (Connor et al., 2007). Stroke could either be ischaemic or haemorrhagic in nature.

1.4.5 Cerebral vascular disease

Cerebrovascular disease is a cluster of brain dysfunctions related to diseases of the blood vessels that supply the brain. Hypertension is one of the conditions which damage the blood vessel lining, exposing the underlying collagen fibres (Preston et al., 2003). Platelets then aggregate to initiate a repairing process which is not always complete and perfect. Sustained elevated blood pressure results in permanent changes in the network and status of the blood vessels making them deformed, narrow, stiff, rough and more susceptible to fluctuations in blood pressure (Zaret et al., 1998). Reduction in blood pressure during sleep can then lead to a marked reduction in blood flow in the narrowed blood vessels causing ischemic stroke in the morning. Conversely, a sudden surge in blood pressure due to excitation during the daytime can cause tearing of the blood vessels resulting in intracranial hemorrhage (Kario et al., 2003). Cerebrovascular disease primarily affects people who are elderly or have a history of DM,
smoking, or ischemic heart disease (Kario et al., 2003). The results of cerebrovascular disease can include an ischaemic or sometimes a hemorrhagic stroke.

1.4.6 Congestive cardiac failure

Congestive cardiac failure also known as congestive heart failure (CHF) is a condition in which there is a problem with the structure or function of the heart. This impairs its ability to supply sufficient blood flow to meet the body's needs (Yancy & Firth 2004). Heart failure is characterized by shortness of breath, aggravated by lying flat, also called orthopnea, a dry cough, ankle swelling and exercise intolerance. Heart failure is often undiagnosed due to a lack of a universally agreed definition and challenges in definitive diagnosis (Zaret et al., 1998). Treatment commonly consists of lifestyle measures (such as decreased salt intake), medications, and in some cases, special devices which help with the cardiac function are implanted through surgical procedures. The prevalence of CHF is reported to be on the rise especially amongst the US population (Masoudi et al., 2002). Even though CHF does not discriminate age, data shows that 1.1% of the Americans under the age of 55 had CHF while it was higher in older individuals between the ages of 55-74 years Masoudi et al., (2002). The Framingham study projected that the individual lifetime risk of developing CHF is 21 and 20% for men and women respectively. This is after a significant percentage of their study cohort developed CHF at follow-up studies (Jones et al., 2002). Studies indicate that the disease is associated with advancing age. For example, a report by Masoudi et al., (2002) showed that 80% of individuals who had CHF were over the age of 65 years. Studies in the sub-Saharan region indicate that CHF affects a significant percentage of individuals at varying rates in different countries (Damasceno et al., 2007).

1.4.7 Coronary artery disease

Coronary artery disease (CAD) (or coronary heart disease) refers to the failure of coronary circulation to supply adequate blood to cardiac muscle and surrounding tissue due to atherosclerosis. It is so far the most common form of CVD and an important cause of premature death (WHO, 2010). Studies, including that of Alexander et al., (2003), reported high prevalences of CAD amongst individuals with MetS and DM. A South African study conducted in Soweto reported 451 cases of CAD amongst its participants (Sliwa et al., 2008).
1.4.8 Myocardial Infarction

When a coronary artery is completely or almost completely obstructed, either by an atherosclerotic plaque or by a blood clot following a plaque rapture or crack, the result is a heart attack, or myocardial infarction (MI), literally, death of heart muscle. Myocardial infarction or acute myocardial infarction is the interruption of blood supply to part of the heart muscle, resulting into death of some heart cells (Zaret et al., 1998). Most heart attacks are caused by atherosclerosis, which is a narrowing and hardening of the coronary arteries resulting from fatty deposits called plaque. Zaret et al., (1998), states that the process, by which the wall of the artery is infiltrated by deposits of cholesterol and calcium, narrows the lumen or diameter of the artery. When the degree of narrowing reaches a critical level, blood flow to the portion of the heart supplied by that artery is stopped and injury (infarction) to the heart muscle that is a heart attack occurs. If the reduction in blood flow is only temporary, relative to muscle needs, permanent damage does not result but the individual may experience angina pectoris due to ischaemia and oxygen shortage to the myocardium.

There is generally paucity of data on myocardial infarction as an entity of the CVD in South Africa. However, available data shows that smoking and dyslipiadeamia were some of the risk factors to the 245 South African Indian myocardial infarction patients who participated in the hospital based study in Durban (Ranjith et al., 2002).

1.4.9 Peripheral vascular disease

Peripheral vascular disease (PVD), also known as peripheral artery disease (PAD) or peripheral artery occlusive disease (PAOD), includes all diseases caused by the obstruction of large arteries in the arms and legs (Kanjwal et al., 2004). PVD can result from atherosclerosis, inflammatory processes leading to stenosis, embolism, or thrombus formation and it predicts a high risk for CVD, (Hirsch & Hiatt, 2001). It causes either acute or chronic ischemia, that is, a lack of blood supply. There is very little data on the epidemiology of PAD, however, it is estimated that PAD affects approximately 27 million people in Europe and North America and about 12 million in the USA (Kanjwal et al., 2004). Available data shows that individuals in advanced age as well as those that are diabetic are most affected by PAD (Hirsch et al., 2001). There is not adequate published data on PVD in South Africa.
1.5 Classification of cardiovascular disease risk factors

Risk factors associated with CVD are classified as non-modifiable and modifiable factors. Non-modifiable risk factors are beyond the control of an individual and include genetic factors. Modifiable risk factors are those that are a result of circumstances and are under the control of an individual including behavioural risk factors. However, it is important to note that some risk factors such as DM fall in both the categories as their aetiology is affected by both behavior and genetics.

1.5.1 Non-modifiable risk factors

1.5.1.1 Age

Simply growing old heightens one’s risk of developing CVD. Studies show that an individual’s risk of developing CVD increases with age (Kingman, 2000). This is because of the morphological and physiological changes that occur over time and alter cardiovascular system function. Advanced age is believed to induce a declining effect on the cardiovascular function no matter whether one has any other underlying CVD risk factors or not. In this regard, several theories on the effect of age on the cardiovascular performance have been suggested. For example, the gradual loss of elasticity in the cardiovascular system is an important feature of the ageing process and plays a significant role in diseases such as atherosclerosis, hypertension, stroke and heart failure (Kingman, 2000). Such elasticity is thought to reduce as one grows older. The other theory is associated with metabolic risk factors which tend to increase with age (Tuomilehto, 2004). For example Mcgil et al., (2008) mentions that the extent of fatty streaks and raised lesions in the right coronary arteries increases with age. The same applied to the extent of abdominal aortic lesions. In another study, Ko et al., (1997) reported that an increase in age was associated with worsening of other cardiovascular risk factors, including worsening in glycaemic status. Studies conducted to evaluate the risk of death from CVD, suggest that age is a significant contributing factor for death from CVD (Pocook et al., 2001).

Population demographics of Bellville South indicate that approximately 25% of its population is middle aged, ranging between 35 to 65 years (Statistics South Africa, 2011). During a previous DM prevalence survey within the Bellville South community, a big population within the above
age group had both known and undiagnosed DM, as well as other cardio-metabolic risk factors hence increasing the risk of CVD (Soita et al., 2009).

1.5.1.2 Gender
Men are more likely to suffer from CVD compared to their female counterparts, particularly those which are manifestations of atherosclerosis (Pilote et al., 2007). Risk assessment models suggest that males score higher risk points for CVD compared to females, with males comparable to females ten years older with similar risk factors (Pocook et al., 2001). It is unclear whether this is because of the increased risk by the male androgen hormones or the protective effect of the female oestrogen, but assumptions are that both play a role through the protective effect of the female oestrogen (Jacques, 2001). Oestrogen is thought to protect against CVD by lowering LDL and raising HDL levels (Jacques, 2001). However, the protective advantage reduces as a woman advances towards menopause. Noteworthy however is the rising incidence of cigarette smoking amongst females even at younger ages, which suppresses the protective effects of oestrogen (Wilansky & Willerson, 2002). This may explain the low incidence of CVD in females before menopause and its rise thereafter.

1.5.1.3 Ethnicity
Even though CVD is a global problem, the current view is that its distribution varies between population groups. For example, South Asians, African-Caribbean’s, African-Americans and Mexican Americans have some of the highest CVD prevalence rates (McKeigue et al., 1991). In particular, South Asians from India, Sri Lanka, Bangladesh, Nepal and Pakistan are known to have high CVD prevalence rates. Furthermore, immigrant South Asians living in the UK and other European countries exhibit greater levels of coronary risk factors compared to other population groups (McKeigue et al., 1991).

There is paucity of data on the prevalence of CVD in South Africa. However, available data describing the burden of CVD shows a steady rise of CVD risk factors amongst the black South Africans. For example a report by Maredza et al., (2011) reveals a worrying 44% and 42% prevalence of hypertension amongst males and females respectively in the Mpumalanga district. Furthermore, a study looking at individuals with previous and newly diagnosed CVD
amongst black South Africans who participated in the Soweto Heart study reported that 56% of CVD patients who had hypertension were also obese (Sliwa et al., 2008).

1.5.2 Modifiable factors

Modifiable factors are factors an individual can have control over in terms of developing CVD and these include;

1.5.2.1 Dyslipidaemia

Elevated levels of blood lipids, particularly cholesterol and triglycerides are important predictors for CVD. Total cholesterol is made up of various forms, however the most studied are the high density lipoproteins (HDL) and the low density lipoproteins (LDL). HDL is regarded as good cholesterol because of its protective nature against atherosclerosis, whilst LDL is considered bad cholesterol because of its predisposition to atherosclerosis. Zaret et al., (1998), states that acceptable levels of LDL cholesterol should range between 130 to 160 mg/dl whilst that of HDL should not be less than 35 mg/dl in individuals without any other current CVD risk factors. Numerous studies, including the INDIANA study have used cholesterol levels as a predictor for CVD (Pocook et al., 2001).

1.5.2.2 Smoking

Despite the harmful health effects associated with smoking, as well as the anti-tobacco campaigns by the relevant authorities, tobacco consumption seems to be increasing globally. It is estimated that the current global number of smokers is 1.3 billion and is predicted to rise to 1.7 billion by 2025 if the incidence remains unchanged, (WHO, 2003; Erhard, 2009). Although smoking is still predominantly a male dominated habit in many countries, the gap is reported to be narrowing rapidly (Wilansky et al., 2002). Available data suggests that tobacco is consumed more in the middle to low income countries (Stenstrom & Anderson, 2000; Prabhat et al., 2002; Pampel, 2008). In Africa, tobacco consumption varies between countries, from 8% in Nigeria to 27% in Madagascar. Tobacco smoking seems to be a socially acceptable habit in the South African communities and as such, it is consumed by people of all status and age groups. Its consumption is believed to be as high as 27% (Wallbeek, 2002).
Tobacco smoking is associated with a mortality of 1.2 million people per year in Europe alone, and 4.9 million globally (Bjorn, 2003; Berlin, 2008). Tobacco smoking has been identified as a risk factor for the development of multiple diseases, including metabolic and cardiovascular diseases (Bjorn, 2003; Elliasson et al., 2004 & Berlin, 2008). CVD predictive models have shown that cigarette smoking conferred a significantly high hazard ratio (Wilson et al., 1998; Grundy et al., 1999), with smoking reported to cause about 14% of CVD deaths in men and 12% in women in 2000. Studies on CHD in both men and women have shown a dose response relationship between elevated risks for CHD and age at smoking initiation and quantity smoked daily (Wilansky et al., 2002) and WHO (2002) reported that smoking related CVD risks are higher amongst younger smokers (Mahonen et al., 2004). Mortality predictions related to tobacco use indicate that if no significant intervention is instituted, 8 million people will die by 2030, accounting for 10% of total deaths (WHO, 2010).

Generally, there is paucity of data on CVD as well as on the association between tobacco smoking and CVD related risk in South Africa. However, studies indicate that tobacco consumption is accountable for 8% of adult deaths in South Africa (Sitas et al., 2004) and reports from the Bellville South Study (Soita et al., 2009) showed that tobacco smoking was highly prevalent amongst the middle age group this population. Further estimates of disease attributable to smoking amongst South Africans indicate that nearly 8-9% of deaths were smoking related (Groenewald et al., 2007).

1.5.2.2.1 The effect of nicotine on endothelial tissue

Nicotine is the active substance found in tobacco and is believed to liberate free radicals once consumed. Free radicals cause morphological and biochemical changes to the internal lining of the blood vessels known as the endothelium. This subsequently promotes the development of atherosclerosis (Erhardt, 2009). Increased oxidative stress results in elevated oxidized LDL, which is consequently engulfed by macrophages and converted into foam cells which form plaques (Erhardt, 2009). Free oxygen radicals produced from cigarette smoke also leads to depression in the production of nitric oxide which is a key element in maintaining endothelial function. Damage to the endothelium interferes with the vasoconstriction properties of the blood vessel as well as contributing to rapid atherosclerosis and vascular dysfunction (Schalkwijk & Stehouwer, 2005; Erhardt, 2009). Smoking is also known to increase the risk of platelet aggregation which can potentially promote thrombosis which may contribute to
Ischaemic Heart Disease (IHD), a condition in which cardiac muscle dies due to lack of sufficient blood supply.

1.5.2.3 Obesity

Obesity is defined by WHO, (2000) as a condition in which there is accumulation of excess body fat to an extent that health may be adversely affected. It is one of the main factors known to fuel the incidence of CVD, type 2 DM as well as many other metabolic diseases (Pettersson et al., 2008; Hossain et al., 2007). Obesity is largely influenced by over consumption of high energy foods or simply, a high fat diet in combination with low or lack of physical activity, although genetic factors have also been reported to play a role (Loktionov, 2003; Giansanti et al., 1999). According to the Canadian body weight classifications an individual is obese if his or her body mass index (BMI) exceeds 30 kg/m² (Douketis et al., 2005). Table 1 describes the different BMI categories and their risk for developing obesity related diseases.

Table 1: Body weight and obesity classification (adapted from Douketis et al., 2005)

<table>
<thead>
<tr>
<th>Measure of BMI in Kg/m²</th>
<th>Weight classification</th>
<th>Risk of health problems</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 18.5</td>
<td>Under weight</td>
<td>Increased</td>
</tr>
<tr>
<td>18.5 - 24.9</td>
<td>Normal weight</td>
<td>Least</td>
</tr>
<tr>
<td>25.0 - 29.9</td>
<td>Overweight</td>
<td>Increased</td>
</tr>
<tr>
<td>≥ 30.0</td>
<td>Obese</td>
<td>Increased</td>
</tr>
<tr>
<td>30.0 - 34.9</td>
<td>Class I obesity</td>
<td>High</td>
</tr>
<tr>
<td>35 - 39.9</td>
<td>Class ii obesity</td>
<td>Very high</td>
</tr>
<tr>
<td>&gt; 40</td>
<td>Class iii obesity</td>
<td>Extremely high</td>
</tr>
</tbody>
</table>

Obesity has been classified as a global epidemic and currently affects 1.3 billion people world wide categorized as overweight or obese (Goedecke et al., 2005; Berke et al., 2007). The prevalence of obesity in the United States is as high as 26% and 32% in adult men and women respectively (Goedecke et al., 2005). Its prevalence elsewhere in the world varies between countries as well as with the level of industrialization.

1.5.2.3.1 Obesity in South Africa

The increasing prevalence of obesity even in developing countries has defied the notion that it is a disease of the affluent. The perception that obesity is associated with economic status is therefore subject to review. Industrialization per se is meant to improve the economic wellbeing.
through household income, but rapid urbanization brings with it unhealthy habits such as consumption of high fat diets which leads to obesity (Cameron et al., 2003; Jebb, 2004 & Apovian, 2010). Nearly 29% of men and 56% of women in South Africa can be classified as overweight or obese (Goedecke et al., 2005). Furthermore, a report from the Bellville South Africa Study revealed that its subjects had a mean waist circumference of 98.5 cm in females and 94.0 cm in males resulting into 87.9% and 42.2% central obesity rates as defined by the IDF (2006) criteria (Erasmus et al., 2012). Somers et al., (2006) classified 15.7% of learners as overweight and 6.2% as obese in a study conducted amongst learners in selected rural and urban schools. This indicates that obesity is not only prevalent amongst adults but also in the younger population. The first South African Demographic and Health Survey (SADHS), conducted in 1998 whose results were published in 2002 reported a 29.2% and 56.6% prevalence rate of obesity amongst South African males and Females respectively. From a Black South African female perspective, some females view obesity as a sign of well-being and happiness, where as being small bodied is associated with being HIV positive (Puoane et al., 2005).

1.5.2.3.2 Physical inactivity and obesity

Furthermore, contributing to the rise in obesity in South Africa is the lack of physical activity amongst its population. For example, a study carried out in Cape Town, South Africa found that 30 to 40% of adults are physically inactive (Lambert et al., 2001; Puoane et al., 2002). This level of physical inactivity nearly corresponds to the prevalence of obesity as reported above. The WHO (2012) defines physical activity as any bodily movement produced by skeletal muscles that requires energy expenditure. Physical inactivity has been linked to DM because of its association with the development of obesity, both of which are known to heighten CVD risk (Proper et al., 2007; Fox & Hillsdon, 2006). Worldwide, WHO (2012) reported that in 2008 about 31% of adults aged 15 years and older were insufficiently active (28% of men and 34% of women), which led to approximately 3.2 million deaths attributable to insufficient physical activity.

Attributable to the rise in physical inactivity is the advance in technology which has promoted passive forms of movements and leisure. Hence, social affluence has been viewed from two perspectives and considered a double edged sword because while on one hand life is made more convenient than ever because of the advances in technology, on the other hand, it
encourages the development of chronic diseases of lifestyle. Television viewing, computerized
work stations, use of modern transport and lifts are some of the current technologies and
habits thought to promote the lack of physical activity (Frank et al., 2004; Proper et al., 2007).
This sedentary lifestyle is more observed amongst urban dwellers who subsequently expend
less energy compared to their rural counter parts who are involved in manual activities
(Hamilton et al., 2008).

It is noted that engagement in physical exercise and adopting a healthy diet is one of the most
prudent means of avoiding overweight and obesity. Available data further recommends that,
being involved in moderate to vigorous physical exercise for 30 minutes daily could prevent or
delay the onset of type 2 DM (Franz, 2001). This is because physical activity stimulates muscle
uptake of circulating glucose and also promotes weight loss particularly in overweight
individuals. A report indicates that some factors associated with physical inactivity are violence
on the streets, high-density traffic, low air quality, pollution, and lack of parks, sidewalks and
sports/recreation facilities (WHO, 2012).

1.5.2.3.3 Dietary lifestyle and obesity
The increasing prevalence of obesity and its subsequent risk for other co-morbid conditions
such as DM, hypertension and CVD can partly be attributed to dietary lifestyle (Loktionov et al.,
2003). Even though obesity has a genetic predisposition, available data shows that over
consumption of high fat diet increases the risk of weight gain (Astrup et al., 1993).
Furthermore, a report by Hu et al., (1997) showed that consumption of high dense
carbohydrates and saturated fat was associated with a risk of developing coronary heart
diseases. The emergence of sugar sweetened beverages also accounts not only for child hood
obesity, but that in adults too, with a further risk of CHD (Malik et al., 2010; Schulze et al.,
2004). South Africa is a country with diverse population and traditions where by most of the
rural populations feed mainly on low fat and low dense carbohydrates. However, individuals
who migrate to the urban setting tend to adopt an unhealthydietary lifestyle characterized by
high fat and high dense carbohydrates which predispose them to weight gain (Steyn et al.,
1998).
1.5.2.3.4 Obesity and cardiovascular disease

Obesity has been documented as an independent and important risk factor for CVD (Wilson et al., 2002; Klein et al., 2004). Obesity has several effects on the vascular system, particularly on the arteries regardless of whether it is globally or regionally distributed (Safar et al., 2006). While visceral obesity has been linked to arterial stiffness, reduced elasticity has also been observed in both central and peripheral arteries (Safar et al., 2006). The above properties have a negative effect on the normal function of the cardiovascular system as subjects may gradually develop hypertension. Although normal weight individuals can develop hypertension, obese people are more likely to develop hypertension (Lavie et al., 2003). According to Garg (2004) and Costa et al., (2012) obesity can predispose the development of other risk factors such as dyslipidaemia, insulin resistance, DM and hypertension. Furthermore, the greater the degree of overweight, the greater the likelihood of developing obesity related complications. Obesity also affects plasma lipids, by increasing triglycerides, which have a damaging effect on the vascular system and decreases the cardio protective levels of high-density lipoprotein cholesterol (Lavie & Milani, 2003).

1.5.2.4 Hypertension

Hypertension is one of the leading causes of cardiovascular mortality and morbidity (Flack et al., 2003). It is defined as a sustained elevated blood pressure measurement of greater than 140/90 mmHg in individuals (Rutherford, 2003). Blood pressure is determined as the product of cardiac output which is the amount of blood expelled by the left ventricle in one minute of pumping and total peripheral resistance which is determined by the tone or tension of the blood vessels (Lindsay & Graw, 1997). Blood pressure is controlled by a complex interaction of hormones, chemical cell receptors, amount of sodium intake and the nervous system. Although the cause of hypertension is unknown in 90% of individuals (primary hypertension), in the remaining 10% of patients, high blood pressure is known to be a symptom of an underlying problem, such as stenosis or narrowing of the arteries supplying the kidneys, a kidney abnormality, tumor of the adrenal gland, or congenital defects of the aorta (Zaret et al., 1998). This is called secondary hypertension.

During the early course of the disease, cardiac output is elevated while total peripheral resistance is normal. As the disease progresses, cardiac output normalizes, but peripheral resistance becomes elevated. This leads to myocardial hypertrophy as a response to raised
peripheral resistance. Particular emphasis is made to a raised pulse pressure (systolic pressure) than the diastolic pressure as this puts the individual at greater risk of cardiovascular complications. A defective rennin angiotensin aldosterone system which results in elevated sodium retention and vaso-constriction, genetic defects within the kidney structure and obesity are believed to cause secondary hypertension (Rutherford, 2003).

Like other cardiovascular risk factors, hypertension is associated with advanced age and overweight. For example, Zipes et al., (2005) note that as the population grows older and obese, the incidence of hypertension continues to increase, not only in developed countries but also in developing countries (Jee et al., 1998). Reports from the Framingham heart study indicate that the residual lifetime risk of developing hypertension in middle aged and elderly individuals is 90% if no primary prevention measures are instituted (Ramachandran et al., 2002). In the South African context, results from Demographic and household survey of 1998 showed that 21% of South Africans were hypertensive (Steyn et al., 1998). However, this prevalence may have risen considering that the study was conducted nearly a decade ago. According to Norman et al., (2007) nearly 8-9% of all deaths in South Africa can be attributed to hypertension.

1.5.2.4.1 Effects of hypertension on the cardiovascular system

The Framingham heart study which was initiated in 1948 to examine the risk factors of CVD provided evidence which showed that high blood pressure increases the likelihood of developing coronary heart disease, stroke, congestive heart failure, peripheral vascular disease and renal dysfunction rises (Ramachandran et al., 2002). Hypertension is a common and known CVD risk factor and of course it is paramount that its effect is clearly understood. Increased pressure within the blood vessels is responsible for driving blood fat and cholesterol through the arteries, which further speeds the process of atherosclerosis (Zaret et al., 1998). This increases the possibility of a stroke or heart attack due to clot formation. In many individuals, hypertension usually present without any symptoms, hence it is referred to as a silent killer. During its advanced stages, it may present with dizziness, headaches, fainting or even convulsions. It is reported that by this time, the kidneys may be damaged leading to renal impairment or dysfunction (Ramachandran et al., 2002). Several studies including Anderson (1991), Cederholm et al., (2008) and Wilson et al., (2002) have used hypertension as a marker in the prediction of CVD events.
1.5.2.5 Chronic kidney disease

CKD, also known as chronic renal disease, is a progressive loss in renal function usually over a period of months or even years. The three most common causes attributed to the development of CKD are DM, hypertension, and glomerulonephritis (Lainscak, 2009). One of the key diagnostic findings in CKD among others is the gradual rise in serum creatinine (Levey et al., 2006). Professional guidelines have recently been developed to classify the severity of CKD. These guidelines comprise stages 1-5, with stage five being the most severe warranting dialysis or kidney transplant (Levey et al., 1999). Stage 5 CKD is often called end stage renal disease (ESRD) The presence of CKD confers reduced life expectancy if untreated as well as a heightened risk of CVD, making it the most common cause of death in people with the disease. It has been noted that individuals with CKD posses multiple CVD risk factors (Lainscak, 2009).

1.5.2.5.1 Epidemiology of chronic kidney disease

CKD has recently been noted as a worldwide public health problem with an increasing incidence. Several sources note that the current burden of CKD might be due to a change of the underlying pathogenicity of the disease (Zhang et al., 2008; Tohidi et al., 2012). Infections leading to glomerulonephritis were one of the leading causes of kidney disease several decades ago. However, following the shift in disease epidemiology, infections have become a less important cause for kidney disease with hypertension and DM being the leading contributors (Zhang et al., 2008). The number of patients with ESRD on renal replacement therapy in the United States, Japan and most European countries have increased by 9%, 7% and 4% per year respectively (Tohidi et al., 2012). There is not much data on the prevalence of CKD in Africa. However, available information from a few studies shows that its incidence is on the rise. For example Matsha et al., (2013) noted a 14.8% prevalence of CKD amongst the mixed ancestry population of South Africa. This is not only one of the few studies conducted in the sub Saharan region, but also one that has reported the highest prevalence of 14.8%.

1.5.2.5.2 Chronic kidney disease and risk of cardiovascular disease

Reports from epidemiological surveys show that CKD heightens the risk for CVD. For example, data from the MONICA study showed that CKD was strongly associated with an increased risk
of incident MI and CVD mortality (Meisinger et al., 2006). A statement issued by the American Heart Association confirms that traditional CVD risk factors as those defined in the Framingham study are highly prevalent in CKD patients. Furthermore, several nontraditional factors, such as hyperhomocysteinemia, oxidant stress, dyslipidemia, and elevated inflammatory markers which are associated with atherosclerosis are present in most CKD individuals (Sarnak et al., 2003).

1.6 Type 2 Diabetes mellitus

Diabetes mellitus is characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both (ADA, 2011). The chronic hyperglycemic status in diabetic individuals is associated with immediate as well as long-term damage, loss of function and failure of various organs, chiefly but not limited to the eyes, kidneys and nerves (Stoner, 2005). Worse still, DM is also an established risk factor for development of heart diseases because of its consequent hyperglycaemic effect on the cardiovascular system. Observational studies have reported hyperglycemia as a risk factor for CVD, including CHD, stroke and intermittent claudication (Meigs et al., 2002). Although CVD could occur to any one, Siscovick et al., (2010) emphasizes that cardiac arrests are a major cause of mortality amongst people with DM.

The global prevalence of DM has reached extremely high proportion (Wild et al., 2004). It has been reported that the number of people with DM is increasing with the global number of diabetic adults, estimated to have been 170 million in the year 2000 and 346 million presently (Roglic et al., 2005; Johnson et al., 2012). However, this figure is still predicted to reach 440 million in 20 years from now, yet a big number remain undiagnosed (Johnson et al., 2012; Qin et al., 2012). Data from the Bellville South Africa study showed that for nearly every one known diabetic, there is another who is undiagnosed (Erasmus, et al., 2012). The health implication of undiagnosed DM is that these individuals are untreated and therefore at risk of developing complications including those related to CVD much sooner than their counterparts who receive diabetic therapy.

Studies have shown a close association between DM and CVD. For example, in a study by Berry et al., (2007), cardiovascular diseases such as myocardial infarction and coronary atherosclerosis were reported to be more prevalent in diabetic subjects than in their non-diabetic counterparts. What further comes out importantly from this study is that age, gender,
LDL cholesterol and hypertension were strong predictors of CVD incidence. Beckman et al., (2002) state that coronary heart disease is known to cause much of the morbidity and mortality in patients with DM and that although the female gender have the cardio-protective effect of hormones, DM blunts these benefits. Furthermore, Berry, et al., (2007) mentions that the prevalence of CHD rises from 2% to 4% in the general non diabetic population to up to as high as 55% in the diabetic subjects. A separate study also shows an association between DM and CVD. Furthermore, the duration of DM has been found to be a key factor in the incidence of CVD amongst the diabetic population (Giansanti et al., 1999).

1.6.1 Diabetes mellitus in South Africa

South Africa is a multiracial society with a population of nearly 50.6 million people according to the recent 2011 mid-year population estimates released by Statistics South Africa. Most of its population is resident in the urban area. The four main ethnic groups with their corresponding national population representations are Black Africans (79.5%), mixed ancestry (coloured) (9%), Caucasians (white) (9%) and Indians (2.5%) (Statistics South Africa, 2011). In South Africa, the prevalence of DM varies from one province to another. This is probably due to the ethnic connotation associated with its distribution. For example, more Indians seem to have settled in Kwazulu Natal (Durban) than elsewhere. The incidence of DM in this province is higher compared to other provinces. Furthermore, variations are also observed within different population groups other than merely regions of settlement (Erasmus et al, 2012). These variations are not an uncommon phenomenon as they have already been previously document by scientist worldwide (Schulz, et al., 2006 and Ramachandran, et al. 1997).

In 2005, the Medical Research Council conducted a survey on the chronic diseases of lifestyle in South Africa. Results from this report revealed that the prevalence of DM was highest among the Indian community at 8.5% and 11.5% for men and women respectively (Goedecke et al., 2005). This was followed by the coloured community whose prevalence was 3.1% and 5.8% for men and women respectively(Goedecke et al., 2005). The prevalence varied according to provinces with the highest 5.9% and 3.3% observed amongst the Kwazulu Natal females and Gauteng males. The lowest rates were observed amongst the North West males and females at 0.9% and 1.1% respectively. Further available data derived from small community studies and compiled by Bradshaw et al., (2007) indicated that the prevalence of diabetes was 5.5%, and as observed in many studies, the prevalence increased with age.
The Mamre study conducted by Levitt, et al. (1999) in a mixed ancestry community in the Western Cape region of South Africa has indicated a prevalence of 10.8%. The same authors (Levitt, et al. 1993) reported a prevalence rate of 8.0% amongst black Africans. A previous study conducted by Charlton, et al. 1997 amongst elderly coloured South Africans in Cape Town documented a prevalence of 28.7%. As mentioned previously, the level of industrialization and/or urbanization which comes with change in lifestyle patterns has a great bearing on the prevalence of DM. For example, a recent study conducted by Erasmus et al. (2012) amongst the middle aged mixed ancestry population of Cape Town, found a positive relationship between the prevalence of DM and rural to urban migration. In this study the crude prevalence of DM was documented to be 28.2%. Other factors associated with DM risk are obesity, consumption of high fat diet, excessive alcohol consumption, cigarette smoking (Wandell et al., 2007; Jee et al., 2010; Hu, 2011).

1.6.2 Association between diabetes and cardiovascular disease

Studies have shown a close association between DM and CVD. For example, in a population based study by Berry et al., (2007), cardiovascular diseases such as coronary atherosclerosis, coronary heart disease and myocardial infarction were reported to be more prevalent in diabetic subjects than were in their non-diabetic counter parts. However, what is interesting is that age, gender, LDL cholesterol and hypertension were strong predictors of CVD incidence. Beckman et al., (2002) state that coronary heart disease is known to cause much of the morbidity and mortality in patients with DM and that although the female gender have the cardio-protective effect of hormones, DM blunts these benefits. Furthermore, Berry, et al., (2007) mentions that the prevalence of CHD rises from 2% to 4% in the general non diabetic population to up to as high as 55% in the diabetic subjects. A separate study also shows an association between DM and CVD. Giansanti et al., (1999), further states that the duration of DM is also a key factor in the incidence of CVD amongst the diabetic population.

1.6.2.1 Pathological mechanism linking diabetes to cardiovascular disease

There is enormous epidemiological and clinical evidence linking DM to the development of cardiovascular disease. The role of DM and CVD risk, compared to other factors, is known to confer the highest risk, to an extent that it has been equated to developing a heart attack. It increases the risk of cardiovascular events two to three folds compared to non-diabetic
individuals (Juutilainen et al., 2005; Chamnan et al., 2009). Evidence shows that once subjected to prolonged hyperglycaemia, body tissues including nerves and blood vessels undergo progressive damage. Vascular endothelial damage affects both micro and macro vessels. Macrovascular effects include coronary vessels. This coupled with alteration in metabolic processes which promote atherosclerosis with its resulting ischaemia, increase an individual’s risk of CVD (Schalkwijk & Stehouwer, 2005; Abbott et al., 2011).

1.6.3 Natural history of diabetes mellitus

Diabetes occurs when the body does not produce enough insulin or when the body cannot effectively utilize the secreted insulin. In type 2 DM, insulin resistance is usually the problem especially in obese individuals (Saini, 2010; Mercurio et al., 2012). Insulin resistance is defined as the inability of insulin to stimulate adequate glucose utilization by the target tissues. It also refers to impaired ability of insulin to control hepatic glucose production and to augment glucose clearance in target tissues (Wilcox, 2005). In insulin resistance, tissues such as peripheral muscles, adipose tissue as well as organs such as the liver are insensitive to the effects of insulin. This consequently results into reduced effect of insulin on lipid and protein metabolism (Luana et al., 2008). This impairment leads to reduced glucose uptake by various tissues whose glucose uptake is insulin dependent. It also leads to increased liver gluconeogenesis as well as production of free fatty acids (Matfin, 2008). Consequently, the cellular demand for insulin rises due to the increasing resistance. In response to the increasing insulin demand, the pancreatic beta cells are forced to secrete more insulin and also reduce the hepatic clearance of insulin which results in hyperinsulinaemia. This situation progressively leads to beta cell exhaustion, hence resulting into impaired glucose metabolism and eventually overt DM (Wilcox, 2005; Stumvoll et al., 2005).

1.6.4. Conversion of glycaemic status

Impaired glucose metabolism is an intermediate phase between normal glucose metabolism and DM. Individuals with impaired glucose metabolism could convert in glycaemic status either way (Nichols et al., 2007). For example, any intervention measures instituted during this phase could result into possible regression to normal glucose metabolism. On the other hand, an individual will possibly progress to full blown DM if no intervention is implemented. Studies, including that of (Erasmus et al, 2012; Olofsson et al., 2010) have reported an association
between multiple components of MetS such as obesity, raised fasting blood glucose (FBG) levels, elevated serum triglycerides (TG), low high density lipoproteins (HDL) values and high blood pressure with glycaemic status as well as an increased risk for CVD.

1.6.4.1 Components of metabolic syndrome

Metabolic syndrome is a constellation of disorders which includes obesity, raised fasting blood glucose (FBG) levels, elevated serum triglycerides (TG), low high density lipoproteins (HDL) values and high blood pressure (HBP) (Thomas et al., 2005). A study by Matsha et al., (2013) which followed up non diabetic hyperglycaemic participants reported a positive association between MetS and progression. Although some components of MetS such as obesity have independently been associated with worsening of glycaemic status elsewhere, Matsha et al., (2012) showed a significant association between the number of MetS risk factors with a high propensity for progression of glyceamic status. Studies elsewhere have found an association between MetS and development of CVD and DM (Olofsson et al., 2010).

1.6.4.2 Haemoglobin A1c

Haemoglobin is the oxygen carrying red pigment found in blood. It is also a component to which glucose binds. Once bound, the heam becomes glycosylated/glycated (Reynolds et al., 2006). Glycosylated haemoglobin or glycated haemoglobin (Haemoglobin A1c, HbA1c) is formed by the attachment of glucose to various amino groups due to its exposure to plasma glucose. A haemoglobin molecule once glycated, remains that way throughout its entire lifespan and is reflective of the amount of glucose it has been exposed to. As the level of plasma glucose increases, the fraction of glycated haemoglobin increases. HbA1c is measured to identify the average plasma glucose concentration over a period of time, usually 12 weeks (Reynolds et al., 2006). Increasing levels of HbA1c indicate rising glycaemia, and hence, the risk for impaired glucose tolerance or DM. Various studies have demonstrated that individuals with impaired glucose metabolism, including DM have elevated HbA1c levels. This has resulted in suggestions to consider HbA1c as a diagnostic variable as well as a predictor for type 2 DM (Leite et al., 2009; Bao et al., 2010; Zemlin et al., 2011).
1.6.5 Cardiovascular intervention measures

The gradual rise in the incidence of NCDs has prompted many governments and other relevant authorities to design and adopt sustainable measures aimed at combating the diseases. Many countries seem to have embraced the strategy of early detection and timely management of CVD risk factors, which also calls for improvement in health care systems. A close analysis of some of the CVD risk factors implicates lifestyle habits such as consumption of unhealthy diets, cigarette smoking, as well as the lack of physical exercises. Hence, addressing these risk factors has been at the forefront of the fight against DM and CVD. Furthermore, because CVD risk factors develop over time and are chronic in nature, efforts towards prevention require multidisciplinary involvement and sustained over a long period of time.

Numerous studies, including Cooper et al., (2012) demonstrated an association between consumption of a healthy diet and reduction in the incidence of DM. Wandell et al., (2006) made recommendations that about 90% of type 2 DM cases can be prevented if individuals adapt a prudent diet. In this regard, efforts at different levels of influence have been directed towards consumption of healthy diets. A controlled trial study involving a cohort of human participants found a significant reduction in weight as well as the incidence of DM compared to their counterparts in the control group (Tuomilehto et al., 2001). Johnson et al, (2012) also state that intervention yield positive results when these programs are delivered in conjunction with professional stake holders within the primary health care system. Even though it might appear costly to implement CVD prevention strategies by involving professional staff at various levels of program delivery, it is eventually cheaper than the cost of DM management (Herman 2011). A report by the WHO, 2012 suggested that only 30 minutes of physical exercise daily is required to prevent overweight or delay the onset of type 2 DM, with a subsequent decrease in the risk of CVD.

The American Diabetes Association issued a report on the standards of medical care of diabetic individuals with suggestions that those with elevated HbA1c should receive intervention therapy through weight loss to prevent progression to DM (ADA, 2013). This is because rising HbA1c has been found to predict development of DM and subsequently heightening the risk of CVD. Other authorities further recommend the use of pharmacological agents such as anti-cholesterol and angiotensin-converting-enzyme inhibitors in the prevention DM and CVD (Mcfarlane et al., 2003).
Other intervention strategies include anti-tobacco campaigns by state owned organizations and Non-Governmental Organizations in which health messages regarding harmful effects of tobacco is communicated to the public. Similarly, the increase in taxes levied on tobacco products by governments is also aimed at reducing its consumption (Chaloupka et al., 2011). Further regulations have been enforced on the amount of salt added to food products as well as reducing the amount of saturated fats in oil which increase the risk of hypertension and a rise in bad cholesterol (Desmond, 2006). Salt reduction in processed foods has been projected to result in CVD mortality and morbidity reduction (Domingo et al., 2010).

In summary of the prevention of CVD and other NCDs, the WHO, (2010) made recommendations to conduct active surveillance of the following risk factors;

1.6.5.1 Behavioral risk factors of cardiovascular disease and other non-communicable diseases
- Prevalence of current daily tobacco smoking among adults
- Prevalence of insufficiently active adults (defined as less than 5 times 30 minutes of moderate activity per week, or less than 3 times 20 minutes of vigorous activity per week, or equivalent)
- Prevalence of adult population consuming more than 5 grams of dietary sodium chloride per day
- Prevalence of population consuming less than five total servings (400 grams) of fruit and vegetables per day
- Adult per capita consumption in litres of pure alcohol (recorded and unrecorded)

1.6.5.2 Physiological and metabolic risk factors of cardiovascular disease and other non-communicable diseases
- Prevalence of raised blood glucose among adults (defined as fasting plasma glucose value ≥ 7.0 mmol/L (126 mg/dl) or on medication for raised blood glucose)
- Prevalence of raised blood pressure among adults (defined as systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg) or on medication for raised blood pressure
• Prevalence of overweight and obesity in adults and adolescents (defined as body mass index greater than 25 kg/m² for overweight or 30 kg/m² for obesity or for adolescents according to the WHO Growth Reference)
• Prevalence of low weight at birth (< 2.5 kg)
• Prevalence of raised total cholesterol among adults (defined as total cholesterol ≥ 5.0 mmol/l or 190mg/dl)

1.6.5.3 Challenges encountered in cardiovascular disease prevention

The rise in obesity is associated with the persistent presence of factors that promote its incidence. For example, despite efforts towards its prevention, factors that promote a sedentary lifestyle as well as reduced energy expenditure such as TV viewing, use of lifts/escalators, lack of physical activity are on the rise. The failure to effectively enforce measures to prevent childhood obesity which often progresses to adulthood has also been viewed as a setback in the prevention of obesity. This is worsened by reduced breast feeding and early weaning where mothers introduce supplementary feeds containing high energy calories, a practice that has been associated with childhood obesity. Mass marketing of unhealthy foods by giant fast foods companies and baby feeds products has also been viewed as factor that has hindered success in the fight against obesity (Sothern, 2004).

There are contradicting reports regarding the effect of tobacco advertising on smoking. While Saffer & Chaloupka (2000) mention that there is little or no evidence linking tobacco advertising to the increasing tobacco consumption, other sources have concluded otherwise (Neuman et al., 2002). However, the general view by most nonsmoking members of the public is that advertising influences continuity and onset of new cigarette smokers.

The state of health care systems in many developing countries is lacking. For example, primary health care providers are the first level contact between communities and the health care system (Gale, 1998). However, evidence shows that these are not adequately staffed to conduct an active surveillance on individuals at risk of developing CVD such as pre-diabetic, hypertensive, undiagnosed DM as well as those with high cholesterol as recommended by the WHO, (2010). Furthermore, the cost of treatment of some CVD risk factors such as DM requires long term commitment. The chronic nature of the disease coupled with the cost of treatment makes compliance inevitably difficult.
Routine physical exercise is an important strategy for the control of many chronic diseases of lifestyle. Studies show that individuals who engage in intensive exercise on a daily basis have a low incidence of CVD risk factors (Franz, 2001; Bassuk & Manson, 2005; Haskell et al., 2007). This is particularly common in rural communities where individuals are involved in physical activities and feed on low energy diets. As for individuals residing in urban areas and who are not physically active, physical exercise is often prescribed as an entire or part of the therapy for many chronic diseases of lifestyle (Haskell et al., 2007). Unfortunately sustainability for physical exercise programs is poor as dropping out affects the outcome (Roumen et al., 2011).

1.7 Cardiovascular disease risk assessment models

The global rise in the prevalence of CVD has led to various authorities coming up with measures to avert the disease. One of the methods is by predicting the future development of the disease so as to institute preventive strategies. In order to perform this, individual or community risk assessment needs to be done. In this regard therefore, numerous studies, including the Framingham study were conducted to develop CVD risk assessment tools (Dawber et al., 1951; Grundy et al., 1999 & Marshall et al., 2008). The Framingham heart study was initiated in 1948 to study cardiovascular related risk factors in the town of Framingham Massachusetts, USA, (Dawber et al., 1951). Over the years, the Framingham heart study participant monitoring was carefully conducted which led to the identification of important risk factors to CVD as well as estimating the participants’ probability of suffering a CVD event in future. Since then, several other heart related studies have been conducted and made reference to this study (Cederholm et al., 2008).

The concept used in risk assessment and prediction is based on presence of cardiovascular risk factors which are used to derive the model (Chamnan et al., 2009). The knowledge of the prevalence of risk factors can also be used to describe the individual or population CVD risk profile. Therefore, risk assessment and prediction is the probability that an individual will experience a CVD episode in an estimated period of time (Cederholm et al., 2008). Risk assessment improves ones clinical judgment of an individual’s cardiovascular health and is thus able to take necessary clinical measures regarding patient management (Coleman et al., 2007). CVD risk prediction is one of the most important epidemiological contributions in the recent evidence based medicine. Therefore the significance of risk assessment is;
(1) To identify high-risk patients who deserve immediate attention and intervention
(2) To motivate patients to adhere to risk-reduction therapies and
(3) To modify intensity of risk-reduction efforts based on the total risk estimate
(Grundy et al., 1999)

1.8 Social economic impact of cardiovascular disease and diabetes mellitus
The global rise in the incidence of CVD and DM has brought with it an enormous financial and social burden to families and governments. The burden could be as a result of direct or indirect costs, in terms of time, money as well as other resources.

1.8.1 Direct cost
There is a huge direct impact conferred by DM both to individuals, families' communities as well as the state and the entire world. Diabetic patients and to some extent those with CVD form a significant bulk of patients admitted for treatment in hospitals globally. Worse still, their length of stay in the hospitals is higher than that of other patients. This therefore means that the cost of treatment (medication, labour and time spent caring for them is higher than that of other patients. This effect is born not only by the state, but also by the families and communities. Data from the National Health Services (NHS) shows that DM care cost nearly £10 billion, which is 10% of the budget allocated to NHS in the United Kingdom (Zhang et al., 2010). For middle-low income countries, the situation is even worse as the cost of managing DM is straining their national health budgets. Resources to manage the disease have to be identified amidst other competing national priorities. A study conduct in Mexico shows that the need for DM care services is projected to rise putting a further strain on scarce resources (Arredondo & Zuniga, 2004). This scenario could be expected in any region, including the developing countries experiencing a high prevalence of CVD, DM and NCDs in general. South Africa is one of the sub-Saharan countries with the highest incidences of DM. The global healthcare expenditure on DM for 2010 and 2030 reported by Zhang et al., (2010) indicates that the total expenditure on diabetic patients for South Africa as of 2010 was estimated at nearly 3 million dollars and further predicted to increase to nearly 4 million dollars in 2030 (Zhang et al., 2010).
1.8.2 Indirect effect

The age of onset of type 2 DM is documented to have been reduced, leading to a young type 2 diabetic population (Winkleby et al., 2004). Furthermore, other CVD risk factors such as obesity and hypertension have been identified in even younger adults which heighten their risk for developing CVD (Winkleby et al., 2004). These individuals are the mainstream workforce within the communities as well as their countries. Because of the debilitating nature of DM and CVD these individuals spend long amounts of time away from work resulting in lack of productivity. For business oriented enterprises, this translates into financial loss, while for service related sectors, it results in loss of man power, regardless of whether they are skilled or not. Further still, these individuals become dependent for economic support since they may be unable to fend for themselves as well as their families. This dependence could strain those immediate to the individual.

1.9. Rationale of the study

Bellville South is a predominantly mixed ancestry, commonly termed ‘coloured’ community with a reportedly high prevalence of type 2 DM (Erasmus et al., 2012). This condition has previously been documented to be a risk factor for development of CVD. Available information shows that the mixed ancestry population has the second highest prevalence of DM to that of the South African Indians (Levitt et al., 1999). The state of CVD risk in the South African population is not adequately described despite the increasing prevalence of CVD risk factors, in particular DM and obesity. Available data regarding cardio-metabolic disease risk stratification in African populations have been derived from developed countries and their validity in this setting is questionable. For instance, studies involving participants from Sub-Sahara Africa, including our own study among coloured South Africans have demonstrated that the waist circumference (WC) cut-off for the prediction of DM and CVD are different from those commonly recommended for use in sub-Saharan populations, 94 cm in men and 80 cm in women (IDF, 2006).

Hence, in the light that the obesity epidemic is known to be the fueling force of developing DM as well as other cardio-metabolic conditions with a subsequent risk of CVD, and also conscious that CVD, particularly CHD carries a high mortality rate, it was therefore warranting that such a study is conducted in the light of attempting to elucidate the CVD risk profile of this population. Clear knowledge of the CVD risk within the community provides a basis on which CVD
prevention strategies can be conducted. This could be either by government at policy formulation level, or by the local population through involvement in lifestyle intervention/modification. This study therefore provides baseline information regarding the state of CVD risk in the mixed ancestry population using a CVD risk estimation tool. It is against this background that this study sought to determine the CVD risk in the population of Bellville South both at baseline and at follow-up.

1.10. Aim of the study

The aim of this study was determine the CVD risk profile of the Bellville South community during the baseline and after the follow-up studies through assessment of their risk factors, MetS, Type 2 DM, Obesity and CKD.

1.10.1 Objectives of the study

- To assess the prevalence of CVD risk factors (MetS, DM, Obesity and CKD) at baseline and 3 year follow-up.
- To determine the burden of DM both at baseline and 3 year follow-up.
- To identify factors associated with glycaemic change
- To determine the prevalence of diagnosed and undiagnosed DM.
- To determine the progression of risk factors from baseline to 3-year follow-up
- To determine MetS
2.1 Introduction
This chapter describes the processes involved in conducting the baseline as well as follow-up studies.

2.2 Ethical statement
The Faculty of Health and Wellness Sciences Ethics Committee of the Cape Peninsula University of Technology approved both studies (Reference Numbers: CPUT/HW-REC 2008/002 and CPUT/HW-REC 2010) respectively and were conducted according to the code of ethics of the World Medical Association (Declaration of Helsinki). All participants signed written informed consent after all the procedures had been fully explained in the language of their choice. Furthermore, permission was also sought from other relevant authorities such as city and community authorities. These authorities granted permission to conduct work in the community and also to make use of designated places such as community halls or nearby schools as data and sample collection venues.

2.3 Study setting and population
Participants were members of a previous cohort study conducted in Bellville-South to determine the prevalence of DM and its risk factors, in the metropolitan city of Cape Town in South Africa. Bellville South is situated within the northern suburbs of Cape Town, South Africa. This community is traditionally a mixed-ancestry township formed in the late 1950s. The mixed ancestry population commonly referred to as coloured, is a population group comprising 32% to 43% Khoisan, 20% to 36% Bantu-speaking African, 21% to 28% European and 9% to 11% Asian ancestry (de Wit et al., 2010). According to the 2011 population census, its population was approximately 24,642, with the people of mixed ancestry making up 87.7% (21,618). Although English and other African languages such as Xhosa are spoken, the predominant language in this community is Afrikaans. Most of the residents of this community have lived there for over five years while others have been there their entire lives. Even though
a significant number of the inhabitants are civil servants employed in the public sector or retired civil servants, Bellville South has a relatively high rate of unemployment

2.4 Criteria for inclusion into the study

Inclusion into the follow-up study was based on satisfaction of the following criteria;

- Resident in Bellville South
- Not pregnant in the case of female participants
- Not acutely sick
- Consents to participation

2.4.1 Exclusion criteria

Exclusion of participants from the study was based on the following criteria:

- Non-resident in Bellville South
- Pregnant mothers
- Participants younger than 35 or older than 65 years. This age group represented the middle aged population in the study area.

2.5 Research design for the baseline and follow-up evaluations

The study was a cross sectional prospective study aimed at determining the prevalence of impaired glucose tolerance and DM as well as establishing a cohort that could be followed up for insulin resistance and its sequel in randomly selected mixed-ancestry subjects aged 35 to 65 years. A more detailed description of the methodology was described in the baseline study MTech thesis (Soita et al., 2009) and also in appendix I. Both dependent and independent data were obtained. Dependent data were the personal demographic information and were collected by means of a structured questionnaire, whilst independent variables which constituted blood and anthropometric data were obtained through participant measurements.

The baseline data was collected between January 2008 and March 2009, whilst that of the follow-up survey commenced in February 2011 on the same participants. The objective was to
determine their CVD risk after a period of three years by repeating measurements conducted during the baseline study.

2.5.1 Selection of participants

The sample size was determined based on the number of the study population as provided by Statistics South Africa in its 2001 population census. According to the 2001 population census, its population was approximately 26 758, with the people of mixed ancestry making up 80.48% (21 536). The target population for this study were subjects between the ages of 35 and 65 years and their number was estimated to be 6500. Based on these statistics and the recommended sample size for a pilot study, usually 10%, the sample size required for this pilot study was 650. By means of a map of Bellville South, random sampling was approached as follows. From a list of streets in each stratum, the streets were then classified as short, medium and long streets based on the number of houses. Streets with 22 or fewer houses were classified as short, streets with 23 to 40 houses were medium, and long streets were those with more than 40 houses. A total of 16 short streets representing approximately 190 houses, 15 medium streets representing approximately 410 houses and 12 long streets representing approximately 400 houses were randomly selected across the different strata and given the code (M). From the selected streets, all household members meeting the selection criteria were eligible to participate in the study. Community authorities requested that participants outside the random selection area should benefit from the study. These were also included as volunteers, but given a different code (X). The total number of volunteers was 304 aged 16-95 years. Hence, the total number of participants was 954.

At follow-up, the database of participants who took part in the baseline study was consulted. Participants were traced through the reference number system which also provided details of participant addresses as well as telephone/cell phone contacts. They were re-visited, invited to participate in the study and underwent the same measurements as was done at baseline.
2.6 Pre-participation instructions
Recruited subjects were visited by the recruitment team the evening before participation and reminded of all the survey instructions. The instructions included overnight fasting, and abstinence from drinking alcohol or consumption of any fluids on the morning of participation as these could interfere with the serological measurements. Since the participants were required to bring in an early morning mid-stream urine sample, they were provided with a sterile container as well as instructions on how to collect the sample. Furthermore, participants were encouraged to bring along their medical/clinic cards and/or drugs they were currently using.

2.7 Data collection
A comprehensive protocol describing data-collection procedures (questionnaires and anthropometric measurements) was developed. The questionnaire was partly adopted from existing standardized questionnaires (Ewing, 1984). It was composed of four sections which were all traceable to either a standardized source or a professional expert. The four sections were personal demographics, family health history, diet, cigarette smoking and alcohol consumption. One of the sources from which the questionnaire was adopted is the Chronic Diseases of Lifestyle in South Africa, (2006) report by the MRC which focused on chronic and lifestyle diseases. From this source, we adopted the personal demographics, family medical history and dietary lifestyle component. This aspect of the questionnaire was designed to obtain data on personal demographics such as age, gender, marital status, duration of stay in the study area as well as level of education. It also sought data on previous medical history of chronic diseases such as DM, high blood pressure and CVDs up to third degree relatives.

Questions related to alcohol use were adopted from the Cut down, Annoyed, Guilt and Eye opener (CAGE) questionnaire (Ewing, 1984) as well as the MRC report of 2006. The CAGE questionnaire is an internationally accepted tool used in alcohol related studies. This questionnaire captured data on type of alcoholic drink, quantity as well as frequency of consumption. It also sought to establish if participant had symptoms of problem drinking. Questions on cigarette smoking focused on whether the participant smoked and how much. It also inquired into duration of the habit. If the habit had been given up, the duration was asked
as well as when it was ended. After a detailed consultation, a final questionnaire was modified to suite our study. It was later pre-tested in a neighbouring community with similar demographics where after further modifications were made. All equipment used in the study were universally accepted and standardized and further pre-tested in the pilot study in order to address issues of reliability and validity. Other details relating to quality control are in appendix J.

2.8 Measurements

Measurements are described under the following sections; Anthropometry, Physiological, Biochemical and Metabolic Syndrome profiling

Anthropometric measurements included height, weight, hip and waist circumferences and blood pressure. These measurements were performed by qualified healthcare professionals who underwent training in order to standardise all measurements prior to the commencement of the study. Part of the training involved routine calibration of data collection equipment so as to ensure reliability of data.

2.8.1 Anthropometric measurements

Anthropometric measurements were performed to determine participant weight, height, hip and waist circumferences and BMI. All measurements were performed in triplicate and the average was recorded as final. They were performed as follows,

2.8.1.1 Weight

Weight was determined on a Sunbeam EB710 digital bathroom scale, which was routinely calibrated and standardised using a weight of known mass. Participants were weighed in light clothing and without shoes on. Subjects with postural imbalances including those in wheel chairs were exempted from this measurement. The subject stood on the middle of the flat surface of the scale after it had been set to zero. They were asked to place their hands on their sides. Weight measurements were recorded to the nearest 0.1 kg.
2.8.1.2 Height

Height was measured to one decimal using a portable stadiometer. Without shoes on, a participant was asked to stand on the flat surface of the stadiometer at right angles to the vertical sliding lever of the stadiometer. The head was placed in the Frankfort plane with hands at the sides. The scapular and buttocks were to be close to the vertical sliding metallic bar. The subject was asked to maintain a fully erect position in order to achieve the required accuracy. The sliding metallic bar was then gently allowed to rest on the subject’s head. Readings were recorded in centimetres. If the participant was taller than the investigator, a platform was used to correctly read the height.

2.8.1.3 Waist circumference

Waist circumference was measured using a non-elastic tape at the level of the narrowest part of the torso as seen from the anterior view. If it was difficult to see the waist narrowing, especially in obese subjects, the waist circumference was measured between the ribs and the iliac crest. Participants were asked to be in an erect position with hands placed on the sides and the feet together with their abdominal muscles relaxed. All anthropometric measurements were performed three times and the average measurements were used for analysis. Measurements equal or above 94 and 80cm for men and women respectively were considered above normal.

2.8.1.4 Hip Circumference

Hip circumferences were measured as the maximal circumference over the buttocks. With the investigator squatted before the fully extended subject, the tape was placed around the buttocks over the widest area in the horizontal plane without pressing tightly against the skin and the measurement taken. Where the hip circumference exceeds the tape, the measurement was not taken but noted.

2.8.1.5 Calculation of BMI

Body mass index is a method used to determine whether someone is overweight or obese. It is calculated as weight (kg) divided by height (m) squared. The various classifications of BMI are seen in table 1 above.
2.8.2 Physiological measurements
These included measurements of blood pressure as well as administration of OGTT. Blood pressure measurements were performed according to WHO guidelines (1999).

2.8.2.1 Blood pressure
Participants were allowed a 10-minute rest period after arrival at the clinic before performing the measurements using a semiautomatic digital blood pressure monitor (Rossmax PA, USA) on the right exposed arm with the participant in a sitting and ambulatory position. The correct adult cuff size was placed 2 cm above the elbow joint in order to ensure accurate readings. Three readings were recorded at five-minute intervals and the lowest of the three readings was taken as the correct blood pressure. During the procedure, the participants were asked not to speak as this could affect the readings. Classification for hypertension was based on the IDF criteria of ≥130/85.

2.8.2.2 Oral glucose tolerance test
As recommended by the WHO, (1999) all participants in this study underwent oral glucose tolerance test (OGTT), except those that self-reported to be diabetic or confirmed through medical forms or anti-diabetic medications. An OGTT is a test performed to assess the ability of the body to metabolize glucose. This test has been used widely to diagnose DM. In this test, subjects are asked to fast for 10 to 14 hours, preferably during the night and then challenged by a standard glucose load (WHO, 1998). In this study, an OGTT was performed on fasting participants using a 75 gram glucose load on the morning after the fasting state. A written instruction as well as a detailed explanation of the procedure was conveyed to each participant. The following steps were followed in OGTT:

- Confirmation that participant was fasting
- A blood sample for glucose analysis was taken before administering
- 75 grams of glucose anhydrous dissolved in 250 to 300 mL of water which was drunk within 3 to 5 minutes and the time recorded
- A second blood sample for glucose was drawn 2 hours after drinking the glucose solution
After administration of OGTT, participants were asked to be less mobile while they waited for the post prandial blood to be drawn. Classifications of glucose tolerance were defined using the WHO (1998) criteria as appears in Table 2 below.

**Table 2: Classification of glucose tolerance status (WHO, 1998)**

<table>
<thead>
<tr>
<th></th>
<th>ADA</th>
<th>WHO</th>
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<tbody>
<tr>
<td>DM</td>
<td>Fasting plasma glucose ≥ 7.0 mmol/L</td>
<td>Fasting plasma glucose ≥ 7.0 mmol/L and/or 2 hr post glucose load ≥ 11.1 mmol/L or both</td>
</tr>
<tr>
<td>IGT</td>
<td>Not Applicable</td>
<td>Fasting plasma glucose &lt; 7.0 mmol/L and 2 hr post glucose load ≥ 7.8 and &lt; 11.1 mmol/L</td>
</tr>
<tr>
<td>IFG</td>
<td>Fasting plasma glucose ≥ 5.6 mmol/L</td>
<td>Fasting ≥ 6.1 mmol/dl and/or (If measured) 2 hr post glucose load &lt; 7.8mmol/L</td>
</tr>
</tbody>
</table>

**2.8.3. Biochemical analyses**

Blood samples were collected and processed for further determinations at an accredited private pathology laboratory. Plasma glucose was measured by enzymatic hexokinase method using the Cobas 6000, Roche Diagnostics analyser series. Glycosylated haemoglobin (HbA1c) was assessed by turbidimetric inhibition immunoassay (Cobas 6000, Roche Diagnostics). This method is National Glycohaemoglobin Standardisation Programme (NGSP) certified according to Roche Diagnostics. High density lipoprotein cholesterol (HDL-C), triglycerides (TG) and γ-glutamyltransferase (GGT) were estimated by enzymatic colorimetric methods (Cobas 6000, Roche Diagnostics). Low density lipoprotein cholesterol (LDL-C) was calculated using Friedwald's formula (Johnson et al., 1997). Creatinine measurements were done using the standardized creatinine (Cobas 6000, Roche Diagnostics). Insulin was determined by a microparticle enzyme immunoassay (AxSYM, Abbot) and urine albumin by immunoturbidimetric assay (Cobas 6000, Roche Diagnostics). Serum cotinine was measured by chemiluminescent assay (Immulate 1000, Siemens). Kidney function was assessed through estimated glomerular filtration rate (eGFR) for which both the Cockcroft-Gault equation (Cockcroft et al., 1976) (with correction for the body surface area using the formula by Du Bois) (Bois et al., 1916), 4-variable Modification of Diet in Renal Disease (MDRD) equation (Levey et al., 1999 & Levey et al., 2006) applicable to standardised serum creatinine values and the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation (Levey et al., 2009) were used, with and
without ethnicity adjustment for all participants. Staging of kidney function was based on the National Kidney Foundation Disease Outcomes Quality Initiative (NKF-KDOQI) classification (Levey et al., 2003). An eGFR<60 mL/min was used to define CKD (or CKD stage 3 to 5). The follow-up examination was conducted in 2011 (3 years from baseline) using similar procedures.

For a detailed description of methods and equipment used in the biochemical analysis, see appendix H.

### 2.8.4 Metabolic Syndrome profile
Metabolic syndrome is a constellation of disorders which includes obesity, raised fasting blood glucose (FBG) levels, elevated serum triglycerides (TG), low high density lipoproteins (HDL) values and high blood pressure (HBP) (Thomas et al., 2005). The following criteria were used to classify MetS:

- Joint Interim statement (JIS),
- National Cholesterol Education Programe, adult treatment panel iii (NCEP ATPIII and International Diabetes Forum (IDF). The table below describes their respective criteria.

<table>
<thead>
<tr>
<th></th>
<th>NCEP ATP III 3 or more of the following</th>
<th>JIS 3 or more of the following</th>
<th>IDF 3 or more of the following</th>
</tr>
</thead>
<tbody>
<tr>
<td>WC (cm)</td>
<td>≥102 (Men) ≥88 (Women)</td>
<td>≥94 (Men) ≥80 (Women)</td>
<td>≥94 (Men) ≥80 (Women)</td>
</tr>
<tr>
<td>HDL-C (mg/dL)</td>
<td>≤40 (Men) ≤50 (Women)</td>
<td>≤40 (Men) ≤50 (Women)</td>
<td>≤40 (Men) ≤50 (Women)</td>
</tr>
<tr>
<td>TGs (mg/dL)</td>
<td>≥150</td>
<td>≥150</td>
<td>≥150</td>
</tr>
<tr>
<td>Glu (mg/dL)</td>
<td>≥110</td>
<td>≥100</td>
<td>≥100</td>
</tr>
<tr>
<td>BP (mm Hg)</td>
<td>≥130/85</td>
<td>≥130/85</td>
<td>≥130/85</td>
</tr>
</tbody>
</table>
2.8.5 Progression and risk prediction
Progression in glycaemic status was determined by comparing baseline and follow up glucose measurements. A rise in glucose measurements meant progression in glycaemic status and so elevates the risk of CVD development, while a reduction meant regression.

2.9 Labelling of samples
In order to avoid errors such as mixing up of samples, stickers bearing participants identification data except names were placed on vacutainer tubes clearly indicating the status of the blood. By so doing, fasting blood samples could easily be identified from postprandial samples. Urine samples were also clearly labelled with the participants reference code as well as their dates of birth.

2.10 Transportation of samples
After samples were appropriately labelled, they were then securely placed in specimen bags then into special cooler boxes containing ice packs. They were then transported to Metropolis private pathology laboratory for processing. The cold chain was maintained from the sample collection site to the laboratory.

2.11 Data management
All data from questionnaires and from laboratory reports was captured into a specially designed excel sheet. Each response was entered under its respective variable column. Data was routinely checked for correctness as well as proper entry. To ensure privacy and confidentiality, the database was password protected and only accessible to authorized personnel in order to avoid divulging participant information. All questionnaires were kept under lock and key in filling cabinets. Only questionnaires whose data were to be entered into the electronic database or for reference purposes were taken out of the cabinet.
2.12 Statistical analysis

After all the data was captured into a data spread sheet, it was then coded appropriately and later cleaned for any possible errors. The data was finally imported into a statistical program (STATISTICA 12, StatSoft Southern Africa, Sandton, South Africa) which was used to run the tests. Basic descriptive statistics were generated to come up various characteristics the data of which was represented as medians (25th, 75th quartile range) as well as numbers and percentages.

Non-parametric tests (Mann-Whitney U test) was used to compare the different independent variables (P-values: P^{ab} and P^{cd}), while Wilcoxon Signed Rank test (P-values: P^{ac} and P^{bd}) was used to compare related samples/variables over time. These generated probability values for different associations. The Pearson Chi square test was used to explore relationships between variables. All tests were performed at a 5% level significance, thus an association was significant if the p-value was less than 0.05 (P-value < 0.05).
CHAPTER THREE
RESULTS

3.1 Introduction
This chapter provides a summary of results for both the baseline and the 3 year follow-up Bellville-South study.

3.2 Baseline results

3.2.1 Diabetes mellitus and metabolic syndrome
A total of 956 subjects participated, comprising of 642 random subjects between the ages 35 to 65 years and 304 voluntary subjects, age range 16 to 95 years. Ten subjects were from other race groups, whilst five did not consent to blood sampling and were excluded resulting in a total of 941 participants. One hundred and twenty two (13 males and 109 females) subjects had previously diagnosed type 2 DM and these subjects were not included for the prevalence of MetS. The general characteristics of the remaining 819 subjects are presented in Table 3 and data are presented as median (25th, 75th quartile range). The BMI, waist circumference, blood glucose, total cholesterol and HDL-cholesterol were significantly higher in females, whilst blood pressure and LDL-cholesterol were significantly higher in males.
Table 4: Characteristics of 819 participants, stratified by gender

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Male (N = 182)</th>
<th>Female (N = 637)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>55.5 (43, 69)</td>
<td>52 (42, 63)</td>
<td>0.0311</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.5 (21.1, 28.8)</td>
<td>30.2 (25.6, 34.8)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Waist-C (cm)*</td>
<td>91.8 (79.3, 102)</td>
<td>97.5 (87, 107)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>WHR</td>
<td>0.92 (0.86, 0.98)</td>
<td>0.87 (0.82, 0.92)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>SBP (mm Hg)*</td>
<td>123 (114, 136)</td>
<td>118 (108, 132)</td>
<td>0.0032</td>
</tr>
<tr>
<td>DBP (mm Hg)*</td>
<td>75 (68, 84)</td>
<td>73 (66, 82)</td>
<td>0.0952</td>
</tr>
<tr>
<td>FBG (mmol/L)</td>
<td>5.2 (4.9, 5.9)</td>
<td>5.5 (5.0, 6.0)</td>
<td>0.0179</td>
</tr>
<tr>
<td>PostBG (mmol/L)</td>
<td>6.4 (5.3, 8.4)</td>
<td>6.9 (5.7, 8.9)</td>
<td>0.0135</td>
</tr>
<tr>
<td>HbA1c (mmol/mol)</td>
<td>39 (37, 44)</td>
<td>39 (36, 44)</td>
<td>0.2245</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>5.7 (5.5, 6.4)</td>
<td>5.7 (5.4, 6.2)</td>
<td>0.2245</td>
</tr>
<tr>
<td>TC (mmol/L)</td>
<td>5.36 (4.5, 6.09)</td>
<td>5.62 (4.83, 6.47)</td>
<td>0.0008</td>
</tr>
<tr>
<td>TG (mmol/L)</td>
<td>1.25 (0.89, 1.70)</td>
<td>1.22 (0.88, 1.22)</td>
<td>0.9458</td>
</tr>
<tr>
<td>HDL-C (mmol/L)</td>
<td>1.16 (0.98, 1.40)</td>
<td>1.26 (1.05, 1.47)</td>
<td>0.0044</td>
</tr>
<tr>
<td>LDL-C (mmol/L)</td>
<td>3.71 (3.07, 4.39)</td>
<td>3.35 (2.64, 4.14)</td>
<td>0.0002</td>
</tr>
<tr>
<td>Smoking %</td>
<td>54.4</td>
<td>38.5</td>
<td>0.00146</td>
</tr>
<tr>
<td>Serum cotinine (ng/mL)</td>
<td>101 (9, 314)</td>
<td>101 (9, 302)</td>
<td>0.0477</td>
</tr>
<tr>
<td>Alcohol consumption %</td>
<td>51.1</td>
<td>22.1</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

Key: * Replicated measurements; Waist-C, waist circumference; WHR, waist to hip ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure; FBG, fasting blood glucose; PostBG, post 2-hour blood glucose; TC, total cholesterol; TG, triglyceride; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol. (Data are presented as Median (interquartile range) for continuous variables and percentage for grouped data).

The prevalence of type 2 DM in the randomly selected subjects (24.0%) did not change significantly by the inclusion of the self-selected individuals, thus the results are presented for the entire study population. The crude prevalence of type 2 DM, including the previously diagnosed type 2 DM was 28.59% (age-adjusted = 33.5%, 95%CI: 30.01 – 36.92), and that of undiagnosed type 2 DM was 17.8% (age-adjusted = 12.4%, 95%CI: 9.8 – 14.8). Pre-diabetes, that is, impaired fasting glucose (IFG) was 4.03% (age adjusted = 4.0%, 95%CI: 2.4 – 5.8),
and impaired glucose tolerance (IGT) was 18.8% (age adjusted 13.6%, 95%CI: 11.0 – 16.1). Whilst pre-diabetes was present in subjects less than 40 years in both sexes, type 2 DM was absent in males in this age group. In both sexes, the type 2 DM peaked at ages 40 to 49 years, but above age 60 years, the incidence of undiagnosed type 2 DM in males was half that of females (Table 4). In multivariate models, increasing age (odds ratio (OR), 1.02; 95% confidence interval [CI], 1.02-1.05, per year increase in age), WaistC (OR, 1.02; 95% CI, 1.00-1.03), or BMI (OR, 1.04; 95% CI, 1.01-1.06), triglycerides (OR, 1.26; 95% CI, 1.04-1.53), female gender (OR, 1.68; 95% CI, 1.09-2.61), alcohol intake (OR, 1.49; 95% CI, 1.01-2.23), absence of DM family history (OR, 0.70; 95% CI, 0.5 – 0.95), and lower education (OR, 0.66; 95% CI, 0.50-0.89) were significantly associated with both DM and pre-diabetes.

Table 5: Age-specific frequency of undiagnosed type 2 diabetes mellitus according to the WHO criterion among the mixed ancestry population of South Africa.

<table>
<thead>
<tr>
<th>Age Group</th>
<th>IFG</th>
<th>IGT</th>
<th>Undiagnosed type 2 diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>16 – 29 (N = 14 M, 38F)</td>
<td>M = 0; F = 2.6</td>
<td>M = 0; F = 2.6</td>
<td>M = 0; F = 5.3</td>
</tr>
<tr>
<td>Total crude</td>
<td>1.9</td>
<td>1.9</td>
<td>3.8</td>
</tr>
<tr>
<td>Age-adjusted (95% CI)</td>
<td>1.0 (1.7 – 3.7)</td>
<td>1.0 (1.7 – 3.7)</td>
<td>2.0 (1.8 – 5.8)</td>
</tr>
<tr>
<td>30 – 39 (N = 16 M, 106F)</td>
<td>M = 6.3; F = 5.6</td>
<td>M = 12.5; F = 12.2</td>
<td>M = 0; F = 7.78</td>
</tr>
<tr>
<td>Total crude</td>
<td>5.7</td>
<td>12.3</td>
<td>6.6</td>
</tr>
<tr>
<td>Age-adjusted (95% CI)</td>
<td>6.0 (1.3 – 10.7)</td>
<td>13.0 (6.1 – 19.8)</td>
<td>7.0 (2.0 – 12.0)</td>
</tr>
<tr>
<td>40 – 49 (N = 39 M, 161F)</td>
<td>M = 5.1; F = 5.6</td>
<td>M = 12.8; F = 15.5</td>
<td>M = 20.5; F = 14.3</td>
</tr>
<tr>
<td>Total crude</td>
<td>5.5</td>
<td>15.0</td>
<td>15.5</td>
</tr>
<tr>
<td>Age-adjusted (95% CI)</td>
<td>11.0 (6.4 – 15.6)</td>
<td>30.0 (22.4 – 37.6)</td>
<td>31.0 (23.3 – 38.7)</td>
</tr>
<tr>
<td>50 – 59 (N = 42 M, 138F)</td>
<td>M = 2.4; F = 5.1</td>
<td>M = 14.3; F = 26.1</td>
<td>M = 19.1; F = 20.3</td>
</tr>
<tr>
<td>Total crude</td>
<td>4.44</td>
<td>23.3</td>
<td>20.00</td>
</tr>
<tr>
<td>Age-adjusted (95% CI)</td>
<td>8.0 (3.9 – 12.1)</td>
<td>42.0 (32.5 – 51.5)</td>
<td>36.0 (27.2 – 44.8)</td>
</tr>
<tr>
<td>60 – 69 (N = 30 M, 119F)</td>
<td>M = 0; F = 4.2</td>
<td>M = 26.7; F = 24.4</td>
<td>M = 13.3; F = 26.9</td>
</tr>
<tr>
<td>Total crude</td>
<td>3.4</td>
<td>24.8</td>
<td>24.1</td>
</tr>
<tr>
<td>Age-adjusted (95% CI)</td>
<td>5.0 (1.4 – 8.6)</td>
<td>37.0 (27.2 – 46.8)</td>
<td>36.0 (26.4 – 45.6)</td>
</tr>
<tr>
<td>≥ 70 (N = 41 M, 91F)</td>
<td>M = 4.9; F = 0</td>
<td>M = 31.7; F = 19.8</td>
<td>M = 17.1; F = 30.8</td>
</tr>
<tr>
<td>Total crude</td>
<td>1.53</td>
<td>23.7</td>
<td>26.0</td>
</tr>
<tr>
<td>Age-adjusted (95% CI)</td>
<td>2.0 (0.42 – 4.4)</td>
<td>31.0 (21.5 – 40.5)</td>
<td>34.0 (24.0 – 44.0)</td>
</tr>
<tr>
<td>Total (N= 819)</td>
<td>4.03</td>
<td>18.82</td>
<td>17.84</td>
</tr>
<tr>
<td>Age-adjusted (N = 819)</td>
<td>4.0 (2.4 – 5.8)</td>
<td>13.6 (11.0 – 16.1)</td>
<td>12.4 (9.8 – 14.8)</td>
</tr>
</tbody>
</table>

Key: M, male; F, female; IFG, impaired fasting glucose; IGT, Impaired glucose tolerance

Undiagnosed type 2 diabetes refers to subjects who were unaware of their glycaemic status. The prevalence of undiagnosed DM increased with advancing age. Data are presented as percentages and median (interquartile range). Significance level was set at P-value < 0.05.
Overall there was good agreement between the MetS criteria \((k = 0.90, 95\% \text{ CI} 0.88 - 0.92)\), between JIS and IDF \((k = 0.96; 95\%\text{CI}: 0.94 – 0.98)\), JIS and ATP III \((k = 0.89, 95\% \text{ CI}: 0.85 – 0.92)\) and IDF and ATP III \((k = 0.85, 95\% \text{ CI}: 0.82 – 0.89)\). In the 815 subjects included in the determination of MetS, the crude prevalence of MetS was higher with the JIS definition (46.5\%) compared to the IDF (44.5\%) and the NCEP ATP III (41.5\%). Irrespective of the method used, MetS was significantly more prevalent in females, \(p < 0.01\). Central obesity was the most common abnormal criterion followed by reduced HDL-cholesterol, hyperglycaemia, blood pressure and triglycerides (Table 5). MetS increased with age and 76.2\% of subjects with undiagnosed type 2 DM and 61.2\% with non-diabetic hyperglycaemia had MetS compared to 31.7\% normoglycaemic subjects using the JIS criteria (Table 6).

Table 6: Prevalence of metabolic syndrome and components of metabolic syndrome by gender.

<table>
<thead>
<tr>
<th></th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central obesity (94/80 \ (N = 815))</td>
<td>82 (45.6%)</td>
<td>554 (87.2%)</td>
<td>636 (78.0%)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Central obesity (102/88 \ (N = 815))</td>
<td>46 (25.6%)</td>
<td>460 (72.4%)</td>
<td>506 (62.1%)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Hyperglycaemia ((N = 819))</td>
<td>67 (36.8%)</td>
<td>296 (46.5%)</td>
<td>363 (44.3%)</td>
<td>0.0208</td>
</tr>
<tr>
<td>Raised SBP ((N = 815))</td>
<td>61 (33.9%)</td>
<td>185 (29.2%)</td>
<td>246 (30.3%)</td>
<td>0.2295</td>
</tr>
<tr>
<td>Raised DBP ((N = 815))</td>
<td>40 (22.2%)</td>
<td>126 (19.9%)</td>
<td>166 (20.4%)</td>
<td>0.4962</td>
</tr>
<tr>
<td>Reduced HDL-C (\text{NCEP ATP III, IDF} \ (N = 818))</td>
<td>61 (33.5%)</td>
<td>344 (54.1%)</td>
<td>405 (49.5%)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Raised TG ((N = 817))</td>
<td>45 (25.0%)</td>
<td>167 (26.2%)</td>
<td>212 (25.9%)</td>
<td>0.7423</td>
</tr>
<tr>
<td>MetS (\text{JIS} \ (N = 815))</td>
<td>66 (36.7%)</td>
<td>313 (49.3%)</td>
<td>379 (46.5%)</td>
<td>0.0027</td>
</tr>
<tr>
<td>MetS (\text{NCEP ATP III} \ (N = 815))</td>
<td>50 (27.8%)</td>
<td>291 (45.8%)</td>
<td>341 (41.8%)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>MetS (\text{IDF} \ (N = 815))</td>
<td>55 (30.6%)</td>
<td>308 (48.5%)</td>
<td>363 (44.5%)</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

Key: SBP, Systolic Blood Pressure; DBP, Diastolic Blood pressure; HDL-C, High Dense Lipoproteins; TG, Triglycerides; MetS, Metabolic syndrome; NCEP ATP III, National Cholesterol Education Program, adult treatment panel III; JIS, Joint Interim Statement; IDF, International Diabetes Forum. Data are presented as count and percentages. Significance level was set at P-value < 0.05.
Table 7: Glycaemic status and age-specific prevalence of metabolic syndrome according to the JIS definition among the mixed ancestry population of South Africa.

<table>
<thead>
<tr>
<th>Age category (years)</th>
<th>Normal</th>
<th>IFG</th>
<th>IGT</th>
<th>Undiagnosed type 2 DM</th>
</tr>
</thead>
<tbody>
<tr>
<td>16 – 29</td>
<td>11.1</td>
<td>0.00</td>
<td>0.00</td>
<td>100</td>
</tr>
<tr>
<td>30 – 39</td>
<td>21.3</td>
<td>83.3</td>
<td>30.8</td>
<td>71.4</td>
</tr>
<tr>
<td>40 – 49</td>
<td>34.4</td>
<td>36.4</td>
<td>66.7</td>
<td>77.4</td>
</tr>
<tr>
<td>50 - 69</td>
<td>38.3</td>
<td>87.5</td>
<td>76.2</td>
<td>75.0</td>
</tr>
<tr>
<td>60 – 69</td>
<td>42.3</td>
<td>100</td>
<td>59.5</td>
<td>69.4</td>
</tr>
<tr>
<td>≥ 70</td>
<td>32.8</td>
<td>100</td>
<td>43.3</td>
<td>82.9</td>
</tr>
<tr>
<td>Total</td>
<td>31.7</td>
<td>70.0</td>
<td>59.5</td>
<td>76.2</td>
</tr>
</tbody>
</table>

Key: IFG, Impaired Fasting Glucose; IGT, Impaired Glucose Tolerance. Significance level was set at P-value < 0.05.

3.3 Chronic kidney diseases

The overall prevalence of CKD was 28.7% (269) and was higher in females (31.4%) compared to 20.2% in males. Of the 269 participants with CKD, 260 (96.7%) had stage 3, eight (2.97%) had stage 4 and only 1 participant had stage 5 CKD (Table 7). The characteristics of participants with CKD (stages 3 to 5) are summarised in Table 8. Generally, the BMI, blood glucose, lipids and age were significantly raised in subjects with CKD, all P < 0.05.

Table 8: Chronic kidney disease stages according to the NKF-KDOQI, using Modification of Diet in Renal Disease Glomerular Filtration Rate estimations and CKD-EPI estimation

<table>
<thead>
<tr>
<th>CKD Stage</th>
<th>Definition (GFR estimation (ml/min/1.73 m²))</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>≥ 90, without urine dipstick abnormality</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>≥ 90, with urine dipstick abnormality*</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>60-89, with urine dipstick abnormality*</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>30-59, with or without urine dipstick abnormality*</td>
<td>260</td>
</tr>
<tr>
<td>4</td>
<td>15-29, with or without urine dipstick abnormality*</td>
<td>4</td>
</tr>
<tr>
<td>5</td>
<td>&lt; 15, with or without urine dipstick abnormality*</td>
<td>1</td>
</tr>
</tbody>
</table>

Key: CKD, Chronic Kidney Disease; GFR, Glomerular Filtration Rate; MDRD, Modification of Diet in Renal Disease. Data are presented as numbers.
Table 9: Characteristics of participants, stratified by the presence of CKD (stages 3 to 5)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>CKD yes (N = 269)</th>
<th>CKD no (N = 667)</th>
<th>P - value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>65 (58, 73)</td>
<td>49 (40, 59)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Males (223)</td>
<td>45 (16.7%)</td>
<td>178 (26.7%)</td>
<td>0.001</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>30.0 (25.7, 34.4)</td>
<td>28.9 (23.9, 33.8)</td>
<td>0.03</td>
</tr>
<tr>
<td>Waist-C (cm)*</td>
<td>98 (88, 107)</td>
<td>97 (85, 107)</td>
<td>0.079</td>
</tr>
<tr>
<td>WHR</td>
<td>0.89 (0.84, 0.94)</td>
<td>0.88 (0.83, 0.94)</td>
<td>0.36</td>
</tr>
<tr>
<td>SBP (mm Hg) *</td>
<td>126 (114, 142)</td>
<td>119 (108, 130)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>DBP (mm Hg)*</td>
<td>74 (67, 82)</td>
<td>74 (66, 82)</td>
<td>0.72</td>
</tr>
<tr>
<td>FBG (mmol/L)</td>
<td>5.9 (5.0, 7.0)</td>
<td>5.5 (5.0, 6.3)</td>
<td>0.002</td>
</tr>
<tr>
<td>PostBG (mmol/L)</td>
<td>7.5 (6.0, 9.3)</td>
<td>6.6 (5.5, 8.4)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>6.0 (5.7, 6.5)</td>
<td>5.8 (5.5, 6.3)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>TC (mmol/L)</td>
<td>5.8 (5.1, 6.7)</td>
<td>5.4 (4.6, 6.2)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>TG (mmol/L)</td>
<td>1.4 (1.1, 2.0)</td>
<td>1.2 (0.7, 1.7)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>HDL-C (mmol/L)</td>
<td>1.5 (1.0, 1.5)</td>
<td>1.4 (1.0, 1.4)</td>
<td>0.004</td>
</tr>
<tr>
<td>LDL-C (mmol/L)</td>
<td>3.8 (3.2, 4.6)</td>
<td>3.5 (2.8, 4.2)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Serum cotinine (ng/ml)</td>
<td>9 (9, 108)</td>
<td>9 (9, 318)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>GGT (IU/L)</td>
<td>26 (19, 39)</td>
<td>28 (19, 43)</td>
<td>0.26</td>
</tr>
<tr>
<td>Any diabetes (%)</td>
<td>100 (37.2)</td>
<td>168 (25.2)</td>
<td>0.0003</td>
</tr>
<tr>
<td>Self-reported diabetes, n (%)</td>
<td>48 (17.8)</td>
<td>73 (10.9)</td>
<td>0.006</td>
</tr>
</tbody>
</table>

Key: BMI, Body Mass Index; Waist-C, waist circumference; WHR, waist to hip ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure; FBG, fasting blood glucose; PostBG, post 2-hour blood glucose; HbA1c, Haemoglobin A 1c; TC, total cholesterol; TG, triglyceride; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; GGT, Gamma Glutamyl Transferase. Data are presented as median (interquartile range) for continuous variables and percentage for categorical variables.
3.3.1 Determinants of chronic kidney disease

In univariable analyses logistic regression models, increasing age (odds ratio [OR], 1.08; 95% confidence interval [CI], 1.06-1.10, per year increase in age), hypertension (OR, 2.05; 95% CI, 1.32-3.19), triglycerides (OR, 1.38; 95% CI, 1.05-1.81), and gamma GT (OR, 1.01; 95% CI, 1.00-1.03) were significantly associated with CKD, stages 3 to 5. The male gender was negatively associated with CKD, stages 3 to 5 (OR, 0.29; 95% CI, 1.02-3.40). These findings were further confirmed by a multiple linear regression analysis using MDRD as the dependent variable. An increase in MDRD was associated with decreasing age, male gender and diastolic blood (Table 9).

Table 10: Multivariable adjusted odd ratios (and 95% confidence intervals) for the determinants of CKD stage 3-5

<table>
<thead>
<tr>
<th>Variables</th>
<th>MDRD</th>
<th>MDRD corrected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (%/year)</td>
<td>1.09 (1.08-1.11)</td>
<td>1.11 (1.09-1.14)</td>
</tr>
<tr>
<td>Female gender</td>
<td>2.88 (1.92-4.38)</td>
<td>2.15 (1.18-4.14)</td>
</tr>
<tr>
<td>Cohort</td>
<td>0.27 (0.16-0.44)</td>
<td>0.50 (0.21-1.04)</td>
</tr>
<tr>
<td>Known hypertension</td>
<td>1.96 (1.35-2.90)</td>
<td>2.42 (1.28-4.94)</td>
</tr>
<tr>
<td>Triglycerides (%/mmol/L)</td>
<td>NS</td>
<td>1.33 (1.04-1.67)</td>
</tr>
<tr>
<td>Body mass index (%/kg/m^2)</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Total cholesterol (%/mmol/L)</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

CKD-EPI, Chronic Kidney Disease Collaboration Epidemiology; 4-v-MDRD, four variable Modification of Diet in Renal Disease. For CKD-EPI, TC was only significant when triglycerides (NS) was removed from the model, however triglycerides in the presence of other covariates except total cholesterol was not significant. For Cockroft-Gault: Hip was significant when replacing waist circumference in the models, not in its presence. And hypertension was significant only in the presence of body mass index in the model.
3.4 The 30-year cardiovascular disease profile

In this study, both lipid and BMI dependent equations were used and the intraclass correlation between the two equations was 0.92 with only a 6% standard error of measurement between the two equations (Figure 2). Thus, the results are presented using the lipid dependent equation. Table 10 presents the general characteristics of the 583 participants eligible for this study. Though the BMI and waist circumference of females were significantly elevated than that of males (P < 0.0001), the CVD risk was significantly higher in males, P < 0.0001. The pattern of the CVD risk factors used in the 30-year risk calculator is shown in Table 11. Generally, DM, hypertension and percent CVD risk increased with age. On the other hand smoking was more prevalent in the younger age group, 20 to 30 years, whilst overweight (BMI ≥ 25 < 30) was similar across age groups. The scatter plot in Figure 3 illustrates the effect of age on increasing CVD risk, even in those subjects younger than 20 years some had CVD risk of 20% or more.
Figure 2. Interclass correlation between BMI and Lipid dependent equation full CVD outcome. Intraclass correlation agreement = 0.920, standard error of measurement (SEM) 6.4%.
**Table 11:** General characteristics of participants stratified by gender

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Male (N = 126)</th>
<th>Female (N = 457)</th>
<th>P - value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>47 (40, 55)</td>
<td>46 (39, 53)</td>
<td>0.31</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.0 (20.8, 29.0)</td>
<td>30.3 (25.9, 35.1)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>WC (cm)*</td>
<td>90.3 (77.8, 100.8)</td>
<td>97.0 (86.5, 108)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>HP (cm)*</td>
<td>98 (91, 99)</td>
<td>112 (103, 112)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>SBP (mm Hg) *</td>
<td>121 (113, 130)</td>
<td>117 (106, 129)</td>
<td>0.0065</td>
</tr>
<tr>
<td>DBP (mm Hg)*</td>
<td>76 (70, 85)</td>
<td>74 (67, 83)</td>
<td>0.0372</td>
</tr>
<tr>
<td>FBG (mmol/L)</td>
<td>5.3 (4.7, 6.1)</td>
<td>5.4 (5.0, 6.1)</td>
<td>0.2717</td>
</tr>
<tr>
<td>PostBG (mmol/L)</td>
<td>6.0 (5.1, 7.9)</td>
<td>6.6 (5.6, 8.2)</td>
<td>0.0068</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>5.7 (5.5, 6.2)</td>
<td>5.7 (5.4, 6.2)</td>
<td>0.7793</td>
</tr>
<tr>
<td>TC (mmol/L)</td>
<td>5.2 (4.4, 5.9)</td>
<td>5.5 (4.7, 6.3)</td>
<td>0.0200</td>
</tr>
<tr>
<td>TG (mmol/L)</td>
<td>1.29 (0.91, 1.78)</td>
<td>1.19 (0.85, 1.71)</td>
<td>0.2462</td>
</tr>
<tr>
<td>HDL-C (mmol/L)</td>
<td>1.13 (0.95, 1.41)</td>
<td>1.21 (1.01, 1.44)</td>
<td>0.0300</td>
</tr>
<tr>
<td>LDL-C (mmol/L)</td>
<td>3.23 (2.54, 3.9)</td>
<td>3.56 (2.94, 4.2)</td>
<td>0.0011</td>
</tr>
<tr>
<td>Lipid Full (%)</td>
<td>41.5 (24, 66)</td>
<td>31 (16, 51)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Lipid Hard (%)</td>
<td>29.5 (15, 52)</td>
<td>17 (8, 32)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>BMI Full (%)</td>
<td>46 (27, 61)</td>
<td>32 (18, 53)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>BMI Hard (%)</td>
<td>32 (17, 55)</td>
<td>18 (9, 33)</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

**Key:** * Replicated measurements; WaistC, waist circumference; HP, hip circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; FBG, fasting blood glucose; PostBG, post 2-hour blood glucose; TC, total cholesterol; TG, triglyceride; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol. Data presented as median (interquartile range). Significance level set at P-value <0.005.
Table 12: Cardiovascular disease risk factors used in the equation in different age groups

<table>
<thead>
<tr>
<th>CVD risk factor</th>
<th>20 - 30</th>
<th>31 - 40</th>
<th>41 - 50</th>
<th>51 - 60</th>
</tr>
</thead>
<tbody>
<tr>
<td>% males</td>
<td>9.5</td>
<td>16.7</td>
<td>36.50</td>
<td>37.3</td>
</tr>
<tr>
<td><strong>BMI (kg/m(^2))</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% BMI &lt; 25</td>
<td>50</td>
<td>22.95</td>
<td>30.81</td>
<td>20.71</td>
</tr>
<tr>
<td>% BMI ≥ 25 &lt; 30</td>
<td>29.17</td>
<td>24.59</td>
<td>25.12</td>
<td>29.80</td>
</tr>
<tr>
<td>% BMI ≥ 30</td>
<td>20.83</td>
<td>52.46</td>
<td>44.08</td>
<td>49.49</td>
</tr>
<tr>
<td>SBP (mm Hg) *</td>
<td>112.7 ± 13.9</td>
<td>113.9 ± 13.7</td>
<td>119.4 ± 17.1</td>
<td>125.6 ± 17.6</td>
</tr>
<tr>
<td>TC (mmol/L) *</td>
<td>4.7 ± 1.1</td>
<td>5.1 ± 1.0</td>
<td>5.4 ± 1.1</td>
<td>6.0 ± 1.2</td>
</tr>
<tr>
<td>HDL (mmol/L) *</td>
<td>1.2 ± 0.26</td>
<td>1.2 ± 0.37</td>
<td>1.3 ± 0.35</td>
<td>1.3 ± 0.36</td>
</tr>
<tr>
<td>% smoking</td>
<td>63.27</td>
<td>49.18</td>
<td>47.42</td>
<td>44.72</td>
</tr>
<tr>
<td>TRTBP</td>
<td>10.42</td>
<td>12.30</td>
<td>25.59</td>
<td>47.45</td>
</tr>
<tr>
<td><strong>Diabetes status</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% IFG</td>
<td>2.04</td>
<td>4.96</td>
<td>5.63</td>
<td>3.52</td>
</tr>
<tr>
<td>% IGT</td>
<td>2.04</td>
<td>13.22</td>
<td>15.02</td>
<td>20.60</td>
</tr>
<tr>
<td>% undiagnosed DM</td>
<td>4.08</td>
<td>5.79</td>
<td>13.62</td>
<td>18.59</td>
</tr>
<tr>
<td>% self-reported DM</td>
<td>0</td>
<td>5.79</td>
<td>6.57</td>
<td>14.07</td>
</tr>
<tr>
<td>Lipid full (%) *</td>
<td>8.5 ± 6.9</td>
<td>19.4 ± 13.0</td>
<td>35.1 ± 17.6</td>
<td>56.6 ± 18.2</td>
</tr>
</tbody>
</table>

**Key:** * Mean ± standard deviation, TRTBP: treatment for blood pressure. Data presented as Mean, Standard deviation and percentage.
Figure 3: Cardiovascular disease risk score for men and women in relation to their age

In normoglycaemic females who were of normal weight (BMI < 25 kg/m²), the CVD risk was significantly lower (P = 0.007) than in obese females, while in hyperglycaemic states, observed differences were not significant. See Table 12.
Table 13: CVD risk stratified by BMI and glycaemic status

<table>
<thead>
<tr>
<th></th>
<th>Females</th>
<th></th>
<th>Male</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Non-diabetic</td>
<td>Diabetic</td>
<td>Non-diabetic</td>
<td>Diabetic</td>
</tr>
<tr>
<td><strong>BMI &lt; 25 (kg/m²)</strong></td>
<td>20.8 (17.7 – 23.9)</td>
<td>49.7 (33.5 – 65.9)</td>
<td>27.6 (22.4 – 32.9)</td>
<td>55.1 (42.5 – 67.7)</td>
</tr>
<tr>
<td><strong>BMI ≥ 25 &lt; 30 (kg/m²)</strong></td>
<td>24.8 (20.4 – 29.1)</td>
<td>65 (57.8 – 72.2)</td>
<td>43.5 (32.6 – 54.4)</td>
<td>72 (64.3 – 79.7)</td>
</tr>
<tr>
<td><strong>BMI ≥ 30 (kg/m²)</strong></td>
<td>31.3 (27.9 – 34.7)*</td>
<td>57.8 (52.3 – 63.3)</td>
<td>42.3 (28.3 – 56.3)</td>
<td>71.9 (60.8 – 83.0)</td>
</tr>
</tbody>
</table>

Median (interquartile range). Diabetic refers to all diabetic subjects including those diagnosed during the survey; nondiabetic excludes those with IGT or IFG. *Significant difference between nondiabetic BMI < 25 and those with BMI ≥ 30, P = 0.007

3.5 At 3-Year follow up

3.5.1 Changes in glucose tolerance status

Of the 946 participants examined during baseline visit, 210 participants took part in the baseline and follow-up examination, of whom 12 were excluded for missing data on covariates. Therefore, the final analytic sample included 198 participants, of whom 153 (72.3%) were women. The baseline glucose tolerance status of participants was distributed as follows [n (%)]: Normal 134 (67.7%), impaired glucose tolerance (IGT) only 44 (22.2%), impaired fasting glycaemia (IFG) only 8 (4.0), both IGT and IFG 12 (6.1%). Progression in glucose tolerance status at 3-year (the study outcome) was the composite of: 1) new onset DM, 2) any worsening in glucose tolerance status in participants with normal status at baseline, 3) acquisition of a dual IFG/IGT status in participants with only one of the statuses at baseline. Thirty two participants acquired a status of progressor during follow up. The characteristics of participants at baseline and follow up are summarized in Table 13 and a comparison of individuals that progressed to those with normoglycaemia in Table 14. No significant differences were observed between age and obesity indices and the progression.
### Table 14: The characteristics of participants at baseline and follow up

<table>
<thead>
<tr>
<th></th>
<th>Males (N = 45)</th>
<th>Females (N = 153)</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>3YR</td>
<td>P - value</td>
<td>Baseline</td>
</tr>
<tr>
<td>Age (Years)</td>
<td>60 (53,67)</td>
<td>63 (53,70)</td>
<td>&lt; 0.0001</td>
<td>56 (46, 62)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27.8 (23.7, 32.3)</td>
<td>27.59 (24.0, 31.7)</td>
<td>0.7355</td>
<td>32.4 (28.2, 37.1)</td>
</tr>
<tr>
<td>WaistC (cm)</td>
<td>99.3 (88, 110)</td>
<td>97.3 (88.9, 107)</td>
<td>&lt; 0.0001</td>
<td>102 (93, 110)</td>
</tr>
<tr>
<td>HP (cm)</td>
<td>103 (98, 109.5)</td>
<td>102 (94.8, 107.3)</td>
<td>&lt; 0.0001</td>
<td>115 (105, 125)</td>
</tr>
<tr>
<td>WHR (cm)</td>
<td>0.97 (0.91, 1)</td>
<td>0.95 (0.9, 1)</td>
<td>0.1276</td>
<td>0.87 (0.83, 0.92)</td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>127 (117, 139)</td>
<td>145 (125, 159)</td>
<td>&lt; 0.0001</td>
<td>121 (111, 134)</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>77 (69, 85)</td>
<td>81 (77, 93)</td>
<td>&lt; 0.0001</td>
<td>75 (67, 83)</td>
</tr>
<tr>
<td>FBG (mmol/L)</td>
<td>5.9 (5.0, 7.0)</td>
<td>5.6 (5.2, 7.4)</td>
<td>0.4094</td>
<td>6.0 (5.0, 7.7)</td>
</tr>
<tr>
<td>PostBG (mmol/L)</td>
<td>6.4 (6.0, 9.0)</td>
<td>5.6 (4.8, 8.5)</td>
<td>0.0290</td>
<td>7.4 (6.0, 9.6)</td>
</tr>
<tr>
<td>HbA1C (%)</td>
<td>6.0 (5.6, 6.8)</td>
<td>6.0 (5.7, 6.8)</td>
<td>0.6461</td>
<td>6.1 (5.7, 6.7)</td>
</tr>
<tr>
<td>FIR</td>
<td>6.8 (2.2, 10.6)</td>
<td>10.5 (6.2, 16.1)</td>
<td>&lt; 0.0001</td>
<td>9.25 (4.5, 15.0)</td>
</tr>
<tr>
<td>FBG/IR</td>
<td>1 (0.65, 2.53)</td>
<td>0.635 (0.35, 1.08)</td>
<td>&lt; 0.0001</td>
<td>0.68 (0.42, 1.58)</td>
</tr>
<tr>
<td>TC (mmol/L)</td>
<td>5.5 (4.8, 6.3)</td>
<td>5.27 (4.8, 6.1)</td>
<td>0.4630</td>
<td>5.63 (5.0, 6.56)</td>
</tr>
<tr>
<td>TG (mmol/L)</td>
<td>1.62 (1.17, 2.02)</td>
<td>1.49 (0.98, 1.99)</td>
<td>0.1589</td>
<td>1.38 (1.06, 1.87)</td>
</tr>
<tr>
<td>HDL (mmol/L)</td>
<td>1.04 (0.94, 1.18)</td>
<td>1.2 (1.02, 1.48)</td>
<td>&lt; 0.0001</td>
<td>1.18 (1.01, 1.4)</td>
</tr>
<tr>
<td>LDL (mmol/L)</td>
<td>3.51 (2.66, 4.34)</td>
<td>3.14 (2.73, 4.03)</td>
<td>0.0092</td>
<td>3.82 (3.08, 4.55)</td>
</tr>
<tr>
<td>TC/HDL (mmol/L)</td>
<td>5.32 (4.27, 5.94)</td>
<td>4.44 (3.46, 5.33)</td>
<td>&lt; 0.0001</td>
<td>4.77 (3.96, 5.67)</td>
</tr>
<tr>
<td>Serum cotinine (ng/mL)</td>
<td>9 (9, 283)</td>
<td>9 (9, 188)</td>
<td>0.1563</td>
<td>9 (9, 245)</td>
</tr>
<tr>
<td>GGT (IU/L)</td>
<td>35 (25, 48)</td>
<td>31 (24, 46)</td>
<td>0.9601</td>
<td>28 (20, 42)</td>
</tr>
<tr>
<td>Creatinine (µmol/L)</td>
<td>96 (86, 107)</td>
<td>88 (81, 105)</td>
<td>0.0026</td>
<td>78 (70, 88)</td>
</tr>
</tbody>
</table>

**Key:** BMI, Body Mass Index; Waist-C, waist circumference; WHR, waist to hip ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure; FBG, fasting blood glucose; PostBG, post 2-hour blood glucose; HbA1c, Haemoglobin 1c; FIR, Fasting Insulin Ratio; TC, total cholesterol; TG, triglyceride; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein; GGT, Gamma Glutamyl Trasferase; Data were presented as median (Interquartile range). Significance level at P-value <0.005.
Table 15: Comparison of individuals that progressed to those with normoglycaemia

<table>
<thead>
<tr>
<th></th>
<th>No progression (N = 166)</th>
<th>Progressed (N = 32)</th>
<th>P - value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>3YR</td>
<td></td>
</tr>
<tr>
<td>Age (Years)</td>
<td>55 (44, 62)</td>
<td>58 (47.65)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>29.3 (24.6, 33.4)</td>
<td>29.8 (24.7, 34.1)</td>
<td>0.1003</td>
</tr>
<tr>
<td>WC (cm)</td>
<td>97 (87, 107)</td>
<td>93.6 (81.1, 104)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>HP (cm)</td>
<td>109 (101, 116)</td>
<td>105 (97, 112)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>WHR (cm)</td>
<td>0.88 (0.84, 0.93)</td>
<td>0.88 (0.82, 0.93)</td>
<td>0.2682</td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>119 (110, 129)</td>
<td>129 (118, 150)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>74 (66, 82)</td>
<td>80 (71, 87)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>FBG (mmol/L)</td>
<td>5.0 (4.7, 5.5)</td>
<td>5.0 (4.7, 5.4)</td>
<td>0.6766</td>
</tr>
<tr>
<td>PostBg (mmol/L)</td>
<td>5.95 (5.1, 6.6)</td>
<td>5.3 (4.8, 6.0)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>HbA1C (%)</td>
<td>5.6 (5.4, 6.0)</td>
<td>5.8 (5.6, 6.1)</td>
<td>0.0001</td>
</tr>
<tr>
<td>FIR</td>
<td>7.35 (3.1, 13.1)</td>
<td>9.95 (6, 15.6)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>FBG/IR</td>
<td>0.66 (0.39, 1.62)</td>
<td>0.49 (0.32, 0.87)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>TC (mmol/L)</td>
<td>5.50 (4.89, 6.39)</td>
<td>5.50 (4.76, 6.29)</td>
<td>0.4152</td>
</tr>
<tr>
<td>TG (mmol/L)</td>
<td>1.15 (0.82, 1.52)</td>
<td>1.21 (0.85, 1.56)</td>
<td>0.3675</td>
</tr>
<tr>
<td>HDL (mmol/L)</td>
<td>1.22 (1.02, 1.49)</td>
<td>1.38 (1.17, 1.7)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>LDL (mmol/L)</td>
<td>3.58 (2.99, 4.41)</td>
<td>3.39 (2.77, 4.11)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>TC/HDL (mmol/L)</td>
<td>4.46 (3.58, 5.39)</td>
<td>3.89 (2.91, 4.78)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Serum cotinine (ng/ml)</td>
<td>9 (9, 287)</td>
<td>9 (9, 296)</td>
<td>0.9164</td>
</tr>
<tr>
<td>GGT (IU/L)</td>
<td>27 (19, 37)</td>
<td>27 (19, 43)</td>
<td>0.6933</td>
</tr>
<tr>
<td>Creatinine (µmol/L)</td>
<td>82 (72, 90)</td>
<td>70 (64, 85)</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

Key: BMI, Body Mass Index; Waist-C, waist circumference; WHR, waist to hip ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure; FBG, fasting blood
3.6 Chronic kidney disease progression
At follow-up, 320 participants were eligible for this analysis. Table 15 summarizes the cross classification of participants by eGFR categories at baseline and at 3 years. In general, 3 (10.0%) with eGFR greater than 90 ml/min/1.73m² at baseline developed CKD stage 3 or above (eGFR<60 ml/min/1.73m²) at three year follow up, whilst those with eGFR less than 30 ml/min/1.73m² at baseline remained unchanged. Consequently, the eGFR did not change in 184 (57.5%) and deteriorated in 23 (7.2%). DM (69.5%) and MetS (78.2%) (MetS) were most common in participants in whom eGFR deteriorated (Figure 4), and their systolic blood pressure, HbA1c, were significantly elevated, P = 0.005 and P < 0.001, respectively.
Table 16: Baseline characteristics by status for chronic kidney disease during follow-up

<table>
<thead>
<tr>
<th>Variables</th>
<th>No change</th>
<th>Deterioration</th>
<th>P - value</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>184</td>
<td>23</td>
<td></td>
<td>320</td>
</tr>
<tr>
<td>Sex (women)</td>
<td>129</td>
<td>20</td>
<td>&lt;0.001</td>
<td>250</td>
</tr>
<tr>
<td>Age (Years)</td>
<td>56.5 (11.7)</td>
<td>57.3 (8.6)</td>
<td>0.88</td>
<td>56.4 (11.4)</td>
</tr>
<tr>
<td>BMI (Kg/m²)</td>
<td>31.9 (7.1)</td>
<td>31.7 (5.9)</td>
<td>0.98</td>
<td>31.9 (6.8)</td>
</tr>
<tr>
<td>WC (cm)</td>
<td>102 (15)</td>
<td>103 (14)</td>
<td>0.60</td>
<td>101 (14)</td>
</tr>
<tr>
<td>Hip (cm)</td>
<td>113 (16)</td>
<td>114 (13)</td>
<td>0.98</td>
<td>113 (15)</td>
</tr>
<tr>
<td>WHR</td>
<td>0.90 (0.10)</td>
<td>0.90 (0.08)</td>
<td>0.44</td>
<td>0.90 (0.09)</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>126 (18)</td>
<td>133 (18)</td>
<td>0.005</td>
<td>125 (18)</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>77 (11)</td>
<td>75 (9)</td>
<td>0.04</td>
<td>75 (11)</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>6.6 (1.8)</td>
<td>7.9 (3.0)</td>
<td>&lt; 0.001</td>
<td>6.6 (1.7)</td>
</tr>
<tr>
<td>Glycemic status</td>
<td></td>
<td></td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>77</td>
<td>5</td>
<td></td>
<td>130</td>
</tr>
<tr>
<td>IGT/IFG</td>
<td>31</td>
<td>2</td>
<td></td>
<td>62</td>
</tr>
<tr>
<td>DM</td>
<td>76</td>
<td>16</td>
<td></td>
<td>128</td>
</tr>
<tr>
<td>MetS (Yes)</td>
<td>117</td>
<td>18</td>
<td>0.30</td>
<td>205</td>
</tr>
</tbody>
</table>

Key: BMI, Body Mass Index; Waist-C, waist circumference; WHR, waist to hip ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure; FBG, fasting blood glucose; PostBG, post 2-hour blood glucose; HbA1c, Haemoglobin 1 c; IFG, Impaired fasting Glucose; IGT, Impaired Glucose Tolerance; DM, Diabetes Mellitus. Data are presented as count and mean (SD).
Figure 4. Diabetes mellitus (69.5%) and metabolic syndrome (78.2%) were most common in participants in whom eGFR was deteriorated. Data are presented as Percentage.
In multinomial logistic regressions analysis adjusted for age and gender, systolic blood pressure (odds ratio (OR), 1.02; 95% confidence interval [CI], 1.00-1.05; p=0.01), HbA1c (1.30; 1.09-1.55; p<0.01), and increasing number of Mets components (1.60; 1.09-2.36; p=0.008) were associated with eGFR deterioration (Table 16). In further adjustment of the model systolic blood pressure (1.07; 1.03-1.11; p=0.002) and HbA1c (1.30; 1.08-1.56; p<0.001) remained the strong predictors of eGFR deterioration (Table 17).

**Table 17:** Predictors of changes in multinomial logistic regressions (age and sex adjusted)

<table>
<thead>
<tr>
<th>Variables</th>
<th>No change</th>
<th>Deterioration</th>
<th>Improvement</th>
<th>P - value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (men)</td>
<td>1</td>
<td>0.34 (0.10-1.20)</td>
<td>0.28 (0.14-0.55)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Age (Years)</td>
<td>1</td>
<td>1.01 (0.97-1.05)</td>
<td>1.00 (0.98-1.02)</td>
<td>0.86</td>
</tr>
<tr>
<td>BMI (Kg/m²)</td>
<td>1</td>
<td>0.97 (0.91-1.04)</td>
<td>0.98 (0.94-1.01)</td>
<td>0.42</td>
</tr>
<tr>
<td>WC (cm)</td>
<td>1</td>
<td>1.00 (0.97-1.03)</td>
<td>0.99 (0.97-1.01)</td>
<td>0.49</td>
</tr>
<tr>
<td>Hip (cm)</td>
<td>1</td>
<td>0.99 (0.96-1.02)</td>
<td>0.99 (0.97-1.00)</td>
<td>0.34</td>
</tr>
<tr>
<td>WHR</td>
<td>1</td>
<td>7.06 (0.06-839)</td>
<td>1.39 (0.08-23.22)</td>
<td>0.73</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>1</td>
<td>1.02 (1.00-1.05)</td>
<td>0.99 (0.97-1.00)</td>
<td>0.01</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>1</td>
<td>0.99 (0.95-1.03)</td>
<td>0.97 (0.95-1.00)</td>
<td>0.06</td>
</tr>
<tr>
<td>No of MetS components</td>
<td>1</td>
<td>1.60 (1.09-2.36)</td>
<td>0.88 (0.73-1.07)</td>
<td>0.008</td>
</tr>
<tr>
<td>Mets (No)</td>
<td>1</td>
<td>0.52 (0.18-1.47)</td>
<td>1.16 (0.70-1.91)</td>
<td>0.29</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>1</td>
<td>1.30 (1.09-1.55)</td>
<td>0.82 (0.68-0.99)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Glycemic status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>1</td>
<td>0.32 (0.11-0.93)</td>
<td>1.39 (0.80-2.43)</td>
<td></td>
</tr>
<tr>
<td>IGT/IFG</td>
<td>1</td>
<td>0.32 (0.07-1.49)</td>
<td>2.11 (1.08-4.11)</td>
<td></td>
</tr>
<tr>
<td>DM</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

Data are presented as count and median (interquartile range).
Table 18: Predictors of changes in multinomial logistic regressions (multivariable adjusted)

<table>
<thead>
<tr>
<th>Variables</th>
<th>No change</th>
<th>deterioration</th>
<th>improvement</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (men)</td>
<td>1</td>
<td>0.28 (0.07-1.06)</td>
<td>0.28 (0.14-0.57)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Age (Years)</td>
<td>1</td>
<td>0.97 (0.93-1.02)</td>
<td>1.00 (0.98-1.02)</td>
<td>0.57</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>1</td>
<td>1.07 (1.03-1.11)</td>
<td>1.00 (0.98-1.02)</td>
<td>0.002</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>1</td>
<td>0.91 (0.85-0.97)</td>
<td>0.97 (0.91-1.05)</td>
<td>0.008</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>1</td>
<td>1.30 (1.08-1.56)</td>
<td>0.83 (0.69-1.00)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Glycemic status

- Normal
  - 1
    - 0.40 (0.13-1.21)
    - 1.30 (0.73-2.30)

- IGT/IFG
  - 1
    - 0.37 (0.08-1.78)
    - 2.02 (1.03-3.97)

- DM
  - 1
    - 1
    - 1

Data are presented as count and median (interquartile range).
CHAPTER FOUR
DISCUSSION

The aim of this study was to assess the CVD risk of the mixed ancestry community of Bellville South, Cape Town, South Africa both at baseline and 3 year follow-up studies. To achieve this, we assessed the prevalence of DM, MetS, CKD and we assessed the lifetime CVD risk profile of participants at baseline. At 3-year follow up we assessed the contributors to DM and chronic kidney diseases progression.

4.1 Cardiovascular risk at baseline
4.1.1 Diabetes mellitus
In South Africa, there is a racial variation in the prevalence of DM, with the highest having been reported amongst the South African Indians followed by the mixed ancestry population (Motala, 2003). In this study, however, we demonstrate that the prevalence of DM has tremendously increased to 28.2% in the mixed ancestry community compared to 10.8% reported in 1999 by Levit and co-workers in the Mamre study. The sharp increase in the prevalence of type 2 DM between these studies may be due to the geographic location of these populations, significant differences in obesity, the economic transition of this population resulting into rapid urbanization, and the different criteria used for the diagnosis of DM. There is a variation in the cut off values for the definition of DM by the 1985 and 1998 WHO criteria. Whilst the 1985 criteria classified an individual with fasting plasma glucose values of ≥ 7.8 mmol/L as diabetic, the revised 1998 criteria cut off value was ≥ 7.0. Hence the 1998 criteria appear more strict and classifies more individuals as diabetic than the 1985 criteria which was used by Levitt (1999).

The limited studies conducted in South Africa have shown a positive rural to urban gradient in terms of the prevalence of type 2 DM, and the sample for this study was taken from an urban mixed ancestry population located approximately 50 km from the previous study (Levitt et al., 1999; Motala et al., 2003). Furthermore, our study subjects were more obese with higher waist circumferences. The mean waist circumference was 102 cm in females and 99.3 cm in males. This was slightly higher as the diabetic population reported by Levitt had a waist circumference of 96.5cm.
More worrisome, we found that more than half, that is 17.8% of those subjects with type 2 DM (28.6%) were not aware of their condition (Table 5). These findings point to the important need for efforts to assist the formulation and implementation of effective early detection, prevention and control strategies for DM in this population. Type 2 DM is usually preceded by IFG and IGT (WHO, 2003; Nichols et al., 2007) and these were found in 4.4% and 15.3% respectively, predicting a further increase in type 2 DM over the next several years. Individuals with undiagnosed type 2 DM or IGT have been shown to exhibit a high prevalence of MetS, and therefore are at a higher risk of future macrovascular complications due to the unmanaged hyperglycaemic state (Matsha et al., 2013).

4.1.2 Metabolic syndrome
To our knowledge this is the first population-based report on the prevalence of MetS in the mixed ancestry population and is the highest observed among sub-Saharan populations (Kengne et al., 2012; Motala et al., 2011) thus far. The JIS definition for the identification of subjects with MetS has been used in only one study from Africa in which a prevalence of 22.1% was reported in rural black South Africans (Motala et al., 2011). In comparison with other sub-Saharan regions that used International Diabetes Forum (IDF) or NCEP ATP III, the prevalence of MetS was much higher in our study population (Kengne et al., 2012). Irrespective of the MetS definition used, we observed MetS to be significantly more prevalent in females, a difference unquestionably due to the increased central obesity in females (Table 6). Central obesity, ≥102cm in men and ≥88cm women (102/88) was observed in 72.4% of females and 25.6% in males, and are much higher than the rates reported by the South African Demographic and Health Survey that reported 42.2% and 9.2% in females and males respectively (Puoane et al., 2002). Thus, it was the most common MetS component in females regardless of the waist circumference cut-off, whilst in males at cut-off 102/88 it was not the most important component. Contrary to our findings, the blood pressure was more common in individuals with MetS from Cameroon and Benin (Kengne et al., 2012 & Ntandou et al., 2008).
4.1.3 Thirty (30)-year Cardiovascular Risk Profile

Various mathematical equations that incorporate the major risk factors (age, sex, high blood pressure, smoking, dyslipidemia, and DM) have been developed for the assessment of CVD risk over a 10-year period in general populations (Anderson et al., 1991; D’Agostino et al., 2008). The performance of the two frequently used models, Framingham Heart Study and the UK Prospective Diabetes Study Risk Engine (UKPDS) (Coleman et al., 2007) have been evaluated in individuals with DM, hyperglycaemia and normoglycemia. The Framingham Heart Study performed better at classifying subjects with a net gain in correct classification of -14% and -12.4% for nondiabetic hyperglycaemia and normoglycaemia respectively (Simmons et al., 2009). However, the 10-year timeframe of these models has been criticised because an individual’s lifetime risk may be high whilst the 10-year risk prediction may be low, therefore delaying efforts to modify that risk. Recently, an algorithm that allows for 30-year risk assessment for individuals with any combination of risk factors has been developed (Pencina et al., 2009) and we have used this algorithm in this study.

The 10-year risk estimates have been criticised because they underestimate the risks, allowing for continued progression of subclinical atherosclerosis. Indeed this is evident in the present study in which we present evidence of a high risk score (> 20%) in young individuals and in those subjects with normoglycaemia. It is well documented that individuals with type 2 DM have increased CVD risk compared to those without DM. The 30-year risk among subjects with DM has been shown to proportionally increase with BMI (Pencina et al., 2009 & Fox et al., 2008). In the Framingham cohort the lifetime risk in obese diabetic subjects was 78.8% and 86.9% in women and men respectively (Fox et al., 2008). Similarly, in the present study the CVD risk was significantly high in subjects with DM, but no significant differences were observed between obese and normal weight diabetics. While significant differences were observed between the estimated CVD risk in non-diabetic (excluding IFG and IGT) normal weight and obese subjects, particularly in females, high risk scores were still evident in the normal weight normoglycaemic individuals. This has important public health implications as CVD is often underestimated in the young. Overall, the data confirm that irrespective of glycaemic or weight status, an evidence based tool is crucial for the identification of high risk subjects.
4.1.4 Chronic kidney diseases
The present study investigated the prevalence of CKD using the MDRD equation. The crude prevalence of CKD stages 3-5 was 26.7% whilst the age-standardized prevalence was 3.9% and 13.0% respectively for the MDRD with and without ethnicity correction (Table 8). Our data also shows that the risk factors for CKD, sex, age and hypertension are similar to those found in developed countries (Eastwood et al., 2010). Based on the South African Renal Society CKD guidelines that omit the correction factor except for black Africans, the prevalence of CKD stages greater than 3 is the highest reported in Africa thus far (Eastwood et al., 2010; Sumaili et al., 2009). To our knowledge, there exist only two detailed reports on the prevalence of CKD in populations from Sub-Saharan Africa (Eastwood et al., 2010; Sumaili et al., 2009). Both studies reported prevalence’s much lower than obtained in this study. Progression of CKD to ESRD is reported to be at a slower rate in women (Xu et al., 2010), but we found a higher CKD prevalence in females than in males similar to other epidemiological CKD screening studies (Zhang et al., 2008; Tohidi et al., 2012) though some studies have reported higher rates in men (Sumaili et al., 2009). Gender-specific differences in glomerular structure, hemodynamic condition and the effect of sex hormones on kidney cells are some of the factors believed to contribute to gender differences (Xu et al., 2010; Kang et al., 2004).

In our population the presence of hypertension doubled the risk of prevalent CKD. Hypertension affects approximately 25% of the adult population and is a cause of CKD in 21% of patients on renal replacement therapy in the South African Registry (National Kidney Foundation, 2010). CKD is also a major contributor of secondary dyslipidaemia and is characterized by specific abnormalities involving all the lipoprotein classes, with variations depending on the degree of renal impairment, etiology of primary renal disease and the method of dialysis (Tsimihodimos et al., 2011). However, in this study, triglycerides were only associated with CKD based on ethnicity corrected MDRD equation, and only in the absence of other covariates in logistic regression models.
4.1.5 Cardiovascular diseases at 3 year follow-up

4.1.5.1 Diabetes mellitus

The natural history of DM is subtle and is preceded by impaired glucose metabolism in a pre-diabetic state, with MetS and obesity, before proceeding to overt DM. The significance of the pre-diabetic phase is that an individual could either regress to normal glycaemia or progress to overt DM depending on whether the individual is involved in any form of lifestyle intervention or not (Chou et al., 1998). In subject with normal glucose tolerance (NGT) components of MetS have been reported to precede the detection of overt DM by as much as 5 years, and the risk of progression is highest amongst those with more than 1 component of the syndrome (Matsha et al., 2012).

Published data including that from the Finnish Diabetes Prevention study have shown that progression to DM can be halted with interventions targeted against obesity and glycaemia (Lindstrom et al., 2003; Alberti, et al., 2007). Because of the lack of data documenting predictors for progression to DM in South Africa, implementation of interventions is restricted. Available data from South African Indians that were followed up for 10 years, the predictors of DM were higher baseline blood glucose levels and obesity (Motala et al., 2003).

In this study we found that HbA1c and components of the MetS (central obesity, hypertension, hyperglycaemia, low HDL and increased triglycerides) are strong predictors of a worsening in glucose tolerance status in the mixed ancestry population (Table 15). However, obesity, a well-known determinant of DM occurrence was not associated with progression on our study sample.

HbA1c, which is formed by the attachment of glucose to various amino groups of haemoglobin, is widely used in DM care as a reliable marker of long term glycaemic control. The results from the present study have identified HbA1c as a strong predictor of DM progression. This is not surprising because recent prospective studies have shown that HbA1c is associated with CVD and mortality (Olofsson et al., 2010). This association has recently been extended to non-diabetic subjects, as the relationship of CVD with glycaemia is believed to be a continuum without a threshold effect (Selvin et al., 2010). The CURES study from India found that the prevalence of all CVD risk factors increased with increasing quartiles of HbA1c, and the difference reached statistical significance in the 3rd and 4th quartiles (Dilley et al., 2007). In our study the median
baseline HbA1c of progressors (6.0%) is similar to that reported by Selvin et al (2010) in a community-based population of non-diabetic adults from the United States. In contrast, Leite et al, (2009) reported a lower level of 5.8% being associated with a higher risk for progression to either IGT or type 2 DM. Our results provide further evidence that HbA1c may be used for the detection of those at an increased risk for new onset type 2 DM. It also has several advantages (Reviewed in Saudek, 2008) over MetS which requires measurement of its five components. However, the use of HbA1c has its limitations which include the overlap in its distribution in the categories of glucose tolerance status.

The WHO recommends use of questionnaires that address age, family history of DM, ethnic origin, simple activity, and diet questions, combined with simple measurements of obesity (BMI, WaistC) and blood pressure for DM screening (WHO, 2003). In the present study, markers of obesity were not associated with risk of progression (Table 15). Similar findings have been reported in other populations such as South African Indians (Motala, 2003), Pima and Nauru Indian population (Saad, 1988), where small or non-significant associations were found between BMI and progression from IGT to type 2 DM. Nevertheless, there’s a belief that obesity is strongly associated with the development of DM, but the presence of high overweight/obesity rates in this population have limited the statistical analysis to demonstrate this association. For example, the BMI of non-progressors was similar to that of progressors at baseline, but remained stable in non-progressors during follow-up. Several lifestyle interventions have consistently shown weight loss to be dominantly associated with reduction in the risk of type 2 DM (Tuomilehto, 2001). For example, a 5 kg weight loss over approximately 3 years of follow-up reduced the risk of DM by 55% (Tuomilehto, 2001), further buttressing the strong relationship between obesity and type 2 DM. Weight loss is also associated with the improvement of nonalcoholic fatty liver diseases (NAFLD) (Riley et al., 2008) a condition characterized by accumulation of liver fat greater than 5% per liver weight in the absence or minimal consumption of alcohol. Nonalcoholic fatty liver diseases are associated with insulin resistance and MetS, and frequently co-exist with DM due to their similar pathogenesis, obesity and insulin resistance.
This is the first study in a mixed ancestry population of South Africa and Africa in general providing detailed analysis of risk factors associated with CKD progression. These findings are of great importance because of the increasing prevalences of DM and hypertension in Africa (Erasmus et al., 2012). In this report we have shown that the prevalence of DM (28.5%) in the mixed ancestry (coloured) population has more than doubled just within a decade. Moreover, about 2/3rd of those with the disease (17.8%) are not aware of their condition, and are therefore not receiving interventions with proven benefits on the adverse health consequences of DM. Several studies have demonstrated that CKD is independently associated with an increased risk of CVD (Lainscak, 2009; Schiffrin et al., 2007). The results from the present study have identified HbA1c as a strong predictor of CKD progression. Also shown is an association between increasing number of MetS and CKD progression (Table 16).

Elevated values of HbA1c at baseline have been associated with an increased risk of CKD even in the absence of DM, whereby HbA1c was shown to be a better predictor compared with fasting glucose (Selvin, 2010). However, there is a conflicting report as to the nature of the relationship, as one study reported no statistically significant association between HbA1c and CKD progression in non-diabetic adults (Schöttker, 2013). In a cohort of 3082 German adults with eight year follow-up, HbA1c was associated with reduced kidney function only in subjects with manifest DM (Schöttker, 2013). Our study does not allow distinction between diabetic and non-diabetic HbA1c/CKD progression association as our analyses included both groups. HbA1c, which is formed by the attachment of glucose to various amino groups of haemoglobin, is widely used in DM care as a reliable marker of long term glycaemic control. In our study, DM was present in 69.5% of individuals with progressive CKD inferring an indirect association between poor glycaemic control and eGFR deterioration (Figure 4).

This study also showed an association between increasing number of MetS, systolic blood pressure and CKD progression (Table 16). Similar findings have been reported in the Atherosclerosis Risk in Communities Study where after adjustment for the subsequent development of DM and hypertension during the 9-year follow-up period, the odds ratio for incident CKD in the participants with MetS was 1.24 (Kurella, 2005). The kidney is involved in the initiation and maintenance of hypertension and in patients with
ESRD, hypertension develops as a result of the fundamental renal disorder (Hostetter, 2002). On the other hand, hypertension is the second most cause of ESRD (Foley & Collins, 2007; Lipworth et al., 2012), consequently, several prevention strategies are targeted towards the reduction of blood pressure to delay the need for dialysis both among diabetic and non-diabetic CKD patients (Kshirsagar, 2000). Other strategies include the modification of lifestyle factors as progression to hypertension is also influenced by modifiable risk factors such physical inactivity, smoking history and body mass index (National Kidney Foundation, 2010). Although a dialysis programme is well established in South Africa, in government funded health care centres more that 50% of potentially eligible participants are turned down for dialysis (Moosa, 2006). Therefore, CKD prevention strategies are of paramount importance and this can be achieved by targeting modifiable risk factors associated with both MetS and hypertension.
CHAPTER 5
CONCLUSION

The aim of this study was to determine the CVD risk profile of the mixed ancestry population in Bellville South Community at Baseline and 3 years follow-up. The aging of populations, globalization, and rapid urbanization are changing disease patterns around the world (Pocook et al., 2001). This has resulted into an epidemiological transition from infectious disease to a high chronic disease burden in many developing countries (Jayawardena et al., 2012). CVD has been noted as the leading cause of death worldwide and believed to account for nearly 30% of all deaths (WHO, 2010). The increased prevalence of CVD risk factors including DM, unhealthy dietary habits contributing to the obesity epidemic, reduced physical activity, increasing blood lipids, and hypertension all reveal significant global changes in behaviour and lifestyle.

This study revealed a high prevalence of CVD risk factors in the mixed ancestry population of Bellville community. The study analysed some of the known traditional CVD risk factors which include DM, obesity, blood lipids, Age and hypertension in a prospective study with a follow-up period of three years. These risk factors were assessed at baseline, and then compared with 3 three year follow-up for any possible improvement or worsening. The prevalence of DM reported by Erasmus et al., (2012) from this community is worryingly high, having increased from 10.8% just over a decade ago (Levitt et al, 1999) to 28.2%. This is in keeping with a previous predicted global rise in the prevalence of DM. In this multi-racial ethnic population of South Africa, DM is most prevalent amongst South Africans of Indian descent. This is followed by the mixed ancestry population. At three year follow-up, some participants were observed to have progressed in glycaemic status, indicating a worsening in CVD risk. Presence of multiple components of MetS was strongly associated with worsening of glycaemic status, a condition which has been closely associated with development of CVD.
Hypertension is globally referred to as a silent killer, yet also a very common CVD risk factor. Evidence shows that a majority of hypertensive individuals develop stroke during their lifetime. Our results reveal that hypertension was prevalent amongst this population, hence increasing the CVD risk even more. Several studies have previously linked MetS to risk of development of DM and subsequently CVD. Our results show a high prevalence of the components of MetS both at baseline and at 3 year follow-up, which shows a heightened risk of CVD. There is overwhelming evidence about the increasing prevalence of CVD risk factors amongst populations of developing nations reportedly as a result of urbanization and increasing lack of physical activity. Our study adds on this growing evidence regarding the global rise in the CVD risk and particularly amongst the mixed ancestry population. Furthermore, the study provides evidence of CKD status amongst the mixed ancestry population. It is notable that the increasing incidence of CKD is probably due to the high prevalence of DM and hypertension amongst the population.
CHAPTER 6
LIMITATIONS

This study provides valuable information regarding the prevalence and distribution of the CVD risk factors amongst the mixed ancestry population resident in Bellville South. However, the study is not without some limitations.

The three year follow-up study was faced with a low response rate, as many individuals who had taken part in the baseline study declined to consent to participation. This resulted in a low response rate. Furthermore, there was skewed gender participation as more female participants turned up compared to the males.

Most of the participants in this study were middle aged and above. The younger eligible participants did not consent to take part in the study. This resulted into a skewed age distribution of the study population.

Tobacco smoking is a known CVD risk factor. Unfortunately, adequate data on its consumption was lacking to provide its role in the CVD risk.

Although a number of deaths were reported within the community during the three year follow-up period, we were unable to obtain data on cause of death. This would have strengthened the study even more, as associations between the CVD risk factors and CVD mortality/morbidity would have been made.
CHAPTER 7
RECOMMENDATIONS

As mentioned earlier, impaired glucose metabolism is a critical stage in the natural history of DM. Any form of lifestyle intervention measures can result into improvement in glycaemic status as evidenced by the Diabetes Prevention Program. With the current global obesity epidemic, which has been established to be the driving force of many cardio-metabolic diseases, efforts by many governments have been directed to its prevention. Our study shows that even without noted supervised intervening efforts, there was an observed change in glycaemic status amongst individuals with impaired glycaemia. It is therefore worth instituting a lifestyle change programme aimed at preventing DM. This will subsequently reduce obesity and in a long run prevent CVD. The following strategies are suggested to implement community based lifestyle change programmes in attempt to prevent DM and CVD.

1. Health/Medical Education institutions, through the Department of Health and in collaboration with various community stakeholders, need to initiate programs directed towards healthy lifestyle with the objective of preventing chronic diseases of lifestyle.

2. Authorities need to establish or make use of existing community based health teams to identify those at risk of developing DM and encourage them to adopt lifestyle intervention programs as well as seeking routine check-up for early detection and management.

3. Every opportunity ought to be taken to give health education talks which encourage the population about the benefits of physical exercises, weight reduction and control as well as consumption of healthy diets with emphasis on prevention of chronic diseases such as DM and CVD.

4. Establish simple but effective lifestyle change strategies such as forming physical exercise clubs of whom all community members are eligible to join. The forms of exercises can be designed to suite their economic circumstances as well as work schedule. Exercises can be conducted either at a central designated physical
fitness venue such as a gym, or at individual homes. These clubs in turn emphasize a minimum amount of exercises per day.

5. Encouraging consumption of healthy home prepared foods as much as possible and minimizing take away foods. This can be achieved with the help of a dietician who may advise the community about available and cost effective healthy foods.

6. Promoting and encouraging low salt consumption at household level. Campaigns at community and legislative levels need to be directed at encouraging food and meat processors to reduce sodium addition in packaged foods.

7. Community based outcome evaluations may be conducted on an agreed routine by health research teams, Community Health Centres, as well as other community based health organizations with a view of determining progress.

8. Involvement of community members in the planning and implementation of these programs is vital as it creates a sense of ownership and increases chances of sustainability.

9. Strengthening the Primary Health Care system through which integrated programs including primary prevention of chronic diseases are implemented. This should be done with a view of early detection and management at the different levels of health care. By so doing chronic diseases can be detected before they progress to cause irreversible complications.

10. Encourage education managers at various levels to adopt and implement these measures within their institutions. Special groups especially the overweight learners need to particularly be encouraged to participate in physical exercises as well as consumption of healthy foods.
CHAPTER EIGHT
REFERRENCES


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APPENDICES

APPENDIX A

ETHICS APPROVAL LETTER

12 October 2010
CPUT/HW-REC 2010/H013

P.O. Box 1906 • Bellville 7535 South Africa • Tel: +27 21 442 6162 • Fax +27 21 447 2963
Symphony Road Bellville 7535

OFFICE OF THE CHAIRPERSON:
HEALTH AND WELLNESS SCIENCES RESEARCH ETHICS COMMITTEE (HW-REC)
Registration Number NHREC: REC- 230408-014

At the meeting of the Health and Wellness Sciences-REC on 4 October 2010 approval was granted to
David Jonah Soita, pending amendments that have now been received and reviewed. This
approval is for research activities related to a DTech: Biomedical Technology at this
Institution.

TITLE:

Development of a non laboratory dependent cardiovascular disease risk prediction model.

INTERNAL SUPERVISOR: Prof T Matsha

Comment:

Research activities are restricted to those detailed in the revised proposal and application submitted in
September 2010.

Approval will not extend beyond 12 October 2011. An extension must be applied for should data
collection for this study continue beyond this date.

Prof PENEOPE ENGEL-HILLS
CHAIR: HEALTH AND WELLNESS SCIENCES RESEARCH ETHICS COMMITTEE
e-mail: engelhills@cpnt.ac.za

- 100 -
APPENDIX B

APPLICATION FOR CHANGE OF TOPIC

HDC 1.10: Application for change of title

Student's surname: Soita
Student no.: 206155654
First names: David Jonah
Postal address: 58 Villa Bianco, Brackenfell, Cape Town, South Africa.
Phone: 0219696015
Cell phone: 0789677308
E-mail: soitadavidjonah@yahoo.com
Gender: M
Ethnic group*: Black
Nationality: Ugandan
Status (full-time):
Indicate whether a 50% dissertation or 100% thesis: 50% dissertation 100% thesis X
Faculty: Health and Wellness Sciences
Department: Biomedical Sciences
Degree: DTech: Biomedical Technology
Supervisor: Professor Tandi Matsha
Position: Professor
Qualifications: PhD

Signed: (Student) [signature]
Date: 14/03/2013

Signed: (Supervisor) [signature]
Date: 14/05/2013

Faculty approval: [signature]
Date of minutes in which recorded: 13/06/2012

Signed: (HOD) [signature]
Date: 14/05/2013

Signed: (Dean/Chair of Faculty Research Committee) [signature]
Date: 25/06/2013
APPENDIX C

LETTER OF INVITATION TO PARTICIPATE

Cape Peninsula
University of Technology
Faculty of Health and Wellness Sciences
Bellville South Cardiovascular disease study

From: Department of Chemical Pathology, Faculty of Health Sciences, University of Stellenbosch, Tygerberg Hospital, P.O.Box 19113, Tygerberg, 7505
Division of Chemical Pathology, Tygerberg Hospital, South Africa.
Telephone number: +27 21 938 4107

And Cape Peninsula University of Technology, Department of Health Sciences, P.O. Box 1906, Bellville, 7535, Cape Town
Telephone number: +27 21 959 6274
Fax +27 21 959 6015

RE; INVITATION TO PARTICIPATE IN A RESEARCH SURVEY

The supervising team of the cardiovascular disease study from the Cape Peninsula University of Technology and University of Stellenbosch do hereby invite you to participate in a Research Survey that will take place in Bellville South. The study targets individuals who were newly diagnosed with the different forms of diabetes.
You will be expected to come to………………………………………on ……………at…………which is the selected venue for participation.
You are requested to keep time and also observe the participation instructions as indicated on the consent form which you will be given later on.

Yours truly
HOD
Invitation to participate in the study
We would like to invite members of the Bellville-South community who participated in a previous research project which determined the prevalence of diabetes to take part in this study. This phase of research is investigating cardiovascular disease (heart diseases) in Bellville South. The study will be conducted by Cape Peninsula University of Technology in conjunction with the University of Stellenbosch.

What is the study about?
The incidence of cardiovascular diseases is increasingly common in our communities. Some of the underlying risk factors for developing cardiovascular disease are hypertension (high blood pressure), diabetes, high cholesterol as well as being overweight. Following the previous research conducted by the Cape Peninsula University of Technology and University of Stellenbosch on diabetes in this community, these factors were found to be highly prevalent. Often people are not aware that they have some of these risk factors. The purpose of this research project is to provide an opportunity for early detection of people that have cardiovascular diseases or are at risk. Cardiovascular diseases are diseases that affect the function of the heart and the blood vessels. Usually before one gets a heart attack, he/she develops signs and symptoms suggesting that in future you might get a heart attack.
Benefits of Participating in this Study

As one grows older, the chances of developing heart diseases also increase. Since you are aged 20 years or older, it would be to your benefit to have your heart examined since you would be informed of the outcome. You would also be advised by professionals on lifestyle changes that would delay the onset and/or prevention of heart disease. For those who will be found to have heart diseases, they will be referred for further examination and follow-up.

What will I need to do?

Should you be selected and agree to take part in the project:

- You will be asked to go to a central data collection site at……………………. (between 7 – 9 am) of any day of the week (Monday-Friday) whichever day is convenient to you.

- At the data collection site, you will be asked questions regarding your general household information, family health history and those related to your heart health. This will take approximately ½ an hour to complete.

- A nursing sister will then take your blood pressure, weight, height, and also measure the amount of fat in your body.

- Radiologists will then check and evaluate your heart health using a special machine for which you will be informed of the outcome. This procedure will be performed in privacy and will require you to expose your chest.

Participation in this study will be voluntary and cost free, except for your time. All information will be confidential. Selection into the study will be on the basis that one participated in the diabetes survey and is also resident in Bellville South. If you don't meet the selection criteria, but would also wish to have your heart health status determined, that can be arranged with the research staff.
Do you have any questions?
If you need more information regarding the project, please feel free to contact the following people during office hours:

1. Prof. Tandi Matsha       Tel. 0219596366
2. Mrs. B. George          Cell Phone 0729581877
3. Mr. M.S Hassan          Tel. 021 9596274
4. Prof. R.T, Erasmus      Tel. 021 938 4107
5. Mr J.D. Soita           Cell Phone 0610070309
APPENDIX E

CONSENT FORM

THE BELLVILLE, SOUTH AFRICA CARDIOVASCULAR STUDY CONSENT FORM

Principal Investigators: Soita David Jonah

Co-investigators: Mr. Shafick Hassan (CPUT)
Prof. RT. Erasmus (University of Stellenbosch)
Prof. Tandi Matsha (CPUT)

Address: Faculty of Health and Wellness Sciences, Cape Peninsula University of Technology (CPUT), Bellville Campus
Symphony Way, 7535

Chemical Pathology Department, Faculty of Health Sciences, University of Stellenbosch (Tygerberg Campus), Tygerberg, 7505.

Contact Numbers: Mr DJ Soita – 078 967 7308
Mr MS. Hassan – 021 959 6274
Prof. RT. Erasmus – 021 938 4107
Prof. T. Matsha – 021 460 3209

Dear Participant,

You are invited to take part in a research project. Please take some time to read the information presented here, which will explain the details of this project. Please ask the study staff or doctor any questions about any part of this project that you do not fully understand. It is very important that you are fully satisfied and that you clearly understand what this research entails and how you could be involved. Also, your participation is entirely voluntary and you are free to decline to participate. If you say no, this will not affect you negatively in any way whatsoever. You are also free to withdraw from the study at any point, even if you do initially agree to take part.

This study has been approved by the Health and Wellness Sciences Research Ethics Committee at the Cape University of Technology and will be conducted according to the ethical guidelines and principles of the international Declaration of Helsinki, South African Guidelines for Good Clinical Practice and the Medical Research Council (MRC) Ethical Guidelines for Research.

What is this research study all about?

Worldwide new causes of certain diseases or conditions are continuously being discovered by research on the cells and molecules of the body. For research to be carried out on certain diseases it is necessary to first establish the incidence and prevalence of the disease. This project aims to determine the incidence, prevalence as well as factors which are predictive of cardiovascular disease. When a large group of
patients with similar diseases has been collected, meaningful research into the disease processes may become possible.

**Why have you been invited to participate?**

The prevalence of cardiovascular disease in South Africa is not well documented and few studies have been conducted since 1994. Many subjects with cardiovascular disease are unknown to the health service, often because they are not yet diagnosed. In order to assess the magnitude of the problem, you have been approached to participate in this project to determine the incidence of cardiovascular disease amongst our adult population.

You have been selected since you previously participated in a diabetes study and that you were aged between 35-65 years at the time. You also meet other criteria used to select participants into this study.

**What will your responsibilities be?**

The participant will be requested to provide information about his/her medical history with specific emphasis on cardiovascular disease. You will also be asked to complete a questionnaire which will take no longer than 10 minutes. A painless procedure known as electrocardiography (ECG) will then be performed to check the health of your heart. No pharmaceutical agents (medication) will be tested in the study.

**Will you benefit from taking part in this research?**

You will be notified of your cardiovascular status by the medical nurse or doctor. Thereafter, you will be referred to your local health centre or general practitioner for further investigations and treatment if necessary.

In the unlikely event that the research may lead to the development of commercial applications, the participant or the participant’s heirs will not receive any compensation, but profits will be reinvested into supporting the cause of further research which may bring benefits to me/the participant’s family and to the community, such as health screening, medical treatment, educational promotions, etc.

**Are there any risks involved in my taking part in this research?**

There are no risks involved when you take part in this study since it will not involve any invasive procedure.

**Who will have access to your medical records?**

The participant’s identity will be kept confidential throughout. Information will not be associated with the participant’s name. The research staff will use only a coded number, access will be limited to authorized scientists and any scientific publications, lectures or reports resulting from the study will not identify me/*the participant.
Some insurance companies may mistakenly assume that taking part in research indicates a higher risk for disease. Thus no information about you or your family will be shared with such companies.

**Will you or your child be paid to take part in this study and are there any costs involved?**

You will not be paid to take part in the study, but your transport, if required will be covered for each study visit. There will be no costs involved for you if you take part in the project.

**Is there anything else that you should know or do?**

You should inform your family practitioner or usual doctor that you are taking part in a research study.

You can contact Prof Erasmus at Tel 938 4107 or rte@sun.ac.za if you have any further queries or encounter any problems.

You can also contact the chairperson of Health and Wellness Sciences Research Ethics Committee of the Cape University of Technology at 021 442 6162 or engelhillssp@cput.ac.za if you have any concerns or complaints that have not been adequately addressed by the research staff.

You will receive a copy of this information and consent form for your own records if it is requested.

**DECLARATION BY PARTICIPANT:**

I declare that:

I have read or had read to me this information and consent form and that it is written in a language with which I am fluent and comfortable.

I have had a chance to ask questions and all my questions have been adequately answered.

I understand that taking part in this study is voluntary and I have not been pressurized to take part.

I may choose to withdraw from the study at any time and will not be penalized or prejudiced in any way.

I may be asked to leave the study before it has finished if the study doctor or researcher feels it is in my best interests, or if I do not follow the study plan as agreed to.

I also consent that my information may be:

- Used and kept for future research studies [ ]
- Used and discarded [ ]

Signed at (place) ............................................. on (date) .......................... 20

Signature of participant------------------------------- Signature of witness-------------------
DECLARATION BY THE INVESTIGATOR

I (name)……………………………………………………… declare that:

I explained the information in this document to (Names of Participant)…………………………………………………………………………

I encouraged him/her to ask questions and took adequate time to answer them.
I am satisfied that he/she adequately understands all aspects of the research, as discussed above

Signed at (place) ........................................... on (date) .............................. 2010.

Signature of investigator----------------------- Signature of witness----------------------
APPENDIX F

QUESTIONNAIRE

THE MODIFIED ROSE ANGINA QUESTIONNAIRE
FOR IDENTIFICATION OF CARDIOVASCULAR DISEASE IN BELLVILLE SOUTH

Principal Investigator: Soita David Jonah
Name of Interviewer: …………………………….
Date of Interview: ……./……./…….   Previous ref No …….

To the respondent:
Thank you very much for your willingness to participate in the completion of this questionnaire. The information obtained in this questionnaire will provide us with information on all the possible health, family, lifestyle and dietary risk factors within your household that might influence the development of cardiovascular disease. The questionnaire should not take long and we hope you find it interesting and enjoyable. All answers provided will be treated as confidential and anonymous.

Note
No special knowledge is needed to complete this questionnaire. Please feel free to ask for clarification if needed.

Postal Address: -----------------------------
 -----------------------------
 -----------------------------

Residential address: -----------------------------
 -----------------------------
 -----------------------------

Telephone or cell phone contact: -----------------------------
Section A. PERSONAL DATA

Instructions:
Please complete the following general information about yourself by ticking in the appropriate box. Please take your time and read through questions carefully.

1. What is your date of birth? 

2. What is your gender?
   Male □ Female □

3. What is your marital status?
   Married □ Single □ Widowed □
   Divorced □ Other □

4. How would you describe yourself?
   Black □ White □
   Coloured □ Asian □

5. What is the highest level of education you have completed?
   (a) Primary School or less □
   (b) High School (Not Completed) □
   (c) High School graduate □
   (d) College Or TechnicalCollege (Not Completed) □
   (e) College or TechnicalCollege Graduate □
   (f) University or Technikon (Not Completed) □
   (g) University or Technikon graduate □

6. What is your profession/occupation?
   Please state........................................................................................................

7. How long have you been living in Bellville South?
   Less than 6 months □ Less than 1 year □
   1-5 years □ 5 years and above □
Section B. FAMILY HEALTH HISTORY

Instructions:

The following questions will tell us about your family health history. Please complete all the questions by placing a tick in the appropriate box or writing the answer.

8. Are you currently on any medication?  Yes ☐  No ☐

9. If Yes, Please list…………………………………………………………………………………………
…………………………………………………………………………………………
…………………………………………………………………………………………
…………………………………………………………………………………………

10. Have you ever been told that you have diabetes?  
Yes ☐  No ☐

11. Have you ever been treated for high blood pressure?  
☐ ☐

12. Did either of your natural parents ever die of a heart attack?  
(a) Before the age of 60?  
Yes ☐  No ☐
(b) After the age of 60?  
Yes ☐  No ☐

Section C. Pain on effort

13. Have you ever had any pain or discomfort in your chest?  
Yes ☐  No ☐

14. If the answer in question 13 was no, have you ever had any pressure or a feeling of heaviness in your chest?  
Yes ☐  No ☐

(If no proceed to section D. If yes continue with next questions in section)
15. Do you get the chest pain when you walk uphill or hurry?
- Yes [ ]
- No [ ]

16. Do you get the chest pain when you walk at an ordinary pace on a flat level?
- Yes [ ]
- No [ ]

17. What do you do when you get the chest pain while you are walking?
- Stop [ ]
- Slow down [ ]
- Carry on [ ]

*(Please indicate if participant carries on after taking Nitroglycerin trinitrate)*

18. What happens to the chest pain when you stand still?
- I feel relieved [ ]
- I do not feel any relief [ ]

19. If there is relief, how soon is it?
- Ten (10) minutes or less [ ]
- More than Ten (10) minutes [ ]
20. Will you show me where the pain was on this picture?
   (a) Breast bone (upper)  Yes ☐  No ☐
   (b) Breast bone (middle)  Yes ☐  No ☐
   (c) Breast bone (lower)  Yes ☐  No ☐
   (d) Left front chest  Yes ☐  No ☐
   (e) Left arm  Yes ☐  No ☐
   Other  Yes ☐  No ☐

21. Did you feel the pain anywhere else? Please indicate on diagram………………..

22. Have you ever had this chest pain or discomfort more than once?  Yes ☐  No ☐

23. Does any other kind of exertion bring it on?  Yes ☐  No ☐

24. Do any of these things tend to bring it on?
   (a) Excitement  Yes ☐  No ☐
   (b) Emotion  Yes ☐  No ☐
   (c) Stooping  Yes ☐  No ☐
   (d) Eating  Yes ☐  No ☐
<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>(e) Breathing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(f) Cold wind</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(g) Coughing</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

25. Does the chest pain get worse if you have a chest cold or bad cough?  
   - Yes  
   - No  

26. Would you describe it as a pain or discomfort?  
   - Pain  
   - Discomfort

27. Would any of these words describe the chest pain sensation?  
   (a) Heaviness  
   - Yes  
   - No  
   (b) Burning  
   - Yes  
   - No  
   (c) Tightness  
   - Yes  
   - No  
   (d) Stabbing  
   - Yes  
   - No  
   (e) Pressure  
   - Yes  
   - No

Section D. Pain due to possible infarction
28. Have you ever had a severe pain across the front of your chest lasting for half an hour or more?  
   Yes ☐  No ☐

29. If yes, how many of these attacks have you had?
   (a) First attack.  Date……….Duration……….Other information……………………
   (b) Latest attack. Date……….Duration……….Other information……………………

30. Have you ever had an electrical recording of your heart (ECG) performed?  
   Yes ☐  No ☐

31. If yes,  Where………………………………. When………………

32. Did you see a doctor because of this pain?  Yes ☐  No ☐

33. If yes, what did he/she say it was………………………………………………

Section E. Intermittent Claudication

34. Did you get pain in either leg on walking?  Yes ☐  No ☐

35. Does this pain ever begin when you are standing still or sitting?  
   Yes ☐  No ☐

36. In what part of your leg do you feel it?
   Pain includes calf/calves ☐   Pain does not include calf/calves ☐

37. Where else in the leg do you feel the pain………………………………………

38. Do you get it when you walk uphill or hurry?  
   Yes ☐  No ☐  None of them ☐
39. Do you get it when you walk at an ordinary pace on a flat level?
   Yes [ ] No [ ]

40. Does the pain disappear while you are still walking?
   Yes [ ] No [ ]

41. What do you do when you get the pain while walking?
   Stop or slacken pace [ ] Continue walking [ ]

Section F. ECG findings by radiologist

42. Is there evidence of infarction?.................................

43. Describe the classification of infarction
   (a) Mild  (b) Moderate  (c) Severe

44. Is there evidence of other cardiovascular disease?
   ...........................................................................

45. Other relevant remarks..............................................
   ...........................................................................
   ...........................................................................
   ...........................................................................
   ...........................................................................
Section G. Researchers check list

1. Have all the participants’ questions been answered?

2. Have radiological findings been reported

3. Has the consent form been attached
APPENDIX G

PHLEBOTOMY PROTOCOL

Phlebotomy is a process of drawing blood for testing. This procedure will be performed by a trained health professional. The following guidelines will be followed in executing the procedure. Although blood can be safely drawn from most venous blood vessels, the antecubital vein is most suitable. The following equipment will be required for sample drawing.

- Needles preferably vacutainer needles.
- Syringe and needles may also be used
- Vacutainer holder
- Tourniquet
- Disinfection Swabs and Cotton swabs
- Adhesive Dressing
- Rubber Gloves
- Needle disposal box

The procedure will be as follows,

- Participant should be sitting and relaxed. Expose the site and support the arm.
- Apply tourniquet to the selected arm and clean area with antiseptic.
- Antiseptic should be allowed to dry off before drawing blood to avoid haemolysis of blood sample.
- Puncture the vein using the vacutainer needle or syringe and needle and immediately release the tourniquet.
- Connect the vacuum tube into the adopter and let blood freely fill in it.
- After getting adequate amounts of the sample, withdraw the needle and place cotton swab and adhesive dressing over the site.
- Samples will thereafter be kept at cool temperatures before transportation to the laboratory.
Pre-processing storage of Blood Samples before transportation

Clearly labeled blood sample tubes will be placed in specimen racks then put in special cooler boxes containing ice packs before transportation to the storage site. This will be done as soon as the samples are obtained from the participants. All sample containers will be packed securely to prevent leakages while at site of collection and during transportation.

At the storage site, different specimen will be stored at the recommended storage temperatures in the freezer or cold rooms.

Since analysis of the samples will not take place within three days, these samples will be stored at -30°C to -70°C, (EHRM, 2002).

Safety Precautions

All used sharp equipment such as needles will be disposed off into the safety disposal box. The safety disposal box should not be allowed to be over full before changing to another one.

If safety measures are taken, blood from HIV and hepatitis B positive participants does not pose any danger to the researcher.

Needle stick injuries

The European Health Risk Monitoring, (2002) recommends that any personnel who sustain a needle stick injury should seek immediate advice from the local health personnel responsible for advising in situations with risk of communicable diseases. The following 'first aid' instructions for personnel in case of needle stick injury were recommended:

1. Make sure that injury does not happen again.
2. Clean the infected area:
   1. Rinse with substantial amount of water.
   2. Don't squeeze wounded area.
   3. If you have blood on eczema or on puncture wound, place a patch with alcohol (at least 70% alcohol) over it for two minutes.
3. Contact the local health professional responsible for infectious diseases for further procedures.

Procedures in Emergency situations
All emergency cases will be attended to by the project doctor who will manage them accordingly. A participant who loses consciousness or feels dizzy during the procedure in circumstances where there might be no doctor on site, the procedure should be discontinued. He/she should be asked to lie down and placed in a recovery position. The principle behind this position is that blood is facilitated to flow towards the brain, while any secretions are allowed to drain out of the patients’ airways. If the subject is willing for the test to be continued after a suitable length of time, the blood sample could be taken. Otherwise the possibility to give the blood sample at a later time may be discussed.
## APPENDIX H.

### METHOD, EQUIPMENT AND REFERENCE VALUES FOR ANALYTES MEASURED IN THE STUDY

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Method</th>
<th>Equipment used</th>
<th>Reference values</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Men</strong></td>
</tr>
<tr>
<td>Plasma glucose (mmol/L)</td>
<td>enzymatic hexokinase</td>
<td>Cobas 6000 Roche Diagnostics</td>
<td>4.1-5.6</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>Turbidimetric inhibition immunoassay</td>
<td>Cobas 6000 Roche Diagnostics</td>
<td>4.50-6.30</td>
</tr>
<tr>
<td>HDL (mmol/L)</td>
<td>enzymatic colorimetric methods</td>
<td>Cobas 6000 Roche Diagnostics</td>
<td>0.9-1.45</td>
</tr>
<tr>
<td>Trigs (mmol/L)</td>
<td>enzymatic colorimetric methods</td>
<td>Cobas 6000 Roche Diagnostics</td>
<td>0.50-2.00</td>
</tr>
<tr>
<td>GGT (mmol/L)</td>
<td>enzymatic colorimetric methods</td>
<td>Cobas 6000 Roche Diagnostics</td>
<td>0-50</td>
</tr>
<tr>
<td>LDL (mmol/L)</td>
<td>Friedwald’s formula</td>
<td>Cobas 6000 Roche Diagnostics</td>
<td>1.0-3.0</td>
</tr>
<tr>
<td>Creatinine (umol/L)</td>
<td>standardized creatinine</td>
<td>Cobas 6000 Roche Diagnostics</td>
<td>53-115</td>
</tr>
<tr>
<td>Insulin (uU/mL)</td>
<td>microparticle enzyme immunoassay</td>
<td>Axsym, Abbot</td>
<td>0.2-9.4</td>
</tr>
<tr>
<td>Serum cotinine (ng/mL)</td>
<td>chemiluminescent assay</td>
<td>Immulite 1000, Siemens</td>
<td>0.0-50</td>
</tr>
<tr>
<td>Urine albumin (mmol/L)</td>
<td>immunoturbidimetric assay</td>
<td>Cobas 6000 Roche Dgntx</td>
<td>0.0-2.0</td>
</tr>
</tbody>
</table>
APPENDIX I

OTHER SOCIAL MARKETING STRATEGIES

1. The community Health Centre

The Community Health Centre Kasselsvlei Community Health Centre is the public health facility offering health services to the population of Bellville South. Situated on one of the main roads, Kasselsvlei clinic is strategically located and thus easily accessible to many individuals living within Bellville South. For this reason, it was identified as one of the venues where the information regarding the study could be disseminated to the public.

2. The local Community Leaders

The existing community structural leadership was utilized in mobilizing the community for this project. Since they are constantly in contact as well as interacting with the community more easily, the local community leaders were able to pass on the information regarding the research project either during their meetings or any other time they had opportunity to speak to the people.

3. Religious and social Groups

The influence of all religious groups in delivering information about the Diabetes and Impaired Glucose Tolerance study was very important. With permission from the religious leaders, the information was passed on to the people during or after prayers highlighting key issues of the project. The aims and objectives of the study were further explained to the religious leaders for purposes of clarity in case the local community needed to know more during other prayer sessions. Bellville South has several social groups with whom the local people identify with. Among these is the club of middle and elderly citizens who refer to themselves as the senior citizens. This club was vital in passing information from one person to another. Since members of this group were mainly senior citizens above the age of forty, it was assumed that they commanded great influence within the community enough to create a positive impact regarding the project.
4. The street advertisement

The street advertisement popularly referred to as the “Road Show” is a social marketing strategy that was initiated in attempt to create diabetes awareness within the study population. On top of creating awareness, the road show was also intended to improve on the response rate by highlighting the objectives of the study. In this strategy, a highly recognized member of the community was identified and invited to speak to the community members. By use of a public address system (megaphone) and on board a moving truck, the spokes person used brief but catching words to relay the message to the community members about diabetes. Such phrases as “You could be diabetic without knowing” and “Diabetes may lead to heart attack” were used to express the severity of diabetes. He was accompanied by the rest of the field team who alongside him issued fliers to the enthusiastic crowds that rushed to take a glimpse of the famous media actor. In this way, a big audience was able to be reached.
QUALITY CONTROL PROCEDURES

A standard operating procedure manual was developed and issued to all research team assistants. In the manual, details of all measurements were clearly explained. Whoever needed clarification about a particular procedure was free to ask for further explanation. One of the quality control measures employed in this study was the use of standardized operational procedures (SOP). All the equipment was calibrated routinely or on daily basis depending on the manufacturer’s instructions. All field staff were pre-trained on questionnaire administration as well as carrying out measurements before embarking on the study. Measurements carried out were traceable to individual measurers since they were required to sign against the measurements they performed. Spot field checks to verify accuracy of measurements by the project supervisors’ also enhanced quality control (Adams et al., 2002). In order to avoid false measurements due to staff fatigue, work load was kept within acceptable limits as had earlier been agreed.

1. Questionnaire

Although the interviewer or researcher effect is avoided in self-administered questionnaires, it is also likely that some errors could occur due to unclear questions leading to inappropriate responses. This can impact negatively on the quality of the data. Considering the fact that some respondents could have some form of impairments such as visual or literacy levels thus rendering the questionnaire understanding difficult, the research team therefore individually administered the questionnaires in order to avoid inaccuracies due to the above effects. During questionnaire administration, the exact answer given by the respondent was then indicated. Participants were asked to indicate when a question was not clear for clarification by the interviewer.

2. Blood and midstream urine Sample collection

Blood and urine samples can either be contaminated by participants or inappropriately labeled by the researcher during surveys. Participants were therefore carefully informed of the instructions on urine collection. The males had to hold the penis and allow the first
stream of the urine to pass down before directing the mid-stream in the container. The container was then to be tightly secured. The female subjects were asked to clean the vulva with a swab, separate the labia’s with fingers of one hand and pass urine into the container held with the other hand. They were however also asked to pass the first stream away before collecting some into the container. By so doing, contamination was minimized. A sticker bearing the participants names, reference number, date of interview as well as his/her date of birth were placed on the urine container. With respect to blood samples, pink coloured stickers bearing the participants details as above were placed on vacutainer tubes for fasting blood samples while post prandial blood samples were marked with orange stickers. By so doing, fasting blood samples could easily be differentiated from postprandial samples. Labelled blood sample tubes were put securely in plastic bags before being placed in special cooler boxes containing ice packs before and sent to the laboratory for analysis. At the storage site, the samples were stored at the recommended storage temperatures of -30 oC to -70oC in the freezer or cold rooms (EHRM, 2002).

3. Measurement of Glucose powder

The recommended weight of glucose to be administered for purposes of diabetes epidemiological surveys is 75g. In order to adhere to these requirements, strict measures were undertaken while measuring glucose since the original packaging was that of 100g. An electronic calibrated scale was used to accurately measure the quantity needed. After being calibrated to zero, only glucose powder was placed on the digital scale. A spoon was used either to add or remove the powder until the required weight was achieved. The final quantity was then put in a dry plastic tin and securely tightened. The tin was only opened and emptied into a glass to make a solution.

4. Anthropometric measurements

All the equipment used in anthropometric measurements were checked and calibrated before starting measurements according to the manufacturers’ recommendations. Weight taking equipment was checked for accuracy by use of standard weights.
Measurements were carried out in repeatedly after which the average was calculated. The correct size of blood pressure cuff was used for individual participants.

5. Classification of subjects’ glucose metabolism status

Study participants were classified in different glucose metabolism status categories depending on their previous history of diabetes, fasting and post prandial glucose results. For example subjects were classified as known diabetics if they were already on antidiabetic treatment following diagnosis by a medical professional. These classifications were based on the WHO, 1999 revised criteria.