b146 22440
U.O.V.S. BIBLIOTEEK
HIERDIE EKSEMPLAAR MAG ONDER
GEEN OMSTANDIGHEDE UIT DIE
BIBLIOTEEK VERWYDER WORD NIE
University Free State
34300001920549
Universiteit Vrystaat

DIABETES MELLITUS, HYPERTENSION AND RELATED FACTORS IN BLACK SUBJECTS RESIDING IN QWAQWA AND BLOEMFONTEIN

Willem Frederik Mollentze

Thesis submitted to comply with the requirements for the degree

Medicinae Doctor

in the Faculty of Health Sciences, School of Medicine, Department of Internal Medicine,
University of the Free State

Promoter: Prof. D.J.V. Weich
Promoter: Prof. G. Joubert
Co-promoter: Dr. K. Steyn
Co-promoter: Prof. A.F. Steyn
2003

Universiteit van die
Oranje-Vrystaat
BLOEMFONTEIN
22 JAN 2004
UOVS SASOL BIBLIOTEEK

TABLE OF CONTENTS

Acknowledgments		**ix**
List of abbreviations		**x**
Abstract		**616**
Uittreksel		**619**
1	**Introduction**	**1**
1.1	Background and motivation	1
1.2	Problem and hypothesis	6
1.3	Objectives	6
1.4	Literature survey	6
1.5	Thesis lay-out	7
	Map of Africa	8
SECTION A. Literature survey		**9**
2	**Diabetes mellitus, impaired glucose tolerance and impaired fasting glucose**	**10**
2.1	Definition, classification and diagnosis of diabetes mellitus, impaired glucose tolerance and impaired fasting glucose	10
2.1.1	Definition of diabetes mellitus	10
2.1.2	Impaired glucose tolerance – historical background	11
2.1.3	Diagnosis and diagnostic criteria	14
2.1.3.1	Biochemical diagnosis of diabetes and other categories of hyperglycaemia	15
2.1.3.2	Severe hyperglycaemia	15
2.1.3.3	Asymptomatic individuals	16
2.1.3.4	Diabetes in children	16
2.1.3.5	Epidemiological Studies	17

2.1.3.6 Change in diagnostic value for fasting plasma /blood glucose concentration 17
2.1.4 Classification 17
2.1.5 The metabolic syndrome 24
2.1.6 Impact of the ADA 1997 and WHO 1998 diagnostic criteria on the prevalence of diabetes and IFG/IGT 25
2.2 Prevalence of diabetes mellitus in black South Africans 31
2.2.1 Type 1 diabetes 31
2.2.2 Type 2 diabetes 33
2.2.2.1 Historical studies 33
2.2.2.2 Studies using WHO 1985 diagnostic criteria 37
2.2.2.3 South Africa's Demographic and Health Survey 38
2.3 Prevalence of diabetes mellitus in sub-Saharan Africa 42
2.3.1 Studies up to 1990 42
2.3.2 Studies since 1990 44
2.4 Prevalence of diabetes mellitus in United States blacks 45
2.5 The increasing global prevalence of Type 2 diabetes mellitus 48
2.5.1 The Who Report 1991 (King et al, 1991) 48
2.5.2 The International Diabetes Institute and Who Collaborating Center for the Epidemiology of Diabetes Mellitus and Health Promotion for non-communicable diseases 51
2.6 Factors predisposing to the development of non-insulin-dependent diabetes mellitus 63
2.6.1 Genetic causes 63
2.6.2 Fetal origins 67
2.6.3 Lifestyle and Stress 74
2.6.3.1 Urbanization 74
2.6.3.2 Physical activity 75
2.6.3.3 Obesity 76
2.6.3.4 Central obesity 78
2.6.3.5 Aging 80
2.6.3.6 Socio-economic factors 80
2.6.3.7 Stress 81
2.6.3.8 Role of insulin resistance and insulin secretory dysfunction in the pathogenesis of type 2 diabetes mellitus 82

2.7	The complications of diabetes mellitus	86
2.8	Economic aspects of diabetes mellitus	96
2.9	Diabetes care in South Africa	98
2.10	The prevention of diabetes	99
3	**Arterial hypertension**	**100**
3.1	Definition, classification and diagnosis of hypertension	100
3.2	Prevalence of hypertension in black South Africans	103
3.3	The prevalence of hypertension in sub-Saharan Africa	110
3.3.1	Early studies (1929-1988)	110
3.3.2	Recent studies (1989-2002)	114
3.4	The prevalence of hypertension in United States blacks	118
3.5	The global prevalence of hypertension	119
3.6	Aetiology and pathophysiology	120
3.6.1	Obesity	120
3.6.2	Central obesity	123
3.6.3	High sodium / low potassium intake	128
3.6.4	Genetic considerations	134
3.6.5	Environmental factors	136
3.6.6	Alcohol and hypertension	139
3.6.7	Low birth weight and blood pressure	141
3.7	End-organ damage in hypertension	142
3.7.1	Mortality due to cardiovascular disease	144
3.7.2	Cerebrovascular disease in hypertension	145
3.7.3	Left ventricular hypertrophy and cardiac failure	147
3.7.4	Coronary heart disease	149
3.7.5	Hypertensive renal disease	150
3.8	Economic aspects of hypertension	152
3.9	Quality of care at primary health care clinics	154
4	**Overweight and obesity**	**155**
4.1	Definition	155
4.2	Classification and diagnosis of overweight and obesity	155

4.2.1 Classification and measurement of obesity 155
4.2.1.1 According to body mass index 155
4.2.1.2 According to body fat distribution 157
4.2.1.3 According to skinfold thickness 158
4.3 Prevalence of obesity in blacks 159
4.3.1 Prevalence of obesity in black South Africans 159
4.3.2 Prevalence of obesity in sub-Saharan Africa 174
4.3.3 Global prevalence of obesity 178
4.3.4 Health consequences of obesity and central obesity 179
4.3.4.1 The health consequences of obesity 179
4.3.4.2 The health consequences of central obesity 181

5 Dyslipidaemia 183

5.1 Basic description of lipids and lipoproteins 183
5.2 Definition, categories and classification of dyslipidaemia 185
5.2.1 Definition 185
5.2.2 Categories and classification of total cholesterol and LDL cholesterol 186
5.2.3 Categories and classification of Triglycerides 187
5.2.4 Categories and classification of Non-HDL Cholesterol 189
5.2.5 Categories and classification of High Density Lipoproteins (HDL) 190
5.2.6 Atherogenic dyslipidaemia 192
5.2.7 Non-lipid risk factors 192
5.3 Prevalence of dyslipidaemia in blacks 194
5.3.1 Prevalence of dyslipidaemia in black South Africans 194
5.3.2 Prevalence of dyslipidaemia in sub-Saharan Africa 197

6 The clustering of cardiovascular risk factors 199

6.1 The metabolic syndrome 199
6.1.1 Definition 199
6.1.2 The pathogenesis of the metabolic syndrome 202
6.1.3 The prevalence of the metabolic syndrome in Finnish Subjects 207
6.2 Cardiovascular risk factors in black South Africans 209
6.2.1 The prevalence of cardiovascular disease in black South Africans 209
6.2.2 The clustering of cardiovascular risk factors in black South Africans 210

6.3	Cardiovascular risk factors in sub-Saharan Africa	211
6.3.1	Cardiovascular disease in Sub-Saharan Africa	211
6.3.2	The clustering of cardiovascular risk factors in sub-Saharan black Africans	211
6.4	Estimating coronary heart disease risk	213
6.4.1	Estimating 10-year risk for men and women (incorporating the Framingham scoring system)	213
6.4.2	Identification of persons with CHD and CHD risk equivalent	214
6.4.3	Identification of persons without CHD or without CHD risk equivalent	214
6.4.4	Estimating 5- or 10-year risk for men and women using Framingham prediction equations	218

SECTION B. Methods **220**

7 Methods **221**

7.1	Study populations and sampling procedures	221
7.1.1	Qwaqwa	221
7.1.2	Mangaung	225
7.2	General comments	225
7.3	Measurements	226
7.4	Laboratory analysis	229
7.5	Statistical analysis	229

SECTION C. Results and Discussion **231**

8 Diabetes mellitus and impaired glucose tolerance **232**

8.1	Description of plasma glucose levels in the study populations	232
8.2	Prevalence of diabetes	241
8.3	Metabolic control of known cases of diabetes	246
8.4	Prevalence of IGT and Type 2 diabetes according to the 1997 ADA and 1985 WHO criteria	247
8.5	Relationship between obesity, body fat distribution and glucose intolerance	251

8.5.1	Obesity and glucose intolerance	251
8.5.2	Central obesity and glucose intolerance	255
8.6	Pharmacological treatment of hypertension and glucose intolerance	262
8.7	Relationship between glucose tolerance status and serum insulin concentrations	265
8.8	Homeostasis model assessment	275
8.9	The relationship between waist-to-hip ratio and serum insulin concentration	278
8.10	Relationship between glucose tolerance status and fasting C-peptide concentrations	280
8.11	Relationship between glucose tolerance status and proinsulin	284
8.12	Serum fructosamine as screening test for glucose intolerance	291
8.13	Relationship between height and 2-hour plasma glucose	293
8.14	Risk factors for glucose intolerance	295
9	**Hypertension**	**300**
9.1	Description of blood pressure levels in the study populations	300
9.2	Prevalence of hypertension	304
9.3	Prevalence of hypertension by region	318
9.4	Previous diagnosis of hypertension and treatment status	320
9.5	Relationship between obesity and hypertension	324
9.6	Relationship between central obesity and hypertension	328
9.7	Relationship between glucose intolerance and hypertension	331
9.8	Relationship between serum insulin and hypertension	338
9.9	Relationship between oral contraceptives and hypertension	348
9.10	Relationship between blood pressure and anthropometrical variables	349
9.11	Correlations between blood pressure and serum lipids and serum urate	354
9.12	Relationship between smoking and blood pressure	356
9.13	Relationship between alcohol intake and blood pressure	359
9.14	Complications of hypertension	363
9.14.1	Electrocardiographic changes associated with hypertension	363
9.14.2	Relationship between hypertension and renal function	387
9.14.3	Hypertension and hypertensive retinopathy	396

10 Overweight and obesity 399

10.1 Descriptive data on height, weight and body mass index 399
10.2 Prevalence of overweight and obesity 404
10.3 Anthropometry 410
10.3.1 Circumferences 410
10.3.2 Circumference ratios 412
10.3.3 Skinfold thickness 415
10.3.4 Percentage body fat 422
10.4 Association between overweight and selected variables 425
10.5 Association between central obesity and selected variables 429
10.6 Macro and micronutrient intake of representative samples of both populations 431

11 Dyslipidaemia 436

11.1 Descriptive data 436
11.2 The prevalence of lipid abnormalities 443
11.3 Association between obesity and dyslipidaemia 448
11.3.1 Obesity and serum cholesterol 448
11.3.2 Overweight and non-protective HDL-C levels 452
11.3.3 Overweight and serum triglycerides 455
11.4 Association between central obesity and dyslipidaemia 458
11.4.1 Central obesity and total cholesterol 458
11.4.2 Central obesity and non-protective HDL-C levels 461
11.4.3 Central obesity and elevated serum triglycerides 464
11.5 Other factors associated with high triglyceride concentrations 467
11.5.1 Fasting hyperinsulinaemia 467
11.5.2 Sum of 60 min and 120 min post-glucose load hyperinsulinaemia 467
11.5.3 Alcohol use 467
11.5.4 Elevated serum GGT concentration 468

12 Clustering of Cardiovascular Risk Factors 479

12.1 The deadly quartet in black dwellers in Qwaqwa and Mangaung 479
12.2 The metabolic syndrome in black dwellers in Qwaqwa and Mangaung 483
12.2.1 Prevalence of the metabolic syndrome 483
12.2.2 The relative risk of abnormal ECG's in subjects with the metabolic syndrome 483

12.3 Framingham CVD Risk Profiles 489

SECTION D. Summary, conclusions, and recommendations 520

13 Summary, conclusions, and recommendations 521
13.1 Summary and conclusions 521
13.2 Recommendations 534
13.2.1 Prevention strategies 534
13.2.2 Improving physical activity levels and healthy eating 535
13.2.3 Public health strategies 536
13.2.4 Improving the quality of primary health care 536
13.2.5 The need for evaluation 536

References 537

Annex 1 Data collection form and informed consent form 584
Annex 2 Repeat anthropometrical measurements 602
Annex 3 Protocol 604

Abstract 616

Uittreksel 619

Acknowledgments

I would like to thank the following persons and organizations:

- My study leaders for their support, encouragement and hard work!
- Professor D Stoker of the HSRC for formulating the sampling procedure
- Professor E Albertyn (late), former head of the Department of Community Health, University of Free State for valuable advice
- The Qwaqwa health authorities for support and infrastructure
- The Qwaqwa Tribal Authorities for their help and support
- The subjects for their participation
- Dr A. Moore for assistance with the field work
- Mr. TD Mofokeng (late) and mrs PM Rakhatla for the dedicated way in which they performed field work under difficult circumstances
- Mr. T Nkomo, mr. M P Khunong and mrs AEK Motshelamadi for fieldwork and data collection
- The Bloemfontein City Council for staff and assistance
- The management of Pelonomi Hospital for providing infrastructure
- Mr Albert Mokoa, Diabetes Clinic, Pelonomi Hospital for assistance
- Mrs. L Vermaak and mr. E Vermaak for technical assistance
- Mr. T Muller and B. Clur and the staff of the Department of Chemical Pathology, UFS, for analyzing endless samples
- Prof. IP Gray for his help with the proinsulin assays
- The Medical Research Council, The Heart Foundation of Southern Africa, Servier Laboratories South Africa (Pty) Ltd., The Department of Internal Medicine, UFS, and the Central Research Fund of the UFS for financial support
- Dr. GM Oosthuizen for taking care of the data base and valuable advice
- Dr. Nelly Silvis and her team from the Potchefstroom University for assistance with the dietary survey

Spesiale dank aan:

♥ My vrou, Marinette, ons kinders, Heidi, Werner en Marieke
vir hul onbaatsugtige liefde en opoffering.

† Ons Hemelse Vader

Abbreviations

ADA	American Diabetes Association
ATP III	Action Treatment Panel III (for dyslipidaemia)
apo B	apolipoprotein B-100
apo C	apolipoprotein C
apo E	apolipoprotein E
BP	Blood pressure
BF	Body Fat
CETP	Cholesteryl ester transfer protein
CHD	Coronary heart disease
CVD	Cardiovascular disease
CI	Confidence intervals
DBP	Diastolic blood pressure
DM	Diabetes mellitus (Type 2)
DXM	Dexamethasone
ECG	Electrocardiograph
FPG	Fasting plasma glucose
FS	Free State
GAD	Glutamic acid decarboxylase
HbA1c	glycosilated haemoglobin
HDL-C	High-density lipoprotein cholesterol
HGP	Hepatic glucose production
HPA	Hypothalamic-pituitary-adrenal axis
HOMA	Homeostasis Model Assessment
IDDM	Insulin-dependent diabetes mellitus
IDF	International Diabetes Federation
IDL	Intermediate Density Lipoprotein
IFG	Impaired fasting glucose
JNC	Joint National Committee (on hypertension)
IGT	Impaired glucose tolerance
LADA	Latent autoimmune diabetes in adults
LDL	Low-density lipoproteins

LPL	Lipoprotein lipase
LV	Left ventricular
MI	Myocardial infarction
NCEP	National Cholesterol Education Program
NEFA	Non-esterified free fatty acid
NIDDM	Non-insulin dependent diabetes mellitus
OGTT	Oral glucose tolerance test
OR	Odds ratio
PCO	Polycystic ovarian syndrome
Qt1	Quantile 1
Qt3	Quantile 3
RR	Relative risk
SA	South Africa
SD	Standard deviation
SADHS	South Africa Demographic Health Survey
SBP	Systolic blood pressure
TC	Total cholesterol
TG	Triglycerides
TGRLP	Triglyceride-rich lipoproteins
UK	United Kingdom
UKPDS	United Kingdom Prospective Diabetes Study
US	United States
VLDL	Very low density lipoproteins
WC	Waist circumference
WHO	World Health Organisation
WBR	Waist-to-buttock circumference ratio
WHR	Waist-to-hip circumference ratio

1 Introduction

1.1 Background and motivation

The disease profile of a modern Western population differs in many important ways from the disease profile of a population still following a traditional lifestyle (Burkitt, 1973). Diseases characteristic of developed populations are known as Western diseases and are simply defined as diseases, which are characteristic of modern affluent Western technological communities (Trowell and Burkitt, 1981a). The following metabolic and cardiovascular diseases are considered to be Western diseases: essential hypertension, obesity, Type 2 diabetes, cholesterol gallstones, cerebrovascular disease, peripheral vascular disease, coronary heart disease, varicose veins, deep vein thrombosis and pulmonary embolism (Trowell and Burkitt, 1981b).

Synonyms for "Western Diseases" include degenerative and man-made diseases (Editorial, 1977), diseases of civilisation (Trowell and Burkitt, 1981b), non-communicable diseases, chronic non-infectious diseases (WHO, 1990a p 11), diseases of modern society (Nakajime, 1991), and chronic diseases of lifestyle or lifestyle-related diseases (Steyn et al., 1992). The terms non-communicable diseases and chronic non-infectious diseases mainly refer to diet-related chronic diseases (WHO, 1990b) while chronic diseases of lifestyle or lifestyle-related diseases are partly caused by an unhealthy lifestyle (Steyn et al., 1992).

The health of a person is heavily influenced by the interaction between his or her genetically controlled biochemistry and a collection of bio-behavioral influences that can be considered lifestyle factors (Eaton et al., 1988). These include nutrition, exercise and exposure to harmful substances such as alcohol and tobacco. Discordance between the ancient, genetically controlled human biology and certain important aspects of our present-day life is considered to be responsible for the emergence of chronic degenerative diseases (Eaton et al., 1988).

The study of Western diseases in Africans in transition in South Africa requires a basic understanding of the anthropology of Africa's indigenous populations. Mankind consists mainly of three major groups of people: Negroid, Caucasoid, and Mongoloid (Akinkugbe, 1985). The Negroid group is broadly classified as African and Oceanic. The African Negroids are again subdivided into the following types (Akinkugbe, 1985):

True Negroes
Forest Negroes
Nilotic Negroes
Nilo-Hamites
Bantu-speaking Negroes
Negrillos (African Pygmies)
Bushmen
Hottentots

The true and forest Negroes constitute most of the indigenes of present-day west Africa, and the Bantu-speaking and Nilo-Hamitic peoples cover the vast expanse of the African sub-Sahara from the Sudan to the Cape (Figure 1/1). The western coastline of this stretch of the continent was inhabited by pockets of negroid populations of Pygmy (Negrillo, in the Congo Basin), Bushman (southern Angola and northern Namibia), and Hottentot stock (just north of the Cape, extending inland to the Kei River). Because of their close physical affinity, the Bushman and Hottentot groups have become better known as the Khoisan peoples. Since the physical anthropology of these populations may differ widely e.g. height, weight, body composition and arm circumference, care must be exercised to directly apply normative data derived from Caucasians, e.g. body mass index, directly to these groups (Akinkugbe, 1985). In this thesis, blacks refer to Africans, those people whose ancestry is from the African continent; whites are Caucasians with European ancestry; coloureds, a uniquely defined South African group, of mixed Khoi, San, Malay, and European ancestry; and Asian/Indian defines those descendents from East Asia and the Indian subcontinent (Steyn et al., 2001).

The agricultural revolution, approximately 10 000 years ago, changed man from a hunter-gatherer to someone with the ability to produce and store food. The industrial revolution in developed countries 200 years ago introduced radical changes in methods of food production, processing, storage and distribution (WHO, 1990). In developed countries, man has crossed an epidemiological boundary and consequently witnessed the emergence of disorders such as obesity, diabetes, hypertension, and certain cancers. These disorders became much more common in contrast to their rarity among remaining pre-agricultural and other traditional-living humans (Eaton et al., 1988). Like many other developing regions of the world, the peoples of Africa are not escaping the emergence of Western diseases.

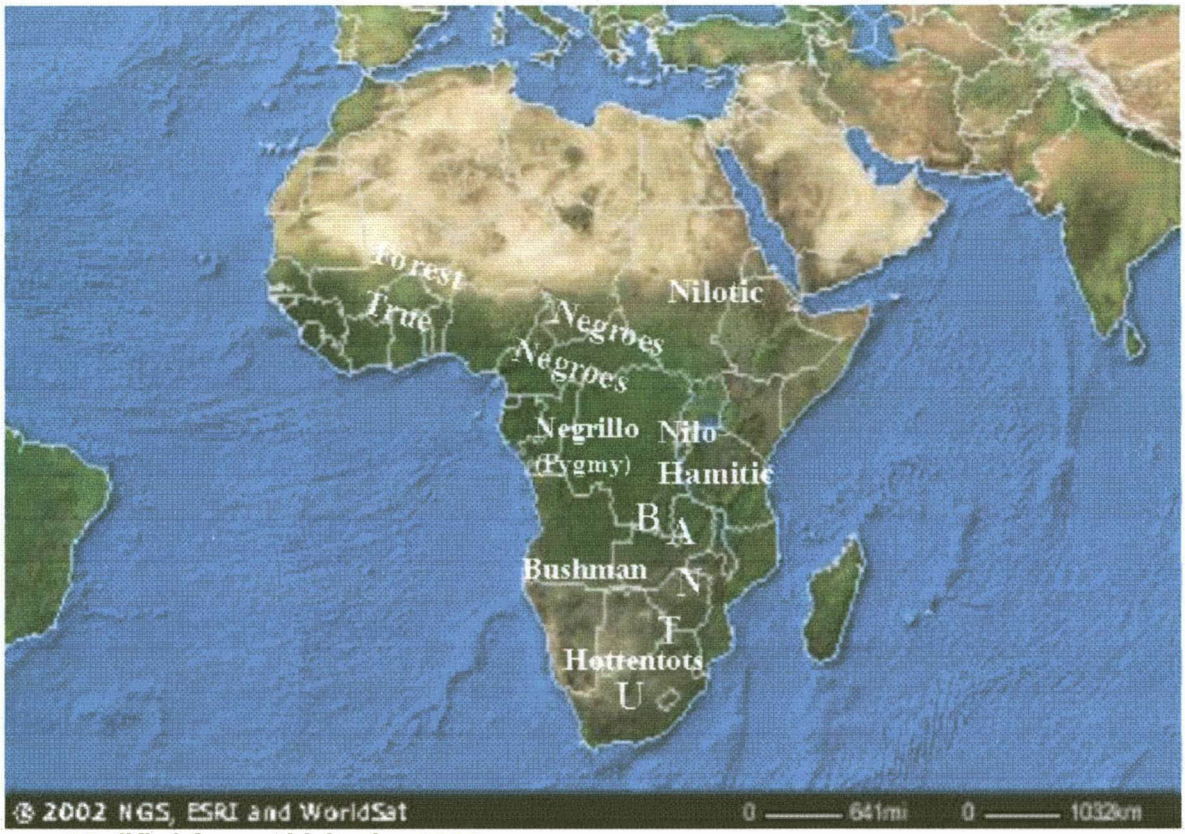


Fig. 1/1. Negroid distribution in Africa. Adapted from Akinkugbe OO, 1985.

The concept of the epidemiological transition provides a useful model to understand changing patterns of health and disease and to relate these changes to mortality in different population groups (Editorial, 1977). Three stages in the epidemiological transition are recognized. The first is the era of pestilence and famine that prevailed in Europe in the Middle Ages. This era persisted throughout the 18th century and was characterized by infectious diseases like typhoid, tuberculosis, cholera, diphtheria and plague. Mortality rates were high, average life expectancy at birth was low, and sustained population growth was impossible. This stage was followed by the stage of receding pandemics during the 19th century. Improved hygiene, sanitation, improved housing and nutrition were major factors responsible for the decline in infectious diseases and mortality. Medical progress played little part in this change. The final stage is characterized by the emergence of degenerative and lifestyle-related diseases like

some cancers, heart disease and stroke. Life expectancy at birth is increased and the old become an increasing burden on the working population (Editorial, 1977).

A nutritional transition accompanies the epidemiological transition as incomes rise and populations become more urbanised (Drewnowski, 1997). Diets high in complex carbohydrates and fibre give way to more varied diets with a higher proportion of fats, saturated fat, and sugars. These shifts in diet structure accompany demographic shifts associated with higher life expectancy and reduced fertility rates. The nutrition transition has also been associated with a higher prevalence of particularly childhood obesity and Type 2 diabetes. Urbanisation is taking place rapidly in South Africa with 43.3% of the population already living in urban areas (Bourne et al., 2002). The epidemiological and nutrition transition accompanying urbanisation in SA is expected to impact negatively in many ways on the health of the previously rural communities. A major dilemma facing the health and nutrition profession in any country, is how best to promote economic growth and prevent or delay the undesirable health effects of the nutritional transition (Drewnowski, 1997).

Western diseases all share the same, or closely similar, epidemiological features (Temple, 1994). In situations in which one of the diseases is common, the others are also prevalent. For instance, the prevalence of particular malignant diseases, such as breast and colon cancer, are often both high in the same population, as are various other conditions, such as coronary heart disease (CHD) and diabetes. Some of these diseases emerge long before others, suggesting that the latter are dependent on a longer exposure to the causative factors or require a much greater intensity of these factors. For example, Type 2 diabetes always seems to appear many years before CHD. However, the precise aetiology of these diseases is uncertain. As well as sharing epidemiological features these diseases often tend to cluster in the same individuals, for instance, diabetes and CHD are associated, as are hiatus hernia and gallstones. Walker hypothesised that a hierarchy is detectable regarding the emergence of the different components of atherosclerotic vascular disease in blacks (Walker, 1975). With increasing sophistication the first arterial disease to emerge is cerebral vascular disease followed by peripheral vascular disease. Coronary heart disease, which is a late event, follows on further sophistication.

More recently a cluster of risk factors for CHD has been noted in some patients with high blood pressure. Reaven (1988) coined the term "Syndrome X" to describe the following combination of conditions: resistance to insulin-stimulated glucose uptake, glucose intolerance, hyper-

insulinaemia, an increased serum concentration of very-low-density lipoprotein triglyceride, a decreased serum concentration of high-density lipoprotein cholesterol and hypertension. The association of insulin resistance with essential hypertension was well documented in Caucasian subjects (Modan et al., 1985). This association could neither be demonstrated in Pima Indians and US blacks (Saad et al., 1991) nor in Pacific Island populations (Collins et al., 1990). Central obesity, causing hyperinsulinaemia, was hypothesized to be the key intermediary in the association of glucose intolerance, hypertriglyceridaemia and hypertension (Kaplan, 1989). Kaplan aptly referred to these four clinical entities as "The Deadly Quartet". The WHO in 1998 formally recognised this entity and adopted the term "Metabolic Syndrome".

A delayed model of the epidemiological transition operates in most of the Third World (Editorial, 1977). Mortality rates have fallen sharply mostly due to imported medical technology, including mass programs to eradicate infectious diseases. Fertility is much less affected, contributing to a rapid population growth. South Africa already carries the triple burden of the continuing high prevalence of some age-old infectious diseases like tuberculosis, diseases of modern society (lifestyle-related diseases including accidents and violence) and new ones such as the Acquired Immune Deficiency Syndrome (AIDS) (Nakajime, 1991). The AIDS epidemic poses a severe threat to the populations of sub-Saharan Africa. Among the countries in this region, South Africa ranks among the first in terms of the largest number of human immuno-deficiency virus (HIV) /AIDS infections. At the end of 2000 the South African infection rate stood at an estimated 4.7 million (van Rensburg et al., 2002).

The leading cause of death in developing countries remains infections, especially of the lower respiratory tract. The second commonest cause of death is ischaemic heart disease. Of the 50 million people globally who died in 1990, 6.3 million succumbed to coronary disease, 57% of which lived in developing nations. The main contributing factor was the health transition that is sweeping the developing world resulting in demographic changes that are increasing up numbers of older people in the population (Editorial, 1998). Chronic diseases of lifestyle were responsible for 24.5% of total mortality in South Africa during 1988 and for 28.5% of deaths in the age group 35-64 years (Steyn et al., 1992). The major causes of mortality in this category were cerebral vascular diseases (7.2% of all deaths, and 7.9% of deaths of persons aged 35-64 years) and ischaemic heart disease (8.7% of all deaths and 9.6% of deaths of persons aged 35-64 years). Amongst blacks, cardiovascular diseases (excluding cardiomyopathy and rheumatic heart disease) were responsible for 10.9% of total mortality in the age group 25 years and older during 1990 (Central Statistical Services Report, 1990). In

1996 cardiovascular diseases were responsible for 16.6% and 24.3% of deaths in males and females respectively in South Africa (Bradshaw et al., 2002).

Studies were recently conducted in mostly urban populations to determine the prevalence of traditional CVD risk factors in black South Africans, for instance hypertension in the Zulu people of Natal (Seedat et al., 1982), the BRISK study in Cape Peninsula blacks (Steyn et al., 1991), the Free State black elderly (Bester and Weich, 1991), the study of diabetes in Cape Town blacks (Levitt et al., 1993), and the THUSA study in blacks in the North West province (Vorster et al., 2000). The first South Africa Demographic and Health Survey conducted in 1998 (SADHS, 1998) focussed mainly on women's health but also collected data on the prevalence of some cardiovascular risk factors such as smoking, hypertension and obesity in the urban as well as rural population.

1.2 Problem and hypothesis

The epidemiological and nutritional transition that is taking place in South Africa has resulted in the emergence of a number of chronic diseases of lifestyle. Because of the lack of information on the prevalence of traditional CVD risk factors in Free State blacks, the need was realised to study the cardiovascular disease risk factor profile of an urban and rural Free State black population.

1.3 Objectives

The primary objectives of the study were to determine the prevalence of and risk factors for glucose intolerance, hypertension and dyslipidaemia in a rural (Qwaqwa) and an urban (Mangaung, Bloemfontein) Free State black population and ultimately to advise on preventative strategies. The hypothesis tested was that these conditions were more common in the urban than in the rural population.

The secondary objectives were to test the hypotheses that the metabolic syndrome existed in the black population and that hypertension was associated with hyperinsulinaemia in these populations.

1.4 Literature survey

It will be audacious to attempt a literature survey in the true sense of the word when dealing with topics such as diabetes mellitus, essential hypertension, obesity and dyslipidaemia.

Therefore, the literature survey is based on a selection of landmark articles covering mainly epidemiological aspects of these topics and generally pertaining to black subjects.

1.5 Thesis lay-out

The lay-out of the thesis is shown in Fig. 1.5/1

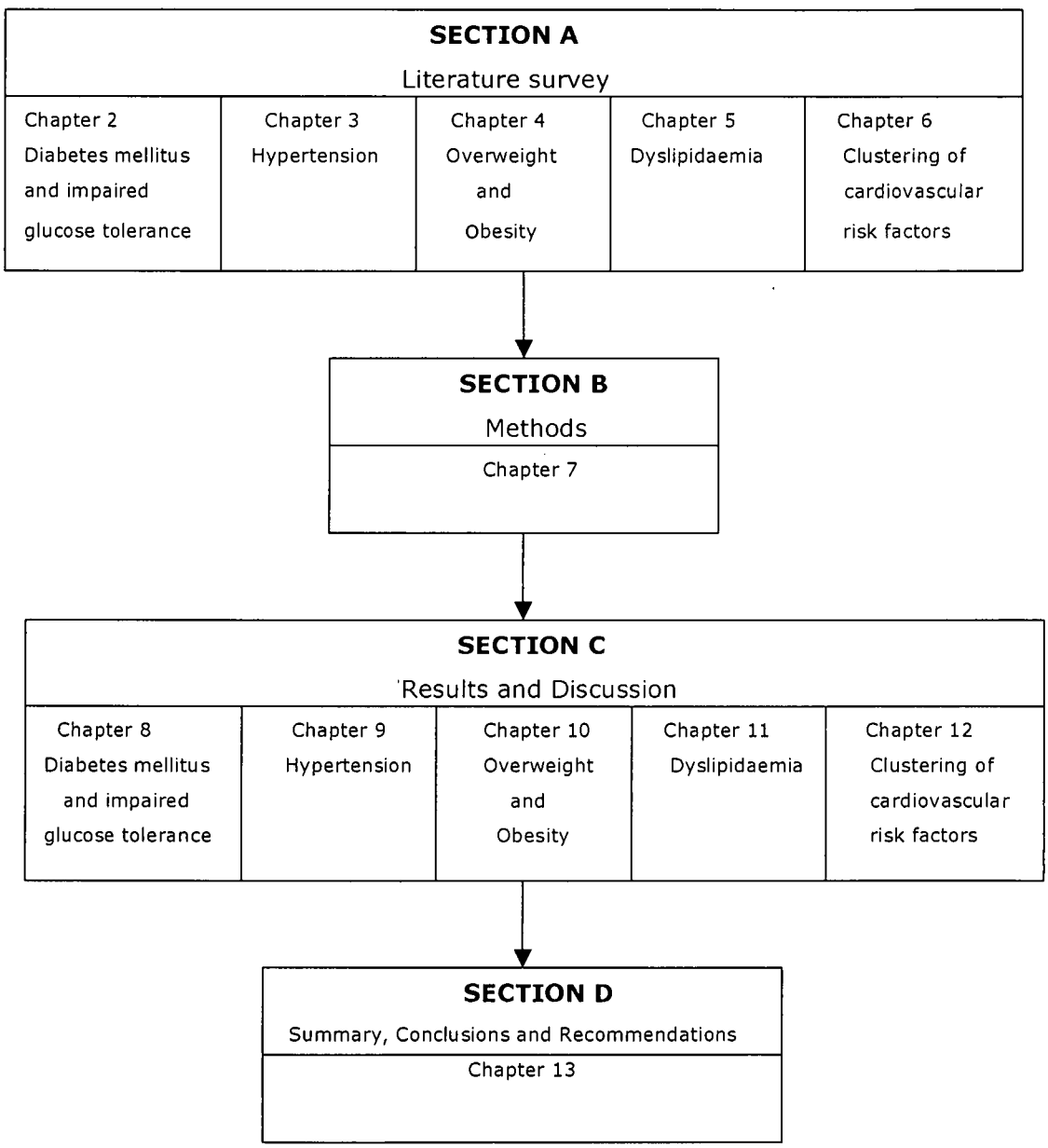


Fig. 1.5/1. Structure of the thesis.

AFRICA
SPAIN
PORTUGAL
MOROCCO
ALGERIA
TUNISIA
LIBYA
EGYPT
TURKEY
GREECE
CYPRUS
LEBANON
SYRIA
IRAQ
IRAN
SAUDI ARABIA
KUWAIT
MALTA
Tropic of Cancer
MAURITANIA
MALI
NIGER
CHAD
SUDAN
ERITREA
ETHIOPIA
SOMALIA
DJIBOUTI
YEMEN
BURKINA FASO
NIGERIA
CÔTE D'IVOIRE
LIBERIA
GHANA
TOGO
BENIN
CAMEROON
CENTRAL AFRICAN REP.
ZAIRE
UGANDA
KENYA
TANZANIA
RWANDA
BURUNDI
ANGOLA
ZAMBIA
MALAWI
MOZAMBIQUE
ZIMBABWE
NAMIBIA
BOTSWANA
SOUTH AFRICA
REP OF SOUTH AFRICA
MADAGASCAR
COMOROS
Equator
Gulf of Guinea
C. Palmas
C. Fria
Etosha Pan
Lake Chad
Lake Victoria
Lake Tanganyika
Lake Malawi
Lake Nasser
Lake Turkana
Ascension Is. U.K.
Georgetown
St. Helena U.K.
Jamestown
Tristan da Cunha U.K.
Edinburgh
SOUTH ATLANTIC OCEAN
INDIAN OCEAN
Rio de Janeiro to Cape Town 3 312 m.
Montevideo to Cape Town 3 662 m.
New York to Cape Town 6 797 m.
Cape Town to Mauritius 2 788 m.
Cape Town to Fremantle 4 212 m.
Cape Town to Adelaide 5 574 m.
Mombasa to Aden 1 625 m.
15° W
0°
15° E
30°
45°
Copyright © Map Studio

SECTION A

Literature survey

2 Diabetes mellitus, impaired glucose tolerance and impaired fasting glucose

2.1 Definition, classification and diagnosis of diabetes mellitus, impaired glucose tolerance and impaired fasting glucose

2.1.1 Definition of diabetes mellitus

Diabetes mellitus is a diverse group of metabolic disorders with varied clinical characteristics initially unified by a common biochemical abnormality – hyperglycaemia. The spectrum ranges from rare genetic defects of beta-cell function to genetic defects in insulin action; from malnutrition-related injury to the developing foetal islets of Langerhans to autoimmune destruction of beta-cells in later life, and from islet cell destruction from toxic substances such as alcohol and iron overload to beta-cell exhaustion due to decades of insulin resistance in the metabolic syndrome. No simple definition exists for diabetes mellitus emphasising the complex nature of the condition.

A working group of the World Health Organisation (WHO) (Alberti et al., 1998) defined diabetes mellitus as a metabolic disorder of multiple aetiology, characterized by chronic hyperglycaemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both. Diabetes mellitus may be asymptomatic or symptoms may be minimal for a long time during which hyperglycaemia may cause pathological and functional changes before the diagnosis is made. On the other hand diabetes mellitus may also present with characteristic symptoms such as thirst, polyuria, blurring of vision, and weight loss. In its most severe forms, ketoacidosis or a non-ketotic hyperosmolar state may develop and lead to stupor, coma and, in the absence of effective treatment, death. Diabetes mellitus is also characterised by the development of specific long-term complications including retinopathy with potential blindness, nephropathy that may lead to renal failure, and/or neuropathy with risk of foot ulcers, amputation, Charcot joints, and features of autonomic dysfunction, including sexual dysfunction. People with diabetes are at increased risk of cardiovascular, peripheral vascular, and cerebrovascular disease.

2.1.2 Definition of Impaired Glucose Tolerance – historical background

IGT was previously defined as a glycaemic response to a standard oral glucose challenge (75g) intermediate between normal and diabetic and can therefore only be determined by an oral glucose tolerance test (OGTT) (WHO, 19f). The previous defining limits are given in Table 2.1.2/1 and the present defining limits in Table 2.1.3/1. The fasting value must not be diagnostic for diabetes. For epidemiological studies the 2-hour value alone was previously regarded as adequate for the diagnosis of diabetes (WHO, 1985). The WHO has recently reclassified 'Impaired Glucose Tolerance' as a stage of impaired glucose regulation, since it can be observed in any hyperglycaemic disorder, and is itself not diabetes (Alberti et al., 1998).

Up to the mid-seventies there were no clear guidelines based on blood-sugar measurements to distinguish between diabetes and normality. Jarrett and Keen (1976) suggested on the basis of the Bedford study as well as on data available from the Pima Indians that a capillary blood glucose of 11.1 mmol/L after a 50g oral glucose load was a reasonable cut-point to divide those at risk of microvascular complications from those not at risk. The lower limit of the 2 hour blood glucose range defining IGT seemed entirely arbitrary although it was shown by Jarrett and Keen that the risk of worsening to diabetes sharply increased when 2 hour blood glucose levels exceeded 7.8 mmol/L.

Jarrett et al. (1979) observed in the Whitehall study that 27 (13.2%) from a group of 204 men with 'borderline diabetes' followed for a period of 5 years with repeated oral glucose tolerance testing, worsened to diabetes. This happened regardless of treatment with carbohydrate restriction with or without 50mg phenformin daily. The authors concluded that the finding of lesser degrees of glucose intolerance did not justify the diagnosis of diabetes or even indicated a necessary progression to diabetes. They suggested the term 'impaired glucose tolerance' to categorize someone with glucose intolerance.

Subjects in the IGT category also had an increased risk of coronary heart disease (CHD). Fuller et al. (Lancet, 1980) reported mortality data for men identified from the Whitehall study. These men were identified from a group of 18403 civil servants aged 40-60 years and followed for 7.5 years for cardio-respiratory disease. From these 281 men with IGT was studied. The end-point was mortality in relation to 2-hour capillary blood glucose concentration following a 50 g oral glucose load, ECG abnormalities at entry, body mass index

TABLE 2.1.2/1

DIAGNOSTIC VALUES FOR THE ORAL GLUCOSE TOLERANCE TEST

	Glucose concentration, mmol/L			
	Whole blood		Plasma	
Diabetes mellitus	Venous	Capillary	Venous	Capillary
Fasting value	>6.7	>6.7	>7.8	>7.8
2 hrs after glucose load[a]	>10.0	>11.1	>11.1	>12.2
Impaired glucose tolerance				
Fasting value	<6.7	<6.7	<7.8	<7.8
2 hrs after glucose load[a]	6.7-10.0	7.8-11.1	7.8-11.1	8.9-12.2

[a] For epidemiological or population screening purposes the 2-hour value after 75 g oral glucose may be used alone or with the fasting value. The fasting value alone is considered less reliable since true fasting cannot be assured and spurious diagnosis of diabetes may more readily occur.

WHO, Technical Report, Expert committee, 1985

(BMI), and various other possible risk factors. They found that CHD mortality doubled when the 2-hour blood glucose concentration exceeded the 95th centile (5.4 mmol/L). This blood glucose concentration was well below the 7.8 mmol/L cut-ff point accepted by the WHO as the lower for IGT. In the IGT group, an increased systolic blood pressure (>153 mm Hg), age and abnormal ECG findings were also independently predictive of CHD death. The increased CHD mortality in the IGT group may have been due to increased serum insulin concentrations (Pÿoräla, 1979) or serum proinsulin concentrations (Temple, 1989).

In the 10-year follow-up of the Bedford survey, Keen et al. (1982) found that 15% of 241 people with 'borderline diabetes' worsened to diabetes while 53% substantially improved their glucose tolerance. The risk of progression to diabetes was predicted by the degree of glucose intolerance while obesity also had a delayed predictive value that only manifested after 5 years. IGT was thus clearly a heterogeneous and unstable category.

Studies in the Pima Indians (Lillioja, 1988) suggested that obese people with IGT have insulin resistance and normal pancreatic function while people with Type 2 diabetes, in contrast, had both insulin resistance and pancreatic secretory deficiency. They developed the hypothesis that moderately elevated glucose levels in subjects with IGT act as a signal to the pancreas that insulin action is impaired and that increased secretion is necessary resulting in hyperinsulinaemia. This process then leads to a cycle of beta-cell unresponsiveness and diabetes. These authors regard the development of diabetes in obese subjects as a two-stage process involving insulin resistance followed by beta-cell failure.

Controversy surrounded the subject of IGT for some time (Jarrett, 1987). Yudkin et al. (1990) emphasized the variability of the blood glucose response to a glucose load and stated examples where coefficients of variation between 20% and 35% in the 2-hour blood glucose concentration were found. The authors of this review also referred to the Tanzanian rural study (vide infra) where a second OGTT was performed within seven days of the first. They found that only 25% of subjects initially classified as diabetic were still diabetic after the second test. Similarly, more than 75% of those with IGT reverted to normal. Possible explanations for this finding were glucose tolerance test variability, regression to the mean, or this population seemed to show a stress effect on glucose tolerance testing. This implies that 2-hour blood glucose concentrations in this population may have responded to investigation with a similar arousal or defence reaction that is found for hypertension (see page 44). This unique phenomenon needs to be confirmed by other studies in similar populations because of the potential to overestimate the prevalence of diabetes by 75%. Furthermore, additional criteria may be required to categorise people with IGT and measures of insulin and of proinsulin-like molecules are possible tools for this task (Yudkin, 1990). More studies are needed to clarify the meaning of IGT especially in black populations.

It is assumed that IGT is a necessary transition state en route to type 2 diabetes (Alberti, 1998 and Alberti, 1999). The prevalence of IGT in different populations ranges between 2-25% in adults and the rates of progression to Type 2 diabetes vary from 2-14% per year (Alberti, 1999). Since IGT also carries an increased risk of the later development of cardiovascular disease, it has also been included in the definition of the metabolic syndrome (Alberti et al., 1998)

2.1.3 Diagnosis and diagnostic criteria (Alberti et al., 1998)

If a diagnosis of diabetes is made, the clinician must feel confident that the diagnosis is fully established since the consequences for the individual are considerable and lifelong (Alberti et al., 1998). The WHO (Alberti et al., 1998) diagnostic criteria for diabetes and other categories of hyperglycaemia are shown in Table 2.1.3/1.

TABLE 2.1.3/1. Values for the diagnosis of diabetes mellitus and other categories of hyperglycaemia

Venous Plasma Glucose (mmol/L)	
Diabetes Mellitus:	
Fasting	≥ 7.0
or	
2-h post glucose load	≥ 11.1
or both	
Impaired Glucose Tolerance (IGT):	
Fasting concentration (if measured)	< 7.0
and	
2-h post glucose load	≥ 7.8 and < 11.1
Impaired Fasting Glycaemia (IFG):	
Fasting	≥ 6.1 and < 7.0
2-h (if measured)	< 7.8

Adapted from Alberti et al. (1998).

For epidemiological or population screening purposes, the fasting or 2-h value after 75 g oral glucose may be used alone. For clinical purposes, the diagnosis of diabetes should always be confirmed by repeating the test on another day unless there is unequivocal hyperglycaemia with acute metabolic decompensation or obvious symptoms. Glucose concentrations should not be determined on serum unless red cells are immediately removed; otherwise glycolysis will result in an unpredictable underestimation of the true concentrations. It should be stressed that glucose preservatives do not totally prevent glycolysis (Alberti et al., 1998).

2.1.3.1 BIOCHEMICAL DIAGNOSIS OF DIABETES AND OTHER CATEGORIES OF HYPERGLYCAEMIA

The biochemical diagnosis of diabetes mellitus and other categories of hyperglycaemia can be made in three different ways i.e. by using a fasting venous PG sample, the 2-hour venous PG after a 75g OGTT and a random venous plasma glucose (PG) sample (Fig. 2.1.3.1/1). In the absence of unequivocal symptoms the diagnosis of diabetes must be confirmed with another test preferably the following day. Venous plasma glucose values are provided since the measurement of venous plasma glucose is widely available and are also the most popular method in South Africa – in the public and private sector.

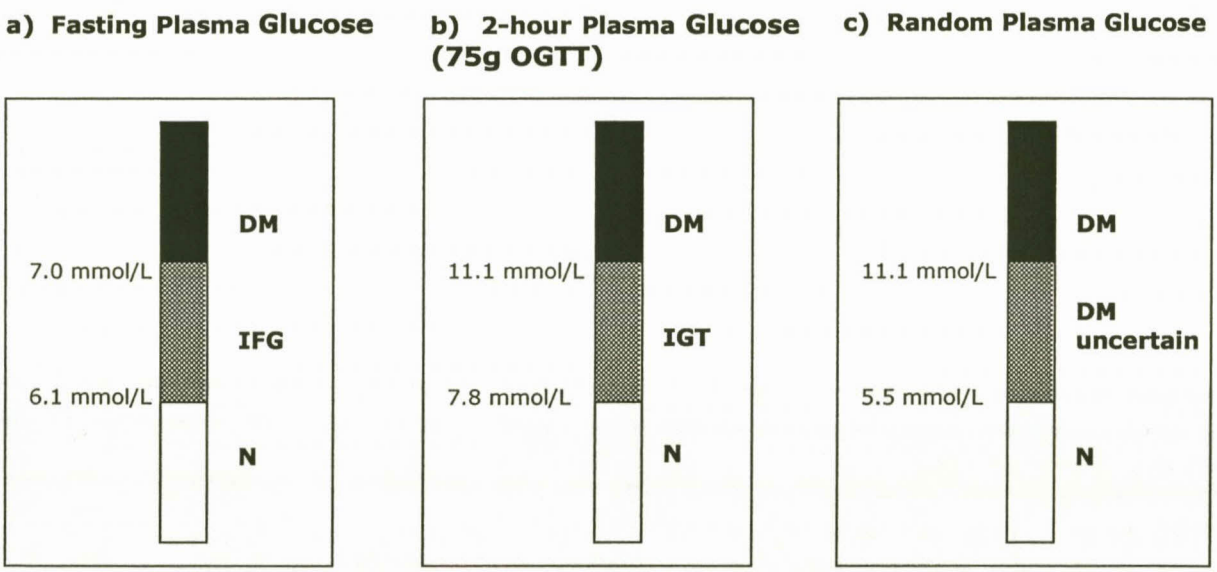


Fig. 2.1.3.1/1. The biochemical diagnosis of diabetes mellitus and other categories of hyperglycaemia. DM = diabetes mellitus, IGT=Impaired Glucose Tolerance, IFG =Impaired Fasting Glucose and N= Normal. (Modified from Alberti et al., 1998).

2.1.3.2 SEVERE HYPERGLYCAEMIA

Severe hyperglycaemia detected under conditions of acute infective, traumatic, circulatory or other stress may be transitory and should not in itself be regarded as diagnostic of diabetes

(Alberti et al., 1998). Other patients with severe hyperglycaemia usually present with symptoms such as increased thirst and urine volume, recurrent infections, and unexplained weight loss and, in severe cases, drowsiness and coma. A **single** casual or random venous plasma glucose concentration (frequently used specimen in South Africa – collected in a sodium fluoride tube) ≥ 11.1 mmol/L establishes the diagnosis of diabetes in such cases (Alberti et al., 1998).

2.1.3.3 ASYMPTOMATIC INDIVIDUALS

The diagnosis of diabetes in the asymptomatic individual should only be made after a **second** plasma / blood glucose concentration in the diabetic range has been found at a different time. The second blood/plasma sample may either be obtained in the fasting state, from a random (casual) sample, or from the oral glucose tolerance test (OGTT). If such samples fail to confirm the diagnosis of diabetes mellitus, it will usually be advisable to maintain surveillance with periodic re-testing until the diagnostic situation becomes clear. Glycated haemoglobin (HbA1c), reflecting average glycaemia over a period of weeks, is not sufficiently well standardized at present for use as a diagnostic test at this time (Alberti et al., 1998).

In non-pregnant asymptomatic subjects with a casual or random venous plasma glucose concentration ≤ 5.5 mmol/L the diagnosis of diabetes is unlikely. The diagnosis of diabetes in asymptomatic subjects is uncertain if the casual venous plasma glucose concentrations lie in the uncertain range (5.6 – 11.0 mmol/L). In such individuals the WHO recommends an OGTT to establish the correct diagnosis. If an OGTT is performed, it is sufficient to measure the blood glucose values while fasting and at 2 h after a 75 g oral glucose load. Diagnostic interpretations of the fasting and 2-h post-load concentrations in non-pregnant subjects are shown in Table 2.1.3/1 (Alberti et al., 1998).

2.1.3.4 DIABETES IN CHILDREN

Diabetes in children usually presents with severe symptoms, very high blood glucose levels, marked glycosuria, and ketonuria. In most children the diagnosis is confirmed without delay by blood glucose measurements, and treatment (including insulin injection) is initiated immediately, often as a life-saving measure. An OGTT is neither necessary nor appropriate for diagnosis in such circumstances. A small proportion of children and adolescents, however, present with less severe symptoms and may require a fasting blood glucose and/or an OGTT for diagnosis (Alberti et al., 1998). For children the oral glucose load is related to body weight: 1.75 g/kg $^{-1}$. The diagnostic criteria in children are the same as for adults. See Annex 1 for the diagnostic criteria of Type 2 diabetes in children.

2.1.3.5 DIAGNOSIS IN EPIDEMIOLOGICAL STUDIES

For population studies of glucose intolerance and diabetes, individuals have been classified by their blood glucose concentration measured after an overnight fast and/or 2 hours after a 75 g oral glucose load (Annex 2). Since it may be difficult to be sure of the fasting state, and because of the strong correlation between fasting and 2-h values, epidemiological studies or diagnostic screening have in the past been restricted to the 2-h values only (Table 2.1.3/1). If the OGTT is difficult to perform for any reason (e.g. logistical, economic) it is now recommended that fasting plasma glucose alone can be used for epidemiological purposes (Alberti et al., 1998). Ideally both should be used.

2.1.3.6 CHANGE IN DIAGNOSTIC VALUE FOR FASTING PLASMA /BLOOD GLUCOSE CONCENTRATION

The major change in the diagnostic criteria for diabetes mellitus from the previous WHO recommendation (WHO, 1985) is the lowering of the diagnostic value of the fasting plasma glucose concentration to 7.0 mmol/L and above, from the former level of 7.8 mmol 1/l and above. The new fasting criterion is chosen to represent a value, which in most persons is of approximately equal diagnostic significance to that of the 2-hour post-load concentration, which is not changed. It also represents an optimal cut-off point to separate the components of bimodal frequency distributions of fasting plasma glucose concentrations seen in several populations. Furthermore, several studies have shown increased risk of microvascular disease in persons with fasting plasma glucose concentrations of 7.0 mmol/L and over, and of macrovascular disease in persons with such fasting concentrations, even in those with 2-h values of <7.8 mmol/L (Alberti et al., 1998). The WHO has defined normoglycaemia arbitrarily as a venous plasma glucose concentration of less than 6.1 mmol/L. There is, however, evidence that values above this are associated with progressively greater risk of microvascular complications.

2.1.4 Classification

In the past numerous attempts were made to classify diabetes e.g. 'insulin sensitive' and 'insulin resistant' types of diabetes (Himsworth, 1936). Advances in the understanding of beta cell function and the insulin receptor made it clear that diabetes is a heterogeneous disorder. The National Diabetes Data Group's provisional consensus classification (National Diabetes Data Group, 1979) paved the way for the World Health Organizations (WHO) classification of diabetes mellitus (WHO, 1980) which was again reviewed in 1985 (WHO, 1985). The latter report provided at the time a classification (Table 2.1.4/1), standardized diagnostic criteria (Table 2.1.2/1), and a uniform terminology suitable for clinical and epidemiological research,

which was internationally accepted and widely applied (Bennett, 1991). The surveys described in this thesis were conducted before the American Diabetes Associations' Expert Committee on the Diagnosis and Classification of Diabetes Mellitus reviewed their previous report (ADA, Expert Committee, 1997). This Expert Committee considered it particularly important to move away from a system that appeared to base the classification of the disease, in large part on the type of pharmacological treatment used in its management toward a system based on disease aetiology where possible. A WHO Consultation also took place in parallel with the report by the American Diabetes Association Expert Committee to re-examine diagnostic criteria and classification (Alberti et al., 1998).

The WHO (1998) proposed a new classification system encompassing both **clinical stages** and **aetiological types** of diabetes mellitus and other categories of hyperglycaemia. The clinical staging reflects that diabetes, regardless of its aetiology, progresses through several **clinical stages** during its natural history. The stage of glycaemia may change over time depending on the extent of the underlying disease processes (Fig. 2.1.4/1). These stages reflect the various degrees of hyperglycaemia in individual subjects regardless of the disease processes, which may lead to diabetes mellitus. Individual subjects may move from stage to stage in either direction (Alberti et al., 1998).

The classification by **aetiological type** results from improved understanding of the causes of diabetes mellitus (Table 2.1.4/2 and Table 2.1.4/3). The aetiological classification reflects the fact that the defect or process, which may lead to diabetes, may be identifiable at any stage in the development of diabetes - even at the stage of normoglycaemia. The severity of the metabolic abnormality can either regress (e.g. with weight reduction), progress (e.g. with weight gain), or stay the same. According to residual beta-cell function some individuals may need insulin for survival, while others according to the severity of the underlying metabolic abnormality, may need insulin for adequate glycaemic control (Alberti et al., 1998).

TABLE 2.1.4/1

1985 WHO CLASSIFICATION OF DIABETES MELLITUS AND ALLIED CATEGORIES OF GLUCOSE INTOLERANCE

A. Clinical classes

Diabetes mellitus (DM)

Insulin-dependent diabetes mellitus (IDDM)

Non-insulin dependent diabetes mellitus (Type 2 diabetes)

(a) Non-obese

(b) Obese

Malnutrition-related diabetes mellitus (MRDM)

Other types of diabetes associated with certain conditions and syndromes:

(1) pancreatic disease;

(2) disease of hormonal aetiology;

(3) drug-induced or chemical-induced conditions;

(4) abnormalities of insulin or its receptors;

(5) certain genetic syndromes;

(6) miscellaneous.

Impaired glucose tolerance (IGT)

(a) Non-obese

(b) Obese

(c) Associated with certain conditions and syndromes

Gestational diabetes mellitus (GDM)

B. Statistical risk classes (subjects with normal glucose tolerance but substantially increased risk of developing diabetes)

Previous abnormality of glucose tolerance

Potential abnormality of glucose tolerance

WHO, Expert committee, 1985

The WHO working group has eliminated the terms 'insulin-dependent diabetes mellitus' and 'non-insulin-dependent diabetes mellitus' and their acronyms 'IDDM' and 'NIDDM'. These terms were confusing and frequently resulted in patients being classified based on treatment rather than on pathogenesis. The terms Type 1 and Type 2 were retained (Alberti et al., 1998). The aetiological type named **Type 1** encompasses the majority of cases, which are primarily due to pancreatic islet beta-cell destruction and are prone to ketoacidosis. Type 1 includes those cases attributable to an autoimmune process, as well as those with beta-cell destruction and who are prone to ketoacidosis for which neither aetiology nor a pathogenesis is known (idiopathic). It does not include those forms of beta-cell destruction or failure to which specific causes can be assigned (e.g. cystic fibrosis, mitochondrial defects). Some subjects with this type can be identified at earlier clinical stages than diabetes mellitus (Alberti et al., 1998).

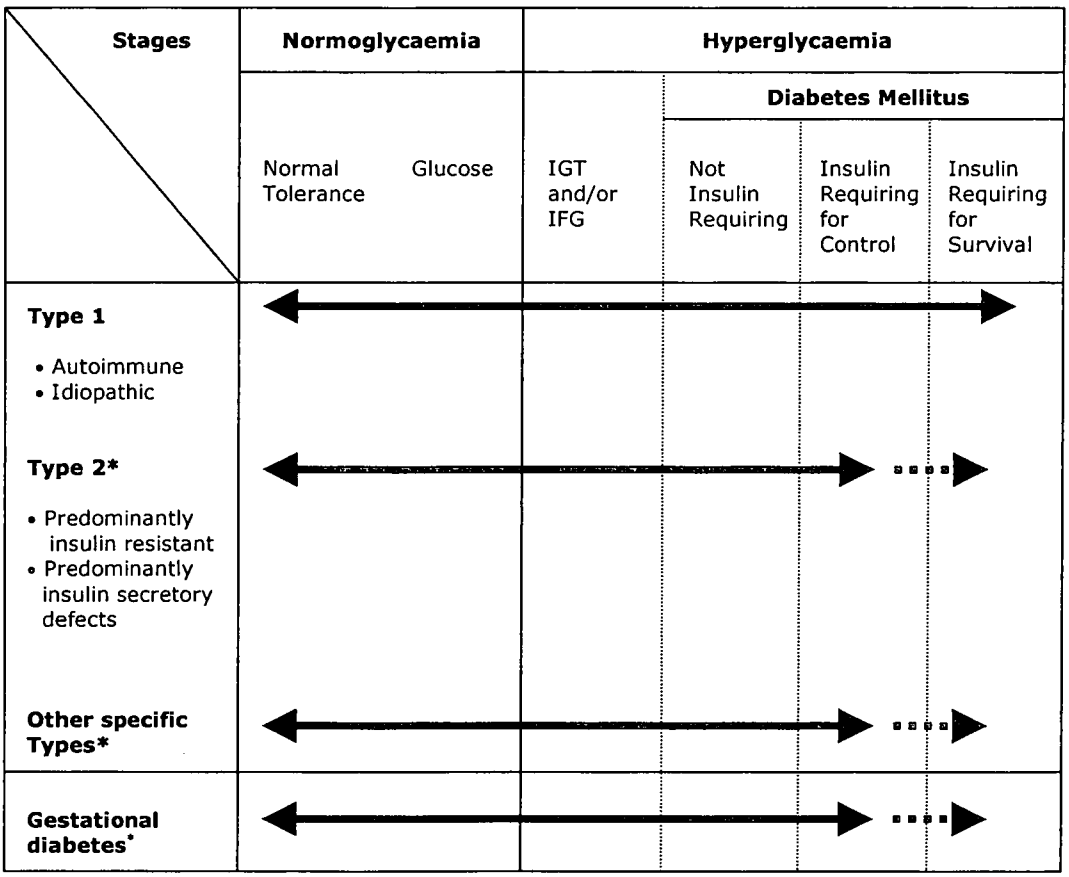


Fig. 2.1.4/1. Disorders of glycaemia: aetiological types and stages. * In rare instances patients in these categories (e.g. Vacor toxicity, Type 1 presenting in pregnancy) may require insulin for survival. (Alberti et al., 1998).

The category **Type 2** includes the common major form of diabetes, which results from defect(s) in insulin secretion, almost always with a major contribution from insulin resistance (Alberti, 1998).

Malnutrition-related diabetes (MRDM) as a class has been deleted. The former subtype of MRDM, protein deficient pancreatic diabetes is no longer recognised as a separate class. The other former subtype of MRDM, fibrocalculous pancreatic diabetes (FCPD), is now classified as a disease of the exocrine pancreas, fibrocalculous pancreatopathy, which may lead to diabetes mellitus (Alberti, 1998).

The terms IGT and IFG refer to a metabolic stage intermediate between normal glucose homeostasis and diabetes mellitus. The WHO has reclassified 'Impaired Glucose Tolerance' as a stage of impaired glucose regulation, since it can be observed in any hyperglycaemic disorder, and is itself not diabetes. Many individuals with IGT are euglycaemic in their daily lives. In the absence of pregnancy, IFG and IGT are not clinical entities in their own right but rather risk factors for future diabetes and cardiovascular disease. Although IGT is frequently associated with the Metabolic Syndrome it may also occur as an intermediate stage in the pathogenesis of any of the conditions listed in Fig. 2.1.4/1. If an OGTT is performed, some individuals with IFG will have IGT and some may have diabetes (Alberti, 1998).

Gestational diabetes was retained as a separate class in the WHO proposal. GDM is defined as any degree of glucose intolerance (WHO criteria for diabetes mellitus or IGT) with onset or first recognition during pregnancy. After the pregnancy ends, the woman should be reclassified as having either diabetes mellitus, or IGT, or normal glucose tolerance based on the results of a 75 g OGGT six weeks or more after delivery. The WHO report emphasized that such women, regardless of the 6-week post-pregnancy result, are at increased risk of subsequently developing diabetes. The significance of IFG in pregnancy remains to be established. Any woman with IFG, however, should have a 75 g OGTT.

TABLE 2.1.4/2

1998 WHO AETIOLOGICAL CLASSIFICATION OF DISORDERS OF GLYCAEMIA*

Type 1 diabetes (beta-cell destruction, usually leading to absolute insulin deficiency)
Autoimmune
Idiopathic
Type 2 diabetes (may range from predominantly insulin resistance with relative insulin deficiency to a predominantly secretory defect with or without insulin resistance)
Other specific types of diabetes#
Genetic defects of beta-cell function
Genetic defects of beta-cell action
Diseases of the exocrine pancreas
Endocrinopathies
Drug- or chemically induced
Infections
Uncommon forms of immune-mediated diabetes
Other genetic syndromes sometimes associated with diabetes
Gestational diabetes

#Other specific types of diabetes are shown in Table 2.1.1/5.

*Alberti et al. (1998)

TABLE 2.1.4/3

OTHER SPECIFIC TYPES OF DIABETES (MODIFIED FROM ALBERTI ET AL., 1998)

Genetic defects of beta-cell function	Drug- or chemically induced
Maturity onset diabetes of the young	Nicotinic acid
(MODY) – at least 4 known subtypes	Glucocorticoids
Others	Thyroid hormone
Genetic defects of beta-cell action	Alpha-adrenergic agonists
Type A insulin resistance	Beta-adrenergic agonists
Lipoatrophic diabetes	Thiazides
Leprechaunism	Diphenylhidantoin
Rabson-Mendenhall syndrome	Pentamidine
Others	Vacor
Diseases of the exocrine pancreas	Interferon-alpha therapy
Fibrocalculous pancreatopathy	Others
Pancreatitis	Infections
Trauma / Pancreatectomy	Congenital rubella
Neoplasia	Cytomegalovirus
Cystic fibrosis	Others
Haemochromatosis	Uncommon forms of immune-mediated diabetes
Others	Insulin autoimmune syndrome (antibodies to insulin)
Endocrinopathies	Anti-insulin receptor antibodies
Cushing's syndrome	Others
Acromegaly	Other genetic syndromes sometimes associated with
Phaeochromocytoma	diabetes
Glucagonoma	Down's syndrome
Hyperthyroidism	Klinefelter's syndrome
Somatostatinoma	Myotonic dystrophy
Others	Porphyria
	Turner's syndrome

2.1.5 The metabolic syndrome

The WHO has suggested the following working definition for the metabolic syndrome: Glucose intolerance (impaired glucose tolerance or diabetes mellitus) and / or insulin resistance together with two or more of the following components (Fig. 2.1.5/1) (Alberti et al., 1998):

1. Impaired glucose regulation or diabetes
2. Insulin resistance (under hyperinsulinaemic euglycaemic conditions, glucose uptake below lowest quartile for background population under investigation)
3. Raised arterial pressure ≥ 160/90 mmHg
4. Raised plasma triglycerides (≥ 1.7 mmol/L1) and/or low HDL-cholesterol < 0.9 mmol/L for men; <1.0 mmol/L for women)
5. Central obesity (males: waist to hip ratio >0.90; females: waist to hip ratio >O.85) and/or BMI >30kgm^{-2}
6. Microalbuminuria (urinary albumin excretion rate ≥ 20 μg min^{-1} or albumin:creatinine ratio ≥ 20 mg g^{-1}).

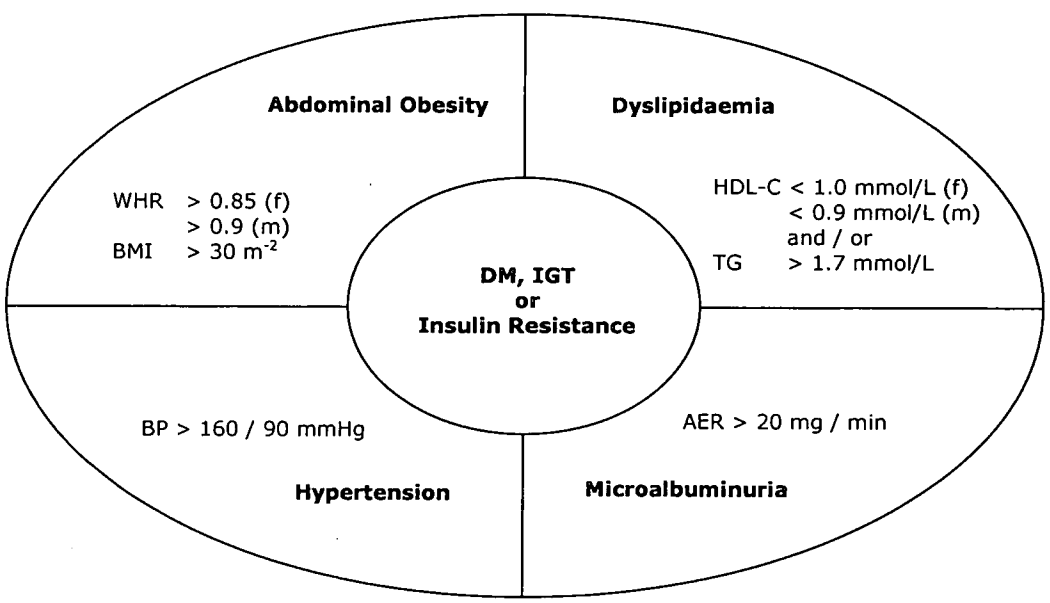


Fig. 2.1.5/1. Components of the metabolic syndrome
Adapted from: Groop and Orho-Melander, 2001.

Several other components of the Metabolic Syndrome have been described (e.g. hyperuricaemia, coagulation disorders, raised PAI-1) but they are not necessary for the recognition of the condition. The presence of the metabolic syndrome was associated with reduced survival, particularly because of increased cardiovascular mortality (Alberti et al., 1998).

Insulin resistance clusters in families and 45% of first-degree relatives of patients with Type 2 diabetes are insulin resistant compared to 20% of individuals without a family history of diabetes (Beck-Nielsen et al., 1994 and Reaven, 1988).

2.1.6 Impact of the ADA 1997 and WHO 1998 diagnostic criteria on the prevalence of diabetes and IFG/IGT

The main advantage of the new ADA diagnostic criteria, requiring only a fasting plasma glucose value for people without overt clinical symptoms of diabetes, is that it provides a much simpler method to diagnose diabetes than the oral glucose tolerance test required by the WHO. Since the 1997 ADA criteria were published, several reports examined the implications of these recommendations. By applying these criteria to the NHANES III data, Harris et al. (1998) found that fewer people were classified as having undiagnosed diabetes than by the WHO system (4.4% vs. 6.4%) (Table 2.1.6/1). Likewise, fewer people were also classified as having impaired fasting glucose by the ADA criteria than as having impaired glucose tolerance by the 1985 WHO criteria. Harris et al. (1998) argues that the prognostic significance of impaired fasting glucose has yet to be defined but is likely to also be a pre-diabetic condition because elevated fasting glucose in general is known to predict subsequent Type 2 diabetes.

In the Pima Indian population, persons in whom Type 2 diabetes developed in later life, had significantly higher plasma glucose concentrations while fasting and two hours after carbohydrate loading than white or black subjects (Saad et al, 1988). In this study the rate of deterioration to Type 2 diabetes increased with increasing plasma glucose concentrations during fasting and after carbohydrate loading. However, the mean fasting plasma glucose in those who developed diabetes after a mean follow-up of 3.3 years was 5.84 mmol/L, which is below the 6.1 mmol/L level defining IFG as suggested as cut-off point by the ADA.

In the Hoorn study (Vegt et al, 1998) the prevalence of diabetes was not affected by applying the 1997 ADA criteria. Compared with the classification according to the 1985 WHO criteria,

18.9% of all subjects shifted to another glucose intolerance group when applying the 1997 ADA criteria, without affecting the overall prevalence of diabetes. However, 38.1 % of the subjects diagnosed as having diabetes by the WHO criteria were classified as either IFG or as NFG by the a ADA criteria. Also, 39.2% of the subjects diagnosed as having diabetes according to the ADA criteria were not diagnosed as having diabetes by the WHO criteria. In the Hoorn study population, the agreement between the 1997 ADA criteria and the 1985 WHO criteria was poor, as was reflected in the overall κ of 0.33 (Table 2.1.6/1).

Unwin et al. (1998) applied the 1997 ADA criteria to three U.K. populations. Using fasting plasma glucose only, the prevalence of diabetes was higher in all ethnic groups than based on 1985 WHO criteria. The absolute difference in the European population was 2.3% (95% CI 1.3%-3.3%); in the Chinese population it was 1.5 % (0.3-2.7); and in the South Asian population it was 1.3% (0.4-2.2) (Table 2.1.6/1). In both the European and Chinese populations the prevalence of the impaired fasting glucose category was higher using the ADA criteria than the 1985 WHO category of impaired glucose tolerance. Again the difference was most marked in the European population (18.9% vs. 12.5%). In the South Asian population the prevalence of impaired fasting glucose and impaired glucose tolerance was very similar (19.0% vs. 18.7%).

There were some marked changes in the classification of individuals between the 1985 WHO and new fasting glucose ADA criteria. For example, 12.5 % of the European population had IGT, yet 5.9 % were normal and 1.8 % had diabetes on the ADA criteria; and of the 20.1% of South Asians classified as having diabetes by WHO criteria 2.1 % were classified as not having diabetes on ADA criteria. Unwin et al. (1998) suggested that according to their data, it would be prudent to treat the ADA recommendation with some caution.

In six of the DECODE populations (DECODE, 1998) the prevalence of diabetes was lower with the ADA criteria than with the 1985 WHO criteria, while in 10 populations it was higher with the ADA than with the WHO criteria. The difference in prevalence with these two criteria ranged from -4.0% to 13.2% and the overall difference was 0.5%. Pronounced disagreement was also found in these studies (Fig. 2.1.6/1).

Table 2.1.6/1

Comparisons of 1997 ADA and 1998 WHO diagnostic categories with the 1980/1985 WHO diagnostic categories

(age yr)	Normal ADA (WHO) %	IFG ADA %	IGT %	DM ADA (WHO) %	Concordance ADA vs WHO (Diabetes) %	Concordance WHO vs ADA (Diabetes) %	Overall agreement k (95% CI)	Reference
NHANES III (44-74)[a]	77.6 (66.8)	10.1	15.6	4.4 (6.4)				Harris et al, 1997
Hoorn (50-75)[b]		12	10.6	5.1 (5.0)	61.9	60.8	0.33 (0.28-0.38)	Vegt et al, 1998
UK[b] European (25-74)	74.1 (82.7)	18.9	12.5	7.1 (4.8)			0.42 (0.28-0.56)	Unwin et al, 1998
Chinese (25-64)	79.3 (83.3)	14.5	12	6.2 (4.7)			0.58 (0.36-0.80)	
South Asian (25-74)	59.7 (61.2)	19	18.7	21.4 (20.1)			0.59 (0.48-0.70)	
DECODE[a] (Overall)				7.7 (7.2)				DECODE, 1998
Seattle[a] (65-100 yr)	77.7 (53.2)	14.6	32.1	7.7 (14.8)			0.275 (SE 0.012)	Wahl et al, 1998
Seattlea Afr.-American (65 -100 (yr)	91.2 (58.4)	6.1	29.8	2.7 (11.8)			0.136 (SE 0.039)	
Melbourne (Overall)				11.3 (11.4)	-19 to +30			Shaw et al, 1999
Cameroon[b]							0.86 (0.58 – 1)	
Evodoula		0.3	3.6	0.7 (0.7)				
Yaounde		0.3	3.4	1.2(1.5)			0.61 (0.30 – 0.93)	
South Africa[b]								Levitt et al, 2000
Cape Town		2.3	7.1	9.2 (8.0)			0.45 (0.28 – 0.62)	
Mamre		12.1	8.1	9.8 (8.5)			0.56 (0.42 – 0.71)	
Mangaung[#]		9.1	14.8	10.6 (8.2)			0.50 (0.36 – 0.65)	
QwaQwa[#]		3.6	12.9	6.0 (6.0)			0.59 (0.42 – 0.75)	
Durban		4.3	9	5.9 (4.4			0.80 (0.62 – 0.97)	
Tanzania[b]								
Dar-es-Salaam		2.7	10.6	2.5 (1.4)			0.17 (-0.19 – 0.45)	
Kilimanjaro		2	6.9	1.2 (0.8)			0.18 (0.02) – 0.34)	
Morogoro		1.7	8.1	1.2 (1.0)			0.23 (.0.08 - 0.39)	
Mara		3.9	8.4	4.1 (1.3)				

a Known diabetics excluded

b Known diabetics included

[#] Age-standardised for prevalence calculated for those $\geq$ 30 years

Values of the k statistic greater than 0.75 indicate good agreement, whereas values less than 0.25 represent poor agreement (Wahl et al, 1998)

A total of 1517 individuals had diabetes according to either the ADA or the WHO criteria. Among 904 who had diabetes according to the WHO criteria, 473 (52%) had a fasting plasma glucose concentration (<7.0 mmol/L) that did not indicate diabetes (Fig. 2.1.6/1). Among 1044 who had diabetes according to the ADA criteria, 59% failed to reach the 2 hour glucose diagnostic value for diabetes (11.1 mmol/L). The authors of the DECODE study pointed out that a change in diagnostic procedure is not a simple issue. Another important consequence of the adoption of the ADA criteria is that the diabetic status of a large number of individuals will be changed. This may result in serious consequences for individuals who will be labelled as diabetic with personal and economical consequences. This disagreement in classification goes in both directions, from diabetes to normal and from normal to diabetes. Among individuals with diabetes according to the ADA criteria but a 2 hour post-load value below 11.1 mmol/L, the median 2 hour blood glucose was 8.0 mmol/L and for individuals with a 2 hour value of 11 mmol/L and a fasting value of <7.0 mmol/L, the median fasting value was 6.0 mmol/L. Therefore, individuals qualifying as diabetic on one criterion but not on the other are not just borderline cases who almost reach the diagnostic level. The WHO criteria were more likely to diagnose diabetes in **lean** individuals, while the ADA criteria were more likely to identify **middle-aged obese** individuals. Thus, the disagreement does not represent a "random

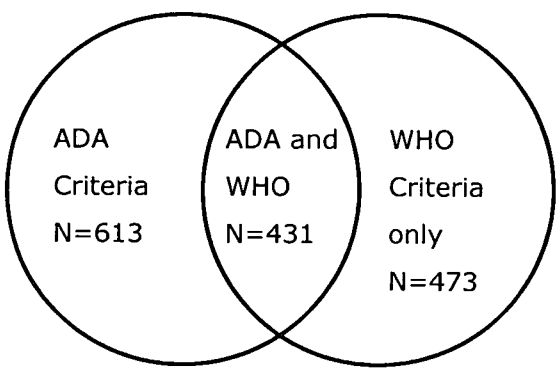


Fig. 2.1.6/1. Prevalence of diabetes with WHO and ADA diagnostic criteria in 16 European populations (DECODE, 1998).

reclassification" but a systematic bias resulting in a change in diabetic phenotype. On the basis of the DECODE study and the fact that prospective data answering some of the above mentioned questions are available for reanalysis, the authors of the DECODE study recommended that changes in the diagnostic criteria should be undertaken only after analysis of solid prospective data that are available and currently being prepared.

The 1997 ADA criteria were also applied to two groups of elderly American subjects (Table 2.1.6/1) (Wahl et al., 1998). Large discrepancies were found in the prevalence of diabetes between the 1985 WHO and ADA diagnostic criteria. The prevalence of normoglycaemia was 77.7% with ADA fasting criteria, versus 53.2% with WHO criteria. By contrast, the prevalence of IFG with ADA fasting criteria was 14,6%, which was less than half the 32.1% prevalence of IGT with WHO criteria. Similarly, for untreated diabetes the prevalence was 7.7% with ADA criteria versus 14.8% with WHO criteria. Overall, among participants who had had no previous treatment for diabetes, substantially fewer men and women were identified with untreated diabetes by ADA fasting criteria than by WHO criteria. 1102 (76%) participants who had IGT by WHO criteria were classified as normoglycaemic by ADA fasting criteria. In the group of elderly African-Americans the WHO classification results were similar to those of the other cohort, whereas the results with ADA fasting criteria had a lower prevalence of IFG and diabetes. Seventy-four of the 78 African-American participants with IGT according to WHO criteria were classified as normal by ADA fasting criteria. There was no association between WHO or ADA categories and age or sex. The κ statistic to measure agreement between the two classification schemes was low: 0.136 (SE 0.039). Thus, differences of similar size, magnitude, and direction were seen in both cohorts. Wahl et al., (1998) suggested that the different prevalence of diabetes among the elderly may be due to the increased sensitivity of the 2 h glucose values to ageing. In the main cohort, WHO diagnostic categories were significantly associated with age, whereas ADA categories based on fasting glucose values, were not. Wahl et al., (1998) concluded that, compared with WHO criteria, ADA fasting criteria significantly underestimate the prevalence of untreated diabetes in older adults. To obtain equivalent WHO and ADA diabetes prevalence estimates in this elderly population, the cut-off point of 2 h glucose values would have had to be increased to 13.32 mmol/L or fasting glucose cut-off points reduced to 6.38 mmol/L.

Shaw et al. (1999) analysed surveys of southern hemisphere island populations coordinated from a single centre (International Diabetes Institute, Melbourne. Australia).

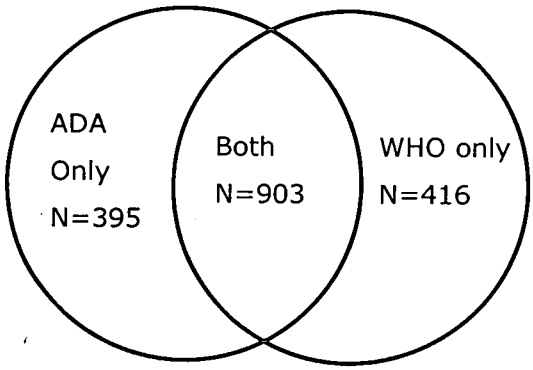


Fig. 2.1.6/2. Number of subjects without previously diagnosed diabetes classified as ADA only (FPG ≥ 7.0 mmol/L and 2-h PG < 11.1 mmol/L), WHO only (FPG < 7.0 mmol/L) or both (FPG ≥ 7.0 mnlol/1 and 2-h PG ≥ 11.1 mmol/L) (Shaw et al., 1999).

The main results from the report are shown in Table 2.1.6/1 and Fig. 2.1.6/2. In three populations, the total prevalence was significantly higher when using the new ADA criteria; in three populations, it was signifcantly lower; and in the remaining three, there were no significant changes. The change in the prevalence varied between – 2.8 percentage points and +4.1 percentage points, but when the ADA prevalence was calculated as a percentage of the WHO prevalence, it varied between a 30% increase (Western Samoa) and a 19% decrease (Kiribati). Obesity was also an important determining factor in this study to determine on which criterion diabetes was diagnosed. This was apparent from the finding that the two studies (Nauru and Western Samoa) with the highest mean population BMI also had the highest proportion of diabetic subjects with FPG ≥ 7.0 mmol/L. This finding was not consistent among all the populations in this study. The influence of age was also not clear-cut and was only significant when comparing those ≥ 64 years or age with the rest. These older people were also more likely to be only in the WHO diagnostic group than were younger people. In conclusion, this study showed that changing over to using the FPG ≥ 7.0 mmol/L cut-off can have variable, unpredictable, and sometimes quite large effects on both the number of people and the specific individuals classified as having diabetes. Furhermore, diabetic subjects defined by the new FPG level, as a group, will be more obese than those identified by the 2-h PG level.

The data from several studies conducted in Africa were also re-analysed to investigate the impact of the 1997 ADA criteria on the prevalence of diabetes and IGT in African subjects

(Levitt et al 2000). Data were available from rural and urban communities in Cameroon (n = 1804), Tanzania (n = 10 013) and South Africa (n = 3 799) (Table 2.1.6/1). The prevalence of diabetes based on the ADA criteria, was higher in all Tanzanian surveys and in four of the five South African surveys, and was unchanged in one South African study and lower in both surveys from Cameroon, than when utilizing the WHO criteria. In all but one instance (Mara), the absolute change in prevalence using the new criteria was small (< 2.5%). When combining both sets of criteria, as in the new WHO criteria, the prevalence of diabetes (crude, non age-standardized) was higher in 10 of the 11 surveys. In the other survey the combined prevalence was the same as that obtained when using the WHO criteria but higher than the prevalence when utilizing the ADA criteria. The prevalence of IFG was lower than the prevalence of IGT with the exception of the Mamre community in South Africa. There was a poor level of concordance in the classification of individuals as diabetic using the ADA and WHO criteria and the range in Kappa statistic between the surveys was considerable. The Kappa statistic was lowest (< 0.25) in the Tanzanian surveys, intermediate in four of the South African surveys and highest (0.86 and 0.61) in the Cameroon and one of the South African surveys. The authors of this study concluded that application of the new WHO criteria (which recommend use of both the new fasting and original post-glucose load levels) based on the data presented in this paper, would increase estimates of the total prevalence of diabetes internationally. In the African surveys agreement between the categories IFG and IGT in the data was even poorer than agreement with diagnoses of diabetes. The present data, and those of others, show that IFG and IGT are not analogous.

A Lancet editorial (Keen, 1998) emphasized that much of the current knowledge of the epidemiology and natural history of glucose intolerance, diabetes, and the health risks associated with them are based on the 2-h blood glucose. Although the new FPG has similar cross-sectional associations, when applied to populations it seems to select a rather different set of people. When applied to individual diagnosis, the new fasting diagnostic strategy is also likely to reshape some of the average characteristics of patients with newly detected Type 2 diabetes i.e. to alter the type 2 phenotype.

2.2 Prevalence of diabetes mellitus in black South Africans

2.2.1 Type 1 diabetes

Insulin dependent diabetes is judged to be present when the classical symptoms of diabetes (thirst, polyuria, wasting and stupor, or coma) are associated with readily detectable

concentrations of glucose and ketone bodies in the blood and urine. Insulin treatment is necessary, not only to control hyperglycaemia, but to prevent spontaneous ketosis and death (WHO, 1985).Technical Report,In some non-Europeans, it may be difficult to distinguish between IDDM and Type 2 diabetes and classification difficulties may be encountered in 20-30% of patients (WHO, 1985).

Historically IDDM was regarded as extremely rare in black children in the first decade of life. Seftel stated in 1963 that they still had to encounter an African case in this age group. Walker (1966) commented on surveys where "thousands" of black schoolchildren were screened for glycosuria and all were negative. The explanation that recently still prevailed was that due to the rapidity of onset of symptoms, death ensued before the patient could present to hospital (Marine , 1969 and Rwiza et al, 1986). It is, however, doubtful whether the same is still true for South Africa.

Gill and Huddle (1991) found that 59,2% of patients who regularly attended the diabetes clinic at Baragwanath Hospital were insulin requiring, confirming other reports of a high proportion of insulin-treated patients attending diabetes clinics in Africa. After categorization of their patients into a young group (age of onset of diabetes < 30 years) and a older group (age of onset ≥ 30 years) and after C-peptide measurement, the authors concluded that the older group of insulin-treated patients most likely had Type 2 diabetes. After recalculation of their data it seems that 16% of patients attending the Baragwanath diabetes clinic are possibly true insulin-dependent patients (Gill and Huddle, 1991). Kalk, et al, (1993) reported that the peak age of onset of Type 1 diabetes in black patients was 22 – 23 years compared with white patients in whom the peak age of onset was 12 – 13 years. Diabetes was diagnosed in childhood in only 7% of the black patients. The reasons for the observed age differences in Africans were not clear.

In a survey of 42981 schoolchildren aged 7-14 years in Khartoum, Sudan, Elamin et al. (1989) found the crude prevalence of IDDM to be 0.95/1000. This is possibly the only reported study from Africa employing WHO guidelines to determine the prevalence of IDDM. McLarty (1990) reported from Dar es Salaam that 21.8% of diabetics attending the Muhimbili Medical Centre required insulin for adequate control. The annual incidence of juvenile diabetes for both sexes was estimated to be 1.5 per 100000 of the population aged 0-19 years in Tanzania (Swai et al, 1993).

Neither from South Africa nor from the rest of Africa is any data available on the prevalence of CHD in black Type 1 diabetic patients. The clinical impression however, is that the prevalence of CHD in black diabetic patients is very low (McLarty et al., 1990). Although heart disease and specifically CHD is regarded as the leading cause of death for blacks and whites in the United States (Saunders et al., 1991), no mention was made of the contribution of diabetes to CHD mortality in US blacks. It is reasonable to assume that the potential of IDDM to contribute to the future emergence of CHD in the South African black population is extremely low and will probably remain so for the foreseeable future.

It is customary when reporting on the prevalence of diabetes not to distinguish between Type 1 and Type 2 diabetes since the prevalence of Type 1 diabetes is relative low compared to Type 2 diabetes. Furthermore, the prevalence of true Type 1 diabetes is unknown in many countries especially in Africa.

2.2.2 Type 2 diabetes

2.2.2.1 HISTORICAL STUDIES

One of the earliest references to the relative rarity of diabetes in the black community came from Natal. Cosnett (1957) commented on the rarity of diabetes as a cause of admission to hospital for Bantu patients. An admission rate of 0.53 diabetics per 1000 admissions for blacks was found compared to 19.2 diabetics per 1000 admissions for Indians admitted to the King Edward VIII Hospital in Durban.

During a 15 month period Sanders (1960) identified 45 known diabetics (including one juvenile diabetic) who attended the Out-patient Department of an urban hospital at the Langa township near Cape Town. The diagnosis was later confirmed by referring the patients to Groote Schuur Hospital Out-patient Department. No mention was made of the methods employed to confirm the diagnosis. According to the estimated size of the township he calculated the prevalence of diabetes to be 0.22% for this population. This report compelled Pollitzer and Schneider (1960) to comment that the percentage of cases in Langa was at least twice that suggested by Sanders since only half of diabetics present to hospital because of their symptoms.

Campbell (1960) also reacted to Sanders' report describing 133 out of 264 Bantu diabetics who attended the King Edward VIII Hospital in Durban in some detail. Campbell failed to

define "fat" but claimed that "no less than 53% of these fat middle-aged diabetics had exposure periods of between 17 and 24 years to city life before developing the disease, and that 40% had exposure periods between 19 and 22 years". Unfortunately he could not provide any indication of the prevalence of diabetes in the black community.

Seftel and Abrams (1960) also conducted a hospital-based survey of urbanized blacks 30 years and older attending the Casualty Department of the Baragwanath Hospital to determine the prevalence of diabetes. They surveyed 2122 subjects (males 1078, and females 1044) and discovered 18 new diabetics (14 females and 4 males) in addition to 9 known cases (7 females and 2 males) yielding a total prevalence of 1.27%. The methods employed in this study was not discussed.

A study comparing the prevalence of diabetes between a rural and an urban black population was reported by Politzer and Schneider in 1962. The rural group comprised 3000 subjects (mean age 36.8 years) selected from patients attending the out-patient section of a hospital in the Butha-Buthe district of Basutoland (Lesotho). The urban group consisted of 3121 new black outpatients (mean age 31.1 years) attending a hospital in Johannesburg. All subjects were 10 years and older and they were screened for post-prandial glycosuria followed by a blood sugar estimation if glycosuria was present. Diabetes was diagnosed when blood sugar levels exceeded 7.8 mmol/L. The prevalence of diabetes was 0.23% and 0.58% for the rural and urban group respectively. Excluding subjects < 30 years, the corresponding prevalences were 0.36% and 1.16%. The study populations differed widely as regards their age and sex distribution and the reported rates were not age and sex adjusted to the respective population.

Until recently, no formal studies on the prevalence of diabetes amongst blacks in Natal were available. Campbell (1963) attributed this to ever-changing urban populations as well as the fact that rural Africans were distrustful towards these kind of surveys. In spite of this Campbell reported a prevalence of 0.17% post-prandial glycosuria in a sample of 1812 black, mostly Xhosa, sugar-cane workers.

Seftel et al. (1963) stated that the true prevalence of diabetes in blacks is unknown since most surveys up to that time were based on hospital populations and were biased to a greater or lesser degree. For the first time an attempt was also made to establish the prevalence of diabetes in the elderly. Seftel et al. (1963) found diabetes to be present in 4% of a sample of

300 black old-age pensioners. Interestingly, in the same paper Seftel also referred to the very first attempt to determine the prevalence of diabetes in the Orange Free State. Dr A.R.P. Walker examined 500 black subjects in the Thaba Nchu district but failed to detect a single case of diabetes. Unfortunately the methodology was not mentioned and the study was never published. Based on this survey as well as Politzer and Schneider's original study (1962), Seftel (1963) concluded that diabetes appeared uncommon in the rural black probably because they were not as obese as city-dwellers.

These early surveys to determine the prevalence of diabetes in black communities were all hospital-based, the methodology was poorly described and sampling was inconsistent, and the results inevitably biased. The prevalence rates reported in these studies merely represented an approximation of the true prevalence of diabetes in the communities.

In the era before the World Health Organisation's citeria for the diagnosis of diabetes were established, the late Prof W.P.U. Jackson's group from Cape Town performed the only scientific, population-based studies examining the prevalence of diabetes in the black communities (Goldberg et al in 1969). The first sampling frame constituted all people 10 years and older and was drawn from Guguletu near Cape Town. A cluster-type sampling procedure was used and 882 respondents were examined and the response rate was 85.5%. Subjects were first screened by means of urine testing (Tes-Tape) and/or a capillary blood-sugar measurement one hour after a 50g oral glucose load. All positive screenees (blood-sugar concentration above 9 mmol/L or glycosuria present) were subjected to a 50g oral glucose tolerance test (OGTT) after an overnight fast. Diabetes was considered present if two of the three estimations of blood-sugar made while fasting, after 60 minutes and after 120 minutes exceeded 6.7, 11.1 and 7.8 mmol/L respectively.

The crude prevalence of diabetes was 2.7% in this study. The prevalence was not age and sex standardized to that of the population. Unfortunately the authors did not state the age distribution of the sample and only commented that the population was young compared with White populations. Previously known diabetes was present in 0.7% and newly discovered diabetes in 2.0% of the study population. A peculiar finding of this study was that the highest prevalence of discovered diabetes occurred in the middle-aged and not in the elderly group as expected. In a different publication Marine et al. (1969) also discussed the results of this study and provided the age structure of the sample. It was evident that only 7.4% of the study-population was older than 55 years, possibly explaining the relative absence of elderly

diabetics. Obesity (15% or more above ideal weight as obtained from Documenta Geigi tables) was present in more than 50% of females and in 8% of males. Recalculation of Marine's data showed that 7% of subjects 35 years and older were diabetic. No known diabetics under the age of 20 years were found - the youngest diabetic in this survey was 35 years old. This finding was in keeping with that of Seftel (1963) who commented that they had never encountered a case in the first decade of life.

In a later publication (Jackson, 1978) a crude prevalence of diabetes of 3.6% in subjects over the age of 15 years was reported for this survey. After adjusting to the age distribution of the white population, this figure rose to 4.2%. Jackson (1978) remarked that the prevalence of diabetes in Cape Town blacks approached that of Cape Town whites and that the potential for diabetes among African people appeared to be similar to that of white people.

Goldberg's second sample (1969) was drawn from Mamelodi near Pretoria and comprised 2015 subjects 10 years and older. The actual method of the sampling procedure was not discussed. In this study diabetes was diagnosed when the 120 minute post glucose load (50g) plasma glucose exceeded 8.4 mmol/L. It was not stated whether the subjects were fasting or not. The crude prevalence of diabetes in this study was 2.9%. Again no age structure was provided and accordingly prevalence rates for the age group 35 years and older could not be calculated. Only one previously known diabetic was encountered in this study possibly reflecting the low level of diabetes awareness in this community. A definite increase in the percentage of newly discovered diabetics with increasing age was evident in this study. Jackson (1978) emphasized that among some African groups (referring to Mamelodi blacks), hyperglycaemia may be frequent, but without symptoms and without general awareness of the condition. Several of the subjects in that study had blood glucose levels above 33.6 mmol/L without symptoms being present.

Although the methodology of these two population-based studies differed slightly, the results were comparable and provided the first evidence that diabetes mellitus was not the rare disorder in the black community as was commonly believed. It also underscored the fact that diabetes in blacks was rare under the age of 35 years and mostly undiagnosed. The notion that diabetes is a rare disorder in rural blacks (Seftel, 1963) persisted until the present time since no population-based studies were ever conducted in South Africa to determine the true prevalence of diabetes in the rural areas.

Walker (1981) predicted that urbanization of blacks and a rise in their socio-economic status will increase this population's proneness to obesity, hypertension, diabetes and strokes. The prediction for diabetes was borne out by at least two published studies performed after the WHO-criteria became established.

2.2.2.2 STUDIES USING WHO 1985 DIAGNOSTIC CRITERIA

In the first survey conducted in the mid-eighties (personal communication) but reported only in 1993, Omar and associates studied the prevalence of diabetes in Zulus living in Umlazi, a township on the outskirts of Durban. A cluster sampling technique was used and 238 households selected. A total of 479 subjects (141 men and 338 women) 15 years and older, participated in the study. The response rate was 78%. Diabetes and IGT was diagnosed according to the revised 1985 WHO criteria. The crude prevalence of diabetes was 4.2% (women 5.2% and men 2.3%). The overall age- and sex-adjusted prevalence was 5.3%. The crude prevalence of IGT was 6.9% (women 5.5% and men 11.5%). The age- and sex-adjusted prevalence of IGT was 7.7%. The authors speculated that a rising BMI and obesity constitute important risk factors in the emergence of diabetes in women.

In the second survey, Levitt and co-workers (1993) studied the prevalence of non-insulin-dependent diabetes mellitus and associated risk factors in urban blacks in the greater Cape Town. The sampling frame consisted of 1000 subjects, 30 years and older selected with a three-stage, proportional, stratified, random cluster method. Diabetes and IGT were diagnosed according to the revised 1985 WHO criteria. The analysis was based on 729 subjects reflecting a response rate of 79%. The crude prevalence of diabetes was 6.3% and of IGT, 5.9%. When age-adjusted to the world population, the prevalence was 8.0% (CI 5.8%-10.3%) for diabetes and 7.0% (CI 4.9%-9.1%) for IGT. The prevalence of diabetes among participants 30-65 years of age, age-adjusted to the world population, was 6.9% (CI 4.7%-9.1%); in men it was 6.1% (CI 4.4%-7.9%) and in women 7.4% (CI 4.6%-10.1%). Similarly, the prevalence of IGT in the 30-65 year age group was 7% (CI 4.6%-9.3%). The crude prevalence of diabetes was similar in men (6.5%) and women (6.4%). The mean age of those with diabetes was 56 years, compared with 44 years in the non-diabetic participants. Of the 46 diabetic subjects, 24 had been diagnosed previously of which only 16 (66%) were seeing a medical practitioner or clinic for their diabetes.

Levitt and co-workers (1993) also performed logistic regression analysis to assess the independent nature of risk factors for diabetes. The following factors independently predicted diabetes: age (odds ratio 4.18 (95% CI 2.48-9.52)), upper segment body fat distribution

(odds ratio 2.94 (95% CI 1.47-5.64)), urbanisation i.e. more than 40% of life spent in an urban area (odds ratio 2.32 (95% CI 1.09-4.95)), and obesity (odds ratio 2.31 (95% CI 1.06-5.02)). The selected model did not indicate sex, physical activity, alcohol intake, or a family history of non-insulin-dependent diabetes, as risk factors. Interestingly, multivariate analysis indicated that age was the only independent predictor of IGT in this survey (odds ratio 4.06 (95% CI 2.06-6.06)).

The more recent Cape Town study (Levitt et al, 1993) indicated that the prevalence of diabetes was considerably higher in Cape Town blacks than rates reported 25 years earlier (Goldberg, 1969) and much higher than rates reported from Tanzania (0.87%) (McLarty et al., 1989). Differences in methodology, degree of obesity and level of urbanisation were considered as factors to explain these differences.

Erasmus and co-workers studied the prevalence of diabetes and IGT in 374 Xhosa factory workers in Umtata, Eastern Cape (Erasmus et al, 2001). The subjects were 20 years and older and the age-adjusted prevalence of diabetes and IGT was 2.4% and 2.7% respectively.

The prevalence of Type 2 diabetes was also studied in the Western Cape in a population of people from mixed ancestry (Levitt et al, 1999). In this sample of 974 participants (age range 15-86 years) the crude prevalence of Type 2 diabetes was 7.1% (5.8% in men and 8.1% in women). The crude prevalence of IGT was 8.0% (7.7% if adjusted for the sample realization); 6.5% in men and 9.2% in women. The mean age of the 69 subjects with diabetes was 55.0 (SD 11.1) years and of these, 44 were previously identified. Age, family history of diabetes, waist circumference and physical inactivity were all identified as independent risk factors for Type 2 diabetes.

2.2.2.3 South Africa's Demographic and Health Survey

South Africa's first demographic and health survey, a landmark study, was conducted during 1998 in which 13827 adults (15 years and over) were interviewed. A response rate of 93% was achieved in this study (SADHS, 1998). Just over 60 percent of respondents lived in urban areas, according to the definition of urban (within a proclaimed municipality or the boundaries of a local authority) used by Statistics South Africa. In this survey the self-reported prevalence of diabetes in males and females ≥ 15 years in South Africa was 2.4% and 3.7% respectively. The self-reported prevalence of diabetes in males living in urban areas was 2.9% compared to

1.7% for those living in non-urban areas. The corresponding figures for females were 4.4% and 2.7% respectively (Table 2.2.2.3/1 and Table 2.2.2.3/2).

Large differences in the self-reported prevalence of diabetes in the different provinces were observed for men (Table 2.2.2.3/1). These rates ranged from 0.9% in the Northern Province to 3.3% in Gauteng. The self-reported rates for the Free State province and Western Cape were 1.3 and 3.2% respectively. Similar differences were observed for women (Table 2.2.2.3/2). The rates for women ranged from 1.1% in North West to 5.9% in KwaZulu Natal. The self-reported rates for Free State and Western Cape women were 2.3% and 4.9% respectively (SADHS, 1998).

Due to differences in methodology between historic and more recent studies, it is unclear whether the prevalence of diabetes is on the increase in South Africa, especially in the rapidly urbanizing black communities. Longitudinal studies conforming to WHO criteria are needed to resolve this issue as well as to confirm previously identified risk factors for the development of IGT and diabetes in our diverse population groups.

Table 2.2.2.3/1 — Self-reported chronic conditions-men

Percentage of male respondents age 15 and above who report that they have various chronic health conditions, according to background characteristics, South Africa 1998

Background characteristic	Chronic condition									Number of adults
	Blood pressure	Ischaemic heart disease	Stroke	Hyper-cholesterolaemia	Diabetes	Emphysema	Asthma	Tuberculosis	Cancer	
Age										
15-24	0.2	0.3	0.0	0.2	0.1	2.3	2.9	0.8	0.0	1,816
25-34	2.7	1.9	0.7	1.2	0.8	2.8	1.9	2.4	0.2	1,123
35-44	7.5	2.8	0.5	1.8	2.5	2.9	4.0	4.1	0.0	1,005
45-54	18.0	4.6	2.0	4.3	5.3	8.6	4.7	5.2	0.5	701
55-64	16.9	6.6	2.0	3.8	7.8	6.6	5.3	4.0	0.1	518
65+	25.0	7.7	2.3	3.7	4.8	8.5	7.2	4.9	1.6	507
Residence										
Urban	9.3	3.1	0.7	2.2	2.9	4.9	4.1	2.6	0.3	3,569
Non-urban	5.5	2.4	1.2	1.2	1.7	3.2	3.2	3.3	0.2	2,102
Province										
Western Cape	9.2	2.8	0.9	1.7	3.2	9.4	4.6	3.2	0.3	721
Eastern Cape	9.0	3.5	0.9	1.3	2.7	5.2	4.7	5.8	0.2	758
Northern Cape	13.2	4.1	1.3	1.8	2.1	5.6	3.2	3.2	0.2	135
Free State	7.2	2.6	0.4	1.4	1.3	0.7	1.3	2.5	0.4	444
KwaZulu Natal	7.5	3.2	1.6	1.7	3.1	3.4	4.9	3.6	0.2	1,064
North West	4.8	2.4	0.3	1.1	0.9	1.4	2.4	1.2	0.0	551
Gauteng	10.7	3.1	0.7	4.0	3.3	5.6	4.5	1.7	0.5	1,099
Mpumalanga	4.9	1.8	1.1	0.9	2.0	2.9	2.9	2.1	0.2	377
Northern	4.4	2.0	0.4	0.2	0.9	1.1	1.3	1.7	0.2	521
Education										
No education	11.6	4.8	2.8	0.3	2.9	4.3	5.4	5.8	0.2	562
Sub A - Std 3	7.2	2.6	0.9	0.4	2.7	4.4	5.7	5.0	0.0	777
Std 4 - Std 5	7.0	2.7	0.4	0.9	1.2	3.2	3.7	3.5	0.2	755
Std 6 - Std 9	6.4	2.1	0.6	1.0	2.3	3.9	2.6	2.2	0.2	2,297
Std 10	8.7	3.0	1.0	3.7	2.7	5.0	4.0	1.5	0.2	801
Higher	10.9	3.5	0.5	8.3	4.0	6.5	3.6	0.4	1.4	440
Ethnicity										
African	5.8	1.9	0.7	0.2	1.5	1.8	3.0	3.0	0.1	4,257
Afr. urban	6.9	1.7	0.5	0.2	1.6	1.5	3.0	2.8	0.2	2,375
Afr. non-urban	4.4	2.0	1.0	0.2	1.5	2.2	3.1	3.2	0.1	1,882
Coloured	9.0	2.9	0.9	1.3	3.1	8.6	4.5	4.5	0.3	637
White	21.1	8.6	1.6	12.4	6.0	16.5	7.7	0.7	1.4	564
Asian	11.9	8.0	1.5	8.4	8.5	6.4	5.5	2.4	0.0	195
Total	7.9	2.9	0.9	1.8	2.4	4.2	3.7	2.9	0.3	5,671

Note: Total includes 40 men with education level missing and 18 men with ethnic group missing.

From: South Africa Demographic and Health Survey, 1998. Preliminary Report, MRC / Department of Health

Table 2.2.2.3/2 — Self-reported chronic conditions-women

Percentage of male respondents age 15 and above who report that they have various chronic health conditions, according to background characteristics, South Africa 1998

Background characteristic	Chronic condition									Number of adults
	Blood pressure	Ischaemic heart disease	Stroke	Hyper-cholesterolaemia	Diabetes	Emphysema	Asthma	Tuberculosis	Cancer	
Age										
15-24	3.8	1.7	0.2	0.5	0.5	3.5	2.5	1.2	0.0	2,084
25-34	8.0	4.2	0.6	0.8	1.6	3.7	3.2	1.8	0.3	1,721
35-44	15.1	4.3	1.0	0.3	2.7	4.4	3.4	2.0	0.6	1,460
45-54	30.5	7.2	1.0	3.0	7.2	6.5	5.6	2.6	0.9	1,116
55-64	40.9	11.7	1.9	2.5	7.6	6.0	5.2	2.2	1.3	914
65+	42.2	14.7	2.6	2.8	8.9	7.6	5.1	3.1	1.7	861
Residence										
Urban	20.6	5.3	1.1	1.6	4.4	5.8	4.3	1.6	1.0	4,999
Non-urban	15.4	6.9	0.7	0.8	2.7	3.3	3.1	2.6	0.1	3,157
Province										
Western Cape	19.3	5.2	2.4	3.0	4.9	11.4	6.2	2.3	2.0	799
Eastern Cape	18.9	6.5	1.2	1.1	3.5	4.9	4.9	4.3	0.6	1,161
Northern Cape	22.8	5.2	0.9	1.1	2.9	5.5	3.3	2.9	0.4	168
Free State	20.4	7.7	0.8	0.0	2.3	0.3	2.7	1.9	0.3	519
KwaZulu Natal	20.7	7.0	1.1	1.0	5.9	3.1	4.5	1.8	0.4	1,608
North West	14.9	5.4	0.9	0.5	1.1	2.0	3.2	1.3	0.0	647
Gauteng	21.7	5.0	0.4	2.2	4.3	7.9	3.5	1.1	0.8	1,887
Mpumalanga	16.7	8.2	1.2	1.1	2.8	3.9	4.0	1.8	1.1	507
Northern	8.7	4.0	0.5	0.4	1.2	0.7	0.8	1.1	0.0	859
Education										
No education	27.0	11.1	1.6	0.7	6.8	3.1	4.1	8	0.3	1,186
Sub A - Std 3	25.6	9.1	1.5	0.5	3.5	4.0	4.9	3.5	0.4	1,088
Std 4 - Std 5	22.5	5.5	0.8	0.7	4.0	2.8	3.9	2.2	0.5	1,136
Std 6 - Std 9	15.6	4.8	0.6	1.6	3.2	4.4	3.3	1.6	0.6	3,094
Std 10	10.1	2.8	0.7	1.9	2.1	8.1	2.8	1.0	1.1	1,120
Higher	11.7	2.2	1.4	3.1	2.5	10.6	6.6	0.7	1.7	495
Ethnicity										
African	17.4	6.1	0.9	0.4	3.0	2.3	2.9	2.0	0.2	6,269
Afr. urban	19.9	5.4	0.9	0.3	3.7	2.6	3.1	1.5	0.3	3,349
Afr. non-urban	14.6	6.9	0.8	0.4	2.2	1.9	2.7	2.5	0.1	2,92
Coloured	22.3	5.4	1.4	1.9	5.8	7.3	5.0	3.3	0.7	806
White	21.4	5.1	1.4	7.6	4.8	23.4	9.1	1.3	4.0	767
Asian	23.7	5.4	1.0	3.9	11.5	3.8	6.2	0.3	0.7	300
Total	18.6	5.9	1.0	1.3	3.7	4.8	3.8	2.0	0.6	8,156

Note: Total includes 37 women not stated as to education and 14 not stated as to ethnic group

From: South Africa Demographic and Health Survey, 1998. Preliminary Report, MRC / Department of Health

2.3 Prevalence of diabetes mellitus in Africa

2.3.1 Studies up to 1990

Prevalence studies of diabetes conducted in Africa before 1990 were extensively reviewed by McLarty (1990) and are summarized in Table 2.3.1/1. Many of these studies were performed before the first WHO diagnostic criteria were published and were based on urine testing. The prevalence of diabetes ranged between 0% (Togo and outpatients in Zimbabwe) to 5.7% in the Ivory Coast. Seven studies reported prevalence rates greater than 1.5% of which 4 were the urban population-based surveys performed in South Africa. McLarty concluded that the range of prevalence estimates may be explained in part by the lack of standardization of diagnostic criteria and methodology in the past.

McLarty et al. (1989) reported the first epidemiological study based on WHO diagnostic criteria, using a 75g glucose load, to determine the prevalence of diabetes in Africans. The WHO diagnostic criteria are considered much stricter for diagnosing diabetes than earlier criteria. They examined 6097 rural subjects aged 15 years and older (mean age 37 years) in 6 villages. The overall prevalence of diabetes in this study was 0.87% and that of impaired glucose tolerance 7.7%. Of the 53 diabetic patients 7 were previously known to be so and 46 were newly diagnosed of whom only 12 had symptoms of hyperglycaemia. The male:female ratio of diabetics was 1.2:1 and did not differ from that in the study population. Multiple regression analysis showed that fasting blood glucose was positively related to systolic blood pressure and negatively to BMI, smoking, drinking, and haemoglobin. The 2-hour blood glucose was related positively to age, systolic blood pressure, and female sex and negatively to BMI, haemoglobin, and smoking. Fasting blood glucose levels were not associated with increasing age although 2-hour blood glucose levels were associated to a small degree with increasing age. From this the authors concluded that for most of the population glucose tolerance did not deteriorate with age. Whether this phenomenon holds true for urban subjects remains to be seen.

During the Tanzanian study a repeat OGTT was carried out within one week of the first, on 498 subjects and blood glucose measured after 2 hours (Swai et al., 1991). Of the 498 subjects, 245 had normal glucose tolerance in the first test and were selected at random for further testing; 223 subjects had impaired glucose tolerance (IGT), and 30 had diabetic

TABLE 2.3.1/1

STUDIES CONDUCTED IN AFRICAN SUBJECTS TO DETERMINE THE PREVALENCE OF DIABETES

Country	First Author	Year	Area	Study population	Sample Size	Method	Prevalence (%)
Ethiopia	Peters	1983	U/R*	Schools/Factories	2381	Urine	0.3
Ghana	Dodu	1958	U	Outpatients	4000	Urine	0.4
	Dodu	1964	U	Males/community	5537	Urine	0.2
Ivory coast	Zmirou	1979	U/R	Community	5000	Blood	5.7
Lesotho	Politzer	1960	R	Outpatients	3000	Urine	0.2
Malawi	Davidson	1963	U/R	Outpatients	4725	Urine	0.1
Mali	Imperato	1976	U/R	Workers/Farmers	297	Blood	1.4
	Fisch	1987	R	Community	7472	Blood	0.9
Nigeria	Ohwovoriole	1988	U	Community	1627	Urine/ Blood	1.7
	Erasmus	1989	U/R	Police/Farmers/ Students	2800	Blood	1.4
South Africa	Seftel	1960	U	Outpatients	2122	Urine	1.3
	Politzer	1962	U	Outpatients	3121	Urine	0.6
	Goldberg	1969	U	Community	882	Urine/ Blood	2.7
	Goldberg	1969	U	Community	2015	Blood	2.9
Tanzania	Ahren	1984	U/R	Community	3145	Blood	0.7
	McLarty	1989	R	Community	6097	Blood	0.9
Togo	Teuscher	1987	R	Community	1381	Blood	0
Tunisia	Papoz	1988	U	Community	3826	Blood	3.8
	Papoz	1988	U	Community	1787	Blood	1.3
Uganda	Tulloch	1964	U/R	Outpatients	7164	Urine	0.2
Zambia	Davidson	1969	R	Community	369	Blood	1.1
Zimbabwe	Carr	1961	U	Community	1007	Urine	0.1
	Wicks	1973	U	Community	1078	Urine	0.3
	Guidotti	1976	R	Outpatients	5456	Urine	0

Adapted from McLarty et al. (1990)

*U = Urban, R = Rural

values. In the second test, 241 (98.4%) of the 245 subjects with normal tolerance continued in this category and 4 (1.6%) showed IGT. Of the 223 with IGT in the first test, 171 (76.2%) reverted to normal on the second test, 7 (3.1 %) had diabetic values, and 45 (20.2%) persisted with IGT. Of the 30 subjects diagnosed as diabetic in the first test, 8 (26.7%) remained with diabetic values, 11 (36.7%) had IGT, and 11 (36.7%) were normal. FPG values were also obtained in 175 subjects. Both FPG and 2-hour plasma glucose values on re-testing showed a significant downward trend. These findings were unique with important implications. The investigators favoured the possibility that anxiety was responsible for this phenomenon much like blood pressure levels during follow-up investigation. They dismissed regression to the mean as an explanation. This publication was thoroughly reviewed by King (1993) who concluded that regression to the mean and unequal selection would appear to be major, if not sufficient, causes of the observed changes. King strongly suggested that IGT as a category should not be abandoned in epidemiological research. Providing that investigators classify subjects according to WHO criteria and select unbiased samples of sufficient size for study, results based on a single test should be valid for comparison between populations.

After examining the available data, McLarty (1990) was still sceptical whether the prevalence of diabetes was on the increase in Sub-Saharan Africa. He was also not convinced of any real difference in the prevalence of diabetes between urban and rural areas, quoting Politzer and Schneider's work (1962). McLarty (1990) estimated the number of non-insulin dependent diabetics on the African continent to be at least 1 million based on a total population of 555 million.

2.3.2 Studies since 1990

The prevalence of Type 2 diabetes and IGT in a rural as well as an urban population was studied in the Cameroon applying 1985 WHO diagnostic criteria (Mbanya et al., 1997). The age range in the sampling frame was 24 to 74 years. The median BMI of rural and urban women was 21.8 kg/m^2 and 26.4 kg/m^2 respectively and the corresponding values for rural and urban men were 21.5 kg/m^2 and 24.5 kg/m^2 . The age-adjusted prevalence of diabetes (treated and screened combined) for rural and urban women was 0.5% and 1.6% respectively and the corresponding rates for men were 0.9% and 0.8%. These rates were very similar to those reported for Tanzania. The rates for IGT in rural and urban women were 2.2% and 2.0% respectively while the corresponding rates for men were 5.8% and 1.8%. The prevalence of IGT in the rural group was unexpectedly high especially in view of the significantly lower mean

BMI in this group. The 2-h plasma glucose concentration distributions were significantly higher in the rural area for both sexes.

In an extension of the Cameroon study the prevalence of diabetes and IGT was also investigated in African-Americans living in Jamaica and Manchester (Mbanya et al., 1999). In order to compare prevalence rates in the study populations with those in other populations, the prevalence of diabetes was age-standardized to the Segi age-distribution (WHO, 1993) for subjects 30-64 years. In this study, these prevalence rates for men were 1.6% in rural Cameroon, 1.6% in urban Cameroon, 7.3% in Jamaica, and 12.4% in Manchester. The corresponding figures for women were 0.6%, 3.7% , 10.8% and 9.9%. The median BMI of Jamaican and Manchester female subjects was 26.8 kg/m^2 and 28.2 kg/m^2 while the corresponding values for men were 22.5 kg/m^2 and 26.8 kg/m^2. Since the subjects in the study populations shared at least some genetic background, it was concluded the transition in glucose intolerance from Cameroon to Jamaica and Britain suggests that environment determines diabetes prevalence in these populations.

In conclusion, the importance and meaning of IGT in African subjects awaits further clarification. The question whether IGT in African subjects is also a risk factor for future of diabetes and atherosclerosis remains to be seen.

2.4 Prevalence of diabetes mellitus in United States blacks

The National Centre for Health Statistics of the Centres for Disease Control and Prevention conducted the Third National Health and Nutrition Examination Survey (NHANES III) during 1988- 1994 (Harris et al, 1998). The survey included a nationally representative sample of the U.S. civilian non-institutionalised population, based on a complex, stratified, multistage probability cluster sampling design with over-sampling of blacks and Mexican-Americans. A total of 18825 people who were ≥ 20 years of age participated and completed a household interview in which information was obtained about demographic characteristics, race, Hispanic ethnicity, and medical history of diabetes. Based on this information, 1503 adults were classified as having previously diagnosed diabetes. A random sample of 8608 non-diabetic subjects was subjected to a 75 g OGTT after an overnight fast. This sample included 1753 non-Hispanic blacks. Both the 1997 criteria of the American Diabetes Association and the 1980-1985 criteria of the World Health Organization were used.

The age-standardized prevalence of diabetes diagnosed by a physician before NHANES III was 5.3% for all people ≥ 20 years of age, 4.8% for non-Hispanic whites, 8.2% for non-Hispanic blacks, and 9.3% for Mexican-Americans. The age-standardized prevalence of undiagnosed diabetes using American Diabetes Association fasting plasma glucose criteria was 2.8% for all people ≥ 20 years of age, 2.5% for non-Hispanic whites, 3.6% for non-Hispanic blacks, and 4.5% for Mexican-Americans. The prevalence increased with age, although for some race/sex groups, there was a decline in the rate for those ≥ 75 years of age. The age-standardized rate for the total sample (all races, known and newly diagnosed) was 8.1% (8.4% and 7.7% respectively for males and females). The age-standardized rate for all non-Hispanic whites was 7.3% (7.9% and 6.5% respectively for males and females). The age-standardized rate for all non-Hispanic blacks was 11.8% (10.0% and 13.6%, respectively for males and females). The age-standardized rate for all Mexican-Americans was 13.8% (13.1% and 14.5% for males and females respectively (Harris et al, 1998).

The age-adjusted prevalence for IFG was 6.9% for the total sample (8.8% and 5.0% respectively for males and females); 6.8% for non-Hispanic whites (8.9% and 4.6% for males and females respectively), 7.0% for non-Hispanic blacks (7.7% and 6.4% respectively for males and females) and 8.9% for Mexican-Americans (11.6% and 6.3% respectively for males and females (Harris et al, 1998).

The previous National Health and Nutrition Examination Survey (NHANES II) was conducted by the National Centre for Health Statistics during 1976-1980 and included a special diabetes medical history supplement and the incorporation of an oral glucose tolerance test (Harris et al, 1987). NHANES II involved a complex sample design and the samples were weighted in order to serve as proxies for the entire US population as it was on March 1, 1978. The full NHANES II sample amounted to 17390 people aged 20-74 years. A subgroup of 3872 people were submitted to a 75g OGTT. Diagnosed diabetics were not separated into IDDM or Type 2 diabetes.

The total prevalence of diabetes (NHANES II) then was 6.8% (1980 WHO diagnostic criteria). Diabetes was also more common in blacks (9.9%) than in whites (6.4%). The ratio of diagnosed to undiagnosed diabetes was 1:1 and there was an age-related increase in the prevalence of diabetes. IGT was present in 11.2% of the population (10.7% for whites and

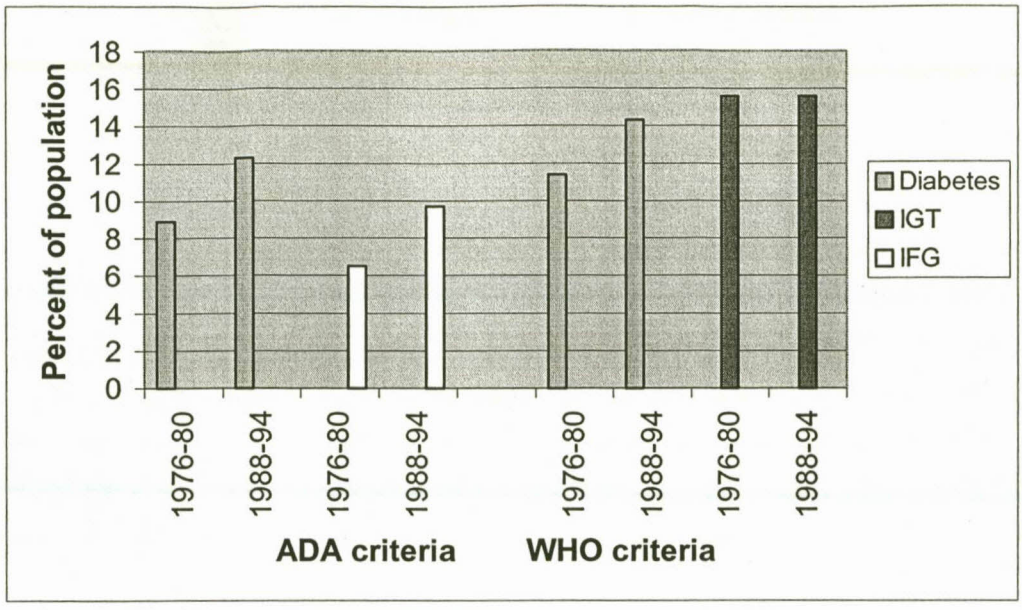


Fig. 2.4/1 - Prevalence of diabetes, impaired fasting glucose, and impaired glucose tolerance in the U.S. population 40-74 years of age, according to NHANES II and NHANES III. Diabetes includes both previously diagnosed subjects and those who meet diagnostic criteria for diabetes but do not have a medical history of the disease. (From Harris et al., 1998).

12.7% for blacks). An alarming increase in the prevalence of diabetes took place since the NHANES II survey (Fig. 2.4/1).

The increase in the prevalence of diabetes, IFG and IGT in the U.S. population 40-70 years of age, according to NHANES II and NHANES III is shown in Fig. 2.4/1. It is clear that the prevalence rates of diabetes, IFG and IGT have increased considerably in the U.S. population over the last 2 decades. The HANES studies have also shown a substantial increase in the prevalence in the U.S. of obesity, which is a major risk factor for diabetes. This increase, together with the high frequency of sedentary lifestyles in the U.S. and the high rates of impaired fasting glucose and impaired glucose tolerance found in NHANES III, portends that diabetes will continue to have a major impact on the health of the U.S. population (Harris et al., 1998).

2.5 The increasing global prevalence of Type 2 diabetes mellitus

2.5.1 THE WHO REPORT 1991 (King et al, 1991)

Since the wide international acceptance of the 1985 WHO criteria (WHO, 1985) for the diagnosis and classification of diabetes, it became possible to directly compare data from different studies. The diabetes programme at WHO Headquarters, Geneva, collated data from many published as well as unpublished studies, in which the diagnosis of diabetes was based upon current WHO diagnostic criteria. Suitable material was obtained in this way for over 70 populations in over 30 countries worldwide, the total study sample being over 150,000 subjects (King, 1991). The prevalence rates were standardized for the age range 30-64 years and adjusted to the standard world population making direct comparisons possible. Data from selected populations is shown in Table 2.5.1/1.

The prevalence of diabetes in these populations varied from 0-50%. In Africa the lowest prevalence recorded was from rural Tanzania (1%). For urban blacks in Dar-es-Salaam the prevalence was 3% for males and 1% for females. This was in contrast to U.S. blacks where the prevalence was 9% and 12% respectively for males and females. Genetic as well as environmental factors were most probably responsible for the wide range in prevalence documented for Indian subjects. In rural South India the prevalence was below 5% and rose

TABLE 2.5.1/1.

PREVALENCE (%) OF DIABETES MELLITUS AND IMPAIRED GLUCOSE TOLERANCE IN THE AGE RANGE 30-64 YEARS IN SELECTED POPULATIONS *

	Diabetes mellitus		IGT	
Region of origin, ethnicity, and location	Men	Women	Men	Women
Africa and Asia				
Arab				
Tunisia	9	8	9	10
Oman	14	14	11	17
Bantu				
Tanzania				
Dar-es-Salaam	3	1	9	16
Wachagga/Masai	1	1	8	10
Indian				
S.India (Dravidian)				
Rural	4	2	9	7
Urban (Madras)	12	11	11	9
S. Africa (Durban)	14	21	12	7
Fiji				
Rural	23	16	10	12
Urban	23	20	12	17
Chinese				
China (Da Qing)	2	2	1	1
Mauritius	16	10	17	22
Americas				
U.S. Non-Hispannic				
White	5	7	10	11
Black	9	12	14	17
U.S. Hispanic				
Rural				
San Luis Valley				
Colorado	7	9	11	18
Urban				
Puorto Rican				
(New York)	18	13	11	16
SanAntonio				
(Texas)				
Upper in corne	7	5	10	14
Middle income	16	12	16	17
Low income	15	19	13	18

TABLE 2.5.1/1.

PERCENTAGE PREVALENCE OF DIABETES MELLITUS AND IMPAIRED GLUCOSE TOLERANCE IN THE AGE RANGE 30-64 YEARS IN SELECTED POPULATIONS* (CONTINUED)

Region of origin, ethnicity, and location	Diabetes mellitus		IGT	
	Men	Women	Men	Women
American Indian				
Mapuche(Chile)	0	1	1	1
Pima (Arizona,USA)	49	51	12	17
Brazilian				
SaoPaulo	7	9	3	3
Europe				
Russian (Novosibirsk, Siberia)	2	4	6	10
Polish (Wroclaw)	4	4	2	3
Italian				
Sanza	8	5	4	9
Laurino	11	10	3	8
Maltese	8	10	5	5
Pacific				
Melanesian				
Papa New Guinea				
Rural	0	0	3	2
Fiji				
Rural	2	2	7	12
Urban	5	12	9	19
Polynesian				
Western Samoa				
Rural	2	6	5	4
Urban	11	10	9	11
Micronesian				
Kiribati				
Rural	4	5	14	17
Urban	16	13	28	19
Nauru	41	42	22	21

* Age-adjusted to standard world population

King and Rewers, 1991

to about 12% in Madras. In South African Indians (a migrant group) the prevalence was 14% and 21% for males and females respectively. The prevalence for mainland Chinese was 2% and for Mauritian Chinese it was above 10%. The highest prevalence recorded (about 50%) was for Pima Indians living in a reserve in Arizona, USA. The Micronesian population of Nauru in the Pacific had a prevalence in excess of 40%. Among U.S. Hispanics the prevalence was approximately 10-20%, and was inversely related to average income in the Hispanic residents of San Antonio. King (1991) made an interesting and important observation from this data. If one takes an arbitrary cut-off point of 10%, above which diabetes in adults can be considered common, it is only among the populations of developing countries, and migrant and minority communities in industrialized countries, that this limit is exceeded. This observation is extremely important for Africa and South Africa in particular. The absence of South African data was conspicuous (Table 2.5.1/1).

The prevalence of IGT was very variable and is also shown in Table 2.1.5/1. In African and Asian populations, the only group in which IGT was rare (1%), was the Chinese in Da Qing. Chinese Mauritians, however, had very high rates (17-22%). Rates of approximately 10% were observed in Bantu and Indians, even in the rural setting. In the USA, IGT was more common among blacks than among whites. The IGT rates for both Pima Indians and the Nauruans were about half of the corresponding figures for diabetes.

2.5.2 The International Diabetes Institute and Who Collaborating Centre for the Epidemiology of Diabetes Mellitus and Health Promotion for non-communicable diseases — Report 1997 (Amos et al., 1997)

Amos et al. (1997) used data from population-based epidemiological studies and estimated that the global burden of diabetes was 118 million in 1995 and that it would likely double to 221 million by 2010. To generate Type 2 diabetes estimates for 1995 and 1997, they applied age-specific prevalence rates from selected studies to the corresponding national demographic age distribution. When Type 2 diabetes prevalence data were unavailable for a given country, data from another country with a similar ethnic composition and level of economic development were applied as a substitute (substitutions were noted). Urban and rural prevalence data, when available, were applied separately to the corresponding populations within each country. Since the prevalence of IGT varies considerably over time and between countries, IGT was not estimated for countries where data were unavailable and no attempt was made to project the prevalence of IGT for 2000 and 2010 in their report. These global and country-specific estimates are shown in Tables 2.5.2/1a-s. According to the estimates of Amos

U.O.V.S. BIBLIOTEEK

et al, 151.3 million people were living with diabetes at the turn of the century. Of these, 9.4 million were living in Africa. AIDS-related deaths were not taken into account not taken into account when these calculations were done.

In developing or newly industrialized countries, the prevalence of IGT is usually higher than the prevalence of type 2 diabetes since susceptible persons first pass through a stage of IGT before becoming diabetic (Alberti et al., 1998). Amos et al. (1997) predicted that the greatest increase in diabetes for the period 1995 to 2010 would likely be seen in Western Asia (3.6 to 11.4 million), South-Central Asia (28.8 to 57.5 million), South-East Asia (8.6 to 19.5 million), East-Asia (21.7 to 44 million).

It is obvious that diabetes is no longer confined to developed nations but is already an escalating health problem in the developing world communities. A serious need exists to maintain surveillance of diabetes and its complications, also in South Africa.

1171126 79

TABLE 2.5.2/1a

GLOBAL ESTIMATES OF DIABETES IN 1997 (IN THOUSANDS)

Region / Country	Population (in thousands)	IDDM < 15 yrs	IDDM ≥ 15 yrs	NIDDM All ages	Total Diabetes	IGT All ages
World	5 846 130	408	3135	119 994	123 537	-
Africa	758 101	21	64	7 644	7 729	-
Asia	3 538 451	220	820	65 008	66 048	-
North America	301 591	53	832	12 463	13 348	-
Latin America	490 971	35	274	12 847	13 156	-
Europe	728 498	74	1 068	21 157	22 299	-
Oceania	28 518	5	77	875	957	-

TABLE 2.5.2/1b

GLUCOSE INTOLERANCE IN NORTH AFRICA (IN THOUSANDS) - 1997

Region / Country	Population (in thousands)	IDDM < 15	IDDM ≥ 15	NIDDM All ages	Total Diabetes	IGT All ages
North Africa	164 729	13.8	48.8	4460.3	4522.9	-
Algeria	29 473	2.6	16.8	314.6	334	-
Egypt	64 465	5.8	15.8	3236	3 257.6	3419.2
Libyan Arab Jamahiriya	5 784	1	2.6	77.4	81	-
Morocco	27 518	2.4	6.6	338.5	347.5	-
Sudan	27 898	1.1	1.1	362.5	364.7	295.7
Tunisia	9 326	0.9	5.9	127.7	134.5	-
Western Sahara	265	-	-	3.6	3.6	-

TABLE 2.5.2/1c

GLUCOSE INTOLERANCE IN WESTERN AFRICA (IN THOUSANDS) - 1997

Region / Country	Population (in thousands)	IDDM < 15	IDDM ≥ 15	NIDDM All ages	Total Diabetes	IGT All ages
Western Africa	221 679	1.5	1.8	1 078.2	1 081.5	-
Benin	5 720	-	-	22.6	22.6	-
Burkina Faso	11 087	0.1	-	43.4	43.5	-
Cape Verde	406	-	0.1	1.6	1.7	-
Cote d'Ivoire	14 230	0.2	0.4	60.2	60.8	-
Gambia	1 169	-	-	5.5	5.5	-
Ghana	18 338	0.2	0.6	78.4	79.2	-
Guinea	7 614	-	-	30.3	30.3	-
Guinea-Bissau	1 112	-	-	5.5	5.5	-
Liberia	2 467	-	-	11.1	11.1	-
Mali	11 480	0.1	-	44.6	44.7	-
Mauritania	2 392	-	-	10.7	10.7	-
Niger	9 788	0.1	-	37	37.1	-
Nigeria	118 369	0.8	0.6	654	655.4	-
Senegal	8 762	-	-	35.7	35.7	-
Sierra Leone	4 428	-	-	19.5	19.1)	-
Togo	4 317	-	0.1	18.1	18.2	-

TABLE 2.5.2/1d

GLUCOSE INTOLERANCE IN EASTERN AFRICA (IN THOUSANDS) - 1997

Region / Country	Population (in thousands)	IDDM < 15	IDDM ≥ 15	NIDDM All ages	Total Diabetes	IGT All ages
Eastern Africa	234 222	1.8	2.7	1 046.9	1 051.4	-
Burundi	6 398	-	-	25.2	25.2	-
Comoros	651	-	-	2.6	2.6	-
Djibouti	634	-	-	5.2	5.2	-
Eritrea	3 409	-	-	14.8	14.8	-
Ethiopia	60 148	0.4	0.3	245.8	246.5	-
Kenya	213 414	0.4	0.8	110.5	111.7	-
Madagascar	15 845	0.1	0.1	62.8	63	-
Malawi	1 0 086	0.1	-	39.9	40	-
Mauritius	1 141	-	0.4	83.8	84.2	95.4
Mozambique	18265	0.1	0.1	79.5	79.7	-
Reunion	673	-	0.3	36.3	36.6	-
Rwanda	5 883	-	-	22.3	22.3	-
Somalia	1 0217	0.1	-	40.1	40.2	-
Uganda	2 0791	0.1	0.2	74.7	75	-
United Rep. Of Tanzania	31 507	0.2	0.2	125.5	125.9	1 152.1
Zambia	8 478	0.1	0.1	31	31.2	-
Zimbabwe	11 682	0.2	0.2	46.9	47.3	-

TABLE 2.5.2/1e

GLUCOSE INTOLERANCE IN MIDDLE AFRICA (IN THOUSANDS)

Region / Country	**Population (in thousands)**	**IDDM < 15**	**IDDM ≥ 15**	**NIDDM All ages**	**Total Diabetes**	**IGT All ages**
Middle Africa	87 967	0.6	0.7	253.9	255.2	-
Angola	11 569	0.1	0.1	30.2	30.4	-
Cameroon	13 937	0.2	0.4	42.3	42.9	81.8
Central African Rep.	3 416	-	-	11.9	11.9	-
Chad	6 702	-	-	20.2	20.2	-
Congo	2 745	-	-	8	8	-
Equatorial Guinea	420	-	-	1.4	1.4	-
Gabon	1 138	-	-	4.8	4.8	-
Zaire	4 8040	0.3	0.2	135.1	135.6	-

TABLE 2.5.2/1f

GLUCOSE INTOLERANCE IN SOUTHERN AFRICA (IN THOUSANDS)

Region / Country	Population (in thousands)	IDDM < 15	IDDM ≥ 15	NIDDM All ages	Total Diabetes	IGT All ages
Southern Africa	49 504	3.5	10.1	804.9	818.5	-
Botswana	1 518	-	0.3	10	10.3	-
Lesotho	2 131	0.1	0.2	16.3	16.6	-
Namibia	1 613	-	-	14	14	-
South Africa	43 336	3.4	9.6	758.4	771.4	-
Swaziland	906	-	-	6.2	6.2	-

TABLE 2.5.2/1g

GLUCOSE INTOLERANCE IN WESTERN ASIA (IN THOUSANDS) - 1997

Region / Country	Population (in thousands)	IDDM < 15	IDDM ≥ 15	NIDDM All ages	Total Diabetes	IGT All ages
Western Asia	175 340	14.7	105.7	3772.6	3 893	-
Armenia	3 642	0.3	3.5	61	64.8	-
Azerbaijan	7655	0.8	8.2	95.6	104.6	-
Bahrain	582	-	0.3	34.2	34.5	-
Cyprus	766	0.1	1.8	30.5	32.4	-
Gaza Strip	863	0.1	0.8	3.2	4.1	-
Georgia	5 434	0.4	4.7	128.1	133.2	-
Iraq	21 177	2.2	6	240	248.2	-
Israel	5 781	0.6	8.9	206.9	216.4	123
Jordan	5 774	0.7	4.5	73.8	79	-
Kuwait	1 731	0.6	7.9	73.1	81.6	-
Lebanon	3 144	0.3	2	56.5	58.8	-
Oman	2 401	0.1	0.8	97.1	98	98
Qatar	569	-	0.2	42	42.2	-
Saudi Arabia	19 494	1	6.2	874.2	881.4	191.8
Syrian Arab Republic	14 951	1.8	11.4	187	200.2	-
Turkey	62 774	5.2	37.1	1291.7	1334	-
United Arab Emirates	2 308	0.1	1.1	155.7	156.9	-
Yemen	16 294	0.4	0.3	122	122.7	-

TABLE 2.5.2/1h

GLUCOSE INTOLERANCE IN SOUTH-CENTRAL ASIA (IN THOUSANDS) - 1997

Region / Country	Population (in thousands)	IDDM < 15	IDDM ≥ 15	NIDDM All ages	Total Diabetes	IGT All ages
South-Central Asia	141 792.1	183.8	559.7	29 397.3	30 140.8	
Afghanistan	22 132	0.5	0.5	178	179	
Bangladesh	122 013	1	1.9	1 391.9	1 394.8	8 050.7
Bhutan	1 862			20	20	
India	960 178	166.3	459.8	20 176.7	20 802.8	43 620.6
Iran (Islamic Rep. of)	71 518	8.8	54.9	707	770.7	
Kazakstan	16 832	1.4	9.3	257.2	267.9	
Kyrgyzstan	4 481	0.4	2.9	43.7	47	
Maldives	273			2.6	2.6	
Nepal	22 591	0.1	0.1	262	262.2	
Pakistan	143 831	1.2	2.9	5 956.4	5 960.5	5 769.9
Sri Lanka	18 273	0.3	3.5	271.9	275.7	336.9
Tajikistan	6 046	0.7	4.4	46.5	51.6	
Turkmenistan	4 235	0.5	3	40	43.5	
Uzbekistan	23 656	2.6	16.5	211.8	230.9	

TABLE 2.5.2/1i

GLUCOSE INTOLERANCE IN SOUTH-EAST ASIA (IN THOUSANDS) - 1997

Region / Country	Population (in thousands)	IDDM < 15	IDDM ≥ 15	NIDDM All ages	Total Diabetes	IGT All ages
South-East Asia	497 992	10	45.7	9114.4	91 70.1	-
Brunei Darussalam	307	-	0.1	8.1	8.2	-
Cambodia	10 516	-	-	55.4	55.4	-
East Timor	843	-	-	17.1	17.1	-
Indonesia	203 480	5.7	13.9	5 328.6	5348.2	8 892.4
Lao (People's Dem. Rep.)	5 194	-	-	25.4	25.4	-
Malaysia	21 018	0.9	8.7	575.6	585.2	-
Myanmar (Burma)	46 764	0.2	0.4	287.6	288.2	-
Philippines	70 724	0.8	5.3	1 518.6	1 524.7	-
Singapore	3 439	0.1	1 .1	219.8	221	347.2
Thailand	59 159	1.6	11.4	607.3	620.3	-
Vietnam	76 548	0.7	4.8	470.9	476.4	624.8

TABLE 2.5.2/1j

GLUCOSE INTOLERANCE IN EAST ASIA (IN THOUSANDS) - 1997

Region / Country	Population (in thousands)	IDDM < 15	IDDM ≥ 15	NIDDM All ages	Total Diabetes	IGT All ages
East Asia	1 447 198	11.3	108.9	22 723.9	22 844.1	-
China	1 243 738	8.5	60.7	14 079.6	14 148.8	12 776.4
Dem. People's Rep. *of* Korea	22 837	0.3	2.9	267.1	270.3	-
Hong Kong	6 249	0.1	2.6	350.7	353.4	557
Japan	125 638	2	37.3	6 223.1	6 262.4	11 194.9
Macau	451	-	-	9.5	9.5	-
Mongolia	2568	-	0.1	18.5	18.6	-
Republic *of* Korea	45 717	0.4	5.3	1775.4	1 781.1	2 305.9

TABLE 2.5.2/1k

GLUCOSE INTOLERANCE IN NORTH AMERICA (IN THOUSANDS) - 1997

Region / Country	Population (in thousands)	IDDM < 15	IDDM ≥ 15	NIDDM All ages	Total Diabetes	IGT All ages
North America	301 591	53.3	831.7	12 462.9	13 347.9	-
Canada	29 943	3.8	63	1 149.7	1 216.5	-
United States	271 648	49.5	768.7	11 313.2	12 131.4	19 114.5

TABLE 2.5.2/1l

GLUCOSE INTOLERANCE IN CENTRAL AMERICA (IN THOUSANDS) - 1997

Region / Country	Population (in thousands)	IDDM < 15	IDDM ≥ 15	NIDDM All ages	Total Diabetes	IGT All ages
Central America	128 302	1.7	15.6	4 095.8	4113.1	-
Belize	224	-	-	5.4	5.4	-
Costa Rica	3 575	0.1	1	127.6	128.7	-
El Salvador	5 928	0.1	0.8	181.8	182.7	-
Guatemala	11 241	0.2	0.6	307.8	308.6	-
Honduras	5 981	0.1	0.8	158.1	159	-
Mexico	94 280	1.1	11.2	3103	3 115.3	-
Nicaragua	4 351	0.1	0.6	111 .7	112.4	-
Panama	2 722	-	0.6	100.4	101	-

TABLE 2.5.2/1m

GLUCOSE INTOLERANCE IN CARIBBEAN (IN THOUSANDS) - 1997

Region / Country	**Population (in thousands)**	**IDDM < 15**	**IDDM ≥ 15**	**NIDDM All ages**	**Total Diabetes**	**IGT All ages**
Caribbean	**35 725**	**2.3**	**27.2**	**1377**	**1 406.5**	**-**
Bahamas	288	-	0.3	10.3	10.6	-
Barbados	262	-	0.3	22.4	22.7	-
Cuba	11 068	0.6	10.5	546.7	557.8	-
Dominican Republic	8 097	0.7	4.8	246.4	251.9	-
Guadeloupe	437	-	0.4	19.2	19.6	-
Haiti	7 395	0.1	0.1	36	36.2	-
Jamaica	2 515	0.2	2.6	170.2	173	-
Martinique	388	-	0.4	33.2	33.6	-
Netherlands Antilles	197	-	0.2	15.9	16.1	-
Puerto Rico	3 771	0.6	6.4	208.2	215.2	-
Trinidad and Tobago	1 307	0.1	1.2	68.5	69.8	-

TABLE 2.5.2/1n

GLUCOSE INTOLERANCE IN SOUTH AMERICA (IN THOUSANDS) - 1997

REGION / COUNTRY	Population (in thousands)	IDDM < 15	IDDM ≥ 15	NIDDM All ages	Total Diabetes	IGT All ages
South America	326 944	31.2	231.7	7 373.9	7 636.8	
Argenti na	35 671	4.3	43.9	1 088.9	1 137.1	
Bolivia	7 774	0.2	0.6	103	103.8	
Brazil	163 132	20.1	134.2	3 768.2	3 922.5	5 178.3
Chile	14 625	0.6	6.5	395.9	403	
Colombia	37 068	2.4	16	687.3	705.7	488.9
Ecuador	11 937	0.8	5.4	177.5	183.7	
Guyana	847		0.1	25.6	25.7	
Paraguay	5 088	0.2	1.2	59.3	60.7	
Peru	24 367	0.3	0.8	474.7	475.8	
Surinam	437		0.2	12.8	13	16.2
Uruguay	3 221	0.4	4.6	99.4	104.4	
Venezuela	22 777	1.9	18.2	481.3	501.4	

TABLE 2.5.2/1o

GLUCOSE INTOLERANCE IN NORTHERN EUROPE (IN THOUSANDS) - 1997

Region / Country	Population (in thousands)	IDDM < 15	IDDM ≥ 15	NIDDM All ages	Total Diabetes	IGT All ages
Northern Europe	**93 079**	**20.6**	**327**	**2220**	**2567.6**	
Denmark	5 248	1.3	21.8	172.9	196	
Estonia	1 55	0.2	1.1	66.4	67.7	
Finland	5 142	2.2	35.1	251	288.3	417
Iceland	274	-	0.7	7.2	7.9	
Ireland	3 359	1	15.7	47	63.7	
Latvia	2 474	0.2	1.2	67.2	68.6	
Lithuania	3 719	0.3	3.9	91.2	95.4	
Norway	4 364	1.1	18.3	126.7	146.1	
Sweden	8 844	2.6	41.5	312	356.1	
United Kingdom	58 200	11.7	187.7	1 078.4	1 277.8	834.9

TABLE 2.5.2/1p

GLUCOSE INTOLERANCE IN WESTERN EUROPE (IN THOUSANDS) - 1997

Region / Country	Population (in thousands)	IDDM < 15	IDDM ≥ 15	NIDDM All ages	Total Diabetes	IGT All ages
Western Europe	**182 434**	**19.5**	**340.9**	**5 120.5**	**5 480.9**	
Austria	8161	0.7	12.6	259.8	273.1	
Belgium	10 188	1.1	19	215.8	235.9	
France	58 542	5.4	88.2	1 170.7	1 264.3	
Germany	82 189	9.6	174.3	2764	2 947.9	
Luxemburg	417		1	12.6	13.6	
Netherlands	15 661	2.1	35.8	461.4	499.3	367.6
Switzerland	7 276	0.6	10	236.2	246.8	

TABLE 2.5.2/1q

GLUCOSE INTOLERANCE IN EASTERN EUROPE (IN THOUSANDS) - 1997

Region / Country	Population (in thousands)	IDDM < 15	IDDM ≥ 15	NIDDM All ages	Total Diabetes	IGT All ages
Eastern Europe	**309 167**	**20.7**	**181.1**	**7 859.4**	**8 061.2**	
Belarus	10 338	1.1	12.1	259.4	272.6	
Bulgaria	8 427	0.6	7.7	235.5	243.8	
Czech Rep	10 237	1.1	13	251.4	265.5	
Hungary	9 990	0.7	5.4	268.4	274.5	
Poland	38 635	2.7	30.6	886	919.3	788.5
Rep of Moldova	4448	0.2	1.4	94.3	95.9	
Romania	22 606	0.8	6.1	570.1	577	
Russian Federation	147 708	12.1	87.7	3 767.2	3867	
Slovakia	5 354	0.6	7.6	112.7	120.9	
Ukraine	51 424	0.8	9.5	1 414.4	1 424.7	

TABLE 2.5.2/1r

GLUCOSE INTOLERANCE IN SOUTH EUROPE (IN THOUSANDS) - 1997

Region / Country	Population (in thousands)	IDDM < 15	IDDM ≥ 15 -	NIDDM All ages	Total Diabetes	IGT All ages
Southern Europe	**14 3818**	**12.9**	**219.2**	**5 956.8**	**6 188.9**	
Albania	3 422	0.2	1.6	50.4	52.2	
Bosnia and Herzegovina	3 784	0.4	4.3	82.9	87.6	
Croatia	4 498	0.4	4.5	124.8	129.7	
Greece	1 0 522	0.7	12	487.9	500.6	
Italy	57 240	4.3	83.2	2 709.4	2 796.9	2 967.4
Malta	371	0.1	1.2	20.6	21.9	16.6
Portugal	9 802	0.9	11.4	436.5	448.8	
Slovenia	1 922	0.2	1.9	51.4	53.5	
Spain	39 717	4.5	85.7	1 683.1	1 773.3	2 134
TFYR Macedonia	2 190	0.1	0.9	46.4	47.4	
Yugoslavia	10 350	1.1	12.5	263.4	277	

TABLE 2.5.2/s

GLUCOSE INTOLERANCE IN OCEANEA (IN THOUSANDS) - 1997

Region / Country	Population (in thousands)	IDDM < 15	IDDM ≥ 15 -	NIDDM All ages	Total Diabetes	IGT All ages
Oceania	**28 518**	**4.9**	**76.8**	**875.2**	**956.9**	
Australia	18 250	4	63.5	663.6	731.1	
Fiji	808			37	37	45
French Polynesia	227			10.8	10.8	
Guam	156			4.2	4.2	
New Caledonia	186			3.5	3.5	6.3
New Zealand	3 641	0.9	13.3	126	140.2	
Papua New Guinea	4 500			22.5	22.5	1.4
Samoa	168			4.8	4.8	4
Solomon Islands	404			1.1	1.1	
Vanuatu	178			1.7	1.7	

Amos et al, 1997

2.6 Factors predisposing to the development of non-insulin-dependent diabetes mellitus

Consensus was recently reached on the causes of Type 2 diabetes by a group of experts who met under the auspices of the WHO and International Diabetes Federation (IDF) in Colombo, Sri Lanka (IDF, 2002). This panel concluded that genetics, foetal history, lifestyle and stress might all contribute to the occurrence of Type 2 diabetes.

2.6.1 Genetic causes

Two decades ago Zimmet (1982) concluded that there appears to be a spectrum of interaction between genetic and environmental factors predisposing to Type 2 diabetes - in certain populations the genetic input may be more important than the environmental and vice versa.

The population geneticist, Neel (1962), regarded diabetes as a frequent disease, with a well-defined genetic basis and as a disease often interfering with reproduction by virtue of an onset during the reproductive years. This enigma of a frequent disease in the face of strong genetic selection against the condition led Neel to propose the 'thrifty genotype' hypothesis. He regarded the diabetic genotype as a thrifty genotype in the sense of being exceptionally efficient in intake and/or utilization of food. This thrifty genotype may have been of great advantage to man in his period as a hunter-gatherer, which was a period of feast and famine. Zimmet (1982) suggested as a possible mechanism for this hypothesis an over-responsive beta cell (a 'quick insulin trigger'). Such a beta cell may have been of great advantage in the days of feast or famine helping to ensure maximum food utilization by promoting fat and glycogen deposition. A steady and plentiful food supply, as is available to modern man, may cause continual over stimulation of the beta cells which may lose their capacity to respond, resulting in type 2 diabetes. The recently described decline in the incidence of epidemic glucose intolerance in Nauruans coupled with the observations that mortality is higher and fertility lower in diabetic Nauruans, is in line with Neel's "thrifty genotype" hypothesis (Dowse et al, 1991).

Studies of migrant populations contributed to the belief that Type 2 diabetes must have a genetic basis. Migrant Indian populations have consistently higher prevalence rates of diabetes than their cohabitants (Dowse et al, 1989). The age and sex adjusted prevalence of diabetes in the Indian community of Durban, which is a migrant community, was reported to be 12.4% for subjects in the 15-69 year old age group (Seedat et al, 1990) compared to 2.1% for

subjects on the Indian continent. The age-adjusted prevalence of diabetes in Natal Indians (13%) (Omar et al., 1994) was considerably than that that reported for blacks (8.0%) (Levitt et al., 1993). Since both populations approximately share the same environment it can be concluded that genetic factors may play an important part in the development of Type 2 diabetes. The age and sex adjusted prevalence of diabetes in the 25-74 year old population of Mauritius, which is 70% of Indian origin, was found to be 11.9% (Dowse et al, 1990). Along with genetic factors Dowse also invoked durable life-style habits such as an unhealthy diet and reduced physical activity to explain the higher prevalence of diabetes in migrant Indian groups.

Although Type 2 diabetes is likely to be a multifactorial disease with a strong genetic component, the progress in identifying genetic markers has been disappointingly slow. HLA-association studies lend some support to the fact that Type 2 diabetes may have a genetic component. A weak association between HLA-A2 and Type 2 diabetes has been reported for Xhosas (Briggs et al, 1980). It has meanwhile become clear that there is no single major gene involved in Type 2 diabetes (nothing akin to HLA in Type 1) (McCarthy, 2001). Hales (2001), however, has argued that the evidence linking a genetic cause to the aetiology of Type 2 diabetes, is poorly founded.

Several candidate genes for the transmission of Type 2 diabetes received attention in the past (O'Rahilly, 1991). The putative gene may either involve insulin secretion or insulin action. The following candidate genes are presently receiving attention: The beta 3-adrenergic receptor, lipoprotein lipase, hormone sensitive lipase, peroxisome proliferator-activated receptor-gamma, insulin receptor substrate-1 and glycogen synthase (Groop, 2000). Several mutations were described in these genes, some of which are associated with the development of diabetes. These types of diabetes are not regarded as type 2 diabetes but as specific types of diabetes in the category "other types of diabetes" (Alberti et al., 1998).

Poulsen et al. (1999) studied a sample of 606 twins (303 pairs) ascertained from the population-based Danish Twin Register. Subjects underwent a standardised 75 g OGTT and diabetes and IGT were diagnosed according to the WHO 1998 criteria. They identified 62 pairs in which one or both had Type 2 diabetes. The proband-wise concordance for Type 2 diabetes was 50% for monozygotic and 37% for dizygotic twin pairs. When the twins with impaired glucose tolerance (IGT) were included, however, the proband-wise concordance for abnormal glucose tolerance was significantly different between monozygotic (63%) and dizygotic (43%)

twin pairs, ($p < 0.01$). The authors calculated the heritability estimates for Type 2 diabetes and found it to be 26%, while that for abnormal glucose tolerance was 61%. In this study, the metabolic variables, insulin resistance and insulin secretion, and anthropometric variables, body mass index and waist to hip ratio, known to be associated with the development of glucose intolerance had a heritability of 26, 50, 80 and 6 % respectively. This study confirmed the notion of a multifactorial aetiology of Type 2 diabetes. The findings also support the contribution of non-genetic aetiological components in the development of Type 2 diabetes. Poulsen et al., (1999) proposed that genetic predisposition is important for the development of abnormal glucose tolerance and that non-genetic factors, however, might play a predominant role in controlling whether a genetically predisposed individual progresses to overt Type 2 diabetes.

In a U.K. study, Medici and co-workers (1999) determined the concordance rate for Type 2 diabetes mellitus in 44 pairs of monozygotic twins, initially ascertained discordant for diabetes in a prospective study. The index patient in each case was referred because of a diagnosis of diabetes and the other twin periodically underwent an OGTT. The mean follow-up was 8 years (range 0-18 years). The percentage of twins who developed Type 2 diabetes was assessed by standardised actuarial life-table methods and the pairwise concordance rate (proportion of concordant pairs over the sum of concordant and discordant pairs) was calculated. The observed rates of concordance for Type 2 diabetes at 1, 5, 10, and 15 years follow-up were 17%, 33%, 57%, and 76%, respectively. The concordance rate for any abnormality of glucose metabolism (either Type 2 diabetes or IGT) at 15 years follow-up was 96%. Since dizygotic pairs were not studied, this study cannot make any claims about genetic or environmental derterminants; the concordance between the monozygotic pairs could be due to shared genes or shared environment (Hopper, 1999).

In an editorial accompanying the 2 previous studies, Hopper (1999) pointed out that twin studies can never prove the existence of a genetic susceptibility, and at best can indicate the extent of genetic determination consistent with a specific model, under certain important assumptions. Hopper suggested that everyone has a "liability" to diabetes and this variable has a normal distribution across the population, but it has not been measured. The probability that a person is diabetic is presumed to depend on his liability. From the pattern of concordance and discordance for disease in twin pairs the correlation between twins in their unmeasured liabilities is estimated. Then, a simple linear model for the effects of genetic and environmental causes of variation in liability is assumed. Heritability is defined to be "the

proportion of variation in liability across the population that the model attributes to genetic factors", and is estimated from the twin data. The problem is that the normal distribution assumption cannot be tested.

Although no twin studies are available from Africa, Swai et al. (1990) reported that 14.4% of blacks with Type 2 diabetes had a first degree relative with diabetes. From the Cameroon Mbanya et al. (2000) showed that diabetes and IGT were more prevalent in the offspring of African Type 2 diabetic parents, and this may be due to an underlying degree of β-cell impairment marked by reduced early-phase insulin secretion. Since the control population was selected on the basis of the tribal and socio-economic status of the diabetic population from Yaoundé, one can assume that both case and control subjects were exposed to the same environmental factors. The findings from this study are thus very likely attributable to genetic factors. Furthermore, there was respectively 16% and 44% glucose intolerance in the offspring when one or both parents were glucose intolerant, implicating a "double dose" of the genetic effect. The sex of the glucose-intolerant parent did not seem to affect the glucose tolerance status of the offspring.

Genetic studies conducted on specific rodent models of Type 2 diabetes are promising. Though there is no guarantee that the genes causing diabetes in these polygenic rodent models are the same as those involved in human disease, these analyses (like those of human subtypes) provide examples of "real" diabetes genes and clues to the key metabolic pathways responsible for the maintenance of normal glucose homeostasis (McCarthy, 2001). Advances in the understanding of the physiology of nutrient regulation and of diabetes pathogenesis, generate a constantly expanding list of candidate genes. The classic approach to study such genes is association analysis relying on linkage disequilibrium for the detection of a signal and positive results are only likely at, or very close to, functional variants. Association studies therefore provide a powerful approach for analysis of small regions, but remain problematical for screens of larger genomic regions (McCarthy, 2001). Examples of loci associated with susceptibility to Type 2 diabetes include the variable region upstream to the insulin gene (insulin variable number tandem repeat (INS-VNTR), and the genes for the insulin promoter factor-1 (IPF-1), the sulphonylurea receptor and insulin-receptor substrate-1 (McCarthy, 2001). The linkage disequilibrium approach has many shortcomings and sometimes yields contradictory results. A further limitation is that many linkage disequilibrium studies have hitherto focused on coding regions, leaving regulatory gene sequences mostly unexplored (McCarthy, 2001). The other approach to study the genetics of Type 2 diabetes is the

genome-wide linkage approach, which attempts to locate such genes through their genomic position alone. The rationale is as follows: if family members share a given phenotype, they will also show excess sharing of chromosomal regions immediately surrounding genes contributing to that phenotype. Diabetes-susceptibility genes can therefore be revealed by finding regions of increased allele-sharing in collections of small multiplex families with affected sib pairs. Because such studies depend on the detection of co-segregation within families (i.e. linkage) and, unlike association studies, do not require allele-specific effects (i.e. linkage disequilibrium), they are capable of detecting a signal over a wide area (10-30 centimorgan), thereby allowing analysis of the entire genome with only a few hundred polymorphic markers (McCarthy, 2001). In his review of the subject, McCarthy pointed out that major advances in statistical methods and technological developments such as single nucleotide polymorphism (SNP) genotyping, proteomics, transcriptional profiling and the development of genomics databases may aid researchers to find the precise site(s) of aetiological variation within regions of interest. The GENNID (Genetics of NIDDM) study in the U.S. that started in 1993 employed the genome-wide search approach. This group subsequently identified a major susceptibility locus on chromosome 2 (Hanis et al, 1996). A similar approach in Finland led to the mapping of a gene associated with an insulin secretion defect (Mathani, 1996).

2.6.2 Foetal origins

Barker's group (1989) examined cardiovascular mortality in men born in Hertfordshire, England, in the early decades of the century, on whom good records had been kept of size at birth and growth in infancy. They showed that subjects with the lowest birth weight and weight at one year had the highest death rates from ischaemic heart disease as adults. In 1992 Hales and Barker proposed the 'thrifty phenotype' hypothesis to explain the pathogenesis of Type 2 diabetes. Central to this hypothesis was the concept that poor nutrition in foetal and early infant life may be detrimental to the development and function of β-cells. They proposed that as long as the foetus/infant persists in the undernourished state there is no need to produce much insulin. However, a sudden move to good or over-nutrition exposes the reduced state of β-cell function and diabetes results. A positive continuous relationship between height and 120 min plasma glucose for both male and female subjects was described (Brown et al, 1991). These authors showed that subjects with IGT were significantly shorter than control subjects. Subsequently, Hales and Barker (1991) proposed that cardiovascular disease might be a 'programmed' effect of interference with early growth and development. The association of Type 2 diabetes and IGT with ischaemic heart disease (Fuller, 1980) and

hypertension (Modan, 1985) led to the suggestion that the thrifty phenotype hypothesis may also be linked to the metabolic syndrome (Hales and Barker, 1991). It is, however, accepted that additional factors such as obesity, ageing, physical inactivity, and other processes leading to insulin resistance must also play a part in determining the time of onset as well as the severity of Type 2 diabetes (Fig.2.6.2/1).

Lawlor et al. (2002) investigated not only the inverse association between height and glucose intolerance but also the association between leg and trunk length and glucose intolerance. They found that total height was weakly inversely associated with diabetes but this masked differences between leg and trunk. Leg length was inversely associated with Type 2 diabetes whereas trunk length was not associated with diabetes. These authors concluded that leg length is an indicator of early childhood environmental circumstances, in particular of infant nutrition. These results suggest that poor infant nutrition is an important causal factor in the development of Type 2 diabetes and insulin resistance in later life.

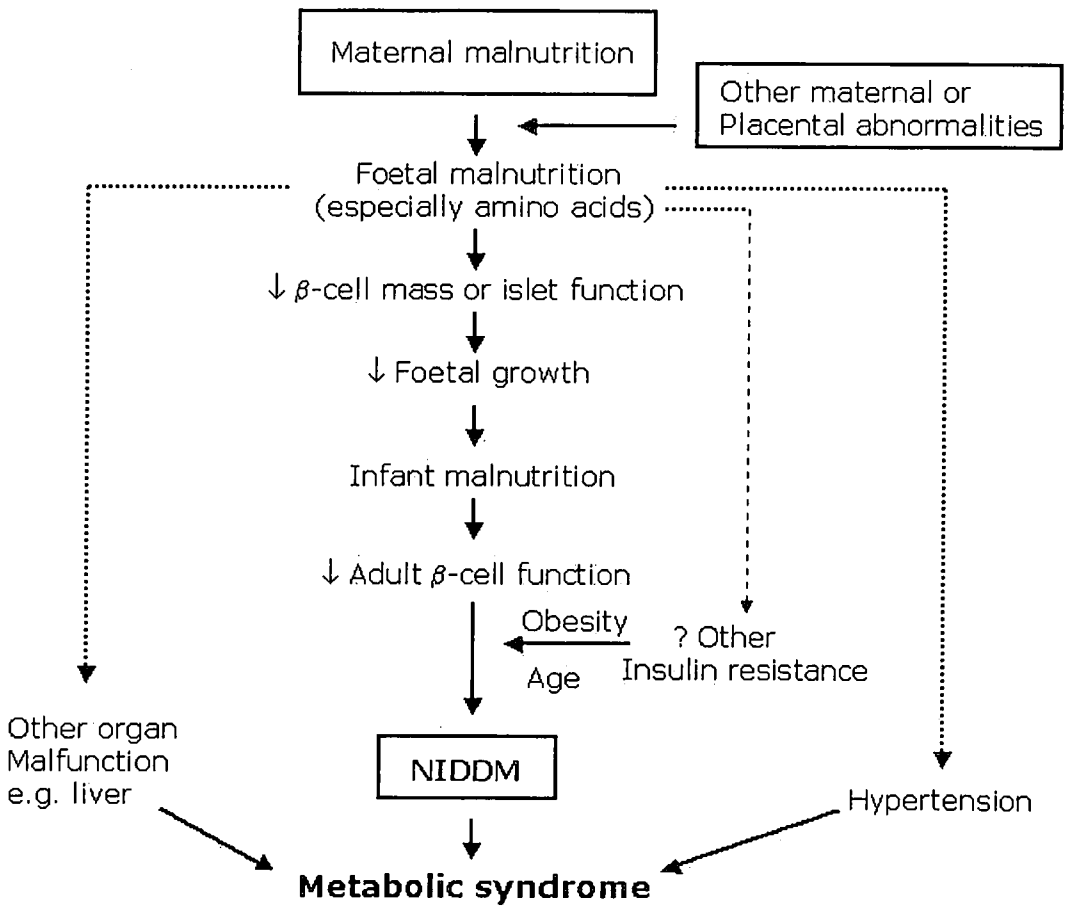


FIG. 2.6.2/1. Pathogenesis of Type 2 diabetes as part of the metabolic syndrome (The thrifty phenotype hypothesis. Hales, 2001).

Since the original descriptions of the relationships between birth weight or thinness at birth, indicated by a low ponderal index (birth weight/length^3) and the later development of Type 2 diabetes and the metabolic syndrome, these findings have been replicated in more than 30 studies in diverse populations around the world (Hales, 2001).

In a recent update on the thrifty genotype hypothesis, Hales (2001) explained that it has become increasingly apparent that the response to foetal malnutrition entrains not only (presumably advantageous) selective preservation of key organs but also metabolic adaptations of advantage for postnatal survival. The thrifty phenotype is thus not only thrifty with respect to antenatal life, but also in relation to the use of poor nutritional resources postnatally. The poorly nourished mother essentially gives the foetus a forecast of the nutritional environment into which it will be born. Processes are set in motion that lead to a postnatal metabolism adapted to survival under conditions of poor nutrition. The adaptations only become detrimental when the postnatal environment differs from the mother's forecast, with an over abundance of nutrients and consequent obesity. An updated version of the diagrammatic representation of the thrifty phenotype hypothesis is shown in Fig. 2.6.2/2.

Foetal hormones promote growth and development in utero by altering both the metabolism and gene expression of the foetal tissues. These hormonal actions ensure that foetal growth rate is commensurate with the nutrient supply and that pre-partum maturation occurs in preparation for extra uterine life (Fowden, 1995). Like other mammals the human foetus responds to under-nutrition by metabolic changes, redistribution of blood flow and changes in the production of foetal and placental hormones that control growth (Fig.2.1.6/3) (Barker (2001). Slowing growth in late gestation leads to disproportion in organ size since organs and tissues that are growing rapidly at the time are affected the most. For example, under nutrition in late gestation may lead to reduced growth of the kidney that is developing rapidly at that time. Reduced replication of kidney cells may permanently reduce cell numbers, since no early postnatal compensation in either nephron number or nephron size takes place (Hinchliffe, 1992).

Shires et al. (1978) studied the insulin response to a glucose load in four groups of subjects: i) obese 'chemical diabetics' (including some individuals with IGT); ii) obese symptomatic but untreated diabetics; iii) non-diabetic non-obese males; and, iv) non-diabetic obese females.

They found a relatively low insulin response to glucose in the normal males. Severe insulinopaenia was observed in the obese symptomatic diabetics. The obese non-diabetic females had a significantly greater insulin response at all times during the OGTT except at 60 minutes compared with the non-obese male subjects. The authors concluded from these data that obesity causes insulin resistance and hyperinsulinaemia, followed by a progressive decline in insulin secretion with increasing glucose intolerance eventually leading to β-cell exhaustion in blacks with diabetes. Joffe et al., (1992) regarded this as (indirect) evidence of the Hales and Barker hypothesis (1991) for the development of Type 2 diabetes in blacks.

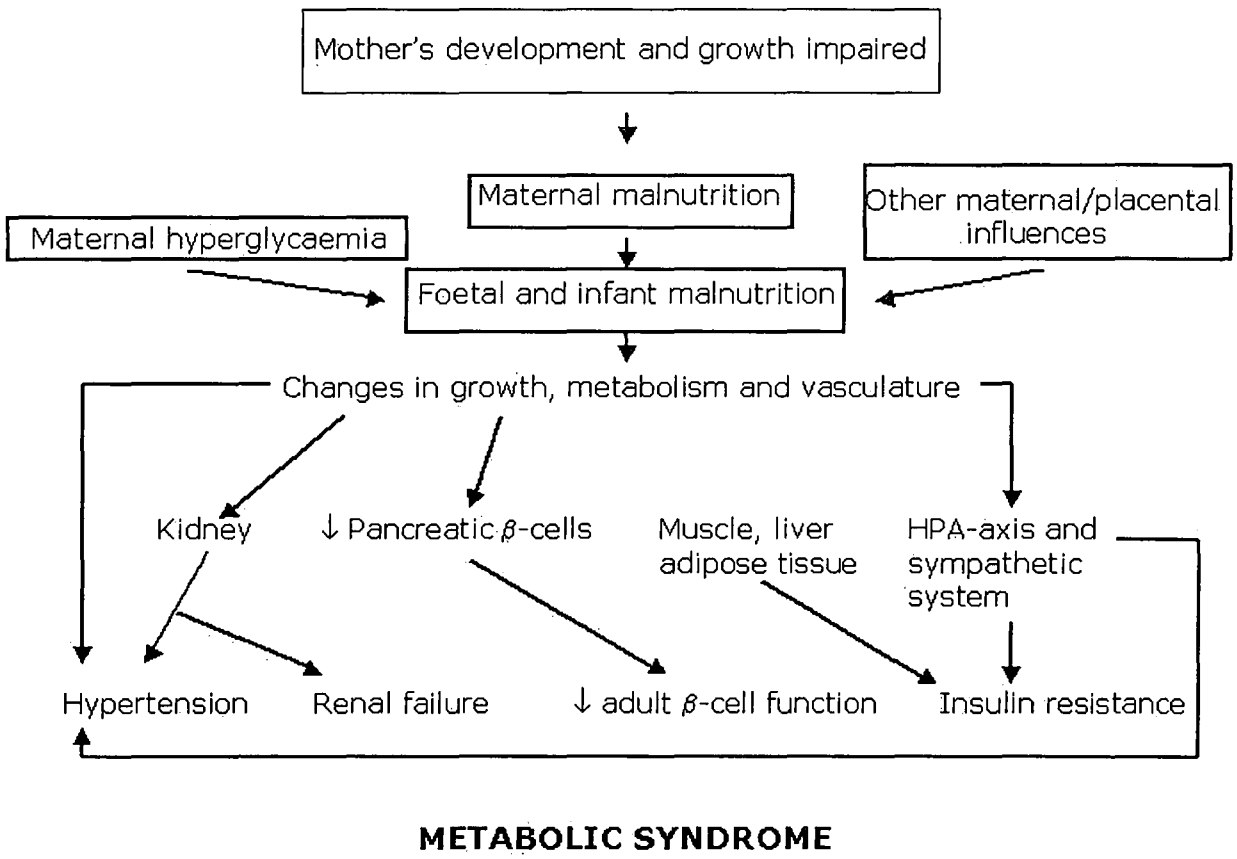


FIG. 2.6.2/2. An updated diagram of the thrifty phenotype hypothesis incorporating recent findings and concepts. Also included are new speculative features: maternal hyperglycaemia as predisposing factor and key roles of the vascular, hypothalamic-pituitary-adrenal axis and sympathetic systems (Hales, 2001). HPA= hypothalamic-pituitary-adrenal axis. (Hales, 2001).

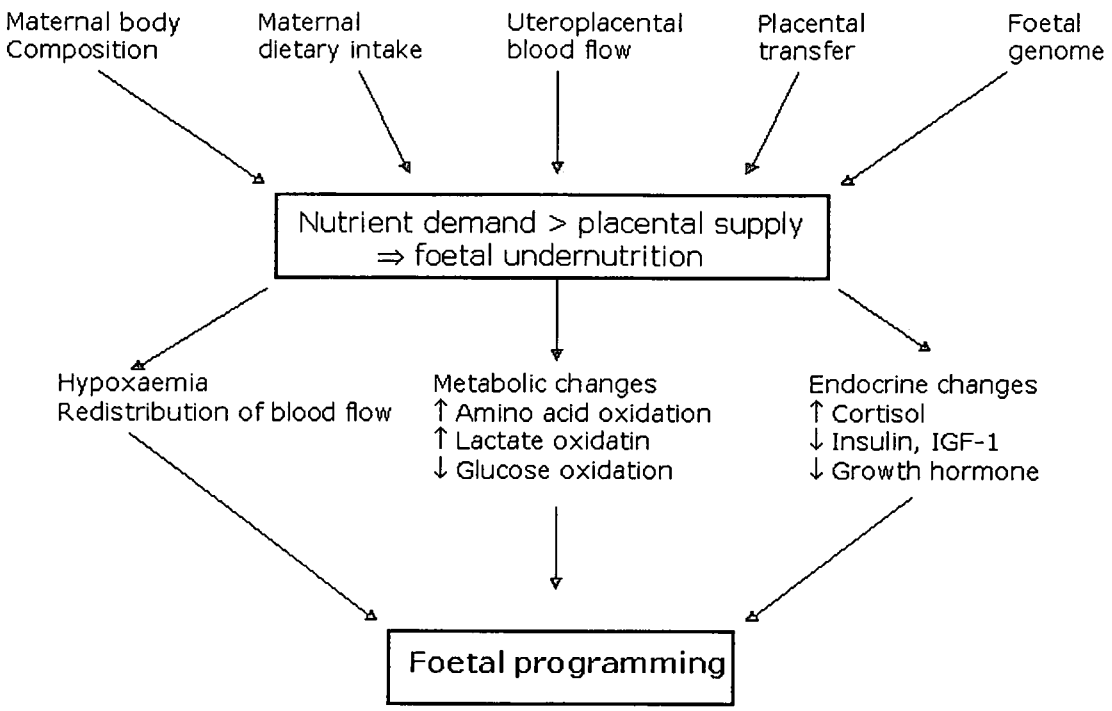


FIG. 2.6.2/3. Foetal adaptations to under-nutrition: a framework (Barker, 2001).

In a subsequent study Shires, et al. (1985) investigated and compared the β-cell response to a glucose challenge followed by intravenous glucagon and tolbutamide (maximal β-cell stimulation) in a group of obese black and white females. The basal insulin levels in the black group were significantly lower compared with the white group. (Interestingly, the mean fasting insulin levels of the obese blacks in this study were only about half that of the obese black females in their earlier study although they were equally obese). The black group also had significantly lower insulin levels at 30 and at 60 minutes post challenge. Basal as well as 30- and 60-minute C-peptide levels were also significantly lower in the black subjects. The authors concluded that β-cell secretory capacity of black obese subjects was less than that of white obese subjects.

The same group (1992) also examined and compared insulin receptor binding characteristics in four groups of ten black women: a young non-obese non-diabetic group (A) ; a middle-aged, non-obese, non-diabetic group (B); a middle-aged, obese, non-diabetic group (C); and a middle-aged, obese group of newly diagnosed but untreated diabetic patients (E). They found that specific insulin binding as well as total receptor concentration decreased significantly from group A through group B and C to group D. Receptor concentrations correlated inversely with fasting plasma glucose, insulin, free fatty acids, and body mass index, suggesting a dependence on these metabolic variables leading to receptor down-regulation. It was concluded that Type 2 diabetes appeared to be preceded by a progressive decline in receptor concentration in middle-aged, obese, non-diabetic individuals in whom fasting hyperinsulinaemia may have led to the down-regulation of insulin receptors.

Using the euglycaemic insulin clamp technique, Wing et al, (1992) showed that glucose utilisation was appreciably reduced in obese, black patients with untreated Type 2 diabetes. This abnormality normalised following sulphonylurea treatment and was accompanied by an increase in insulin receptor concentration but not with changes in basal insulin secretion as determined from C-peptide measurements.

Following these studies Joffe and co-workers (1992) proposed an alternative hypothesis for the pathogenesis of Type 2 diabetes in black South Africans (Fig. 2.6.2/4). This concept was also partly based on the Hales and Barker hypothesis (1992) that proposed that one of the major long-term consequences of inadequate early nutrition is impaired development of the endocrine pancreas and a greatly increased susceptibility to the development of Type 2 diabetes. As was eloquently outlined by Joffe and Seftel (1994) their hypothesis had important therapeutic implications. It was predicted that the therapeutic response to oral sulphonylureas would be rather brief in black patients with Type 2 diabetes before secondary failure develops. This has, however, yet to be proved in prospective studies. The frequent need for permanent or intermittent insulin therapy in these patients has also been mentioned.

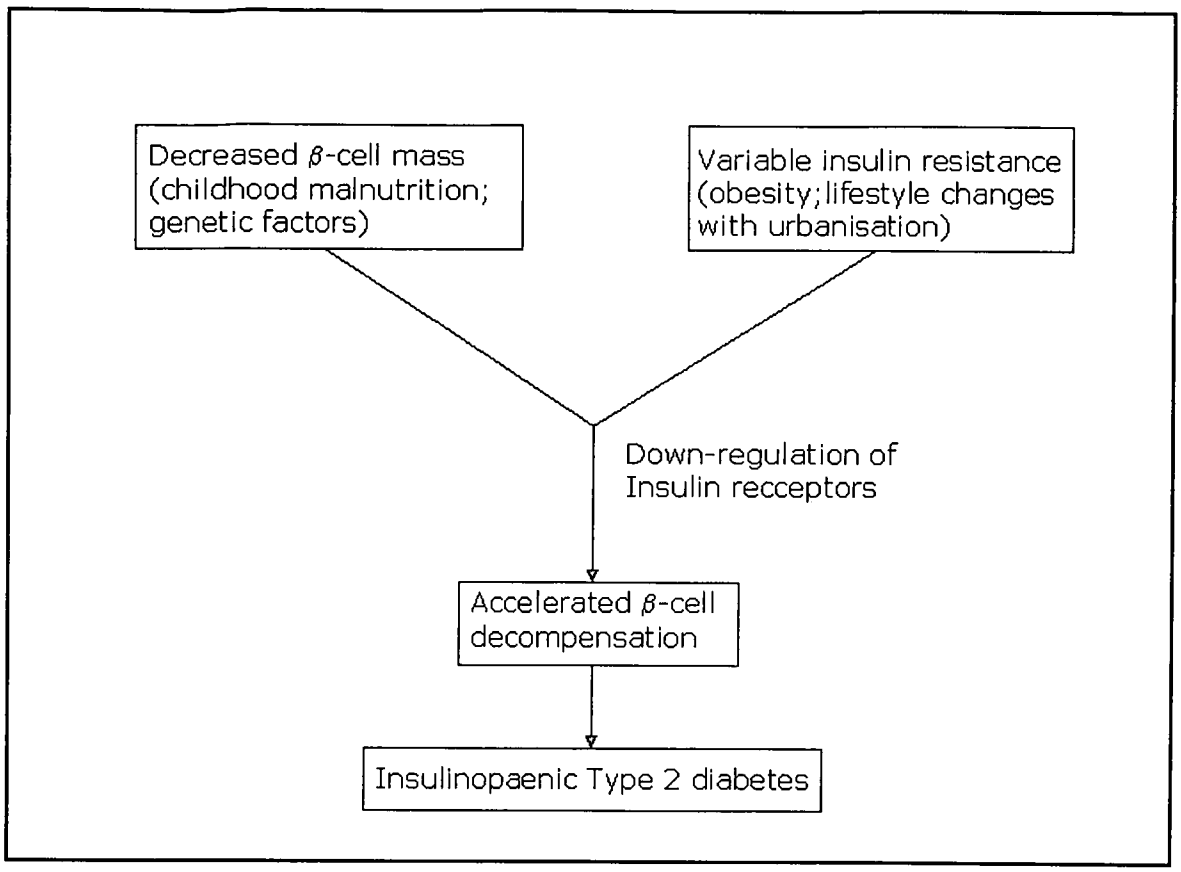


FIG. 2.6.2/4. Proposed scheme for the pathogenesis of Type 2 diabetes in the black population of southern Africa (Joffe et al., 1992).

Crowther et al. (1998) investigated the relation between glucose tolerance and birth weight in a group of 7-year-old black South Africans for whom longitudinal anthropometric data were available. OGTT's were carried out on 152 subjects and inverse correlations were found between birth weight and insulin secretion during the first 30 minutes as well as at 90 minutes and also between birth weight and the 30 min glucose concentrations. Children born with low birth weights but who had high weights at 7 years had higher insulin concentrations and indices of obesity compared with those with low birth weights and low weights at 7 years. The authors concluded that low birth weight in conjunction with rapid childhood gains in weight especially as subcutaneous fat, produces poor glucose tolerance in 7-year-old children and can make them susceptible to the development of Type 2 diabetes later in life.

In South Africa Levitt and co-workers (2000) examined the association between low birth weight and glucose intolerance, blood pressure, and dyslipidaemia in young, non-obese adults from mixed ancestry and a community undergoing the health transition. Hypothalamic-pituitary-adrenal function and responsiveness to ACTH was also studied. A group of low birth weight 20-year old subjects (n=59) was compared to a control group (n=54). After controlling for body weight, the mean fasting plasma glucose concentration in the low birth-weight group was significantly higher than in the control group (4.9 mmol/L vs. 4.7 mmol/L). Furthermore, 6 subjects had IGT and one subject was diagnosed with Type 2 diabetes in the under-weight group vs. no one with abnormal glucose tolerance in the control group. After controlling for body weight and gender, systolic and diastolic blood pressures were significantly higher in the underweight group. There were no significant differences in plasma triglycerides and cholesterol concentrations and cholesterol sub-fractions between groups, a finding that was somewhat unexpected. An ACTH stimulation test was done at 09h00 on a subset of both the underweight and control groups (n=32 and n=36 respectively). Plasma cortisol concentrations at 0900 h were significantly higher in the group who was underweight at birth than the normal birth weight group. After ACTH stimulation plasma cortisol levels were significantly higher in the low birth weight group across all time points from 0 to 60 min than in the control group. Similarly the area under the plasma cortisol curve from 0 to 60 min was greater in the low birth weight group than in the control group.

The evidence for the association of adverse adult outcomes with lower birth weight is strongest for blood pressure and impaired glucose tolerance. Fewer studies link heart disease and stroke to low birth weight. The foetal origins of adult disease is no longer just an hypothesis; it is widely accepted and may be critically important in developing countries (Robinson, 2001).

2.6.3 Lifestyle and Stress

2.6.3.1 URBANIZATION

Urban-rural differences in the prevalence of diabetes have been well described and are widely acknowledged (King et al, 1991). In Southern Africa Politzer (1960) and Politzer and Schneider (1962) found that the prevalence of diabetes was 0.23% and 0.58% for a rural and urban group of blacks respectively. Excluding subjects < 30 years, the corresponding rates were 0.36% and 1.16%. Levitt (1993) found that urbanization, defined as 40% or more of life spent in the city, was a risk factor for Type 2 diabetes in the black population of Cape Town.

2.6.3.2 PHYSICAL ACTIVITY

Physical inactivity as a risk factor for type 2 diabetes was examined in several studies and yielded inconsistent results. Helmrich et al. (1991) used questionnaires to study physical activity in relation to the subsequent development of type 2 diabetes over a period of 14 years in 5990 male alumni of the University of Pennsylvania. They found that the age-adjusted risk of type 2 diabetes was reduced by 6% for every increment of 500 kcal per week in leisure-time physical activity. Although vigorous sports activity was most effective in decreasing the risk of type 2 diabetes, moderate sports activity was also effective.

Dowse et al. (1991) reported on the effect of physical activity and abdominal obesity as risk factors for Type 2 diabetes and IGT in the inhabitants of Mauritius. This study showed for the first time an association between physical inactivity and risk of both type 2 diabetes and IGT after controlling not only for age and BMI but also for WHR and family history of diabetes. On the other hand Jarrett et al. (1986) failed to find an association between 2-hour blood glucose levels and physical activity in British male civil servants. Inconsistencies in results between studies may reflect methodological differences rather than true heterogeneity of effects (Dowse et al, 1991). The question remained whether physical activity was universally related to insulin concentrations (and therefore insulin sensitivity) in different populations at high risk for diabetes but that greatly differed by location, ethnic group and BMI. Kriska and co-workers (2001) estimated insulin sensitivity by mean insulin concentrations at zero and 120 minutes post glucose load, and assessed physical activity by questionnaire in a group of non-diabetic Pima Indian men and women and a group of non-diabetic men and women from Mauritius. They found that after controlling for BMI and fat distribution physical activity was negatively associated with insulin concentrations both in the Pima Indians, who tend to be overweight, and in Mauritians, who are leaner. These findings suggested a beneficial role of activity on insulin sensitivity that is separate from any influence of activity on body composition.

The Da Qing study investigated whether diet and exercise interventions in subjects with IGT may delay the development of type 2 diabetes (Pan et al, 1997). In 1986, 110 660 men and women in the city of Da Qing, China, were screened for IGT and type 2 diabetes. Of these individuals, 577 were classified (using WHO 1985 criteria) as having IGT. Subjects were randomised into a clinical trial, either to a control group or to one of three active treatment groups: diet only, exercise only, or diet plus exercise. The cumulative incidence of diabetes at 6 years was 67.7% (95% CI, 59.8-75.2) in the control group compared with 43.8% (95% CI,

35.5-52.3) in the diet group, 41.1% (95% CI, 33.4-49.4) in the exercise group, and 46.0% (95% CI, 37.3-54.7) in the diet plus exercise group ($p < 0.05$). The relative decrease in rate of development of diabetes in the active treatment groups was similar when subjects were stratified as lean or overweight (BMI $<$ or $\geq$ 25 kg/m^2). After adjusting for differences in baseline BMI and glucose, the diet, exercise, and diet-plus-exercise interventions were associated with 31 % ($P < 0.03$), 46% ($P < 0.0005$), and 42% ($P < 0.0005$) reductions in risk of developing diabetes, respectively. The Da Qing study thus convincingly showed that diet and/or exercise interventions led to significant decrease in the incidence of diabetes over a 6-year period among those with IGT.

2.6.3.3 OBESITY

The relationship between obesity and diabetes has been recognized for many years. Joslin reported in 1921 that rates of diabetes were 6-12 times greater in "fat" people than in "thin" (West, 1978 page 232). The prevalence of carbohydrate intolerance in grossly obese subjects is around 50% (Bray, 1990). The relationship between obesity and diabetes is, however, a complex one and influenced by several factors like age, magnitude of obesity, location of fat, the duration of obesity, familial relationships, exercise and population studied.

The Whitehall survey (Jarrett, 1979) found that initial fasting and 2-hour blood glucose levels were the most powerful and equally important variables in predicting subsequent worsening to diabetes. In this study obesity did not predict worsening to diabetes when blood sugar levels were taken into account.

Data for 113 861 nurses (98% white), age 30-55 years, from the Nurses health study, was collected from 1976 onwards until 1984 to determine the contribution of obesity and weight gain at different periods of life on the subsequent development of Type 2 diabetes (Colditz, 1990). An extremely strong relation between Type 2 diabetes and BMI was observed across the age groups. The relative risk of diabetes was elevated for women with body mass index greater than 22 kg/m^2 and was particularly pronounced for those with a body mass index greater than 25 kg/m^2. In these women current BMI correlated stronger with the development of Type 2 diabetes than BMI at age 18 years. Unfortunately waist and hip circumferences were not measured in this study.

In the Pima Indians, however, diabetes incidence was strongly related to obesity. Knowler et al. (1981) reported that age-sex adjusted diabetes incidence rates increased steadily from 0.8 cases/1000 person-years in the least obese to 72.2 cases/1000 person-years in the most

obese group. In the same study, after adjusting simultaneously for age and obesity, it was estimated that the incidence rate of diabetes was 2.3 times higher in subjects with one diabetic parent compared to subjects with both parents non-diabetic. The corresponding figure when both parents were diabetic was 3.9, emphasizing the importance of family history in this population. The authors concluded that both obesity and hereditary factors appeared to be important for the development of diabetes.

Modan and co-workers (1986) found in Israeli subjects that the past degree of overweight determined the rates of both Type 2 diabetes and IGT ten years later. A concurrent high degree of overweight at the time of examination affected the rate of IGT but not of diabetes. These workers also found a threshold effect of BMI > 27 on the rate of glucose intolerance and BMI > 31 on the rate of Type 2 diabetes.

Seftel (1961) commented that 67% of African diabetics attending the diabetic clinic at Baragwanath Hospital were obese, but the definition of obesity was not stated. Scanty information is available on the body fat distribution of blacks in South Africa.

Type 2 diabetes in children is an emerging public health problem and is increasingly being reported in children from industrialised countries (Fagot-Campagna, 2001). Most children with Type 2 diabetes are diagnosed over the age of 10 years and are in middle to late puberty. Obesity is a hallmark of Type 2 diabetes, with up to 85% of affected children either overweight or obese at diagnosis. A family history of diabetes is also usually present. Type 2 diabetes in children occurs more commonly in girls and is also associated with low birth weight in Pima Indians. The prevalence of Type 2 diabetes in children in populations in North America ranges from 4.1 to 509 per 1000 . Acanthosis nigricans and polycystic ovarian syndrome (PCO) are associated with insulin resistance and obesity and both are common in youth with type 2 diabetes (ADA, 2000).

Obesity-related cytokine production was recently postulated as another possible mechanism linking obesity and Type 2 diabetes. In the women's health study, Pradham et al. (2001) found that elevated levels of C-reactive protein (CRP) and interleuken-6 (IL-6) predicted the development of Type 2 diabetes. In this study that started in 1992, a nationwide cohort of 27 628 women were followed for 4 years. Blood samples were collected for CRP and IL-6 at baseline. After 4 years 188 women developed diabetes. These subjects were defined as cases and their levels of CRP and IL-6 at baseline were compared with those of 362 disease free

matched controls from the same study. The relative risks of future diabetes for women in the highest vs. lowest quartile of these inflammatory markers were 7.5 for IL-6 (95% CI 3.7-15.4) and 15.7 for CRP (95% CI 6.5-37.9).

2.6.3.4 CENTRAL OBESITY

Not only obesity, but also body fat distribution is important in the eventual development of diabetes. Vague already observed in 1956 that android obesity was associated with a frequent tendency to diabetes and vascular accidents (Vague, 1956). Ohlson (1985) reported that 6.3% of 629 men aged 54 years at baseline and followed for 13.5 years, developed diabetes. New cases of diabetes were significantly more obese at baseline than non-cases. In this study Ohlson also found an exponential "dose-response" relationship between the incidence of diabetes and waist-to-hip circumference ratio (WHR) as well as body mass index (BMI). The risk for diabetes in the upper 5% of the distribution of the WHR was 16.6 times higher than the risk in the lowest quintile (95% CI 4.4-76.7). Furthermore, 21.4% of men within the upper 5% of the BMI distribution developed diabetes. The combined influence of BMI and WHR on the risk of diabetes was also examined in Ohlson's study. The highest risk (15.2%) was seen in the highest tertile for both BMI and WHR. The conclusion from this important study was that not only the degree of obesity but also a certain localization of adipose tissue is a risk factor for diabetes mellitus. These two factors seem to be independent of each other and to potentiate each other as risk factors for the development of diabetes.

More evidence of an association between central obesity and glucose intolerance came from the Mauritius study (Dowse et al, 1991). This study showed that although BMI and WHR were independently significant risk factors for Type 2 diabetes and IGT, WHR conveyed relatively stronger risk for Type 2 diabetes than BMI in women, whereas the converse was true for men. This was also the first report of an association between abdominal obesity and IGT.

Evans et al. (1983) found that increasing localization of fat in the upper body was associated with a continuous decline in sex hormone binding globulin and an increase in percentage free testosterone. The authors suggested that increased androgenic/estrogenic activity is an important factor in the pathogenesis of central obesity by promoting redistribution of body fat, enlargement of adipocytes and a decrease in sex hormone binding globulin levels.

Peiris et al. (1986) presented evidence that obesity was associated with increased insulin secretion and that this association was related to the magnitude of adiposity but not to central obesity. Central obesity, on the other hand, was accompanied by a progressive decline in the

hepatic insulin extraction fraction resulting in increased systemic delivery of insulin. Combined, these effects accounted for the pronounced peripheral hyperinsulinaemia characteristic of upper body obesity.

In the Health Professional's Follow-up study, a large cohort (n=27,983) of U.S. men were prospectively examined according to nine strata of BMI and waist-to-hip ratio (WHR) to determine more precisely at what levels the risk of diabetes is increased (Chan et al, 2000). Absolute weight-gain since early adulthood was also examined as a potential risk factor for diabetes. In this study, an extremely strong association was found between BMI and risk of diabetes, and the risk of diabetes increased continuously with increasing levels of BMI. Men with a BMI of 25.0-26.9 kg/m^2 had a risk 2.2 times (95% CI 1.3-3.8) greater than men with a BMI<23.0 kg/m^2 after adjusting for age, family history, and smoking habits. Risk rose markedly for men with a BMI ≥ 29 kg/m^2. The men in the highest category of BMI (≥ 35 kg/m^2, had the highest RR (multivariate RR = 42.1, 95% CI 22.0-80.6). When WHR was added to the model (controlling for family history, age, and smoking), the relative risks associated with nine categories of BMI were only modestly attenuated. Early obesity (at age 21 years) and weight gain since then also independently predicted diabetes in later years. Recent weight gain (within the last 5 years) was also strongly associated with the risk of diabetes. Waist circumference was positively associated with the risk of diabetes and the magnitude of excess risk was stronger than with WHR. Chan et al concluded that because waist circumference has less measurement error than WHR, it might be a better indicator of the relationship between abdominal adiposity and the risk of diabetes. In this study fat distribution appeared to be a modest independent risk factor for diabetes among men in the top 5% of WHR, but the strong relative risks associated with even moderate BMI levels suggested that overall obesity is the dominant risk factor for diabetes in men.

Recently Levitt et al. (1993) described an association between central obesity and diabetes in South African blacks. The risk factors for Type 2 diabetes were studied in the Western Cape in a population of people from mixed ancestry (Levitt et al, 1999). In this sample of 974 participants (age range 15-86 years) the crude prevalence of Type 2 diabetes was 7.1% and IGT 8.0%. Age, family history of diabetes, waist circumference and physical inactivity were all identified as independent risk factors for Type 2 diabetes. The population attributable risk fraction for upper segment fat distribution and physical inactivity were 52.4% and 21.2% respectively. These findings implied that the prevalence of Type 2 diabetes in the community

might fall from 7.1 % to 4% should both upper segment fat distribution and low levels of physical activity be removed.

In a cross-sectional survey Okosun and co-workers (1998) examined the relationship between waist circumference, blood pressure and fasting glucose levels in a group of 5042 African, Afro-Caribbean or Afro-American subjects, 25-74 years of age, from Nigeria, Jamaica, and the U.S. respectively. They observed a positive association between weight, BMI, waist, hip, and WHR and increased risk of high blood pressure in all three populations. A similar association of increased risk of Type 2 diabetes was observed in the Jamaica and the U.S. populations. In addition a gradient in the direction of Nigeria, Jamaica, and U.S. for risk factors (waist circumference, weight, BMI, hip, WHR) and prevalence of hypertension and Type 2 diabetes was observed. The authors concluded that studies are needed to investigate waist circumference as a marker of the insulin resistance syndrome in African subjects.

More studies are needed to better describe the relation between central obesity and glucose intolerance in black subjects – a need that was also recognized in the U.S. (Gavin, 1990).

2.6.3.5 AGING

Due to the health transition that is sweeping around the world, the number of older people (aged 60 years or more) in less developed countries will increase from 171 million in 1998 to 1594 million by 2050 (Editorial-Lancet, 1998). The effect of ageing on glucose tolerance had been extensively studied and still remains controversial. In most population studies the prevalence and incidence of diabetes increase with age (West, 1978). The mechanism of glucose intolerance with ageing is multifactorial and insulin resistance is regarded as the principal abnormality (DeFronzo, 1981).

2.6.3.6 SOCIO-ECONOMIC FACTORS

Socio-economic factors also contribute to the development of Type 2 diabetes. King et al. (1991) remarked that glucose intolerance reaches its greatest frequency in developing countries, among minority groups and the disadvantaged in the industrialized countries. In Scotland, Evans et al. (2000) found that the prevalence of Type 2 diabetes (not Type 1 diabetes) varied by deprivation. The most deprived people in this large study were 1.6 times (95% CI 1.4-1.8) more likely to have Type 2 diabetes than those least deprived. In this study there was also a significant increase in BMI with increasing deprivation in Type 2 diabetes. Also from Scotland, Roper et al. (2001) reported that the mortality of patients with diabetes (both Type 1 and Type 2) was increased across all ages compared with the local population

without diabetes. The excess mortality was 2.2 times the national average, and increased with worsening material deprivation. The increased mortality was mostly attributed to cardiovascular disease and renal disease. The accompanying editorial (Williams, 2001) commented that "this study presented a depressing snapshot of the prospects for diabetic people in the UK today, which shows diabetes to be particularly mean: sexist, ageist, and with a clear tendency to kick the underdog".

2.6.3.7 STRESS

In spite of intensive research the primary cause of insulin resistance has not yet been identified. Since insulin resistance and Type 2 diabetes are strongly associated with central obesity, the pathophysiology of central obesity might provide a clue to the primary defect in the pathogenesis of insulin resistance (Björntorp, 1992 and Björntorp et al, 1999). The latter group designed a study to investigate the hypothalamic-pituitary-adrenal axis (HPA) in a large group of free-living people based on measurement of the concentration of free cortisol in saliva. Physiological stimuli such as perceived stress and lunch were recorded in addition to frequent sampling to establish circadian rhythm and a 0.5 mg dexamethasone suppression test to investigate the sensitivity of the HPA to feedback control. Subgroups of patients were selected on the basis of waist/hip circumference for further study. In a subgroup of men, Björntorp and co-workers found two extreme types of diurnal salivary cortisol curves: The first was characterized by a high variability, with high morning values and low afternoon-evening values, and a brisk response to lunch. The DXM test showed a marked suppression of cortisol secretion. The second showed a low variability, with low morning values, little response to lunch, poor response to dexamethasone, and low total cortisol secretion. The first pattern of response was significantly associated with low values of BMI, WHR, total and LDL-cholesterol as well as blood pressures, and high IGF-1. The second pattern of response was significantly associated with elevated BMI, WHR and saggital diameter, and an unfavourable lipid profile. Blood pressure and heart rate were also elevated. Serum testosterone and IGF-1 (a substitute measurement of growth hormone concentrations) were low. Björntorp and co-workers thus demonstrated in free-living non-diabetic men a dramatic difference between healthy subjects with a normally regulated, undisturbed HPA axis, and subjects with a suppressed HPA axis regulation and features of the metabolic syndrome. Björntorp hypothesised that the presumed chain of events in the development of insulin resistance starts with environmental stressors which in genetically susceptible individuals are followed by a central arousal syndrome and endocrine, anthropometric, metabolic and haemodynamic perturbations. Since genetic factors are also important, the glucocorticoid receptor gene was studied for mutations. They found a

Bcl I polymorphism associated with the metabolic syndrome (Björntorp et al, 1999). Homozygotes with this polymorphism were found in no less than 13.7% of Swedish males (Björntorp and Rosmond, 1999). O'Rahilly (1999) reviewed this study in depth and concluded that although the model is attractive, the available data do not, as yet, add up to compelling proof of the accuracy of their theoretical model.

2.6.3.8 ROLE OF INSULIN RESISTANCE AND INSULIN SECRETORY DYSFUNCTION IN THE PATHOGENESIS OF TYPE 2 DIABETES MELLITUS

For more than 2 decades the pathogenesis of Type 2 diabetes was considered to be due to two fundamental defects, insulin deficiency and insulin resistance (De Fronzo, 1988). These two defects are intimately related to one another in the pathogenesis of Type 2 Diabetes mellitus. Each of them can lead to the other secondarily and by more than one mechanism (De Fronzo, 1988). The relative contribution of each to the development of hyperglycaemia may differ due to heterogeneity of the disease but under most circumstances, insulin resistance is the earliest detectable defect (Groop, 2000). Much controversy still surrounds the basic mechanisms underlying these defects (Reaven, 1995 and Weyer, 2002). These concepts are summarised in Fig. 2.6.3.8/1.

De Fronzo presented evidence that the main sites of insulin resistance are at the level of the liver and muscle (De Fronzo, 1988). Progression from normal to IGT is associated with a reduction in insulin sensitivity at these tissues. Initially, glucose tolerance is only mildly impaired because of a compensatory increase in insulin secretion post-prandially and thus post-prandial hyperinsulinaemia. As glucose tolerance worsens due the progressive nature of β-cell dysfunction, the plasma insulin response will become insufficient to return the elevated glucose level to its basal level and fasting hyperglycaemia will ensue. The persistent basal and stimulated hyperinsulinaemia will lead to down-regulation of insulin binding and action. In the early stages of glucose intolerance hepatic glucose production (HGP) would remain within the normal range due to the suppressive effects of hyperglycaemia. As the plasma insulin response becomes progressively more impaired, either as a result of the initial defect or glucose toxicity, both the early and late phases of insulin secretion will become absolutely deficient. When the fasting plasma glucose concentration exceeds 7.8 mmol/L the restraining effect of hyperinsulinaemia on the liver is lost, and HGP increases progressively and is directly correlated to the rise in fasting glucose concentration. Interestingly, whole body glucose clearance decreases until FGP concentration reaches a level of 7.8 to 10.0 mmol/L after which it increases linearly with the further rise in plasma glucose levels. This linear increase in glucose disposal at plasma glucose concentrations >180 mg/dl can be viewed as a protective

mechanism that prevents the further development of severe hyperglycaemia and associated intracellular dehydration (De Fronzo, 1988). With further rises in FPG concentrations, the activity of glucose transport systems becomes severely impaired, intracellular enzymatic steps involved in glucose metabolism become depressed and plasma free fatty acid (FFA) concentrations increase, all contributing to a further increase in fasting and post-prandial glucose concentrations.

A question that was not yet fully answered was why glucose levels started to rise in diabetic patients at insulin levels that were not much different from that of normal control subjects Reaven (1995). In normal individuals adipose tissue is very insulin sensitive (Swislocki, 1987) while adipose tissue of patients with Type 2 diabetes is also insulin resistant and that these patients have elevated levels of non-esterified free fatty acid (NEFA) concentrations (Fraze, 1985). Reaven (1995) proposed that the increase in plasma NEFA concentration that occurs when insulin-resistant individuals cannot maintain a state of compensatory hyperinsulinaemia is primarily responsible for the development of significant hyperglycaemia in patients with Type 2 diabetes. NEFA decreases serum insulin-stimulated glucose uptake and the increased NEFA flux to the liver stimulates hepatic glucose production (Reaven, 1995). In addition chronic increases in NEFA concentration in rats as distinct from acute elevations, also inhibit β-cell response to glucose (lipotoxicity) (Sako et al., 1990 and Zhou et al., 1994). In addition, the increase in plasma NEFA and glycerol concentrations will stimulate hepatic VLDL-TG secretion, and render such individuals at risk of developing HTG, and a series of associated changes in lipoprotein concentration and composition (Reaven, 1995). Frank decompensation of glucose homeostasis only supervenes when circulating plasma insulin concentrations fall to a level which is no longer able to suppress NEFA and glycerol release from adipose tissue. Once this happens, fasting hyperglycaemia is the inevitable pathophysiological consequence, often in association with hypertriglyceridaemia. Based upon these considerations, Reaven (1995) suggested "that it is necessary to acknowledge the central role of the adipose tissue in the pathophysiology of Type 2 diabetes and to expand the triumvirate (De Fronzo, 1988) into a foursome, and accord the adipose tissue the recognition that is its due."

Studies performed on the Pima Indians contributed substantially to our knowledge of the pathogenesis of Type 2 diabetes in this ethnic group (Weyer, 2002). When early insulin secretion (AIR) and insulin sensitivity (M-low) in Pima Indians with NGT are plotted against one another, a hyperbolic relation emerges. This finding indicates that early insulin secretion increases with increasing insulin resistance and vice versa (Fig. 2.6.3.8/2A).

The signals involved in this feedback loop by which pancreatic β-cells are able to sense and compensate for changes in peripheral insulin sensitivity, are unknown (Weyer, 2002). These authors recently showed that both insulin resistance and impaired early insulin secretion are pre-diabetic abnormalities (primary defects) that are present many years before the onset of hyperglycaemia when glucose tolerance is still normal. Weyer et al. (2002) recently identified 17 Pima Indians who had measurements of insulin sensitivity and early insulin secretion initially when they had NGT, and again as they developed IGT and ultimately type 2 diabetes during an average follow-up of 5 years. The longitudinal changes in their insulin sensitivity and early insulin secretion were compared with those in a group of 31 non-progressors who remained NGT during a similar period of rime. The changes in their insulin sensitivity and early insulin secretion were superimposed onto the cross-sectional hyperbolic relation between AIR and M-low as established in a reference population of 277 Pima Indians with NGT (Fig. 2.6.3.8/2B.).

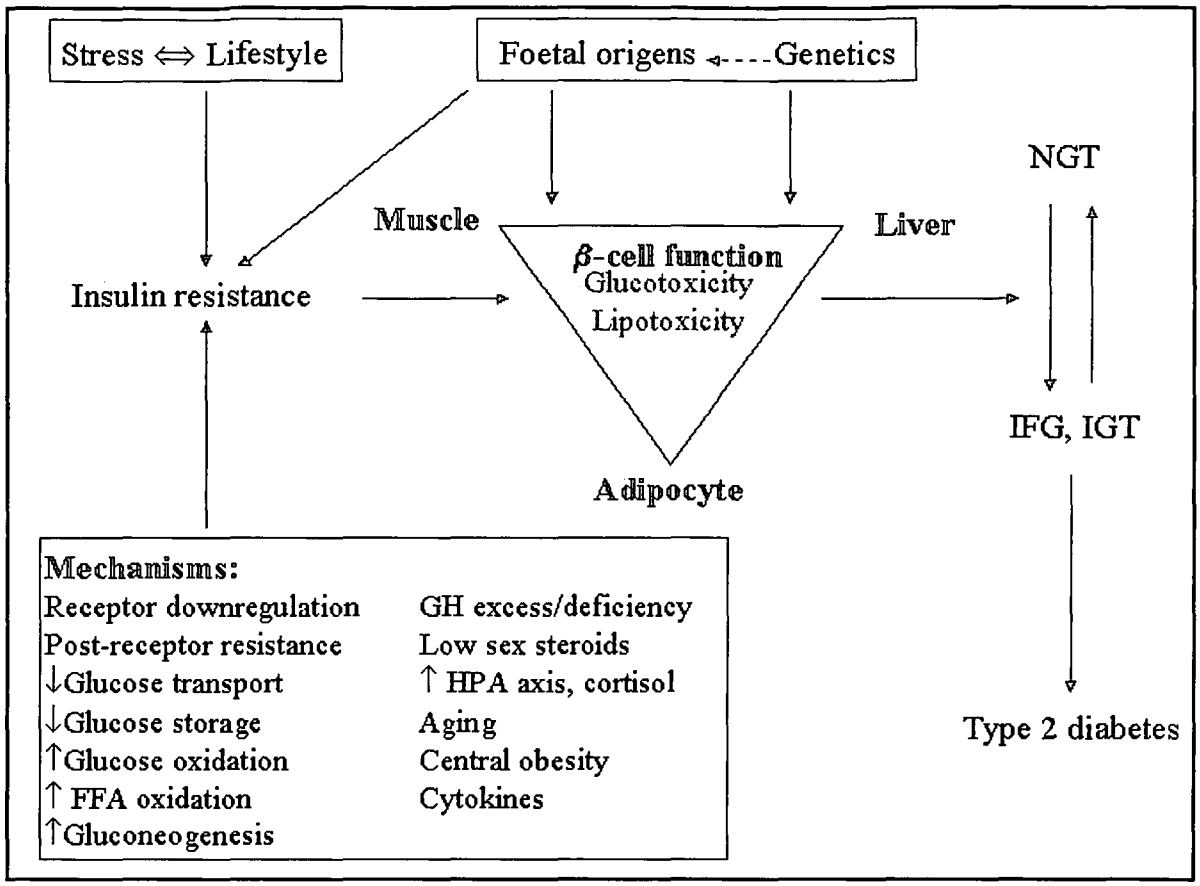


FIG. 2.6.3.8/1. Simplified scheme of contributing factors and key events in the pathogenesis of Type 2 diabetes (De Fronzo, 1981, DeFronzo 1988, Reaven 1995, Björntorp, 1999, Pickup, 1998, IDF 2002, Weyer 2002).

Both insulin resistance and early insulin secretion progressively worsened as people made the transition from NGT to IGT to diabetes (secondary defects), causing these people to deviate further and further from the normal range. The non-progressors also manifested a decrease in insulin sensitivity over time but were able to compensate with an appropriate, simultaneous increase in early insulin secretion, gradually climbing up the hyperbolic curve. Thus, in these patients, the inability of pancreatic β-cells to compensate for insulin resistance with an appropriate increase in insulin secretion appears to be a critical event in the pathogenesis of type 2 diabetes that distinguishes people who develop diabetes from those that are able to maintain NGT.

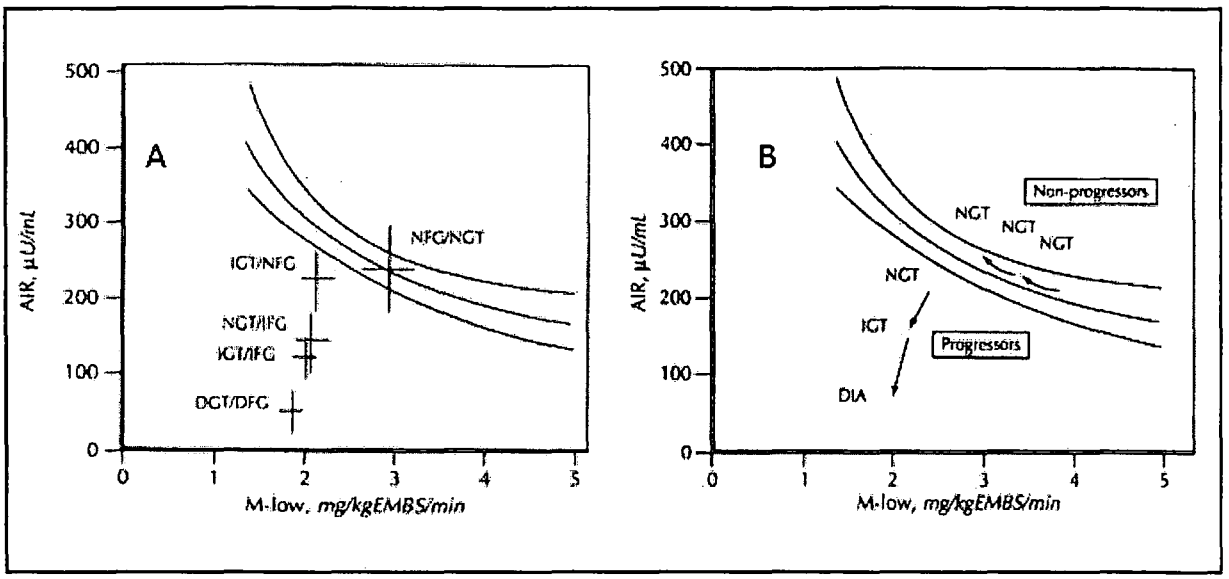


FIG. 2.6.3.8/2. Relation between early insulin secretion and insulin resistance in Pima Indians cross-sectional and longitudinally (Weyer, 2002).

2.7 The complications of diabetes mellitus

Diabetes has a serious impact on life and health and is therefore an important public health problem (Eko, 1988 p237). The major threat to life and health of those afflicted with the disease is the progressive damage to the eyes, kidneys, nerves and arteries that, unfortunately, results in early disability and death.

In most developed countries, diabetes ranks between fourth and eighth as a cause of death (WHO, 1985). In South Africa, diabetes ranked as the 7th (at 4.0%) and 10th (at 1.9%) commonest cause of death in 1996 for women and men respectively (Bradshaw et al, 2002). This is probably an underestimation for several reasons: Firstly, many related diseases are grouped together in international death statistics e.g. cardiovascular diseases, cancers, and lung diseases and, collectively, these rank higher than deaths from diabetes (WHO, 1985). Secondly, although diabetes may have caused or contributed to cardiovascular mortality, only the terminal event will be entered on the death certificate e.g. stroke, myocardial infarction, renal failure. During 1990 (before the AIDS epidemic) diabetes was responsible for 2.8% of total mortality in blacks 25 years and older in South Africa. In this age group diabetes was the

cause of death in 709 men (1.9%) and 1098 women (4.1%). Seventy-four deaths below the age of 25 years were attributed to diabetes (Central Statistical Services, 1990).

McLarty and co-workers investigated diabetes as a cause if death in one urban and two rural areas in Tanzania (McLarty, 1996). The adult male mortality rates associated with diabetes were 34, 30, and 15 per 100000 per year in the urban and two rural districts respectively. The figures for women were 21, 18, and 4 per 100000 per year, respectively. The percentages of all adult male deaths associated with diabetes were 2.6%, 2.1% and 0.7 % respectively. For women the percentages were 1.7%, 1.8%, and 0.2% respectively. Acute metabolic complications, infection, and stroke each accounted for approximately 30 % of all diabetic deaths. The authors concluded that most patients died from preventable causes, indicating a need for improved case-management of diabetic emergencies as well as better detection and treatment of hypertension.

Specific long-term complications of diabetes include the microvascular diseases namely retinopathy, nephropathy and neuropathy. Non-specific macrovascular complications are caused by accelerated occlusive atherosclerotic disease affecting the heart, brain and legs. The most common causes of death in 10 European countries are shown in Table 2.7/1. Overall mortality in Type 2 diabetes is increased 2-3 fold and life-expectancy is reduced by 5-10 years compared with the general population (Gill, 1991).

TABLE 2.7/1. Cause of death of patients with Type 2 diabetes in the WHO Multinational Study.

Cause of death	Pecentage of total
Ischaemic heart disease	34
Cancer	14
Renal disease	11
Stroke	9
Other CV disease	7
Gastrointestinal disease	7
Diabetes*	3
Infectious disease	2
Respiratory disease	2
Other	11

* Excludes diabetic renal disease and diabetes with peripheral circulatory disease (included under other cardiovascular disease).

Adapted from Stephenson et al., 1995

Diabetes accounts for approximately 25% of all patients with end-stage renal disease in the United States (Rostand, 1989). Cowie et al. (1989) analyzed the data in the Michigan Kidney Registry and found that the incidence of diabetic end-stage renal disease was 2.6 fold higher among blacks than whites after adjusting for the higher prevalence of diabetes among blacks. In the same study it was also found that 77% of blacks with end-stage renal disease had Type 2 diabetes in contrast to 58% of white people with end-stage renal disease. This was true although the risk of end-stage renal disease was 5.8% among patients with IDDM and 0.5% among those with Type 2 diabetes (both races combined). This paradox was explained by the greater frequency of Type 2 diabetes. A possible explanation for the excess of black diabetics with end-stage renal disease in this study may have been the higher mean diastolic blood pressure of black patients (92.6 mmHg vs 88.2 mmHg for white patients) before the onset of end-stage renal disease.

The number of diabetic patients in South Africa with end-stage renal disease on chronic dialysis programs, differs drastically from that in the US. Seedat (1990) reported that there were 22/million of the population in Natal on chronic dialysis. Of these, 2/million were black, 20/million "mixed" race (coloured), 55/million Indian and 59/million white. This should be

seen against the background of blacks comprising 78% of the population of Natal. The most important reason for this disparity was the divergence of the socioeconomic status of the racial groups. Diabetes was not mentioned as a cause of end-stage renal disease in 1131 patients registered by the South African Dialysis and Transplant Registry (Seedat, 1990).

Combined, diabetic retinopathy and cataracts affect 31% of Type 2 diabetes patients. These and other common medical problems of patients with Type 2 diabetes are shown in Table 2.7/2. Like diabetic nephropathy, little is known about the prevalence and incidence of diabetic retinopathy in southern African black patients suffering from Type 2 diabetes.

The prevalence of diabetic retinopathy, nephropathy and neuropathy reported in studies from Africa was recently reviewed (Table 2.7/3-5). The prevalence of retinopathy ranged between 4% (Sudan) to 39.4% (Johannesburg). In a random sample of black patients examined at Pelonomi hospital, Mollentze et al. (1990) detected diabetic retinopathy in 30%. The prevalence of diabetic nephropathy ranged between 6.1% (Ethiopia) and 23.8% (Zambia). Few studies examined the prevalence of neuropathy which ranged from 9.4% (Ethiopia) to 31.2% (Zambia). In a Johannesburg study of 50 patients with Type 1 diabetes with a mean duration of only 4 years, Tuch et al. (1994) reported that 32% had evidence of autonomic neuropathy. It is well-known that the prevalence of microvascular complications are more common in smokers than in non-smokers (Telmer et al, 1984). In a study of the smoking habits of diabetic patients at Baragwanath hospital, Gill et al. (1996) found that 20% of patients smoked compared to 28% of the black general population.

Levitt and co-workers (1997) reported on the prevalence of diabetes complications and level of glycaemic and blood pressure control in 243 black African patients attending community health care centres in Cape Town. The mean duration of diabetes was 8 years and the mean HbA1 concentration of 10.5% reflected sub-optimal diabetes control. Blood pressure control was satisfactory (SBP <140 mmHg and DBP < 90 mmHg) in 38.5% of patients taking anti-hypertensive medications. The prevalence of complications found in this study is shown in Table 2.7/6.

TABLE 2.7/2

MEDICAL PROBLEMS AND DIABETIC COMPLICATIONS IN TYPE 2 DIABETES

Retinopaty	17%
Cataracts	14%
Painful neuropathy	8%
Foot ulcers	3%
Angina	17%
Claudication	12%

(Gill 1991)

TABLE 2.7/3.

DIABETIC RETINOPATHY IN AFRICAN STUDIES

Region or country	Author, year published	Age range (yrs)	Sample size	Type of diabetes	All retinopathy(%)
Northern Africa					
Sudan	Elamin et al, 1992	0-14	101	Type 1	4
Sudan	Elmahdi et al, 1991	20-72	413	Type 2	17.4
Sudan	Elbagir et a, 1995	15-75	91	Ins-treated	42.8
Eastern Africa					
Eth iopia	Seyoum et al, 1997	14-85	302	All	37.8
Zambia	Rolfe, 1988		600	All	33.8
Southern Africa					
South Africa	Omar et al., 1984		133	Type 1	14.1
South Africa	Kalk et al, 1997	>30	507	All	39.4

Amos et al, 1997

TABLE 2.7/4.

DIABETIC NEPHROPATHY IN AFRICAN STUDIES

Region or country	Author, year published	Age range (yrs)	Sample size	Type of diabetes	All nephropathy (%)
Northern Africa					
Sudan	Elamin et al,. 1992		101	Type 1	8.9
Sudan	Elmahdi et al., 1991	20-72	413	Type 2	9.2
Egypt	Al-Kassab et al., 1997	>20	250	All	12.4
Eastern Africa					
Ethiopia	Lester, 1984	All ages	847	All	6.1
Zambia	Rolfe, 1988		600	All	23.8
Southern Africa					
South Africa	Levitt et al., 1995		30	Type 1	16.7
	Kalk et al., 1997	>30	448	All	14.5

Amos et al, 1997

TABLE 2.7/5.

DIABETIC NEUROPATHY IN AFRICAN STUDIES

Region or country	Author, year published	Age range (yrs)	Sample size	Type of diabetes	All neuropathy (%)
Northern Africa					
Sudan	Elbagir et al., 1995	15-75	128	Ins-treated	30.5
Eastern Africa					
Ethiopia	Lester, 1984	All ages	847	All	9.4
Zambia	Rolfe, 1988		600	All	31.2
Southern Africa					
South Africa	Omar et al., 1984		133	Type 1	21.7

Amos et al, 1997

TABLE 2.7/6

FREQUENCY OF COMPLICATIONS OF DIABETES IN 243 BLACK PATIENTS ATTENDING A COMMUNITY HEALTH CARE CLINIC IN CAPE TOWN

	% (95% CI)
Feet	
Peripheral neuropathy	27.6 (15.2-39.9)
Peripheral vascular disease	8.2 (5.2-12.6)
Ulcers, sepsis, deformities	5.4 (2.1-8.7)
Amputation	1.4 (O.4-2.4)
Any foot problem	36.6 (23.3-50.0)
Eyes	
Cataracts	
unilateral	6.2 (1.0-11.5)
bilateral	1.7 (O.O-3.4)
Retinopathy	
background	35.4 (30.6-40.2)
preproliferative	14.3 (7.9-20.7)
proliferative	4.3 (1.0-7.5)
Macular changes	13.1 (7.9-18.4)
Visual acuity	12.0 (8.8-15.3)
normal	53.2 (47.0-59.4)
bilateral moderate	12.0 (7.4-16.6)
unilateral mod/unilateral severe bilateral severe	9.2 (4.7-13.6)
Renal	
Proteinuria	5.3 (2.5-8.1)
Elevated serum creatinine	5.9 (3.6-8.1)
Abnormal albumin-creatinine ratio	36.7 (29.0-44.4)

Levitt *et al.*, 1997

In his description of diabetes mellitus in the Johannesburg African, Seftel (1961) noted that 8 (3.2%) out of 250 new patients presented with stroke and 1 presented with peripheral vascular disease and gangrene. Diabetes was diagnosed in 22 (10.4%) of 211 black patients with stroke seen at Kalafong Hospital, Pretoria (Rosman, 1989). In this study successive patients with stroke were analyzed for the presence of risk factors. The role of diabetes as a risk factor for stroke in black patients has not been studied adequately and needs to be prospectively addressed.

CHD is the most important cause of mortality in patients with Type 2 diabetes. The relative risk of all-cause mortality after 15 years of follow-up in diabetic men compared to non-diabetic

men was 2.05 in the Whitehall study (Fitzgerald, 1991). In the same study the corresponding relative risk for mortality due to CHD was 2.71. Females with Type 2 diabetes are even more prone to death from CHD than males with Type 2 diabetes. Barrett-Conner (1991) reported the relative risk of mortality for female diabetics after 14 years of diabetes to be 3.3 compared to non-diabetics. In his review of the subject, Jarrett (1984) could not find an association between the duration of diabetes and CHD mortality. Haffner et al., (1998) found that the seven-year incidence rates of myocardial infarction (MI) in diabetic subjects without prior MI compared to non-diabetic subjects was 20.5% and 3.5% respectively. The incidence rates for MI for diabetic subjects with a previous history of MI compared to non-diabetic subjects were 45.0% and 18.0% respectively.

The mechanism of the increased risk of death due to CHD in diabetics remains the subject of much controversy. In the Whitehall study Fitzgerald and Jarrett (1991) found that elevated systolic blood pressure was the only significant risk factor for CHD mortality. A modest but insignificant effect of total cholesterol, current smoking and a previous history of smoking was also found in this study. BMI was not significantly associated with mortality. Reporting on the risk factors of mortality from CHD in diabetics in the NHANES I study, Ford and DeStefano (1991) also found hypertension to be a risk factor.

In the London cohort of the WHO Multinational Study of Vascular Disease in Diabetics, Morrish et al. (1990) could not find any association between blood pressure and CHD mortality. However, in this study cigarette smoking and proteinuria was positively associated with CHD mortality. Nine years after a diagnosis of Type 2 diabetes, 29% of UKPDS subjects had experienced some type of diabetes-related complication, with 20% of subjects experiencing macrovascular complications (e.g., myocardial infarction, angina, stroke) of which one-third of the subjects have died (Turner, 1998). In the UKPDS Turner et al., (1998) found that a quintet of potentially modifiable risk factors for coronary artery disease exists in patients with Type 2 diabetes mellitus. A reduction in HbA_{1c} of 1% was associated with a 14% reduction in risk of myocardial infarction in this study (Stratton et al., 2000). These risk factors were increased concentrations of low-density lipoprotein cholesterol, decreased concentrations of high density lipoprotein cholesterol, raised blood pressure, hyperglycaemia, and smoking. A meta-analysis of 20 studies showed that the relationship between glucose and incident cardiovascular events extends below the diabetic threshold (Coutinho et al., 1999). This finding may partly explain why tight blood glucose control in clinical studies reduces microvascular complications but fails to reduce the incidence of cardiovascular events.

In the Wisconson study (Moss et al, 1991), which investigated causes of death in a non-clinic population of diabetic patients, the most common causes of death in patients with Type 2 diabetes were heart disease (48.8%), diabetes (15.3%), malignant neoplasms (9.9%), and cerebrovascular disease (9.5%). Not only is the prevalence of ischaemic heart disease increased in patients with Type 2 diabetes but the prognosis after acute chest pain or myocardial infarction is also worse. In a Finnish population the hazard ratio for death from coronary heart disease after a MI was similar in diabetics without a prior history of MI than in non-diabetic subjects with a prior history of MI suggesting similar risks for infarction in the two groups (Hafner et al., 1998).

Approximately 50% to 75% of deaths in patients with diabetes are attributable to cardiovascular disease (Huang et al., 2001). Therefore, most guidelines for the management of diabetes advise on the management of traditional risk factors such as hypercholesterolaemia, hypertension and levels of glycaemia. The evidence from interventional studies trials demonstrates that lipid and blood pressure lowering in patients with Type 2 diabetes is associated with substantial cardiovascular benefits. While intensive glucose lowering is essential for the prevention of microvascular disease, improvements in cholesterol and blood pressure levels are central to reducing cardiovascular disease in these patients (Huang et al., 2001).

In his analysis of diabetes mellitus in the Johannesburg African, Seftel (1961) did not detect a single case of CHD in 250 newly diagnosed diabetics who presented before 1958. In a later report he mentioned 4 cases of black diabetics with CHD detected between 1958 and 1963. He also described electrocardiographic evidence of CHD in 8 patients out of a cohort of 52 diabetics (Seftel, 1963). This finding was in keeping with the low prevalence of CHD in the general black population as pointed out by Walker and Walker (1985). They calculated the annual incidence of myocardial infarction for the population of Soweto to be 10/100 000 as compared to 400/100,000 for Scotland. The actual prevalence of CHD in the black population of South Africa as well as in black diabetics is unknown. Atherosclerotic vascular disease comprising ischaemic heart disease, peripheral vascular disease and cerebrovascular disease – was recorded in 5.1% of patients attending a community health care clinic in Cape Town (Levitt et al., 1996).

In a study unique to Africa, McLarty et al. (1990) reported on the course and prognosis of 1250 Tanzanian diabetic patients followed for 6 years. From this group 205 (16.4%) were known to have died and a further 71 patients (5.7%) were likely to have died. Mortality was highest in the six months after presentation during which time 42.4% of deaths occurred. In patients requiring insulin, diabetic keto-acidosis and infections including pulmonary tuberculosis were important causes of death. In patients not requiring insulin, cardiovascular, renal and liver diseases were important causes of mortality. These authors stressed the problems of follow up of patients with chronic diseases in Africa.

Urgent studies are needed to address the prevalence and incidence of long-term complications of diabetes in African blacks. Likewise, data on survival rates and causes of death in black patients suffering from diabetes are also needed.

2.8 Economic aspects of diabetes mellitus

In most countries for which data exist, diabetes is sufficiently common and its adverse effects on morbidity, employment, productivity and premature mortality sufficiently great for it to rank as one of the most important influences on world health. Two decades ago diabetes accounted for 2.8% of the total hospital admissions recorded for England and Wales compared to 7.2% of all hospital admissions in the U.S. In the U.S. this was 2.4 times that for the non-diabetic population, the most hospitalisations being for complications and for cardiovascular disease. Diabetic patients were 22 times more likely to be admitted for skin ulcers and gangrene, 15 times more for peripheral vascular disease, 10 times more for atherosclerosis, and 6-10 times more frequently for heart disease and cerebrovascular accidents (Bransome, 1992). While exact figures for outpatient services and primary care are unknown for the U.K., consultations for diabetes care made up 1.6% of total consultations in the U.S.A. in 1980 (Williams, 1997).

The direct and indirect costs of diabetes during 1987 in the United States were estimated to be $20.4 billion (American Diabetes Association, 1988). Direct medical costs accounted for 47.1% of total costs; indirect costs accounted for 52.9% of the total. Institutional care accounted for 38.6% of total costs, outpatient care 8.5%, premature mortality 36.8%, long-term disability 15.4%, and short-term morbidity 0.7%.

In a cross-sectional analysis of expenditures for individuals with diabetes over age 65 years from a nationwide sample of Medicare beneficiaries it was found that individuals with diabetes

were 1.5 times as expensive as all Medicare beneficiaries (Krop et al, 1998). However, there were wide variations, with the most expensive 10% of beneficiaries with diabetes accounting for 56% of expenditures for individuals with diabetes and the least expensive 50% accounting for 4%. Acute care hospitalisations accounted for the majority (60%) of total expenditures, whereas outpatient and physician services accounted for 7% and 33%, respectively. There were no differences in the number of complications for all older adults with diabetes compared with those with the highest expenditures. However, the average number of hospitalisations was 1.6 times higher, and the average length of stay was 2 days longer, among older adults with diabetes.

An alternative approach to healthcare expenditure is to calculate disability-adjusted life-years (DALYs) (Jönsson, 1998). This approach measures the intangible costs associated with diabetes and combines the healthy life-years lost as a result of premature mortality with those lost because of disability. This is an important concept to consider when trying to estimate the economic impact of diabetes, as a considerable proportion of the health care expenditure on this disease is directed toward improving quality of life. Using this approach the World Bank demonstrated that the burden of diabetes due to loss of quality of life and decreased life expectancy is concentrated in those countries with the lowest health care budgets. The estimated total cost of diabetes care in several countries for 1995 is shown in Table 2.8/1.

Both the prevalence of diabetes as well as the size of the population is expected to increase in developing countries over the next decade. Developing countries will thus be faced with a need for a significant increase in health care expenditure during this period. The situation in South Africa is much more complex. The prevalence of diabetes is expected to increase, a period of a negative population growth rate may be seen during the next 1 or 2 decades and the proportion of the national health care budget spent on HIV/AIDS may also increase, possibly resulting in a smaller proportion of the budget available for diabetes care.

TABLE 2.8/1.

An Estimate of the Total Cost of Diabetes in Several Countries in 1995

Country	Currency	Total health care cost (billions)	Cost of diabetes (billions)	% of total health care cost
Denmark	Krone	64	3.8	6%
Finland	Finmark	44	2.6	6%
France	Franc	753	45.2	6%
Germany	Deutsche Mark	331	19.7	6%
Italy	Lira	137000	8220	6%
Japan	Yen	34500	2070	6%
Spain	Paseta	5330	320	6%
Sweden	Krona	125	7.5	6%
U.K.	Pound	48	2.9	6%
U.S.	U.S. Dollar	1007	60	6%

Jönsson B, 1998

A useful study on the costs of diabetes care in Africa comes from Tanzania (Chale et al, 1992). Direct outpatient costs amounted to $229 per year for diabetics requiring insulin, and $69 per year for diabetics not requiring insulin. Of the $229 for insulin-requiring diabetics, $156 (68.2%) was for the provision of insulin. The total direct cost of diabetes care in Tanzania amounted to $4 million a year and represented 8% of the total Government Health budget (compared to 4-5% of that for the United Kingdom). The average annual per capita income in Tanzania was $160-$200. The authors concluded that in spite of the low prevalence of diabetes in Tanzania, diabetes placed a severe strain on the limited resources of that country. Furthermore, should African patients with diabetes have to pay for their own treatment; most will be unable to do so and may die. Presently no reliable estimates are available on the costs of diabetes care in South Africa.

2.9 Diabetes care in South Africa

Diabetes care on the African continent is fraught with numerous problems and the view was expressed that in South Africa, the situation for many black people is not too different from that experienced on the rest of the continent (Huddle, 1995). The new order in South Africa has created an opportunity to improve care for chronic diseases including diabetes care.

Few published studies have addressed the quality and availability of diabetes care in South Africa. In one such study, on the quality of diabetes care at primary health care level in Cape Town, Levitt et al. (1996) found that only 35% of patients fulfilled the criteria for optimal attendance. Good clinic attenders had better glycaemic control than bad attenders and good attendence was more common among pensioners. Ophthalmological examination was performed on only 3.2% and examination of the feet was recorded for only 4.7% patients. This paper concluded that their data suggested that this system of chronic care in the community was failing to provide effective diabetes care for a large proportion of the people who use it, and planners and managers should pay special attention to improving the effectiveness and quality of care of diabetes.

2.10 The prevention of diabetes

The Da Qing IGT study has shown that Type 2 diabetes may be a preventable condition in a large number of susceptible or high-risk individuals (Pan et al., 1997). The diabetes prevention programme (DPP) was recently launched in the U.S. (DPP research group, 1999). The DPP is a randomised clinical trial testing strategies to prevent or delay the development of type 2 diabetes in 3000 high-risk individuals with elevated fasting plasma glucose concentrations and impaired glucose tolerance. The primary research goal is a comparison of the efficacy and safety of each of three interventions: an intensive lifestyle intervention or standard lifestyle recommendations combined with metformin or placebo, in preventing or delaying the development of diabetes. The trial was meant to continue until the middle of 2002.

A recent review article in Nature highlighted the escalating Type 2 diabetes epidemic (Zimmet et al., 2001). The authors suggested the establishment of a multidisciplinary international task force representing all parties that can help reverse the underlying socio-economic causes of the problem and address the issues that have led to the epidemic. Africa and in particular South Africa, should also respond to this call to ensure its place in these ranks.

3 Arterial hypertension

3.1 Definition, classification and diagnosis of hypertension

In the past many attempts were made to classify blood pressure into normotension and hypertension (Pickering, 1968). However, confusion in definitions has resulted from the failure to distinguish between the aims of the definitions (Rose, 1985). Definitions of hypertension were based on four different concepts depending on how the definition was to be applied (Rose, 1985): a statistical definition (purely descriptive with no biological meaning), a clinical definition (identifies pressures which are likely to be associated with current ill-health), a prognostic definition (subjects, although well at present, are at an increased risk of future complications or shortening of life) and an operational definition ("that level of blood pressure above which action is preferred to inaction").

A statistical definition can be determined by differentiating between normal and abnormal pressures strictly on the basis of the frequency with which they occur in the population. Hypertensive subjects would then be identified as those at the higher end of the systolic and diastolic distribution curve e.g. those with pressures in the upper 5% of the population and thus above the 95th percentile (Master et al., 1952). The statistical method has important disadvantages. Firstly, distribution curves differ between different populations and would thus make a uniform definition impossible. Furthermore, some populations are "low pressure" populations e.g. the !Kung bushmen (Trusswell, 1972) whose blood pressure also do not rise with age. Secondly, in most populations blood pressure increases with age and this age-associated blood pressure relationship can be expected to skew the distribution curve further to the right and to raise mean pressures (Master, 1952).

Results from the Framingham heart study showed that cardiovascular risk increased in proportion to blood pressure (Kannel, 1996). The impact of systolic blood pressure seems to be greater than that of diastolic blood pressure on the occurrence of cardiovascular disease. In persons with systolic blood pressure elevation, knowledge of diastolic blood pressure is not helpful in assessing cardiovascular risk (Kannel, 1996). In the Framingham study combined systolic and diastolic hypertension carried only a marginally greater risk of cardiovascular disease than isolated systolic hypertension (Kannel, 1996). While the risk associated with blood pressure elevation supplies the rationale for treatment, the continuous nature of the relationship does not by itself define thresholds for initiating treatment (Pickering, 1968).

3 Arterial hypertension

3.1 Definition, classification and diagnosis of hypertension

In the past many attempts were made to classify blood pressure into normotension and hypertension (Pickering, 1972). However, confusion in definitions has resulted from the failure to distinguish between the aims of the definitions (Rocella, 1987). Definitions of hypertension were based on at least three different concepts depending on how the definition was to be applied (Rose, 1985 and Rocella, 1987): a definition based on the normal distribution curve, a risk-related definition and a clinical definition.

A statistical definition can be determined by differentiating between normal and abnormal pressures strictly on the basis of the frequency with which they occur in the population. Hypertensive subjects would then be identified as those at the higher end of the systolic and diastolic distribution curve e.g. those with pressures in the upper 5% of the population and thus above the 95th percentile (Rocella, 1987). The statistical method has important disadvantages. Firstly, distribution curves differ between different populations and would thus make a uniform definition impossible. Furthermore, some populations are "low pressure" populations e.g. the !Kung bushmen (Trusswell, 1972) whose blood pressure also do not rise with age. Secondly, in most populations blood pressure increases with age and this age-associated blood pressure relationship can be expected to skew the distribution curve further to the right and to raise mean pressures (Roccela, 1987).

Attempts to define blood pressure in the context of a risk factor for future life-threatening complications also proved to be elusive (Roccela et al., 1987). Results from the Framingham heart study showed that cardiovascular risk increased in proportion to blood pressure (Kannel, 1996). The impact of systolic blood pressure seems to be greater than that of diastolic blood pressure on the occurrence of cardiovascular disease. In persons with systolic blood pressure elevation, knowledge of diastolic blood pressure is not helpful in assessing cardiovascular risk (Kannel, 1996). In the Framingham study combined systolic and diastolic hypertension carried only a marginally greater risk of cardiovascular disease than isolated systolic hypertension (Kannel, 1996). While the risk associated with blood pressure elevation supplies the rationale for treatment, the continuous nature of the relationship does not by itself define thresholds for initiating treatment (Roccela et al., 1987).

The best clinical definition of hypertension according to Rose (1985), is the level of arterial pressure at which the benefits of intervention exceed those of inaction. Clinical trials have previously demonstrated the benefits of antihypertensive treatment in patients with severe hypertension with diastolic blood pressure in the range of 115 through 129 mm Hg (Veterans Administration Cooperative Study Group, 1967) as well as in patients with diastolic blood pressure averaging 90 through 114 mm Hg (Veterans Administration Cooperative Study Group, 1970). More recently MacMahon et al. (1990) have demonstrated a log-linear relationship between diastolic blood pressure and stroke and between diastolic blood pressure and CHD. Disease rates were lowest among those individuals whose usual (long-term average) diastolic blood pressure was about 73 mm Hg.

The purpose of a classification of hypertension is to provide an easy and reliable method for the characterization of each patient. It allows assessment of severity of disease by reference to epidemiological data so that risk can be defined and appropriate treatment instituted (WHO Expert Committee, 1978). This WHO expert committee (1978) defined normal adult blood pressure arbitrarily as a systolic pressure equal or below 140 mm Hg, together with a diastolic (fifth Korotkoff phase) equal to or below 90 mm Hg. Hypertension in adults was defined as a systolic pressure equal to or greater than 160 mm Hg and/or a diastolic pressure (fifth phase) equal to or greater than 95 mm Hg. This definition of hypertension was previously widely used in epidemiological surveys both internationally (Nissinen et al., 1988) as well as in South Africa (Steyn et al., 1991, Seedat et al., 1992). The WHO (1978) used the term 'borderline hypertension' to describe blood pressure values between normal and hypertensive. The 1978 WHO Technical report have meanwhile been replaced by revised guidelines.

The definition of hypertension in South Africa was only recently changed from the 1978 WHO definition of ≥ 160/95 mmHg or taking antihypertensive medication to ≥ 140/90 mm Hg based on the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure guidelines (Joint National Committee, 1997)(JNC VI). The JNC VI Expert Committee defined hypertension as SBP 140 mm or greater, DBP of 90 mm Hg or greater or taking antihypertensive medication while normal blood pressure was defined as < 130/85 mm Hg (Joint National Committee, 1997). These values were like previous definitions chosen in a somewhat arbitrary way from a continuous distribution of pressure readings.

The JNC 7 report defined a normal blood pressure as < 120/80 mm Hg, introduced a new category designated pre-hypertension in the blood pressure range 120-139 mm Hg systolic or 80-89 mm Hg diastolic and combined the JNC VI stages 2 and 3 hypertension (Chobanian et al, 2003). The JNC 7 classification of blood pressure is shown in Table 3.1/1.

TABLE 3.1/1. JNC 7 Classification of Blood Pressure for Adults Aged 18 years or Older*

BP Classification	Systolic BP, mm Hg[a]		Diastolic BP, mm Hg[a]
Normal	<120	and	<80
Prehypertension	120-139	or	80-89
Stage 1 hypertension	140-159	or	90-99
Stage 2 hypertension	≥160	or	≥100

* Chobanian et al, 2003

[a] Treatment determined by highest BP category

This classification is based on the mean of 2 or more properly measured seated BP readings on each of 2 or more office visits (Chobanian et al, 2003). When SBP and DBP fall into different categories, treatment should be determined by the higher category. Both the JNC VI and JNC 7 guidelines recognised that the prevalence, severity, and impact of hypertension are increased in African-Americans.

Neither the JNC 7 (Chobanian et al, 2003) nor the SA Hypertension Clinical Guideline (Milne, 2000) retained the terms accelerated or malignant hypertension although these terms are still clinically widely used (Williams, 2001). Malignant hypertension is characterised by the presence of papilloedema, usually accompanied by retinal haemorrhages and exudates, rather than by the absolute BP level although BP levels are often above 200/140 mm Hg. Accelerated hypertension is defined as a significant recent increase over previous hypertensive levels associated with evidence of vascular damage on funduscopic examination but without papilloedema (Williams, 2001).

3.2 Prevalence of hypertension in black South Africans

Before 1978 few studies of good quality on hypertension were performed in SA (Seftel, 1978). Common deficiencies included poor sampling techniques, inadequate numbers and lack of standardization of methods. An additional problem was the relative unavailability of rural black males because of the migrant labour system (Seftel, 1978). In a rural hospital in Sekhukhuneland for example, few male patients compared to females were admitted and hypertension was a rare cause of admission (Edginton et al., 1972).

The blood pressure of other ethnic groups in Southern Africa was studied as well. Truswell et al. (1972) described a Botswana !Kung Bushmen community in which blood pressure did not rise with age. Blood pressure was only measured in 152 subjects, aged 15-83 years. In men both mean systolic and diastolic blood pressure showed a downward trend with increasing age. In women older than 45 years there was a slight increase in mean systolic blood pressure while their mean diastolic blood pressure stayed the same until the two oldest age groups in which there was a slight drop. They consumed very little salt, had no alcohol but smoked tobacco.

Seedat et al. (1978) reported on the prevalence of hypertension in a sample consisting of 994 urban Zulus (459 males and 535 females) 15 years and older, who lived in Durban for at least 5 years. The overall prevalence of hypertension was 21.4% based on the single criterion of blood pressures of 160 mm Hg systolic and/or 95 mm Hg diastolic for all ages. Diastolic blood pressure was diagnosed at Korotkoff phase four and readings were recorded to the nearest 5 or 10 mm Hg gradation below the observed figures. Slightly more females (27%) than males (23%) had hypertension. Both mean systolic and diastolic blood pressure rose with age in both sexes, but the rise in systolic BP was greater than in diastolic blood pressure. A family history of hypertension was obtained from 8% of subjects. Interestingly, the mean number of years of residence in Durban was significantly greater in hypertensive subjects compared to normotensive subjects. Seventeen percent and 28% of male and female hypertensive subjects respectively were aware of the fact they had hypertension. In this study approximately 90% of subjects who had hypertension were either undiagnosed or untreated or inadequately treated. The prevalence of hypertension in this study was comparable to the prevalence of hypertension in American blacks.

Concurrently with the previous study, a similar study was done among the rural Zulu of Ubombo in the northeastern part of Natal (Seedat et al., 1982). The sample consisted of 987

subjects (327 men, 660 women). Although this was a population-based study, it was probably not a truly representative sample. An aneroid sphygmomanometer was used to measure blood pressure and the measurements were standardized between the two studies. The 4th phase Korotkoff sound was also used to define diastolic blood pressure. The crude prevalence of hypertension (systolic blood pressure ≥ 160 mm Hg and/or diastolic blood pressure ≥ 95 mm Hg) was 10.% (10%men, 11% women). Both systolic and diastolic blood pressure increased with increasing age for both sexes. There was thus a pronounced difference in the prevalence of hypertension between the rural and urban groups. The onset of hypertension occurred earlier in women than in men in both populations. The authors also found that rural Zulus were less obese than urban Zulus and both rural and urban Zulu women were more obese than Zulu men. Interestingly, 27% of the rural Zulus with hypertension were on treatment compared to 10% of urban Zulus. A family history of hypertension was reported by 2.9% of the rural Zulus.

In a third study, Seedat et al. (1978) reported on the prevalence of hypertension in the Indian community of Durban. In this study 476 males and 524 females 15 years and older were examined. Hypertension (≥ 160/95 mm Hg) was present in 17% of males and 23% of females.

In a fourth study, Seedat et al. examined the prevalence of hypertension in the white population of Durban (1980). In this sample, comprised of 492 males and 514 females 15 years and older, the prevalence of hypertension was 20.2% and 19.1% respectively in males and females.

In a landmark study Seftel et al. (1980) described the distribution and biosocial correlations of blood pressure levels in Johannesburg blacks. The sample consisted of 5018 men and 5028 women 16 years and older, selected at random from subjects attending the Johannesburg labour bureau. Because of the study design subjects older than 60 years were underrepresented in this study. Unfortunately, WHO criteria defining hypertension were not used, making direct comparisons with other studies difficult. The prevalence of hypertension was not age and sex adjusted (Table 3.2/1).

TABLE 3.2/1. The Prevalence of Raised Phase IV Diastolic Blood Pressure in Black Males and Females

	N	DBP (%) > 90 mm Hg	DBP (%) > 100 mm Hg
Males (age in yr)			
16-19	585	4.3	0.3
20-29	2227	14.8	2.8
30-39	1151	32.6	12.9
40-49	647	44.2	19.9
50-59	300	63.7	33.3
60+	108	57.4	26.9
Females (age in yr)			
16-19	622	5.9	0.2
20-29	1979	10.9	2.1
30-39	1268	33.0	10.4
40-49	829	58.4	30.3
50-59	287	73.9	47.7
60+	43	72.1	39.5

Seftel et al. (1980)

Systolic and diastolic blood pressure increased with age until the 5th decade. From the 6th decade diastolic levels started to decrease in both sexes, while the systolic level in men also started to decline but continued to rise in women. Obesity was, although modestly so, positively correlated with both systolic and diastolic blood pressure. Weak relationships between educational status, occupation and blood pressure was found. The correlation between blood pressure and urban or urban-rural status was varied and of uncertain significance. In summary, this large study showed that hypertension was common and severe in urban blacks and that in both sexes and at most ages the blood pressure of Johannesburg blacks were higher than those of London whites and approximated the same as those of Georgia blacks.

The CORIS baseline study of CHD risk factors in white, mostly Afrikaans-speaking subjects commenced in 1979 (Rossouw et al., 1983). In this study blood pressure was measured in 3831 males and 3831 female subjects between the ages of 15-64 years. Hypertension (≥160/95) was present in 22.1% of males and 22.3% of females.

The prevalence of hypertension in the coloured community of the Cape Peninsula, was also studied (Steyn et al., 1986). The sample was age- and sex-stratified, included age groups 15-64 years and consisted of 976 subjects, 478 males and 498 females. Korotkoff phase 4 sound was used to define diastolic blood pressure. The methodology was well standardized and results age-standardized to the local population. Hypertension (WHO criteria) was present in 17% and 18% of males and females respectively. Isolated systolic hypertension was present in 11.6% of women and 3.3% of males in the age group 55-64 years. Total hypertension (defined as systolic blood pressure ≥ 140 mm Hg and/or a diastolic blood pressure ≥ 90 mm Hg) was present in 35.6% of males and 24.7% of females. A history of stroke was present in 3.9% of males and 2.6% of females with hypertension. Of the male hypertensives 10.9% and of the female hypertensives 9.2% reported having had angina, and 4.7% of male hypertensives and 3.9% of female hypertensives had had a myocardial infarction. A family history of hypertension-associated disease was obtained from 58.6% of men and 62.8% of women with hypertension. No significant correlation between the amount of alcohol used and either systolic or diastolic blood pressure was found although drinkers as a group had higher systolic and diastolic blood pressures than the non-drinkers. A weak association between blood pressure and BMI was found. Male smokers had significantly higher systolic and diastolic blood pressures than non-smokers. Those with hypertension had significantly lower levels of education than those without hypertension.

Steyn et al. (1991) also studied the prevalence of cardiovascular risk factors in the black population of the Cape Peninsula. The study population consisted of 986 persons (442 males and 544 females) aged 15-64 years. The sample was drawn from several black residential as well as squatter areas. The WHO definition (1978) of hypertension was used in the analysis while mild hypertension was equivalent to WHO (1978) 'borderline' hypertension. Korotkoff sound phase 5 was used to define diastolic blood pressure. Hypertension was present in 7.7% and 8.9% of male and female subjects respectively and mild hypertension in 6.7% and 4.8% of males and females respectively. The prevalence of hypertension increased with age in this study. The highest recorded prevalence of hypertension in males was 40.3% in the age group 55-64 years and in females 44.2% in the corresponding age group.

Bester and Weich (1991) studied the prevalence of hypertension in elderly black subjects in the FS. The sample consisted of 400 subjects 65 years and older (182 men and 218 women), randomly selected from 10 Free State towns and cities. Applying WHO criteria, hypertension was present in 42% of males and 61% of females. Systolic hypertension, defined as a systolic

blood pressure ≥ 160 mm Hg and a diastolic blood pressure < 90 mm Hg was present in 13% and 14% of males and females respectively. These prevalence rates were similar to that reported for United States elderly blacks i.e. 56% for males and 60% for females.

Seedat and co-workers (1992) studied the prevalence of coronary heart disease risk factors in the black population of Durban. The sample consisted of 458 subjects (192 men, 179 women) 15-69 years of age and was drawn from patients attending a dental clinic in Durban. The sample was not truly representative of the population and subjects in the age group 45-69 years were under-represented. The prevalence of hypertension (WHO 1978 guidelines) in this sample was 12.6% and 13% for males and females respectively.

South Africa's first Demographic Health Survey was conducted in 1998 and overcame most of aforementioned difficulties. The overall age-adjusted prevalence of hypertension (≥160/95 mmHg or on treatment for hypertension) in this cross-sectional study of 5738 men and 8064 women 15 years and older was 10.9% for men and 13.9% for women (Steyn et al., 2001). In the SADHS the prevalence of hypertension was 9.3% in black men and 12.4% in black women. By applying the JNC VI cut-points of ≥ 140/90 mm Hg the overall prevalence rates for men and women were 20.9% and 21.2% respectively (22.9% and 24.6% for black men and women respectively). Translated into numbers, 3.3 million South Africans were suffering from hypertension in 1998 using the ≥ 160/95 mm Hg cut-point and 6 million if the ≥ 140/90 mm Hg cut-point was used. Two-thirds of hypertensive women were overall aware that they had hypertension while 1% (young) to 52% (older) of men was aware of their diagnosis. Among black subjects, 64% of hypertensive women and 32% of men were aware that they had hypertension. Hypertension was overall controlled (<160/95 mm Hg) in 38% of women and 26% of men who were taking medication. The prevalence of hypertension (>160/95) in the different SA ethnic groups is shown in Fig.3.2/1.

In summary, results of population-based epidemiological studies conducted before the SADHS showed that the prevalence of hypertension in South African blacks ranged from 8% in the Cape Peninsula to 22% in the urban Zulus of Durban, that an urban-rural gradient was present, and that hypertension was extremely common in elderly blacks in the Free State (42% in males, 61% in females). Direct comparison between the different studies is flawed by different methodologies used in these studies e.g. sampling frame, sampling methods, instruments used, observers (one versus many), standardization of measurements, site of

measuring blood pressure (house versus clinic), phase 4 and phase 5 Korotkoff sound to define diastolic blood pressure.

The prevalence rates of hypertension obtained from the SADHS differ fairly widely from those obtained from other much smaller studies in different ethnic groups (Fig.3.2/2). It is therefore not possible to make any conclusions about time-trends in the prevalence of hypertension in different ethnic groups. Possible reasons for these differences are that blood pressure measurements in the SADHS were made with Omron electronic devices versus mercury shygmomanometers in most of the other studies and that in the SADHS blood pressure readings were done in the homes of the respondents versus clinics and hospitals in most of the other studies.

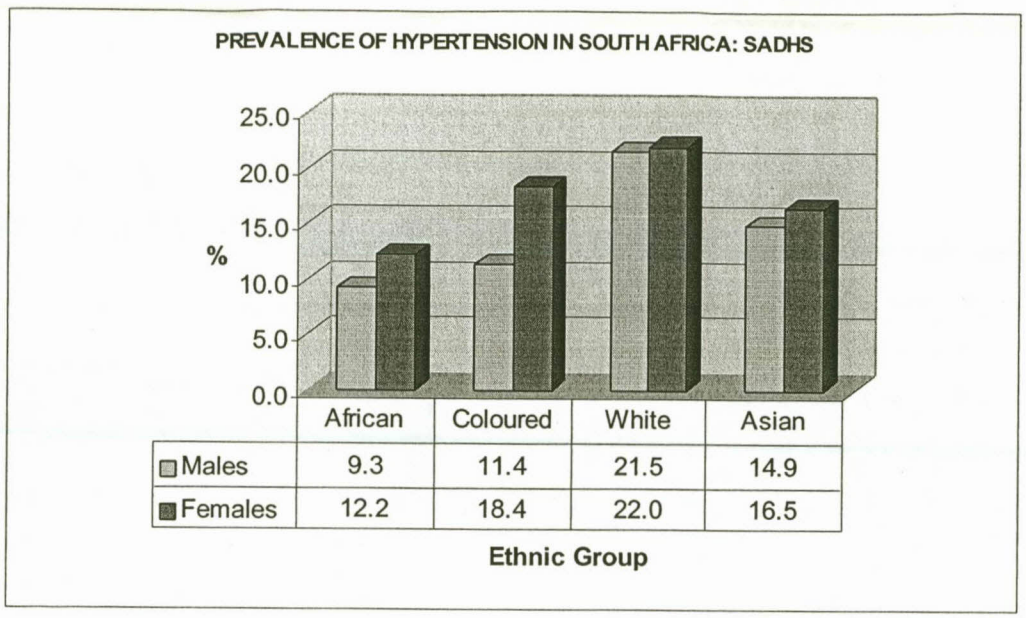


Fig. 3.2/1. The age-adjusted prevalence of hypertension (≥160/95) in South Africa by gender and ethnic group. (Steyn et al., 2001).

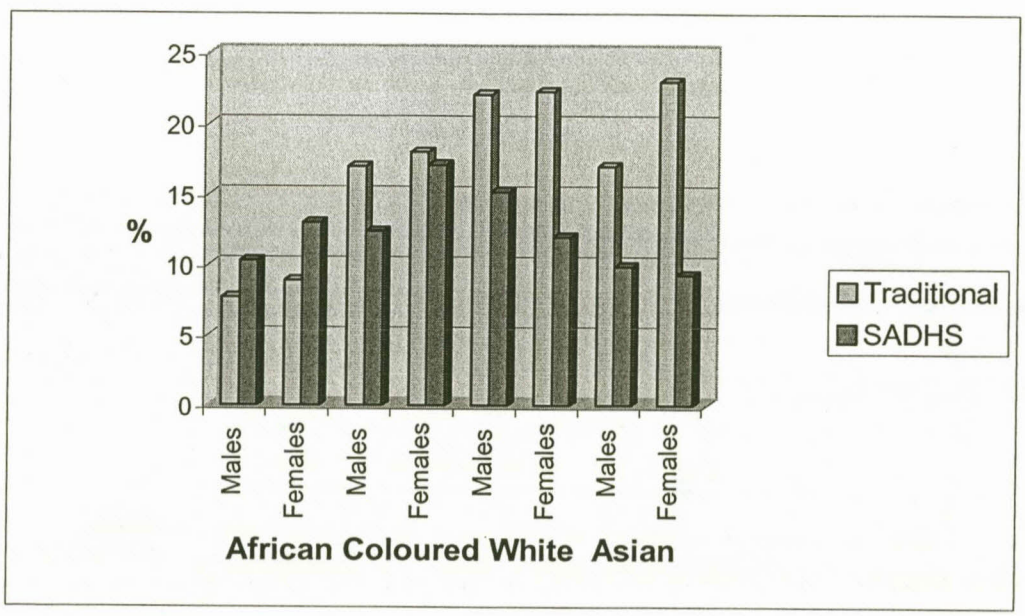


Fig. 3.2/2. The prevalence of hypertension in South Africa in different ethnic groups comparing SADHS data with observations from previous studies. (African: Steyn et al., 1991; Coloured: Steyn et al., 1986; White: Rossouw et al., 1983; Asian: Seedat et al., 1978). (Traditional = mercury shygmomanometry)

3.3 The prevalence of hypertension in sub-Saharan Africa

3.3.1 Early studies (1929-1988)

In the past blood pressure studies in Africa were criticized for poor quality and few of these studies met established criteria for methodology or were capable of withstanding the rigors of epidemiological assessment (Akinkugbe, 1985b).

The pioneer of blood pressure studies in Africa, Donnison (1929) commented on the rarity of certain diseases associated with civilization in indigenous races living under conditions that have been but little influenced by the civilization of white races. In this regard he was specifically interested in a group of allied diseases "which occupies much attention nowadays, namely, hyperpiesia (abnormally high blood pressure - Webster's New Collegiate Dictionary, 1951), arterio-sclerosis, and chronic interstitial nephritis".

Donnison (1929) reported on the distribution of blood pressure in a series of a 1000 examinations made on apparently healthy male Kenyan subjects between the ages of 15 and 70-80 years (estimated). An aneroid sphygmomanometer was used and an attempt at standardization was made. The average systolic blood pressure of males aged 15-19 years was 123 mm Hg and diastolic blood pressure was 82 mm Hg. In this series SBP increased with age up to the age 30-34 years and then started to decrease with further aging. DBP behaved in the same way. Donnison also commented on the absence of hypertension in 1800 patients admitted to a rural hospital although abnormally low blood pressure was not uncommonly noted. He did comment on occasional cases of hemiplegia seen in young males without obvious cardiovascular abnormalities. In his historic monograph Donnison concluded that his "investigation thus lends support to the view that hyperpiesia and arterio-sclerosis are diseases associated with civilisation".

Another early study came from Uganda (William, 1941). This study was also not a population-based study. Subjects were outpatients, visitors, and women attending ante-natal clinics and baby clinics. The actual method of blood pressure measurement was not mentioned except that William favoured 5 mm Hg intervals and chose the figure immediately above the point at which the sound began to fade. The lowest average systolic as well as diastolic blood pressure was observed in the 16-20 years age group (120 mm Hg systolic, 74 mm Hg diastolic). The highest average systolic blood pressure was recorded in subjects 51 years and older (127 mm

Hg) while the highest diastolic pressure was measured in the 41-50 year age group (79 mm Hg). A slight but progressive rise occured with age. Although subjects were not weighed, the author remarked that obesity was unusual except in the most prosperous of families.

Shaper and Saxton (1969) studied blood pressure and body build in subjects living in a rural area close to Kampala, Uganda. Baganda subjects were considerably lighter than age- and height-matched American subjects. For both males and females systolic as well as diastolic blood pressure increased with increasing age. The overall prevalence of hypertension (systolic blood pressure ≥ 160 mm Hg and/or diastolic blood pressure ≥ 100 mm Hg since Korotkoff phase 4 was used) was 13% for men and 15% for women compared to 15% and 28% for American white and black males respectively and 16% and 28% for American white and black females respectively. Shaper and Saxton concluded from this study that body-bulk in this population did not contribute significantly to blood pressure levels.

An increase in systolic blood pressure was noted in nomadic warriors after they entered the Kenyan army, compared to a control group (Shaper et al., 1969). The duration of service was also associated with higher systolic blood pressure. Shaper ascribed these changes to changes in lifestyle including dietary pattern and an increase in salt intake.

Akinkugbe and Ojo (1969) reported the results of an urban-rural study from Nigeria. The rural sample was a random one and consisted of 3602 subjects of an uncertain age range. The urban sample consisted of 821 workers (566 males, 255 females) from a tobacco factory and a shopping centre. Systolic as well as diastolic blood pressure increased with advancing age for both populations and both sexes. Mean systolic and diastolic blood pressure in the urban group appeared higher than the rural group. No mention was made of the prevalence of hypertension in this study.

Williams (1969) compared the blood pressure levels of settled agricultural Kikuyu people with that of the nomadic Samburu tribe in Kenya. Both systolic and diastolic mean blood pressure levels were higher in virtually all age groups in the Kikuyu than in the Samburu subjects. Systolic blood pressure rose appreciably with advancing age in the Kikuyu but hardly at all in the Samburu. The results of this study must be interpreted with caution because of the methodological deficiencies.

In a collaborative study, (Akinkugby 1977) compared blood pressure levels between black American, white American and Nigerian school children. It was found that Nigerian school children had higher systolic and diastolic blood pressure levels than American school children at all ages. Since the ancestors of the black American children were supposedly from West Africa, the observed difference in blood pressure levels were ascribed to possible environmental differences.

In a study of 608 rural subjects between 25 and 64 years in Tanzania, Vaughan et al. (1979) found that a rise in blood pressure with age occurred only in women and even that rise was a comparatively small one. Only 2% of subjects were hypertensive (WHO 1978 criteria). A random zero sphygmomanometer was used in this study. Weight and subscapular skin fold thickness was positively associated with diastolic blood pressure while subscapular skin fold thickness was also associated with systolic blood pressure in men. In women, age and triceps skin fold was positively associated with diastolic blood pressure. This is possibly the first study in sub-Saharan Africa that draws attention to the association between blood pressure and central adiposity.

In a more recent study from Kenya, Poulter et al. (1984) studied the blood pressure of a group of rural (n=861) and a group of urban (n=310) subjects and measured their urinary sodium excretion. Diastolic blood pressure did not rise in rural males but systolic blood pressure did after the age of 65. Both systolic and diastolic blood pressure increased with age in both sexes in the urban group as well as in rural females. The average urinary sodium excretion of the rural group was approximately 90 mmol/day that was well in excess of the 51 mmol/24 hours reported for Kenya in the Intersalt study (1988).

In Malawi, central Africa, Simmons et al. (1986) studied blood pressure and salt intake in an urban and rural population. The sample was not truly representative but subjects were identified from a house-to-house survey until sufficient numbers were generated. A Hawkesley random zero sphygmomanometer was used and measurements were fully standardized. The urban sample consisted of 509 subjects (270 males, 239 females) and the rural one of 499 subjects (207 males, 292 females). The age range of the respondents was 15 to 65 years and older. Urban dwellers had consistently higher mean systolic and diastolic blood pressures. This difference was present even in the 15-24 year group. Both systolic and diastolic blood pressure increased with increasing age for both populations and sexes although the rise in diastolic blood pressure was not as pronounced in females. Urinary sodium output in the urban

sample was twice that in the rural sample but potassium output was the same for both samples. Crowding as measured by room-density had no effect on blood pressure. No reference was made to the prevalence of hypertension in the study populations.

Idahosa et al. (1987) compared blood pressure levels between a group of Nigerian policemen (594, mean age 26.2 years) and a group of male civil servants (521, mean age 28.6 years). Hypertension (WHO criteria, 1978) was present in 8.2% of policemen and in 8.8% of civil servants.

A blood pressure survey was conducted in a rural area of Ghana in 1973 (Pobee et al., 1977). Most adults in the area were involved in subsistence farming. The sample consisted of 809 males and 861 females. Little increase in mean systolic blood pressure until the late middle age was noted in the study population. A diastolic blood pressure exceeding 95 mm Hg was present in 3.8% of all males and 4.3% of all females. Overall, the prevalence of diastolic hypertension was 4.1%. This population was clearly a young population with a median age of 17 years.

Nissinen et al. (1988) reviewed the prevalence of hypertension in selected African countries. Overall, blood pressure was higher in older age groups of both sexes. Men had higher values than women, the difference between the sexes being greater among the younger age group in most countries. Blood pressure in African subjects was highest among urban men in Zaire in 1983-1984 (137/88 mm Hg at age 40-49 years) and among urban Malawian men in 1983 (141/87 mm Hg at age 45-54 years). These blood pressure levels were approximately the same as for subjects in developed countries e.g. the Japanese rural population in the late 1970s and Finnish men in rural areas in 1982. Urban Bantu women in Zaire during 1983-1984 had a mean blood pressure of 133/79 mm Hg in the 40 to 49 year age group. Urban Zulu women of the same age had a somewhat higher blood pressure level (136/89 mm Hg) in 1976. Nissinen et al. (1988) observed that these values were of the same magnitude as the blood pressure levels in Finland in 1982 but they were somewhat higher than that recorded in Japan in 1983.

Nissinen et al. (1988) concluded that the prevalence of hypertension was lowest in the Tanzanian population in the late 1970s (2%) and highest in urban men in Zaire during 1983-1984 (33%). These authors were of the opinion that the poorest countries had the lowest

prevalence of hypertension and that the prevalence increased in developing countries parallel to affluence.

The prevalence of hypertension in some sub-Saharan countries (except South Africa) is summarized in Table 3.3.1/1.

TABLE 3.3.1/1 The Prevalence of Hypertension in sub-Saharan African Countries - Early Studies

Population	Year of Study	Age (yr)	Males	Females	Total	Reference
Uganda	1963	18-75+	13.0	15.0	-	Shaper et al., 1969
Ghana	1973	16+	3.8	4.3	4.1	Pobee et al., 1977
Tanzania	< 1979	25-64	1.5	2.5	2.0	Vaughan et al., 1979
Nigeria	1983	20-64	8.5	-	-	Idahosa et al., 1987

3.3.2 Recent studies (1989-2002)

Hypertension research in Sub-Saharan Africa entered a new era during the previous decade resulting in several epidemiological studies of outstanding quality that are summarised in Table 3.3.2/1. Although these studies are much more standardised than previously, between-population comparisons are still hampered by differences in sample size, age categorisation, and most importantly by different techniques of blood pressure measurement.

The highest prevalence of hypertension (≥ 160/95 mm Hg or on treatment) in Africa at present is found in Zimbabwe (18% in males and 28% in females) ((Mufunda et al., 2000) followed by Tanzania (17.2% in rural males and 17.7% in urban females) (Table 3.3.2/1) (Edwards et al., 2000). The lowest prevalence rates are found in rural Gambia (7.6% males and 6.3% females)(van der Sande 2000) and Nigeria (6.9% males and females) (Cooper et al., 1997). Using the SADHS data, SA blacks have rates in between Tanzania and Gambia (9.3% males and 12.2%) females (Edwards et al., 2000 and Steyn et al., 2001). The SA coloured population has a prevalence of hypertension close to that of West Indies blacks (Steyn et al., 2001).

The Seven Populations Study (Cooper et al., 1997) with its meticulous methodology showed a clear gradient in the prevalence rates of hypertension between Nigeria, the Cameroon, the

West Indies and U.S. blacks (Fig. 3.3.1). Cooper attributed this gradient to the cross-cultural differences in the prevalence of the main risk factors for hypertension including obesity, high sodium-low potassium intake, psychosocial stress, physical inactivity, and alcohol. The unexpectedly high prevalence of hypertension in Zimbabwe does not fit in with the socio-cultural gradient-hypothesis put forward by Cooper et al. (1997). The high prevalence of hypertension in Zimbabwe is not attributable to differences in BMI (Mufunda et al., 2000).

An unexpected observation from Table 3.3.3/1 and Fig. 3.3.2/1 is the relatively low prevalence of hypertension in black South Africans compared to other sub-Saharan African populations. This finding is even more striking in the context of the extremely low prevalence of diabetes in Tanzania (MacLarty et al., 1989 and Bovet et al., 2002). Previous studies of black populations in SA, although characterised by limitations such as small sample sizes, confined to particular regions and ethnic groups, provided prevalence rates significantly different from that of the SADHS. The prevalence of hypertension in urban Zulus (21.4%, Seedat et al., 1982) for example was well above that reported for urban Africans (11.2% and 14% for males and females respectively) in the SADHS (SADHS, 1998). Similarly the prevalence of hypertension previously reported for coloureds (17.2% males, Steyn et al., 1986) and Asians (17% males, 23% females, Seedat et al., 1978) was also different from the SADHS results. A further possible explanation may be the different techniques used to measure blood pressure. The Omron M1 electronic blood pressure manometer was exclusively used in the SADHS. However, these instruments were previously properly validated (Steyn et al., 2001). One remaining explanation for the lower prevalence obtained during the SADHS may be the escalating AIDS epidemic by way of modifying the mean BMI of the population on a large scale. Although the findings of the SADHS are more reassuring concerning the prevalence of hypertension in SA, efforts should be made to reconcile the disparate results of the SADHS and previous hypertension studies.

TABLE 3.3.2/1. Prevalence of Hypertension in Africa, West-Indies and US Blacks – Recent Studies

		>140/90 mm Hg				>160/95mm Hg		
		Males		Females		Males	Females	Reference
Country	Age(yr)	n	%	n	%	%	%	
West Africa[a]								Cooper et al.1997
Nigeria	25-55+	1171	14.7	1338	14.3	6.9	6.9	
Cameroon								
Urban	25-55+	612	22.8	749	16.0	8.7	8.7	
Rural	25-55+	745	14.2	722	16.3	4.7	7.4	
Caribbean								
Jamaica	25-55+	524	19.1	733	28.2	12.9	20.6	
St. Lucia	25-55+	491	24.1	598	27.4	13.9	20.8	
Barbados	25-55+	330	25.9	483	28.2	18.0	22.9	
U.S.								
Maywood	25-55+	708	31.3	810	33.6	23.1	28.2	
Cameroon[2 a]								Mbanya et al., 1998
Rural	25-74	308	-	438	-	5.4	5.9	
Urban	25-74	461	-	591	-	16.4	12.1	
Tanzania[a]								Edwards et al., 2000
Ilala (Ur)	15+	330	30.0	437	28.6	14.4	15.4	
Shari (Ru)	15+	401	32.2	527	31.5	17.2	15.6	
Gambia[f]								van der Sande et al., 2000
Banjul (Ur)	Adults	1028	22.0	1138	16.9	7.5	7.3	
Farafenni (Ru)	Adults	1200	20.6	2023	16.0	7.6	6.3	
Zimbabwe[e] (Ur)	25+	384	28.0	391	41.0	18.0	28.0	Mufunda et al., 2000
South Africa[1 b]								Steyn et al., 2001
African	15-65+	4283	18.6	6174	20.1	9.3	12.2	
Coloured	15-65+	772	22.9	1008	24.7	11.4	18.4	
White	15-65+	500	34.4	603	27.1	21.5	22.0	
Asian	15-65+	183	24.8	279	20.3	14.9	16.5	
Tanzania[c 2] (Ur)	35-64	1729	27.1	2053	30.2	13.1	17.7	Bovet et al., 2002

[1] Age-adjusted

[2] Adjusted to the world population

[a] Mercury shygmomanometer

[b] Omron M1 electronic BP manometer

[d] Omron HEM

[c] Visomat

[e] Omron HEM-713C

[f] Omron HEM-705-CP

55+ and 65+: subjects older than 55 years and 65 years were grouped together.

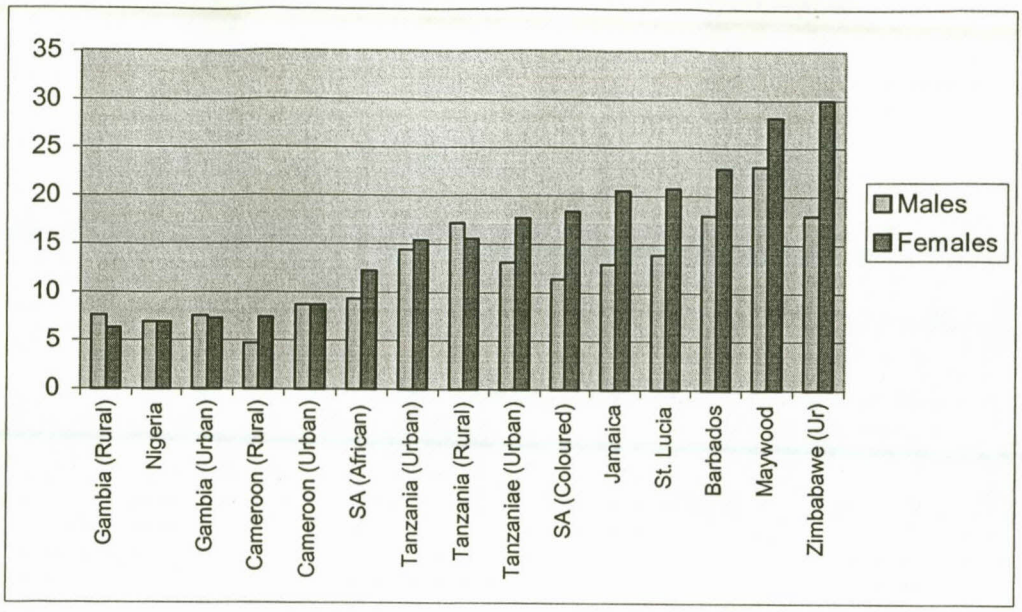


Fig. 3.3.2/1. Prevalence of hypertension (≥160/95 mm Hg) in populations of African origins.

3.4 Prevalence of hypertension in United States blacks

Hypertension and elevated blood pressure levels among black people in the United States are common and excessive compared to those in the white population. This excess is greatest among adults, less so among adolescents, and not apparent in children (Prineas et al.1985). Hypertension in black Americans tends to appear earlier than in white Americans and often is not treated early enough or aggressively enough. The result is a higher prevalence of severe hypertension in black patients, frequently accompanied by target-organ damage.

Home blood pressure measurements were done in the United States in 14 communities during 1973-1974 as part of the Hypertension Detection and Follow-up Program (HDFP) and 151,668 individuals participated (1977). The prevalence of hypertension was higher for blacks than whites and for men than women, except in the older age group. In the age group 30 to 49 years 25.6% of black men and 14.1% of white men were classified as hypertensive (5th phase diastolic blood pressure > 95 mm Hg not on medication for high blood pressure and plus those with a diastolic blood pressure < 95 mm Hg currently taking antihypertensive medication). In the age group 50 to 69 years the corresponding prevalence of hypertension was 41.7% and 24.3%. Likewise for women the prevalence in the 30 to 49 year group was 22.7% and 9.4% for black and white women respectively and in the 50 to 69 year group 45.1% and 25.7% respectively. Severe hypertension (diastolic blood pressure ≥ 115 mm Hg) was five times more common in black than white men and approximately seven times more common in black women than in their white counterparts.

In the Maryland State-wide Household Surveys conducted in 1978 and 1982, it was found that 56.2% of black males over 50 years and 59.7% of black females over 50 years had diastolic blood pressure levels ≥ 90 mm Hg, or < 90 mm Hg on medication (Saunders, 1985).

The National Health and Nutrition Examination Survey I (NHANES I) Epidemiologic Follow-Up Study (NHEFS) is one of the few longitudinal studies reporting on the incidence of hypertension in both white and black Americans (NHEFS, 1989). The NHEFS included 14235 participants (12036 white, 2199 black) who were 25 to 74 years old at baseline examination and who were followed for an average period of 9.5 years. Total incidence rates of definite hypertension (>160/95) for white men and women followed for an average of 9.5 years, were 12.1% and 10.2% respectively. For black men and women the corresponding rates were

23.3% and 22% respectively. Incidence rates of hypertension calculated from the NHEFS data emphasized dramatically what was implied in previously reported prevalence rates. The

3.5 The global prevalence of hypertension

During the last 15 to 20 years the methodology used for measuring blood pressure in surveys has become more standardized and results are also reported in a more uniform manner (Nissinen et al., 1988). Furthermore, the definition of hypertension follows generally the recommendations laid down by the WHO in 1978.

Nissinen and co-workers (1988) reviewed total mortality, mortality from hypertensive disease and stroke, and the prevalence of hypertension in developing countries. Sadly, mortality statistics for Africa were either not available or not included as is the case for South Africa. On the whole mortality rates for hypertensive disease in most countries showed a downward trend since the 1960s. The three countries with the highest mortality rates (per 100 000) for the 1980s in the 55-64 year age group were Trinidad and Tobago 85.7 (1983), Mauritius 100.0 (1984) and Kuwait 184.7 (1986). Hypertension as a cause of death has clearly decreased in Barbados, Chile and Singapore, whereas in Kuwait the rates are increasing. In developing countries the prevalence of hypertension is now of the same magnitude as in Finland which has one of the highest mortality rates for ischaemic heart disease among the middle-aged population (Nissinen, 1988).

3.6 Aetiology and pathophysiology of hypertension

Patients with arterial hypertension and no definable cause have primary, essential, or idiopathic hypertension (Williams 2001). It is more likely that separate disease entities are involved in the development of primary hypertension than a single abnormality in a specific organ system (Williams 2001). The principle risk factors for hypertension are obesity, high sodium/low potassium intake, psychosocial stress, physical inactivity, and alcohol (Cooper et al., 1997).

3.6.1 Obesity

The association between obesity and hypertension is well documented (van Italie, 1985). In the 1976-80 US National Health and Nutrition Survey II (NHANES II), overweight was defined as a body mass index exceeding 27.8 kg/m^2 for men and 27.3 kg/m^2 for women (Van Italie, 1985). Hypertension was defined according to WHO (1978) criteria. Fig. 3.6.1/1 shows the relation between overweight and hypertension in this survey.

The overall relative risk of hypertension for overweight Americans aged 20-75 years was threefold that for non-overweight persons. This risk was strongly influenced by age. Among overweight Americans aged 20-44 years, the relative risk of hypertension was 5.6 times that of non-overweight Americans of the same age group (Fig.3.6.1/1). This is in contrast to the relative risk for hypertension of 1.9 in overweight Americans aged 45-74 years compared to non-overweight persons in the same age group.

It is also evident from Fig. 3.6.1/1 that compared to overweight black men and women, overweight white men and women were at slightly greater risk of being hypertensive. Thus, blood pressure in black Americans may be less affected by overweight than blood pressure in white Americans. Since hypertension is commoner in black Americans than white Americans, other factors apart from overweight must contribute to hypertension in blacks. The risk of hypertension was also slightly greater in overweight individuals from poor socio-economic status compared to more affluent individuals.

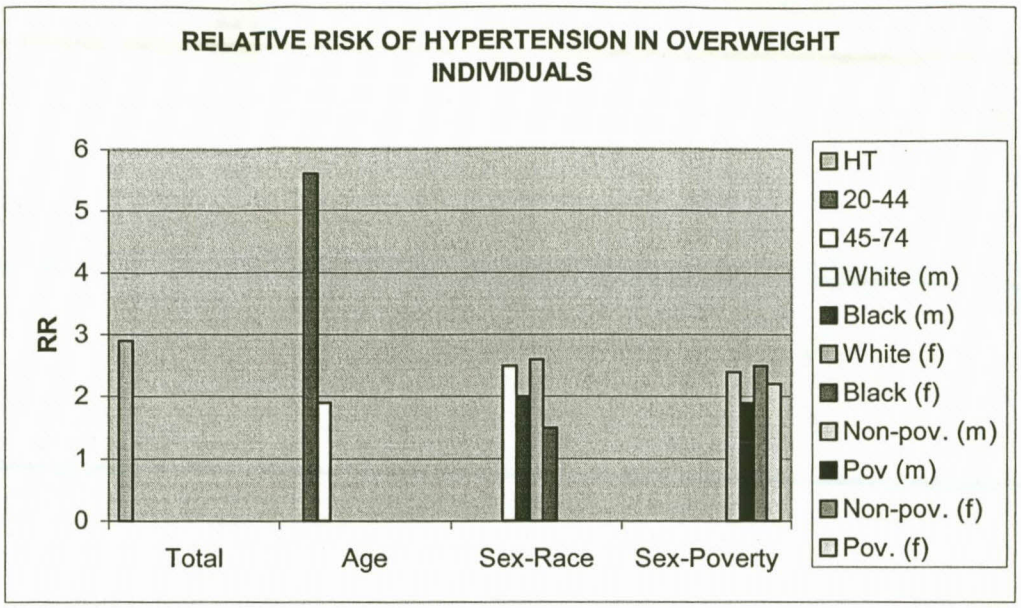


Fig.3.6.1/1. Relative risk of hypertension in overweight individuals. (van Italie, 1985) (pov. = poverty)

Overweight patients with hypertension can reduce both their systolic and diastolic blood pressure significantly by losing weight without restricting salt intake at the same time (Reisin et al., 1978). In the latter study a weight reduction of 13.5% in 24 patients with a initial mean weight of 85.5 kg resulted in a decrease in SBP of 21-28 mm Hg and a decrease in DBP of 18 and 23 mm Hg while maintaining the same salt intake. The individual response of blood pressure to weight loss in this study, however, varied considerably.

The association between obesity and hypertension is not so firm in less-developed societies (Dustan, 1991). A group of 152 !Kung Bushmen, studied by Truswell (1972), were lean, short, of delicate build and none of them were hypertensive. William (1969) reported from Kenya that neither blood pressure nor ponderal index changed with increasing age in Samburu men (Nilo-Hamites, a northern subgroup of the Masai tribe). Kenya was also one of the Intersalt (1988) populations that had a low median blood pressure, low prevalence of hypertension, and only a small increase in blood pressure with increasing age. The median BMI of this population was only 20.5 kg/m^2 (the second lowest of the 52 participating populations).

Several studies in South Africa also confirmed the association between obesity and hypertension. Seftel et al. (1980) found in their study of 10046 blacks that females were considerably more obese than males. Both diastolic and systolic blood pressure correlated positively but modestly with obesity. In the Cape Coloured population Steyn et al. (1986) also found a correlation between body mass index and systolic as well as diastolic blood pressure for both sexes. This correlation was spurious when the systolic and diastolic blood pressures were corrected for arm circumference.

TABLE 3.6.1/1 Relationship between Obesity and Hypertension in Blacks: African Studies

	Males	Females	Level of Risk	Reference
Cape Peninsula blacks	-	Positive	Not calculated	Steyn et al., 1991
Seven Populations	Positive	Positive	RR=1.02 (1.01-1.12)	Cooper et al., 1997
Tanzania	Negative	Positive	Not calculated	Edwards et al., 1999
Nigeria	Negative	Positive	Not calculated	Olatunbosun et al., 2000
Gambia	Positive	Positive	Not calculated	van der Sande et al., 2000
Zimbabwe	Positive	Positive	Not calculated	Mufunda et al., 2000
THUSA	n.a.	Positive	Not calculated	Kruger et al., 2001
Tanzania	Positive	Positive	SBP (m) 1.01 mmHg/kg	Bovet et al., 2002
			SBP (f) 0.91 mmHg/kg	
			DBP (m) 0.76mmHG/kg	
			DBP (f) 0.72 mmHg/kg	

m=male, f=female

The relationship between obesity and hypertension in Africans or subjects with an African origin from more recent studies is summarised in Table 3.6.1/1. The relationship is consistent for women but not for men. Few attempts were made to quantify the risk associated with obesity. A possible explanation for the inconsistent association between obesity and hypertension in male subjects is the fact that the prevalence of obesity was overall relatively low in male subjects.

The exact mechanism linking hypertension to obesity remains unclear. Several possibilities were suggested including increased cardiac output with failure of appropriate reduction in systemic vascular resistance, stimulation of the renin-angiotensin-aldosterone system, and increased salt intake with increased caloric intake (van Gaal and Mertens, 1998).

3.6.2 Central obesity

Fat distribution correlates with several cardiovascular risk factors including hypertension (van Gaal en Mertens, 1998). As long ago as 1956 Vague observed a relationship between android obesity and hypertension, diabetes, atherosclerosis and gout (Vague, 1956). A decade after the first NHANES survey, Blair et al. (1984) reported the correlation between subscapular skin fold thickness and systolic as well as diastolic blood pressure whilst triceps skin fold thickness correlated only weakly with blood pressure. The implication was that fat located mainly over the trunk, correlated better with both systolic and diastolic blood pressure than fat situated more peripherally.

Selby et al. (1989) attempted to answer the question whether the fat distribution pattern as determined by subscapular and/or triceps skin fold thickness, was a predictor of hypertension. These authors did a retrospective case-control study among the participants of the Kaiser Permanente Medical Care Program. A total of 1031 case-control pairs were matched for sex, race, age and dates of the case's baseline normotensive examination as well as the first examination where the case was found to be hypertensive. Subscapular and triceps skin folds were routinely measured at baseline and follow-up as well as blood pressure. Baseline BMI, subscapular skin fold thickness and triceps skin fold thickness were each predictive of the development of hypertension. The association of triceps skin fold with risk disappeared after correcting for body mass index. A change in subscapular skin fold thickness from baseline over 5.7 years conferred some increase in risk for women only. This study clearly showed the relative importance of central versus peripherally deposited fat in the development of clinically recognized essential hypertension. This was probably the first study that demonstrated that the risk of hypertension associated with body fat distribution is independent of the overall level of obesity. Although black subjects were included in this study, results were not presented separately.

Hartz et al. (1984) investigated the relationship between central fat distribution and hypertension in 21 065 health conscious white women between the ages of 40-59 years. He found that the RR of hypertension in women with central obesity compared to women with predominantly lower body fat distribution was 1.74. Diseases were self-reported and waist and hip measurements were self-performed.

In the historic Gothenburg-study, Larsson et al. (1984) examined the relationship between the various distributions of body fat and an increased risk of cardiovascular disease in 792 men followed for a period of 13 years. Significant positive associations were found between the waist to hip ratio on the one hand and systolic and diastolic blood pressures, body mass index, and sum of three skin fold thickness (triceps, subscapular and parathoracic) on the other hand.

An even earlier observation made by Ruderman et al. (1981) suggested that there are individuals who by standard weight tables are not obese or overweight, but who have metabolic abnormalities that are characteristically associated with adult-onset obesity i.e. hyperinsulinism, hypertriglyceridaemia, diabetes and hypertension. He referred to these subjects as 'metabolically-obese', normal-weight individuals. This interesting concept still awaits epidemiological description.

The relation between central obesity and hypertension in black Africans or subjects of African descent has not been adequately studied. Although methods for measuring waist- and hip-circumferences have been standardised, cut-points for WHR and waist circumferences for black Africans have not been standardised. Most researchers used US cut-points or sex- and region-specific means or WHR in the upper quartile of the sex-specific distributions to diagnose central obesity (Table 3.6.2/1). In all the available studies of sub-Saharan subjects where WHR or waist circumferences were measured a positive association between central obesity and hypertension emerged (Table 3.6.2/1). In the only study where OR's were calculated, the OR for hypertension in subjects with central obesity compared to subjects with lower body fat distribution was 1.6 for rural as well as the urban samples (van der Sande et al.2000). Consensus needs to be reached for appropriate cut-points including possible validation of the WHO suggestions in this regard for measures of central adiposity in black African subjects.

TABLE 3.6.2/1. Relationship between Central Obesity and Hypertension in Blacks: African Studies

	Males	Females	Level of Risk	Reference
Tanzania[a]	Positive	Positive	Not calculated	Edwards et al., 2000
Nigeria[b]	Positive	Positive	Not calculated	Olatunbosun et al., 2000
Zimbabwe	Positive	Positive	Not calculated	Mufunda et al., 2000
Gambia[c] (rural)	Positive	Positive	OR=1.6(1.2-2.2)	Van der Sande et al., 2000
Gambia[c] (urban)	Positive	Positive	OR=1.6(1.1-2.3)	Van der Sande et al., 2000
THUSA	n.a.	Positive	Not calculated	Kruger et al., 2001

[a] mean WHR hypertensive males 0.87 vs. 0.85 in non-hypertensive males -rural

[a] mean WHR hypertensive males 0.90 vs. 0.84 in non-hypertensive males urban

[a] mean WHR hypertensive females 0.84 vs. 0.82 in non-hypertensive females -rural

[a] mean WHR hypertensive females 0.82 vs. 0.78 in non-hypertensive females -rural

[b] US criteria for WHR (men > 0.95 and women >0.80)

[c] Central obesity = WHR in upper quartile of sex-specific distribution

While the mechanisms linking central fat patterning with increased blood pressure are incompletely understood, several hypotheses have been advanced to explain this association. The results of a study from Israel provided an early clue to a possible link between insulin resistance and hypertension (Modan et al., 1985). They found in a population-based study of middle-aged and elderly subjects that glucose intolerance and hypertension were strongly associated. The prevalence of glucose intolerance was 27.8% in normotensive subjects, 48.1% in untreated hypertensive subjects and 61.7% in treated hypertensive subjects. This association was independent of the effect of age, obesity, and use of antihypertensive medication. Hyperinsulinaemia was defined in this study as fasting insulin levels, or the sum of 60 and 120 min post glucose load serum insulin levels, exceeding the 75th percentile of corresponding insulin levels of a non-obese and normotensive control group. Hypertension was significantly associated with hyperinsulinaemia, independent of BMI, age, sex and glucose tolerance. A possible critique on this study is that the study population was mainly middle-aged and older and that the influence of body fat distribution was not explored.

In a later study, Donahue et al. (1987) reported that fasting serum insulin concentrations were directly related to systolic and diastolic blood pressure in young adults, independent of body mass index and fasting serum glucose. Donahue et al. (1990) also emphasized that because the insulin/blood pressure link was present in healthy young people, the mechanisms linking blood pressure with insulin are present before obesity, clinical hypertension, or glucose intolerance develops.

A link between insulin resistance and central adiposity was already established. Kissebah et al. (1982) studied the glucose and insulin response to an oral glucose load in 16 obese women with predominantly central obesity, 9 obese women with predominantly lower body fat distribution and 9 non-obese control subjects. Plasma glucose levels were significantly higher at 30 min, 60 min, 90 min and 120 min in the group with central obesity compared to normal subjects, and glucose levels were in between for subjects with lower segment body fat distribution. Analogous results were obtained for serum insulin levels. Krotkiewski et al. (1983) confirmed these results in 930 obese individuals (930 women, 260 men). Interestingly, in the latter study fasting serum insulin concentrations were significantly higher in men than in women with the same degree of overweight (23.5 mU/l compared to 17.6 mU/l respectively) implying greater insulin resistance in men. Analogous results were obtained for plasma glucose levels.

In an epoch-making lecture, Reaven (1988) reviewed the biochemical evidence linking insulin resistance and arterial hypertension, Type 2 diabetes and CHD. Reaven also reviewed two possible mechanisms whereby insulin may cause hypertension. Firstly, increases in plasma insulin concentration are associated with significant increases in plasma catecholamine concentration and secondly, insulin infusion acutely causes sodium retention in humans, a fact previously established by DeFronzo et al. (1975). Reaven did not consider a role for obesity or central obesity in this syndrome he referred to as Syndrome X.

In the studies cited thus far the following interrelations were shown: hypertension was associated with obesity and was even more strongly associated with central obesity; hypertension was associated with hyperinsulinaemia independent of body mass index, age and fasting serum glucose in both older as well as younger subjects; and central obesity was associated with increased plasma glucose levels and hyperinsulinaemia. Kaplan (1989) consolidated these findings into a single hypothesis and included the association of central obesity with hypertriglyceridaemia (Fig. 3.6.2/1). Another paradigm shift was thus established

drawing attention to the clustering of CV risk factors. Kaplan referred to this clustering of CV risk factors as the "Deadly Quartet".

Although several subsequent epidemiological studies confirmed the hyperinsulinaemia/insulin resistance hypothesis of essential hypertension, other epidemiological studies did not. Saad et al. (1991) investigated the relationship between plasma insulin concentration, insulin-mediated glucose disposal by euglycaemic-hyperinsulinaemic clamp, and blood pressure in healthy Pima Indians, whites, and American blacks. They found that after adjusting for age, sex, body weight, and percentage of body fat, the fasting plasma insulin concentration

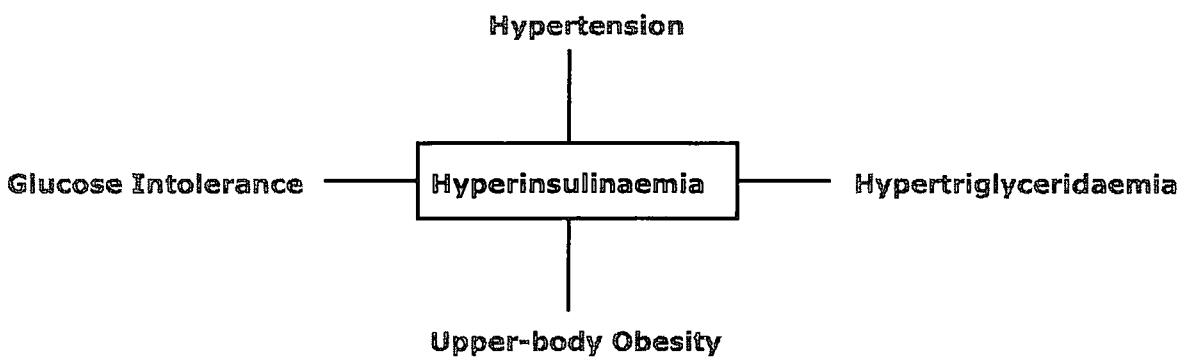


Fig. 3.6.2/1. The Deadly Quartet (Kaplan, 1988).

remained significantly related to mean blood pressure in whites but not in the other two groups. After similar adjustments, glucose disposal also remained significantly related to mean blood pressure only in whites.

Mbanya et al. (1988) investigated the relation between hypertension and insulin resistance in a small number of non-obese normotensive and hypertensive diabetic and non-diabetic subjects. They found that hyperinsulinaemia was not causally related to essential hypertension but that it may contribute to the hypertension of non-insulin-dependent diabetes in association with low hepatic extraction of insulin.

In a study comprising 3 ethnic groups (106 Afro-Caribbean, 107 Gujerati Indian and 101 white European subjects), Cruickshank et al. (1991) found no consistent relationship between blood pressure and fasting or 2 hour C-peptide or insulin concentrations.

In 3 Pacific Island populations, susceptible to obesity, non-insulin-dependent diabetes, hyperinsulinaemia and hypertension, Collins et al. (1990) found an inconsistent and weak association between insulin and blood pressure.

It is not possible to explain the discrepant results among these studies, but different definitions of obesity, ignoring body fat distribution, differing proportions of males and female participants and ethnic or genetic differences may account for some of the divergent findings. The distribution of blood pressure in a population is also affected by a variety of genetic and environmental influences, and it would be surprising if insulin concentration explained more than a portion of the blood pressure variance (Donahue et al., 1990).

As long ago as 1991 Dustan commented that the hypothesis was intriguing, but the gaps in knowledge did not permit a conclusion as to insulin's role in arterial pressure control. In addition, he expressed the sobering thought that sophisticated statistical analyses are commonly used to explain human disease, resulting in the possibility that the relationship of arterial pressure with a single factor is more apparent than real. The role of insulin in controlling arterial pressure is still vaguely understood and its role in the pathogenesis of arterial hypertension remains unclear (Williams, 2001).

3.6.3 High sodium / low potassium intake

Luft et al. (1985) studied urinary sodium excretion in a series of volume expansion and contraction experiments in black and white subjects. In the 24 hours after volume expansion with saline, sodium excretion of blacks was less than of whites. During volume contraction with furosemide, black subjects actually demonstrated a greater natriuresis than white subjects. It must be pointed out that although statistically significant, these differences were mild. Luft et al. (1985) also extensively examined plasma renin activity (PRA) in normotensive blacks. Free-living normotensive black and white subjects seem to have renin values that are not greatly different. However, when subjected to volume contraction, the increase in plasma renin of white subjects was greater than that observed in black subjects. Luft suggested that the difference was related to relative volume expansion in blacks. The latter observation supported earlier work by Chrysant et al. (1979) who showed that 43% of black patients with uncomplicated essential hypertension were volume expanded compared to 21% of white patients. There is thus a segment of black patients with essential hypertension in whom

arterial pressure, intravascular volume, and PRA do not demonstrate the interrelations among these variables that were found in white patients. Other researchers had difficulty in repeating these purported differences in plasma volume between black and white hypertensive subjects (Sagnella, 2001).

Sagnella extensively reviewed available information on the reasons for lower PRA in black subjects (2001). The most plausible explanation is the abnormal renal sodium handling mechanisms in black subjects with hypertension. Hypertension in blacks shares some significant similarities with Liddle's syndrome such as an apparent greater sodium sensitivity and low PRA. Liddle's syndrome is characterised by a molecular defect leading to increased activity of the renal epithelial sodium channel. The increased renal sodium reabsorption and sodium retention leads to high blood pressure and suppression of PRA. This hypothesis stemmed from the finding of a mutation in the sodium channel β-subunit, the T594M mutation, which was more common in hypertensive than in normotensive black subjects (Baker et al., 1998). This increased tendency for sodium retention may reflect an evolutionary adaptation for more efficient mechanisms to conserve sodium in people originally inhabiting semitropical regions where sodium intake was traditionally low and difficult to obtain. Furthermore, the more sluggish renin system in blacks provides a basis for the greater reduction in blood pressure in response to dietary sodium restriction (Sagnella, 1998).

In South Africa, Sever et al. (1980) compared blood pressure and PRA of 126 rural Xhosas with that of 125 urban Xhosas. Mean plasma renin activity was similar in both groups although mean blood pressure was significantly greater in the urban group. The authors speculated that the low renin activity in blacks may be largely genetically determined, and therefore a true ethnic phenomenon.

Hoosen et al. (1985) also compared plasma renin activity of rural Zulus with that of urban Zulus and urban Indian patients. PRA levels were lower in urban than in rural Zulus and the plasma renin activity levels of urban Zulus were the same as that of Indians. Only hypertensive urban Zulus had significantly lower plasma renin activity levels than their normotensive counterparts. An inverse association between plasma renin activity and blood pressure was found in urban Zulus and Indians but not in rural Zulus. Hoosen concluded that the difference in observed in plasma renin activity between the urban and rural Zulus was not

due to genetic factors. They also studied urinary sodium and potassium excretion and found no difference between rural and urban Zulus.

The Intersalt study (1988) was launched to investigate in a systematic and standardised way the relations between electrolyte excretion and blood pressure based on samples from many countries. Globally, 10648 subjects were enrolled in 52 centres. The study was designed to test three hypotheses: 1) that there is a direct correlation between 24-hour sodium excretion and blood pressure values across populations, 2) there is an inverse correlation between 24-hour potassium excretion and blood pressure values across populations, and 3) the ratio of urinary sodium and potassium excretion is directly correlated with blood pressure (Luft, 1989). The lowest 24-hour urinary sodium excretion (< 50 mmol/24 hours) was seen in four isolated and less developed populations. In these societies BP tended not to increase with age. In the age and sex standardized analysis a significant linear relation was shown between the median 24- hour sodium excretion for the 52 centres and mean systolic blood pressure. However, this relationship was lost if the 4 primitive centres were deleted from the analysis (Intersalt Cooperative Research Group, 1988). The main conclusions of the Intersalt study were: 1) Within centres sodium excretion was significantly related to blood pressure in individual patients and across centres to the blood pressure slope with age. Thus lower average sodium intake might have a favourable influence on blood pressure, on change of blood pressure with age, and hence on cardiovascular mortality. 2). Potassium excretion was negatively and independently associated with blood pressure of individual subjects within centres after adjustment for sodium excretion, body mass index, and alcohol intake. 3) The relation of the urinary sodium to potassium ratio to blood pressure in individual subjects followed a pattern similar to that for sodium but more strongly and consistently.4) BMI and high alcohol intake were strongly, positively, and independently associated with blood pressure in individual subjects.

Two African populations participated in the Intersalt project: Kenya where the 24-hour sodium excretion rate was 51.3 mmol and the prevalence of hypertension (systolic pressure ≥ 140 mm Hg or diastolic ≥ 90 mm Hg) was 5.0% and Zimbabwe, where the 24-hour sodium output was 129.7 mmol and the prevalence of hypertension 24% (Intersalt Cooperative Research Group, 1988). Hoosen et al. (1985) also could not find an association between sodium excretion and blood pressure. Following the Intersalt study, Luft (1989) warned against giving prescriptive advice on the basis of weak epidemiological relations. An editorial in the Lancet (1989)

suggested that the debate about optimum sodium intake should move from an anthropological setting to that of properly conducted intervention trials.

Cutler et al. (1997) reviewed 32 properly conducted randomised trials of the effect of reduced sodium intake on blood pressure with outcome data for 2635 subjects (Fig. 3.6.3/1). The effects on blood pressure of lowering sodium intake in hypertensive and normotensive subjects, were -4.8/-2.5 mm Hg and -1.9/-1.1 mm Hg for systolic and diastolic blood pressure respectively. There was no evidence that sodium reduction as achieved in these trials presented any safety hazards. The authors suggested that the blood pressure reduction that would result from a substantial lowering of dietary sodium in the US population could reduce cardiovascular morbidity and mortality. The development of hypertension appears to require a threshold level of salt intake (Kaplan, 2002). Thus, essential hypertension is seen primarily in societies in which salt intake is above 100 meq/day (2.3 g sodium). In contrast, hypertension is a rare disorder in societies in which salt intake is less than 50 meq/day (1.2 g sodium). This effect appears to be independent of other risk factors for hypertension, such as obesity and increased alcohol intake.

A different meta-analysis of 56 trials on the effect of reduced dietary sodium on blood pressure, however, came to different conclusions (Midgley et al., 1996). Dietary salt restriction reduced systolic blood pressure levels in hypertensive patients significantly by 3.7 mm Hg and DBP level by 0.9 mm Hg (not significantly). The reduction in BP levels in normotensive subjects was also not significant. The magnitude of change was greater for older subjects. The authors recommended that dietary sodium restriction might be considered for older subjects and also cautioned that more information on long-term benefits and safety-issues are needed.

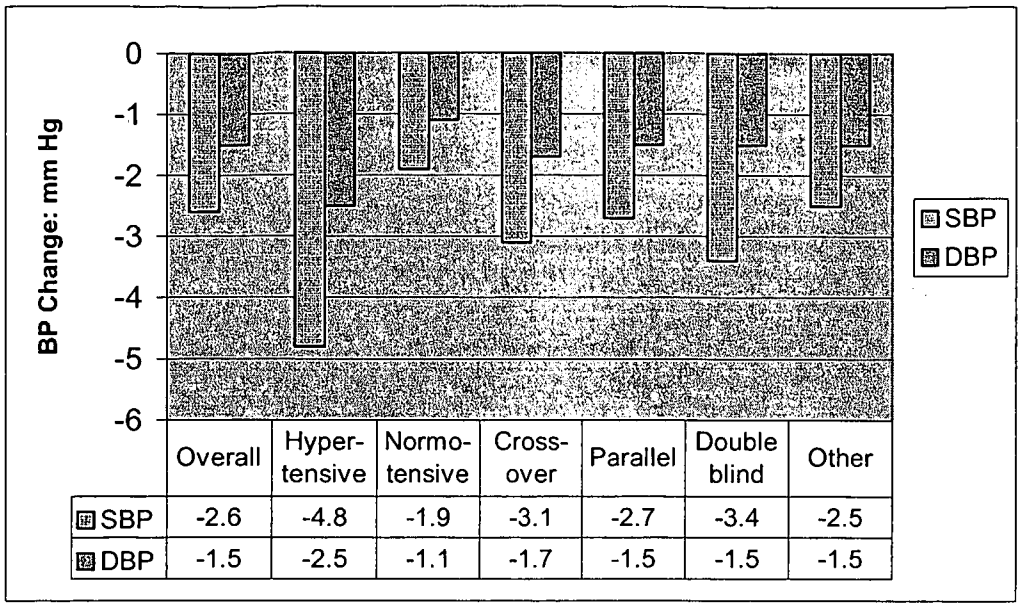
Part of the difficulty in documenting a significant fall in blood pressure with sodium reduction may reflect the natural variation in pressure responsiveness, a characteristic known as sodium sensitivity (Kaplan, 2002). Although the extent of BP change in response to reduced sodium intake varies considerably from individual to individual, it is likely that excess sodium intake over many years plays a role in most people who develop hypertension (Kaplan, 2002).

Several possible mechanisms for increased sodium sensitivity were proposed including a defect in renal salt excretion (Campese, 1994), increased activity of the sodium-hydrogen exchanger in the proximal tubule (Siffert et al., 1995), and a defect in the gene for adducin (a cytoskeletal protein) (Tripodi et al., 1996).

The role of potassium in the pathogenesis of essential hypertension has also received attention. Animal experiments suggested that dietary potassium afforded protection against hypertension by, at least in part, promoting natriuresis (Luft, 1991). The Intersalt study showed that potassium excretion was negatively and independently associated with blood pressure of individual subjects within centres after adjusting for sodium excretion, body mass index, and alcohol intake. In clinical practice, however, conflicting results were obtained by increasing the potassium intake of hypertensive patients. Grimm et al. (1990), on the other hand, concluded from a study that oral potassium supplementation in hypertensive patients did not reduce the need for antihypertensive medication. Kaplan (1990), however, pointed out that the latter study involved only white men and that dietary potassium supplements might benefit black patients with hypertension who have a diet high in sodium and low in potassium as was commonly found in dietary surveys. Subsequently Morris et al. (1999) showed that in most normotensive black men but not in white men, salt sensitivity occurred when dietary potassium was deficient. This phenomenon was prevented when dietary potassium was increased into the normal range. A potassium intake of 40-60 mmol/day may have a beneficial effect on the level of blood pressure (Linas, 1991). Potassium supplementation should be withheld in individuals with decreased renal function, in the elderly, and in individuals taking potassium-sparing diuretics, ACE-inhibitors or non-steroidal anti-inflammatory drugs.

Salt-sensitivity is not synonymous with sodium-sensitivity. Kurtz et al. (1987) showed in 5 hypertensive men who became normotensive on salt restriction that the administration of sodium chloride but not sodium citrate induced significant increases in both systolic and diastolic BP.

The possible contribution of other vasoactive substances to the development of essential hypertension has also been studied. Urinary excretion of kallikrein was examined during usual diet and after sodium restriction in normotensive and hypertensive subjects, including both blacks and whites (Levy



	Overall	Hyper-tensive	Normo-tensive	Cross-over	Parallel	Double blind	Other
SBP	-2.6	-4.8	-1.9	-3.1	-2.7	-3.4	-2.5
DBP	-1.5	-2.5	-1.1	-1.7	-1.5	-1.5	-1.5

Fig. 3.6.3/1. Blood pressure and sodium reduction (Cutler et al., 1997).

et al., 1977). Urinary kallikrein excretion at baseline was lower in black subjects than in white subjects. With dietary sodium restriction, urinary kallikrein excretion increased significantly in all groups except hypertensive blacks. Since kinin was associated with vasodilatation, lower levels of kinin and thus kallikrein implied less vasodilatation. Unfortunately blood kinin levels were not necessarily correlated with urinary kallikrein excretion (Shulman, 1985).

Sever et al. (1980) measured plasma noradrenaline concentrations in a sample of urban and rural Xhosas and found no difference between the two groups and between the sexes. Furthermore, no correlation was found between age, noradrenaline and blood pressure in this study. Similarly, no evidence of increased sympathetic activity on studying heart rate variability was found in black subjects of African descent in London (Guzetti et al., 2000).

Yanagisawa and co-workers discovered the novel and potent vasoconstrictor, endothelin in 1988. This protease-sensitive substance is a 21-aminoacid peptide produced by endothelial cells. Kohno et al. (1990) reported increased levels of endothelin in hypertensive subjects compared to normotensive and borderline hypertensive subjects. Levels were elevated in many patients in whom blood pressure was particularly high or in whom renal function was impaired. Their findings suggested that endothelin might be more strongly associated with the progress than the onset of essential hypertension. The exact role of endothelin in the pathogenesis and maintenance of essential hypertension is still unknown.

3.6.4 Genetic considerations

Hypertension is about twice as common in subjects who have one or two hypertensive parents and genetic factors may account for approximately 30 percent of the variation in blood pressure in various populations (Kaplan, 2002b). Most studies of likely genes, however, have failed to document linkage or consistent association with hypertension (Williams, 2001). Cooper et al. (1997) holds the view that available data do not allow either the genetic or environmental hypotheses to be tested rigorously since measures of both components are still very imprecise. It is also likely that gene-environment interactions occur, with specific genotypes expressed differently in settings where the mix of exposures differs (Cooper et al., 1997). The results of some human genetic studies on the aetiology of essential hypertension are shown in Table 3.6.4/1.

Cooper et al.(2000) compared the familial patterns of angiotensinogen (AGT) and angiotensin-converting enzyme (ACE) levels in black subjects residing in Maywood, US with that of Nigerians. Strong evidence for familial aggregation of AGT and ACE was found in Nigerians but only weak aggregation was found in US blacks. Heritability estimates for AGT were 76%-78% in Nigerians and 15%-23% in US blacks. A similar pattern was observed for ACE. AGT is influenced by body composition and some factors associated with the obesity syndrome may be the cause of this phenomenon. Lifestyle patterns and environmental exposures may likewise influence these traits.

TABLE 3.6.4/1. Some Human Genetic Studies on the Aetiology of Essential Hypertension

Gene	Intermediate Phenotype	Statistical Approach	Reference
α&βG Subunit of epithelial Na^+ Channel	None	Linkage positive (SBP)	Wong et al., 1999
B&G Subunit of epithelial Na^+ Channel	Liddle's syndrome	Association Negative	Melander et al., 1998
Glucocorticoid receptor receptor gene	angiotensinogen cortisol 18-OH corticosterone	Association Positive	Watt et al., 1992
AGT M235T	None	Association Positive (HT)	Tiret et al., 1998
AGT T174M	None	Association Neg (HT)	
ACE I/D	None	Association Neg (HT)	
AGT1RA1166C	None	Association Positive (HT, females)	
CYP11B1	11 beta hydroxylase	Linkage negative (HT)	Brand et al., 1998
CYP11B2	aldosterone synthase	Association Positive (HT)	
Adducin (Gly 460 Trp)	actin skeleton	Linkage positive	Cusi et al., 1997
Chromosome 17[a]		Association Positive (SBP & DBP)	Levy et al., 2000
AGT	angiotensinogen-levels	Segregation analysis: recessive major gene effect	Guo et al., 1999
ATG	angiotensinogen-levels	Aggregation	Cooper et al., 2000
ACE	angiotensin-cnverting enzyme	Heritability for ATG and ACE in Nigerians but less in US blacks	
B2-Adrenoreceptor polymorphism	None	Association Negative	Candy et al., 2000
G-protein 825 T allele		Association Negative	Carlos Poston et al.
AGT-235 T-allele	PRA, ACE activity	Association Negative	2001
ACE I/D		Association Negative	

[a] Close to WNK4 gene (mutations involved in Type 2 pseudohypoaldosteronism-Gordon's syndrome)

SBP=systolic blood pressure

DBP=diastolic blood pressure

HT=hypertension

3.6.5 Environmental factors

The historical debate over the predisposition of US blacks to hypertension has focussed almost exclusively on black-white comparisons with a prominent emphasis on genetic predisposition (Cooper et al., 1997). The possibility that the primary determinant of the black-white differences might be environmental received less attention. Several studies, however, contributed to the body of knowledge in this field.

In the US the Hypertension Detection and Follow-up Program (1977) screened 158 906 adults and examined the relationship of education to the racial difference in the prevalence of hypertension. The level of education was inversely associated with hypertension and this "education effect" was strongest in blacks and in females. Overweight diminished the inverse effect but did not eliminate it (Fig.3.6.5/1). The mechanism responsible for higher rates of hypertension in those with least education was not clear. The authors hypothesized that cultural traditions related to economic status and food choices such as higher dietary salt intake were involved. Education, as an index and symbol of social status, could be reflecting the relative social and psychological stress. Education alone did not fully explain the black-white difference but did account for a portion of it.

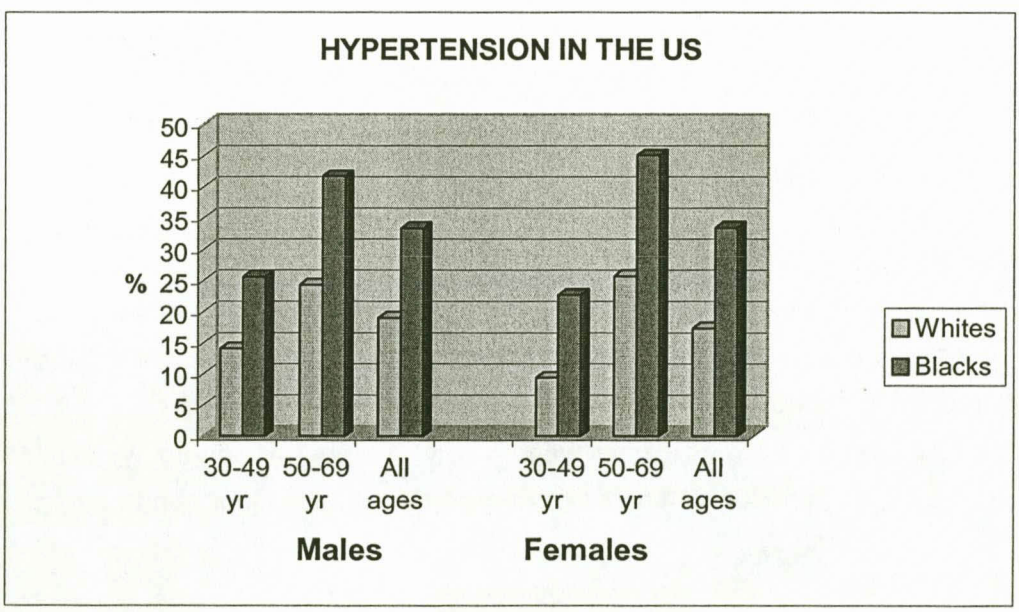


Fig. 3.6.5/1. Prevalence of hypertension in the US adjusted for age, weight and education (HDFP, 1977).

Klag and co-workers (1991) investigated whether skin colour was associated with blood pressure in a community-based sample of US blacks, independent of socio-economic status and other co-variables. Skin colour was measured on the medial aspect of the upper arm with a reflectometer. The sample had a broad range of socio-economic status, with a low average score. Skin reflectance was associated inversely with both systolic and diastolic blood pressure. For a 1-SD increase in skin pigmentation, SBP and DBP both increased by about 2 mm Hg. This effect was seen only in the lower two tertiles of socio-economic status. When level of education was used an indicator of socio-economic status, a similar interaction was seen. In persons who had not completed high school, blood pressure was higher in darker persons. The change in blood pressure for increases in variables frequently associated with blood pressure is shown in Fig. 3.6.5/2. The authors hypothesised that skin colour is a marker of psychosocial stress.

James et al. (1987) studied the relationship between socio-economic status, John Henryism and hypertension in black and white Americans. John Henryism refers to a strong personality predisposition to cope actively with psychosocial stressors. The authors found that among high levels of John Henryism, black males and females from low socio-economic status were nearly 3 times as likely to be hypertensive than blacks form higher socio-economic status. This was not the case for white subjects.

In South Africa, Seftel et al. (1980) investigated 1046 Johannesburg blacks for biosocial correlations of blood pressure. Little or no relationship between educational status and blood pressure and between occupation and blood pressure was found.

Seedat et al. (1982) also reported on biosocial factors related to hypertension in urban and rural Zulus. In their study the following variables were positively associated with hypertension: age, obesity, marital status, urbanization, number of dependents (men only), insomnia, cigarette smoking (men only), alcohol (women only), certain conditions of work, low educational status (women only), low income (women only), number of unemployed children, non-attendance of a recreation club (men only), non-participation in sport and overcrowding (women only).

In a longitudinal study, Somova et al. (1995) investigated psychosocial predictors of hypertension in black and white students at the University of Zimbabwe. After controlling for

biological factors, anxiety, coefficient of family instability, and suppressed hostility all remained independent predictors of hypertension in black students. None of the psychological variables alone predicted hypertension in the white students.

In a group of Nigerian civil servants, subjects at higher salary grade level or socio-economic status were more likely to be hypertensive (Olatunbosun et al., 2000). Unfortunately it was not clear whether the authors controlled for BMI but age and male sex may have confounded their results. No relationship was found between regular exercise, smoking, and alcohol or family history of hypertension in this sample.

In a study comparing lifestyle and psychosocial predictors of hypertension (psychological well-being and perceived racism) between African-American health care workers with a group of first-generation African immigrant health care workers, no differences were found (Carlos-Poston et al., 2001). Smoking was, however, more common in the group of African-Americans.

In summary, conflicting results were obtained in studies examining relationships between biosocial factors and hypertension in the US and Africa. Cooper et al. (1997) interpreted the finding of a definite gradient in the prevalence of hypertension across populations with the same genetic background from Nigeria to Jamaica to the US as evidence of the impact of social and cultural factors, supporting the environmental hypothesis of hypertension in blacks. Measures of both the genetic and the environmental component of hypertension are still too imprecise to allow rigorous testing of these hypotheses at present.

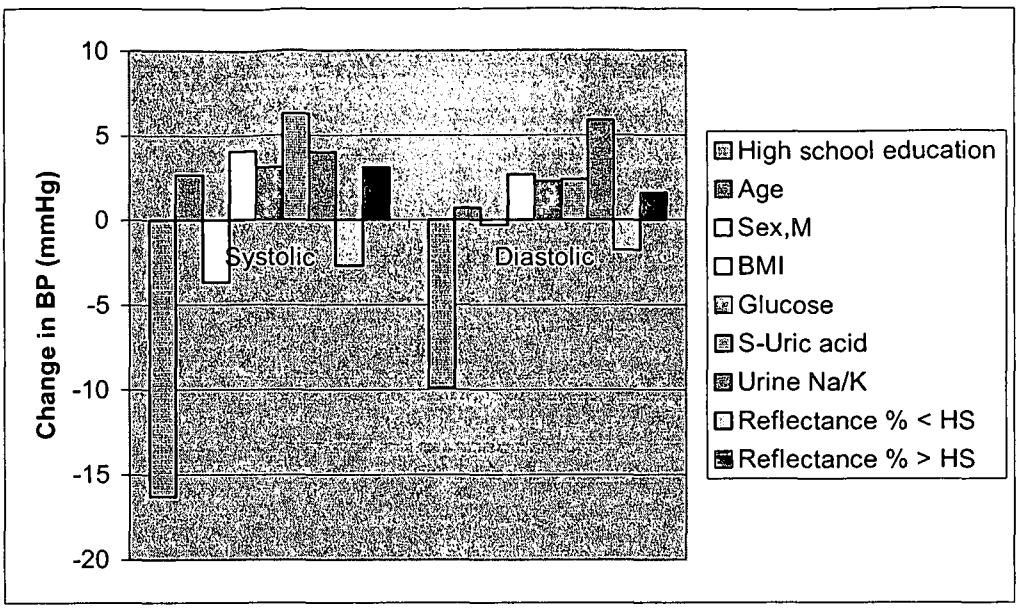


Fig. 3.6.5/2. Change in BP for increase in independent variables from a multiple linear regression model in 457 blacks (Klag et al., 1991). (Change in blood pressure is shown for a 1 SD increase in continuous variables. For education level, the blood pressure difference between persons with education compared to those with less than high school education is given. For gender, blood pressure in males compared with females. Glucose=p-glucose 1 hour after glucose load. HS=high school)

3.6.6 Alcohol and hypertension

Many epidemiological studies have indicated a positive association between the amount of alcohol consumed and the development of stroke. Hypertension is also a risk factor for stroke and it has been suggested that the relationship between alcohol consumption and stroke might be mediated via alcohol-induced hypertension (Regan, 1990).

In the Tecumseh study (1980) men who ingested one and a half drinks per week and women who had four drinks per week had lower blood pressure levels than non-drinkers. Higher intakes in both groups were associated with higher systolic and diastolic blood pressures. The relationship between alcohol intake and blood pressure was U-shaped in this study.

The Kaiser-Permanente study (Klatsky, 1977) reported on the association between alcohol intake and blood pressure of 83 947 people including 10 475 blacks. The relationship between alcohol intake and blood pressure was also U-shaped for females in this study. White and black men who drank 2 or fewer drinks per day had approximately the same blood pressure levels as non-drinkers. White and black women who drank 2 or fewer drinks per day had

slightly lower blood pressure levels than non-drinkers. The ingestion of 3 to 5 drinks per day was associated with higher systolic as well as diastolic blood pressure levels for both sexes and ethnic groups. White men taking six or more drinks per day had a systolic blood pressure 11 mm Hg higher than non-drinkers and a diastolic blood pressure 5 mm Hg higher than non-drinkers. Blacks who drank heavily showed no further increase in either systolic or diastolic blood pressure beyond those who took 3 or more drinks per day. Among white as well as black women, mean systolic blood pressure was 3mm Hg lower in those who took 2 or fewer drinks per day than non-drinkers. White women, like white men, showed a progressive increase in systolic pressure associated with 3 to 5 and 6 or more drinks per day. The mean difference between those taking 6 or more drinks per day and non-drinkers was 5 mm Hg. Black women like black men showed a levelling off of systolic blood pressure at 3 to 5 drinks per day. The mean difference between black women taking 3 or more drinks per day and non-drinkers was also 5 mm Hg. Diastolic pressures in white and black women who took 2 or fewer drinks per day were also slightly lower than in non-drinkers. The diastolic pressure of women taking 6 or more drinks per day was 2 mm Hg higher in white women compared to non-drinkers. The corresponding figure for black females was 2.5 mm Hg.

Klag et al. (1990) compared the association between alcohol consumption and blood pressure in a group of white American men with a group of Japanese men living in Tokyo. Blood pressure rose in the Japanese men with each successive level of alcohol intake. Compared to abstainers, systolic blood pressure was 9.4 mm Hg higher in those who drank 30-58 ml/ alcohol per day and 13.5 mm Hg higher in those who drank more than 58 ml/day. In the Americans, blood pressure was lower in the 2 lightest drinking categories than in abstainers and heavier drinkers. In the Americans, systolic blood pressure was 5.6 mm Hg higher in those who drank 30-58 ml/day than in abstainers. Diastolic blood pressure in heavy Japanese drinkers was 8.9 mm Hg higher than abstainers. In the Americans, diastolic blood pressure was 3.6 mmHg higher in those who drank 30-58 ml/day compared to abstainers, but was lowest in lighter drinkers. This J-shaped curve in American men was due primarily to the higher blood pressures in the abstainers which in turn was due to under-reporting of alcohol as was suggested by using uric acid levels as a proxy for alcohol intake.

In a small number of Johannesburg black males Touyz et al. (1989) found an association between alcohol intake (as defined by elevated GGT levels) and systolic blood pressure. In a

group of coloured males in the same study, GGT levels were positively related to blood pressure independently of age and weight.

In the coloured population of the Cape Peninsula Steyn et al. (1986) found that the drinkers as a group had significantly higher diastolic and systolic blood pressure levels than the non-drinkers. No significant correlation could be demonstrated between the amount of alcohol consumed and the systolic or diastolic blood pressure levels.

In the Intersalt study (1988) a high alcohol intake was strongly, positively, and independently associated with blood pressure levels.

Not all studies of hypertension in black populations found a positive association between alcohol intake and hypertension. No association existed between a history of alcohol intake and hypertension in rural Zulu subjects but an association did exist between alcohol intake and hypertension in urban Zulu women (Seedat et al., 1982). The relation between a history of alcohol intake and hypertension in African subjects in the Seven populations Study was weak and inconsistent (Cooper et al., 1997)

In summary, a definite association between alcohol intake and hypertension has not yet been demonstrated for African subjects.

3.6.7 Low birth weight and blood pressure

A series of observations were reported in the United Kingdom linking cardiovascular disease mortality in 47-54 year old adults to infant mortality at the time of their birth and shortly after (Barker and Osmond, 1986). In 1989 Barker and his co-workers reported an inverse relation between systolic blood pressure and birth weight in 10 year olds as well as in adults. This association was attributed to factors relating to the intrauterine environment. Shortly following this publication, Barker et al. (1990) reported the unexpected and surprising association between birth weight and placental weight on the one hand and blood pressure in adult life on the other. The highest systolic as well as diastolic pressures were among people who had been small babies with large placentas and the lowest pressures were among people who had been large babies with small placentas. Mean systolic pressure at age 46 -54 years rose by 15 mm Hg as placental weight increased from < 0.45 kg to > 0.68 kg and fell by 11 mm Hg as birth weight increased from < 2.5 kg to > 3.4 kg.

Two possible mechanisms were proposed for this observation (Barker et al.1986). Firstly, greater placental weight was associated with a decrease in the ratio of foetal length to head circumference. This disproportionate growth is consistent with diversion of blood away from the trunk in favour of the brain (as might possibly happen during hypoxia). Reduced blood flow to the trunk in a foetus that is small in relation to his placenta could have irreversible consequences, perhaps by influencing arterial structure. Secondly, the mother's external conjugate diameter is strongly related to foetal birth weight. Since a women's physique depends partly on her nutrition in childhood, the nutrition during this period may be linked to blood pressure in the next generation.

Similar observations regarding low birth weight and type 2 diabetes in later life followed and led to the development of the "thrifty phenotype" hypothesis (Hales et al., 1992). A logical next step was to link the thrifty phenotype hypothesis to the metabolic syndrome (Barker et al., 1993). Many studies have subsequently shown that lower birth weight is associated with higher blood pressure in childhood and adult life (Robinson, 2001). The hypothesis predicts that more heart disease and impaired glucose tolerance will be seen in a population that is undergoing transition from sparse to better nutrition (Robinson, 2001). Systolic BP in a cohort of 779 5-year old Johannesburg black children was inversely related to birth weight (Steyn et al., 2000). This finding might predict higher blood pressures in later life for this subgroup.

3.7 End-organ damage in hypertension

Hypertension is responsible for 35% of atherosclerotic CV events in the population due to its high prevalence (Kannel, 1996). Hypertension predisposes to all of the major cardiovascular outcomes including cardiac failure (CF), stroke, CHD, and peripheral vascular disease (PVD). Risk ratios are larger for CF and stroke, but CHD is the most common and the most lethal sequela of hypertension equalling all the other CV outcomes combined (Fig. 3.7/1)(Kannel, 1996).

Hypertension in blacks develops earlier in life, is frequently more severe, and results in a higher mortality at a younger age, more commonly from strokes than from CHD (Finnerty, 1971). Remarkable progress has been made over the last 2 decades towards hypertension control among blacks in the U.S. Mean systolic pressures have dropped 30 mm Hg over the

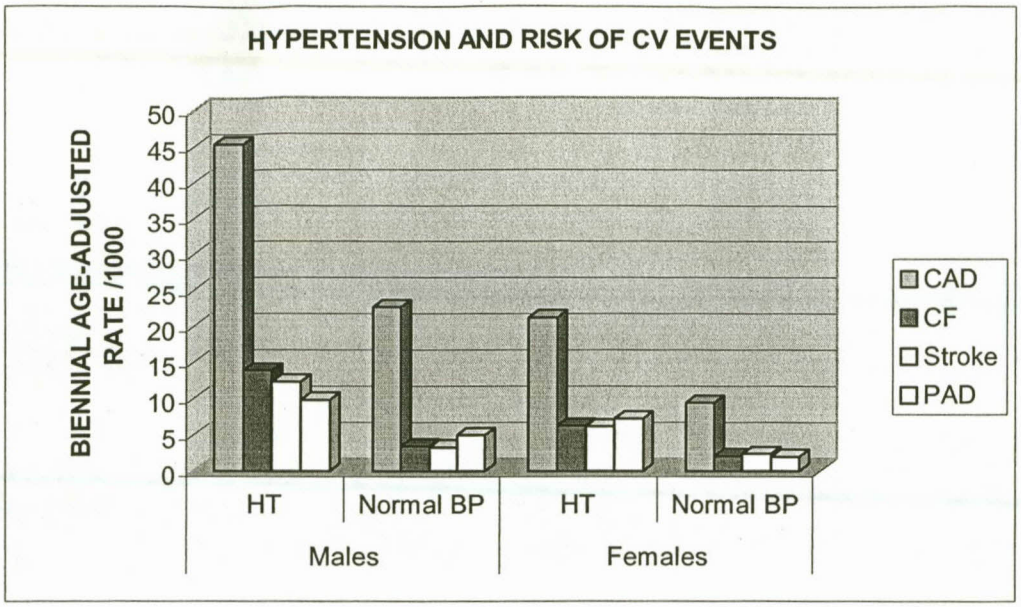


Fig. 3.7/1. Risk of CV events by hypertensive status in subjects aged 35-64 years (Kannel, 1996). CF=Cardiac failure, PAD=Peripheral arterial disease.

last 4 decades among subjects over 55 years of age (Cooper, 1997). This reduction is difficult to explain but may be due to a reduction in the force of the disease as well as to treatment.

3.7.1 Mortality due to cardiovascular disease

In South Africa, as in the United States, hypertension-related mortality among blacks is reaching alarming proportions. In 1996 cardiovascular diseases accounted for 24.3% of female and 16.6% of all male deaths in all age groups and in all populations (Bradshaw et al., 2002). In females the CV causes were stroke (9.0%), heart failure (6.5%), ischaemic heart disease (3.9%), hypertensive heart disease (2.6%) and unspecified (2.3%). In males the CV causes were stroke (5.3%), ischaemic heart disease (4.3%), heart failure (4.1%), hypertensive heart disease (1.1%) and unspecified (1.8%). Ill-defined causes were responsible for 13.1% of deaths in males and 16.7% of deaths in females. Injuries were responsible for 23.3% of deaths in males and 9% of deaths in females.

Previously, mortality rates for hypertension among blacks and whites in the United States differed considerably. Age-race-sex-specific mortality rates for hypertension was linear for whites but not for non-whites (mostly blacks) where an excess of deaths occurred in the 25 to 65 year age group. A decline in the mortality rate for hypertension disease, however, became apparent starting at about 1940 for whites and 1950 for blacks (Prineas and Gillum, 1985b). The age-adjusted death rate for hypertension in persons 35 years and older declined from 1968 to 1977 with 30.4% and 25.2% for non-white and white males respectively and with 32.8% and 30.3% for non-white and white females respectively.

Mortality from hypertension can be effectively reduced by therapy. Treatment dramatically lowered mortality in a group of subjects with severe hypertension (diastolic blood pressure ≥ 115 mm Hg) (Veterans Administration Cooperative Study, 1967). The estimated risk of a morbid event was reduced from 55% to 18% by active pharmaco-therapy over a period of approximately 3 years in subjects with diastolic blood pressures averaging 90 to 114 mm Hg (Veterans Administration Cooperative Study, 1970). The sample size in this study was relatively small (380 at the outset).

In the much larger Hypertension and Detection and Follow-up Program Cooperative Group study involving 10940 persons aged 30-69 years at entry (HDFP, 1979a), all-cause mortality was reduced by 17% over a 5-year period in its Stepped Care group compared to its Referred Group emphasizing the quality of control. Blacks comprised 44% of the study group. The corresponding reduction in mortality among black males was 19% and for black females 28%

(HDFP, 1979b). These reports also showed that systematic stepped care therapy was effective in decreasing all-cause mortality in persons with mild, moderate and severe hypertension.

3.7.2 Cerebrovascular disease in hypertension

Hypertension is considered the most important risk factor for stroke in the U.S., mainly because of the high prevalence of hypertension (Cooper, 1985). The risk of stroke in patients with hypertension compared to patients with normotension is increased 4- to 5-times (Sacco, 1995). Systolic hypertension may be of particular importance in the development of CVD including stroke (Kannel, JAMA 1996). Pulse pressure was also a useful indicator of heart failure and stroke risk in elderly subjects being treated for isolated systolic hypertension (Vaccarino et al., 2001). Khaw et al. (1987) reported lower stroke mortality in older people who consumed a diet high in potassium, presumably by lowering the blood pressure.

Stroke was the third most common cause of death in SA during 1990 and accounted for 7.35% of all deaths (Bradshaw et al., 1995). The highest stroke rates are found in the coloured and Asian communities of SA with age-standardised mortality rates (1984-1986) of approximately 125-175/100,000 per annum compared to an estimated 70/100 0000 in the white community (Fritz, 2000). No accurate figures were available for blacks.

Rosman (1986) studied hospital admissions (mostly blacks) for acute stroke over a one-year period at the Kalafong hospital, Pretoria. Only patients 20 years and older were studied. The overall incidence for the population at risk was calculated to be 101/100 000. There was a marked rise in incidence with age, with a peak in the male group at 65 to 70 years (1031/100,000 population). Cerebral haemorrhage was present in 32.8%, large artery thrombosis in 31.9%, cerebral embolism in 13.8% and lacunar infarctions were found in 20.7% of cases. Hypertension was present in 69.8% of patients, highlighting the importance of this risk factor in blacks. The one month case fatality rate for the group was 33.6%, that for cerebral haemorrhages 57.9%, and for cerebral infarctions 22.4%. Rosman also concluded that blacks with stroke tended to have little extra-cranial carotid vascular disease, and the source of thrombosis was more frequently in the intra-cranial vasculature.

Joubert (1991) investigated 316 black stroke patients admitted to Garankua Hospital, Pretoria. The majority of the patients had cerebral infarction (71.2%). Parenchymal cerebral haemorrhage was diagnosed in 25.6% of patients. The prevalence rates of these entities were

very similar to that found by Rosman (1986) making the type of pathology very similar to that found in Western countries. The major risk factors for stroke were age (mean age 55.4 yr) and hypertension that was present in 42.4% of patients. The 1-month mortality rate in this series was also 33%.

Mortality from stroke in the United States has been declining for several decades paralleling and usually exceeding the decline in mortality from other cardiovascular diseases. This decline was greatest in non-white women, in whom, from 1960 to 1975, there was a 48.5% drop in stroke deaths among those aged 35 to 74 years (Cooper et al., 1991). The decline in stroke and other cardiovascular morbid and mortal events has been attributed to improved hypertension awareness, treatment and control (Hildreth et al., 1991). A significant decline in the severity of the neurological deficit from stroke over the last decade was also recorded in the Framingham study while the prevalence of all stroke events over 3 decades increased mostly due to an increase in the prevalence of transient ischaemic attacks (Wolf et al., 1992). A systematic review of the outcome of treating hypertension in older persons showed that 5-year morbidity and mortality benefits were greater for older than younger persons (Mulrow, 1994).

Cruickshank et al. (2001) determined the prevalence in and compared the level of control of hypertension between two Cameroon populations (rural and urban), a Jamaican population and a Manchester sample containing both African-Caribbean and European subjects. The prevalence of hypertension (≥160/95 and or on treatment) ranged between 6.3% in rural Cameroonian women to 39% in Manchester African-Caribbean women. For those hypertensives during the survey, treatment rates were 34% in urban Cameron up to 70% in Jamaican- and Manchester-Caribbean women. Blood pressure control (<140/90 mm Hg) was achieved in less than half (30-88%) of the groups treated (supporting the "rule of halves" for hypertension). Calculating the attributable risk for stroke for blood pressure levels >160/95, the authors concluded that 32%-48% of future strokes might be prevented by proper BP control. Since stroke is the most common CV complication of hypertension in black communities with a high morbidity to mortality ratio rate (2:1) the potential benefit of improving the tightness of blood pressure control once treated would be greatest on stroke mortality (and morbidity).

3.7.3 Left ventricular hypertrophy and cardiac failure

Initial success in the therapy of hypertension resulted largely from the reduction of morbidity and mortality from stroke as was shown by the early Veterans Administration studies (1967, 1970). Following this initial success it was realised that in order to continue improvements in morbidity and mortality, more emphasis will have to placed on the cardiac effects of hypertension. Hypertension not only affects the heart directly, but also indirectly by promoting the development and expression of atherosclerotic coronary heart disease (Gottdiener, 1991).

The principal structural alteration of the heart in hypertension is a relatively uniform increase in the thickness of the left ventricular wall (concentric left ventricular hypertrophy) with little change in the left ventricular (LV) diastolic volume (Gottdiener, 1991).

Kannel (1983) reviewed the prevalence and natural history of electrocardiographic LVH in the Framingham study. In 10% of subjects some evidence of ECG LVH developed in the first 12 years of follow-up. At systolic blood pressures exceeding 180 mm Hg some evidence of ECG LVH developed in 50% of subjects. ECG LVH was associated with a two- to nine-fold increased risk of stroke, cardiac failure, coronary heart disease and peripheral vascular disease over a period of 20 years. Within 5 years of the appearance of LVH, 35% of men and 20% of women were dead in this study, reflecting the ominous character of this ECG abnormality.

Echocardiography soon established its superiority over the electrocardiogram as a measure of LVH. Reicheck and Devereux (1981) reported that neither the Romhilt-Estes (1969) nor the Sokolow-Lyon (1949) ECG criteria for LVH correlated closely with LV weight. M-mode echocardiography, however, showed excellent sensitivity, specificity and accuracy to diagnose LVH.

Casale et al. (1986) followed 140 men with hypertension for 4.8 years to assess whether echocardiography could predict cardiovascular morbid events. Of the 29 men who had echocardiographic evidence of LVH, 24% developed one or more morbid events compared to 6% of subjects without LVH. This study provided the first documentation that echocardiographically measured LV mass is an important predictor of subsequent cardiovascular morbid events. LV mass is, however, a continuous variable based upon body size, physical activity, obesity, and other physiologic and pathologic variables (Gottdiener, 1991 p136 CV diseases in blacks). Therefore, the prevalence of LVH will depend upon the cut-point selected for LV mass to divide normals from abnormals.

The Framingham Heart Study provided the opportunity for Levy et al. (1988) to examine the prevalence and potential determinants of LVH in the general population. Echocardiographic LVH occurred in 16% to 19% of the study population (compared to a 3.2% ECG prevalence). Echocardiography probably underestimate the prevalence of LVH since it is technically difficult to obtain studies of adequate quality in elderly or obese persons, who are at particularly high risk for LVH. Advancing age dramatically increased the prevalence of LVH from 6% in persons less than 30 years to 43% in those over age 69. In elderly women the prevalence of LVH approached 50%. The role of age was independent in this study. For every 10-year increment in age, the risk for LVH increased with 15% for men and 67% for women. This study also showed a constant and graded effect of systolic blood pressure levels, which were within the limits of normal, on increasing prevalence of LVH. These data suggested a dose-response relationship between blood pressure and LVH, supporting the hypothesis that both the duration and severity of hypertension contribute to the occurrence of LVH. The role of blood pressure was independent to promote LVH. Every 20 mm Hg increase in systolic blood pressure was associated with a 43% increase in the prevalence of LVH for men and a 25% increase for women. Obesity also had an independent and graded effect upon the prevalence of LVH. Across the BMI range of the study population, there was an approximate tenfold increase in the prevalence of LVH. A history of myocardial infarction conferred more than a threefold increase in risk for LVH in both sexes. The significance of these findings is that hypertension control and weight reduction are two possible ways to minimize development of LVH and to promote its regression.

The Framingham Heart Study also showed that the estimation of LV mass by echocardiography offers prognostic information beyond that provided by the evaluation of traditional cardiovascular risk factors (Levy et al., 1990). In this study 3220 subjects, 40 years and older, were followed for 4 years. Echocardiographic LVH was present in 16% of men and 21% of women. During the follow-up period there were 208 incident cardiovascular events, 37 deaths from cardiovascular disease, and 124 deaths from all causes. Echocardiographic LV mass was, independent of other cardiovascular risk factors, associated with all outcome events. In spite of the results the authors did not advocate the routine use of echocardiography for risk factor assessment or patient care. The most important reason being that the benefits of primary prevention and secondary management of LVH remain largely unproved. Possible mechanisms suggested for the association between morbidity and mortality and LVH include: an increased myocardial oxygen consumption while reducing coronary blood

flow reserve; coronary reserve is impaired in hypertrophied ventricles and, alternatively, LV mass may simply be a marker of risk by serving as a sensitive indicator of cardiac end-organ damage.

Coresh et al. (1991) studied 551 black men and women aged 34 to 57 years and reported an ECG prevalence (Minnesota coding) of LVH of 14% (18% in men, 11% in women) that was significantly greater than the 3% reported in the Framingham study. LVH was strongly associated with both systolic and diastolic blood pressure but not to skin colour as determined with a reflectance meter. The authors concluded that black individuals do not have a genetic susceptibility to the effects of blood pressure on the myocardium.

The Framingham study also provided useful information in patients with hypertension and the long-term risk of developing cardiac failure (Levy et al., 1996). A total of 2334 men and 2809 women were followed for 36 years. Hypertension was defined as blood pressure ≥140/90 mm Hg. Cardiac failure was diagnosed when 2 major criteria or 1 major and 2 minor criteria were present. During a mean period of 14.1 years 392 new cases of cardiac failure developed. Hypertension antedated the development of cardiac failure in 91% of these patients. After controlling for age and other risk factors, the hazard ratio (HR) of cardiac failure in men with hypertension compared to men without hypertension was 2.07 (95%CI: 1.34-3.20). The HR in women was 3.35 (95%CI:1.67-6.73). Median survival following the diagnosis of cardiac failure in hypertensive subjects was 1.37 years in men and 2.48 years in women. Other important risk factors for cardiac failure in hypertensive patients in this study included myocardial infarction, LVH, diabetes and valvular heart disease.

3.7.4 Coronary heart disease

The CHD death rates in 1970 for blacks in the age group 55-64 years in South Africa were 51/100 000 compared to 1118/100 000 for whites, 1047/100 000 for Asians, and 491/100 000 for coloureds (Seftel, 1978). Seftel reviewed the prevalence of CHD risk factors in black South Africans and concluded that the rarity of CHD was appropriate for the low level of a combination of risk factors. He supported the view that CHD (atherosclerosis) is a multifactorial condition requiring a "nutritional-metabolic milieu" characterized by a high intake of fat and hyperlipidaemia and that the duration of risk factor exposure is extremely important, particularly during childhood. The high prevalence of hypertension in the absence of other major CV risk factors was thus not sufficient to cause CHD over a relatively short

time. With hindsight Seftel's remarks were almost prophetic of the modern views of the metabolic syndrome and clustering of CV risk factors.

Isaacson (1977) reviewed autopsy records of black patients for the years 1959, 1960 and 1976 that died at Baragwanath hospital and examined the deaths from cardiac disease in detail. A striking finding was the increase in deaths from myocardial infarction. Expressed as a percentage of the total number of necropsies done on cardiac patients, cases of myocardial infarction have increased from 0.9% in 1959 and 0.81% in 1960 to 11.7% in 1976. Unfortunately, the author did not comment on any post-mortem findings indicative of chronic hypertension in these autopsy cases. In this series hypertension was by far the commonest cause of heart disease at Baragwanath hospital. It comprised 5.7% of all autopsies in 1959, 6.9% in 1960 and 7.5% in 1976. Again, the cardiac findings in these cases were not discussed in any detail.

Seedat et al. (1977) commented on the rarity of myocardial infarction in the urban African patient in spite of the high prevalence of hypertension. In their study the incidence of cardiac failure in 1000 hypertensive patients followed for 13 years was 16% while ischaemic heart disease was not observed. A 10-year post-mortem study (1965 to 1974) of 434 African patients suffering from hypertension showed that 42% had cerebrovascular complications, 25% had renal complications, 33% had cardiovascular complications in the form of congestive cardiac failure, while only 2% had myocardial infarction. Intracranial haemorrhage was responsible for 95% of cases suffering from cerebrovascular accident, and cerebral thrombosis constituted only 5%. These results are in stark contrast to the findings of Rosman (1989) mentioned earlier.

A decade ago it became apparent in the United States that contrary to earlier impressions of blacks' relative immunity to coronary heart disease, African Americans started to experience greater mortality from coronary heart disease than whites. This was not unexpected from the greater prevalence of established risk factors, including hypertension, in their black population. (Lewis et al., 1991).

3.7.5 Hypertensive renal disease

Epidemiological evidence suggests that not only do blacks have a greater prevalence and incidence of hypertension, but they are also at increased risk for target organ damage, especially to the kidney. Rostand et al. (1982) reported that between 1974 and 1978 the

annual rate of referral for treatment of end-stage renal disease in Jefferson County, Alabama, United States, was 9.1 per 100 000 population. The rate for blacks (18.8 per 100 000) was 4.2 times greater than that for whites (4.4 per 100 000). The risk of end-stage renal disease from hypertension was 17.7 times greater in blacks than whites. Interestingly, the relative risk for any of the other causes of end-stage renal disease was also significantly greater for blacks than for whites. The authors considered that blacks may have a greater susceptibility to end-stage renal disease than whites.

A decade later (Qualheim et al. 1990) reviewed the risk of end-stage renal disease from hypertension and found that the rate was still 15.4 times greater in blacks than whites. In his study it was noted that black women older than 50 years had the highest rates of end-stage renal disease due to hypertension whereas a decade earlier it was black males younger than 50 years who had the highest rates. Blacks were referred to nephrologists at a later stage in their disease than whites and with a significantly less controlled blood pressure. The reasons for the delay in the onset of hypertensive end-stage renal disease were in whites uncertain but might have been due to better awareness and treatment of hypertension.

The explanation for the increased risk of end-stage renal disease in hypertensive blacks was largely attributed to the increased frequency of more severe blood pressure elevation in blacks (Weir et al., 1991). Levy et al. (1978) demonstrated that black hypertensives had reduced renal blood flow compared to white patients with comparable severity of hypertension and other end-organ damage. They also found that the grade of severity of arcuate artery nephrosclerosis was greater in the black group. These morphologic differences may also contribute to the higher prevalence of end-stage renal disease in hypertensive blacks. Other congenital, environmental or dietary factors may also be involved to explain the excessive risk. Blacks more frequently ingest a high sodium-low potassium diet, a combination that can raise the BP and increase the risk of cardiovascular complications (Veteran's Administration Study, 1987). In addition there is also ample evidence to suggest that kidneys of blacks are at a greater risk for target organ damage compared with those of whites (Weir et al., 1991). Overall in the United States, blacks have 7.3 times greater risk than non-blacks for end-stage renal disease from hypertension, 3.7 times greater from diabetes, 2.6 times higher risk from glomerulonephritis, and 1.2 times greater risk from polycystic kidney disease.

Seedat et al. (1984) analysed the characteristics of patients accepted into the chronic renal failure programme in Durban. Glomerulonephritis was the commonest lesion (27%) followed

by hypertension (24%). Proportionally very few blacks were accepted for the chronic renal failure programme because of poor socio-economic status, inadequate sanitary conditions, lack of motivation and poor acceptance of chronic diseases with prolonged therapy by this group. The authors suggested that more efficient screening and therapeutic programmes for hypertension should be initiated to alleviate the problem.

The hallmark of malignant nephrosclerosis in black patients is myxoid myo-intimal hyperplasia of the interlobular arteries while fibrinoid necrosis is not as frequent as it is among whites (Isaacson et al.1989). Isaacson et al. also found that more effective treatment changed the spectrum of pathological findings in patients who died of hypertension complications. Previously the accent was on death from uraemia whereas congestive cardiac failure was more prominent since the introduction of improved antihypertensive agents.

The paucity of data on the prevalence, morbidity and mortality of CV disease in South African blacks suffering from hypertension as well as the absence of information obtained from properly designed interventional studies on risk reduction, are noted. It is also clear from this review that it is not possible to extrapolate from findings of studies done elsewhere in Africa, nor from the U.S. to advise local policy makers. South Africa, and in particular those carrying the burden of hypertension in this country, should benefit greatly from establishing our own Framingham-type of longitudinal cardiovascular research project focussing on CV disease in blacks. The HIV/AIDS epidemic is currently dominating the research agenda in SA, and rightly so. SA can however, not afford to emerge from the HIV/AIDS epidemic after one or two decades finding ourselves in the midst of an escalating epidemic of cardiovascular disease.

3.8 Economic aspects of hypertension

The HDFP findings (1979a, 1979b and 1982) clearly indicated that the systematic effective management of hypertension has great potential for reducing morbidity and mortality. Unfortunately, many of those with limited resources, the working poor, and the aged have needlessly suffered from preventable strokes, heart disease, and renal failure because of financial barriers to proper antihypertensive management (Shulman, 1991). Table 3.8/1 depicts the estimated economic costs of hypertension in the United States for 1988/1989. The cost/benefit of treatment becomes more impressive at higher blood pressure levels. If medication is provided for those patients with severely elevated blood pressure levels (above 115 mm Hg) a reduction in morbidity from 33% to 3% could be anticipated in 14 months (Shulman, 1991). This should result in a substantial saving.

TABLE 3.8/1. Economic Costs of Hypertension in the United States [1]

Economic Consequences of Hypertension

* Hypertension is the major risk factor for stroke, which cost Americans $12.9 billion in 1988
* Hypertension is the major cause of kidney failure in blacks which cost Americans $3 billion in 1989
* Hypertension is an important factor in heart attack

Cost of Antihypertensive Drug Treatment

* An estimate of the US antihypertensive drug marked in 1989 was $2.9 billion
* Yearly cost per patient varied from $3.46 for hydrochlorothiazide to $816 for Capoten (3 times a day)
* About 50% of patients require 2 or more drugs.

Economic Consequences of Poor/ No Treatment

* The costs of both stroke rehabilitation and work years lost because of stroke were estimated at $12.9 billion in 1988.
* Dialysis treatment of renal failure cost $25,000 per year per patient

[1] Adapted from Shulman, 1991

Opie (1989) addressed the economy of hypertension treatment in South Africa in a very constrained way. He concluded that cost-effectiveness can best be shown when large numbers of patients are subjected to blunderbuss diuretic therapy with minimal sophisticated care or when high-risk patients are chosen for sophisticated therapy. Although quality of life was referred to, this issue was not addressed. Cruickshank et al. (2001) approached the issue differently. According to their comparative study, between 23% and 47% of strokes might have been prevented by proper and effective treatment of blood pressure aiming for BP levels <140/90 mm Hg. A central issue discussed by Cruickshank et al. is that presently the main aim at primary care clinics is to *initiate* treatment rather than to *achieve blood pressure control* on treatment. He made the point that the former approach is a waste of money (the "blunderbuss approach"). Although one must be careful to extrapolate from UK/Cameroon data, this hypothesis deserves to be tested in a SA context.

3.9 Quality of care at primary health care clinics

Common sense dictates that the essential ingredients of the successful management of a chronic disease like hypertension at primary health care level requires adherence to approved treatment guidelines in addition to essential knowledge, appropriate skills and a positive attitude. The work environment must also meet minimum required standards and a realistic patient to health care worker ratio is also a prerequisite. In many ways just the opposite were found when Daniels et al. investigated the responses of health care professionals in primary care to receipt of hypertension and diabetes management guidelines in the Western Cape (Daniels et al., 2000). Although the subsequent SA guidelines for the management of hypertension were published a year ago, no official implementation program has followed to date of this writing. The same is true for the SA Medical Association's Heart Failure Guideline published in 1998 (SAMA Heart Failure Working Group, 1998). The SA Hypertension Society did however initiate a few workshops to introduce the guidelines and a website has also been created (www.hypertension.org.za) (Milne et al., 2002).

In an Audit of diabetes care at primary health care level Levitt et al. (1997) found that 38.5% of hypertensive diabetic patients' blood pressure was controlled on treatment (SBP <140 and DBP < 90 mmHg). Of the remainder, 31.4% had a SBP ≥ 160 or DBP ≥ 95 mm Hg. Steyn et al. (1999) investigated the level of blood pressure control at a community health care centre in the Western Cape. Two hundred and two hypertensive patients were evaluated. Blood pressure was ≥ 160/95 mm Hg in 41.6% and only 42.2% had a BP < 140/90. mm Hg. One third of the patients felt they were not properly examined while urine and eye examinations were done infrequently. Patients suggested the reinstitution of dedicated hypertension clubs. Steps to make patients more compliant and knowledgeable were also suggested.

It is clear that an enormous and concerted effort involving both public and private sector is needed to achieve the goals set forward by the SA Hypertension Society namely "to promote evidence-based, accessible and comprehensive management of hypertension by health care professionals" (Milne, 2001).

4 Obesity

4.1 Definition

Obesity is the disease in which excess body fat has been accumulated to such an extent that health may be adversely affected (WHO, 2000). The WHO Technical Report (2000) recognises that the amount of fat, its distribution within the body, and the associated health consequences vary considerably between obese individuals.

4.2 Classification and diagnosis of overweight and obesity

4.2.1 Classification and measurement of obesity

4.2.1.1 ACCORDING TO BODY MASS INDEX

It must be realised that body weight and weight indices adjusted for height are variables that are continuously distributed just as is the case for blood pressure, blood glucose and serum cholesterol (Stallone, 1985). The graded classification of overweight and obesity makes it possible to (a) make meaningful comparisons of weight status within and between populations; (b) to identify individuals and groups at increased risk of morbidity and mortality; (c) to identify priorities for intervention at individual and community levels; and (d) provide a firm basis for the evaluation of interventions (WHO, 2000).

Body mass index (BMI) is a simple index of weight-for-height that is commonly used to classify underweight, overweight and obesity in adults (WHO, 2000). BMI is the name given by Keys et al. (1972) to the ratio of weight to the square of height (according to Garrow et al., 1985). Garrow et al. (1985) acknowledged Quetelet who in 1869 was the first person to observe that the weight of normal adults was proportional to their height squared: in other words that W/H^2 was constant for people of normal built. BMI is defined as weight in kilograms divided by height (in metres) squared (kg/m^2) (WHO, 2000). There is a good correlation between BMI and the percentage of body fat (Seidel, 1998). In the French population the proportion of a person's body fat mass increases with age in both sexes until the age of 65 years and decrease thereafter (Rolland-Cachera et al., 1991). BMI does not differentiate between weight associated with muscle and weight associated with fat (Seidel, 1998). The relationship between BMI and body fat content varies according to body build and

TABLE 4.2.1.1/1. Classification of Adults According to BMI

Classification	BMI	Risk of co-morbidities
Underweight	< 18.50	Low (but risk of other clinical problems increased)
Normal range	18.50-24.99	Average
Overweight:	≥ 25.00	
Pre-obese	25.00-29.99	Increased
Obese class I	30.00-34.99	Moderate
Obese class II	35.00-39.99	Severe
Obese class III	≥ 40.00	Very severe

WHO, 2000

proportion (WHO, 2000). Furthermore, to interpret BMI in terms of body composition in more detail it is necessary to take into account sex, age, shape and ethnicity (Norgan, 1994). Asians, in general, have low correlations between BMI and body composition (Norgan, 1994). In blacks, BMI did not correlate with height while the BMI correlation with height was excellent in men from the Pacific area and in women from the Indo-Mediterranean region (Norgan, 1994). Unfortunately very little data is available on BMI and measured body composition from the Africa.

The classification of adults according to BMI as suggested by the WHO 2000 is shown in Table 4.2.1.1/1. These BMI values are age-independent and the same for both sexes. Table 4.2.1.1/1 shows a simplistic relationship between BMI and the risk of co-morbidity, which can be affected by a range of factors, including the nature of the diet, ethnic group and activity level. The risks associated with increasing BMI are continuous and graded and begin at a BMI below 25. The interpretation of BMI gradings in relation to risk may differ for different populations. Both BMI and a measure of fat distribution are important in calculating the risk of obesity co-morbidities (WHO, 2000).

The measurement of BMI is suitable to provide at the population-level an estimate of obesity but care must be exercised to use BMI to account for the wide variation in the nature of obesity between different individuals and populations (WHO, 2000).

4.2.1.2 ACCORDING TO BODY FAT DISTRIBUTION

The apparent heterogeneity of human obesity has resulted in a number of attempts to identify subgroups. Vague (1956) realized that fat distribution is a sexual characteristic and distinguished two types of obesity namely gynoid and android obesity. The gynoid type is characterized by the elective localization of fat on the lower part of the body while the android type is characterized by the localization of fat on the upper part of the body. Vague also realized that a high degree of overlapping of fat distribution between the sexes exists, especially at the two extremes of life. Ahead of his time, Vague (1956) documented that android obesity carries with it the tendency to hypertension, plethora, atherosclerosis, vascular accidents, diabetes and gout.

Abdominal fat mass can vary dramatically within a narrow range of total body fat or BMI (WHO, 2000). Lemieux et al. (1993) measured visceral adipose tissue area and volume with computed tomography and compared it with total body fat mass. It was concluded from this study that the proportion of visceral adipose tissue was greater in men than in women after correcting for sex differences in total body fat, that obesity was associated with a greater proportion of visceral adipose tissue in men than in women, and that the preferential accumulation of visceral fat depots in men may be a determining factor for the greater health hazards of obesity in men than in women.

The WHO Technical Report (2000) accepts that a waist-to-hip ratio > 1.0 in men and > 0.85 in women indicates abdominal fat accumulation. Although waist circumference alone may provide a better correlate of abdominal fatness and associated ill health than WHR, the latter measurement is still useful and should not be abandoned (WHO, 2000). Sex- and population-specific cut-off points for waist circumference should be developed since the level of risk is different for different populations (WHO, 2000). Not all measures of abdominal obesity were consistently related to features of the metabolic syndrome across three ethnic groups (Europeans, South-Asian and Chinese) studied by Patel et al. (1999). There is a need to investigate the validity of the proposed WHR cut-off points and to develop local sex- and population-specific cut-off points for waist-circumference in South African blacks.

4.2.1.3 ACCORDING TO SKINFOLD THICKNESS

Skinfold thickness measurements provide additional rather than primary information in population studies (WHO, 2000). The measurement of skinfold thicknesses at a number of sites has been used for many years to estimate body fat stores (Jebb, 1998). Subcutaneous fat is measured using callipers which exert a standard pressure and it is assumed that the thickness of subcutaneous fat at the selected sites is representative and that there is a known relationship between subcutaneous fat and total fat mass, after allowing for gender differences and skinfold thickness changes with age. Measurement of skinfold thickness is a more direct index of obesity as well as of body fat distribution. Durnin et al. (1973) measured skinfold thicknesses at four sites (biceps, triceps, subscapular and supra-iliac) and determined total body density by underwater weighing. With these results linear regression equations were calculated for the estimation of body density and thus body fat by using single skinfolds or the sum of two or more skinfolds.

Garn et al. (1971) examined the relationship between subscapular and triceps skinfold thickness as well as the sum of the two measurements with body weight. Garn et al. (1971) concluded that skinfold measurement provided indications of fatness and thus nutrition under field conditions in a mass-scale survey. Gray et al. (1990) also evaluated the accuracy of skinfold thickness measurements in the assessment of body composition in the obese by cross-validation analysis comparing density calculated from underwater weighing with density calculated from commonly used skinfold equations. In this study the correlation between % body fat calculated from skinfold equations and % body fat measured by underwater weighing was in the same range as that between %body fat estimated from impedance and underwater weighing. However, %body fat calculated from skinfold equations and bio-electrical impedance tended to underestimate %body fat calculated from underwater weighing in the most obese subjects. Gray et al. (1990) also commented that existing callipers are not large enough to accommodate some skinfolds in very obese people. This was particularly true for the abdominal and thigh folds. Another problem encountered was the difficulty in raising an adequate skinfold for measurement in obese people.

Other disadvantages of skinfold measurements include difficulty in reproducibility (especially in the obese), only subcutaneous fat is measured, and the measurements are influenced by elasticity of the subcutaneous tissues, which decline in old age (Epstein and Higgins, 1992). Gray (1990) also commented on the difficulty of training other observers to measure skinfolds,

especially in obese subjects. The accurate measurement of skinfold thickness is also very time-consuming in large epidemiological studies.

Must et al. (1991) published age-, sex- and race specific population-based reference data for the 85th and 95th percentiles of BMI and triceps skinfold thickness. These reference ranges are based on the National Health and Nutrition Examination Survey I done in the United States. No other generally accepted normative data for the categorization of obesity is available.

4.3 The prevalence of obesity in blacks

4.3.1 In black South Africans

Very little population-based data is available on the prevalence of overweight and obesity in black South Africans that goes back more than one or two decades. It is therefore almost impossible to comment on trends during this phase of the nutritional transition. Weight, height, BMI and skinfold thickness measurements that were available or that could be calculated from published studies, are presented in an attempt to form an impression of time trends in BMI, if any. Most of these samples were not representative.

Referring to obesity in the Zulu nation, Campbell (1960) remarked that since the passing of the great militant kings and beginning with the enormously fat Mpande, the royal family has lived in comparative ease, and their obesity has been legendary.

Slome et al. (1960) described the weight, height and triceps skinfold thickness of adult Zulus in Durban. The mean crude age- and sex-specific weight and height as well as triceps skinfold thickness of the subjects is shown in Table 4.3.1/1 (pounds were converted into kg and inches into cm). BMI was calculated for each age decile. A weakness of this study was the low response rate for males (45.2%). Women were heavier than men and the mean BMI for women was well above 25 kg/m^2. The mean BMI for females 40 years and older was above 30 kg/m^2. For both sexes mean BMI increased from 20 to 49 years and then declined in both sexes after the age of 50 years. Slome et al. (1960) commented on the shortness of the men compared with Zulu men studied 31 years earlier (Kark et al., data not available). Comparing the 85th percentile reference ranges for BMI and triceps skinfolds published by Must (1991) the Zulu males in all age groups were much leaner than US black males and the Zulu females were less obese than U.S. black females.

TABLE 4.3.1/1. Mean Height (cm), Weight (kg), BMI and

Triceps Skinfold Thickness (mm) of Urban Zulu Subjects

	n	Height cm	Weight kg	BMI kg/m^2	Triceps skinfold mm
Males (age in yr)					
20-29	33	165.9	61.3	22.3	8.56
30-39	32	167.1	65.6	23.5	8.38
40-49	20	164.8	64.6	23.8	9.00
50+	21	167.1	69.6	24.9	11.55
Women (age in yr)					
20-29	69	156.5	65.8	26.9	20.32
30-39	67	158.2	68.5	27.4	21.08
40-49	44	155.7	79.2	32.7	24.90
50+	39	155.2	73.1	30.4	22.12

Slome et al., 1960

O'Keefe et al. (1983) studied and compared the nutritional status of 803 patients admitted to the medical wards at King Edward VIII Hospital in Durban to a control group of factory workers as well as to a group of female hospital domestic workers. The mean BMI of male and female patients were 18.8 kg/m^2 and 20.1 kg/m^2 respectively compared to the control group's BMI of 25.3 kg/m^2 for men and 27.8 kg/m^2 for women. Of the latter group of women 89% were overweight (BMI $\geq$ 25 kg/m^2). The mean BMI of the female domestic staff was 31.6 kg/m^2. The female patients had a high prevalence of cardiovascular disease including hypertension and cardiomyopathy. These diseases were at that stage the most common cause of death in women. O'Keefe et al. (1983) reiterated the belief that obesity was well accepted in the black African culture, and was indeed often considered a sign of health and prosperity. These authors hypothesized that since women were responsible for feeding the family, the close proximity to food resulted in overeating and obesity. The absence of obesity among females elsewhere in Africa argues against this viewpoint (Zinyowera et al., 1994).

Loots et al. (1971) performed an anthropometrical study of 247 urban and 260 rural Venda males. In addition to height and weight, 5 skinfold measurements were also taken and the percentage body fat calculated. The crude mean age-specific height and weight of the subjects

TABLE 4.3.1/2. Mean Height (cm), Weight (kg), BMI and Triceps Skinfold Thickness (mm) of Urban and Rural Male Vendas.

	n	Height cm	Weight kg	BMI kg/m^2	Triceps skinfold mm
Rural males (age in yr)					
20-29	134	167.6	56.8	20.2	6.8
30-39	41	169.0	58.9	20.6	6.7
40-49	44	166.7	56.7	20.4	6.3
50+	41	166.1	54.9	19.9	6.1
Urban males (age in yr)					
20-29	39	167.6	60.1	21.4	6.3
30-39	49	166.7	63.5	22.9	8.2
40-49	102	168.2	64.6	22.8	8.1
50+	57	168.6	65.8	23.1	8.8

Loots et al., 1971

as well as the mean triceps skinfold thickness is shown in Table 4.3.1/2. BMI was also calculated for each age decile. Judging from the mean BMI and the triceps skinfold thickness, the rural group was much leaner than the urban group and the nutritional status of the former bordered on under-nutrition with mean BMI's at lower end of the reference range. The mean BMI of the oldest group was below the lower cut-off point of 20. No consistent change in BMI with increasing age was evident from this study. The Venda men were slightly taller than the Zulu men studied by Slome (1960). Both the BMI and triceps skinfold thickness showed that the urban Venda men tended to be slightly thinner than the urban Zulu men of corresponding age. Other skinfold measurements as well as calculated percentage body fat for the same Venda subjects are presented in Table 4.3.1/3.

TABLE 4.3.1/3. Mean Biceps, Subscapular and Suprailiac Skinfold Thickness (mm) and Calculated % Body Fat of Urban and Rural Male Vendas.

	Biceps SF[1] mm	Subscapular SF[1] mm	Suprailiac SF[1] mm	Body Fat %
Rural males (age in yr)				
20-29	3.7	8.0	5.6	10.8
30-39	3.3	8.7	5.8	10.8
40-49	3.5	8.4	5.3	9.9
50+	2.9	8.9	6.0	10.2
Urban males (age in yr)				
20-29	3.2	8.3	5.0	10.3
30-39	3.5	11.5	7.1	12.7
40-49	2.8	11.2	8.3	12.9
50+	3.5	12.5	8.7	13.7

Loots et al., 1971

[1] SF=skinfold

Loots et al. (1971) commented that the urban Venda had higher percentages body fat than the rural Venda. Percentage body fat also increased with age only in the urban group. The rural Venda gave the impression of being thin with a mean percentage body fat of 10.5 (range 4.3%-21.7%). The mean energy intake of 3976 kcal of urban subjects was slightly higher than that of the rural subjects who had an average intake of 3664 kcal (Lubbe, 1971).

Jackson et al. (1978) reviewed the findings of two epidemiological surveys amongst black subjects by to determine the prevalence of diabetes. The prevalence of obesity was 7% in males and 52% in females. The exact criterion used to define obesity was not stated. Furthermore, the study population also included children, limiting the usefulness of this data.

TABLE 4.3.1/4. Mean Height (cm), Weight (kg) and BMI of Black Adults in Johannesburg

	n	Height cm	Weight kg	BMI kg/m^2
Men (age in yr)				
20-24	42	167	59	21. 2
25-29	24	167	59	21. 2
30-34	11	170	63	21. 8
35-39	11	169	69	24.2
40-44	25	169	67	23.5
45-49	20	169	64	22.4
50-55	13	167	66	23.7
55+	37	164	62	23.1
Females (age in yr)				
20-24	62	155	59	24.6
25-29	34	156	61	25.1
30-34	30	157	68	27.6
35-39	36	156	66	27.1
40-44	33	156	70	28.8
45-49	25	153	69	29.5
50-54	21	154	74	31.2
55+	42	152	69	29.9

Shuenyane, 1977

In a socioeconomic and health survey aimed mainly at the paediatric population of Diepkloof, Johannesburg, Shuenyane et al. (1977) weighed and measured 466 subjects (183 men, 283 women) 20 years and older (Table 4.3.1/4). This survey also showed a slight increase in the BMIs of men with increasing age. A similar but more pronounced increase in BMI was also observed for females. From 25 years and upwards the mean BMI of women fell in the overweight category.

In a hypertension-survey involving 10 000 subjects, Seftel (1978) reported that in each age category black women were more obese than white men and women (referring to British subjects) and black men. Table 4.3.1/5 shows the age-and sex-specific mean BMI of the

subjects the in the study by Seftel et al. (1978) after converting the obesity index to BMI. Johannesburg black women had a lower BMI in each age category than Zulu women (Slome, 1960).

TABLE 4.3.1/5. Mean BMI of Johannesburg Blacks According to Age and Sex

Age (in yr)	Males	Females
20-29	21.9	24.7
30-39	22.7	27.4
40-49	22.9	28.6
50-59	23.0	28.7

Seftel, 1978

Body-build was also studied in a relatively small sample of rural and urban Xhosa subjects (Sever, 1980). Table 4.3.1/6 shows the mean age- and sex-specific height, weight and subscapular skinfold thickness as well as the calculated BMI of the subjects. Neither of the study populations could be regarded as representative of their communities. The composition of the urban group was biased towards members of the domestic staff of Groote Schuur hospital that has implications as far as nutrition is concerned. This study is of interest since rural females were included, which was not the case in the previous studies. The mean BMI of the rural women was 27.4 kg/m^2 that exceeded the upper limit of normal while the mean BMI for rural males (22.5 kg/m^2) implied higher energy intake or less physical activity in rural Xhosa males than in rural Venda males. Sever et al. (1980) commented that gross obesity was very common in the urban group.

TABLE 4.3.1/6. Mean Height (cm), Weight (kg), BMI and Subscapular Skinfold Thickness (mm) of Rural and Urban Xhosa Subjects

	n	Height cm	Weight kg	BMI kg/m^2	Subscapular SF mm
Rural (mean age)					
Men (43.7 yr)	35	167.9	63.5	22.5	12.0
Women (42.3)	91	158.0	68.3	27.4	21.1
Urban (mean age)					
Men (46.1)	64	166.8	73.5	26.4	16.0
Women (38.2)	61	153.6	80.4	34.1	28.6

Sever et al. (1980)

In a population-based urban-rural study of hypertension in Zulu subjects, Seedat et al. (1982) reported the body mass indices of the subjects (Table 4.3.1/7). Unfortunately the height and weight of individual subjects were not available for comparison. Although this was a population-based study, the rural sample was possibly not truly representative of the population due to the selection process followed. There were also relatively few females in the age group 50 years and older (89 rural and 87 urban). Results were not age-adjusted. The mean BMI of urban females in each age category was greater than that of rural females. Neither the mean BMI of urban females nor that of rural females showed a clear tendency to rise with age. The mean BMI of urban Zulu females studied by Slome et al. (1960) was overall less than that reported by Seedat et al. (1982). In the latter study the mean BMI of both rural and urban females was 25 or above but below 30 except for rural females in the age group 21-30 years who had a mean BMI of 24.4 kg/m^2.

TABLE 4.3.1/7. Mean BMI of Rural and Urban Zulu Subjects

	n	BMI
Rural		
Males (age in yr)		
21-30	72	23.0
31-40	81	23.5
41-50	86	23.6
51-60	45	23.5
61-70	21	26.2
Females (age in yr)		
21-30	226	24.4
31-40	163	26.3
41-50	130	26.2
51-60	71	25.1
61-70	18	25.9
Urban		
Males (age in yr)		
20-29	145	22.0
30-39	100	23.3
40-49	87	23.5
50-64	58	24.2
65+	15	22.0
Females (age in yr)		
20-29	169	26.5
30-39	108	29.0
40-49	75	29.0
50-64	64	28.5
65+	23	29.5

Seedat et al., 1982

TABLE 4.3.1/8. Mean BMI (kg/m^2) and Prevalence (%) of Underweight[1] and Obesity[2] in Cape Town Blacks

	n	BMI	Underweight	Obesity
Males (age in yr)				
25-34	110	23.4	21.7	5.5
35-44	84	24.4	22.1	10.7
45-54	56	24.5	14.3	10.7
55-64	42	27.4	9.5	28.6
Females (age in yr)				
25-34	147	27.8	4.1	30.6
35-44	109	30.3	2.8	47.7
45-54	64	31.7	1.6	59.4
55-64	53	31.9	5.7	56.6

Steyn et al., 1998

[1] BMI < 20 kg/m^2 (males)

BMI < 19 kg/m^2 (females)

[2] Obesity ≥ 30 kg/m^2

In a cross-sectional study of cardiovascular risk factors in 986 Cape Town blacks, Steyn et al. (1991) also reported on the BMI of the subjects as well as on the prevalence of obesity applying modern criteria (Table 4.3.1/8). An outstanding feature of this study was the high prevalence of obesity among females, with 44.4% of females having a BMI of 30 or greater compared to only 7.9% of males. Another interesting feature was the high prevalence of obesity in males in the age group 55-64 years (28.6% compared to 10.7% in the category 45-54 years). In both males and females BMI increased with age. The mean BMI exceeded 30 kg/m^2 for females in all age categories except in the group 25-34 years.

The familiar pattern of black females being heavier than their male counterparts was also evident in this study. In both sexes BMI increased with increasing age and the mean BMI exceeded 25 kg/m^2 in all three groups of females. The prevalence of obesity was somewhat lower in Durban females compared to Cape Town females but still ranged between 26.9% and 43.5% (Table 4.3.1/9)(Seedat et al., 1991). Although overweight was not uncommon in males,

Table 4.3.1/9. Mean BMI (kg/m^2), Sum of Skinfolds[1] (mm), Prevalence (%) of Overweight[2] and Obesity[3] in Durban Blacks

	n	BMI	Sum of skinfolds	Over-weight	Obesity
Males (age in yr)					
25-34	60	22.2	36.01	11.7	-
35-44	36	23.6	48.17	22.9	5.7
45-69	29	25	55.83	51.7	17.2
Females (age in yr)					
25-34	54	26.3	97.78	61.5	26.9
35-44	30	29.3	16.9*	76.7	36.7
45-69	23	29.7	113.9	82.6	43.5

[1] Sum of biceps, triceps, subscapular and suprailiac skinfolds

[2] Overweight = BMI ≥ 25

[3] Obesity = BMI ≥ 30

Seedat et al. (1991)

* An error in original publication

obesity occurred only in 5.7% and 17.2% of males in the age group 35-44 years and 45-69 years respectively.

Levitt et al. (1993) conducted a study amongst Cape Town blacks 30 years and older to determine the prevalence of diabetes. In this study a mean BMI of 24.2 kg/m^2 for males and 30.9 kg/m^2 for females was found. These figures are in line with the high prevalence of obesity among black women in the Cape Town area as reported by Steyn et al. (1991).

The anthropometry of the Cape Coloured has also been well described (Steyn et al., 1990). The mean BMI of coloured women was 27.1 kg/m^2 and that of males 23.4 kg/m^2. Most of the women were overweight and obese. Above 24 years of age the mean BMI was above the cut-off point for overweight for women and above 45 years it was above the cut-off point for obesity. On the other hand, underweight was a problem among coloured men. Overall 17.8% of the men were underweight and in the age group 16-25 years 39.4% of males had a BMI below 20 kg/m^2.

TABLE 4.3.1/10. Time Trends in Mean BMI (kg/m^2) In SA Blacks

	Zulu[1]	Venda	Venda	JHB	JHB	Zulu	Zulu	CPT	Zulu	Thusa
		Rural	Urban	Urban	Urban	Rural	Urban	Urban	Urban	Mixed
	1960(1)	1971(2)	1971(2)	1977 (3)	1978 (4)	1982 (5)	1982 (5)	1998 (6)	1991 (7)	2001(8)
Males										
(age-yr)										
20-24	22.3	20.2	21.4	21.2	21.9	23.0	22.0			
25-29				21.2				23.4	22.9	
30-34	23.5	20.6	22.9	21.8	22.7	23.5	23.3			
35-39				24.2				24.4	23.6	
40-44	23.8	20.4	22.8	23.5	22.9	23.6	23.5			
45-50				22.4				24.5	25.0	
50-54	24.9	19.9	23.1	23.7	23.0	23.5	24.2			
55-59				23.1				27.4		
60-69						26.2	22.0			
Females										
(age-yr)										
20-24	26.9			24.6	24.7	24.4	26.5			
25-29				25.1				27.8	26.3	26.7
30-34	27.4			27.6	27.4	26.3	29.0			
35-39				27.1				30.3	29.3	28.9
40-44	32.7			28.8	28.6	26.2	29.0			
45-50				29.5				31.7	29.7	27.9
50-54	30.4			31.2	28.7	25.1	28.5			
55-59				29.9				31.9		28.0
60-69						25.9	29.5			

(1) Slome et al., 1960 (2) Loots et al., 1971 (3) Shuenyane et al., 1977

(4) Seftel et al., 1978 (5) Seedat et al., 1982 (6) Steyn et al., 1998

(7) Seedat et al., 1991 (8) Kruger et al., 2001

Time trends in mean BMI for SA blacks are shown in Table 4.3.1/10. The sexual dimorphism for BMI is evident in all the studies with females heavier than males. The mean BMI of rural men and women was lower than that of urban subjects of the corresponding sex. The mean BMI of Zulu men in 1982 was the same in the respective age categories as in 1960. No consistent change was evident for Zulu women between 1960 and 1982. Although the later sample of Seedat et al. (1991) was not representative of the population, the mean BMI of both males and females were still very similar to that of their counterparts 3 decades earlier.

The categories of BMI of South Africans 15 years and older from the SADHS is shown in Tables 4.3.1/11 and Table 4.3.1/12. In males and females the prevalence of obesity increased with age across the age deciles until the age group of 55-64 years was reached whereafter the prevalence started to decline (SADHS, 1998). The sexual dimorphism of BMI is again obvious (Fig.4.3.1/1). The prevalence of obesity among black males was 7.7% (urban 9.4% and non-urban 5.4%) and among black females 30.5% (urban 35.7% and non-urban 24.6%). The prevalence of obesity was 3-4 times higher in females than in males for all the age categories. In the SADHS survey the highest rates of obesity were present among blacks, but fewer than 5% of men and 15% of women perceived themselves to be obese (Bourne et al., 2002). Education-status had a striking impact on the prevalence of obesity and on the sexual dimorphism of BMI. The prevalence of obesity declined in women (mostly black) with increasing education while the prevalence increased in men (mostly black). This is possibly a unique phenomenon (Fig.4.3.1/2).

Although the macronutrient intake of blacks in the Cape Peninsula met the requirements of the SA Diet Consensus Panel, it was regarded as a diet in transition that had the potential to change in the direction of a more atherogenic diet (Bourne et al., 2002). Total energy and fat intake was found to be contributing factors to obesity in women in the North West Province, while higher levels of physical activity was associated with a lower risk of obesity in these women (Kruger et al., 2002). While excessive energy intake is partially responsible for the high rates of obesity among SA blacks, a significant proportion of the SA population is underweight (12.9% of males and 4.8% of females) (Bourne et al., 2002).

Although data from the earlier studies cannot be directly compared with data from the more recent studies due to methodological differences, it is evident that obesity is a major public health problem especially among black females in South Africa.

TABLE 4.3.1/11. Distribution of Body Mass Index (kg/m^2) by Categories In Men Age 15 Years and Above, According to Background Characteristics, (SADHS,1998)

Characteristic	Underweight < 18.5	Normal 18.5-24.9	Overweight 25-29.9	Obese 30+	Number
Age					
15-24	21.1	66.7	8.3	2.7	1 816
25-34	8.4	61.7	20.4	7.6	1 123
35-44	8.4	52	24.5	12.6	1 005
45-54	8.9	43.8	27.2	16.7	701
55-64	9	46.7	27.9	14.2	518
65+	9.4	45.4	27.1	13.2	507
Residence					
Urban	10.6	54.2	21.7	10.9	3 569
Non-urban	16.2	60.5	15.4	6.2	2 102
Province					
Western Cape	5.7	54.1	24.8	12.8	721
Eastern Cape	11.4	57	20.3	9.9	758
Northern Cape	22.7	53.3	14.2	7.5	135
Free State	18.6	56.1	16.2	8	444
KwaZulu Natal	10.9	55.9	21.1	10.2	1 064
North West	17.3	60.6	15.2	5.4	551
Gauteng	9.3	56.4	20.4	9.8	1 099
Mpumalanga	16.4	57.4	16.1	7.2	377
Northern	19.4	57.1	15.8	6.1	521
Education					
No education	11.9	56.9	20.8	8	562
Sub A - Std 3	14.3	57	18	8	777
Std 4 - Std 5	15.7	57.8	17.3	7.3	755
Std 6 - Std 9	14.7	58.8	16.9	7.5	2 297
Std 10	5.6	57.5	21.7	13.1	801
Higher	6.9	40.7	32.7	17.3	440
Population Group					
African	13.7	59.9	16.9	7.7	4 257
Afr. urban	11.6	58.3	18.4	9.4	2 375
Afr. non-urban	16.5	61.9	14.9	5.4	1 882
Coloured	11.2	55.7	21.8	9.1	637
White	4.5	36.5	34.3	19.8	564
Asian	16.1	49	22.9	8.7	195
Total	12.6	56.5	19.4	9.1	5 671

TABLE 4.3.1/12. Distribution of Body Mass Index (kg/m^2) by Categories in Women Age 15 Years and Above According to Background Characteristics, (SADHS, 1998)

Characteristic	Underweight < 18.5	Normal 18.5-24.9	Overweight 25-29.9	Obese 30+	Number
Age (in yr)					
15-24	9.3	59.5	19.6	9.4	2 084
25-34	4.9	37.4	28.5	26.3	1 721
35-44	2.7	26.7	30.2	38.7	1 460
45-54	3.6	23.3	25.8	44.3	1 116
55-64	2.7	25.1	25.1	45.1	914
65+	7.1	31.3	25.5	32.0	861
Residence					
Urban	4.9	34.8	25.4	32.4	4 999
Non-urban	6.3	40.9	25.6	24.5	3 157
Province					
Western Cape	4.8	37.3	25.6	30.8	799
Eastern Cape	5.7	37.7	25.0	28.9	1 161
Northern Cape	12.3	37.0	24.5	24.5	168
Free State	6.9	37.7	25.8	29.1	519
KwaZulu Natal	5.2	30.1	26.5	34.2	1 608
North West	8.1	46.5	25.6	18.8	647
Gauteng	3.3	33.4	26.0	34.7	1 887
Mpumalanga	4.8	43.2	24.6	25.4	507
Northern	7.0	47.0	23.2	19.4	859
Education					
No education	5.7	33.8	26.7	32.0	1 186
Sub A - Std 3	6.2	31.3	24.4	34.9	1 088
Std 4 - Std 5	4.6	32.4	27.2	32.3	1 136
Std 6 - Std 9	5.5	40.5	23.8	28.2	3 094
Std 10	6.1	38.0	29.4	24.2	1 120
Higher	3.9	47.3	22.5	22.4	495
Population Group					
African	4.8	37.0	25.4	30.5	6 269
Afr. urban	3.9	33.5	25.1	35.7	3 349
Afr. non-urban	5.9	41.0	25.8	24.6	2 921
Coloured	9.8	35.9	25.1	28.3	806
White	2.8	42.1	26.1	24.3	767
Asian	14.7	34.0	25.9	20.2	300
Total	5.5	37.2	25.5	29.4	8 156

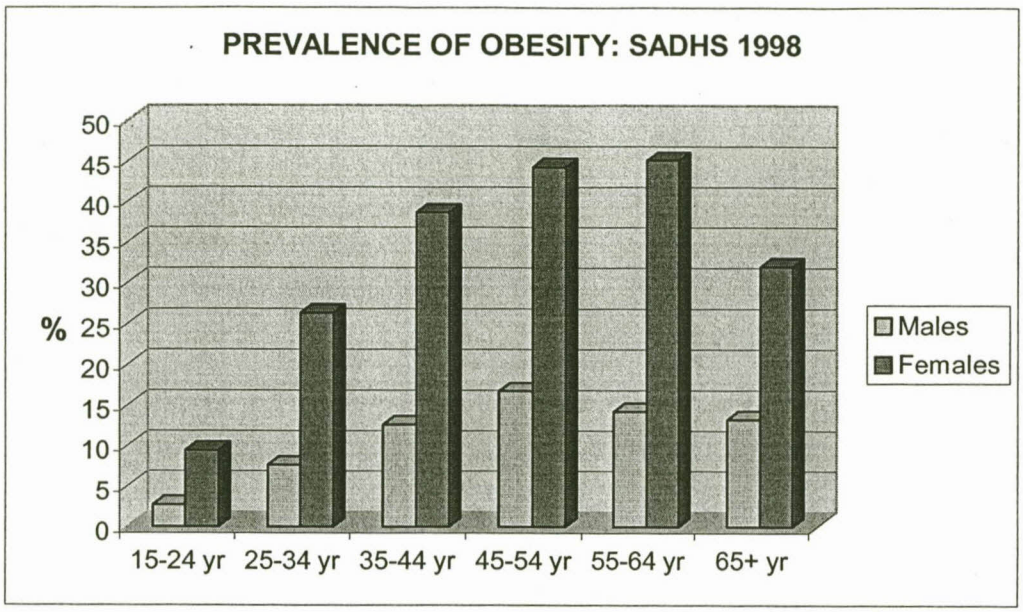


Fig. 4.3.1/1. Prevalence of obesity according to age and sex (SADHS, 1998)

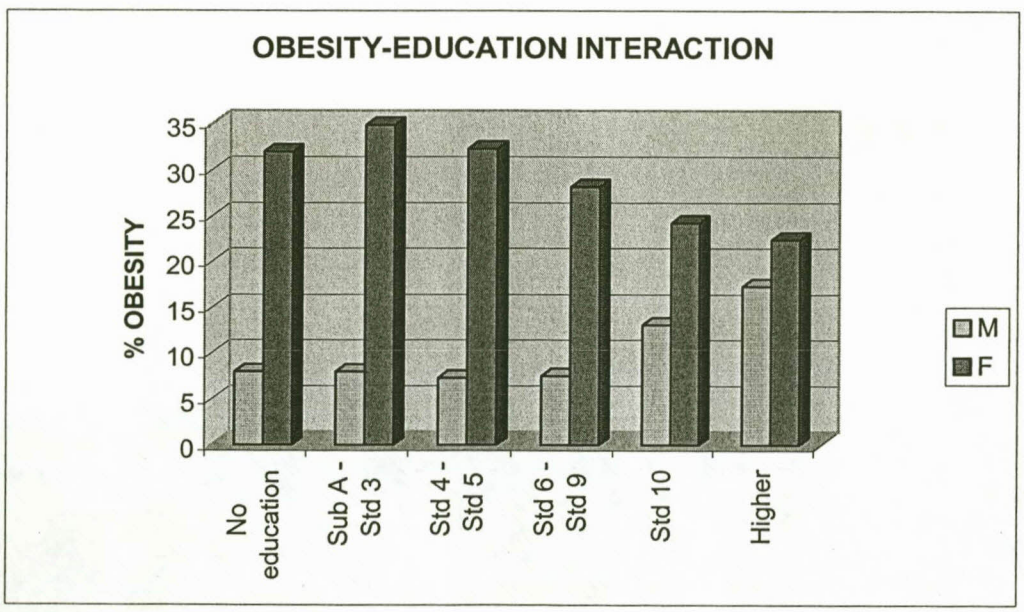


Fig. 4.3.1/2. **Prevalence of obesity according to level of education and Sex (SADHS, 1998)**

4.3.2 Prevalence of obesity in Sub-Saharan Africa

Although data on obesity is fragmentary and limited for this region, it is evident that obesity does exist (WHO, 2000). Available data, mostly from blood pressure surveys was adapted and is presented in Tables 4.3.2/1 and Table 4.3.2/2.

Of interest are the studies performed on the San (Bushmen) (Table 4.3.2/1). These studies were performed on small numbers of subjects. Kaminer et al. (1960) studied 37 subjects and remarked that after adolescence, weight does not increase with age. Bronte-Stewart et al. (1960) specifically mentioned that no obese Bushmen were encountered and that there was more fat on women during childbearing age as is evident from the difference in triceps skinfold thickness. Infertility did occur and the number of children was usually less than 5.

The authors of the early blood pressure studies rarely referred to obesity (Table 4.3.2/2). The sexual dimorphism of BMI is evident with females being slightly heavier than males. The mean BMI of male subjects from this era was low-normal while the mean BMI of women was within the normal range and did not change much with age.

TABLE 4.3.2/1. Mean Body Mass Index (kg/m^2) of the San (Bushmen)

Reference		Height mm	Weight kg	BMI kg/m2	Triceps SF[1] mm
Kaminer et al., 1960					
	Males	1579	47.1	18.9	
	Females	1479	41.3	18.9	
Bronte-Stewart et al.1960					
	Males	1597	47.1	18.5	3
	Females	1470	38.3	17.7	8
Truswell et al., 1972					
	Males	1610	48	18.5	
	Females	1500	40	17.8	

[1] SF= Skinfold

TABLE 4.3.2/2. Mean Body Mass Index (kg/m^2) From Early Studies on African Subjects

	Uganda[1]	Kenya[2] Kikuyu	Kenya[2] Samburu	Kenya[3] Luo (Ru)	Kenya[3] Luo(Ur)
	1969	1969	1969	1984	1984
Males					
(Age in yr)					
20-24	NA	19.2	17.8	20.1	19.5
25-34	22.0	21.1	18.7	21	20.3
35-44	22.0	21.2	18.4	20.1	21.6
45-54	21.7	20.4	18.3	20.2	20.9
55-64	21.9	18.1	17.8	19.9	21.1
65+	20.1	17.8	18.3	19.3	NA
Females					
(Age in yr)	NA	NA	NA	NA	NA
20-24	NA	NA	NA	21.5	21.1
25-34	23.0	NA	NA	20.8	22.8
35-44	23.7	NA	NA	20.6	22.9
45-54	23.1	NA	NA	19.7	23.4
55-64	20.6	NA	NA	18.6	17.4
65+	20.3	NA	NA	18.1	25.5

NA=Not available

Ru=rural, Ur=urban

Shaper et al. (1969) (2) Williams (1969) (3) Poulter et al.(1984)

Few of the recently published hypertension surveys in Sub-Saharan Africa refer to the prevalence of obesity, which is perhaps an indication of the low prevalence of overweight and obesity in this region. Cooper et al. (1997) compared the mean BMI of urban and rural West Africans with that of Jamaicans and US blacks of African origin. A gradual increase in mean BMI was evident along the historical migration path of the West African Diaspora that was attributed to a cross-cultural gradient of physical inactivity and diet (Cooper et al., 1997). The greater prevalence of obesity and higher mean BMI in urban compared to rural areas is a universal finding wherever studied. South Africa has the highest prevalence of obesity in black

men and women reported in Africa. The prevalence of obesity among urban black females in SA already exceeds that of women in the US (Fig. 4.3.2/1) (Cooper et al., 1997, SADHS 1998).

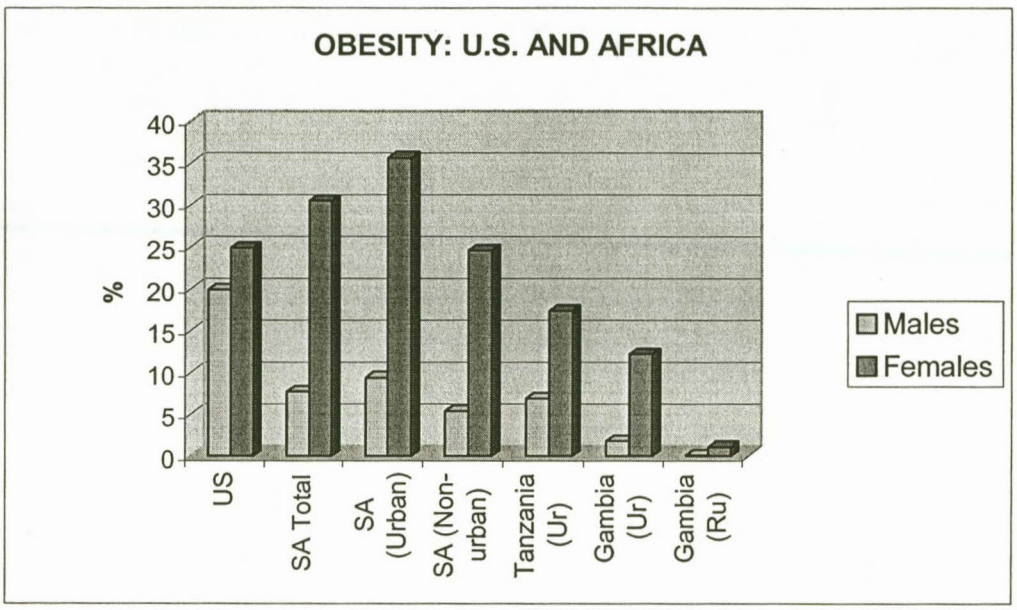


Fig. 4.3.2/1. Prevalence (%) of obesity (BMI ≥ 30 kg/m^2) in Africa and the US. Ur=urban, Ru=rural. (Cooper et al., 1997, SADHS 1998)

The prevalence of obesity in Sub-Saharan populations as obtained from recent studies is shown in Table 4.3.2/3. Unfortunately anthropometrical data from African studies is rarely published in such a way that direct comparisons can be made. Percentage body fat of subjects was only calculated in one study while the prevalence of obesity was calculated in 3 studies (Table 4.3.2/3). The prevalence of obesity in South African and Tanzanian (urban) men was very similar while the prevalence of obesity in South African women was almost double that of urban women in the Gambia and Tanzania. The gradual increase in mean BMI of blacks in West Africa to blacks in the West Indies to Afro-Americans was interpreted by Cooper et al. (1997) as evidence of a socio-cultural gradient along the migration route.

TABLE 4.3.2/3. Means of Anthropometrical Variables From Studies on Black Subjects Performed in Sub-Saharan Africa, Jamaica and U.S. by Sex and Population

Population	n	Height	Weight	BMI	Waist	Hip	WHR	Obese	% BF[1]	Reference
		cm	kg	kg/m²	cm	cm		%		
Males										
Nigeria	1171	168.3	61.5	21.7	77.3	88.3	0.88			Cooper et al., 1997
Cameroon										
Urban	612	172.3	74.5	25.1	83.3	96.8	0.86			
Rural	745	170.1	68.1	23.5	80.4	90.7	0.89			
Jamaica	524	172.1	70.6	23.8	80.8	95.8	0.84			
St. Lucia	491	173.5	73.0	24.3	82.7	95.3	0.87			
Barbados	330	171.9	76.4	25.9	86.2	97.8	0.88			
U.S.(Maywood)	708	176.5	84.5	27.1	92.4	103.4	0.89			
South Africa (Black)	4 527							7.7		SADHS, 1998
Cameroon										Mbanya et al., 1998
Urban	461			25						
Rural	308			21						
Zimbabwe (Urban)	384	171	63.0	21.7	79.0	91.0	0.86		21.1	Mufunda et al., 2000
Gambia										van der Sande et al., 2000
Urban	1028			20.8				1.8		
Rural	1200			19.8				0.1		
Tanzania										
Urban	3659							6.9		Bovet et al., 2002
Females										
Nigeria	1338	158.3	56.6	22.6	73.9	93.5	0.79			Cooper et al., 1997
Cameroon										
Urban	749	162.1	71.0	27.0	82.5	102.5	0.81			
Rural	722	160.7	60.6	23.5	80.9	92.6	0.87			
Jamaica	733	160.7	72.2	27.9	83.2	104.3	0.80			
St. Lucia	598	162.3	72.3	27.3	85.5	103.7	0.82			
Barbados	483	160.1	75.2	29.4	87.1	106.7	0.82			
US (Maywood)	810	163.4	82.4	30.8	91.4	111.8	0.82			
South Africa (Black)	6 269							30.5		SADHS, 1998
Cameroon										Mbanya et al., 1998
Urban	591			26.0						
Rural	438			22.0						
Zimbabwe (Urban)	391	160	67.0	21.7	82.0	101.0	0.82		36.5	Mufunda et al., 2000
Gambia										
Urban	1138			23.9				12.2		
Rural	2023			20.5				1.1		
Tanzania										Bovet et al., 2002
Urban	5654							17.4		

[1] BF=Body Fat

4.3.3 Global prevalence of obesity

The prevalence of obesity is increasing worldwide at an alarming rate in both the developed and the developing world (WHO, 2000). In many developing countries including South Africa, obesity co-exists with undernutrition (SADHS, 1998 and WHO, 2000). The prevalence of obesity in selected countries is shown in Table 4.3.3/1. Childhood obesity is seen as an emerging global problem with rates in the U.S. and Japan already escalating (WHO, 2000). The prevalence of obesity (as defined as two standard deviations above the reference median weight for-height of the National Centre for Health Statistics population) in preschool children in Lesotho is already approaching 5% (WHO, 2000).

TABLE 4.3.3/1. Obesity (BMI ≥ 30 kg/m^2) Prevalence in Selected Countries of the World[1]

Country	Year	Age (yr)	Men	Women
Canada	1986-1990	18-74	15.00	15.00
U.S.A.	1988-1994	20-74	19.90	24.90
Brazil	1989	25-64	6.00	13.00
England	1995		15.00	16.50
Finland	1991-1993	20-75	14.00	11.00
Sweden	1988-1989		5.30	9.10
Netherlands	1995		8.40	8.30
Kuwait	1994	18+	32.00	41.00
Saudi Arabia	1990-1993	15+	16.00	24.00
Australia	1989	25-64	11.50	13.20
New Zealand	1989	18-64	10.00	13.00
Nauru	1987	25-69	64.80	70.30
Japan	1993	20+	1.70	2.70
China	1992	20-45	1.20	1.64

[1] WHO, 2000

4.3.4 The health consequences of obesity and central obesity

4.3.4.1 THE HEALTH CONSEQUENCES OF OBESITY

It has been known for more than two decades that obesity contributes to cardiovascular disease, diabetes mellitus, gallbladder disease, psychosocial disability, and musculoskeletal disorders (Van Itallie, 1979). Sjöström (1993) reviewed 51 studies examining the relationship between obesity and mortality. He concluded that 40% of all employee, community, and random population studies have failed to demonstrate a relationship between body weight and mortality. Negative studies clustered among small and/or short-term studies. Studies including more than 20 000 participants showed a positive relationship between overweight and mortality. Twenty out of 21 cohort studies with more than 7000 participants also showed positive relationships between overweight and mortality. The critical period for follow-up in these studies was 5 years. The health problems associated with obesity are shown in Table 4.3.4.1/1. Although the absolute risk of certain obesity-related diseases may vary between populations, the relative risk of any particular disease is fairly similar throughout the world (WHO, 2000).

TABLE 4.3.4.1/1 Relative Risk (RR) of Health Problems Associated with Obesity[1]

Greatly increased RR > 3	Moderately increased RR 2-3	Slightly increased RR 1-2
Type 2 diabetes	CHD	Cancer: breast cancer in postmenopausal women, endometrial cancer colon cancer
Gallbladder disease	Hypertension	Reproductive hormone abnormalities
Dyslipidaemia	Ostheoarthritis (knees)	Polycystic ovary syndrome
Insulin resistance	Hyperuricaemia and gout	Impaired fertility
Breathlessness		Low back pain due to obesity
Sleep apnoea		Increased risk of anaesthesia complications
		Foetal defects associated with maternal obesity

[1] WHO, 2000

The American Cancer Society's study of the variations in mortality among 750 000 men and women according to weight is a landmark study on obesity (Lew et al., 1979). The major findings of this study of middle-class Americans in good health followed for 11 years are summarized in Table 4.3.4.1/2. The results clearly indicated that increasing overweight was associated with rising mortality. The lowest mortality was found among those of average weight and among those 10-20% below average weight. Mortality among both men and women 30-40% heavier than average was nearly 50% higher than that among those of average weight and nearly 90% higher among those 40% or more above average weight. CHD mortality was 55% greater among those 30-40% above average weight and about double among those 40% or more overweight. Cancer mortality was significantly increased only among those 40% or more overweight – 33% higher in men and 55% higher in women. Cancer of the colon and rectum was the principal site of higher cancer mortality among markedly overweight men while cancer of the gall bladder and biliary passages, breast, cervix, endometrium, uterus and ovary were the causes of higher cancer mortality among markedly overweight women. Mortality from diabetes was particularly high among overweight women, being nearly eight times higher among women whose weight was 40% or more above average than among women of average weight. Mortality among men in this group was increased five times. In this study male and female smokers of 20 or more cigarettes per day recorded by far the highest mortality from all causes in all weight index categories.

Walker et al. (1990) compared the prevalence of hypertension, hypertriglyceridaemia, hypercholesterolaemia and fasting plasma glucose concentrations of 50 obese urban black South African women with an age-matched group of non-obese urban women and found no significant difference in these variables. In a similar study on elderly rural black women significantly higher blood pressure and serum lipid levels were found in the obese group although plasma glucose levels did not differ significantly (Walker et al., 1991).

In a unique study of 1040 black South African women from the North West Province stratified according to level of urbanisation, Kruger et al. (2001) found a positive association between BMI and diastolic blood pressure, fasting serum TG, fasting glucose, and log fasting serum insulin and a negative association with serum HDL cholesterol.

The association of obesity and diabetes and obesity and hypertension in other studies on black

TABLE 4.3.4.1/2. Mortality Ratios For All Ages Combined In Relation to The Death Rate of Those 90-109% of Average Weight (n=750 000)[1]

		Weight Index						
	Sex	< 80	80-89	90-109	110-119	120-129	130-139	140+
Total deaths	M	1.25	1.05	1.00	1.15	1.27	1.46	1.87
	F	1.19	0.96	1.00	1.17	1.29	1.46	1.89
CHD	M	0.88	0.90	1.00	1.23	1.32	1.55	1.95
	F	1.01	0.89	1.00	1.23	1.39	1.54	2.07
Cancer	M	1.33	1.13	1.00	1.02	1.09	1.14	1.33
(all sites)	F	0.96	0.92	1.00	1.10	1.19	1.23	1.55
Diabetes	M	0.88	0.84	1.00	1.65	2.56	3.51	5.19
	F	0.65	0.61	1.00	1.92	3.34	3.78	7.90
Digestive	M	1.39	1.28	1.00	1.45	1.88	2.89	3.99
diseases	F	1.58	0.92	1.00	1.66	1.61	2.19	2.29
CVD	M	1.21	1.09	1.00	1.15	1.17	1.54	2.27
	F	1.33	0.98	1.00	1.09	1.16	1.40	1.52

1 Lew et al., 1979

Africans was addressed in chapters 2 and 3.

4.3.4.2 THE HEALTH CONSEQUENCES OF CENTRAL OBESITY

Vague (1956) defined android obesity as the elective localization of fat on the upper part of the body. He also observed that this type of fat distribution was associated with hypertension, plethora, atherosclerosis and diabetes. In the First Health and Nutrition Examination Survey (HANES), a cross-sectional study, subscapular skinfold thickness was found to be associated with both systolic and diastolic blood pressure in both sexes and in both black and white participants (Blair et al., 1984). The latter authors recommended that since central deposition of body fat was more directly related to the cardiovascular complications of obesity than

peripherally distributed fat, changes were needed in the techniques of measuring and assessing obesity.

Larsson et al. (1984) found in a 13-year prospective study of middle-aged men that the distribution of body fat as measured by the WHR was a better predictor of cardiovascular disease and death than the degree of adiposity. In this study smoking was a strong confounding factor in the association between obesity and CHD and death. The highest incidence of CHD and death was in those men with the lowest BMI and the highest WHR. In a similar study in women, Lapidus et al. (1984) found a significant positive association with the 12-year incidence of myocardial infarction, angina pectoris, stroke and death. In the Honolulu Heart Programme it was found that men in the highest tertile of sub-scapular skinfold thickness compared to men in the lowest tertile experienced a more than two-fold increase in the risk of CHD over 12 years (Donahue et al., 1987). This study is of importance since it is one of few directly linking the degree of central obesity to increasing levels of serum total cholesterol, serum triglycerides and plasma glucose.

In the black women in the THUSA study (Kruger et al., 2001) WHR correlated positively with fasting serum triglycerides and negatively with serum HDL-cholesterol while triceps skinfold thickness correlated positively serum cholesterol, LDL-cholesterol, plasma fibrinogen and the insulin sensitivity index.

The relationship between central obesity and diabetes was reviewed in section 2.6.3.4 and central obesity and hypertension in 3.6.2.

The postulated mechanisms linking intra-abdominal fat to metabolic disturbances and thus the metabolic syndrome include more adipocytes per unit mass, higher blood flow, more cortisol receptors, more androgen receptors and greater catecholamine-induced lipolysis than peripheral adipocytes (WHO, 2000).

5 Dyslipidaemia

5.1 Basic description of lipids and lipoproteins

The six major types of lipoproteins are chylomicrons, chylomicron remnants, very low-density lipoproteins (VLDL), low density lipoproteins (LDL), intermediate density lipoproteins (IDL) and high-density lipoproteins (HDL) (Table 5.1/1) (Mahley et al., 1998). The contribution of Lipoprotein (a) to the pathogenesis of atherosclerosis and CHD as well as issues relating to its measurement, have not yet been fully resolved (ATP III, 2001). The latter report adopted a negative position on the usefulness of Lp (a) measurement in clinical practice.

A brief overview of some of the salient features of lipoproteins is provided (Table 5.1/1). Chylomicrons are the largest of the plasma lipoproteins, consist of 85%-90% triglycerides, and are manufactured by the epithelial cells of the small intestine (Mahley et al., 1998). Newly synthesised chylomicrons possess apo B48, apo AI, and apo AIV (Mahley et al., 2001). Endothelial lipoprotein lipase (LPL) is responsible for the hydrolysis of the TG content of chylomicrons and convert them into triglyceride-poor cholesterol-enriched remnants (Tchernof et al., 1998). Because of their large size, chylomicrons filter poorly through the endothelium and into subintimal spaces, minimizing their atherogenic capability (Grundy, 1994). Chylomicron remnants are cleared rapidly from the plasma by the liver via remnant receptors with the interaction of apo E present on the surface of chylomicron remnants (Mahley et al., 2001).

Very-low-density lipoproteins (VLDL) are secreted by the liver and are composed of about 55% triglycerides, 20% cholesterol, 15% phospholipid and 10-15% protein (Table 5.1.1). The distinctive apolipoprotein of VLDL is apo B100, the hepatic form of apo B (Mahley et al., 1998). The production of VLDL by the liver is stimulated by increased delivery of free fatty acids to the liver either from a high intake of dietary fat or from mobilization of fatty acids from adipose tissue (Mahley et al., 1998). The cholesterol component of VLDL can be synthesized de novo in the liver like the TG and phospholipid component or it can be reutilised from LDL cholesterol. VLDL triglycerides are hydrolysed by LPL and hepatic lipase and converted into smaller and smaller particles that become increasingly rich in cholesterol (Mahley et al., 1998). The products of VLDL metabolism are IDL that are processed to LDL by

LPL and hepatic lipase. In the fasting state, almost all plasma triglycerides are present in VLDL (Mahley et al., 1998).

Low-density lipoproteins (LDL) normally transport most of the cholesterol in the plasma. They originate from catabolism of VLDL through IDL or VLDL remnants. LDL is composed of approximately 75% lipid (about 35% cholesteryl ester, 10% free cholesterol, 10% TG and 20% phospholipid) and 25% protein (Mahley et al., 1998). Apo B100 is the major protein of these particles. About 75% of LDL is taken up by hepatocytes of which two-thirds via LDL receptors and the remainder by a poorly defined process (Mahley et al., 1998). LDL levels can be increased by two primary mechanisms. The first is increased production of VLDL by increased flux of free fatty acids from adipocytes or from dietary fats. The second mechanism is defective catabolism due to down-regulation of LDL receptors on hepatocytes and extrahepatic tissues, defective LDL receptors or defective apo-B100 incapable of normal interaction with LDL receptors (Mahley et al.1998). Increased numbers of high-affinity apo E containing lipoproteins that compete with LDL for receptor interaction may also increase LDL levels (Mahley et al., 1998).

TABLE 5.1/1. The Major Classes of Plasma Lipoproteins

Type	Density (g/mL)	Electrophoretic Mobility	Site of Origin	Major Lipids	Major Apolipoproteins
Chylomicrons	<0.95	Origin	Intestine	85% TG	B48, AI, AIV (E, CI, CII, CIII-by transfer from HDL)
Chylomicron remnants	<1.006	Origin	Intestine	60% TG 20% Cholesterol	B48, E
VLDL*	<1.006	pre-beta	Liver	55% TG 20% Cholesterol	B100, E, CI, CII, CIII
IDL*	1.006-1.019	beta	Derived from VLDL	35% Cholesterol 25% TG	B100,E
LDL	1.019-1.063	beta	Derived from IDL	60% Cholesterol 5% TG	B100
HDL	1.063-1.21	alpha	Liver, intestine, plasma	25% Phospholipid 20% Cholesterol 5% TG (50% protein)	AI, AII, CI, CII, CIII, E
HDL3	1.125-1.21	alpha			
HDL2	1.063-1.025	alpha			

*The term VLDL remnants often refers to small, partially lipolyzed VLDL and IDL

Mahley et al., 1998

HDL are small particles that contain about 50% lipid (25% phospholipid, 15% cholesteryl ester, 5% free cholesterol and 5% TG) and 50% protein (Mahley et al., 1998). The major apolipoproteins of HDL are apo AI and apo AII (Table 5.1/1). HDL originate from three sources: the liver secretes apo-AI-containing phospholipid discs called nascent or immature HDL particles, the intestine synthesizes small apo-AI-containing particles, and HDL is also derived from surface material from chylomicrons and VLDL during lipolysis (Mahley et al., 1998). The nascent HDL particles are excellent acceptors of limited amounts of free cholesterol from cell membranes or other lipoproteins. The capacity of nascent HDL particles to accept cholesterol is less limited when cholesterol is present in its esterified form. The plasma enzyme lecithin:cholesterol acyltransferase (LCAT) esterifies cholesterol with long-chain fatty acids after which the complex is taken up by HDL changing its structure from a disc to a small spherical particle (Mahley et al., 1998). As the particle accepts more free cholesterol it increases in size, forming HDL_2. The latter particle can be further enriched in cholesteryl ester and at the same time acquire apo-E, forming HDL_1 which is a minor but metabolically active subclass of HDL (Mahley et al., 1998). The apo-E containing HDL_1 is directed to cells expressing LDL receptors e.g. hepatocytes completing the reverse cholesterol transport pathway which directs cholesterol away from tissues with excess cholesterol to the liver for excretion (Mahley et al., 1998). A more important mechanism or reverse cholesterol transport is provided by the action of CETP (cholesteryl ester transfer protein) that transfers cholesteryl ester from HDL_2 to VLDL, IDL and remnants delivering cholesterol indirectly to the liver (Mahley et al., 1998).

5.2 Definition, categories and classification of dyslipidaemia

5.2.1 Definition

Dyslipidaemia is defined as a clinically significant alteration in the circulating lipids and lipoproteins predisposing to CHD and related disorders (Berger et al., 2000). The ATP III report (2001) also refers to dyslipidaemia but does not define the condition. In clinical practice the most common dyslipidaemia is hypercholesterolaemia (Berger et al., 2000). The term hyperlipidaemia emphasises the importance of excess lipid in the circulation generating the adverse consequences of the common lipoprotein disorders (Berger et al., 2000). The chief exception is a low HDL-cholesterol concentration, which is independently atherogenic (Berger et al., 2000).

5.2.2 Categories and Classification of total cholesterol and LDL cholesterol

LDL is the primary target for cholesterol-lowering therapy based on extensive observational and experimental data accumulated over years (ATP III, 2001). Earlier studies like the Framingham Heart Study (Kannel et al., 1961) and the Multiple Risk Factor Intervention Trial (MRFIT) (Stamler et al., 1986) measured only total cholesterol (TC) although at least 60% of TC is contained in LDL (Table 5.1/1).

The quantitative importance of serum cholesterol as a risk factor for the later development of coronary heart disease was highlighted in an early report on the Framingham study (Kannel et al, 1961). In this study 5127 subjects (2283 males, 2844 females) in the age range 30 to 62 years were re-examined after 6 years for the development of CHD. The overall 6-year incidence of CHD was 36.3 per 1000 (54.8 per 1000 for males and 21.4 per 1000 for females). Higher mean cholesterol levels were observed among subjects who developed CHD than in the population at risk. The cut-points dividing the population into tertiles of serum cholesterol levels were 5.4 mmol/L and 6.3 mmol/L. A gradient of risk for the development of CHD was observed across the tertiles of serum cholesterol. Subjects with serum cholesterol levels above 6.3 mmol/L had more than three times the incidence of those with serum cholesterol levels less than 5.4 mmol/L. The rarity of CHD in younger females (2 per 1000) was in sharp contrast to the incidence of this disease in males of the same age (25 per 1000). Importantly, this study also demonstrated a progressive rise in the incidence of CHD with increasing levels of blood pressure, and a combination of the two risk factors augmented the risk.

In the MRFIT that included 356 222 men who were initially free of CHD, it was found that the relationship between serum TC and CHD was not a threshold one, but a continuously graded risk (Stamler et al., 1986). The relationship between CHD mortality (plotted on a logarithmic scale) and serum cholesterol is, however, linear (Law, 1999). The robust relationship between TC and CHD found in the MRFIT (Stamler et al., 1986) as well as in other epidemiological studies implies that LDL cholesterol is a powerful cardiovascular risk factor (ATP III, 2001). Total cholesterol is considered a good surrogate for LDL cholesterol. In population studies, (ATP III Panel, 2001). The risk for CHD associated with elevated levels of TC is not restricted to men without a prior history of myocardial infarction. In the Framingham study it was found that patients (men and women) who recovered from a myocardial infarction and who had elevated serum TC levels were also at increased long-term risk of re-infarction, death from CHD, and all-cause mortality (Wong et al, 1991).

Although the risk associated with increasing concentrations of serum TC and thus serum LDL-cholesterol is continuous, any LDL cholesterol concentration above 2.6 mmol/L appears to be atherogenic (ATP III, 2001). This is true over a broad range of LDL cholesterol concentrations and the higher the level the greater the risk (Stamler., 1986). Although the mortality from CHD has fallen substantially in the US over the past three decades, the lifetime risk for developing CHD at age 40 years in this population is estimated to be 49% for men and 32% for women (Lloyd-Jones, 1999).

The ATP III Panel (2001) considers LDL-cholesterol concentrations below 2.6 mmol/L as *optimal* since levels as low as this throughout life are associated with a very low risk of CHD (Table 5.2.2/1). Atherogenesis starts to occur at LDL cholesterol concentrations of 2.6-3.3 mmol/L and therefore levels in this range are called *above-optimal* (ATP III, 2001). At concentrations that are *borderline high* (3.4-4.1 mmol/L), atherogenesis proceeds at a significant rate, whereas at levels that are *high* (4.2-4.9 mmol/L) and *very high* (≥5.0 mmol/L) atherogenesis is markedly accelerated due to the log-linear relationship between elevated TC concentrations and atherosclerosis (Law, 1999).

TABLE 5.2.2/1. ATP III Classification of Total Cholesterol and LDL Cholesterol[1]

Total Cholesterol (mmol/L)		LDL Cholesterol (mmol/L)	
		< 2.6 mmol/L	Optimal
< 5.2	Desirable	2.6-3.3 mmol/L	Near optimal/above optimal
5.2-6.1	Borderline High	3.4-4.1 mmol/L	Borderline High
≥ 6.2	High	4.2-4.9 mmol/L	High
		≥5.0	Very High

[1] ATP III, 2001

5.2.3 Categories and classification of triglycerides

After many years of controversy, raised serum triglycerides are now considered as an independent risk factor for CHD (ATP III, 2001). Assmann et al. (1992) for example found that hypertriglyceridaemia was a powerful CHD risk factor when excessive TG coincided with a high ratio of plasma LDL cholesterol to HDL cholesterol (>5). The meta-analysis performed by Austin et al. (1998) showed that the risk for CVD associated with a 1 mmol/L increase in

serum TG levels was 32% for men and 76% for women over a period of 8-11 years. The atherogenicity of raised serum triglyceride concentrations is blamed on the presence of triglyceride–rich lipoproteins (TGRLP) that harbour small LDL particles, remnant VLDL and IDL (ATP III, 2001). These particles are cholesterol enriched and share many of the properties of LDL (ATP III, 2001). Some causes of hypertriglyceridaemia in the general population are listed in Table 5.2.3/1.

TABLE 5.2.3/1. Common Causes of Raised Serum Triglyceride Concentrations

Physical inactivity	Other diseases:	Drugs:
Cigarette smoking	Overweight and obesity	Corticosteroids
Excess alcohol intake	Type 2 diabetes	Protease inhibitors
Very high carbohydrate diets	Chronic renal failure	Beta-adrenergic blocking agents
(> 60% toal energy)	Nephrotic syndrome	Oestrogens
Genetic factors		

ATP III, 2001

Previously, conservative definitions of serum TG ranges were adopted based on a weak association between TG and CHD (ATP II, 1994). Raised serum TG can now be considered a marker for several atherogenic factors (Grundy, 1998). These factors include increased levels of atherogenic TGRLP, the lipid triad and the metabolic syndrome. The lipid triad consists of elevated serum TG, small dense LDL particles and low HDL cholesterol (Grundy, 1998). According to Grundy (1998) the metabolic syndrome includes the coexistence of the lipid triad, elevated blood pressure, insulin resistance (plus glucose intolerance), and a pro-thrombotic state. Lemieux et al. (2000) for example showed that more than 80% of 185 healthy men with a waist circumference ≥ 90 cm and with elevated TG levels (≥2.0 mmol/L) were characterized by the atherogenic metabolic triad of hyperinsulinaemia, elevated apo B, and small dense LDL. Since the association between elevated TG levels and all of these atherogenic factors became more obvious, the ATP III (2001) reduced the cut-off points for intervention for raised serum TG. The categories and classification of raised serum triglyceride concentrations are shown in Table 5.2.3/2.

TABLE 5.2.3/2. Classification of Serum Triglycerides[1]

Triglyceride Category	ATP II Levels	ATP III Levels
Normal TG	<2.3 mmol/L	<1.7 mmol/L
Borderline High TG	2.3-4.5 mmol/L	1.7-2.2 mmol/L
High TG	4.6-11.3 mmol/L	2.3-5.7 mmol/L
Very High TG	>11.3 mmol/L	>5.7 mmol/L

ATP III, 2001

5.2.4 Categories and Classification of Non-HDL Cholesterol

Non-HDL cholesterol is defined as the difference between TC and HDL cholesterol concentrations (Cui et al., 2001). Non-HDL cholesterol is also simply the sum of LDL cholesterol and VLDL cholesterol (Gordon et al., 1989). Data from the Lipid Research Clinics (LRC) Program Follow-up Study demonstrated that Non-HDL cholesterol was a slightly better predictor of CVD mortality than LDL cholesterol (Cui et al., 2001). One reason for the improved predictive power of non-HDL cholesterol is that this measurement includes all of the potentially atherogenic lipid fractions such as LDL, lipoprotein (a), IDL and VLDL remnants (Cui et al., 2001). Furthermore, LDL levels are calculated by the Friedewald formula (see below) that is inaccurate in the presence of elevated serum TG levels (Cui et al 2001). Highly atherogenic small dense LDL particles are associated with serum TG levels > 1.7 mmol/L and by utilizing non-HDL cholesterol to predict risk, these particles will be included (Cui et al., 2001).

Non-HDL cholesterol is highly correlated with total apolipoprotein B (apo B) in normolipidaemic men and apo B is the major apolipoprotein of all atherogenic lipoproteins including LDL, IDL and VLDL (Abate et al., 1993). Avogaro et al (1979) focussed attention on the possible role of apo B in atherosclerosis. In the latter study apo B discriminated better between subjects with and without CHD than did levels of TC. The ATP III (2001) therefore recommends that non-HDL cholesterol be used as an acceptable surrogate marker for total apo B in routine clinical practice. This measurement is reliable in non-fasting serum in contrast to calculated serum LDL cholesterol that can be erroneous in the presence of postprandial hypertriglyceridaemia (ATP III, 2001).

Most clinical laboratories measure plasma levels of total TG, total cholesterol, and HDL cholesterol. HDL cholesterol is measured after precipitation of apo-B containing lipoproteins from the plasma with an agent such as heparin (Mahley et al., 1998). The Friedewald Formula is then used to calculate the plasma LDL concentration from these measurements (Mahley et al., 1998).

LDL cholesterol=total cholesterol-HDL cholesterol-TG÷5

This formula relies on an estimate of the VLDL cholesterol that is about 20% of the plasma TG level and is only reliable for TG levels of 4.5 mmol/L or less (Mahley et al., 1998). When TG levels are high (2.3-5.7 mmol/L), a significant fraction of non-HDL cholesterol is contained in VLDL and therefore LDL may under these circumstances not be the only risk factor for atherosclerosis (ATP III, 2001). Under the latter circumstances non-HDL cholesterol will better represent the concentrations of all atherogenic lipoproteins than will LDL cholesterol alone. This is, however, no longer the case when serum TG concentrations are very high (>5.7 mmol/L) when some of the cholesterol in triglyceride rich lipoprotein (TGRLP) resides in non-atherogenic forms of larger VLDL and chylomicrons, and non-HDL cholesterol may then be less reliable as a predictor of CHD risk (ATP III, 2001).

Normal VLDL cholesterol can be defined as follows: when triglyceride levels are < 1.7 mmol/L this value is typically < 0.8 mmol/L (ATP III, 2001). When triglyceride levels are > 1.7 mmol/L, VLDL cholesterol is usually > 0.8 mmol/L (ATP III, 2001). A reasonable therapeutic goal for non-HDL cholesterol is one that is 0.8 mmol/L higher than the LDL cholesterol goal (0.8 mmol/L+2.6 mmol/L=3.4 mmol/L) (ATP III Panel, 2001). This panel recommended that triglyceride concentrations should be measured but did not define any therapeutic goals for TG for two reasons: (a) TG levels have more day to day variability than non-HDL cholesterol levels and are thus less reliable, and (b) non-HDL cholesterol as a target allows more flexibility in choice of therapies to reduce atherogenic lipoproteins contained in the combined LDL+VLDL fraction. The ATP III Panel chose non-HDL cholesterol as a secondary target of therapy (after LDL cholesterol) and recommended that non-HDL cholesterol be used in clinical practice as an affordable alternative to apo B measurement (ATP III Panel, 2001).

5.2.5 Categories and Classification of High Density Lipoproteins (HDL)

Epidemiological studies consistently show that low HDL cholesterol is an independent risk factor for CHD and in prospective studies HDL cholesterol proves to be the lipid risk factor

most highly associated with CHD risk (ATP III, 2001). Gordon et al. (1989) undertook a systematic re-examination of four studies, the Framingham Heart Study (FHS), the Lipid Research Clinics Prevalence Mortality Follow-up Study (LRCF), the Coronary Primary Prevention Trial (CPPT) and the MRFIT. In this analysis a 0.026 mmol/L increment in HDL cholesterol was associated with a significant reduction in CHD risk of 2% in men (FHS, CPPT, and MRFIT) and 3.0% in women (FHS). In the LRCF where only fatal outcomes were monitored, an 0.026 mmol/L increment in HDL level was associated with significant decreases in CVD mortality (3.7% in men and 4.7% in women) (Gordon et al., 1989).

Although the association between low HDL cholesterol and atherogenesis is very strong, other factors are also implicated since a low serum HDL concentration correlates with elevations of serum TG and remnant lipoproteins while low HDL levels are also linked to small dense LDL (ATP III, 2001). Austin et al. (1990) described two distinct phenotypes of LDL cholesterol denoted A and B in 301 subjects from 61 families selected by sequential sampling of informative kindreds. Phenotype A was characterized by predominance of large buoyant LDL particles and phenotype B by small, dense LDL particles. Phenotype B was associated with increases in plasma levels of TG and apo B, with the mass of VLDL and IDL and with decreases in plasma levels of HDL cholesterol and plasma levels of apo AI. The tight association between low HDL cholesterol, small LDL particles and elevated serum TG levels are called the "lipid triad" (ATP III, 2001). A low HDL cholesterol level is not as strongly independent a predictor of CHD as was previously accepted due to these confounding variables (ATP III, 2001). It also comes as no surprise that the same conditions that cause serum TG levels to rise also cause HDL levels to decline (ATP III, 2001).

The inverse association between HDL cholesterol concentrations and CHD risk is a continuous variable therefore any categorical definition of low HDL cholesterol must be arbitrary (ATP Panel III, 2001). The ATP III Panel (2001) has decided to increase the cut-off point for low HDL concentrations from the previous 0.9 mmol/L to 1.0 mmol/L for both men and women (Table 5.2.5/1). The motivation for this step by the ATP III (2001) is that the association between HDL-C and CHD is a continuous variable and the risk for CHD already starts at HDL-C concentrations above 0.9 mmol/L. Furthermore, obesity and physical inactivity which are considered risk factors for atherosclerosis cause only moderate reductions in HDL-C concentrations (ATP III, 2001). A high HDL cholesterol concentration is associated with a reduced risk for CHD and its presence is referred to as a *negative risk factor*, making possible the removal of one risk factor from the risk factor count (see Chapter 6).

TABLE 5.2.5/1. ATP III Classification of HDL Cholesterol

Serum HDL Cholesterol	
<1.0 mmol/L	Low HDL cholesterol
≥1.6 mmol/L	High HDL cholesterol

ATP III, 2001

5.2.6 Atherogenic dyslipidaemia

The strong association between low HDL cholesterol, small LDL particles and elevated serum TG levels have already been referred to as the "lipid triad" (ATP III, 2001). This phenotype has also been referred to as an atherogenic lipoprotein phenotype and is not uncommon (Austin et al., 1990). The lipoprotein concentrations in this triad are often not categorically abnormal, but are marginally altered (ATP III Panel, 2001). Sophisticated technology such as gradient gel electrophoresis that is not clinically available is needed to measure small LDL concentrations (Austin et al., 1990).

The lipid triad occurs commonly in persons with premature CHD (ATP III Panel, 2001). Typical characteristics of persons with the lipid triad or atherogenic dyslipidaemia include obesity, abdominal obesity, insulin resistance, and physical inactivity (ATP III Panel, 2001). Atherogenic dyslipidaemia is also common in persons with Type 2 diabetes mellitus (Kreisberg 1998). Since the relative quantitative contribution of the individual components of the lipid triad on the development of atherosclerosis cannot be determined, the ATP III Panel (2001) recommended that the lipid triad as a whole should be regarded as a risk factor.

5.2.7 Non-lipid risk factors

The presence of certain non-lipid risk factors including modifiable and fixed factors are associated with increased risk for CHD and signals the need for more intensive lowering of LDL cholesterol (ATP III, 2001). These factors are shown in Table 5.2.7/1.

TABLE 5.2.7/1. Non-Lipid Risk Factors[1] for CHD

Modifiable Risk Factors	Non-modifiable Risk Factors
Hypertension	Age
Cigarette Smoking	Male Sex
Thrombogenic/haemostatic state	Family History of Premature CHD
Diabetes	
Obesity	
Physical inactivity	
Atherogenic diet	

[1] ATP III, 2001

The ATP III Panel's (2001) recommendations also take selected factors into account to set lower thresholds for initiating treatment as well as lower LDL cholesterol goals for those at higher risk. A low HDL cholesterol level (<1.0 mmol/L) also counts as a major risk factor for setting lower LDL goals, whereas a higher HDL cholesterol level (≥1.0 mmol/L) takes away one other risk factor (Table 5.2.7/2).

TABLE 5.2.7/2. LDL Cholesterol Goals for Three Risk Levels[1]

Risk Level	LDL-C Goal
CHD and CHD Risk Equivalent	< 2.6 mmol/L
Multiple (2+) Risk Factors	< 3.4 mmol/L*
0-1 Risk Factor	< 4.1 mmol/L

* LDL-C goal for multiple-risk-factor persons with 10-year risk > 20% = <2.6 mmol/L.

[1] ATP III Panel, 2001

5.3 Prevalence of dyslipidaemia in blacks

5.3.1 South African blacks

Seftel et al. (1995) reviewed the early studies on cholesterol levels in the various populations of South Africa. Mean total cholesterol levels in middle aged black men were about 4.0 mmol/L compared to 5 mmol/L in coloured men and 6 mmol/L in white men (Seftel et al., 1995). Since the mean TC concentrations of newborn black and white babies were almost the same, the differences in TC levels that were found between middle-aged men belonging to different ethnic groups were likely to be largely environmental (Seftel et al., 1995). Serum triglyceride levels in black male subjects under the age of 40 years were about 1 mmol, but rose in white middle-aged men to 2 mmol/L while it decreased slightly in middle-aged black men (Antonis et al. (1960). These differences were clearly diet related (Antonis et al., 1960). Seftel (1978) reported on the TC levels of a large group of Johannesburg black males and females. Mean TC levels varied from about 3.7 mmol/L in the younger age groups to 5.5 mmol/L in the middle-aged group (Table 5.3.1/1). A clear increase in TC levels with age was evident for males and females. TC levels were higher in females for all age groups, a phenomenon that Seftel contributed to the higher prevalence of obesity in the females in this study. Unfortunately cut-points were not available at that stage to calculate the prevalence of elevated levels of TC in the sample.

TABLE 5.3.1/1. Mean Serum Cholesterol Levels (mmol/L) in Johannesburg Black Males and Females[1]

	Males		Females	
	n	TC (mmol/L)	n	TC (mmol/L)
Age (in yr)				
16-19	53	3.7	56	4.2
20-29	228	4.2	185	4.3
30-39	112	4.6	130	4.7
40-49	71	4.8	106	5.0
50-59	35	5.0	26	5.5
Total	499		503	

[1] Seftel, 1978

The fasting serum lipid profile of black subjects in the Cape Peninsula was studied in detail (Table 5.3.1/2) by Steyn et al. (1991). Again, TC levels were higher in females than in males in all age groups and rose with age in both sexes. The HDL cholesterol levels were high in all sub-groups but the HDL cholesterol level for the females was not higher than that for males. The mean HDL/TC ratio for males and females was 35.2% for males and that for females 34.1%. Very few participants (1.1% of males and 2.3% of females) had hypercholesterolaemia at a high level of risk while 15.4% of males and 23.5% of females had a moderate level of risk.

TABLE 5.3.1/2. Mean Serum Lipid levels (mmol/L) and HDL/TC Ratio (%) in Black Subjects in the Cape Peninsula[1]

	n	TC	HDLC	HDL/TC Ratio
Males (age in yr)				
15-24	150	3.6	1.3	37.7
25-34	110	4.0	1.4	35.6
35-44	84	4.2	1.4	34.2
45-54	56	4.2	1.3	32.3
55-64	42	4.7	1.4	30.6
Total	442	4.0	1.3	35.2
Females (age in yr)				
15-24	171	3.8	1.3	34.9
25-34	147	4.1	1.4	35.1
35-44	109	4.4	1.4	33.8
45-54	64	4.7	1.4	31.2
55-64	53	5.1	1.5	29.7
Total	544	4.2	1.4	34.1

[1] Steyn et al., 1991

Seedat et al. (1992) measured the serum lipids of 458 subjects attending the dental clinic at King George V Hospital. The sample included both sexes and the age range was 15-69 years. The mean TC concentration for males was 4.48 mmol/L and that for females 4.64 mmol/L. The HDL/TC ratio for males and females were 28% and 29.4% respectively. Serum TG levels were 1.15 mmol/L for males and 0.93 for females. In this study, the prevalence of hypercholesterolaemia at a high level of risk (≥6.5 mmol/L) was 5.5% for males and 5.0% for

females and at low level of risk (TC≥5.7 mmol/L) was 12.3% for males and 12.4% for females. There was a significant correlation between serum TC and HDL cholesterol levels, BMI, serum TG and alcohol consumption. The level of cholesterol also increased with age.

In a unique study, Seftel et al. (1993) measured and compared the lipid levels of 859 male scholars between the ages 15 and 20 years from different ethnic groups and different socio-economic status. This study included two groups of black boys, one rural and the other urban. The mean TC concentration was 3.24 mmol/L and 3.65 mmol/L for the rural and urban black boys. The difference was statistically significant. The TC concentration of the rural black boys was the lowest of the four ethnic groups studied (black, white, Indian and coloured). The mean apo B concentration was 0.63 g/dL and 0.70 g/dL for the rural and urban black boys respectively. These levels did not differ significantly. One percent of the urban and 2% of the rural black boys had TC concentrations in the high-risk category (TC>5.2mmol/L). This level of risk was well below that of boys belonging to the other ethnic groups.

The lipid profiles of 852 five-year old black children was measured as part of the birth to ten study in Johannesburg and Soweto (Steyn et al., 2000). The mean TC level for these children was 3.7 mmol/L compared to 3.9 mmol/L for coloured, 4.1 mmol/L for Indian and 4.4 mmol/L for white children. The corresponding HDL-C/TC ratios were 30.6%, 28.9%, 27% and 25.8% repectively. The percentages of children with protective HDL-C/TC ratios (≥20%) were 86% (black), 73% (coloured), 89% (Indian) and 78% of white children.

Kruger et al. (2001) measured serum lipids in 1040 black women aged 15-70 yers in the North West province. TC levels increased from 3.72 mmol/L in the youngest age decile to 5.09 mmol/L in the oldest age decile, LDL cholesterol from 2.20 mmol/L in the youngest to 3.42 mmol/L in the oldest decile, and serum TG from 0.89 mmol/L in the 25-34 year old group to 1.44 mmol/L in the 55-70 year group. The HDL-C/TC ratio decreased from 29% in the 25-34 year old group to 25% in the 55-70 year old group. In this study, serum TG levels correlated positively with BMI, HDL cholesterol correlated negatively with BMI while the triceps skinfold thickness correlated positively with TC. Waist circumference correlated positively with serum TG and negatively with HDL cholestrerol.

It is not possible to directly compare the lipid levels of the different ethnic groups in South Africa due to methodological differences between (Vermaak, et al., 1988). The overall picture that emerged from these studies was that blacks had, until now, the most favourable lipid

profile of all the ethnic groups in South Africa. This profile was, however, by all means not ideal (Seftel et al., 1995). It was emphasized in the latter review that TC levels in blacks correlated with their total fat intake and that the favourable lipid profile of blacks may thus deteriorate with increasing urbanisation.

5.3.2 Sub-Saharan Africa

Due to the low prevalence of CHD in Sub-Saharan countries, few hypertension and diabetes surveys included the measurement of serum lipids (Table 5.3.2/1). Comparison of the results of lipid measurements between different studies is further hampered by the use of different cut-points (Table 5.3.2/1). Hopefully the National Education Program's ATP III Report (2001) will result in the standardization of reporting on the results of lipid measurements in population studies.

Swai et al. (1993) measured the TC concentrations of 8581 rural Tanzanians (3705 males and 4876 females) between the ages of 15 and older (Table 5.3.2/1). Mean serum cholesterol concentrations were significantly higher in women than in men. In only one out of three regions was a trend of increasing TC concentrations with increasing age observed. In the region with the lowest serum TC concentrations (Morogoro) the levels ranged between 3.2 mmol/L and 3.6 mmol/L in men and between 3.5 mmol/L and 3.4 mmol/L in women. The prevalence of hypercholesterolaemia at a high level of risk (≥ 6.5 mmol/L) ranged between zero and 9.8%. In the economically more advanced region (Kilimanjaro) almost a third of subjects had TC levels of 5.5 mmol/L or above (Table 5.3.2/1). The prevalence of hypertriglyceridaemia (≥1.7 mmol/L) ranged between 6.3% and 12.2%.

In the Gambian study (van der Sande et al., 2000) serum lipids were also studied in some depth. The lowest prevalence of hypercholesterolaemia at a level of moderate risk (≥5.2 mmol/L) was 2.3% in male subjects in a rural area while the highest prevalence was recorded in urban females (29.1%).

Serum lipids and its sub-fractions have not been studied adequately in black populations in Sub-Saharan Africa, including South Africa. At this stage there is still very little known about LDL sub-fractions in black populations and the way it is influenced by the nutritional transition. Similarly, very little is known about the prevalence of the atherogenic phenotype in black populations.

TABLE 5.3.2/1. Mean Lipid Levels (mmol/L) and Prevalence of Dyslipidaemia in Sub-Saharan African Subjects

Country (age in yr)	N	TC mmol/L	HDL-C mmol/L	TG mmol/L	% TC ≥ 5.2 mmol/L	% TG ≥ 1.7 mmol/L	Reference
Tanzania							Swai et al.,1993
Kilimanjaro (Ru)							
Males (55+)	413				26.9	12.6	
Females (55+)	478				35.5	11.5	
Mara							
Males (55+)	198				6.6	8.1	
Females (55+)	133				6.1	12.2	
Morogoro							
Males (55+)	79				12.7	6.3	
Females (55+)	74				9.5	12.1	
Nigeria							Kadiri et al., 1997
Males	110				7.3		
Females	36				19.5		
Gambia						TG ≥1.8	van der Sande et al., 2000
Normotensive						mmol/L	
Urban males	1028	4.1		0.68	12.5	4.0	
Urban females	1138	4.6		0.68	29.1	0.6	
Rural males	1200	3.6		0.81	2.3	4.3	
Rural females	2023	3.9		0.76	8.3	2.1	
Hypertensive							
Urban males	77	4.9		1.13	24.5	4.1	
Urban females	85	5.0		0.79	39.1	4.7	
Rural males	91	4.0		1.17	4.1	1.4	
Rural females	127	4.4		0.83	13.7	2.9	
Tanzania							Njelekela et al., 2001
Rural males	93	3.4	1		4.4		
Rural females	91	4.4	1		22.5		
Nomadic males	41	5.1	1.1		48.6		
Nomadic females	61	5.3	1.3		53.7		
Urban males	81	4.7	1.2		29.5		
Urban females	79	5.3	1.3		50.0		

6 The clustering of cardiovascular risk factors

6.1 The metabolic syndrome

6.1.1 Definition

Reaven (1988) produced convincing evidence that the cluster of risk factors (Table 6.1.1/1) commonly seen in patients with hypertension are linked to insulin resistance and went on to hypothesise that insulin resistance plays a major role in the pathogenesis of CHD. Reaven (1988) referred to this cluster of risk factors as Syndrome X. Missing from the original descriptions of Syndrome X, is obesity or central obesity.

TABLE 6.1.1/1. The Cluster Of Cardiovascular Risk Factors

(Syndrome X)[1]

Resistance to insulin-stimulated glucose uptake
Glucose intolerance
Hyperinsulinaemia
Increased very low density lipoprotein triglyceride
Decreased high-density lipoprotein cholesterol
Hypertension

[1] Reaven, 1988

The traditional view before 1989 was that obesity by itself did not contribute to CHD and that obesity only became a problem when accompanied by other risk factors such as glucose intolerance, hyperlipidaemia, and hypertension (Kaplan, 1989). Kaplan argued that obesity, hypertension, hypertriglyceridaemia, and glucose intolerance coexist more commonly than by chance suggesting a shared pathogenesis in at least some subjects who suffer from two or more of these conditions (Kaplan, 1989). Since the association between obesity and these other disorders are stronger in the presence of predominantly upper-body fat distribution or central obesity, Kaplan (1989) developed a hypothesis that linked hyperinsulinaemia to central obesity. The cluster of upper-body obesity (central obesity), glucose intolerance,

hypertriglyceridaemia, and hypertension was referred to as " The Deadly Quartet" (Kaplan, 1989) (Fig. 6.1.1/1).

Various other names were given to this cluster of CV risk factors including the insulin resistance syndrome (Haffner et al., 1992), the metabolic syndrome (van Gaal et al., 1998b), and the dysmetabolic syndrome (Groop et al., 2001). The WHO adopted the name metabolic syndrome and suggested the working definition referred to in Chapter 2 (section 2.1.5). Various other components of the metabolic syndrome have been described but were not included in the WHO definition (Table 6.1.1/2).

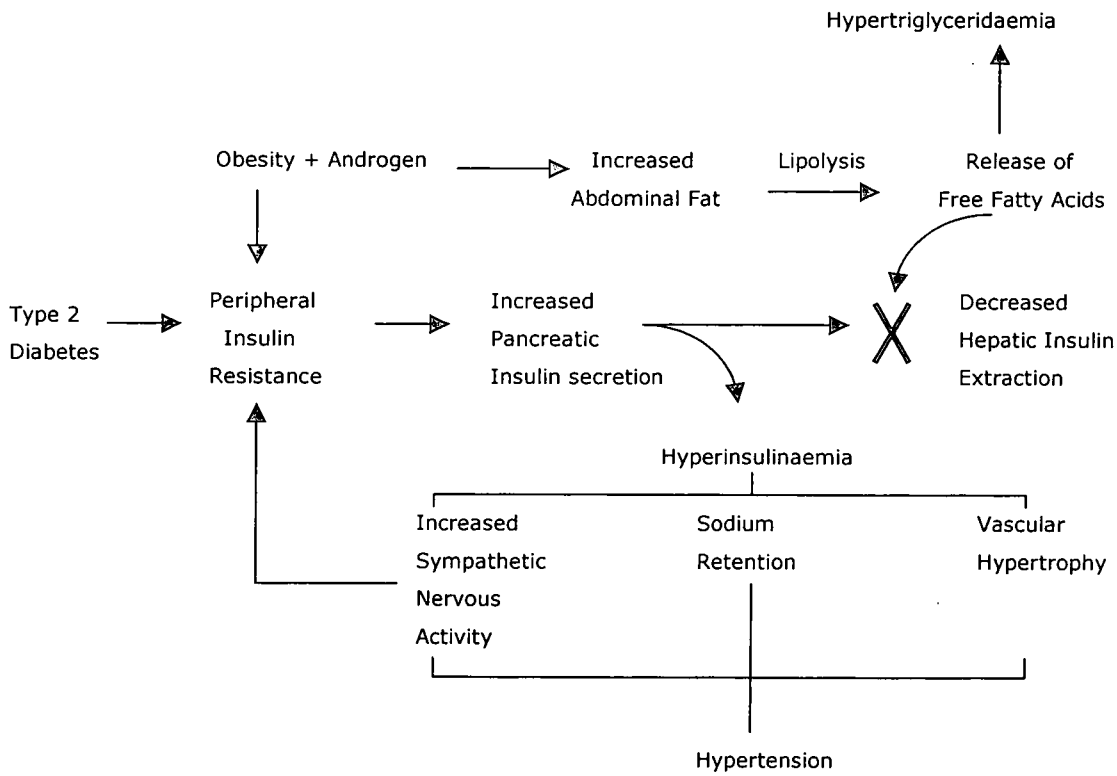


Fig. 6.1.1/1. Postulated mechanism of upper-body obesity promoting glucose intolerance, hypertriglyceridaemia, and hypertension via hyperinsulinaemia (Kaplan, 1989).

TABLE 6.1.1/2. Expanded View of the Metabolic Syndrome[1]

Insulin resistance and hyperinsulinaemia
Glucose intolerance/ Type 2 diabetes
Hypertension
Reduced LDL cholesterol
Hypertriglyceridaemia
Small dense LDL particles
Elevated PAI-1 levels, disturbances in haemostasis
Fibrinolytic abnormalities
Hyperuricaemia

[1] van Gaal et al. ,1998

The saga of different definitions and diagnostic criteria for the metabolic syndrome continues as the Expert Panel (2001) published their recommendations. This body recognised the factors in Table 6.1.1/3 as being characteristic of the syndrome.

TABLE 6.1.1/3. Factors Characteristic of the Metabolic Syndrome[1]

Abdominal obesity	Insulin resistance or glucose intolerance
Atherogenic dyslipidaemia	Pro-thrombotic state
Raised blood pressure	Pro-inflammatory state

[1] Expert Panel, 2001

The ATP III (2001) recommended that a clinical diagnosis of the metabolic syndrome is justified by the presence of three or more of the criteria listed in Table 6.1.1/4. The ATP III (2001) did not find adequate evidence to recommend routine measurement of insulin resistance (e.g. serum insulin), pro-inflammatory state (e.g. high-sensitivity C-reactive protein), or pro-thrombotic state (e.g. fibrinogen or PAI-1) in the diagnosis of the metabolic syndrome. The ATP III (2001) also acknowledged that some male persons may develop multiple metabolic risk factors when the waist circumference is only marginally increased, e.g. 94-102 cm. Such persons may have a strong genetic contribution to insulin resistance. They should benefit from changes in life style, similarly to men with categorical increases in waist circumference.

TABLE 6.1.1/4. Clinical Identification of the Metabolic Syndrome[1]

Risk Factor	Defining Level
Abdominal obesity	Waist circumference
Males	>102 cm
Females	> 88cm
Triglycerides	>1.7 mmol/L
HDL cholesterol	
Men	<1.0 mmol/L
Women	<1.3 mmol/L
Blood pressure	>130/85
Fasting glucose	6.1-7.0 mmol/L

[1] ATP III, 2001

6.1.2 The pathogenesis of the metabolic syndrome

Presently there are two schools of thought on the pathogenesis of the metabolic syndrome. The first, the thrifty phenotype or the foetal origins hypothesis, was already dealt with in Chapter 2 (section 2.6.2). The second and opposing view (Groop et al., 2001 and Ukkola et al., 2001) supports the original thrifty genotype hypothesis of Neel (1962) who proposed that individuals living in a harsh environment with unstable food supply would maximise their probability of survival if they could maximise storage of surplus energy. Genetic selection would thus favour energy conserving genotypes in such environments. Storage of energy as fat rather than as glycogen would ensure energy during periods of starvation (Groop et al., 2001). The different metabolic abnormalities of the metabolic syndrome are strongly inherited (Groop et al., 2001 and Ukkola et al., 2001). The current evidence is summarised in Table 6.1.2/1.

The candidate genes for the metabolic syndrome were recently reviewed (Groop et al., 2001) and are summarized in Table 6.1.2/2. It is most probable that for insulin resistance to manifest, an interaction between genetic and environmental factors is necessary (Groop et al., 2001). Likewise, abdominal obesity most likely results from gene-gene interaction and an affluent environment (Groop et al., 2001). It is also possible that a low birth weight (foetal

environment) could be a phenotype for a thrifty gene (Groop et al., 2001). Amongst the different genes contributing to the metabolic syndrome, those regulating lipolysis, thermogenesis and glucose uptake in skeletal muscle still remain prime candidates worthwhile of examining with the genome wide approach (Groop et al., 2001). Ukkola and Bouchard (2001) expressed the view that insulin resistance and hyperinsulinaemia do not represent the fundamental causes of the metabolic abnormalities, but they rather represent frequent traits of the syndrome.

Groop et al. (2001) hypothesised that the thrifty genotype is not a monogenic condition but that genes regulating lipolysis, thermogenesis, and glucose uptake are involved. These candidate genes are summarised in Table 6.1.2/3.

An understanding of the role of genes in the development of the metabolic syndrome and thus the clustering of its components, may help to identify at risk individuals with the aim of delaying the onset or preventing the syndrome altogether. The reduction of excess body fat, the most common clinical feature observed with the syndrome, should be the first line of attack in the treatment of the condition when prevention has failed (Ukkola and Bouchard, 2001).

TABLE 6.1.2/1. Inheritance of the Components of the Metabolic Syndrome

Component	Heritability	Reference
Insulin resistance	45% of first degree relatives of patients with type 2 diabetes are insulin resistant compared to 20% of individuals without a family history	Beck-Nielsen et al., 1994
Obesity	25% of the variation in body fat is attributed to genetic factors	Bouchard 1992
Abdominal fat	The distribution of subcutaneous fat in the trunk relative to the limbs exhibits a genetic effect of about 20%	Bouchard 1992
Abdominal fat	60% of the variance in abdominal fat in postmenopausal women is genetic	Samaras 1997
Hypertension	Associated with insulin resistance See Table 3.6.4.1	Ferranini 1987, Modan 1985
HDL cholesterol	Associated with insulin resitance	Hong et al., 1998
HDL cholesterol	Associated with insulin resistance	Widén 1992
Hypertriglyceridaemia	Associated with insulin resistance	Widén 1992
Microalbuminuria	Heritability 30% and clusters in families	Forsblom et al., 1999
Microalbuminuria	Associated with insulin resistance	Mykkänen et al., 1998 Groop et al 1993

Modified from Groop et al. 2001

TABLE 6.1.2/2. Candidate Genes for the Thrifty Genotype[1]

Gene(s)	Intermediate Phenotype	Reference
Monogenic obesity:		
Leptin 7q31.3,	Obesity	Montague et al., 1997
codon 133, single deletion		
Arg105Trp replacement	Obesity, hypogonadism	Strobel et al., 1998
LEPR 1p31 mutation	Obesity and hypogonadism	Clement et al.,1998
Leptin Receptor		
MC4R 18q22 mutation	Agouti protein	Yeo et al., 1998
Melanocortin Receptor 4	Morbid obesity in humans	Hinney et al., 1999
		Vaise et al 2000
		Farooqi et al., 2000
MC4R, MC5R	Obesity	Chagnon et al., 1997
POMC 2p21	Leptin levels, basal metab. rate	Comuzzie et al., 1997
POMC 2p21	Regulator of leptin levels	Hixson et al.,1999
POMC 2p21	Agouti-like obesity, red hair	Krude et al., 1998
null mutations	Adrenal insufficiency	
POMC 2p21	Weight extremes	Hinney et al., 1998
mutations		
POMC 2p21	Obesity	Delplanque et al., 2000
point mutations		
Prohormone convertase 1	Obesity, hypogonadism, elevated	Jackson et al., 1997
mutation	proinsulin, cortisol, POMC	
Lipolysis and FFA metabolism:		
Beta-3-adrenoreceptor (β3AR)	Increased lipolysis in abdom fat	Lonnquist et al., 1995
β3AR Trp64Arg	Abdominal obesity, hyperinsulin.,	Watson et al., 1995
	insulin resistance, higher BP	Widèn et al., 1995
		Clement et al., 1995
β3AR 8p12-p11.1	High BMI in Mexican Americans	Mitchell et al., 1998
β3AR Trp64Arg	Higher fasting NEFA levels	Carlsson et al., 2001
β3AR Arg 16 homozygote	Hypertension and Type 2 DM	Bengtson et al., 2001a
β3AR Cys19-Arg16-Gln27	Hypertension and obesity	Carlsson et al., 2001
β2AR Gln27	Increased NEFA levels	Carlsson et al., 2001
β2AR plus β3AR	Type 2 DM	Carlsson et al., 2001
variations		Bengtson et al., 2001a
β1AR Arg389Gly	Higher BP and heart rate	Bengtsonn et al., 2001b
Fatty Acid Binding Protein 2	Higher serum TG, TC levels,	Carlsson et al., 2000
polymorphism: Thr54	increased risk for stroke	

[1] Adapted from Groop et al., 2001

TABLE 6.1.2/2. Candidate Genes for the Thrifty Genotype[1] (ctd.)

Gene(s)	Intermediate Phenotype	Reference
Lipases		
Hormone Sensitive Lipase		
HSL 19q13.1-13.2 polymorphism	Type 2 DM, metabolic syndrome	
Lipoprotein Lipase (LPL) 8p22		
LPL Asn291Ser	High serum TG, low HDL, increased risk for CVD	Reymer et al., 1995 Knudsen et al., 1997
LPL Asn291Ser	Dyslipidaemia, high SBP	Klannemark et al., 2000
Hepatic Lipase (HL) 15q21-23		
polymorphism -514 promoter	HL activity, LP levels	Tahvanainen et al., 1998
Uncoupling proteins		
UCP1 4q31		
polymorphism promoter region	Weight gain	Clement et al 1996
polymorphism plus B3AR Trp64Arg	Weight gain accentuated	
UCP3 mutations	Obesity in Type 2 DM	Argyrpoulos et al 1998
Insulin sensitivity		
Tumor necrosis factor alpha (TNFα)	Role in metab. syndr. unlikely	Groop et al.,2001
PPARγ 3p4 (peroxisome proliferator-activated receptor gamma)		
mutation Pro115Gln	Obesity	Ristow et al 1998
mutation Pro12Ala	Increased insulin sens., lower BMI, lower risk for diabetes	Deeb et al., 1998 Altshuler et al., 2000
Resistin 19p13	Downregulated by thiazolidenediones	Steppan et al., 2001
Glycoprotein PC1 6q22-23	Inhibit insulin receptor tyrosine kinase	
Lys121Gln variant (?K12Q)	Insulin resistance, features of metabolic syndrome	Pizzutti et al., 1999
Insulin receptor substrates (IRSs)		
IRS1 codon 972 polymorphism	Insulin resistance, metab. syndrome	Clausen et al., 1995
Glycogen synthase		
GYS1 19q13.3 Xba1 polymorphism	Type 2 DM, insulin resistance	Groop et al., 1993
GYS1 A2 allele	More insulin resistant than A1 allele	Orho-Melander et al 1999

[1] Adapted from Groop et al.,2001

TABLE 6.1.2/3. Genes that May Contribute to the Thrifty Genotype[1]

Glycogen synthase	GYS1	Calpain 10	CAPN10
Leptin Receptor	LEPR	Uncoupling protein 1	UCP1
Pro-opiomelanocortin	POMC	Fatty acid binding protein 2	FABP2
Beta-1-adrenoreceptor	β1AR	Hormone sensitive lipase	HSL
Beta-2-adrenoreceptor	β2AR	Lipoprotein lipase	LPL
Beta-3-adrenoreceptor	β3AR		
Peroxisome proliferator-activated receptor gamma	PPARγ		

[1]Adapted from Groop et al., 2001

6.1.3 The prevalence of the metabolic syndrome in Finnish Subjects

Isomaa et al. (2001) published the first report on the prevalence of the metabolic syndrome applying the WHO 1998 definition on a high-risk Scandinavian population (Table 6.1.3/1). The prevalence of obesity was high in all groups in this study, especially in male subjects (76% of males with normal glucose tolerance). The most common combination was obesity plus dyslipidaemia or obesity plus hypertension. The prevalence of the metabolic syndrome in this study was more common in non-diabetic men than in women and the sex-specific differences almost disappeared in the type 2 diabetic patients. The prevalence of the metabolic syndrome also increased with age in this study.

The prevalence of CV disease in relation to the metabolic syndrome was also recorded in the Finnish study over a mean period of 6.9 years (Isomaa et al., 2001). In all subjects a history of CHD, myocardial infarction and stroke was more common in those with the metabolic syndrome than those without the metabolic syndrome. CHD was almost four times as common in subjects with the metabolic syndrome than in subjects without the metabolic syndrome (21.4% vs. 5.5%). Dyslipidaemia was associated with an increased risk of CHD especially in subjects with type 2 diabetes. Hypertension was associated with an increased risk of CHD especially in subjects with normal glucose tolerance.

The Finnish study also investigated total and CV mortality over a mean period of 6.9 years in relation to the metabolic syndrome and its components (Isomaa et al., 2001). Total as well as CV mortality was increased in subjects with the metabolic syndrome compared to subjects without the syndrome (18.0% vs. 4.6% and 12.0% vs. 2.2% respectively). The RR of CV

mortality in subjects with the metabolic syndrome compared to subjects without the metabolic syndrome was 1.81 (95% CI 1.24-2.65). The RR of CV mortality in subjects with microalbuminuria compared to subjects without microalbuminuria was 2.8 (95% CI 1.62-4.83). The latter risk exceeded that of the other components of the metabolic syndrome. Isomaa et al. (2001) concluded that the prevalence of the metabolic syndrome as defined by the WHO 1998 criteria was 10% in subjects with normal glucose tolerance, 50% in subjects with IFG/IGT, and 80% in subjects with type 2 diabetes. Since the metabolic syndrome conferred an increased risk of CV morbidity and mortality, its identification may be important in risk assessment and treatment of patients.

TABLE 6.1.3/1. The Prevalence (%) of Different Combinations of the Individual Components of the Metabolic Syndrome in 35-70-Year-Old Finnish Male and Female Subjects[1]

	NGT[2]		IFG/IGT[3]		Type [2] diabetes	
	Male	Female	Male	Female	Male	Female
Obesity + dyslipidaemia	25	9	41	21	51	49
Obesity + hypertension	20	11	28	23	50	50
Obesity + hypertension + dyslipidaemia	7	3	15	10	29	31
Hypertension + dyslipidaemia	8	5	16	14	31	36
Obesity + microalbuminuria	3	2	6	3	21	11
Hypertension + microalbuminuria	2	2	3	3	16	10
Dyslipidaemia + microalbuminuria	1	1	4	2	14	9

[1] Isomaa et al., 2001

[2] Normal Glucose tolerance

[3] Impaired fasting glucose/impaired glucose tolerance

NGT: n=1988 (males 855, females 1133)

IFG/IGT: n=798 (males 401, females 397)

Type 2 diabetes: n=1697 (males 804, females 893)

6.2 Cardiovascular risk factors in black South Africans

6.2.1 The prevalence of cardiovascular disease in black South Africans

Coronary heart disease was regarded as very rare in blacks in the 1970's (Walker, 1973). In spite of significant overlap in the prevalence of the traditional CV risk factors between the different ethnic groups in South Africa, CHD was less common in urban blacks than was expected. Walker (1973) hypothesized that the different risk factors did not have the same weight in all populations and that the "degree of noxiousness" of a particular risk may be different between communities. From the available literature at that stage, Walker (1975) concluded that the first atherosclerotic disease to emerge in a population in transition is cerebrovascular disease, followed much later by peripheral vascular and coronary heart disease in that order. Even today little information of any quality is available to support or to refute this view.

In 1978 Seftel confirmed that the prevalence of CHD in the black population was low but not absent. The previous low incidence of CHD in the black population was not unusual and was explained by the absence of the required nutritional-metabolic milieu, low cholesterol levels, short duration of risk factor exposure, and a low frequency of a combination of risk factors (Seftel, 1978).

Walker et al. (1993) commented that the death rate from CHD in white South Africans declined from 1978 to 1989 while CHD mortality remained unchanged for blacks. Ischaemic heart disease accounted for about 4% of all deaths in SA during 1996 (Bradshaw et al., 2002). This figure included all racial groups and both sexes while separate figures for blacks were not available. During the same period 9% of all women and 5.3% of all men died from stroke. Contributing factors to the emergence of stroke as a major health problem in SA are the increase in prevalence of hypertension, obesity, smoking habit and hyperfibrinoginaemia (Vorster, 2002). Black South Africans may be protected against CHD because of their favourable lipid profiles and low homocysteine levels (Vorster, 2002).

The prevalence of CHD in black stroke patients was found to be about 30% (Joubert et al., 2000). Seedat et al. (1992) examined the risk factors for CHD in black patients attending a

dental clinic in Durban. The prevalence of CHD in this sample of 458 patients (16-69 years) was 2.4% based on clinical history and Minnesota ECG-coding. Hypercholesterolaemia was uncommon and more than 80% of subjects had protective levels of HDL cholesterol. This was the only recent study in black South Africans aimed at determining the prevalence of CHD in this population.

The estimated total cost of CV disease in South Africa during 1991 was about R4.5 billion (Pestana et al., 1996). The direct health care cost was approximately 42% of which two-thirds were carried by the private sector and the rest by the public sector.

6.2.2 The clustering of cardiovascular risk factors in black South Africans

Twenty eight percent of black males in the Cape Peninsula had at least one risk factor at a high level of CHD risk while 2.7% had two risk factors and 31% had one or more risk factors (Steyn et al., 1991). The prevalence of the metabolic syndrome in these men was probably low since only 8% were obese (BMI ≥30 kg/m^2). Twelve percent of females had at least one risk factor at high level of risk, less than 1% had one risk factor and one or more risk factors were present in 12.5%. Although 44% of females were obese no estimate can be made about the prevalence of the metabolic syndrome in this group. In males the bulk of the risk was due to smoking and in females it was due to hypertension. An outstanding feature of this population was the high level of HDL cholesterol and the high prevalence of protective HDL cholesterol levels.

In the Durban study, 55% of males and 79% of females were free of any major CV risk factor that included hypercholesterolaemia, hypertension, smoking and diabetes (Seedat et al., 1992). The most frequent risk factor in males was smoking (28%), followed by hypertension (12.6%) whereas in females, hypertension was the most frequent (13%). Hypercholesterolaemia at high level of risk occurred in 5.5% of males and in 5% in females. The combination of hypercholesterolaemia and smoking occurred in 1.6% of males and in none of the women, while hypercholesterolaemia and hypertension occurred in 1.2% of females and in none of the males. Again, no estimate about the prevalence of the metabolic syndrome was possible from this study.

6.3 Cardiovascular *risk factors in sub-Saharan Africa*

6.3.1 Cardiovascular disease in Sub-Saharan Africa

Like South Africa, no population-based studies are available describing the prevalence of CV disease in this region. Records from the Abidjan Institute of Cardiology indicate that the prevalence of proven CHD in blacks as a percentage of patients with CV diseases admitted to this unit increased from 1.4% in the period 1964-1965 to 6.5% in the period 1988-1990 (Bertrand, 1995). During the period 1977-1981 to 1988-1990 the percentage of Caucasians with proven CHD admitted to this unit declined from 39% to 36%. More than 90% of admissions were black males and their clinical presentation was no different form their Caucasian counterparts.

6.3.2 The clustering of cardiovascular risk factors in sub-Saharan black Africans

The prevalence of CHD risk factors was overall low in rural Tanzanians (Swai et al., 1993). Of 8581 subjects, 19% or less had TC levels in the moderate risk category (≥5.2 mmol/L), 7.5% or less had hypertension (BP ≥160/95 mm Hg), 3% to 43% of males smoked cigarettes while less than 4% of women smoked, and the prevalence of overweight or obesity was less than 11% in females and less than 4% in males. Q-wave abnormalities on ECG were present in 2.7% of men and 3.7% of women. Very few subjects in this study had one or more CV risk factor while the prevalence of obesity was low (Table 6.3.2/1). Waist and hip circumferences were not measured and therefore the prevalence of the metabolic syndrome in this study was not available. Risk factors were higher in the Kilimanjaro region but few people had more than one risk factor. Thus, levels of CV risk factors were low in Tanzania with the exception of smoking and myocardial disease as indicated by ECG abnormalities were rare.

In a smaller study of 496 Tanzanian subjects Njelekela et al. (2001) found that the prevalence of hypercholesterolaemia at moderate risk increased significantly over an eleven-year period from 1.4% to 4.4% in a rural and from 16.7% to 29.5% in an urban sample of men. The corresponding increases for women were 2.2% to 22.5% (rural) and 7.4% to 50% (urban).

TABLE 6.3.2/1. The Clustering of Cardiovascular Risk Factors[1] in Tanzanian Subjects[2]

	Kilimanjaro		Mara		Morogoro	
Risk factors	Male	Female	Male	Female	Male	Female
	n=1754	n=2680	n=481	n=585	n=1468	n=1609
0	41.7	65.8	75.6	77.3	61.7	73.8
1	45.9	26.9	22.4	18.7	32.4	21.6
≥2	12.4	7.3	2.0	4.0	5.9	4.6

[1] TC ≥ 5.2 mmol/L, diabetes mellitus or IGT, hypertension, smoking and BMI ≥ 25 kg/m2

[2] Swai et al. (1993)

Ezenwaka et al. (1997) measured the prevalence of CV risk factors in two low socio-economic populations in Nigeria. The proportion of subjects with no risk factors at all was considerably lower than that reported by Seedat et al. 91992) in Durban blacks, as well as by Swai et al. (1993) in Tanzanian subjects. About 12% of males and 22% of females had of subjects had >4 risk factors (Table 6.3.2/2). The most frequent risk factor in males was central obesity followed by sedentary lifestyle and in women sedentary lifestyle insulin resistance and physical inactivity. The overall prevalence of hypercholesterolaemia at moderate level of risk in this study was less than 1%. The prevalence rates of hyperinsulinaemia, insulin resistance, and physical inactivity were twice as high in women compared to men. Women also had more combinations of multiple risk factors than men (Table 6.3.2/2). The low prevalence of CHD in this population was attributed to the low prevalence of hypercholesterolaemia and diabetes (Ezenwaka et al., 1997).

In a different and smaller Nigerian study of 146 middle-aged subjects, multiple risk factors were infrequent in individual subjects (Kadiri et al., 1997). Two or more risk factors occurred in only 4.5% of men and none of the women had more than one risk factor. Okesina et al. (1999) also reported an absence of hypercholesterolaemia (≥5.2 mmol/L) in a similar study involving 500 subjects in rural Nigeria. The prevalence of obesity was 2% in this sample.

Van der Sande et al. (2000) also commented on the frequent co-existence of hypertension, obesity, diabetes and hyperlipidaemia especially in the urban population of the Gambia suggesting that the metabolic syndrome may be emerging in the capital Banjul.

TABLE 6.3.2/2. The Clustering of Cardiovascular Risk Factors (%)[1] in Nigerian Subjects[2]

Risk factors	All % n=500	Males % n=295	Females % n=205
0	29.8	31.5	27.3
≥1	70.2	68.5	72.7
≥2	47.6	44.4	52.2
≥3	27.8	25.1	31.7
≥4	16.2	12.2	22.0
≥5	9.2	6.4	13.2

[1] Smoking, alcohol intake, sedentary lifestyle, hypertension (≥160/95), obesity, truncal obesity, hyperinsulinaemia, insulin resistance, diabetes, hypercholesterolaemia (≥5.2 mmol/L and hypertriglyceridaemia (≥ 2.5)

[2] Ezenwaka et al. ,1997

6.4 Estimating coronary heart disease risk

6.4.1 Estimating 10-year risk for men and women (ATP III, 2001, incorporating the Framingham scoring system)

The guiding principle of ATP III (2001) was that the intensity of LDL-lowering therapy should be adjusted to the individual's absolute risk for CHD. Short term (≤ 10-year risk) as well as long-term risk (>10 years) must be taken into consideration. ATP III (2001) identified three categories of risk for CHD that modify goals of LDL-lowering therapy (Table 6.4.1/1).

TABLE 6.4.1/1. Categories of Risk for CHD That Modify LDL Cholesterol Goals[1]

Risk Categories	LDL Goal
Established CHD & CHD risk equivalents	<2.6 mmol/L
Multiple (2+) risk factors	<3.4 mmol/L
0-1 risk factor	<4.1 mmol/L

[1] ATP III, 2001

6.4.2 Identification of persons with CHD and CHD risk equivalent (ATP III, 2001)

- Coronary heart disease

Persons with CHD are at very high risk for future CHD events (10-year risk >20 percent). Clinical patterns that constitute a diagnosis of CHD include history of acute myocardial infarction, evidence of silent myocardial infarction or myocardial ischaemia, history of unstable angina and stable angina pectoris, and history of coronary procedures (coronary angioplasty and coronary artery surgery).

- Other clinical atherosclerotic diseases

Persons in this subcategory have a CHD risk equivalent. Included are those with peripheral arterial disease, abdominal aortic aneurysm, carotid artery disease, and other forms of clinical atherosclerotic disease e.g. renal artery disease.

- Diabetes mellitus

ATP III 2001 counts diabetes as a CHD risk equivalent.

- Multiple risk factors and when 10-year risk for CHD >20 percent

Based on a 10-year risk assessment using Framingham scoring, a person in this category can be said to have a CHD risk equivalent.

6.4.3 Identification of persons without CHD or without CHD risk equivalent (ATP III 2001)

Risk status in persons without clinically manifest CHD or CHD equivalents is determined by a 2-step procedure (ATP III, 2001). The number of risk factors is counted (Table 6.4.3/1) followed by 10-year risk assessment according to Framingham scoring (Table 6.4.3/2 and Table 6.4.3/3) for those individuals with multiple (2+) risk factors. In patients with high HDL cholesterol 1 risk factor is subtracted. Framingham scoring divides persons with multiple risk factors (2+) into those with 10-year risk for CHD >20%, 10-20% and <10%. If the 10-year risk >20% then that person is regarded as having a CHD risk equivalent and the target for LDL cholesterol lowering would be <2.6 mmol/L and not <3.4 mmol/L. The risk factors included in the Framingham calculation of 10-year risk are: age, total cholesterol, HDL cholesterol, SBP, treatment for hypertension, and cigarette smoking. The Framingham scoring system applies to "hard" CHD including myocardial infarction and CHD death (ATP III 2001).

When 0-1 risk factor is present, Framingham scoring is not necessary because 10-year risk rarely reaches levels for intensive intervention (ATP III 2001).

TABLE 6.4.3/1 Major Risk Factors (Exclusive of LDL Cholesterol) That Modify LDL Goals* [1]

Positive Risk Factors
1. Age
Male: >45 years
Female: >55years
2. Family history of premature CHD (definite myocardial infarction or sudden death before 55 years of age in father or other male first-degree relative, or before 65 years of age in mother or other female first-degree relative)
3. Current cigarette smoking
4. Hypertension (>140/90, or on antihypertensive medication)
5. Low HDL cholesterol (<1.0 mmol/L)
Negative (protective) Risk Factor
6. High HDL cholesterol (>1.6 mmol/L)

[1] ATP III, 2001

* Diabetes is regarded as a CHD risk equivalent.

Table 6.4.3/2. Estimate of 10-Year Risk for Men (Framingham Point Scores)

Age, y	Points
20 – 34	-9
35 – 39	-4
40 – 44	0
45 – 49	3
50 – 54	6
55 – 59	8
60 – 64	10
65 – 69	11
70 – 74	12
75 - 79	13

	Points				
Total Cholesterol , mmol/L	Age 20 – 39 y	Age 40 – 49 y	Age 50 – 59 y	Age 60 – 69 y	Age 70 – 79 y
<4.2	0	0	0	0	0
4.2-5.1	4	3	2	1	0
5.2–6.1	7	5	3	1	0
6.2–7.1	9	6	4	2	1
≥7.2	11	8	5	3	1

	Points				
	Age 20 – 39 y	Age 40 – 49 y	Age 50 – 59 y	Age 60 – 69 y	Age 70 – 79 y
Nonsmoker	0	0	0	0	0
Smoker	8	5	3	1	1

HDL, mg/dL	Points
≥1.6	-1
1.3–1.5	0
1.0 – 1.2	1
<1.0	2

Systolic BP, mm Hg	If Untreated	If Treated
<120	0	0
120 – 129	0	1
130 – 139	1	2
140 – 159	1	2
≥160	2	3

Points total	10-Year Risk, %
<0	<1
0	1
1	1
2	1
3	1
4	1
5	2
6	2
7	3
8	4
9	5
10	6
11	8
12	10
13	12
14	16
15	20
16	25
≥17	≥30

Table 6.4.3/3. Estimate of 10-Year Risk for Women (Framingham Point Scores)

Age, y	Points
20 – 34	-7
35 – 39	-3
40 – 44	0
45 – 49	3
50 – 54	6
55 – 59	8
60 – 64	10
65 – 69	12
70 – 74	14
75 - 79	16

	Points				
Total Cholesterol , mg/dL	Age 20 – 39 y	Age 40 – 49 y	Age 50 – 59 y	Age 60 – 69 y	Age 70 – 79 y
<4.2	0	0	0	0	0
4.2–5.1	4	3	2	1	1
5.2–6.1	8	6	4	2	1
6.2–7.1	11	8	5	3	2
≥7.1	13	10	7	4	2

	Points				
	Age 20 – 39 y	Age 40 – 49 y	Age 50 – 59 y	Age 60 – 69 y	Age 70 – 79 y
Nonsmoker	0	0	0	0	0
Smoker	9	7	4	2	1

HDL, mg/dL	Points
≥1.6	-1
1.3–1.5	0
1.0–1.2	1
<1.0	2

Systolic BP, mm Hg	If Untreated	If Treated
<120	0	0
120 – 129	1	3
130 – 139	2	4
140 – 159	3	5
≥160	4	6

Points total	10-Year Risk, %
<9	<1
9	1
10	1
11	1
12	1
13	2
14	2
15	3
16	4
17	5
18	6
19	8
20	11
21	14
22	17
23	22
24	27
≥25	≥30

6.4.4 Estimating 5- or 10-year risk for men and women using Framingham prediction equations

The best strategy for the prevention of CHD is a multifactorial approach that takes into consideration all the risk factors (Anderson et al., 1990). Prediction equations based on measurements of several known risk factors were developed from the Framingham heart study (Anderson et al., 1990). Mathematical equations were developed for the following outcomes: myocardial infarction, death from CHD, CHD, stroke, cardiovascular disease (including all those outcomes mentioned as well as congestive heart failure and peripheral vascular disease), and finally death from CVD. The following risk factors are used: age, gender (female sex is a protective factor), SBP (average of two office measurements), DBP (average of two office measurements), total serum cholesterol, HDL cholesterol, cigarette smoking, diabetes, and ECG-LVH (Table 6.4.4/1 and Table 6.4.4/2). These prediction equations may be used for estimating outcome probabilities over a range of 4 to 12 years for persons of both sexes aged 30-74 years based on SBP or DBP or both. These prediction equations were validated and performed well among whites and blacks in different settings (D'Agostino et al., 2001). The formulae for these equations are provided in Table 6.4.4/1 and Table 6.4.4/2.

The following is an example of a predicted probability (Anderson et al., 1991): As an example of how to compute a predicted probability, consider the CHD equation for a 55-year-old woman with diabetes who smokes, has an SBP of 135 mm Hg, total cholesterol 5.96 mmol/L, HDL cholesterol of 1.24 mmol/L, and no ECG-LVH. Using Table 6.4.4/1, begin by computing $\mu=\beta_0+ \beta_1 X\text{female}+ \beta_2 x\log(\text{age})+ \beta_3 x\log(\text{age})x\text{female}+ \beta_4 X[\log(\text{age})]^2 X\text{female}+\beta_5 X\log(\text{SBP})+ \beta_6 X\text{cigarettes}+\beta_7 X\log(\text{total cholesterol} \div \text{HDL cholesterol}) + \beta_8 X\text{diabetes} + \beta_9 X\text{diabetes}X\text{female}=15.5305+28.4441-(1.479+14.4588)x\log(55)+1.8515X[\log(55)]^2-0.9119x\log(135)-0.2767-0.7181X\log(230/48)-0.1759-0.1999=3.588.$

Next compute: $\log(\sigma)=\theta_0+ \theta_1\mu=0.9145-0.2784X\mu= -0.08430$, so $\sigma = e^{-0.0843} = 0.9192$. If t = 10 years, we have

$$\mu= \frac{\text{Log}(10)-\mu}{\sigma} = -1.398$$

Thus the 10-year predicted probability for CHD is 1 – exp(-exp(-1.398)) = 0.22 (or 22%).

Table 6.4.4/1. SBP prediction equation coefficients

Coefficients	*CHD*	*MI*	*CHD death*	*Stroke*	*CVD*	*CVD death*
θ_0	0.9145	3.4064	2.9851	-0.4312	0.6536	0.8207
θ_1	-0.2784	-0.8584	-0.9142	--	-0.2402	-0.4346
β_0	15.5305	11.4712	11.2889	26.5116	18.8144	-5.0385
female	28.4441	10.5109	0.2332	0.2019	-1.2146	0.2243
log(age)	-1.4792	-0.7965	-0.9440	-2.3741	-1.8443	8.2370
$(\log(age))^2$	-	-	-	-	-	-1.2109
log(age) x female	-14.4588	-5.4216	-	-	0.3668	
$(\log(age)^2$ x female	1.8515	0.7101	-	-	-	
log (SBP)	-0.9119	-0.6623	-0.5880	-2.4643	-1.4032	-0.8383
cigarettes (Y/N)	-0.2767	-0.2675	-0.1367	-0.3914	-0.3899	-0.1618
log(total-C ÷ HDL-C)	-0.7181	-0.4277	-0.3448	-0.0229	-0.5390	-0.3491
diabetes	-0.1759	-0.1534	-0.0474	-0.3087	-0.3036	-0.0831
diabetes x female	-0.1999	-0.1165	-02233	-0.2627	-0.1697	-0.2061
ECG-LVH	-0.5865	-	-0.1237	-02355	-0.3362	-0.2946
ECG-LVH x male	-	-0.1588	-	-	-	

Table 6.4.4/2. DBP prediction equation coefficients

Coefficients	*CHD*	*MI*	*CHD death*	*Stroke*	*CVD*	*CVD death*
Θ_0	0.9341	3.4587	2.1249	-0.4212	0.6761	0.907
Θ_1	-0.2825	-0.8647	-0.6860	-	-0.2421	-0.452
β_0	15.5222	11.0436	12.0963	25.1067	17.5392	-9.021
Female	32.4811	5.1559	0.2619	0.1558	-0.8019	0.210
log(age)	-1.6346	-0.9302	-1.3025	-3.0997	-2.1231	9.522
$(\log(age))^2$	-	-	-	-	-	-1.399
log(age) x female	-16.4933	-2.6310	-	-	0.2584	
$(\log(age))^2$ x female	2.1059	0.3472	-	-	-	
log(DBP)	-0.8670	-0.5132	-0.4762	-1.7556	-1.0117	-0.507
cigarettes (Y/N)	-0.2789	-0.2721	-0.1553	-0.3975	-0.3900	-0.154
log(total-C ÷ HDL-C)	-0.7142	-0.4228	-0.4056	-0.0297	-0.5365	-0.342
diabetes	-0.2082	-0.1764	-0.0860	-0.4047	-0.3575	-0.117
diabetes x female	-0.1973	-0.1184	-0.2539	-0.2506	-0.1661	-0.198
ECG-LVH	-0.7195	-	-01591	-0.2801	-0.3847	-0.318
ECG-LVH x male	-	-0.1702	-	-	-	

Anderson et al. (1991).

SECTION B

Methods

7 Methods

7.1 Study populations and sampling procedures

7.1.1 Qwaqwa

Qwaqwa with its population of 183 000 (1985 census) was during the Apartheids-era regarded as the traditional homeland of the Sesotho-speaking people and was previously the most rural black population within the borders of the Orange Free State. Qwaqwa is situated in the foothills of the Drakensberg and shares borders with Natal, Lesotho and the Orange Free State. In recent years urbanisation and industrialisation have affected this region profoundly and the capital, Phuthaditjhaba, has typical urban elements. Outside the city the majority of the population still followed a rural or partly rural lifestyle.

Professor D. Stoker of the Human Sciences Research Council designed the sampling frame which included adults 25 years and older. Prof. E. Albertyn, a former head of the Department of Community Health, University of the Free State, advised on the sampling procedure used with the aerial photographs. All villages, including Phuthaditjhaba were proportionally represented in the random sample based on the 1985 census population. In that census the population of Phuthaditjhaba, the main urban area, numbered 20 999 while the rural and semi-rural population numbered 182 629. 37.1% of the population was 25 years and older. Qwaqwa consisted of 12 tribal regions and permission was obtained from each tribal leader before entering and recruiting subjects (Table 7.1.1/1). Based on an estimated prevalence of diabetes of approximately 3%, the calculated sample size was 1900. Since an unrelated male and/or female respondent had to be selected in a standardised way from each household, 950 households had to be identified. The sample was drawn in such a way that a proportional number of households, rounded off to 4, were allocated to each village according to the known number of inhabitants based on the 1985 census (Table 7.1.1/2). Small villages where the number of inhabitants was not known were combined with adjacent villages.

TABLE 7.1.1/1. Sampling Frame of Qwaqwa Region*

Region	Population	Number of persons 25 years and older	Proportional Sample Size	Adjusted Sample Size
1	26800	9943	236	236
2	30800	11427	271	272
3	8600	3191	76	76
4	31400	11649	276	276
5	29700	11019	261	260
6	7200	2671	63	64
7	7100	2634	62	60
8	19000	7049	167	168
9	28050	10407	247	248
10	14100	5231	124	124
11	3830	1421	34	32
12	9500	3525	83	84
TOTAL	216080	80167	1900	1900

* Based on the 1985 census

TABLE 7.1.1/2. Sample Allocation per Village per Region

Region	Village	Sample Size Number of Households	Character	PHC* Clinic
1	Monontsa	52	Rural	18
	Hlatseng	80	Rural	
	Poelong	104	Semi Rural	
	Marallaneng	-	Rural	
	Sehlajaneng	-	Rural	16
2	Kudumane	60	Rural	
	Dithotaneng	108	Semi Rural	
	Makgalwaneng	68	Semi Rural	14
	Mabolela	36	Rural	
	Paballong	-	Semi Rural	15
3	Tseki	76	Semi Rural	11
4	Puthaditjhaba	188	Urban	1 and 7
	Botjahabela	76	Rural	
	Mpatlalatsane	12	Rural	
5	Phahameng	24	Semi Rural	13
	Ha-Nchabeng	112	Rural	
	Matsieng	40	Rural	
	Makong	48	Semi Rural	
	Sebokeng	36	Semi Rural	
	Bolata	-	Rural	12
6	Boiketlong	64	Semi Rural	10
	Phamong	-	Rural	
	Ha-Rankopane	-	Rural	
	Khatleng	-	Rural	
	Maqhasane	-	Rural	
	Namahadi	-	Rural	
7	Mangaung	32	Semi Rural	
	Ha-Sethunya	32	Semi Rural	4
8	Makwane	44	Rural	2
	Comet	48	Rural	
	Tebang	76	Rural	19
9	Thabane-Tsooana	120	Rural	6
	Makeneng	84	Semi Rural	5
	Tsirela	28	Rural	
	Thabang	16	Rural	
	Sekgutlang	-	Rural	

TABLE 7.1.1/2. Sample Allocation per Village per Region (ctd.)

Region	Village	Sample Size Number of Households	Character	PHC* Clinic
10	Mafikeng	44	Rural	7
	Thaba Tshweu	8	Rural	
	Thibella	48	Rural	9
	Lejwaneng	24	Rural	
	Ha-Polane	-	Rural	
	Moeding	-	Rural	
	Masionokeng	-	Rural	
	Phomolong	-	Rural	
	Sejwaleuwale	-	Rural	
	Malekunutu	-	Rural	
11	Rietpan	12	Rural	20
	Makhemeng	20	Rural	
	Matsoakeng	-	-	
	Theseng	-	-	
12	Thaba Bosiu	84	Rural	3
	Qoqolosing	-	-	

*PHC=Primary Health Care Clinic Number

In Phuthaditjaba, 188 households had to be selected. A household was defined as a group of people who cooked and ate together. A recent map of this urban settlement was obtained from the town developers and civil engineers. Street blocks were numbered and 47 (188÷4=47) street blocks were randomly selected with the aid of a table of random numbers (Stoker, 1977). The number of plots per block was counted in a standard way and 4 plots were selected from each block, again with the aid of a table of random numbers. The field workers visited these plots and if a dwelling was present the purpose of the study was explained to the dwellers. A male and/or an unrelated female were selected if and recruited if they were willing to participate. The following exclusion criteria were adhered to: Pregnancy, being bedridden, mental retardation, known malignancies, antituberculous drug therapy, and hospitalisation of more than 1 week during the previous 3 months. Those who are unwilling were also excluded. Those who were willing constituted the actual sample. If no dwelling was present, the next dwelling on the right-hand side, standing in front of the plot was selected. If nobody was home, two more attempts were made at a later date before the dwelling was replaced.

The Department of Water Affairs conducted an aerial survey of the Qwaqwa region 6 months before the commencement of the study and these photographs were available for sampling purposes in the rural and semi-rural areas. The village of interest was identified on the photograph(s) and outlined on transparent wax paper. The outline was transposed onto graph paper and the number of complete squares contained within the outline was counted. If, for example, 12 households had to be selected from this village, 12 squares were selected by a table of random numbers (Stoker, 1977) and the dwelling closest to the centre of the square selected. If nobody was found at home after 3 visits, the dwelling was replaced by another closest to the chosen one.

7.1.2 Mangaung

The population of Qwaqwa was 79 330 according to the 1985 census. From maps of the area all the residential blocks were counted and numbered and 950 housing units were randomly selected following the same procedures as outlined for Phuthaditjaba. An unrelated male and/or female respondent was also selected from each household in the same standardised way as in Qwaqwa.

7.2 General comments

Data collection in Qwaqwa started in June 1989 and was completed in December 1990. The dietary survey took place in March 1991. Data collection in Mangaung commenced in February 1990 but had to be interrupted because of political unrest. It was resumed again in April 1990 and was completed in October 1991 including the dietary survey. The response rates for available subjects were 68% for Qwaqwa subjects and approximately 62% for Mangaung subjects. Unless otherwise indicated the term diabetes in this section is used to refer to Type 2 diabetes.

The sample size in Qwaqwa was 853 (females 574 and males 279). The female to male ratio was 2.1:1. For Mangaung the sample size was 758 (females 468 and males 290). The female to male ratio was 1.6:1. Table 7.2/1 shows the age structure of both populations as well as the corresponding samples.

TABLE 7.2/1. Age and Sex Structure of the Study Populations (%) (Structure of Samples in Parenthesis)

	Age groups (years)				
	25-34	35-44	45-54	55-64	65+
Qwaqwa					
Females	25 (33)	19 (22)	17(14)	18 (15)	21 (16)
Males	20 (36)	24 (25)	10 (16)	16 (10)	30 (13)
Mangaung					
Females	22 (36)	27 (27)	22 (18)	15 (11)	14 (9)
Males	23 (36)	22 (27)	22 (19)	19 (11)	14 (7)

7.3 Measurements

Two fieldworkers of whom at least one was a staff nurse visited the households identified. These visits usually took place on a Friday and a Monday. The study was explained and selected respondents were requested to attend a local clinic in the case of Qwaqwa or the outpatient department at Pelonomi Hospital in the case of Mangaung on a specific day when actual data collection took place at these locations. Subjects who could not travel on their own to these locations were provided with transport on the days their visits were scheduled. Data was collected from small groups of subjects (approximately 8) on a Tuesday, Wednesday and on a Thursday. Subjects were requested to fast overnight. At the clinic or hospital the details of the study were again explained to the participants in their own language by a registered nurse and signed consent was obtained from all participants. Data collection was completed for each subject during one morning visit. Oral temperature was recorded and if abnormal, measurements were postponed. Fasting blood samples were collected for the measurement of plasma glucose, serum insulin, serum C-peptide (Mangaung subjects only), serum pro-insulin, total serum cholesterol (TC), HDLC, TG levels and a biochemistry profile. This was followed by a standard 75 g oral glucose tolerance test (OGTT) and blood samples were obtained at 60 and 120 minutes for the measurement of serum insulin, serum proinsulin and serum C-peptide (Mangaung). Questionnaires were administered, subjects were examined and anthropometric measurements were taken while subjects were waiting for the completion of the OGTT and also after completion of the OGTT. All blood samples were kept on ice until they could be spun down. Serum and or plasma samples were stored at minus 20^0 C until the specimens could be analysed which was done on a weekly basis. Serum samples for proinsulin measurements

were stored at minus 20^0 C and was analysed all at once at the end of the study.

Height was recorded and subjects was weighed dressed in light indoor clothing with the aid of a Seca beam scale and measuring column. Body mass was rounded off to the nearest 0.5 kg. All skinfold measurements were performed in the standing position. Skinfold measurements were made on the left side of the body with a Harpenden skinfold caliper as described by Weiner and Lourie (1969).

Triceps skinfold: While standing in the upright position, subjects were asked to keep the left arm relaxed but flexed 90 degrees at the elbow. A horizontal mark was made with a black koki pencil exactly half way between the inferior border of the acromial process and the tip of the olecranon process. The acromion was defined as the inferior edge of the most external border of the acromial process. The arm was allowed to hang down just away from the body. A skinfold was picked up between the thumb and the forefinger at the back of the arm about 1 cm above the mark on the skin with the skinfold directly in line with the olecranon process. The caliper jaws were applied at exactly the level of the koki mark. The measurement was made 2 seconds after the full pressure of the caliper jaws was applied to the skinfold.

The biceps skinfold: The skinfold was picked up at the front of the arm, with the arm still hanging at the side, directly above the center of the cubital fossa, at the same level that the triceps skinfold measurement was made.
Upper arm circumference: A nylon tape measure was used. While the subject's left arm hanged relaxed but just away from the side, the upper arm circumference was measured in the horizontal plane at the level marked with the koki pen.

The subscapular skinfold: The skinfold was picked up below the angle of the left scapula with the crest at 45 degrees to the vertical.

Parathoracic skinfold: The skinfold was picked up midway between the axilla and iliac crest.

Suprailiac skinfold: Was picked up just above the iliac crest in the mid-axillary line.

Waist circumference: While standing, with the abdomen relaxed and breathing normally, the waist circumference was recorded to the nearest 0.5 cm with fiberglass tape at the end of normal expiration. In male subjects, the tape was held behind the subject with one edge in the

horizontal plane through the center of the umbilicus. The tape was then carefully wrapped around the subject's torso. Care was taken not to exert pressure to the skin. Waist circumference was measured to the nearest 0.5 cm at the level of the umbilicus at the end of expiration while the subject was breathing normally. In female subjects waist circumference was measured in the same way but at the narrowest point between the rib cage and the iliac crest. Hip circumference was measured at the level of the greater trochanter. Both measurements were taken in the horizontal plane. The maximum circumference over the buttocks was also recorded.

Thigh circumference: Thigh length was first measured. While standing, the subject was asked to stand with the left knee slightly flexed, leg abducted and with the left foot remaining on the floor. The skin was marked halfway between the greater trochanter and the inferior border of the lateral epicondyle of the femur. Thigh circumference was measured at this level. Care was taken that the tape remained horizontal and that the skin was not indented by the tape.

All anthropometric measurements, clinical examinations and blood pressure measurements were performed by myself and one medically qualified co-worker (Dr. A Moore) after initial and periodic standardisation of techniques. Duplicate anthropometric measurements were recorded in every 10th respondent as a quality control measure. Results for these standardisation techniques are shown in Annex 2.

A standardised clinical examination was performed on all subjects including fundoscopy through dilated pupils. Blood pressure was measured twice in the supine position by means of a Hawksley random zero sphygmomanometer and a standard 12,5 x 23 cm cuff. The diastolic pressure was taken as the point of disappearance of Korotkoff phase V sounds and the set of readings with the lowest diastolic reading was used for analysis. When the mid-upper arm circumference exceeded 35 cm a large-size cuff (15,5 x 32,5 cm) was used. Finally, a 12 lead resting ECG was performed with a Marquette ECG machine. ECG's were analysed independently by myself and a qualified cardiologist using the Minnesota code for resting ECG's (Rose et al., 1968).

A questionnaire was administered in Sesotho by one of two trained staff nurses to collect data on demography, socio-economic status, physical activity, cardio-respiratory status, health perception, smoking and drinking habits as well as breast-feeding and contraception. Respondents were informed of abnormal clinical or laboratory findings and a referral letter was

provided for participants in need of further medical attention.

7.4 Laboratory analysis

Plasma glucose levels were measured by the glucose oxidase peroxidase method. TC levels were measured by the cholesterol esterase oxidase peroxidase method (Boehringer Mannheim kit). HDLC was measured after precipitation of major lipoproteins by phosphotungstate MgCl by the same method as for TC. Low-density lipoprotein cholesterol (LDLC) was calculated by means of the Friedewald formula." Serum TG levels were determined by the lipoprotein lipase glycerokinase peroxidase method (Boehringer Mannheim kit). Assay precision for TC measurement had a coefficient of variation (CV) of 3-4%; HDLC a CV of 5-6% and TG a CV of 6-7%. Serum insulin was measured with a radio-immune assay (Coat-A-Count®). Serum C-peptide was also measured with a radio-immune assay (Incstar®). Serum intact proinsulin was measured with an immunoradiometric assay with materials provided by Dr. IP Gray. The latter assay was also directly supervised by Dr. IP Gray.

7.5 Statistical analysis

For each population, frequencies and percentages were computed by age group and sex for categorical variables and categorised continuous variables. Age-standardised prevalences were calculated for each population and sex using the sex-specific age structure of the specific target population. Age and sex standardised prevalences were also calculated for each population using the age and sex structure of the specific population. To compare the prevalences between Qwaqwa and Mangaung the prevalences in Mangaung were also standardised to the age and sex structure of the the Qwaqwa population, and 95% confidence intervals were calculated for the differences between these Mangaung and Qwaqwa prevalences.

Means and standard deviations were calculated by age and sex for normally distributed continuous variables. Medians were calculated for continuous variables with skew distributions.

The associations between categorical variables were analysed using relative risks with 95% confidence intervals, and Mantel-Haenszel summary relative risks and 95% confidence intervals, adjusting for age and sex.

The correlations between continuous variables were analysed using partial correlations adjusting for sex. In the case of skew distributions Spearman rank partial correlations were

calculated. The comparison of continuous variables between subgroups were done using t-tests (or Mann-Whitney tests in the case of skew distributions).

In selected cases logistic regression and analysis of covariance was used to investigate the multivariate association between variables.

The homeostasis model assessment method (HOMA) (Mathews et al, 1985) was used to calculate percentage β-cell function and insulin resistance by utilizing fasting plasma glucose and insulin concentrations according to the following formulae: Assuming that normal-weight normal subjects aged < 35 years have 100% β-cell function, and an insulin resistance of 1, the values for a patient can assessed from the insulin and glucose concentrations by the formaulae: β-cell function (%) = 20xinsulin/(glucose-3.5), and (near approximation) resistance = insulin/($22.5e^{-lnglucose}$).

The Framingham equations (Anderson et al., 1991) were applied to calculate the 5 and 10 year risk for various cardiovascular events of respondents 25-74 years old. These equations are given in section 6.4.4.

SECTION C

Results and Discussion

8 Diabetes mellitus and impaired glucose tolerance

8.1 Description of plasma glucose levels in the study populations

Fasting plasma glucose concentrations, concentrations 60 minutes and 120 min after a standard 75 g oral glucose load are shown in Table 8.1/1. A clinically significant rise in mean fasting, 60 min and 2-hour plasma glucose concentration was noted for both sexes and populations with increasing age. The elderly group of women in Qwaqwa was the exception where a slight decrease in fasting glucose concentration was noted compared to the 55-64 year old group.

In the Tanzanian study (McLarty et al., 1989) fasting plasma glucose concentrations were not related to age but 2-hour levels were positively related to age. The progressive decline in glucose metabolism with aging has been shown to correlate with increasing insulin resistance especially at the site of muscle (De Fronzo, 1981). Following oral glucose ingestion, the 1-hour plasma glucose response has been shown to increase by 0.5 mmol/L per decade and the 2-hour plasma glucose value by 0.28 mmol/L per decade (De Fronzo, 1981). This phenomenon of aging, also present in our study populations, may have serious implications for the diagnosis of diabetes using ADA instead of WHO diagnostic criteria. Due to an increased sensitivity of the 2-hour glucose values to aging, WHO criteria which use 2-hour glucose values for the diagnosis of diabetes might be expected to give a higher estimated prevalence of diabetes in older subjects than ADA criteria (Wahl et al., 1998). By using ADA fasting criteria in our study populations, the prevalence of diabetes in elderly subjects may be underestimated.

TABLE 8.1/1. Mean Plasma Glucose Concentration (mmol/L) after a 75 g Oral Glucose Load. Results by Age, Gender and Population (Standard Deviation in Parenthesis)

	n	Time 0 min[a]	n	Time 60 min[b]	n	Time 120 min[b]
Qwaqwa						
Men (age in yr)						
25-34	56	4.6 (0.7)	56	6.4 (2.1)	56	5.1 (1.3)
35-44	68	4.9 (0.6)	68	7.1 (2.1)	68	5.0 (1.6)
45-54	27	5.2 (1. 7)	25	7.8 (2.2)	25	5.9 (1.8)
55-64	45	5.4 (2.0)	43	7.8 (2.0)	41	6.2 (2.0)
65+	82	5.8 (3.3)	75	8.2 (3.2)	77	6.9(3.7)
Women (age in yr)						
25-34	141	4.7 (0.6)	140	6.3 (1.9)	140	5.7 (1.6)
35-44	109	5.2 (2.1)	107	6.8 (3.0)	106	6.4 (2.9)
45-54	99	5.4 (2.0)	99	8.0 (3.7)	98	7.2 (3.9)
55-64	102	6.0 (3.1)	92	8.3 (3.3)	91	7.3 (3.4)
65+	121	5.6 (2.5)	116	8.3 (2.8)	116	7.3 (2.8)
Mangaung						
Men (age in yr)						
25-34	66	5.3 (1.0)	66	6.0 (2.0)	65	5.5 (2.0)
35-44	65	5.4 (0.9)	65	6.5 (1.9)	64	5.8 (1.4)
45-54	64	5.7 (1.8)	62	8.0 (3.5)	62	7.0 (3.2)
55-64	53	6.0 (2.6)	53	8.1 (4.5)	52	6.8 (4.2)
65+	39	6.0 (2.1)	37	8.5 (3.6)	38	6.7 (3.6)
Women (age in yr)						
25- 34	105	5.1 (0.8)	105	6.1 (1.6)	103	5.9 (1.4)
35-44	125	5.5 (1. 7)	124	7.0 (3.2)	121	7.0 (3.1)
45-54	103	5.8 (2.2)	95	7.7 (3.6)	96	7.3 (3.3)
55-64	67	6.0 (2.0)	65	8.1 (3.2)	65	7.9 (3.1)
65+	63	6.4 (2.7)	60	9.1(4.3)	59	8.4 (4.4)

[a] Fasting plasma glucose

[b] Known diabetics excluded

Centiles for fasting and 2-hour plasma glucose concentrations are shown Table 8.1/2 and Table 8.1/3 as well as in Fig. 8.1/1 to Fig. 8.1/4. The median fasting value for Qwaqwa females aged 25-34 years was 4.67 mmol/L and increased to 5.07 mmol/L in the group 65 years and older. The corresponding values for Mangaung females were 4.95 mmol/L and 5.74 mmol/L. The corresponding median fasting values for Qwaqwa and Mangaung males ranged from 4.62 mmol/L to 5.04 mmol/L and 5.15 mmol/L to 5.48 mmol/L. The median 2-hour plasma glucose concentration for Qwaqwa females aged 25-34 years was 5.59 mmol/L and increased to 6.85 mmol/L for those 65 years and older. Corresponding values for Mangaung females were 5.61 mmol/L and 7.37 mmol/L. The corresponding median 2-hour values for Qwaqwa and Mangaung males ranged from 5.04 mmol/L to 6.09 mmol/L and 5.19 mmol/L to 5.7 mmol/L respectively. The rise in median 2-hour plasma glucose concentrations with increasing age was thus more pronounced for females in both populations. Median fasting and 2-hour glucose concentrations were thus overall higher in the urban group compared to the rural group with the exception of elderly males in Mangaung. In the Cameroon study median values for both FPG and 2-hour plasma glucose concentrations were slightly but not always higher in the rural than in the urban group (Mbanya et al., 1997). In Tanzanian subjects fasting blood glucose values did not rise significantly with age but there was a small but significant increase in 2-hour blood glucose levels in older subjects. This increase was related mainly to changes in the upper centiles (McLarty et al., 1989). This may well have been the case in our study populations too. No evidence of bimodality was observed in the distribution of 2-hour plasma glucose concentrations in any of the two FS populations.

SUMMARY

Fasting as well as 2-hour plasma glucose concentrations increased in both samples with age with the exception of the elderly group of women in Qwaqwa. The increase in 2-hour glucose concentrations with aging may result in an underestimation of the prevalence of diabetes should ADA diagnostic criteria be used instead of WHO criteria in FS black populations. This may also possibly be true for other black populations in South Africa as well as in other Sub-Saharan African populations.

TABLE 8.1/2. Centiles of Fasting Plasma Glucose (mmol/L) by Age, Gender and Population

		Centiles					
	n	10th	25th	50th	75th	90th	95th
Qwaqwa							
Males (age in yr)							
25-34	56	3.79	4.20	4.60	5.03	5.46	5.79
35-44	68	4.17	4.51	4.93	5.40	5.63	5.79
45-54	27	4.01	4.45	4.76	5.28	5.90	7.95
55-64	43	4.19	4.59	4.97	5.56	6.39	7.71
65+	80	4.44	4.63	5.04	5.52	6.05	9.52
Females (age in yr)							
25-34	140	4.12	4.44	4.67	5.03	5.31	5.41
35-44	107	4.22	4.54	4.84	5.18	5.86	6.16
45-54	98	4.37	4.63	4.91	5.38	6.63	7.19
55-64	100	4.58	4.75	5.13	5.89	7.66	9.28
65+	121	4.44	4.69	5.07	5.53	6.72	8.22
Mangaung							
Males (age in yr)							
25-34	65	4.37	4.72	5.15	5.56	6.34	6.59
35-44	64	4.68	4.88	5.31	5.67	6.57	6.76
45-54	64	4.22	4.84	5.37	5.93	7.08	7.89
55-64	52	4.23	4.75	5.20	5.71	6.57	7.50
65+	39	4.63	4.87	5.48	6.11	8.25	13.88
Females (age in yr)							
25-34	103	4.27	4.65	4.95	5.51	5.87	6.02
35-44	123	4.53	4.82	5.19	5.60	6.15	7.03
45-54	102	4.20	4.87	5.36	6.16	7.07	7.95
55-64	67	4.58	4.91	5.46	6.17	7.93	9.85
65+	62	4.69	5.10	5.74	6.34	8.96	10.52

TABLE 8.1/3. Centiles of 2-Hour Plasma Glucose (mmol/L) by Age, Gender and Population

		Centiles					
	n	10th	25th	50th	75th	90th	95th
Qwaqwa							
Males (age in yr)							
25-34	56	3.56	4.13	5.04	5.87	6.83	7.36
35-44	68	3.93	4.85	5.52	6.91	8.60	8.75
45-54	27	3.93	4.85	5.65	7.16	8.92	9.02
55-64	43	4.07	5.09	5.75	7.01	8.53	9.90
65+	80	4.19	5.05	6.09	7.32	10.62	14.16
Females (age in yr)							
25-34	140	4.31	4.78	5.59	6.40	7.32	7.74
35-44	107	4.75	5.19	5.87	6.51	7.88	9.40
45-54	98	4.69	5.57	6.25	7.18	9.90	13.40
55-64	100	4.69	5.37	6.86	8.21	10.67	11.03
65+	121	4.94	5.80	6.85	7.81	9.26	12.68
Mangaung							
Males (age in yr)							
25-34	65	3.51	4.11	5.19	5.82	8.35	9.47
35-44	64	4.16	4.62	5.75	6.60	7.70	7.87
45-54	64	3.09	4.84	6.21	7.41	8.81	12.59
55-64	52	3.77	4.73	5.82	7.26	8.65	13.61
65+	39	4.30	5.28	5.70	7.36	9.11	10.47
Females (age in yr)							
25-34	103	4.35	4.84	5.61	6.75	7.35	8.34
35-44	123	4.67	5.20	6.25	7.14	9.09	10.39
45-54	102	4.80	5.55	6.72	7.92	9.67	12.39
55-64	67	5.25	6.27	7.13	8.40	10.61	14.10
65+	62	5.13	6.15	7.37	8.71	12.28	22.32

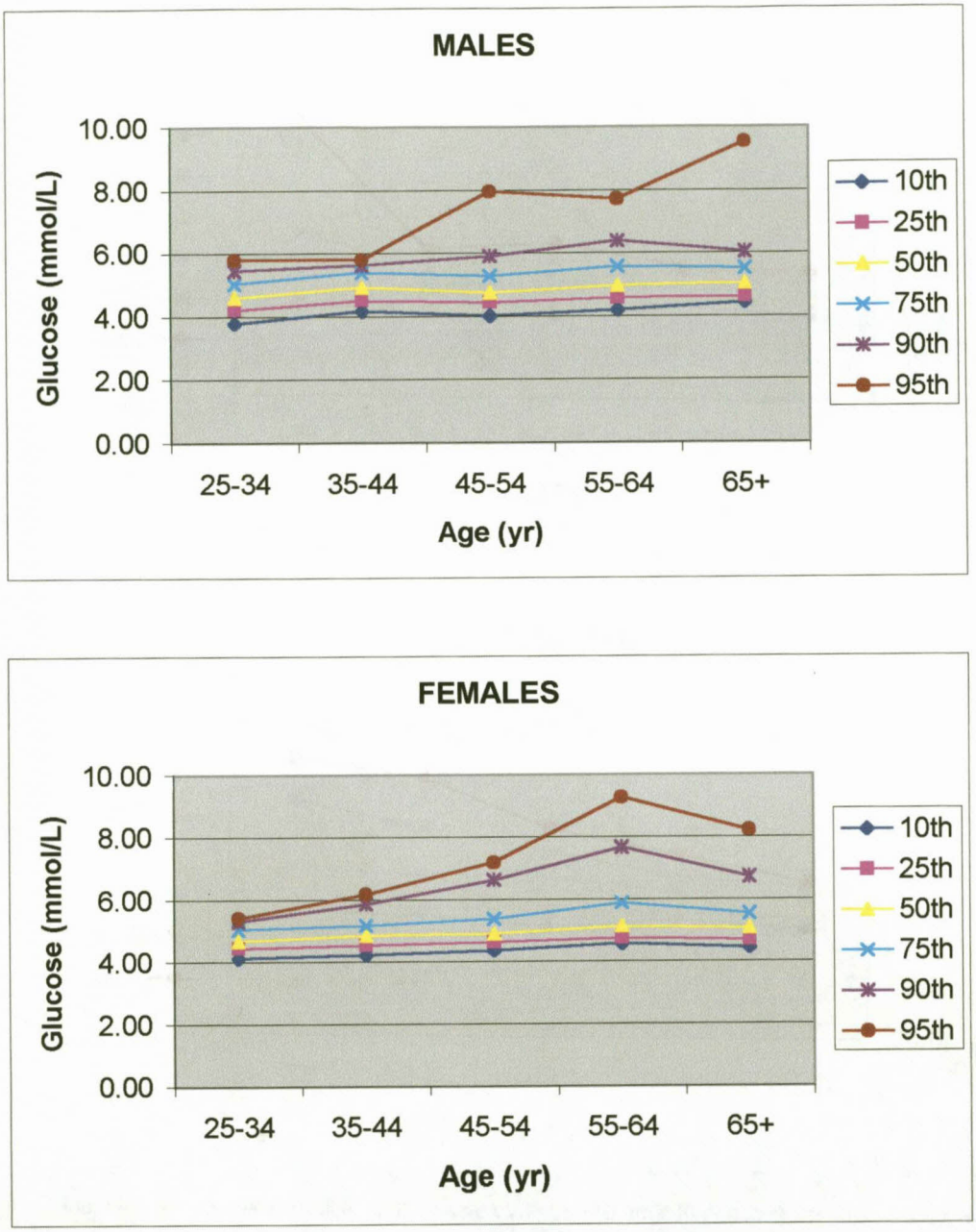


Fig. 8.1/1. Centiles of Fasting Plasma Glucose by Age and Gender for the Qwaqwa Population.

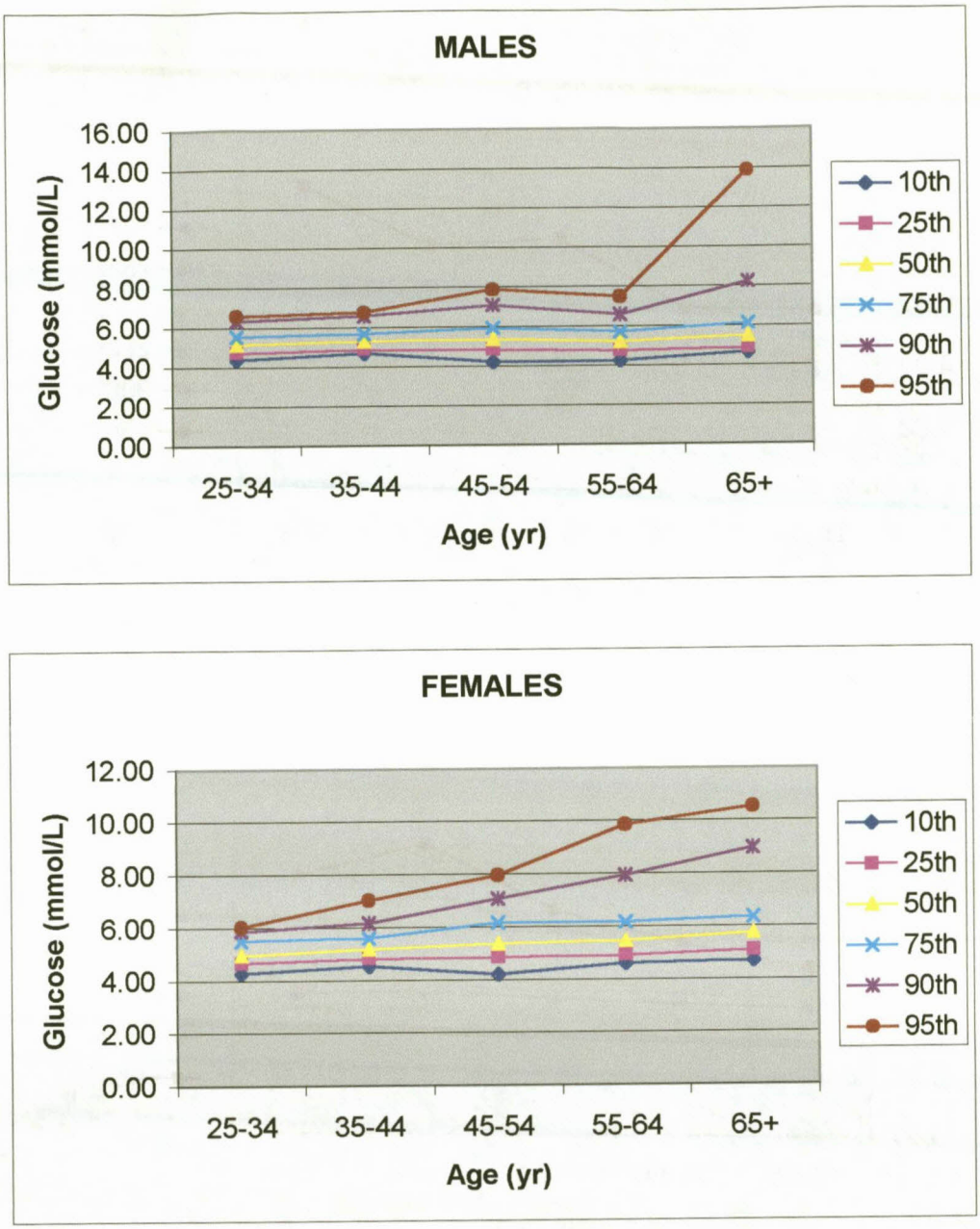


Fig. 8.1/2. Centiles of Fasting Plasma Glucose by Age and Gender for the Mangaung Population

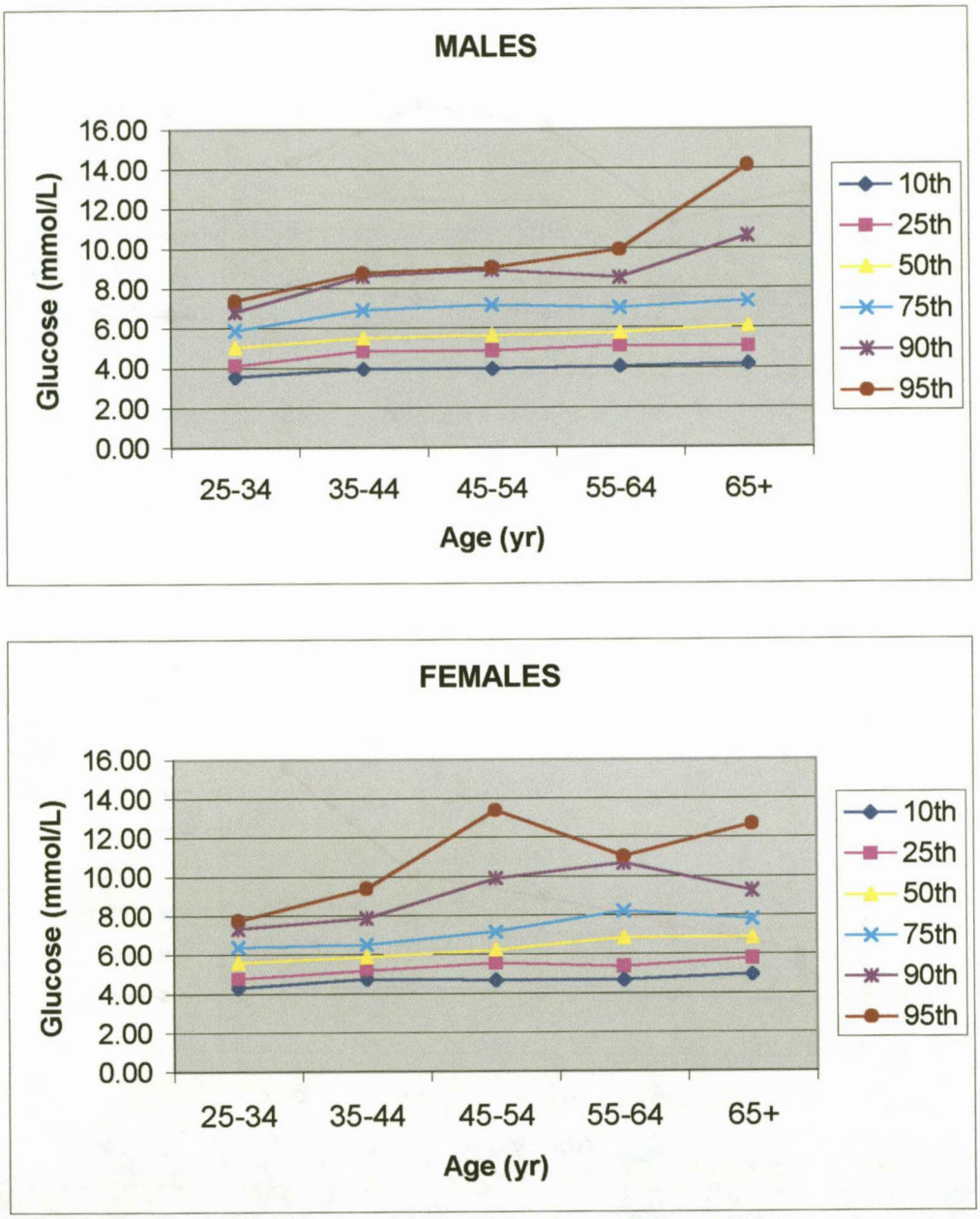
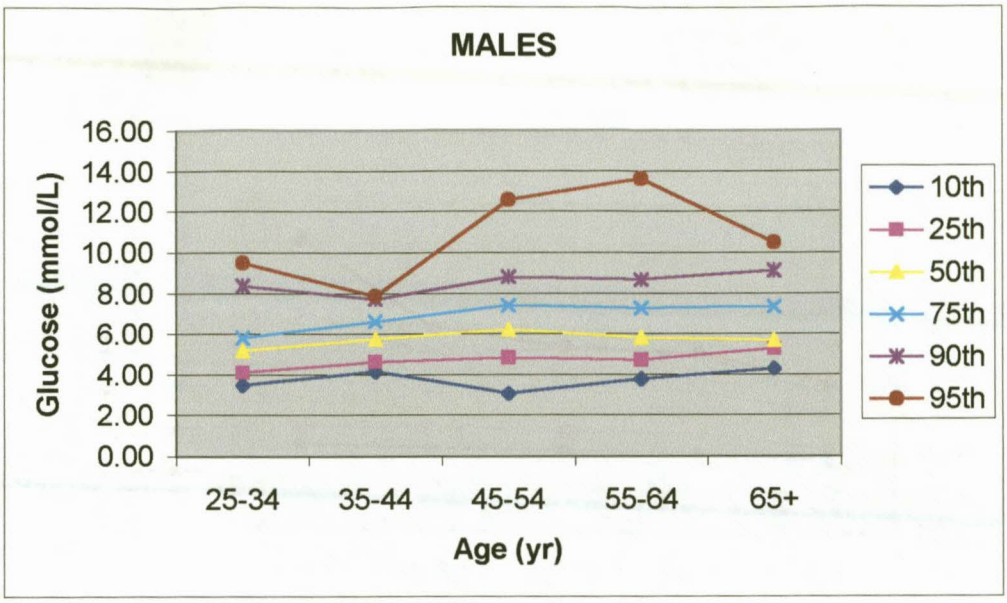


Fig. 8.1/3. Centiles of 2-Hour Plasma Glucose by Age and Gender for the Qwaqwa Population.



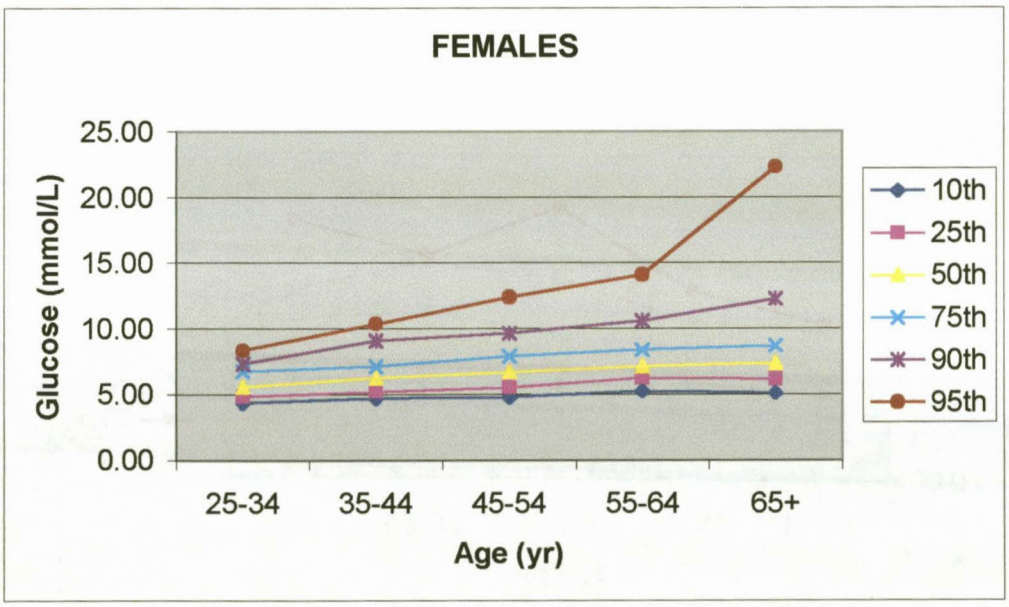


Fig. 8.1/4. Centiles of 2-Hour Plasma Glucose by Age and Gender for the Mangaung Population

8.2 Prevalence of diabetes and impaired glucose tolerance

The mean plasma glucose concentrations according to glucose tolerance status for younger (<45 years) and older subjects (45+ years) are compared in Table 8.2/1. In the normal group the difference in mean FPG concentrations between younger and older patients in both populations was 0.2 mmol/L, while the mean 120-minute concentrations differed by 0.3 mmol/L and 0.4 mmol/L for the Qwaqwa and Mangaung samples respectively. As was expected all the glucose concentrations in both the IGT and the diabetes strata for both populations were significantly different from that of the normal group except for fasting plasma glucose concentrations in the IGT group in Qwaqwa.

TABLE 8.2/1. Mean Plasma Glucose Concentration (mmol/I) According to Glucose Tolerance Status and Age (Standard Deviation in Parenthesis)

	QWAQWA				MANGAUNG			
	n	< 45 yr	n	45+ yr	n	< 45 yr	n	45+ yr
Normal								
0 min	342	4.8 (0.6)	342	5.0 (0.6)	311	5.1 (0.7)	270	5.3 (0.8)
60 min	342	6.2 (1.6)	342	7.2 (1.8)	311	6.0 (1.6)	268	6.9 (2.0)
120 min	342	5.5 (1.1)	342	5.8 (1.1)	311	5.5 (1.1)	270	5.9 (1.3)
IGT								
0 min	24	5.2 (1.1)	81	5.4 (0.8)*	35	6.1 (1.3)*	68	6.0 (1.0)*
60 min	24	9.9 (1.6)*	80	9.8 (1.8)*	35	8.9 (1.9)*	68	9.5 (2.2)*
120 min	24	9.1 (0.9)*	81	9.0 (1.0)*	35	9.0 (0.9)*	68	8.8 (0.8)*
Diabetes								
0 min	5	11.9 (6.8)*	46	11.0 (6.1)*	8	9.1 (5.1)*	47	9.9 (4.3)*
60 min[a]	4	19.0 (7.2)*	24	16.1 (5.7)*	7	15.2(7.7)*	34	16.2 (5.9)*
120 min[a]	4	18.9 (7.5)*	25	16.9 (6.2)*	7	15.3 (8.3)*	34	16.0 (6.0)*

* Significantly different from normal ($p < 0.01$)

[a] For newly diagnosed diabetics only

The age standardised prevalence of diabetes in Qwaqwa was 4.8% (3.5% and 5.7% in males and females, respectively) and of IGT 10.7% (9.9% and 11.3%) (Table 8.2./2). The prevalence of diabetes after adjusting for age in Mangaung was 6.0% (5.0% and 6.8% in males and females, respectively) and of IGT 12.2 % (10.0% and 14.0%) (Table 8.2/2). IGT was twice as common as diabetes in both

populations. The age and sex standardised prevalence of glucose intolerance (diabetes and IGT combined) in Qwaqwa was 15.5% and in Mangaung 18.2%. Overall, a tendency towards a higher prevalence of glucose intolerance was observed in the Mangaung population compared to the Qwaqwa population. The prevalence of diabetes was 6.6% and that of IGT 13% in Mangaung after the sample was sex- and age-standardised to the population structure in Qwaqwa (Table 8.2/2). These differences were not statistically significant.

In the Qwaqwa sample one female and in the Mangaung sample two male diabetics under the age of 35 were identified. Clinically these patients were not obviously Type 1 diabetics although the possibility could not be ruled out completely. The prevalence of diabetes increased across the age intervals in Mangaung females but such an increase was not that evident in the other groups although diabetes was clearly more common in males and females > 45 years. The same observation was made for IGT. Overall, however, a rise in the prevalence of both diabetes and IGT was noted with increasing age. In the age group 65 years and older, a slight decline in the prevalence of diabetes was noted in Qwaqwa females. An unexpected observation was the exceptionally high prevalence of diabetes (14.1%) in Mangaung males in the age group 45-54 years. Apart from pure chance, sampling bias may be a possible explanation.

The two Free State studies were similar to the Cape Town study (Levitt et al., 1993) in many respects including time frame, sample size and methodology. Two exceptions are, however, noteworthy: Firstly, the age distribution differed slightly in that subjects in the Cape Town study were 30 years and older, and secondly their sample was age standardized to the world population as the standard. The age-standardised prevalence of diabetes of 8.0% for the Cape Town study was somewhat higher than that obtained in the Free State (5% for Qwaqwa and 7.1% for Mangaung). In the KwaZulu Natal study, Omar et al. (1992) reported an

TABLE 8.2/2. Prevalence (%) of Impaired Glucose Tolerance (IGT) and Diabetes Mellitus by Sex and Population

	Qwaqwa			Mangaung		
	n	IGT	DM	n	IGT	DM
Men (age in yr)						
25-34	56	3.6	0	65	9.2	3.1
35-44	68	11.8	0	64	7.8	0
45-54	27	14.8	7.4	64	9.4	14.1
55-64	43	16.3	7	52	13.5	7.7
65+	80	12.5	12.5	39	18	5.1
All ages	274	11.3	5.5	284	10.9	6
Age-standardized prevalence		9.9	3.5		10	5
Women (age in yr)						
25- 34	140	4.3	0.7	103	7.8	0
35-44	107	7.5	3.7	123	13	5.7
45-54	98	14.3	7.1	102	18.6	12.8
55-64	100	21	14	67	23.9	13.5
65+	121	19	9.9	62	21	17.7
All ages	566	12.7	6.7	457	15.8	8.8
Age-standardised prevalence		11.3	5.7		14	6.8
Total						
All ages		12.3	6.3		13.9	7.7
Age- and sex-standardized prevalence	840	10.7	4.8	741	12.2	6
Sex- and Age-standardised to the Qwaqwa population structure		10.7	4.8		13.0[a]	6.6[b]
Total (25+ yr)		11.5	5		13.1	7.1
Men		11.2	4.1		10.7	5.7
Women		11.9	5.9		15.5	8.5
Total (30-64 yr)		12.3	4.8		13	7.3
Men		12.2	3.6		9.4	6.3
Women		12.3	6		16.7	8.4

a: (95% CI for difference Qwaqwa-Mangaung −5.8;1.2)

b: (95% CI for difference Qwaqwa-Mangaung −4.1;0.5)

age-and sex-standardised prevalence of 5.3% for diabetes and 7.7% for IGT. The sample size (479) was possibly not optimal for such a study and subjects of 15 years and older were included. The prevalence of diabetes may thus have been underestimated in this study. An obvious difference between these studies was the relative low age-standardised rates of 7.0% and 7.7% for IGT in the Natal and Cape Town studies respectively compared to 12.3% and 13.9% in Qwaqwa and Mangaung respectively. These prevalence rates of IGT are the highest to have been reported in any population in SA as well as in any other Sub Saharan African country thus far. The age-standardised prevalence of IGT in a recent study from Ghana was 10.7% and thus very close to the FS prevalence rates for IGT (Amoah et al., 2002). IGT is regarded as a stage in between normal glucose tolerance and diabetes through which all cases of Type 2 diabetes have to pass (Expert Committee 1997 and WHO, 1998). A potential implication of this observation is that African subjects living in Cape Town and Durban are further advanced on the road of urbanization than Free State blacks and that the prevalence of diabetes in these areas may not increase much in future contrary to the Free State where the prevalence of diabetes may be expected to increase.

The prevalence rates of Type 2 diabetes in the two FS samples were less than that reported for subjects from mixed ancestry in a peri-urban Western Cape community (age-standardised prevalence 10.8%)(Levitt et al., 1999) and approximately half of that reported for a South African Indian community (age- and sex standardised prevalence 13%)(Omar et al., 1994). The odds of being a female in the diabetic group compared to being a female in the non-diabetic group for the Qwaqwa sample was 1.3 (95% CI 0.69 - 2.45). The corresponding odds ratio in females in the Mangaung sample was 1.5 (95% CI 0.84 - 2.7). In both samples the odds of Type 2 diabetes occurring more often in females was statistically significant. The number of known compared to newly diagnosed diabetics is shown in Table 8.2./3. The ratio of known to newly discovered diabetics was almost one. In the NHANES III study (Harris et al., 1998), undiagnosed diabetes constituted 44% of total diabetes in the age group 40-74 years while this figure dropped to 35% when using 1997 ADA criteria. The self-reported prevalence of diabetes in blacks in the SADHS was 1.5% for men and 3.0% for women. Applying the principle of a 1:1 ratio for

known and newly diagnosed cases (Ekoé, 1988) this means that the total prevalence of diabetes in Africans in South Africa is 3.0% and 6.0% respectively for men and women. These rates correspond to a large extent with those found in Cape Town, Durban and the Free State with the exception of male subjects in Cape Town (6.1%) and in Mangaung (5.0%). The true prevalence of diabetes in males may thus have been underestimated in the

TABLE 8.2/3. Characteristics of Newly Diagnosed and Known Cases of Diabetes (Median Age in Years in Parenthesis)

	Known Cases	Newly Diagnosed Cases	Known: New	Female: Male
Qwaqwa				
Males	7 (64.6)	7 (71.6)		
Females	18(63.4)	19(50.1)		
Ratio			1:1.04	2.6:1
Mangaung				
Males	9 (54.5)	8 (51.2)		
Females	20(52.5)	20 (57.2)		
Ratio			1.04:1	2.4:1

SADHS. It is, however, clear that the prevalence of diabetes is presently much higher in black South Africans than was previously accepted (Goldberg et al., 1969).

Compared to black Africans from other sub-Saharan populations the prevalence of Type 2 diabetes in the South African black population is exceedingly high. The prevalence of diabetes in rural Tanzania was 0.87% (McLarty et al., 1989) and in Cameroon the prevalence of diabetes ranged between 0.5% and 1.6% for rural and urban women and 0.9% to 0.8% for rural and urban men respectively (Mbanya et al., 1999). Ghana seems to be an exception among other Sub-Saharan countries with an age-standardised prevalence of diabetes of 6.4%. The stepwise increase in the prevalence of diabetes in black subjects from the African Diaspora described

from the Cameroon to Jamaica and to Britain (Mbanya et al., 1999), as well as from Nigeria to the Caribbean and to the U.S. and the U.K. (Cooper et al., 1997) predict that the prevalence of diabetes in South African blacks may reach levels currently seen in U.K. blacks (10.8%) and U.S. blacks 13.4% (Harris et al., 1998) unless urgent preventative measures are taken.

The median age of known and newly discovered diabetics tended to be higher in the Qwaqwa population. The median age of known as well as newly diagnosed diabetics in Mangaung was very similar to that reported for black subjects in Cape Town (56 years). In Qwaqwa, however, the median age of known cases were almost a decade older than Mangaung subjects while the median age of newly diagnosed cases in Qwaqwa were 7 years younger for females and a decade older for males than in Mangaung. The reason for this discrepancy may be due to the fact that relatively more male subjects were included in the age group ≥ 65 years in the Qwaqwa sample due to the age structure of the population. Although the prevalence of diabetes was very low in the younger age groups in the Free State and Durban studies, a significant number of subjects in the younger age groups in all these studies had IGT (range 3.0% in Durban females to 9.2% in Mangaung males) which may predict more cases of Type 2 diabetes in future in these age groups.

8.3 Metabolic control of known cases of diabetes

The ADA recommends that non-pregnant diabetic individuals should aim for FPG levels of 5.0 to 7.2 mmol/L and that additional action should be taken when FPG levels exceed 8.3 mmol/L (ADA, 2002). The quality of metabolic control of known diabetics in the two studies is shown in Table 8.3/1. Glycaemic control was good in only 4% of known diabetics in Qwaqwa and in 33% of known diabetics in Mangaung (fasting plasma glucose concentration less than 7 mmol/L). This finding is not surprising since patients with diabetes in Mangaung had access to a dedicated diabetes clinic at Pelonomi hospital while patients in Qwaqwa only had access to primary health care at clinic level. The percentage of patients with poor diabetes control in both regions is alarming. These findings are lower than those of Levitt et al. (1997) who demonstrated that approximately 50% of patients attending primary health care clinics in Cape Town had acceptable glycaemic control. A need clearly

exists in both Qwaqwa and Mangaung to improve the quality of care provided to diabetic patients to improve morbidity and mortality outcomes.

TABLE 8.3/1. Control of Diabetes based on Fasting Plasma Glucose

(Percentage in Parenthesis)

	Good FPG<7 mmol/L n (%)	Fair FPG 7-12 mmol/L n (%)	Poor FPG >12 n (%)
Qwaqwa	1 (4)	12 (48)	12 (48)
Mangaung	9 (33)	8 (30)	10 (37)

8.4 Prevalence of IGT and Type 2 diabetes according to the 1997 ADA and 1985 WHO criteria

The ADA proposed in 1997 that new diagnostic criteria should be adopted for the diagnosis of diabetes. The most important recommendation was that diabetes be diagnosed on fasting blood glucose recommendations only. Additionally, a new diagnostic class was created –impaired fasting glucose – to replace IGT. These new criteria were also applied to the Qwaqwa and Mangaung database. These calculations were done for subjects in the age groups 30 years and older for both Qwaqwa and Mangaung as part of a study examining the implications for epidemiological studies applying the 1997 ADA fasting plasma glucose recommendations as the main diagnostic test for diabetes in Sub-Saharan Africa (Levitt et al., 2000).

The numbers of patients with diabetes, IGT and normal glucose tolerance bsed on 1997 ADA and 1985 WHO diagnostic criteria are shown in Fig. 8.4/1 and Fig. 8.4/2. The concordance is especially poor between subjects with IFG and IGT. Since IGT as such has not been properly studied in black subjects in South Africa, it would be premature to abandon the 1985 WHO criteria at this stage. Both sets of criteria should be used and compared until greater clarity emerges as to the prognosis of subjects falling outside either the one or the other set of criteria.

Summary

The prevalence of diabetes and IGT did not differ significantly between the rural and the urban samples indicating that the rural community is possibly already well advanced in the transition process. Similarly, the prevalence of diabetes and IGT also did not differ significantly between males and females and was more common in subjects older than 45 years. The age-standardised prevalence rates of diabetes in black subjects in two FS populations are somewhat lower than that of blacks from a Cape Town urban area but are several fold higher than in black African subjects in Cameroon and Tanzania. The prevalence rates of IGT in the FS studies are the highest recorded for any population in SA thus far. A potential implication of this finding is that the prevalence of diabetes may increase in these populations in the near future. The poor glycaemic control in known diabetics in both samples is a matter of concern but it has to be kept in mind that due to the small number of subjects in this category this observation needs to be investigated further. Measures to prevent an increase in the prevalence of diabetes and to improve the quality of health care for those already affected, should be taken urgently in these communities.

The 1985 WHO diagnostic criteria should be retained and used alongside the WHO 1997 criteria until greater clarity emerges as to the prognosis of subjects falling outside either the one or the other set of criteria. This may be especially important for subjects with IGT.

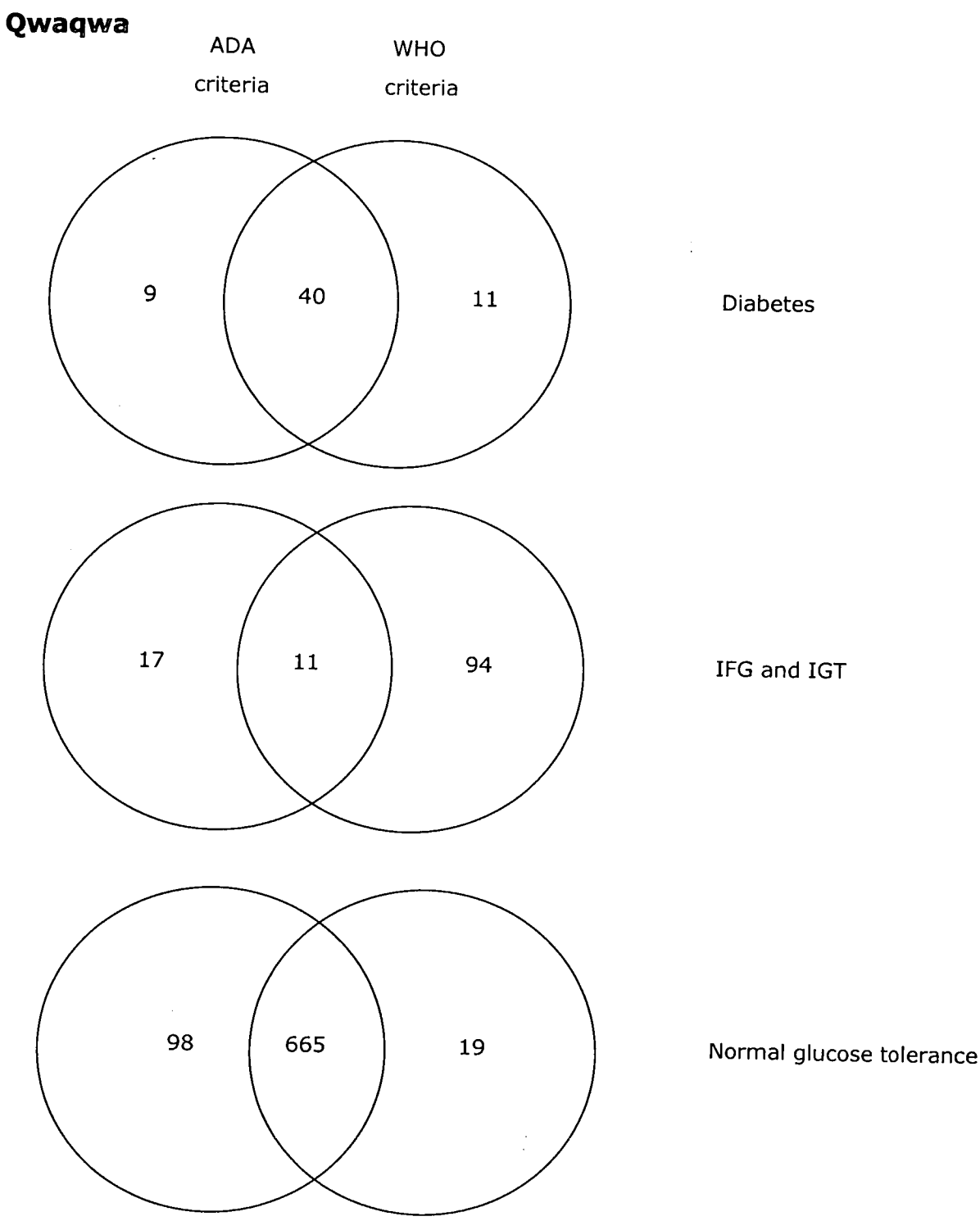


Fig. 8.4/1. Numbers of participants with WHO and ADA diagnostic criteria in the Qwaqwa sample (n= 749, 30 years and older).

Mangaung

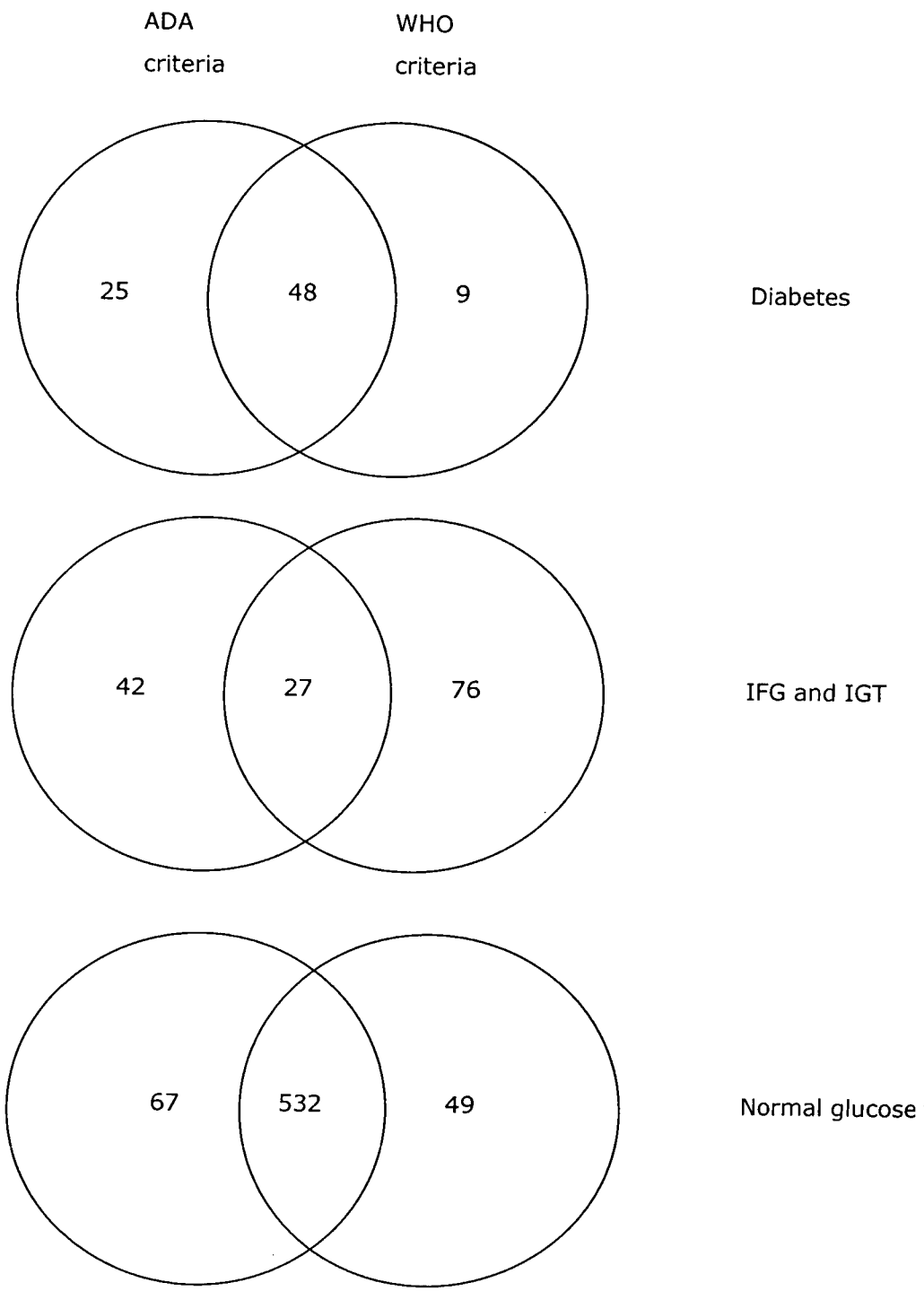


Fig. 8.4/2. Numbers of participants with WHO and ADA diagnostic criteria in the Mangaung sample (n=653, 30 years and older).

8.5 Relationship between obesity, body fat distribution and glucose intolerance

8.5.1 Obesity and glucose intolerance

The relationship between glucose intolerance and pre-obesity after adjusting for age and sex is shown in Table 8.5.1/1. Pre-obesity was defined as a BMI ≥ 25-29.9 kg/m^2 for both sexes (WHO, 1997). The majority of females (in both the younger and older age groups) in both populations had a BMI ≥ 25 kg/m^2 while the majority of men (in both the younger and older age groups) in both populations had a BMI < 25 kg/m^2. The relative risk of glucose intolerance in pre-obese subjects compared to normal weight subjects after adjusting for age and sex is shown in Table 8.5.1/2. In the Qwaqwa sample the summary relative risk of glucose intolerance in pre-obese people compared to non-obese people was 1.3 and failed to reach statistical significance (95% CI 0.93-1.7). In females younger than 45 years this relationship was significant with a relative risk of 4.7 (95% CI 1.1-20). When the relationship between pre-obesity and diabetes and pre-obesity and IGT was examined separately in this sample, it was noteworthy that pre-obesity was significantly associated with diabetes (summary RR = 2.4) whilst IGT was not (Summary RR = 1.0). In the Mangaung sample a more consistent relationship was present between pre-obesity and glucose intolerance. The summary relative risk of glucose intolerance in pre-obese subjects compared to non-obese subjects was 1.9 (95% CI 1.4-2.5). In this population pre-obesity was also significantly associated with both diabetes and IGT (summary RR 2.2 and 1.8 respectively). It may be hypothesized that this tendency towards a more consistent association between pre-obesity and glucose intolerance in Mangaung subjects may be due to more advanced urbanization of the urban group. In the diabetic subgroups in both populations the association between diabetes and pre-obesity was mainly due to the strong association between diabetes and obesity in the older group of females.

The relation between BMI and glucose tolerance in studies from Africa is not consistent. A decade ago Walker et al. (1990) compared random plasma glucose concentrations at least 3 hours after a limited breakfast in a group of 50 healthy obese women (mean BMI=36.8 kg/m^2) matched for age and height with 50 non-obese women (mean BMI=20.2 kg/m^2) from Soweto and found no significant

difference. He attributed this apparently "healthy obesity" to a low fat diet. The sample in the latter study can at best be described as a convenience sample, only apparently healthy subjects were selected, WHR was not determined and semi-fasting plasma glucose levels may not give a true reflection of glucose tolerance in such a small sample. Similar results were obtained in a limited sample of elderly rural women (Walker et al., 1991). In the Durban study significantly higher age-standardised BMIs were present in both diabetic subjects as well as in subjects with IGT (Omar et al., 1992). In Cape Town blacks BMI was associated with diabetes but in peri-urban subjects of mixed ancestry BMI was not associated with diabetes (Levitt et al 1993 and 1999). BMI was negatively related to both FPG and 2-hour plasma glucose in the Tanzanian study (McLarty et al., 1989). In the latter study closer analysis of the BMI association revealed a U-shaped relation with glucose values and the majority of subjects being in the lower BMI group caused the overall negative association. In the Cameroon study the BMI percentiles, FPG and 2-hour glucose percentiles followed the same trends (Mbanya et al., 1997) while BMI and diabetes was positively related in the Ghanaian study (Amoah et al., 2002). The association between pre-obesity and diabetes as well as IGT in both the FS studies is in keeping with the findings of at least two other studies: In the massive health professionals study Chan et al. (1994) showed that even men with a BMI between 23.0 kg/m^2 and 24.9 kg/m^2 at age 21 had an increased risk of diabetes in later life. In another massive study, the nurses health study, Colditz et al. (1990) showed that in women the risk of diabetes starts to increase when BMI exceeds 22 kg/m2 and women at BMI 25-26.9 kg/m2 had more than a fivefold increase in risk of diabetes. Enough epidemiological evidence has now been accumulated to challenge the concept of "healthy obesity" in the South African black population.

TABLE 8.5.1/1. The Prevalence of Glucose Intolerance by Body Mass Index Category, Age and Sex

		Glucose tolerance status		
		Glucose intolerance	Diabetes	IGT
	n	%	%	%
Qwaqwa (age in yr)				
Females (<45)				
BMI ≥ 25	159	10.7	3.1	7.8
BMI < 25	88	2.3	-	2.3
Females (≥45)				
BMI ≥ 25	213	29.6	12.7	19.4
BMI < 25	106	26.4	4.7	22.8
Males (≥45)				
BMI ≥ 25	41	12.2	-	12.2
BMI < 25	82	6.1	-	6.1
Males (≥45)				
BMI ≥ 25	42	21.4	11.9	10.8
BMI < 25	106	25.5	8.5	18.6
Mangaung (age in yr)				
Females (≥45)				
BMI ≥ 25	153	15.7	2.6	13.4
BMI < 25	71	9.9	4.2	5.9
Females (≥45)				
BMI ≥ 25	170	38.8	17.7	25.7
BMI < 25	61	24.6	4.9	20.7
Males (≥45)				
BMI ≥ 25	36	22.2	2.8	20
BMI < 25	92	5.4	1.1	4.4
Males (≥45)				
BMI ≥ 25	53	34	15.1	22.2
BMI < 25	102	16.7	6.9	10.5

TABLE 8.5.1/2. The Relative Risk (RR) of Glucose Intolerance in Obese Subjects (BMI > 25 kg/m^2) Compared to Non-obese Subjects Adjusted by Sex and Age (95% Confidence Interval in Parenthesis)

	Glucose Intolerance	Diabetes	IGT
Qwaqwa (age in yr)			
Females (45)	4.7 (1.1-20)*	a	3.4 (0.79-15.0)
Females (45+)	1.1 (0.8-1.6)	2.7 (1.1-6.8)*	0.85 (0.5-1.4)
Males (45)	2.0 (0.6-6.5)	a	2.0 (0.6-6.5)
Males (45+)	0.8 (0.4-1.6)	1.4 (0.5-3.9)	0.6 (0.2-1.6)
Summary RR	1.3 (0.93-1.7)	2.4 (1.3-4.7)*	1.0 (0.7-1. 5)
Mangaung (age in yr)			
Females (45)	1.6 (0.7-3.5)	0.6 (0.1-2.7)	2.3 (0.8-6.4)
Females (45+)	1.6 (0.98-2.5)	3.6 (1.1-11.4)*	1.2 (0.7-2.2)
Males (45)	4.1 (1.4-11.6)*	2.6 (0.2-40.0)	4.5 (1.4-14.5)*
Males (45+)	2.0 (1.1-3.6)*	2.2 (0.8-5.7)	2.1 (0.95-4.7)
Summary RR	1.9 (1.4-2.5)*	2.2 (1.2-4.0)*	1.8 (1.3-2.7)*

* Statistically significantly different from 1 at the 0.05 level

a Cannot be calculated

8.5.2 Central obesity and glucose intolerance

The WHO (2000) Technical Report recommended the use of a waist-to-hip ratio (WHR) cut-point of 1.0 in men and 0.85 in women as the clinical method of choice to identify patients with central obesity. Since these cut-points have not been adequately validated in black subjects it was decided to use the median values of WHR for males and females specific for each sample instead. The median WHR for Qwaqwa males and females was 0.97 and 0.85 and for Mangaung males and females 0.98 and 0.85 respectively. These values corresponded closely to the WHO cut-points.

The influence of age and body fat distribution on glucose tolerance status is shown in Table 8.5.2/1. In each age category, diabetes, IGT and total glucose intolerance was more common in persons with central obesity than in those with peripheral body fat distribution. In Qwaqwa, no person younger than 45 years and with peripheral body fat distribution had diabetes. On the other hand, glucose intolerance was present in 34.5% of females and 31.2% of males in the age group 45 years and older with central body fat distribution compared to 18.4% of females and 15.5% of males with peripheral obesity. In Mangaung only one person (a male) below the age of 45 years and with peripheral body fat distribution had diabetes while glucose intolerance was present in 43.4% of females and 26.2% of males with central obesity in the age group 45 years and above.

The relative risk for glucose intolerance according to body fat distribution after adjusting for age and sex is shown in Table 8.5.2/2. Glucose intolerance was significantly associated with central obesity in both populations. In the Qwaqwa sample the summary relative risk of glucose intolerance in subjects with central obesity (WHR > median) was 2.3 (95% CI 1.7-3.2). The corresponding summary relative risk for the Mangaung population was 2.8 (95% CI 2.0-3.8). In the IGT subgroup of both populations central obesity was also significantly associated with IGT as was evident from the summary relative risk of 2.1 (95% CI 1.4-3.0) and 2.4 (95% CI 1.6-3.5) for Qwaqwa and Mangaung subjects respectively. The RR for diabetes associated with central obesity in both sexes combined was particularly high namely 3.9 (95% CI 2.0-7.3) in the Qwaqwa sample and 5.0 (95% CI 2.5-

10.1) in the Mangaung sample. It may again be hypothesized that the greater RR in the urban sample might be due to more advanced urbanization.

The relationship between central obesity, age and glucose intolerance is further explored in Fig. 8.5.2/1 and Fig. 8.5.2/2. The prevalence of both diabetes and IGT increased from the lower to the upper WHR tertile groups for females in both samples. The same was true for the prevalence of diabetes in Qwaqwa and Mangaung males. In Qwaqwa, however, no male diabetic was found under the age of 45 years while in Mangaung only 2 male diabetics were younger than 45 years. The relationship between IGT and WHR tertiles for males in both populations was not consistent.

Central obesity was after age the most important predictor of diabetes in the Cape Town study with an OR of 2.94 (95% CI 1.47-5.64), (Levitt et al.1993). In the latter study the OR for obesity to predict diabetes was somewhat lower at 2.31 (95% 1.06-5.02). The cut-off points for WHR in this study were 0.92 for males and 0.84 for females. In the Mamre sample of respondents from mixed ancestry the mean waist circumference of diabetic subjects was 96.5 cm and different significantly from that of non-diabetic subjects (81.7 cm). In the THUSA study conducted in the North West province WHR and waist circumference (WC) correlated positively in black women with fasting serum glucose while logarithmically transformed fasting serum insulin correlated positively with BMI, WC and WHR (Kruger et al., 2001). WHR was not used in any other study from Sub-Saharan Africa making direct comparisons impossible. Probably enough epidemiological evidence has now been accumulated to consider central obesity an important risk factor for diabetes in both black males and females. The first WHO criterion for the existence of the metabolic syndrome in urban and rural black South Africans has been satisfied (Alberti et al., 1998).

TABLE 8.5.2 /1. The Prevalence of Glucose Intolerance by WHR, Age and Sex

		Glucose tolerance status		
		Glucose intolerance	Diabetes	IGT
	n	%	%	%
Qwaqwa (age in yr)				
Females < 45)				
(WHR ≥ Median)	76	19.7	6.6	14.1
(WHR < Median)	170	2.4	-	2.4
Females (≥ 45)				
(WHR ≥ Median)	203	34.5	13.3	24.4
(WHR < Median)	114	18.4	4.4	14.7
Males (≥ 45)				
(WHR ≥ Median)	57	12.3	-	12.3
(WHR < Median)	66	4.6	-	4.6
Males (≥ 45)				
(WHR ≥ Median)	77	31.2	14.3	19.7
(WHR < Median)	71	15.5	4.2	11.8
Mangaung (age in yr)				
Females < 45)				
(WHR ≥ Median)	73	30.1	9.6	22.7
(WHR < Median)	153	5.9	-	5.9
Females (≥ 45)				
(WHR ≥ Median)	159	43.4	18.2	30.8
(WHR < Median)	72	16.7	5.6	11.8
Males < 45)				
(WHR ≥ Median)	34	17.7	2.9	14.7
(WHR < Median)	94	7.5	1.1	6.5
Males (≥ 45)				
(WHR ≥ Median)	107	26.2	13	14.9
(WHR < Median)	48	14.6	2.1	13

(For median values, see text)

TABLE 8.5.2/2. The Relative Risk (RR) of Glucose Intolerance in Subjects with Central Obesity[1] Compared to Subjects with Lower Segment Body Fat Distribution[2] by Age and Sex (95% Confidence Intervals in Parenthesis)

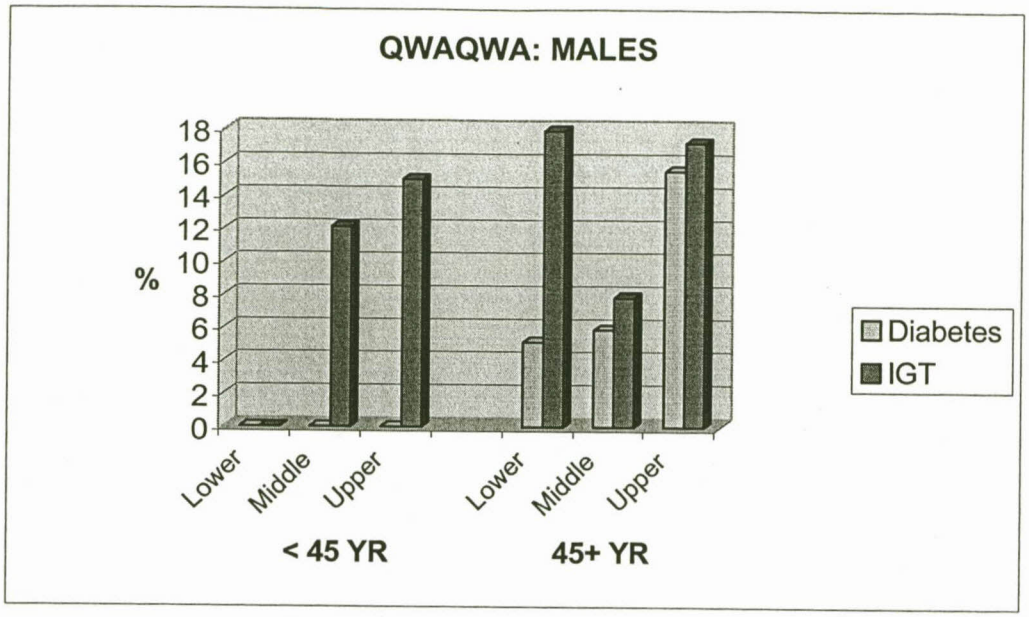
	Glucose		
	Intolerance	Diabetes	IGT
Qwaqwa (age in yr)			
Females (<45)	8.4 (2.9-24.4)*	a	6.0 (1.9-18.5)*
Females (≥45)	1.9 (1.2-2.9)*	3.0 (1.2-7.7)*	1. 7 (0.99-2.8)
Males (<45)	2.7 (0.7-10.0)	a	2.7 (0.73-10.0)
Males (≥45)	2.0.(1.1-3.8)*	3.4 (0.98-11. 6)	1. 7 (0.74-3.8)
Summary RR	2.3 (1.7-3.2)*	3.9 (2.0-7.3)*	2.1 (1.4-3.0)*
Mangaung (age in yr)			
Females (<45)	5.1 (2.5-10.5)*	a	3.9 (1.8-8.4)*
Females (≥45)	2.6 (1.5-4.5)*	3.3 (1.2-9.0)*	2.6 (1.3-5.3)*
Males (<45)	2.4 (0.86-6.5)	2.7 (0.2-41.3)	2.3 (0.74-6.9)
Males (≥45)	1.8 (0.84-3.8)	6.1 (0.8-45.0)	1.1 (0.47-2.8)
Summary RR	2.8 (2.0-3.8)*	5.0 (2.5-10.1)*	2.4 (1.6-3.5)*

[1] WHR ≥ median (Median WHR for females : 0.85 Qwaqwa and Mangaung; Median WHR for males: Qwaqwa 0.97 and Mangaung 0.98)

[2] WHR < median

a Cannot be calculated

* Statistically significantly different from 1 at the 0.05 level



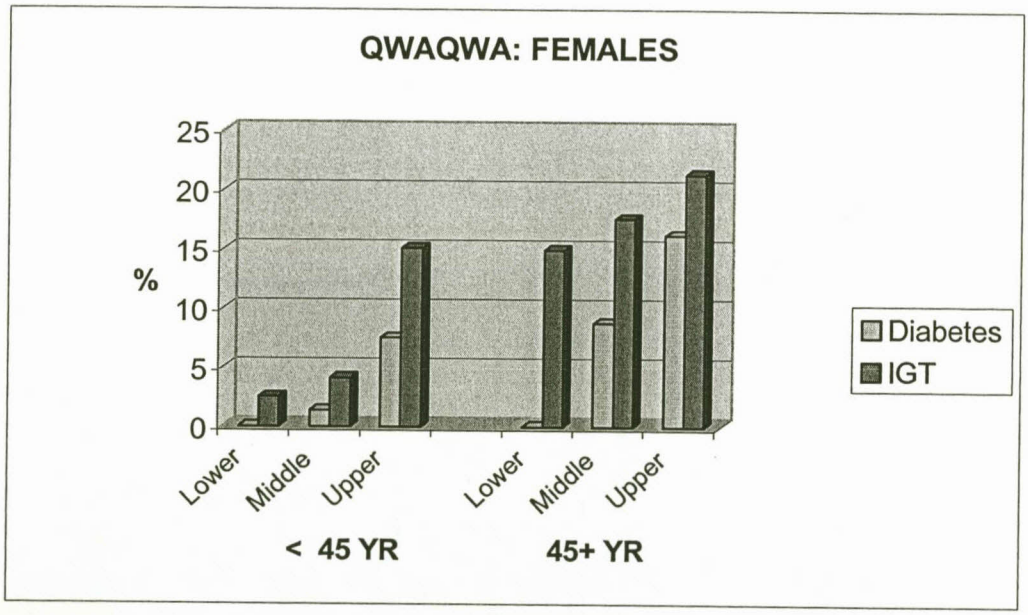
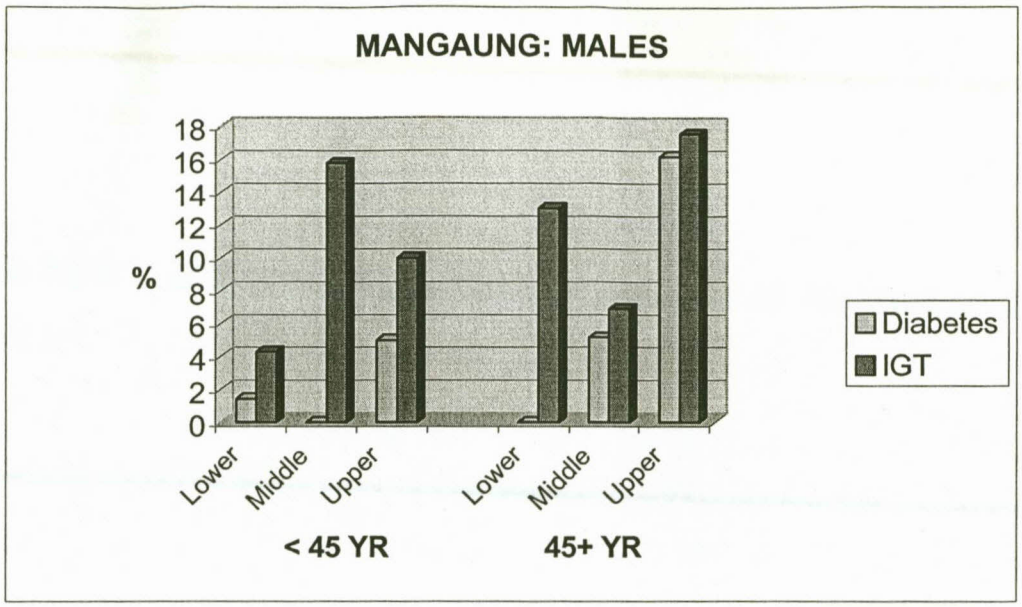


Fig. 8.5.2/1. Prevalence of Diabetes and IGT by WHR Tertiles, Age and Sex in Qwaqwa



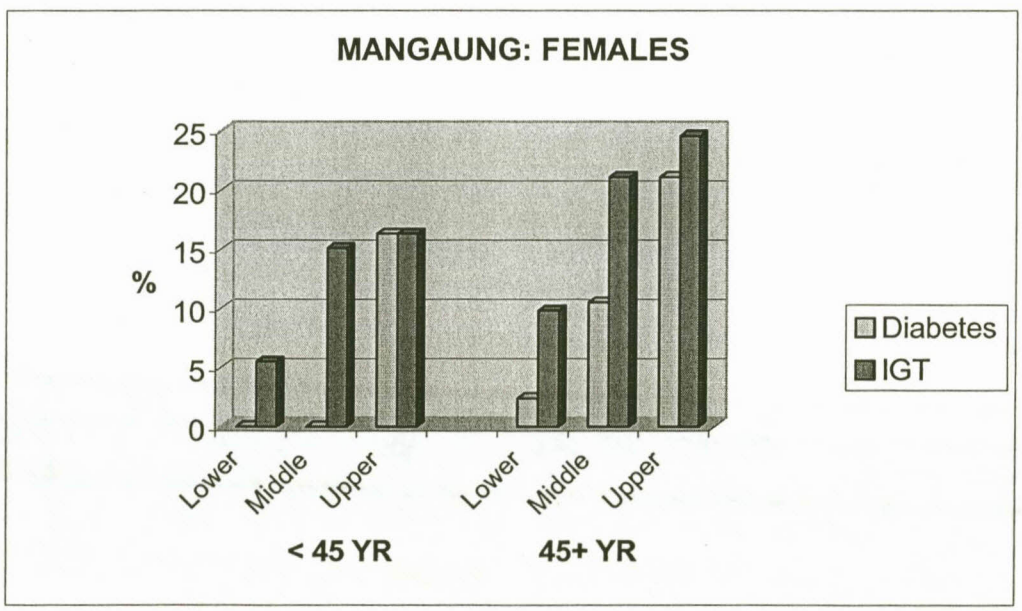


Fig. 8.5.2/2. Prevalence of Diabetes and IGT by WHR Tertiles, Age and Sex in Mangaung

Summary

An important finding is that even mild excess in body fat as indicated by pre-obesity (BMI 25-29.9 lg/m^2) was associated with diabetes in both the FS populations. Pre-obesity was also associated with IGT in the urban sample. The relationship between pre-obesity and glucose intolerance was more consistent in the subgroups in the urban sample than in the rural group. Enough epidemiological evidence has been accumulated to challenge the concept of "healthy obesity" in both urban and rural black South Africans.

Central obesity was significantly associated with diabetes in both the urban and rural samples while central obesity was associated with IGT only in the urban sample. It may be hypothesized that the urban group might be more urbanized than the rural group. In the populations studied the RR for diabetes associated with central obesity was higher than that for pre-obesity. Enough epidemiological evidence has been accumulated to satisfy the first WHO criterion for the existence of the metabolic syndrome in black South Africans.

8.6 Pharmacological treatment of hypertension and glucose intolerance

The relationship between pharmacological treatment of hypertension and glucose intolerance is shown in Table 8.6/1. In the Qwaqwa sample 4.6% of normotensive subjects and 4.9% of untreated hypertensive subjects were diabetic respectively while 16.8% of treated hypertensives were diabetic. Likewise was IGT present in 10.3% of normotensive subjects and
in 13.4% of untreated hypertensive subjects (rate for IGT in population=10.7%) while 23.2% of treated hypertensives had IGT. Similar results were obtained in Mangaung with two exceptions: The prevalence rates of both diabetes and IGT in untreated hypertensives were higher at 9.4% and 18.8% respectively (rate for IGT in the population=12.2%). Glucose tolerance appeared to be worse in treated hypertensives compared to both untreated hypertensives and normotensive subjects in both populations with the exception of IGT in the group of untreated hypertensives in Mangaung.

Since age and BMI may influence the rate of glucose intolerance, these variables were controlled for in calculating the relative risk for glucose intolerance in persons receiving treatment for hypertension (Table 8.6/2). In Qwaqwa subjects, after adjusting for age and BMI, the summary relative risk of glucose intolerance in pharmacologically treated hypertensives compared to untreated hypertensives was 2.2 (95% CI 1.5-3.3). The summary relative risk of glucose intolerance in pharmacologically treated hypertensives compared to normotensives was 1.9 (95% CI 1.32-2.63). The corresponding summary relative risks for the Manguang subjects were 1.3 (95% CI 0.95-1.9) and 1.6 (95% CI 1.1-2.3). The association between pharmacological treatment for hypertension and glucose intolerance was more consistent in the rural sample in both older and younger overweight subjects. A possible explanation for the discrepancy between the two populations may be that high dose thiazide therapy for hypertension was used more frequently in the Qwaqwa sample.

The relationship between hypertension and diabetes as well as between hypertension and IGT is complex even before embarking on pharmacological management. At least five different possibilities exists:

- Hypertension and glucose intolerance may be associated by pure co-incidence since both conditions occur frequently in populations;
- hypertension and glucose intolerance are linked by a common factor (e.g. insulin resistance) which has not been conclusively shown in black South Africans;
- The pharmacological management of hypertension may cause glucose intolerance (Thiazides have been implicated in the past (Alberti et al., 1998));
- The pharmacological management of diabetes (and IGT) may cause hypertension. This possibility is highly unlikely (UKPDS 33, 1998);
- Diabetes (but not IGT) may cause hypertension. 30% of black patients with Type 2 diabetes had persistent proteinuria after 10 years (Motala et al., 2000).

TABLE 8.6/1. The Prevalence (%) of Diabetes and IGT according to Blood Pressure Status[1] and Population

	Normotensives	Untreated Hypertensives	Treated Hypertensives
QWAQWA			
Diabetic	25 (4.6)	10 (4.9)	16 (16.8)
New cases	9 (1.7)	1 (0.5)	1 (1.0)
Known cases	16 (2.9)	9 (4.5)	15 (15.8)
IGT	56 (10.3)	27 (13.4)	22 (23.2)
	462 (85.1)	165 (81.7)	57 (60.0)
Total	543	202	95
MANGAUNG			
Diabetic	21 (4.5)	17 (9.4)	18 (19.0)
New cases	12 (2.6)	10 (5.5)	6 (6.3)
Known cases	9 (1.9)	7 (3.9)	12 (12.7)
IGT	51 (11.0)	34 (18.8)	18 (19.0)
Normal	391 (84.5)	130 (71.8)	59 (62.1)
Total	463	181	95

[1] WHO, 1978

TABLE 8.6/2. The Relative Risk (RR) of Glucose Intolerance in Subjects Treated for Hypertension Compared to subjects not Receiving Treatment Standardised to BMI and Age. (95% Confidence Interval in Parenthesis)

	Treated Hypertensives Compared to Untreated Hypertensives	Treated Hypertensives Compared to Normotensives
Qwaqwa (age in years)		
BMI < 25 kg/m^2, Age <45 yr	a	a
BMI < 25 kg/m2, Age ≥45 yr	1.4 (0.7-3.1)	1.4 (0.69-2.82)
BMI ≥ 25 kg/m2, Age <45 yr	4.1 (0.9-18.4)	2.9 (1.24-6.71)*
BMI ≥ 25 kg/m2, Age ≥45 yr	2.3 (1.4-3.8)*	1.9 (1.22-2.88)*
Summary RR	2.2 (1.5-3.3)*	1.9 (1.32-2.63)*
Mangaung (age in years)		
BMI < 25 kg/m2, Age <45 yr	a	1.6 (0.24-11.0)
BMI < 25 kg/m2, Age ≥45 yr	1.3 (0.54-3.0)	1.8 (0.78-4.0)
BMI ≥ 25 kg/m2, Age <45 yr	0.8 (0.28-2.2)	1.7 (0.66-4.4)
BMI ≥ 25 kg/m2, Age ≥45 yr	1.5 (0.99-2.2)	1.6 (1.0-2.4)
Summary RR	1.3 (0.95-1.9)	1.6 (1.1-2.3)*

a Cannot be calculated

* Statistically significantly different from 1 at the 0.05 level

Summary

A positive association was found between the pharmacological management of hypertension and glucose intolerance in Qwaqwa but not in Mangaung except when treated hypertensives were compared to normotensive subjects in the latter population. The possibility exists that high dose thiazide therapy was used more frequently in Qwaqwa than in Mangaung. The situation might have changed since the introduction of a primary health care Essential Drug List and hypertension management guidelines since 1994. However, it is recommended that this association deserve further investigation.

8.7 Relationship between glucose tolerance status and serum insulin concentrations

Mean age- and sex-specific fasting and post-glucose load serum insulin concentrations for the two populations are shown in Table 8.7/1. No consistent change in mean fasting, 60 min or 120 min serum insulin concentrations were noted with increasing age for either sex or population. Fasting, 60 min and 120 min serum insulin concentrations for both sexes and in all age groups appeared overall higher among Mangaung subjects than Qwaqwa subjects except the 60 min and 120 min mean serum insulin concentration for Mangaung males in the age group 25-34 years which were lower. This difference, however, disappeared when median insulin values were examined. Apart from a true difference, the difference in mean values may also be due to sample handling since Qwaqwa samples were transported on ice in cool boxes from Qwaqwa to the laboratory in Bloemfontein. As expected 60 min serum insulin concentrations were higher than 120 min concentrations in both populations. The same information is also portrayed in graph form in Fig. 8.7/1 and Fig. 8.7/2.

Fig. 8.7/3 and Fig. 8.7/4 portray median serum insulin concentrations in relation to glucose tolerance status in the study populations. Median rather than mean serum insulin concentrations are shown since the SD for insulin measurements were wide. Median fasting serum insulin concentration in Qwaqwa subjects with normal glucose tolerance was 10 µIU/ml. It increased to 50 µIU/ml 60 minutes after a 75g glucose load and decreased again to 39 µIU/ml after 120 minutes. The corresponding values in the Mangaung subjects were 12 µIU/ml, 54µIU/ml and 39 µIU/ml. In the Qwaqwa group of subjects with IGT, the median fasting, 60 and 120 min serum insulin concentrations were 10 µIU/ml, 61 µIU/ml and 56 µIU/ml respectively which is in keeping with increased insulin secretion due to increased insulin resistance in people with IGT (De Fronzo 1988). These values were mirrored in the Mangaung group with IGT. The corresponding values were 15 µIU/ml, 80 µIU/ml and 80 µIU/ml. The median fasting serum insulin concentration for Qwaqwa diabetics (known and new diabetics combined) was 13 µIU/ml. For newly diagnosed diabetics the 60 and 120 min post glucose load median serum insulin concentrations were 36 µIU/ml and 42 µIU/ml respectively.

In Mangaung diabetics the corresponding median serum insulin concentrations were 15 μIU/ml, 44 μIU/ml and 57 μIU/ml. The decreased serum insulin concentrations at 60 min and 120 min in newly diagnosed diabetic subjects compared to the corresponding serum insulin values in subjects with IGT in the face of higher plasma glucose concentrations are clearly indicative that insulin secretion in these subjects are on the downward slope of the Starling curve of the beta cell (De Fronzo, 1988). The 120 min median serum-glucose concentrations in diabetic subjects were also higher than that of normal subjects at the same time point (Fig. 8.8/2). Although these values were elevated compared to normal it was still inadequate to normalise blood glucose.

To further examine the effect of age on serum insulin concentrations, each population was divided into a group younger than 45 years and a group 45 years and older (Table 8.7/2). In the subjects with normal glucose tolerance mean serum insulin concentrations were very similar for both age groups and both populations. In subjects with IGT, mean serum insulin concentrations were overall lower in the older groups in both populations and this was especially the case for Qwaqwa subjects. In the older diabetic subjects from both populations mean fasting serum insulin concentrations very slightly higher than in younger subjects. In older subjects in the Mangaung sample 60 min and 120 min serum insulin concentrations were lower than in the younger group.

Since standard deviations for insulin were wide, median serum insulin concentrations according to glucose tolerance status and age is also shown alongside the corresponding plasma glucose concentrations (Table 8.7/3). The effect of age on post-glucose load insulin secretion is particularly obvious when median values are examined. Older subjects with IGT and diabetes secreted less insulin than younger subjects in both populations. Because the data in the groups were skew, the nonparametric Mann-Whitney test was used to compare median insulin concentrations between the groups. In the Qwaqwa sample, median serum insulin concentrations at 60 min and 120 min in persons younger than 45 years with IGT were significantly different from corresponding concentrations in subjects with normal glucose tolerance, while in those older than 45 years only the 120 min concentration was significantly different from normal. This indicates poor beta cell function in this group. In the Mangaung sample, median fasting, 60 min and 120

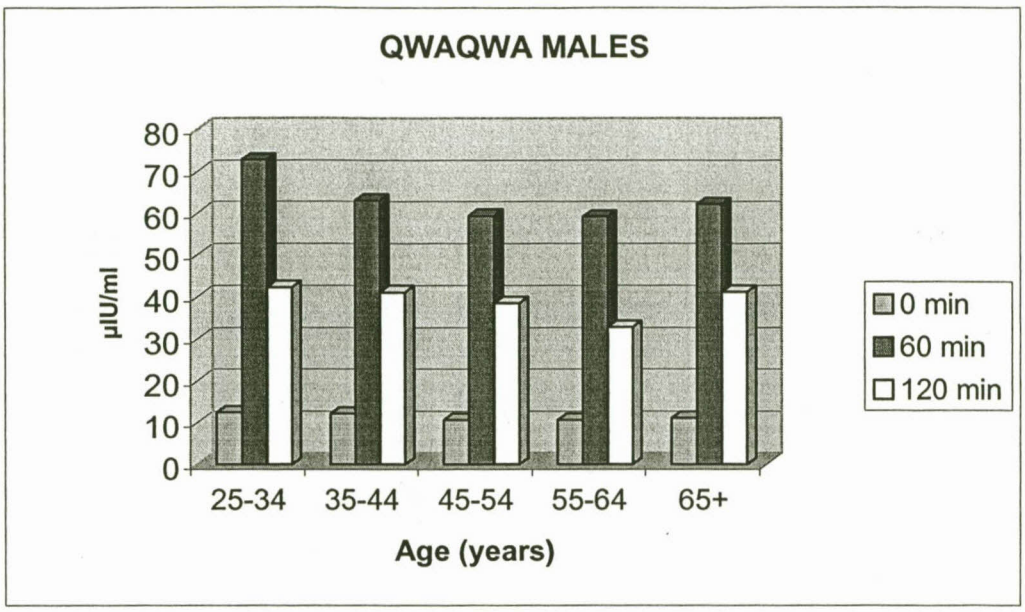
min serum insulin concentrations in persons with IGT were significantly different from normal in both age categories except for subjects older than 45 years in whom median fasting serum insulin concentration failed to be statistically different from normal. Median insulin concentrations in persons with diabetes from both populations and both age groups were not significantly different from those with normal glucose tolerance except in one subgroup (Qwaqwa, older than 45 years). This reflects inadequate insulin secretion in subjects with diabetes since plasma glucose concentrations were higher in diabetics than in both subjects with IGT or normal glucose tolerance (Table 8.7/3). In none of the other epidemiological studies investigating diabetes and IGT in black subjects in South Africa or Sub-Saharan Africa were insulin measurements reported as part of the OGTT. It is therefore not possible to compare the insulin response to the OGGT of the subjects in the FS studies to other subjects from the same ethnic background. In the Cameroon offspring study a different insulin assay was used making direct comparisons difficult.

TABLE 8.7/1. Mean Serum Insulin Concentration (μIU/ml) after a 75 g Oral Glucose Load. Results by Age, Gender and Population (Standard Deviation in Parenthesis)

	Time		
	0 min[a]	60 min[b]	120 min[b]
Qwaqwa			
Men (age in yr)			
25-34	12.4 (9.3)	72.8 (92.0)	42.3 (55.6)
35-44	12.1 (8.3)	63.1 (57.8)	41.1 (32.3)
45-54	10.6 (6.9)	59.4 (48.0)	38.5 (31.6)
55-64	10.6 (7.8)	59.2 (39.9)	32.8 (23.9)
65+	11.1 (8.6)	62.2 (36.1)	41.2 (23.3)
Women (age in yr)			
25-34	12.7(7.4)	67.6 (45.1)	55.8 (31.2)
35-44	15.0 (11.8)	68.4 (62.8)	56.8 (52.1)
45-54	15.3 (36.1)	62.2 (37.1)	48.2 (32.1)
55.64	14.4 (16.3)	66.9 (47.0)	55.3 (42.3)
65+	13.1 (10.4)	70.2 (54.0)	54.6 (44.5)
Mangaung			
Men (age in yr)			
25-34	14.9 (12.9)	49.5 (23.9)	34.8 (36.8)
35-44	15.3 (16.3)	72.0 (49.8)	43.6 (40.9)
45-54	17.8 (29.7)	67.1 (64.8)	45.0 (45.2)
55-64	14.0 (12.2)	68.2(42.1)	53.8 (50.2)
65+	23.5 (47.7)	85.0 (61.4)	47.6 (41.7)
Women (age in yr)			
25-34	17.8 (13.6)	73.5 (53.7)	59.2 (45.8)
35-44	18.6 (22.9)	75.1 (66.1)	65.0 (71.3)
45- 54	20.6 (15.5)	76.0 (48.4)	62.5 (41.0)
55-64	19.0 (20.5)	64.9 (31.8)	62.5 (37.1)
65+	19.3 (25.6)	89.3 (62.2)	65.2 (45.9)

[a]Fasting serum insulin

[b] Known diabetics excluded



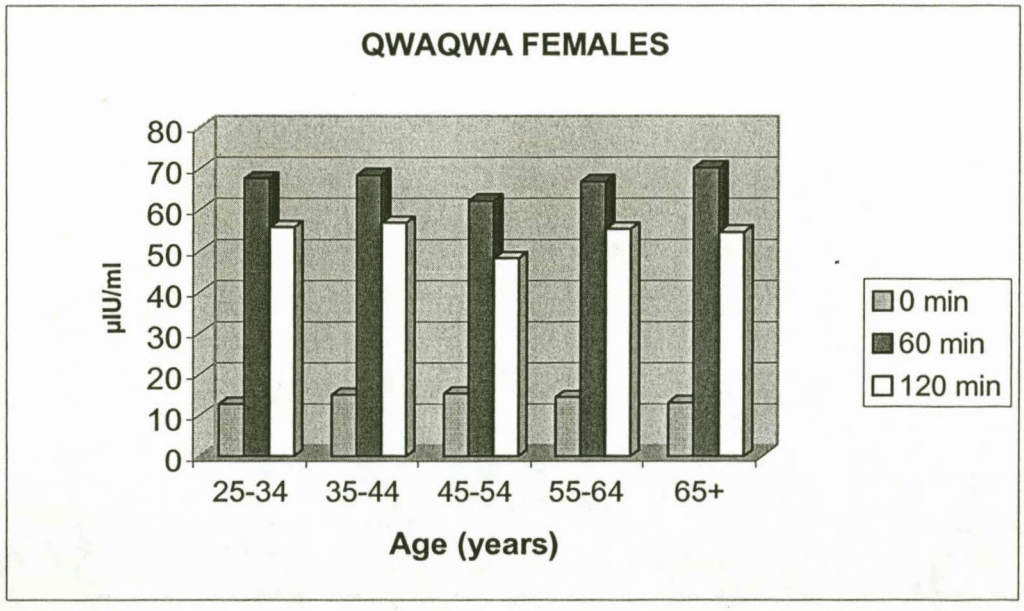
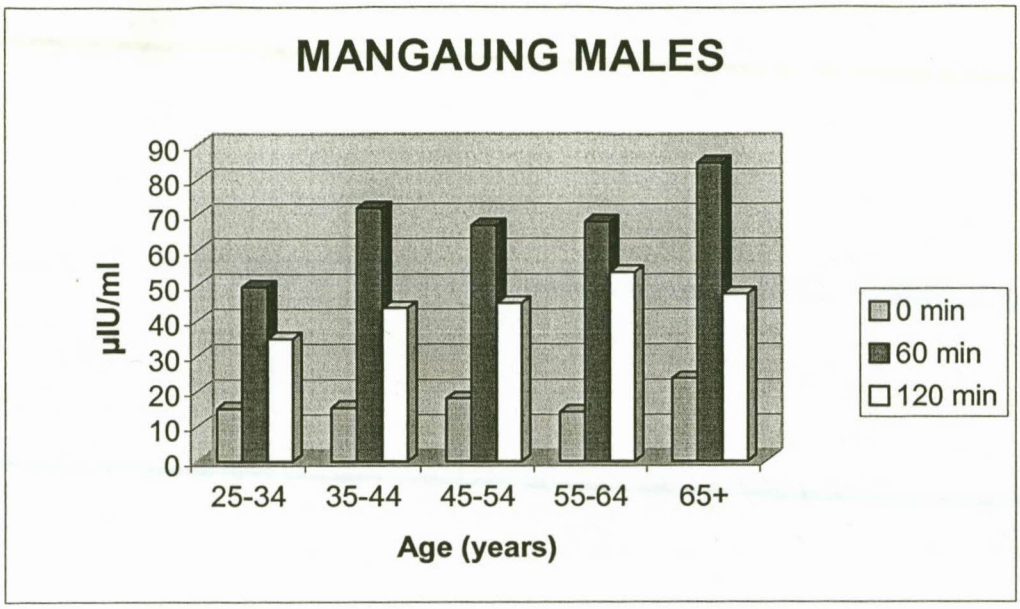


Fig. 8.7/1. Serum insulin concentrations during 75 g OGTT in Qwaqwa males and females



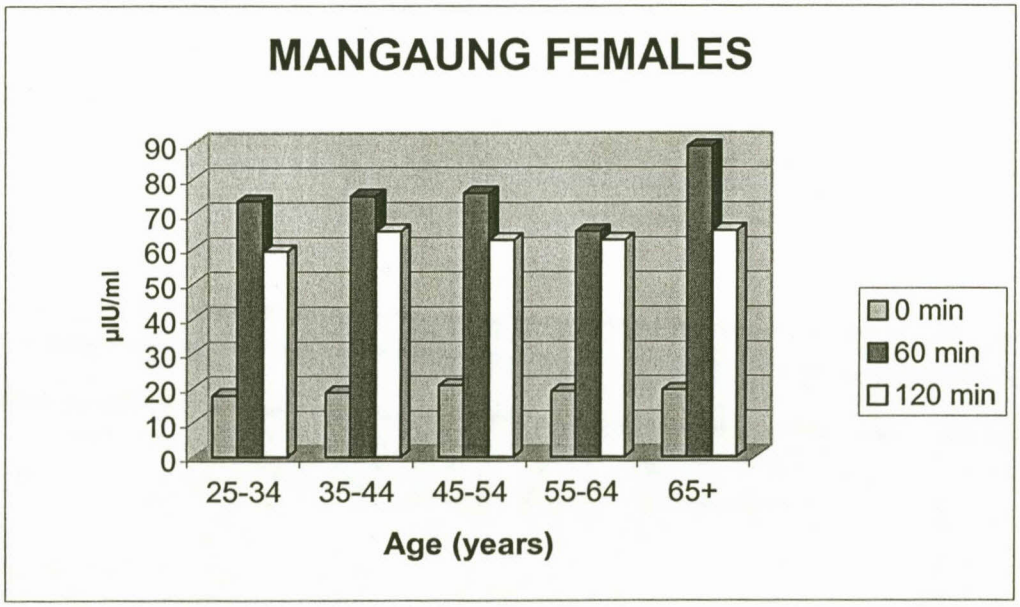
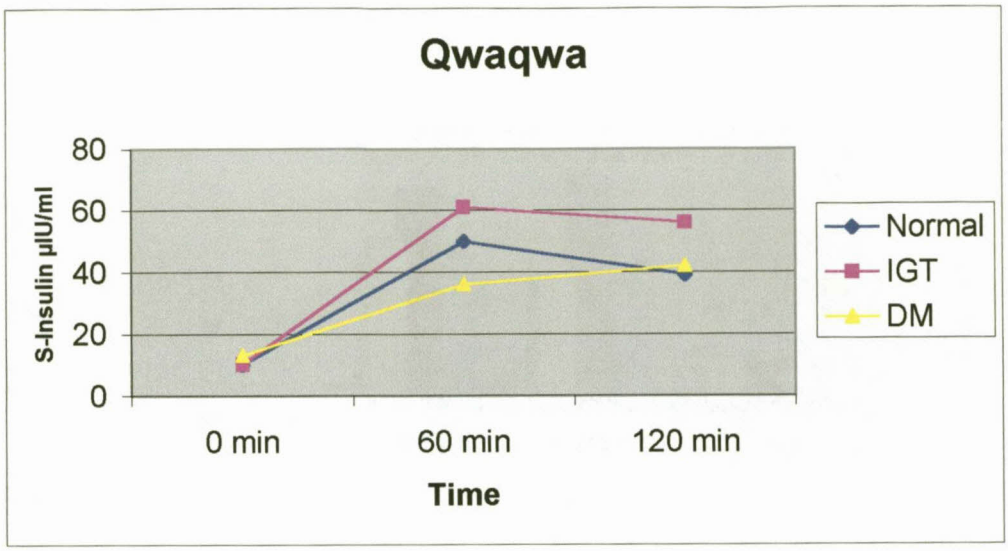


Fig. 8.7/2. Serum insulin concentrations during 75 g OGTT in Mangaung males and females



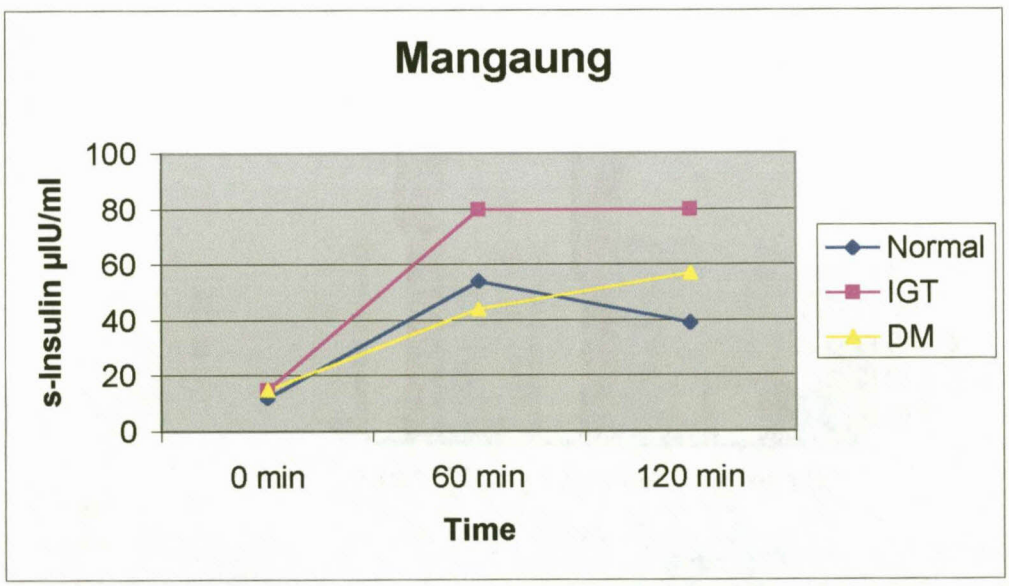
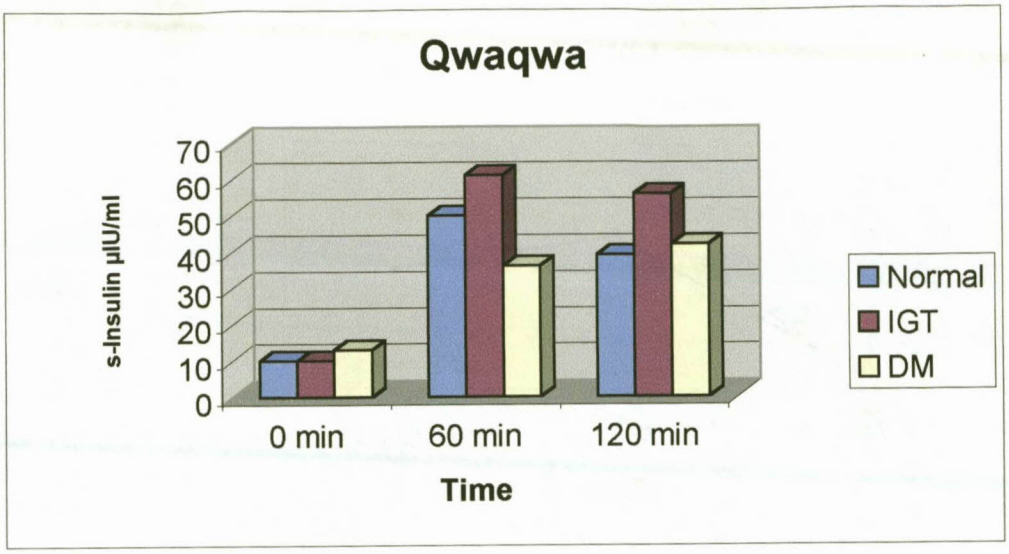


Fig. 8.7/3. Median serum insulin concentrations after a 75 g OGTT according to glucose tolerance status and region.



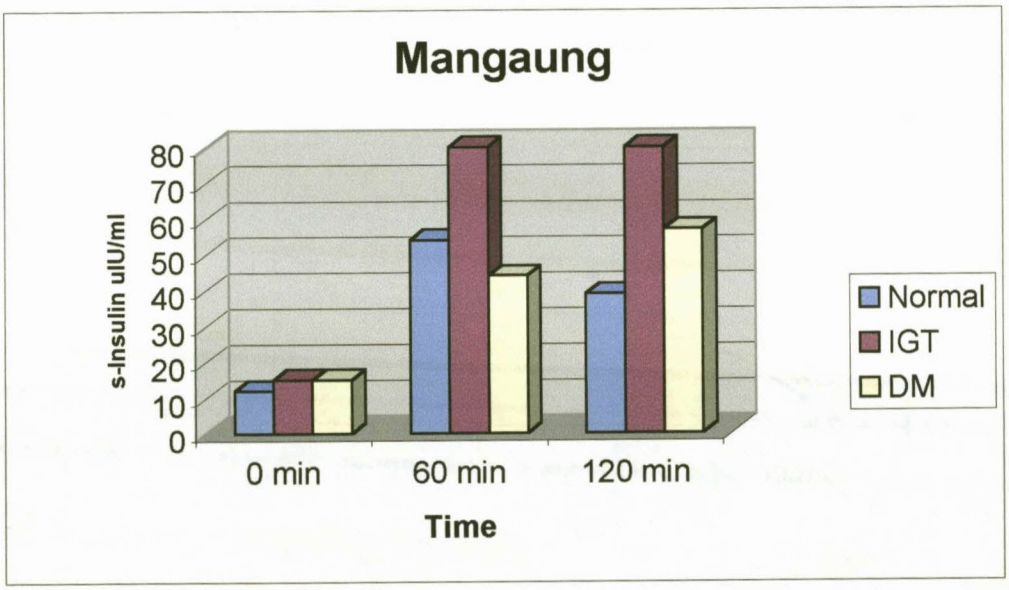


Fig. 8.7/4. Median s-insulin concentrations after a 75 g OGTT according to glucose tolerance status and region.

TABLE 8.7/2. Mean Serum Insulin Concentration (μIU/ml) According to Glucose Tolerance Status and Age (Standard Deviation in Parenthesis)

	QWAQWA		MANGAUNG	
	< 45 yr	45+ yr	< 45 yr	45+ yr
Normal				
0 min	13 (8.8)	12 (20.7)	16(13.1)	16 (16.0)
60 min	65 (58.7)	65 (39.7)	64 (43.2)	69 (43.1)
120 min	46 (29.8)	43 (27.0)	44 (30.7)	48 (32.8)
IGT				
0 min	19 (15.0)	13(10.7)	31 (38.5)	26 (39.0)
60 min	110 (88.3)	69 (63.0)	117 (94.3)	101 (78.2d)
120 min	130 (100)	71.4 (59.7)	127 (100.3)	93 (59.8)
Diabetes				
0 min	17(6.4)	19 (21.7)	23(16.1)	27(37.7)
60 min[a]	39 (24.0)	50 (38,0)	86 (103.6)	67 (49.6)
120 min[a]	52 (39.2)	49 (29.5)	125 (142.5)	63 (49.5)

[a] For newly diagnosed diabetics only

TABLE 8.7/3. Mean Plasma Glucose and Median Serum Insulin Concentrations According to Glucose Tolerance Status, Age and Region (SD)

	QWAQWA		QWAQWA		MANGAUNG		MANGAUNG	
	< 45 yr		45+ yr		< 45 yr		45+ yr	
	Glucose mmol/l	Insulin µIU/ml	Glucose mmol/l	Insulin µIU/ml	Glucose mmol/l	Insulin µIU/ml	Glucose mmol/l	Insulin µIU/ml
Normal								
0 min	4.8 (0.6)	10	5.0 (0.6)	10	5.1 (0.7)	12	5.3 (0.8)	12
60 min	6.2 (1.6)	49	7.2 (1.8)	53	6.0 (1.6)	51	6.9 (2.0)	59
120 min	5.5 (1.1)	41	5.8 (1.1)	38	5.5 (1.1)	37	5.9 (1.3)	42
IGT								
0 min	5.2 (1.1)	13	5.4 (0.8)*	10	6.1 (1.3)*	18*	6.0 (1.0)*	13
60 min	9.9 (1.6)*	94*	9.8 (1.8)*	49	8.9 (1.9)*	96*	9.5 (2.2)*	80*
120 min	9.1 (0.9)*	106*	9.0 (1.0)*	51*	9.0 (0.9)*	93*	8.8 (0.8)*	77*
Diabetes								
0 min	11.9 (6.8)*	13	11.0 (6.1)*	13*	9.1 (5.1)*	20	9.9 (4.3)*	14
60 min[a]	19.0 (7.2)*	39	16.1 (5.7)*	36	15.2(7.7)*	54	16.2 (5.9)*	44
120 min[a]	18.9 (7.5)*	48	16.9 (6.2)*	42	15.3 (8.3)*	79	16.0 (6.0)*	52

[a] For newly diagnosed diabetics only

* Significantly different from normal ($p < 0.01$)

8.8 Homeostasis model assessment

The Homeostasis model assessment (HOMA) (Matthews et al., 1985) was used to determine beta-cell function and insulin resistance from fasting plasma glucose and median serum insulin concentrations. Beta-cell function and insulin resistance in the age- and glucose tolerance subgroups for both populations are shown in Table 8.8/1 and Fig 8.8/1.

The HOMA model equations were developed assuming that normal-weight normal subjects aged < 35 years have 100% β-cell function, and an insulin resistance value of 1 (Mathews et al., 1985). In neither of the populations was any consistent relationship found between median fasting plasma insulin, beta-cell function and insulin resistance between the categories of glucose tolerance. Beta-cell function in normal subjects in both samples ranged from 137%-175%. Relative insulin resistance ranged between 2.1 and 2.8. Insulin resistance was significantly higher in all diabetic subjects in both populations compared to normal subjects with the exception of younger subjects in Mangaung. Beta-cell function was significantly decreased in both older groups of diabetic subjects compared to normal subjects. In subjects with IGT β-cell function was significantly lower in older Qwaqwa subjects compared to older normal subjects. Insulin resistance was significantly higher in the younger group with IGT compared to young normal subjects in Mangaung.

The HOMA model has not been validated in black South Africans and therefore these results should be interpreted with some reservation. According to the model most subjects with diabetes are 2-3 times more insulin resistant than normal subjects. Significant insulin resistance could, however, not be demonstrated in all subjects with IGT. Beta-cell function was decreased according to the model in at least older subjects. Overall, Mangaung subjects tended to be more insulin resistant than Qwaqwa subjects especially in the IGT group. It may again be hypothesized that more advanced urbanization may be the mechanism. Other methods to investigate and quantify insulin resistance in the different categories of glucose tolerance may be necessary to better understand the pathophysiology of IGT and Type 2 diabetes in these populations.

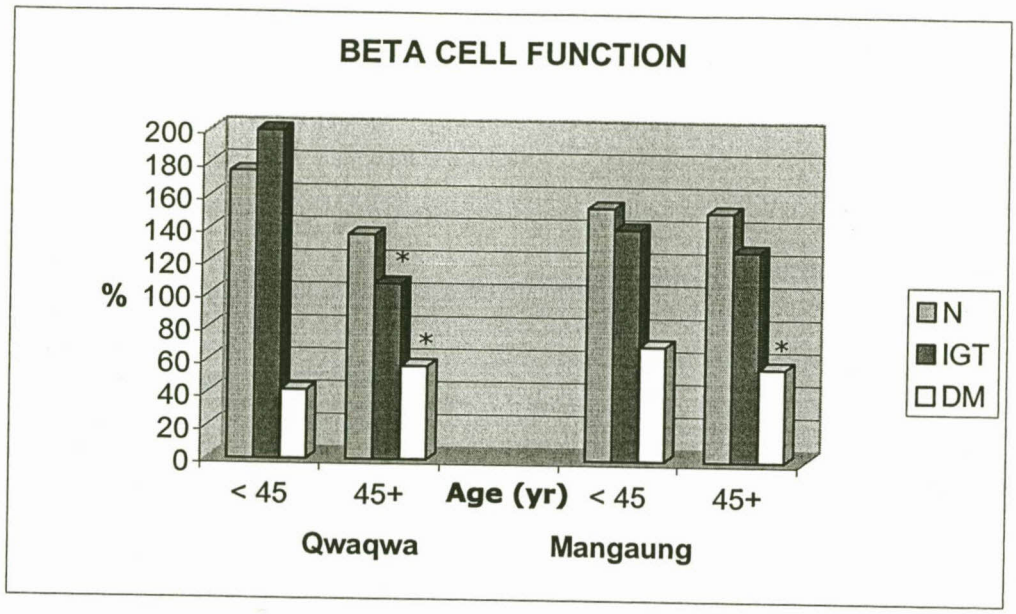
TABLE 8.8/1. Mean Fasting Plasma Glucose (mmol/L) and Median Fasting Serum Insulin (μIU/ml) Concentrations, Median Beta-Cell Function (%) and Median Relative Insulin Resistance by Glucose Tolerance Status, Age and Population

	QWAQWA		MANGAUNG	
	< 45 yr	45+ yr	< 45 yr	45+ yr
Normal				
n	342	342	311	270
p-Glucose	4.8	5	5.1	5.3
s-Insulin	10	10	12	12
BCF[a]	175	137	154	152
IR[b]	2.2	2.1	2.8	2.8
IGT				
n	24	81	35	68
p-Glucose	5.2	5.4	6.1	6
s-Insulin	13	10	18.0*	13
BCF[a]	200	107*	141	128
IR[b]	2.7	2.4	4.7*	3.4
Diabetes				
n	5	46	8	47
p-Glucose	11.9	11	9.1	9.9
s-Insulin	13	13	20	14
BCF[a]	42	57*	70	57*
IR[b]	6.9*	6.8*	7	7.0*

* Significantly different from normal ($p < 0.05$)

[a] BCF = Beta-cell function

[b] IR = Insulin resistance



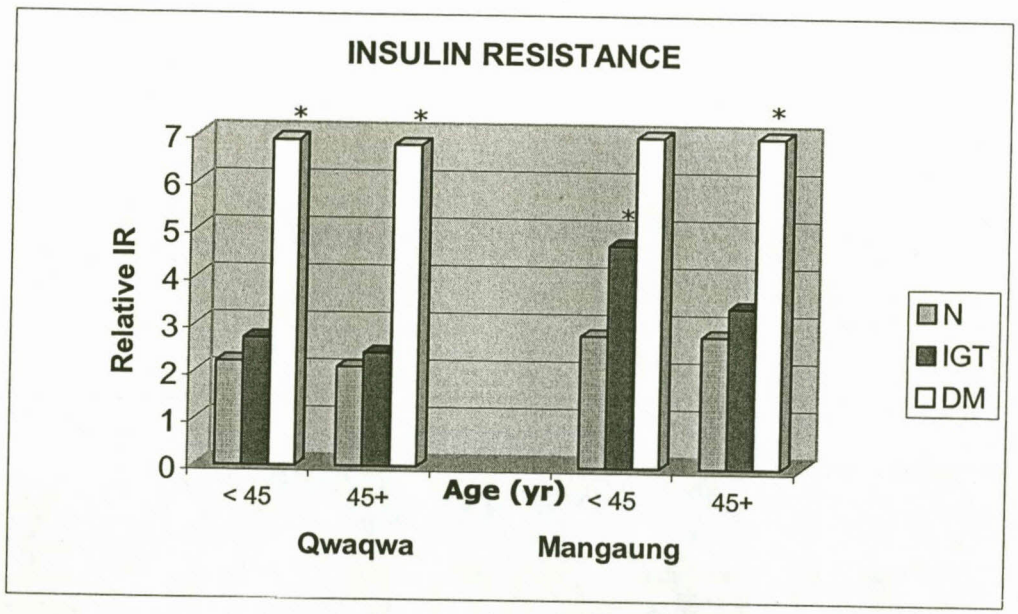


Fig. 8.8/1. Beta Cell Function and Insulin Resistance According To the HOMA Model by Age and Population.

*Significantly different from normal ($p<0.05$)

8.9 The relationship between waist-to-hip ratio and serum insulin concentration

The relationship between WHR tertiles, age, sex and median 2-hour serum insulin concentrations are shown in Fig. 8.9/1. The similarity of the data for the 2 populations is striking. Median serum insulin concentrations in all tertiles for females in both populations exceeded those for males in the corresponding age groups. This may be explained by the higher prevalence of obesity in females. Overall, for male subjects, median 2-hour serum insulin concentrations tended to increase from lower to upper WHR tertiles. This was not as evident for females, although median 2-hour serum insulin concentrations in the upper two tertiles exceeded concentrations in the lower tertile. The tendency of 2-hour insulin levels to

increase across WHR tertiles provides more evidence for increasing insulin resistance with

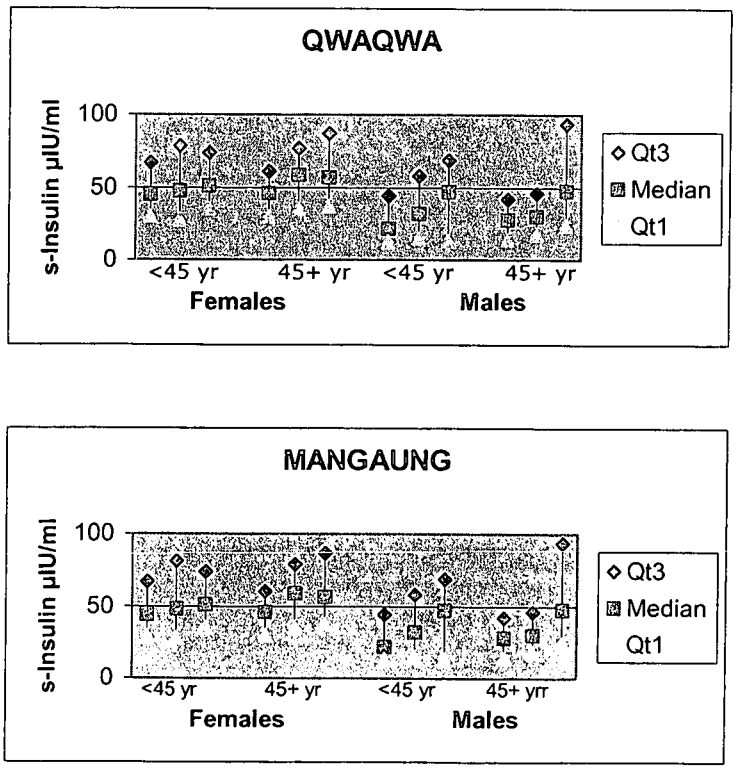


Fig. 8.9/1. Median 2-hour Serum Insulin Concentration by WHR Tertiles, Age, Sex and Population.

increasing central adiposity in the populations studied. This was especially evident in the younger groups of males. This observation suggests that increasing glucose intolerance with increasing central obesity may be at least partly preventable.

Summary

This study provides for the first time serum insulin measurements as part of the 75g OGTT test in the epidemiological study of diabetes and IGT in black South Africans or possibly even in Sub-Saharan Africa. No direct comparisons were therefore possible with other African subjects. Overall, mean serum insulin levels tended to be somewhat lower in Qwaqwa subjects than in urban subjects but levels were fairly comparable. When median insulin values were examined, this difference almost disappeared. Technical reasons like the transport of specimens may contribute to this mild difference. Fasting, 60 min and 120 min serum insulin concentrations post-glucose load were higher in subjects with diabetes and even still higher in subjects with IGT than in subjects with normal glucose tolerance. The decrease in serum insulin concentrations at 60 and 120 minutes in diabetic subjects compared to subjects with IGT in the face of higher plasma glucose levels supports the concept of a Starling curve for the β-cell also in these populations. Diabetic subjects older than 45 years secreted relatively less insulin in the fasting state (relative to the fasting hyperglycaemia) and absolutely less insulin at 120 min than normal subjects indicating β-cell failure. The HOMA model assessment supported this observation. It also showed that older diabetic subjects were particularly insulin resistant compared to normal subjects, again supporting De Fronzo's (1988) previous observations in older subjects in both these populations. The HOMA model is a very useful epidemiological tool but deserves to be evaluated and validated in the South African black population as well. Urban subjects tended to be more insulin resistant than rural subjects, but more statistical analysis will have to done to explore this possibility. The positive association between WHR and serum insulin levels demonstrated for both males and females in both populations supports the importance of central obesity in the development of insulin resistance and glucose intolerance. These observations provide more evidence to challenge the concept of healthy obesity in black females. A possible mechanism for the association between central obesity and diabetes also in black South Africans is thus provided by these

population-based studies. Since central obesity is potentially preventable as well as reversible, these findings provide epidemiological support for these efforts.

8.10 Relationship between glucose tolerance status and fasting C-peptide concentrations

The motivation for examining C-peptide concentrations in this population was twofold: Firstly to better characterize subjects with IGT and diabetes and secondly as another possible indicator of β-cell function. Fasting C-peptide concentrations were available only for the Mangaung population and the mean and median age- and sex-specific concentrations for this population are shown in Table 8.10/1. Standard deviations were wide. Fasting C-peptide levels were higher among females than males in all age groups except in elderly females. Overall, there was no obvious change in C-peptide concentrations with increasing age. No other population-based studies of C-peptide concentrations in black South Africans were available to compare these results with.

TABLE 8.10/1. Mean and Median Fasting Serum-C-Peptide Concentration (pmol/L) by Age and Sex for the Mangaung Population (Standard Deviations in Parenthesis)

	n	Mean C-Peptide	Median C-Peptide
Men (age in yr)			
25-34	65	535 (316)	484
35-44	65	599 (410)	482
45- 54	63	565 (384)	462
55-64	53	475 (401)	355
65+	39	679 (513)	563
Women (age in yr)			
25-34	105	630 (300)	544
35-44	123	661 (462)	533
45- 54	102	703 (381)	634
55-64	67	670 (408)	583
65+	62	630 (332)	556
Total	744		

Mean and median serum C-peptide concentrations according to age and glucose tolerance status are examined in Table 8.10/2. Median fasting C-peptide concentrations in both age groups were significantly higher in subjects with IGT than in subjects with normal glucose tolerance ($p < 0.01$). Elevated mean fasting C-peptide concentrations in this group may be the result of insulin resistance. Although mean fasting C-peptide concentrations among diabetics in the age group 45 years and older were clearly higher than in normal subjects, this difference failed to reach statistical significance. The relatively high mean fasting serum C-peptide concentrations among diabetics in both age groups were consistent with the diagnosis of Type 2 diabetes. The distribution of serum C-peptide levels in Figure 8.10/1 again demonstrates the phenomenon of a Starling curve of the β-cell.

TABLE 8.10/2. Mean Fasting Serum C-Peptide Concentration (pmol/L) According to Glucose Tolerance Status And Age (Standard Deviations in Parenthesis) for the Mangaung Population

	< 45 year			45+ year		
	n	Mean C-Peptide	Median C-Peptide	n	Mean C-Peptide	Median C-Peptide
Normal	307	578 (304)	524	266	592 (376)	512
IGT	34	959 (718)*	774	67	746 (495)*	642
Diabetes	9	737 (532)	516	45	659 (342)	617

* Significantly different From normal

Among subjects with normal glucose tolerance in both age groups combined (Table 8.10/2), fasting C-peptide concentrations ranged between 17 and 2652 pmol/L and 64 (11.2%) of normal subjects had fasting C-peptide concentrations below 300 pmol/L. Among diabetic subjects younger than 45 years, mean fasting C-peptide concentration ranged between 177 and 1668 pmol/L and only one subject (11.1%) had a C-peptide concentration below 300 pmol/L. GAD 65 antibody measurements were not available at the time to characterize this subject any further. Among diabetics 45 years and older, C-peptide concentrations ranged between 86 and 2215 pmol/L and 3 diabetics (6.7%) had values below 300. Amongst subjects of all

ages with IGT, C-peptide concentrations ranged between 141 to 4004 pmol/L. Three subjects with IGT (3%) had C-peptide concentrations below 300 pmol/L and all of them were 45 years or older.

A decline in mean fasting serum C-peptide concentration was noted in male subjects in the age group 55-64 years and this was followed by a rise in elderly subjects (Table 8.10/1). A corresponding decrease in fasting s-insulin concentrations in men in this age group was also noted (Table 8.7/1). A rise in mean serum C-peptide concentrations in middle-aged females was also. S-creatinine concentrations were examined to investigate the possibility that reduced renal function might have been associated with these observations. No relationship was found (Data not shown).

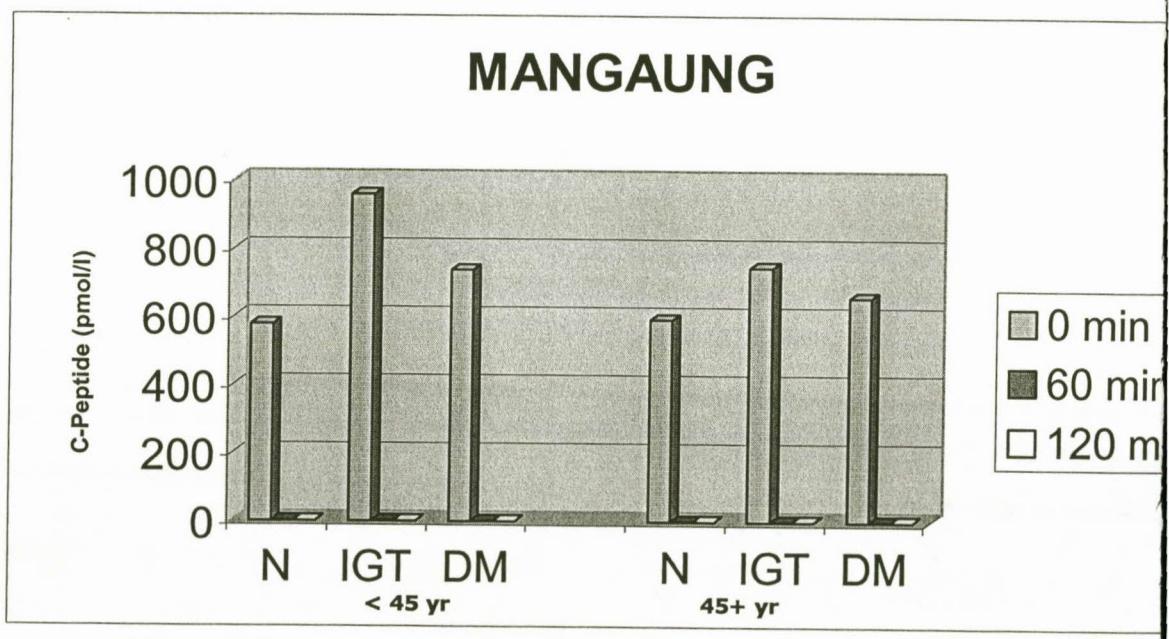


Fig. 8.10/1. Mean serum C-Peptide Concentration According to Glucose Tolerance Status and Age

Summary

Fasting serum C-peptide concentrations < 300 pmol/L were present in 11.2% of normal subjects. Fasting C-peptide concentrations in subjects with IGT were

significantly higher than in normal subjects while in diabetics it did not differ significantly from normal although fasting plasma glucose levels were higher in diabetics. This observation supports a diagnosis of Type 2 diabetes in the vast majority of cases. This observation is also indicative of failing β-cell function. An unexpected decrease in C-peptide levels was observed in men in the age group 55-64 years that corresponded to a similar decrease in insulin concentrations. This phenomenon was unrelated to renal function. Overall, C-peptide concentrations provided much the same information than serum insulin concentrations with the exception that no obvious age-related decline in C-peptide concentrations could be detected.

8.11 Relationship between glucose tolerance status and proinsulin concentrations

Fasting and 60 min post glucose load proinsulin concentrations were measured in both populations to examine the relation between proinsulin and blood pressure levels and also to better characterise β-cell function in the study populations. Due to the theft of a deep freeze with its content some stored serum samples were lost explaining the missing observations. Age- and sex-specific serum proinsulin concentrations for the study populations are shown in Table 8.11/1 and Table 8.11/2 and in Fig. 8.11/1 and Fig. 8.11/2. In both populations and both sexes fasting serum proinsulin levels tended to rise with age with the exception of young males in Qwaqwa who had higher fasting proinsulin concentrations than any other age group. Sixty-minute proinsulin concentrations in females in the Qwaqwa sample in the age group 45 years and older showed a clear tendency to increase with age. The same was observed for males in the age group 55 years and older. Overall, proinsulin concentrations in the Qwaqwa population appeared to be lower than in the urban population and in males compared to females. This observation has to be treated with caution due to the missing samples. A much clearer picture emerged in the Mangaung sample where an increase in fasting and 1-hour serum proinsulin concentrations with age in both sexes was most obvious. This is a unique finding. Due to the scarcity of epidemiological studies examining proinsulin secretion and the lack of comparable studies in blacks, one can only speculate about the meaning of this observation.

In section 8.7 it was shown that neither fasting nor 60 min or 120 min serum insulin concentrations changed much with age in any of the two populations with the possible exception of older subjects in Mangaung where levels may have increased slightly (summarised in Fig. 8.11/3). Both fasting and 60 min proinsulin concentrations increased with age in both populations and this was especially evident in the Mangaung sample. Although β-cell function declined with worsening glucose tolerance (Starling effect) it did not change much with aging (comparing normal subjects < 45 years of age with normal subjects ≥ 45 years). The same is true for fasting C-peptide levels and proinsulin levels. A plausible explanation for the increase in proinsulin concentrations with aging in the presence of largely

unchanged insulin levels, is that an alternative variety or specie of proinsulin was secreted that is not normally a precursor of insulin (Temple et al., 1992).

The Starling curve phenomenon is recognisable at 60 min post-glucose load in younger subjects in Qwaqwa sample and in both age groups in the Mangaung sample. Further research is needed to confirm these findings and to better understand the pathophysiology of Type 2 diabetes and β-cell function in older subjects.

SUMMARY

Although some stored samples were lost enough duplicate samples were left to examine proinsulin levels in the different age groups at 0 and 60 minutes. Proinsulin levels appeared higher in urban than in rural subjects. Again one may speculate that the difference is due to more advanced urbanisation of the former. A unique finding was that fasting and 60 min proinsulin concentrations increased with aging in normal subjects in the face of unchanged β-cell function and increased insulin resistance while corresponding insulin concentrations (and fasting C-peptide concentrations) nearly remained the same. This finding is in accordance with the concept that altered β-cell pathways of insulin secretion may operate in glucose intolerance and possibly also in the aging process. This hypothesis deserves further investigation.

TABLE 8.11/1. Mean Serum Proinsulin Concentration (pmol/L) after a 75 g Oral Glucose Load. Results by Age, Gender and Population (Standard Deviation in Parenthesis)

	0 min		60 min	
	n	Proinsulin[a]	n	Proinsulin[b]
Qwaqwa				
Men (age in yr)				
25-34	50	2.4 (4.0)	51	5.6(4.1)
35-44	58	1.7 (1.5)	62	6.1 (6.2)
45-54	24	1.6 (1.4)	24	5.8 (3.6)
55-64	37	1.6 (2.8)	38	6.3 (11.5)
65+	72	1.8 (1.9)	69	6.6 (3.7)
Women (age in yr)				
25-34	118	1. 7 (0.9)	126	6.5 (4.2)
35-44	89	1.9 (1.4)	96	6.2(4.4)
45-54	80	2.0(1.7)	86	6.9 (5.8)
55-64	79	2.0 (1.5)	80	8.3(7.4)
65+	96	2.3 (2.4)	102	8.5 (7.9)
Mangaung				
Men (age in yr)				
25-34	57	1.9 (1.3)	58	5.0 (3.7)
35-44	57	2.2 (2.0)	57	6.0 (5.3)
45-54	56	2.4 (1.9)	55	7.2 (6.7)
55-64	36	3.0(4.7)	36	9.6 (12.7)
65+	32	2.8 (2.9)	32	9.2 (6.6)
Women (age in yr)				
25-34	93	2.2 (1.6)	92	6.9 (5.5)
35-44	117	2.2 (1. 7)	115	7.2 (7.1)
45-54	85	3.2 (3.2)	76	7.8 (6.3)
55-64	58	3.6 (3.9)	57	10.2 (6.9)
65+	60	3.0 (2.4)	59	11.1 (9.4)

(Qwaqwa 150 missing observations)

(Mangaung 142 Observations missing)

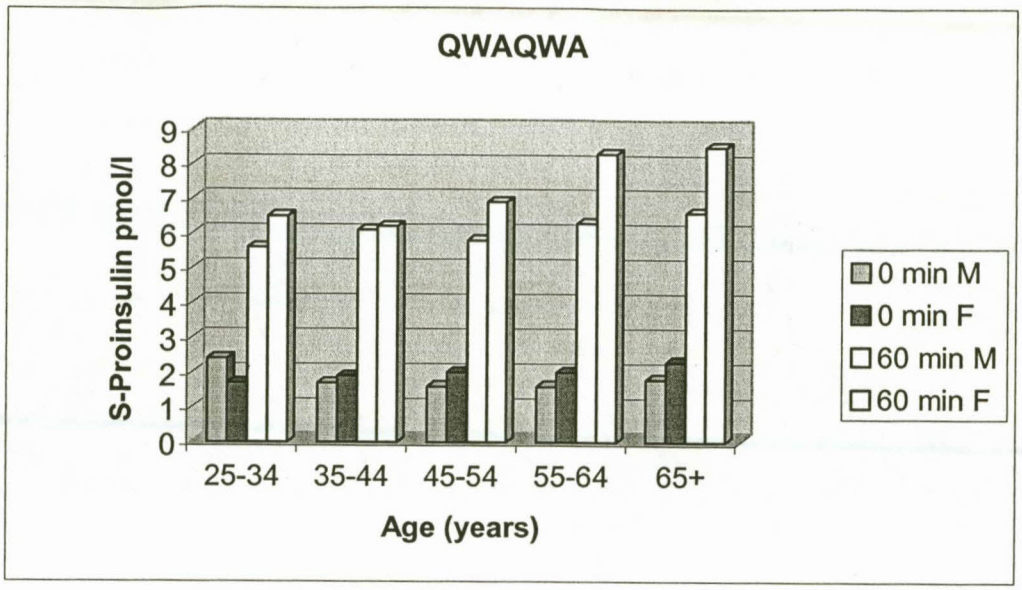
[a] fasting serum proinsulin

[b] known diabetics excluded

TABLE 8.11/2. Mean Serum Proinsulin Concentration (pmol/L) According to Glucose Tolerance Status and Age (Standard Deviation in Parenthesis)

	QWAQWA		MANGAUNG	
	< 45 yr	45+ yr	< 45 yr	45+ yr
Normal				
0 min	1.8 (1. 9)	1.9 (1.8)	2.0 (1.5)	2.6 (2.3)
60 min	5.9 (4.3)	7.3 (7.1)	5.8 (4.7)	8.0 (7.2)
IGT				
0 min	2.7 (2.4)	1.6 (1.4)	3.3 (2.2)*	3.6 (3.7)
60 min	10.3 (7.6)*	7.4 (6.9)*	11.3 (7.8)*	12.2 (10.4)*
Diabetes				
0 min	4.8 (3.1)	3.4 (3.4)	3.0 (2.0)	4.7 (5.5)*
60 min	7.9 (3.2)	8.2 (7.3)	7.1 (6.5)	10.5 (8.0)

* Significantly different from normal $p < 0.01$



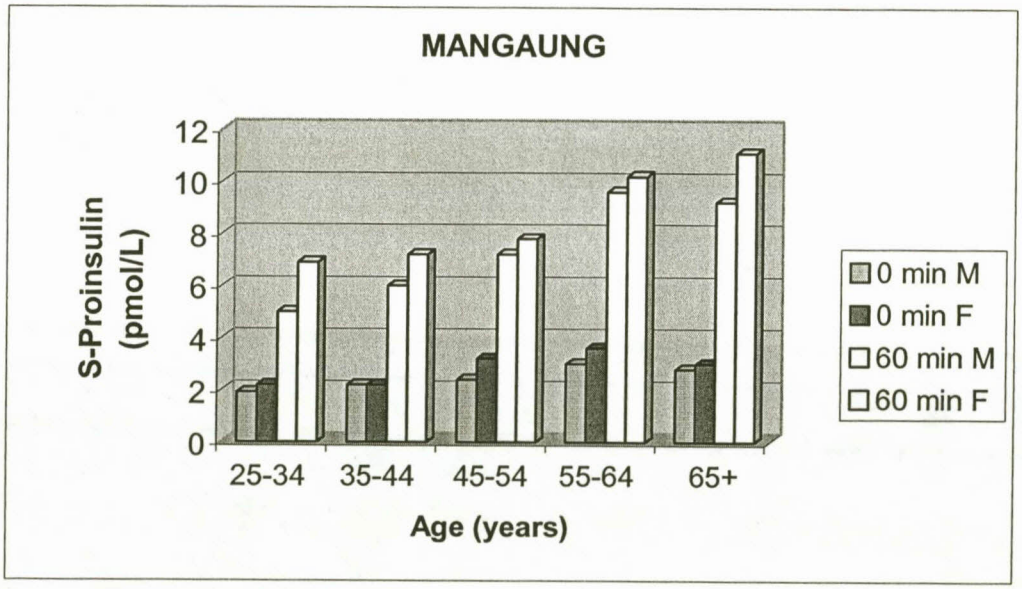
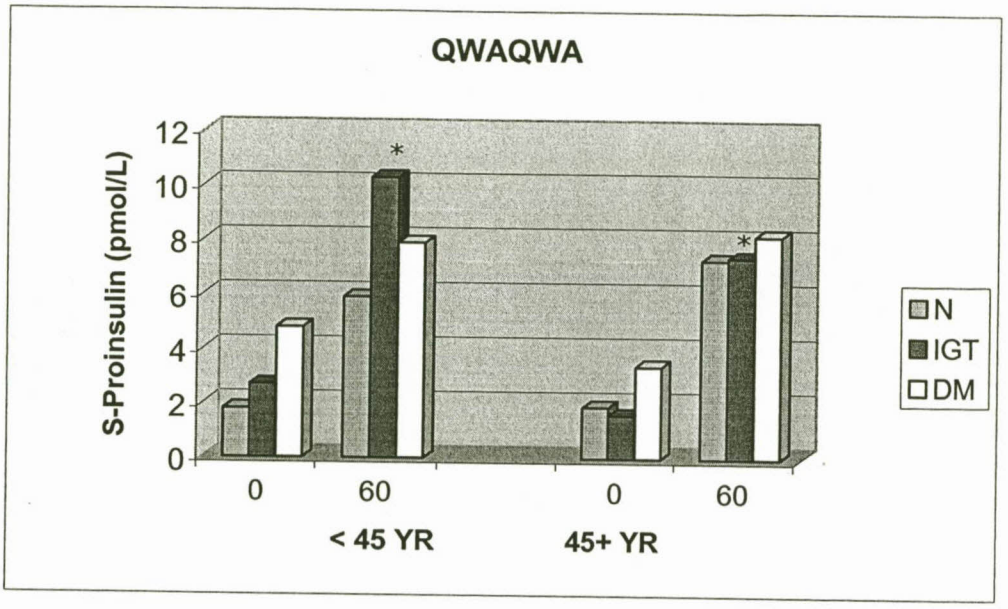


Fig. 8.11/1. Fasting and 60 min s-Proinsulin Concentrations by Age, Sex and Population



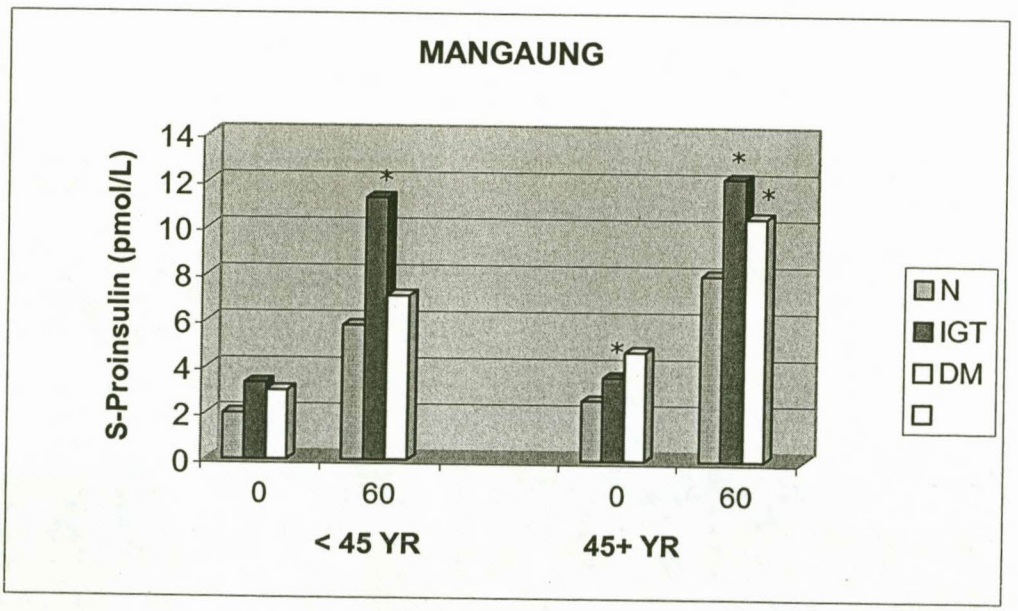


Fig. 8.11/2. Mean S-Proinsulin Concentration According to Glucose Tolerance Status, Region and Age.

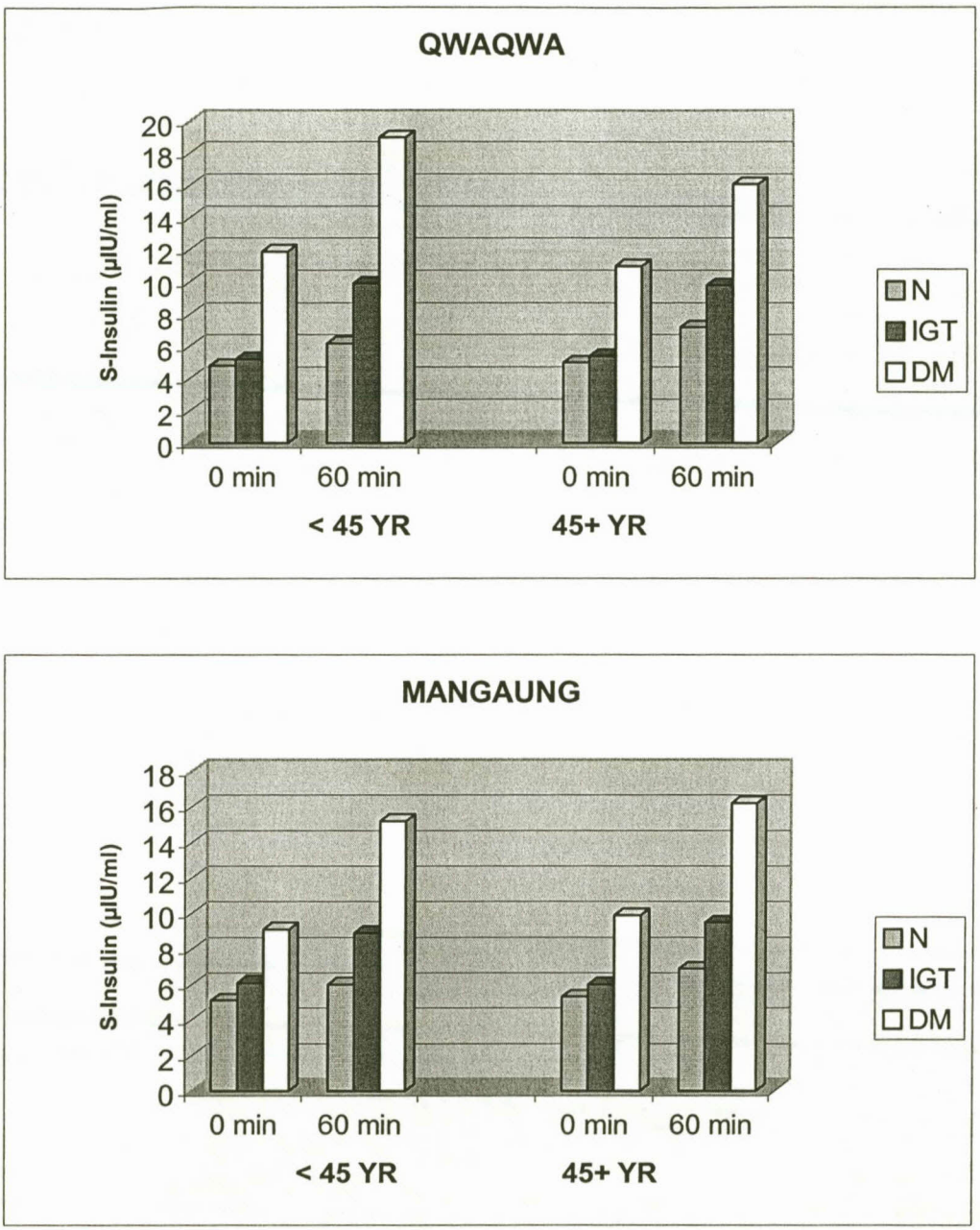


Fig. 8.11/3. Mean Fasting and 60 min s-Insulin Concentrations by Age, Sex and Region.

8.12 Serum fructosamine as a screening test for glucose intolerance

The motivation for the ADA to review the diagnostic criteria or diabetes was to simplify the diagnosis of diabetes and to eliminate the OGTT as a diagnostic test (ADA, 1997). Glycosilated haemoglobin was investigated as such a test but due to a lack of standardised methodology attempts were unsuccessful up to now. The sensitivity and specificity of serum fructosamine to detect newly diagnosed cases of diabetes was examined in the two study populations. In the Qwaqwa sample the sensitivity and specificity was 42.3% and 98.3% respectively (Table 8.12/1). The sensitivity and specificity in the Mangaung sample was 28.6% and 98.8%.

TABLE 8.12/1. Sensitivity and Specificity of Serum Fructosamine to Detect

Newly Diagnosed Cases of Diabetes (Known Cases Excluded)

	2-h Glucose ≥ 11.1 mmol/L		
	Positive	Negative	Total
Qwaqwa			
(Serum fructosamine > 2.1 mmol/L)			
Positive	11	13	24
Negative	15	769	784
Total	26	782	808
Sensitivity = 42.3%			
Specificity = 98.3%			
Mangaung			
(Serum fructosamine > 2.1 mmol/L)			
Positive	8	8	16
Negative	20	673	693
Total	28	681	709
Sensitivity = 28.6%			
Specificity = 98.8%			

The sensitivity and specificity of serum fructosamine to detect glucose intolerance (IGT and diabetes) is shown in Table 8.12/2. The sensitivity and specificity in the Qwaqwa sample was 12.2% and 98.8% respectively. The corresponding values in Mangaung were 6.9% and 98.8%.

TABLE 8.12/2. Sensitivity and Specificity of Serum Fructosamine to Detect Newly Diagnosed Cases of Glucose Intolerance (Excluding known diabetics)

	≥ 7.8 mmol/L 2-h Glucose		
	Positive	Negative	Total
Qwaqwa			
(Serum fructosamine > 2.1 mmol/L)			
Positive	16	8	24
Negative	115	669	784
Total	131	677	808
Sensitivity = 12.2%			
Specificity = 98.8%			
Mangaung			
(Serum fructosamine > 2.1 mmol/L)			
Positive	9	7	16
Negative	122	571	693
Total	131	578	709
Sensitivity = 6.9%			
Specificity = 98.8%			

Summary

Serum fructosamine is neither a useful test for the diagnosis of diabetes nor for the diagnosis of glucose intolerance.

8.13 Relationship between height and 2-hour plasma glucose

The relationship between height and 2-hour post glucose load was also examined (Table 8.13/1). No significant correlation could be demonstrated between height and 2-hour plasma glucose for either population or sex. There was, however, a tendency towards a negative correlation between height and 2-hour plasma glucose most pronounced in Qwaqwa females.

A negative correlation between height and 120 min plasma glucose was found in British subjects irrespective of their glucose tolerance status. Furthermore, subjects with IGT were found to be significantly shorter than matched control subjects from the same population (Brown et al., 1991). In the latter study height in postmenopausal females was strongly and negatively related to age. The authors suggested that since BMI was usually used as the main anthropometrical variable in most studies, height is eliminated as independent analytical variant. It was, however, found in a French study that reduced final height is related to intrauterine growth retardation (Leger et al., 1997). In a Nigerian study some association (negative) was found between blood glucose and height in an African community with a low prevalence of diabetes and IGT (Olatunbosun and Bella, 2000). Levitt et al. (2000) demonstrated in subjects from mixed ancestry a link between low birth weight and adult glucose intolerance and elevated blood pressure. The absence of an association between final adult height and blood glucose concentrations in the two FS populations did not lend support to the foetal origins hypothesis in these populations. One pitfall must however be considered when interpreting such data in a developing country. An important difference between growth retardation in industrialised and non-industrialised countries is that growth retardation in the former is disproportionate ("asymmetrical") whereas in the latter proportionate growth retardation is common (Barker, 2001). It follows that it may be much more difficult to prove or disprove the foetal origins hypothesis in non-industrialised countries using adult height as variable.

SUMMARY

In neither of the two FS populations was any correlation found between plasma glucose concentrations and adult height. Adult height was the only available variable to examine the foetal origins hypothesis in the pathogenesis of Type 2

diabetes these communities. The contribution of the foetal origins hypothesis in the pathophysiology of Type 2 diabetes in FS communities deserves further study.

TABLE 8.13/1. Correlation between height and 2-hour plasma glucose (excluding known diabetics).

	n	Correlation	p-value
Qwaqwa (age in yr)			
Females			
25-34	140	-0.05	0.52
35-44	105	0.08	0.44
45-54	98	-0.04	0.69
55-64	90	-0.17	0.10
55+	115	-0.09	0.33
All	548	-0.09	0.04
Males			
25-34	55	0.08	0.56
35-44	68	-0.29	0.02
45-54	25	-0.14	0.49
55-64	41	-0.12	0.46
55+	75	0.05	0.68
All	264	-0.09	0.13
Mangaung (age in yr)			
Females			
25-34	101	-0.08	0.40
35-44	120	0.06	0.49
45-54	94	0.02	0.88
55-64	64	-0.03	0.80
55+	56	-0.10	0.45
All	435	-0.07	0.13
Males			
25-34	65	-0.18	0.16
35-44	63	-0.01	0.92
45-54	59	-0.18	0.18
55-64	50	-0.03	0.79
55+	37	0.07	0.69
All	274	-0.11	0.06

8.14 Risk factors for glucose intolerance

Backward selection logistic regression analysis was used to identify possible predictors of glucose intolerance in the study populations (Table 8.14/1).

In the Qwaqwa population, age (odds ratio (OR) 3.7), WHR (OR 2.7), treated hypertension (OR 1.9) and elevated serum cholesterol (OR 1.9) were all independent risk factors for glucose intolerance. Elevated serum triglycerides (OR 1.6) just failed to reach statistical significance. Sex, alcohol, smoking and obesity were not retained in the final model as risk factors for glucose intolerance. In the Mangaung population, WHR (OR 3.3), elevated serum triglycerides (OR 1.9), age (OR 1.8), obesity (OR 1.8) and treated hypertension (OR 1.8) were independent risk factors for glucose intolerance. Sex and untreated hypertension just failed to reach statistical significance. In this model and this population, alcohol, serum cholesterol and smoking were not retained as risk factors for glucose intolerance.

Since IGT in addition to Type 2 diabetes are widely regarded as cardiovascular risk factors (Alberti et al., 1998), these two related metabolic disorders were combined in the regression analysis. It is interesting that pre-obesity came out as a risk factor in Mangaung but not in Qwaqwa. This finding may again point towards more advanced urbanisation of the urban sample. In the Cape Town study obesity (BMI $\geq$ 27 kg m^2 for men and > 25 kg/m^2 for women) as well as WHR were risk factors for diabetes (Levitt et al., 1993). In the FS studies WHR was a risk factor in both populations with the OR higher in Mangaung than in Qwaqwa – again supporting the hypothesis of more advance urbanisation of the urban population. It is also evident that central obesity appeared a stronger risk factor than pre-obesity in both populations. It is surprising that cholesterol was a risk factor in the rural population while triglycerides were a risk factor in the urban sample. Serum triglyceride concentrations just failed to reach statistical significance in Qwaqwa. Overall a clustering of cardiovascular risk factors was observed in this risk analysis. However, association does not imply causality and it is impossible to determine which abnormality came first. As expected, age was a risk factor as was the case in the Cape Town blacks. Obesity was also a risk factor for diabetes in the Cameroon study (Mbanya, 1997) while BMI was negatively related to glucose values in the Tanzanian study (McLarty, 1989). In the latter study age and systolic blood

pressure were also positively related to diabetes. The traditional risk factors for glucose intolerance (age, BMI, WHR) were confirmed while treatment for hypertension alongside the metabolic abnormalities, hypercholesterolaemia and hypertriglyceridaemia emerged as risk factors for glucose intolerance – a unique finding in Africans. A second criterion (dyslipidaemia) satisfying the existence of a metabolic syndrome in black South Africans was met.

Independent risk factors for impaired glucose tolerance are shown in Table 8.14/2. For the Qwaqwa population, independent risk factors for IGT were age (OR 2.8), WHR (OR 2.2), and elevated serum cholesterol (OR 1.9). Variables not retained in the model were sex, alcohol, smoking and pre-obesity. For Mangaung, the independent risk factors for IGT were WHR (OR 2.6) and pre-obesity (OR 1.8) while elevated serum triglycerides and age just failed to reach statistical significance. Variables not retained in this model were alcohol, serum cholesterol, smoking and hypertension. Since the Qwaqwa and Mangaung populations have such unusually high IGT prevalence rates, the identification of these risk factors are of paramount importance. It was convincingly shown that IGT could be prevented from proceeding to Type 2 diabetes (Pan et al, 1997). Measures to identify subjects at risk of IGT and to intervene with lifestyle modification is strongly recommended for the FS.

TABLE 8.14/1. Odds Ratio (OR) of Factors Predicting Glucose Intolerance in the Study Populations

Factors	Odds Ratio	95% Confidence Interval
Qwaqwa		
Age[1]	3.7	(2.3-5.9)
WHR[2]	2.7	(1.8-4.1)
Cholesterol[6]	1.9	(1.3-2.8)
Hypertension[4]	1.9	(1.1-3.3)
(Treated)		
Triglyceride[5]	1.6	(0.9-2.9)
Hypertension[3]	0.67	(0.42-1.1)
(Untreated)		
Mangaung		
WHR[2]	3.3	(2.1-5.2)
Triglyceride[5]	1.9	(1.1-3.4)
Hypertension[4]	1.8	(1.3-3.1)
(Treated)		
Pre-Obesity[7]	1.8	(1.2-2.8)
Age[1]	1.8	(1.1-2.7)
Sex[8]	1.4	(0.93-2.2)
Hypertension[3]	1.2	(0.73-1.8)
(Untreated)		

1 >45+ VS. <45yr

2 > sex-specific median vs. < sex-specific median

3 Hypertensives (> 160/95) vs. normotensives

4 Treated hypertensives vs. normotensives

5 > 2.3 mmol/L vs. < 2.3 mmol/L

6 > 5.2 mmol/L v. < 5.2 mmol/L

7 BMI > 25 kg/m2 vs. < 25 kg/m2

8 Females vs. males

Variables not retained in the model for Qwaqwa: Sex, alcohol, smoking and obesity

Variables not retained in the model for Mangaung: Alcohol, cholesterol, smoking

TABLE 8.14/2. Odds Ratio (OR) of Factors Predicting Impaired Glucose Tolerance in the Study Populations (Diabetes Excluded)

Factors	Odds Ratio	95% Confidence Interval
Qwaqwa		
Age[1]	2.8	(1.7-4.7)
WHR[2]	2.2	(1.4-3.6)
Cholesterol[6]	1.9	(1.2-2.9)
Hypertension[4] (Treated)	1.8	(0.95-3.3)
Triglyceride[5]	1.7	(0.88-3.2)
Hypertension[3] (Untreated)	0.76	(0.45-1.3)
Mangaung		
WHR[2]	2.6	(1.6-4.3)
Obesity[7]	1.8	(1.1-2.9)
Triglyceride [5]	1.8	(0.96-3.5)
Age[1]	1.6	(0.99-2.6)
Sex[8]	1.5	(0.93-2.6)

1 >45+ vs. <45yr

2 > sex-specific median vs. < sex-specific median

3 Hypertensives (> 160/95) vs. normotensives

4 Treated hypertensives vs. normotensives

5 > 2.3 mmol/L vs. < 2.3 mmol/L

6 > 5.2 mmol/L vs. < 5.2 mmol/L

7 BMI > 25 kg/m^2 vs. < 25 kg/m^2

8 Females vs. males

Variables not retained in the model for Qwaqwa: Sex, alcohol, smoking and obesity

Variables not retained in the model for Mangaung: Alcohol, cholesterol, smoking and hypertension

Summary

The traditional risk factors for diabetes namely age, WHR and pre-obesity were also identified as risk factors for glucose intolerance (IGT + diabetes) in both the FS populations studied. Other additional unique risk factors for Africans were also identified namely hypercholesterolaemia and treated hypertension in the Qwaqwa population and hypertriglyceridaemia, treated hypertension and pre-obesity in the Mangaung population. A clustering of cardiovascular risk factors was observed in patients with glucose intolerance. With regression analysis pre-obesity emerged as a risk factor for diabetes only in Mangaung subjects, while the odds ration (OR) for WHR as a risk was also higher in Mangaung subjects. It may be hypothesised that urbanisation is more advanced in Mangaung than in Qwaqwa.

As mentioned previously the FS populations have the highest prevalence rates for IGT in South Africa as well as in Sub-Saharan Africa. For the first time were modifiable risk factors for IGT in black South Africans identified. These were WHR for subjects in both studies as well as hypercholesterolaemia in Qwaqwa subjects and pre-obesity and hypertriglyceridaemia in Mangaung subjects.

9 Hypertension

9.1 Description of blood pressure levels in the study populations

In both populations, diastolic blood and systolic blood pressure increased with increasing age and this increase was more pronounced for systolic blood pressure (Fig. 9.1/1). Mean diastolic blood pressure measurements in the youngest age decile were very similar for the corresponding sexes in the two populations (Table 9.1/1). The mean diastolic blood pressure in Qwaqwa males and females aged 25-34 years was 77.9 and 73.7 mm Hg respectively. Thereafter it increased by 5.5 mm Hg to 83.4 mm Hg in males and by 12.3 mm Hg to 86 mm Hg in females in the age group 65 years and older. The mean diastolic blood pressure in Mangaung males and females aged 25-34 years was 76.8 and 72.8 mm Hg respectively. In males, mean diastolic blood pressure increased by 11 mm Hg to 87.8 mm Hg and in females by 13.3 mm Hg to 86.1 mm Hg, from the youngest to the oldest age decile. The rise in diastolic blood pressure with increasing age in Mangaung males was twice as great as in Qwaqwa males.

Mean systolic blood pressures were 129.2 mm Hg and 125 mm Hg for Qwaqwa males and females respectively in the youngest age decile. In males, mean systolic blood pressure increased by 19.9 mm Hg to reach 149.1 mm Hg in the oldest age decile while in females it increased by 35 mm Hg to reach 160 mm Hg in the corresponding age decile. In Manguang males mean systolic blood pressure increased by 32.4 mm Hg from 127.9 mm Hg in the youngest age decile to 160.3 mm Hg in the oldest age decile. For Mangaung females the corresponding rise was 44.7 mm Hg from 124.7 mm Hg to 169.4 mm Hg. The rise in systolic blood pressure was thus greater in Mangaung subjects than in Qwaqwa subjects and the greatest rise occurred in Mangaung females.

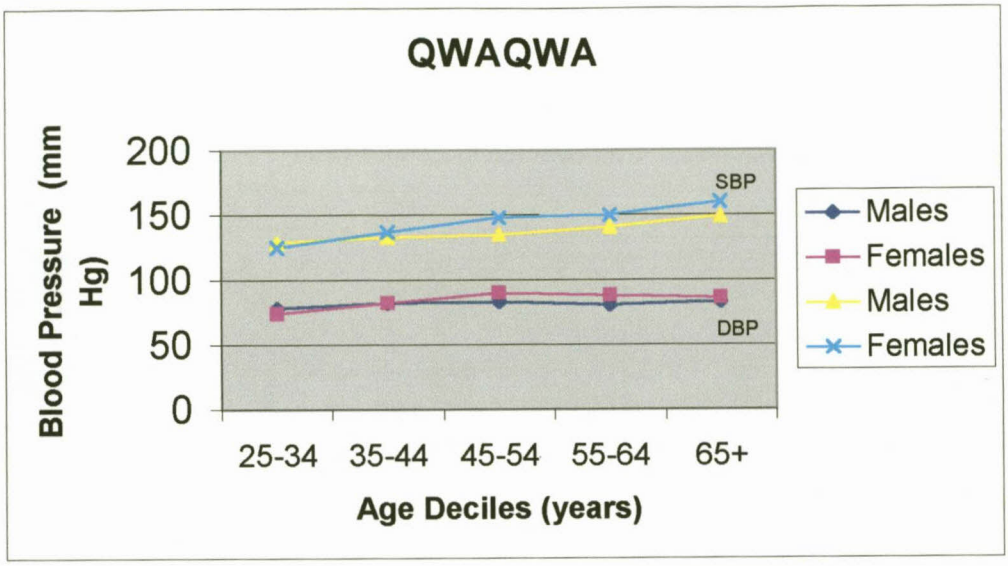
The rise in diastolic blood pressure from the youngest to oldest decile in Qwaqwa males was 5.5 mmHg compared to 11 mmHg in Mangaung males. This difference was clinically significant. The corresponding rise in diastolic blood pressure for females was 12.3 mmHg and 13.3 mmHg respectively. The most striking difference between the two populations was the increase in systolic blood

pressure. In Qwaqwa the increase from the youngest to the oldest decile in males was 19.9 mmHg and in Mangaung 32.4 mmHg. The corresponding increase in females was 35 mmHg and 44.7 mmHg. Both these differences were clinically significant. It appears thus in this cross-sectional study that although young males and females have comparable diastolic and systolic blood pressure levels in the 25-34 year age decile group, the rise in blood pressure with age was more pronounced in the urban group than in the rural group. This difference may possibly be attributable to more advanced urbanisation of the Mangaung population. Before definite conclusions can be reached more analysis will have to be performed.

The mean diastolic blood pressure of females in the age group 45-54 years in both populations exceeded the 90 mm Hg the cut-point for borderline hypertension. The mean systolic blood pressure in females 45 years and older in both populations as well as in Mangaung males in the same age group exceeded the 140 mm Hg cut-point for hypertension. Qwaqwa males reached this cut-point a decade later. The mean systolic blood pressure in females 65 years and older in both populations exceeded the hypertension cut-point of 160 mm Hg. This was also the case for older Mangaung males. The difference in mean systolic blood pressure in males 65 years and older in the two populations was 11.2 mmHg that was clinically significant. These differences in blood pressure patterns between the two populations deserve more study for instance the influence of BMI and WHR must be examined.

Summary

The expected rise in mean diastolic and systolic blood pressure with age was observed for both sexes and populations. This rise was more pronounced for systolic blood pressure. The increase in mean diastolic as well as mean systolic blood pressure across the age centiles for men as well as for mean systolic blood for women was more pronounced in the urban than in the rural group. This important observation should be explored further to establish whether this was a true difference possibly attributable to a more advanced urbanisation process in the Mangaung population.



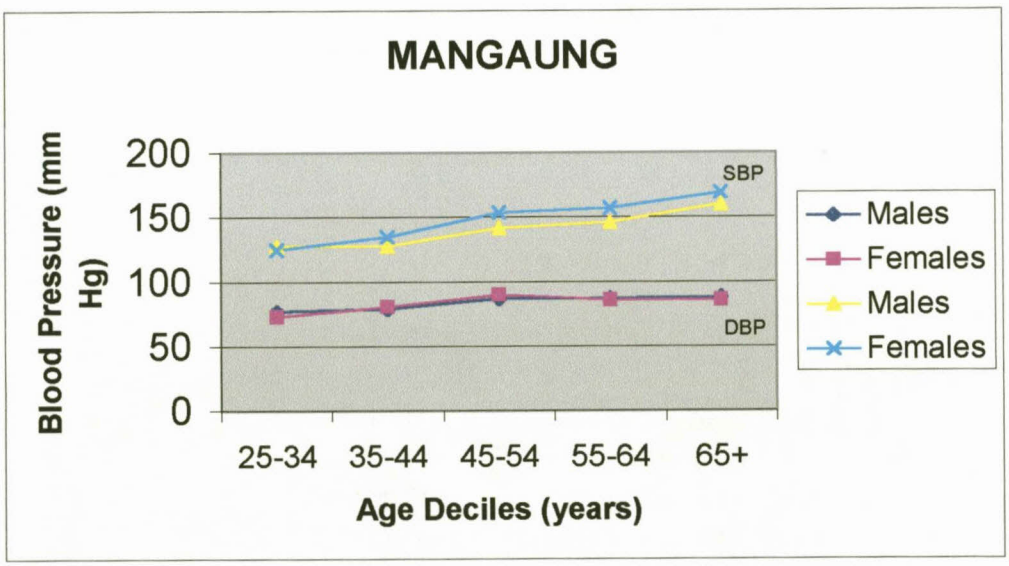


Fig. 9.1/1. Mean Systolic and Diastolic Blood Pressure by Age, Sex and Population (SBD=Systolic Blood Pressure and DBP=Diastolic Blood Pressure).

TABLE 9.1/1. Mean Diastolic and Systolic Blood Pressure (mm Hg) by Age and Study Population (Standard Deviation in Parenthesis)

	No	Diastolic	Systolic
Men (age in yr)			
25-34	56	77.9 (13.8)	129.2 (19.1)
35-44	68	81.3 (15.1)	132.7 (19.8)
45-54	27	83.2 (13.3)	134.7 (22.0)
55-64	45	81.2 (10.4)	140.8 (21.8)
65+	83	83.4 (14.0)	149.1 (27.0)
Women (age in yr)			
25-34	142	73.7 (14.7)	125.0 (19.8)
35-44	110	81.9 (13.9)	137.3 (24.2)
45-54	99	90.3 (17.2)	148.2 (29.3)
55-64	102	88.3 (14.8)	150.1 (26.6)
65+	121	86.0 (20.0)	160.0 (30.5)
Mangaung			
Men (age in yr)			
25-34	67	76.8 (12.6)	127.9 (14.4)
35-44	65	79.4 (11.3)	128.4 (14.2)
45-54	64	86.6 (13.9)	141.8 (23.3)
55-64	54	87.3 (14.9)	146.4 (27.3)
65+	40	87.8 (13.1)	160.3 (26.3)
Women (age in yr)			
25-34	105	72.8 (13.1)	124.7 (17.1)
35-44	126	81.0 (13.4)	134.8 (21.6)
45- 54	105	90.3 (15.5)	153.6 (31.8)
55-64	68	86.2 (14.1)	156.7 (30.8)
65+	64	86.1 (19.2)	169.4 (36.9)

9.2 Prevalence of hypertension

Total hypertension is defined as a systolic blood pressure ≥ 140 mm Hg and/or a diastolic blood pressure ≥ 90 mm Hg or on treatment for hypertension. The age- and sex-specific and age-adjusted prevalence rates of total hypertension are shown in Table 9.2/1. The prevalence of total hypertension increased across the age deciles for both sexes and both populations. The age-standardized rates of total hypertension in the two populations were remarkably similar for the corresponding sexes but were higher in females than males (44.3% and 43.4% for Qwaqwa and Mangaung males respectively, and 51.3% and 50.4% for Qwaqwa and Mangaung females respectively). The prevalence of total hypertension in elderly subjects ranged from 74.7% among Qwaqwa males to 90.6% of elderly females in Mangaung. The overall age- and sex-adjusted prevalence of total hypertension in Qwaqwa and Mangaung was 48.4% and 47.3% respectively.

The prevalence of total hypertension in the Cape Peninsula black population was 14.4% for males and 13.7% for females (Steyn et al., 1991). This huge discrepancy in the prevalence of total hypertension between the FS and Cape Peninsula studies may partly be explained by the inclusion of younger subjects and the exclusion of elderly subjects in the latter study. Another possible contributing factor might be technical. The FS studies were the only studies in SA to use the Hawksley random zero (RZ) sphygmomanometer to measure blood pressure in epidemiological studies. The prevalence of total hypertension in males and females in a study of subjects from mixed ancestry in the Cape Peninsula was also much higher than that of black subjects from the same are (Steyn et al., 1986). The rates were 35.6% for males and 24.7% for females. The age range of the sample was 15-64 years. In a neighbouring country, Zimbabwe, the prevalence of hypertension (systolic BP ≥ 140 and or diastolic BP ≥ 90) was 21% for men and 30% for women 25 years and older (Mufunda, 2000). Prevalence rates of total hypertension in different ethnic groups from different socio-economic backgrounds making the transition in SA vary considerably with rates in the FS exceeding those from most other communities.

TABLE 9.2/1. Prevalence (%) of Total Hypertension[1] According to Age Group, Sex and Population

	Qwaqwa		Mangaung	
	n	%	n	%
Men (age in yr)				
25-34	56	28.6	67	31.3
35-44	68	47.1	65	30.8
45-54	27	40.7	64	53.1
55-64	45	60	54	70.4
65+	83	74.7	40	82.5
All ages	279	53.1	290	50.3
Age-standardized prevalence		44.3		43.4
Women (age in yr)				
25-34	142	21.1	105	21.9
35-44	110	50	126	49.2
45-54	99	70.7	103	71.8
55-64	102	70.6	68	79.4
65+	121	80.2	64	90.6
All ages	574	56.5	466	58.2
Age-standardized prevalence		51.3		50.4
Total				
Age- and sex-standardized	853	48.4	756	47.3

[1] Systolic blood pressure ≥ 140 and/or diastolic blood pressure ≥ 90 mm Hg or on treatment for hypertension

Hypertension was defined according to WHO guidelines as a systolic pressure equal to or greater than 160 mmHg and/or diastolic (fifth phase) equal to or greater than 95 mmHg (WHO, 1978). Hypertension was extremely common in both sexes and in both populations. The overall age-and sex-adjusted prevalence was 29.2% in Qwaqwa 30.3% in Mangaung (Table 9.2/2). The prevalence of hypertension in the Mangaung sample was 33.3% after the sample was sex- and age standardised to the Qwaqwa population structure. The difference in the prevalence of hypertension was not statistically significant (95% CI -9.5;1.3).

The prevalence of hypertension increased sharply in both sexes and populations with increasing age, especially in the groups older than 44 years with the exception of Qwaqwa males where the increase occurred after the age of 54 years. Hypertension was already common at a young age as was evident from rates ranging from 9.9% in Qwaqwa women to 14.3% in Qwaqwa men. In all age groups hypertension was more common among women than men except in the age group 25-34 years where it was more common in Qwaqwa men than women. Among men in both populations the prevalence of hypertension was only about half the prevalence of total hypertension while among women the rate of hypertension was about two-thirds the rate of total hypertension.

Seedat et al. (1982) reported an overall prevalence of hypertension (≥ 160/95 mmHg) in random samples of urban and rural Zulus of 21.4% (18.7% men and 23.9% women) and 10.7% (10% men and 11% women) respectively. The samples included subjects below 20 years and above 70 years. Compared to urban Zulus the prevalence of hypertension (≥160/95 mmHg) was remarkably low in Cape Peninsula blacks (Steyn et al., 1991). In the latter study the prevalence was 6.7% in males and 8.9% in females. In subjects from mixed ancestry from the same region the age-adjusted prevalence rates were 17.2% for men and 18.4% for women. In the SADHS 11% of men and 13% of women had a blood pressure above 160/95 mmHg or were taking anti-hypertensive drugs. The SADHS rates for the FS were 14.5% for men and 15.5% for women (the vast

majority of the population is African). The prevalence of hypertension in a group of older people (mean age 65.4 years) of mixed ancestry from West Coast villages near Cape Town was 71.1% for men and 76% for women (Charlton et al., 2001). These extremely high rates are higher than in the 65-year and older group of subjects in the FS studies. The prevalence of hypertension in a Gambian study including 5389 subjects was 7.1% (van der Sande et al., 2000). Interestingly, the prevalence of hypertension in subjects from Afro-Caribbean descent participating in the Intersalt study in Birmingham, was 31% in men and 34% in women. The Hawksley RZ was also used in this study. The prevalence of hypertension in the two FS black populations was considerably higher than that previously reported for Durban and Cape Peninsula blacks as well as for people of mixed ancestry in in the Western Cape. The prevalence of hypertension in black subjects from different populations are summarised in Fig. 9.2/1. Using the hypertension prevalence data from the SADHS (Steyn et al., 2001) the prevalence of hypertension in SA adults compares favourably with rates found in subjects of Afro-Caribbean descent in the UK (Fig.9.2/1).

The disparity in results obtained between the Omron aneroid method and the Hawksley (RZ) measurements, were obvious in spite of the different age structures of the samples. The Omron method is relatively simple and is widely used internationally. The Hawksley method, however, is cumbersome and requires greater concentration on the part of the operator than a traditional mercury sphygmomanometer. It also takes much longer to do a single blood pressure measurement. For this very reason the results obtained with the Hawksley might be more reliable. In the FS studies, all BP measurements were performed in duplicate by two trained observers, with regular quality control sessions. Since great care was also taken with quality control during the SADHS, other reasons for the disparity in hypertension prevalence should be sought. Possible explanations include a true difference between the two techniques, a difference in sampling procedure, and BP measurements were done in subject's homes during the SADHS and in community health centres during the Qwaqwa and Mangaung studies. Furthermore, at least two reports appeared in the literature of the Hawksley RZ underestimating systolic BP by as much as 3.4 mmHg and diastolic BP by as much as 3.7 mmHg (Brown et al., 1997 and O'Brien et al., 1990). If anything, the prevalence of hypertension might have been underestimated in the

FS studies compared to other studies where mercury sphygmomanometers were used. One possible solution to solve this intriguing dilemma is to do a field study using both instruments.

Since the WHO (1978) definition of hypertension is a broad definition, the actual composition of this category was also analysed. Among females with hypertension in the Qwaqwa sample, 58.2% had a diastolic blood pressure of ≥ 95 mm Hg, 65.8% had a systolic blood pressure ≥ 160 mm Hg and 40.9% had both elevated systolic and diastolic blood pressure readings above these cut-points. For male subjects the corresponding percentages were 49.4%, 65.6% and 27.8%. Among females in Mangaung the corresponding figures were 49.8%, 62.2% and 37.8% and for males 70.2%, 53.6% and 32.1%.

TABLE 9.2/2. Prevalence (%) of Hypertension[1] (WHO Definition)

According to Age Group, Sex and Population

	Qwaqwa		Mangaung	
	n	%	n	%
Men (age in yr)				
25-34	56	14.3	67	11.9
35-44	68	20.6	65	10.8
45-54	27	14.8	64	34.4
55-64	45	37.8	54	42.6
65+	83	43.4	40	60
Age-standardized prevalence		22.1		22.8
Women (age in yr)				
25-34	142	9.9	105	12.4
35-44	110	29.1	126	31
45-54	99	44.4	103	61.2
55-64	102	53.9	68	52.3
65+	121	66.1	64	78.1
Age-standardized prevalence		34.5		36.3
Total				
Age- and sex-standardised	853	29.2	756	30.3
Sex- and age-Standardised to Qwaqwa population		29.2		33.3[a]

[1] Systolic blood pressure ≥160 and/or diastolic blood pressure ≥95 mm Hg or on treatment for hypertension

[a] 95% CI for the difference Qwaqwa-Mangaung −9.5;1.3

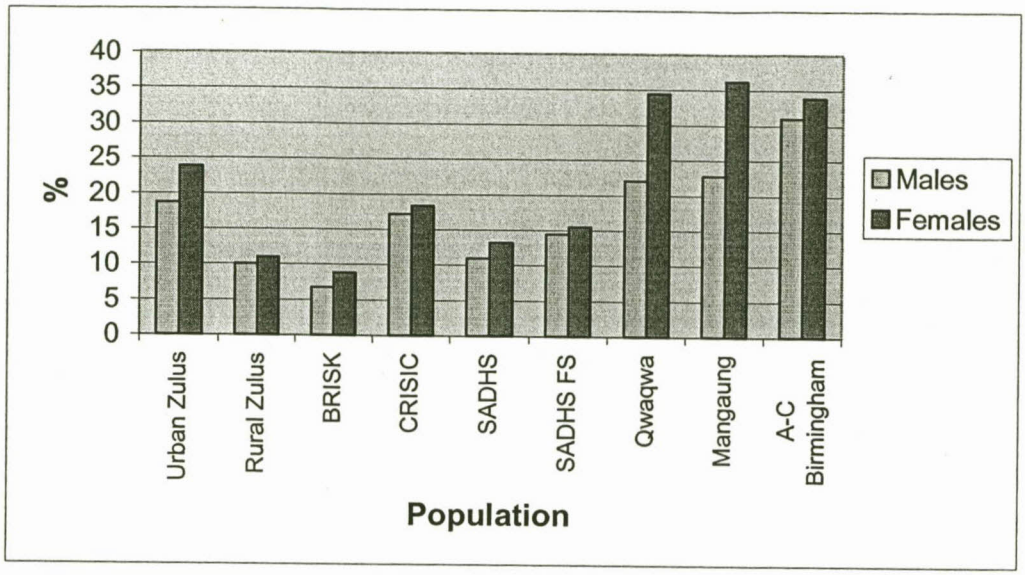


Fig. 9.2/1. Prevalence of Hypertension (SBP ≥160, DBP ≥95) in Different Populations in SA compared with Birmingham Subjects of Afro-Caribbean Descent.

The age- and sex-specific rates of borderline hypertension (WHO, 1978) in the two populations are shown in Table 9.2/3. In Qwaqwa 22.2% of males and 16.7% of females had borderline hypertension while in Mangaung the respective rates were 20.6% and 17%.

TABLE 9.2/3. Prevalence (%) of Borderline Hypertension[1]

According to Age Group, Sex and Population

	Qwaqwa		Mangaung	
	n	%	n	%
Men (age in yr)				
25-34	56	14.3	67	19.4
35-44	68	26.5	65	20
45-54	27	25.9	64	18.8
55-64	45	22.2	54	27.8
65+	83	31.3	40	22.5
Age-standardized prevalence		22.2		20.6
Women (age in yr)				
25-34	142	11.3	105	9.5
35-44	110	20.9	126	18.3
45-54	99	26.3	103	10.5
55-64	102	16.7	68	26.5
65+	121	14.1	64	12.5
Age-standardized prevalence		16.7		14.1
Total				
Age- and sex-standardized	853	19.2	756	17

[1] Systolic blood pressure ≥ 140 but < 160 and diastolic blood pressure ≥ 90 but < 95 mm Hg and not on treatment for hypertension

The age- and sex-specific rates of other categories of hypertension are shown in Table 9.2/4. As expected, isolated systolic hypertension was common in the older age groups in both populations. Among Qwaqwa male subjects in the age group 55-64 the prevalence of isolated systolic hypertension was 22.2% and among females 14.7%. Among elderly males and females the prevalence was 19.3% and 26.5% respectively. Among Mangaung male subjects severe isolated systolic hypertension was present in 9.3% in the age group 55-64 years, while in females it was present in 20.6% in the same age group. In elderly subjects isolated systolic hypertension was present in 25% of both sexes.

TABLE 9.2/4a. Age- and Sex-Specific Rates of Other Categories of Hypertension in the Study Populations

	Isolated Systolic Hypertension ≥160/<95 mmHg	Severe Diastolic Hypertension [1] > 115 mmHg	Diastolic Hypertension[2] >100 mmHg
Qwaqwa			
Men (age in yr)			
2.5-34	1.8	1.8	10.7
35-44	1.5	2.9	11.8
45-54	3.7	7.4	7.4
55-64	22.2		6.7
65+	19.3	3.6	10.8
Prevalence	6.3	3	10.1
Women (age in yr)			
25-34	0.7	1.4	6.3
35-44	2.7	1.8	8.2
45-54	5.1	9.1	28.3
55-64	14.7	5.9	24.5
65+	26.5	5.8	26.5
Age Standardized Prevalence	8	3.9	15.8
Total			
Age- and sex-standardized	7.4	3.5	13.2

[1] As defined by the JNC, 1988

[2] Diastolic blood pressure level above which treatment is mandatory according to the Consensus Report, MRC/Heart Foundation, 1992 (figures include patients on inadequate treatment)

TABLE 9.2/4b. Age- and Sex-Specific Rates of Other Categories of Hypertension in the Study Populations

	Isolated Systolic Hypertension ≥ 160/<95 mmHg	Severe Diastolic Hypertension [1] > 115 mmHg	Diastolic Hypertension[2] >100 mmHg
Mangaung			
Men (age in yr)			
25-34	-	-	6
35-44	-	-	4.6
45-54	4.7	3.1	21.9
55-64	9.3	1.6	22.2
65+	25	7.5	20
Age Standardized Prevalence	3.7	1.3	11.5
Women (age in yr)			
25-34	-	-	3.8
35-44	7.1	1.6	7.9
45-54	9.5	6.7	26.7
55-64	20.6	5.9	19.1
65+	25	7.8	23.4
Age Standardized Prevalence	8.1	2.9	12.4
Total			
Age-standardized prevalence	6.1	2.2	12

[1] As defined by the JNC, 1988

[2] Diastolic blood pressure level above which treatment is mandatory according to the Consensus Report, MRC/Heart Foundation, 1992 (figures include patients on inadequate treatment)

The Joint National Committee (1988) advised that all patients with a diastolic blood pressure equal to or exceeding 115 mm Hg should be evaluated or referred for immediate care. This means that in Qwaqwa 3.5% and in Mangaung 2.2% of the population were in urgent need of medical attention because of a serious blood pressure problem. In Qwaqwa the highest rates in this category were found in the age group 45-54 years (males 7.4%, females 9.1%) and in Mangaung in the elderly group (males 7.5%, females 7.8%).

For the southern African situation it was suggested that pharmacologic treatment should be reserved for patients with diastolic blood pressures in excess of 100 mm Hg (Management Guidelines, 1992). This means that in Qwaqwa 13.2% and in Mangaung 12% of the population was either in need of drug therapy or had inadequately controlled hypertension.

After adjusting the Qwaqwa population to the world standard population, the prevalence of hypertenson among subjects 25 years and older was 29.7% (23.4% males, 36.0% females). After the same adjustment, the prevalence of hypertension among subjects 30 years and older was 41.6% (25.9% males, 33.8% females). Corresponding rates of hypertension in Mangaung subjects 25 years and older was 34.9% (males 27.6%, females 42.1%) while in the age group 30 years and older, rates adjusted to the world standard population were 39.9% for the total population (males 30.6%, females 49.2%).

To correct for the possible influence of arm circumference on blood pressure measurement, Maxwell's correction factor was applied to the data (Maxwell, 1982). Table 9.2/5 shows the prevalence of hypertension (WHO, 1978) after correction. The percentage change in the prevalence of hypertension after correction is shown in Table 9.2/6. Amongst male subjects in both populations, the age-standardized prevalence of hypertension was slightly higher after applying the correction factor. In Qwaqwa males the prevalence increased by 2.5% to 24.6% and in Mangaung males by 1.7% to 24.5%. In females, however, the prevalence was reduced by 1% among Qwaqwa females to 33.5% and in Mangaung females by 2% to 34.3%. Overall, the total age- and sex-adjusted prevalence of hypertension was not clinically significantly influenced by the

correction factor. Consistently using a large blood pressure cuff when arm circumference exceeds 33 cm, as was done in both studies, eliminates the need to do any further corrections for arm circumference.

TABLE 9.2/5. Prevalence (%) of Hypertension[1] (HT) According to Age Group, Sex and Population After Correcting for Arm Circumference[2]

	Qwaqwa		Mangaung	
	HT	CHT[3]	HT	CHT[3]
Men (age in yr)				
25-34	14.3	14.3	11.9	13.4
35-44	20.6	25	10.8	13.9
45-54	14.8	18.5	34.4	35.9
55-64	37.8	37.8	42.6	44.4
65+	43.4	49.4	60	57.5
Age-standardized prevalence	22.1	24.6	22.8	24.5
Women (age in yr)				
25-34	9.9	9.9	12.4	13.3
35-44	29.1	25.5	31	27.8
45-54	44.4	46.7	61.2	56.3
55-64	53.9	51	52.3	48.5
65+	66.1	65.3	78.1	76.6
Age-standardized prevalence	34.5	33.5	36.3	34.3
Total				
Age- and sex-standardized	29.2	29.7	30.3	30

[1] Systolic blood pressure ≥ 160 and/or diastolic blood pressure ≥ 95 mm Hg or on treatment for hypertension

[2] Corrected for arm circumference with Maxwell's (1982) correction factor.

[3] CHT = corrected hypertension

TABLE 9.2/6. Impact of Correcting for Arm Circumference[1] on the Prevalence of Hypertension (95% Confidence Intervals in Parenthesis)

	Increase or decrease (%)	95% CI
Qwaqwa		
Males (age in yr)		
25-34	-1.0	-2.8 to 0.9%
35-44	3.2	-1.2 to 7.5%
45-54	4.9	0.7% to 9.0
55-64	4.4	-1.9 to 10.8%
65+	1.6	-3.7 to 6.9%
Females (age in yr)		
25-34	1.6	-8.0 to 5.0%
35-44	-1.5	-9.1 to 2.9%
45-54	-1.6	-4.6 to 1.5%
55-64	-1.9	-5.4 to 1.7%
65+	2.5	-6.0% to 11.0%
Mangaung		
Males (age in yr)		
25-34	0.0	-2.8% to 2.8%
35-44	3.6	-1.4 to 8.6%
45-54	-2.0	-7.6% to 3.6%
55-64	2.9	-0.3 to 6.2%
65+	0.8	-2.8 to 4.4%
Females (age in yr)		
25-34	0.0	-4.9% to 4.9%
35-44	-4.4	-10.8% to 1.9%
45-54	-3.7	-10.8% to 3.4%
55-64	0.0	-7.9% to 7.9%
65+	-6.0	-11.1% to -0.9%

1 Maxwell's correction factor (1982)

Summary

Application of a reasonably strict definition of hypertension such as a systolic blood pressure equal to or exceeding 140 mm Hg and / or a diastolic blood pressure equal to or exceeding 90 mm Hg, resulted in an age-standardised prevalence of hypertension of 48.4% (44.3% in males and 51.3% in females) in Qwaqwa and 47.3% (43.4% in males and 50.4% in females) in Mangaung. These rates are considerably higher than that reported for black subjects in the Cape Peninsula or in Zimbabwe.

By applying the more conservative WHO definition, the age- and sex-adjusted prevalence of hypertension was 29.2% (22.1% in males and 34.5% in females) in Qwaqwa and 30.3% (22.8% in males and 36.3% in females) in Mangaung. Up to 14% of subjects in the young age group of 25-34 years had hypertension according to this definition. These rates are higher than that previously reported for urban and rural Zulus as well as for Cape Peninsula blacks. The SADHS reported much lower rates for hypertension in the FS although these rates were also among the highest in the SA. Methodological differences such as the sampling procedure, technique of BP measurement and the place where BP was measured (community health centre vs. home) may account for some of the difference. It is interesting that the prevalence of hypertension in FS blacks are very similar to that reported for Afro-Caribbean subjects in Birmingham. Up to 83% of elderly subjects was hypertensive while isolated systolic hypertension was present in up to 25% of the elderly. Overall, these rates are unacceptably high and calls for action not only to detect and aggressively manage hypertension at an earlier stage but also to implement preventative measures.

9.3 Prevalence of hypertension by region

On the basis of previous surveys for the Qwaqwa Department of Health, the Human Sciences Research Council was able to provide guidelines for dividing Qwaqwa into an urban area (Phuthaditjhaba), a semi-rural and a rural area. Since all villages were proportionally represented in the sample, the prevalence of hypertension could also be computed for the semi-rural and rural areas (Table

9.3/1). Due to the relative small number of subjects in the urban area, it was not feasible to calculate a separate rate for this area.

Among men in the semi-rural areas the age-standardized prevalence of hypertension (WHO, 1978) was somewhat lower (17.4%) than among men from the rural areas (21.3%). The prevalence of hypertension was very similar among females in both areas. The overall age-standardized prevalence of hypertension in the semi-rural (26.3%) and rural (28.9%) areas did not differ clinically significantly from the sample prevalence of 29.9%. One can speculate that in spite of living in the more rural areas of Qwaqwa these subjects were already urbanised to the same extent than those living in the semi-rural areas.

TABLE 9.3/1. The Prevalence (%) of Hypertension in Qwaqwa

According to Area (Phuthaditjhaba excluded)

	Semi-Rural		Rural	
	n	%	n	%
Men (age in yr)				
25-34	19	10.5	19	10.5
35-44	28	10.7	29	24.1
45-54	10	10	12	16.7
55-64	21	33.3	21	38.1
65+	39	46.2	42	38.1
Age-standardized prevalence	117	17.4	123	21.3
Women (age in yr)				
25-34	50	10	63	9.5
35-44	47	23.4	49	30.6
45-54	39	41	49	44.9
55-64	44	54.6	50	52
65+	58	67.2	56	67.9
Age-standardized prevalence	238	33.1	267	34.8
Total				
Age-standardized prevalence	355	26.3	390	28.9

9.4 Previous diagnosis of hypertension and treatment status

Table 9.4/1 shows the age- and sex-specific rates of a previous diagnosis of hypertension. A low proportion of subjects with hypertension (known and newly diagnosed) were receiving treatment (range 21.4% to 39.3%). Of these on treatment a disappointingly low proportion had their hypertension controlled (range 20.0% to 41.8%) (Table 9.4/2). The percentage of subjects whose hypertension was under control was greater in Mangaung than in Qwaqwa. Hypertension was poorly controlled in an alarming percentage of known hypertensives on treatment (Table 9.4/3). An urgent need exists for a strategy to improve the level of blood pressure control amongst subjects taking medication. This finding is in keeping with the results of the SADHS survey (1998).

TABLE 9.4/1. Percentage of Persons Aware of a Past Diagnosis of Hypertension by Age, Sex and Population

	n	%
Qwaqwa		
Men (age in yr)		
25-34	56	7.1
35-44	68	8.8
45-54	27	11.1
55-64	45	13.3
65+	83	15.7
Age-standardized prevalence	279	9.9
Women (age in yr)		
25-34	142	7.8
35-44	110	18.2
45-54	99	33.3
55-64	102	41.2
65+	121	42.3
Age-standardized prevalence	574	24.1
Total		
Age-standardized prevalence	853	17.8
Mangaung		
Men (age in yr)		
25-34	67	4.5
35-44	65	13.9
45-54	63	25.4
55-64	54	37
65+	40	40
Age-standardized prevalence	289	17.2
Women (age in yr)		
25-34	105	13.3
35-44	126	31.8
45-54	105	61.9
55-64	68	57.4
65+	64	68.8
Age-standardized prevalence	468	36.6
Total		
Age-standardized prevalence	757	28

TABLE 9.4/2. Number of Hypertensives on Treatment and Level of Control of Hypertension (Percentage in Parenthesis)

	na	Receiving Treatment	Hypertension Controlled b
Qwaqwa			
Males	79	20 (25.3)	4 (20)
Female	225	77 (34.2)	25 (32.5)
Mangaung			
Males	84	18 (21.4)	4 (22.2)
Females	201	79 (39.3)	33 (41.8)

[a] Total number of hypertensives

[b] Systolic BP < 160 mm Hg **and** diastolic BP < 95

TABLE 9.4/3. Hypertension and Treatment Status According to Region, Sex and Age.

	Among those with hypertension[1]			
	% Who knows	% Taking medication	% Whose HT is controlled	Number with hypertension
Qwaqwa				
Males				
25-34	37.5	37.5	0	8
35-44	28.6	28.6	21.4	14
45-54	50	25	25	4
55-64	29.4	17.7	11.8	17
65+	27.8	25	13.9	36
Females				
25-34	64.3	35.7	21.4	14
35-44	62.5	34.4	31.3	32
45-54	59.1	31.8	13.6	44
55-64	67.3	40	12.7	55
65+	60	31.3	15	80
Mangaung				
Males				
25-34	37.5	25	0	7
35-44	28.6	0	0	7
45-54	57	22.7	13.6	22
55-64	73.9	30.4	8.7	23
65+	54.2	16.7	8.3	24
Females				
25-34	61.5	46.2	38.7	13
35-44	66.7	43.6	38.5	39
45-54	81	46	22.2	63
55-64	80.6	36.1	16.7	36
65+	74	28	24	50

[1] ≥ 160/95 mm Hg.

9.5 Relationship between obesity and hypertension

The prevalence of hypertension (WHO, 1978) after adjusting for age, sex and body mass index, is shown in Table 9.5/1. Obesity was defined as a BMI ≥ 25 kg/m^2 to include the WHO pre-obesity category (WHO Technical Report, 2000). In both the older and younger subgroups in both populations hypertension and borderline hypertension was more common in the obese subjects than in those with normal BMI with the exception of older females in Mangaung. In Qwaqwa females, the prevalence of hypertension ranged between 5.6% in the young non-obese group to 60.9% in the older obese group. The corresponding rates for Mangaung females were 16.4% to 67.8%.

The relative risk (RR) for hypertension (obese compared to non-obese) after adjusting for age and sex is shown in Table 9.5/2. In Qwaqwa, obese respondents were more likely to have hypertension than non-obese respondents with the exception of older male subjects. The summary relative risk for the total sample was 2.9 (95% CI 1.3-6.2) indicating a significant association between hypertension and BMI in this population. Young obese females were 4.5 times more likely to have hypertension than young non-obese females. Such a high relative risk in younger subjects with obesity indicates that obesity is not an innocent condition or a "healthy" condition in females in this population. Young obese females in the Mangaung sample on the other hand, showed no increased risk of hypertension although the older females did. Great care must be exercised when interpreting epidemiological data such as these. If the findings in this regard for the Qwaqwa sample were ignored, it would have been possible to conclude that obesity in young females is "a healthy obesity" as far as hypertension is concerned. This is clearly not the case for young females in Qwaqwa. The explanation for this paradox between the two samples is not simple and other factors such as diet, exercise and family history will have to be considered as well. The age and sex-adjusted summary relative risk for hypertension in obese subjects compared to non-obese subjects in Mangaung was 1.4 (95% CI 1.1-1.7) indicating that, overall, obesity in this population is not "healthy". The age- and sex-adjusted summary relative risk for borderline hypertension in Qwaqwa was

also significant in obese compared to non-obese subjects but just failed to be significant in the Mangaung sample. The association between obesity and hypertension in the Mangaung sample was not as strong as in the Qwaqwa sample. Again, other factors such as diet, exercise and family history will have to be considered.

Obesity was associated with hypertension in both rural and urban Zulus (Seedat et al., 1982). Hypertension was also independently related to obesity in black subjects in the Cape Peninsula (Steyn et al., 1997). In the study of hypertension in the coloured population of Cape Town a weak association was found between hypertension and obesity, an association that disappeared when arm circumference was corrected for (Steyn et al., 1986). In the Zimbabwe study it was shown that systolic blood pressure increased by 0.84 mm Hg per kg/m2 for women and with 1.85 mm Hg per kg/m^2 for men (Mufunda et al., 2000). Obesity was also significantly associated with hypertension in a study performed in the Gambia (van der Sande et al., 2000). In the Birmingham study age, BMI and ethnicity predicted hypertension in Afro-Caribbean subjects (Lane et al., 2002). The findings of a significant association between obesity and hypertension in FS black subjects from both populations are in line with the findings in these studies. The confirmation of an association between obesity and hypertension in the FS populations is of significance and provides evidence to support weight management programmes as called for in the WHO initiative (1997).

Summary

After adjusting for age and sex, the risk of hypertension was clearly increased in obese (BMI $\geq$ 25 kg/m^2) subjects in both Qwaqwa and Mangaung. This finding is in agreement with other studies in black populations in SA, in Africa and in the U.K. Overall this increased risk was higher in Qwaqwa subjects than Mangaung subjects and cannot be explained on the grounds of urbanisation. Other factors such as family history of hypertension, physical activity and dietary factors need to be investigated in an attempt to explain this paradox. The confirmation of obesity as a risk factor for hypertension in the FS populations supports the call for weight management programmes also in the FS.

TABLE 9.5/1. The Prevalence of Hypertension By Age, Sex and Body Mass Index by Population (Percentage in Parenthesis)

	Hypertension[a]		Borderline[b] HT	
	Size of Group n	Subjects with HT n (%)	Size of Group n	Subjects with HT n (%)
Qwaqwa (age in yr)				
Females <45)				
BMI ≥ 25	163	41 (25.2)	122	25 (20.5)
BMI < 25	89	5 (5.6)	84	14 (16.7)
Females (≥45)				
BMI ≥ 25	215	131 (60.9)	84	41 (48.8)
BMI < 25	107	48 (44.9)	59	19 (32.2)
Males (<45)				
BMI ≥ 25	41	13 (31.7)	28	12 (42.9)
BMI < 25	82	9 (11.0)	73	14 (19.2)
Males (≥45)				
BMI ≥ 25	44	20 (45.5)	24	13 (54.2)
BMI < 25	109	36 (33.0)	73	29 (39.7)
Mangaung (age in yr)				
Females (<45)				
BMI ≥ 25	156	40 (25.6)	116	25 (21.6)
BMI < 25	73	12 (16.4)	61	8 (13.1)
Females (≥45)				
BMI ≥ 25	171	116 (67.8)	55	22 (40.0)
BMI < 25	64	33 (51.6)	31	15 (48.4)
Males (45)				
BMI ≥ 25	37	5 (13.5)	32	10 (31.3)
BMI < 25	94	10 (10.6)	84	16 (19.1)
Males (≥45)				
BMI ≥ 25	55	29 (52.7)	26	16 (61.5)
BMI < 25	103	40 (38.8)	63	20 (31.8)

[a] Systolic Blood pressure ≥ 160 and / or diastolic blood pressure ≥ 95 mm Hg or on treatment for hypertension (WHO, 1978)

[b] Systolic Blood pressure ≥ 140 but < 160 and / or diastolic blood pressure ≥ 90 but < 95 mm Hg (WHO, 1978)

TABLE 9.5/2. The Relative Risk (RR) for Hypertension in Obese Subjects (BMI > 25 kg/m^2) Compared to Non-obese Subjects After Adjusting for Age and Sex (95% Confidence Interval in Parenthesis)

	RR Hypertension[a]	RR Borderline Hypertension [b]
Qwaqwa (age in yr)		
Females (<45)	4.5 (1.8-10.9)	1.2 (0.68-2.2)
Females (≥45)	1.4 (1.1-1.7)	1.5 (0.99-2.3)
Males (<45)	2.9 (1.3-6.2)	2.2 (1.2-4.2)
Males (≥45)	1.4 (0.9-21)	1.4 (0.86-2.2)
Summary RR	2.9 (1.3-6.2)	1.5 (1.2-1.9)
Mangaung (age in yr)		
Females (<45)	1.6 (0.87-2.8)	1.6 (0.79-3.4)
Females (≥45)	1.3 (1.07-1.7)	0.83 (0.51-1.3)
Males (<45)	1.3 (0.47-3.5)	1.6 (0.83-3.2)
Males (≥45)	1.4 (0.96-1.9)	1.9 (1.2-3.1)
Summary RR	1.4 (1.1-1.7)	1.4 (1.0-1.9)

* Statistically significantly different from 1 at the 0.05 level

[a] Systolic Blood pressure> 160 and / or diastolic blood pressure > 95 mm Hg or on treatment for hypertension (WHO, 1978)

[b] Systolic Blood pressure> 140 but < 160 and / or diastolic blood pressure> 90 but < 95 mm Hg (WHO, 1978)

9.6 Relationship between central obesity and hypertension

The prevalence of hypertension and borderline hypertension by age, sex and waist-to-hip ratio (WHR) is shown in Table 9.6/1. The prevalence of hypertension ranged between 7.6% among Qwaqwa males with a peripheral body fat distribution and age under 45 years, to 58.8% in females 45 years and older with central obesity. Corresponding rates for Mangaung males and females were 6.3% and 67.3%. Overall, in each age group and in both populations, the prevalence of hypertension was higher in subjects with central obesity than in subjects with peripheral body fat distribution. The same was observed for borderline hypertension with the exception of young females in Qwaqwa and older females in Mangaung.

The relative risk of hypertension in subjects with central obesity compared to subjects with peripheral body fat distribution after adjusting for age and sex is shown in Table 9.6/2. In both samples, the summary relative risk for hypertension among subjects with central obesity compared to peripheral body fat distribution was 1.5 (95% CI 1.2-1.8). The risk was particularly high for young males (RR=3.9 Qwaqwa and RR=4 Mangaung). This was not the case for women with the exception of young females in Qwaqwa who had a RR of 1.8 (95% CI 1.1-3.0). This was also the group in whom obesity was associated with hypertension. Subjects with central obesity were not significantly more likely to have borderline hypertension than subjects with peripheral body fat distribution with the exception of the younger subgroup of males in Mangaung (Table 9.6/2). The possibility that waist circumference might be a better predictor of hypertension in males as well as in females needs to be explored as well.

Few other studies examined the relation between central obesity and hypertension in black subjects. The Zimbabwean study also found a highly significant association between waist circumference and WHR and hypertension in both sexes (Mufunda et al., 2000).

TABLE 9.6/1. The Prevalence of Hypertension According to Median WHR After Adjusting For Age and Sex (Percentage in Parenthesis)

	Hypertension[a]		Borderline[b] HT	
	Size of Group n	Subjects with HT n (%)	Size of Group n	Subjects with HT n (%)
Qwaqwa (age in yr)				
Females <45)				
WHR > Median	80	21 (26.3)	59	9 (15.3)
WHR < Median	171	25 (14.6)	146	30 (20.6)
Females (≥45)				
WHR > Median	204	120 (58.8)	84	39 (46.4)
WHR < Median	116	58 (50.0)	58	20 (34.5)
Males (<45)				
WHR > Median	57	17 (29.8)	40	11 (27.5)
WHR < Median	66	5 (7.6)	61	15 (24.6)
Males (≥45)				
WHR > Median	80	36 (45.0)	44	21 (47.7)
WHR < Median	72	19 (26.4)	53	21 (39.6)
Mangaung (age in yr)				
Females <45)				
WHR > Median	74	20 (27.0)	54	14 (25.9)
WHR < Median	157	32 (20.4)	125	19 (15.2)
Females (≥45)				
WHR > Median	159	107 (67.3)	52	21 (40.4)
WHR < Median	76	42 (55.3)	34	16 (47.1)
Males (<45)				
WHR > Median	35	9 (25.7)	26	10 (38.5)
WHR < Median	96	6 (6.3)	90	15 (16.7)
Males (≥45)				
WHR > Median	109	57 (52.3)	52	22 (42.3)
WHR < Median	49	12 (24.5)	37	14 (37.8)

[1] Median WHR for Qwaqwa subjects: females 0.85, males 0.97

Median WHR for Mangaung subjects: females 0.85, males 0.98

[a] Systolic Blood pressure ≥ 160 and / or diastolic blood pressure > 95 mm Hg or on treatment for hypertension (WHO, 1978)

[b] Systolic Blood pressure ≥ 140 but < 160 and / or diastolic blood pressure ≥ 90 but < 95 mm Hg (WHO, 1978)

TABLE 9.6/2. The Relative Risk (RR) for Hypertension in Subjects with Central Obesity1 Compared to Subjects with Peripheral Obesity After Adjusting for Age and

	RR Hypertension[a]	RR Borderline Hypertension[b]
Qwaqwa (age in yr)		
Females (<45)	1.8 (1.1-3.0)*	0.74 (0.38-1.5)
Females (≥45)	1.2 (0.95-1.46)	1.3 (0.88-2.1)
Males (<45)	3.9 (1.6-10.0)*	1.1 (0.57 2.2)
Males (≥45)	1.7 (1.1-2.7)*	1.2 (0.77-1.9)
Summary RR	1.5 (1.2-1.8)*	1.1 (0.87-1.5)
Mangaung (age in yr)		
Females (<45)	1.3 (0.82-2.2)	1.7 (0.93-3.1)
Females (≥45)	1.2 (0.97-1.5)	0.86 (0.53-1.4)
Males (45)	4.0 (1.6-10.8)*	2.3 (1.2-4.5)*
Males (≥45)	2.1 (1.3-3.6)*	1.1 (0.66-1.9)
Summary RR	1.5 (1.2-1.8)*	1.3 (0.98-1.7)

[1] Median WHR for Qwaqwa subjects: females 0.85, males 0.97

Median WHR for Mangaung subjects: females 0.85, males 0.98

* Statistically significantly different from 1 at 0.05 level

[a] Systolic Blood pressure> 160 and / or diastolic blood pressure > 95 mm Hg or on treatment for hypertension (WHO, 1978)

[b] Systolic Blood pressure> 140 but < 160 and / or diastolic blood pressure> 90 but < 95 mm Hg (WHO, 1978)

Summary

In both FS populations WHR was significantly associated with increased risk of hypertension, a risk that was particularly high for young male subjects. A second criterion to satisfy the WHO definition for the existence of the metabolic syndrome in FS blacks has been established.

9.7 Relationship between glucose intolerance and hypertension

The relationship between pharmacological treatment of hypertension and glucose tolerance has been addressed in section 8.7. The prevalence of hypertension in diabetic subjects compared to subjects with normal glucose tolerance according to BMI and age is shown in Table 9.7/1 and Fig. 9.7/1.

No specific pattern or gradient in the prevalence of hypertension between the different categories of glucose tolerance could be detected for the different BMI and age categories in any of the populations except in the young group in the Mangaung sample (Fig. 9.7/1). Among subjects 45 years and older in the Qwaqwa population, the prevalence of hypertension in the stratum BMI < 25 kg/m^2 was very similar in the different categories of glucose tolerance (38.2% in group with normal glucose tolerance, 39.0% in group with IGT and 42.9% in group with diabetes). In the stratum BMI ≥ 25 kg/m^2 hypertension was more prevalent in subjects with IGT in both age groups than in subjects with normal glucose tolerance and diabetes. In the Mangaung population in the BMI < 25 kg/m^2 stratum and age group older than 45 years, the prevalence of hypertension (80%) in the small number of diabetics was double that of subjects in the normal and IGT group. In the BMI ≥ 25 kg/m^2 stratum, the highest prevalence rates of hypertension were found in the younger age group with diabetes (60.0%) and in subjects with IGT in the older age group (71.7%).

The relative risk for hypertension in subjects with glucose intolerance compared to subjects with normal glucose tolerance after adjusting to BMI and age was computed and is shown in Table 9.7/2. In the Qwaqwa population no significant association was found between hypertension and glucose tolerance. Overall, in the Mangaung population, no significant association could be demonstrated between hypertension and glucose tolerance. However, in the BMI < 25 kg/m2 and age ≥ 45 years subgroup, as well as in the BMI ≥ 25 kg/m^2 and age < 45 years subgroup the risk of hypertension in diabetics compared to normal subjects was significantly increased with a RR = 2.0 (95% CI 1.4-2.9) and 2.9 (95% CI 1.4-6.4) respectively.

Since treatment of hypertension may bias the association between hypertension rates and glucose tolerance, the association between hypertension and glucose tolerance was also determined after excluding those hypertensives currently on treatment (Table 9.7/3). This step yielded similar results and did not change the preceding conclusion.

TABLE 9.7/1. The Prevalence (%) of Hypertension in Subjects With Normal Glucose Tolerance, Diabetes and IGT in the Study Populations After Adjusting for BMI and Age

	Normal Glucose Tolerance		Diabetes		IGT	
	n	%	n	%	n	%
Qwaqwa						
BMI < 25 kg/m2						
Age < 45 yr	163	8.6	-	-	7	
Age ≥ 45 yr	157	38.2	14	42.9	41	39
BMI ≥ 25 kg/m2						
Age < 45 yr	178	24.7	5	20	17	41.2
Age ≥ 45 yr	183	56.3	32	59.4	40	65
Mangaung						
BMI < 25 kg/m2						
Age < 45 yr	151	13.3	4	-	8	12.5
Age ≥ 45 yr	131	40.5	10	80	9	40.9
BMI ≥ 25 kg/m2						
Age < 45 yr	157	20.4	5	60	27	33.3
Age ≥ 45 yr	138	60.9	37	64.9	46	71.7

These results were unusual since in the United Kingdom Prospective Diabetes Study 38% of newly diagnosed patients with Type 2 diabetes had hypertension defined as a systolic BP of ≥ 160 mmHg and / or a diastolic BP ≥ 90 mmHg or receiving antihypertensive treatment as a systolic BP ≥ 150 mmHg and /or a diastolic BP of 85 mmHg (UKPDS 38, 1998). The association between hypertension and newly diagnosed Type 2 diabetes may be explained by several mechanisms. These may include coincidental hypertension, the metabolic syndrome, diabetogenic antihypertensive drugs, drugs causing both diabetes and hypertension and rare endocrine disorders (Nilsson, 1997). A quintet of cardiovascular risk factors usually associated with the metabolic syndrome existed in the UKPDS patients with Type 2 diabetes, explaining the relative high prevalence of hypertension in their patients (UKPDS 38, 1998). Since insulin resistance is presumed to be the common factor linking glucose intolerance and

hypertension (Reaven, 1988) it was expected that patients with diabetes and IGT in the FS studies would have a higher prevalence of hypertension than non-diabetic subjects. Possible explanations for these unexpected negative findings may be that the pathophysiology of type 2 diabetes and / or hypertension is different in this ethnic group compared to the subjects participating in the UKPDS. These possibilities may be worth exploring. Another possibility is that the number of patients with glucose intolerance was to small to demonstrate the expected increase in prevalence of hypertension. This is unlikely since in Qwaqwa 156 subjects and in Mangaung 146 subjects with glucose intolerance were studied.

Summary

An important negative finding from the FS studies was the absence of an expected increase in the prevalence of hypertension in at least the diabetic subjects. The prevalence of hypertension in subjects with IGT and diabetes in the FS studies was not different from non-diabetic subjects. A potential implication of this finding is that the pathophysiology of type 2 diabetes and / or hypertension may be different in this population.

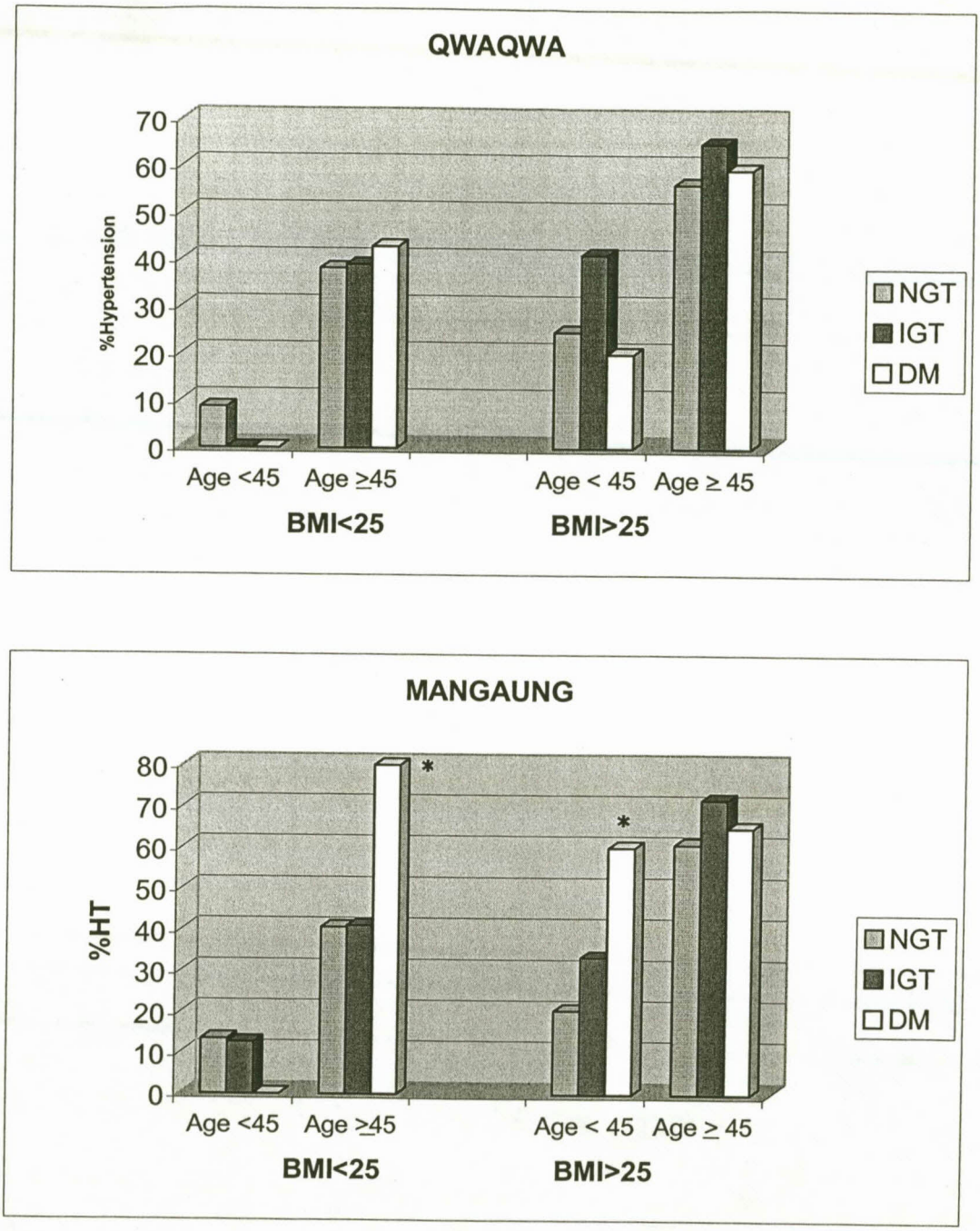


Fig. 9.7/1. Prevalence of Hypertension According to Glucose Tolerance Status, Age and BMI.

TABLE 9.7/2. The Relative Risk (RR) for Hypertension in Subjects with Abnormal Compared to Normal Glucose Tolerance After Adjusting for BMI and Age in the Study Populations (95% CI in Parenthesis)

	Diabetics Compared to Normal: RR	IGT Compared to Normal: RR
Qwaqwa		
BMI < 25 kg/m2, Age < 45 yr	a	a
BMI < 25 kg/m2, Age ≥ 45 yr	1.1 (0.6-2.1)	1.0 (0.7-1.6)
BMI ≥ 25 kg/m2, Age < 45 yr	0.8 (0.1-4.8)	1.7 (0.9-3.1)
BMI ≥ 25 kg/m2, Age ≥ 45 yr	1.1 (0.8-1.4)	1.2 (0.9-1.5)
Summary RR	1.1 (0.8-1.4)	1.1 (0.9-1.4)
Mangaung		
BMI < 25 kg/m2, Age < 45 yr	a	0.9 (0.1-6.2)
BMI < 25 kg/m2, Age ≥ 45 yr	2.0 (1.4-2.9)*	1.0 (0.6-1.7)
BMI ≥ 25 kg/m2, Age < 45 yr	2.9 (1.4-6.4)*	1.6 (0.9-3.0)
BMI ≥ 25 kg/m2, Age ≥ 45 yr	1.1 (0.8-1.4)	1.2 (0.9-1.5)
Summary RR	a	1.2 (0.96-1.5)

a Cannot be calculated

* Statistically significantly different from 1 at the 0.05 level

TABLE 9.7/3. The Relative Risk (RR) for Hypertension in Subjects with Abnormal Compared to Normal Glucose Tolerance After Adjusting for BMI and Age in the Study Populations and After Excluding Hypertensives Currently on Treatment (95% CI in Parenthesis)

	Diabetics Compared to Normal: RR	IGT Compared to Normal: RR
Qwaqwa		
BMI < 25 kg/m2, Age < 45 yr	a	a
BMI < 25 kg/m2, Age> 45 yr	1.3 (0.7-2.4)	0.9 (0.5-1.5)
BMI > 25 kg/m2, Age < 45 yr	a	0.96 (0.3-3.6)
BMI > 25 kg/m2, Age> 45 yr	0.5 (0.2-1.2)	1.1 (0.7-1.6)
Summary RR	0.7 (0.5-1.2)	0.95 (0.7-1.3)
Mangaung		
BMI < 25 kg/m2, Age < 45 yr	a	a
BMI < 25 kg/m2, Age> 45 yr	2.2 (1.3-3.7)*	0.96 (0.5-2.0)
BMI > 25 kg/m2, Age < 45 yr	3.8 (1.3-11.0)*	1.9 (0.8-4.3)
BMI > 25 kg/m2, Age> 45 yr	0.8 (0.5-1.4)	1.2 (0.9-1.6)
Summary RR	a	1.2 (0.9-1.6)

a Cannot be calculated

* Statistically significantly different from 1 at the 0.05 level

9.8 Relationship between serum insulin and hypertension

Fasting hyperinsulinaemia (Modan, 1985) was defined as fasting serum insulin levels above the 75th percentile of that of a reference group who was non-obese (BMI < 25 kg/m^2), normotensive and with normal glucose tolerance. For Qwaqwa and Mangaung subjects this insulin concentration was 11 μIU/ml and 14 μIU/ml respectively. Post-glucose load hyper-insulinaemia was defined as the sum of the 60 min and 120 min insulin levels after a 75 g oral glucose load, exceeding the 75th percentile of the sum insulin concentration of the reference group. For Qwaqwa and Mangaung this insulin concentration was 108 μIU/ml and 113 μIU/ml respectively.

Table 9.8/1 shows the rate of hypertension in fasting compared to normo-insulinaemic subjects after controlling for BMI and glucose tolerance status. Among Qwaqwa subjects with BMI < 25 kg/m^2 the rate of hypertension was higher in normo-insulinaemic subjects with IGT and normal glucose tolerance than in hyperinsulinaemic subjects. In persons with BMI ≥ 25 kg/m^2 and with diabetes and IGT, the rate of hypertension was higher in hyperinsulinaemic than normo-insulinaemic persons. In the small number of Mangaung subjects with BMI < 25 kg/m^2 and with diabetes and IGT, the rates of hypertension in hyperinsulinaemic persons exceeded the rates in normo-insulinaemic persons. The same was true of diabetic and normal subjects with BMI ≥ 25 kg/m^2.

The summary relative risk of hypertension in fasting hyperinsulinaemic compared to normo-insulinaemic subjects after controlling for BMI and glucose tolerance was 0.9 (95% CI 0.7-1.1) in the Qwaqwa sample and 1.1 (95% CI 0.9-1.3) in the Mangaung sample (Table 9.8/2). The relative risk was thus in neither population statistically significant. After excluding subjects on antihypertensive therapy, the summary relative risks were 0.8 (95% CI 0.6-1.0) and 0.99 (95% CI 0.8-1.3) for Qwaqwa and Mangaung subjects respectively and also not statistically significant.

When the sum of 60 and 120 minute definition of hyperinsulinaemia was used, the rates of hypertension were also not consistent for the two populations (Table 9.8/3). In the Qwaqwa population the rates of hypertension in the subgroups were all higher in the normo-insulinaemic group than the hyperinsulinaemic group

except for overweight diabetics. In Mangaung subjects the rates of hypertension were higher in the hyperinsulinaemic group with the exception of non-obese diabetics.

The summary relative risk for hypertension in the Qwaqwa sample using the sum insulin definition of hyperinsulinaemia was 0.9 (95% CI 0.7-1.1) and 0.8 (95% CI 0.7-1.1) after excluding persons taking antihypertensive drugs (Table 9.8/4). This relative risk was thus also not statistically significant. In the Mangaung population the summary relative risk for hypertension in hyperinsulinaemic compared to normo-insulinaemic subjects almost reached statistical significance. The relative risk was 1.2 (95% CI 1.0-1.5) and after excluding subjects taking antihypertensive drugs, 1.2 (95% CI 0.9-1.6).

Glucose tolerance was not found to be significantly associated with blood pressure in analysis of covariance containing sex and glucose tolerance (normal, IGT and diabetes) as grouping factors, and BMI and age as covariates (Table 9.8/5). Treated hypertensives were excluded. BMI and age were significantly associated with systolic and diastolic blood pressure in both samples.

The relationship between hypertension and fasting as well as post-glucose load serum insulin response was also analysed by analysis of covariance using age and BMI as covariates and sex, hypertension and glucose tolerance as grouping factors (Table 9.8/6). Since serum insulin concentrations were not normally distributed these values were log-transformed.

In the Mangaung sample, fasting insulin in the total group is significantly related to BMI and glucose grouping, and close to significant with age, but not significantly related to hypertension. The results were similar in the group excluding the treated hypertensives except that fasting insulin was no longer significantly related to glucose grouping.

Reaven (1988) suggested that insulin resistance and elevated circulating insulin levels are characteristic of a proportion of patients with hypertension. Modan et al. (1985) demonstrated in a population-based study that hyperinsulinaemia might be the link between hypertension and glucose intolerance. In the San Antonio Heart Study, Haffner et al. (1988) also showed that hyperinsulinaemia was

positively associated with blood pressure in men. Mbanya et al. (1988) suggested that hyperinsulinaemia is not causally related to essential hypertension but that it may contribute to the hypertension of type 2 diabetes. In the two FS studies, however, it was not possible to repeat the findings of Modan et al. (1985). Our findings also failed to show an association between hyperinsulinaemia and hypertension in subjects with type 2 diabetes. Several other studies also failed to demonstrate an association between blood pressure and serum insulin concentration. Collins et al. (1990) found that after controlling for age and BMI, mean fasting and 2-hour post-glucose load insulin levels were not significantly different between hypertensive and non-hypertensive Pacific islanders. In the U.S. Saad et al., (1991) found that mean blood pressure was significantly correlated with fasting plasma insulin concentration and insulin resistance in whites but not in Pima Indians or blacks. In a comprehensive study of Mauritian including Asian Indian, Creole and Chinese subjects Dowse et al., (1992) could not find any support for the hypothesis that circulating insulin concentration is an independent determinant of blood pressure in those populations. To explain the inconsistencies in findings from clinical studies and population-based studies on the relationship between insulin and blood pressure Dowse suggested that possibilities such as subject selection, sample size, differing methods of analysis, inadequate controlling for confounding factors, differences in the specificity of insulin assays or real differences between ethnic groups.

Enough evidence has accumulated to reach consensus on the existence of a metabolic syndrome (WHO, 1998) but there is still much controversy on the exact role of insulin resistance in the pathogenesis of hypertension. The FS study is the first population-based study in SA that could be considered representative of the black population in a rural and an urban population to examine the relationship between insulin concentration and hypertension. The negative findings of this study might contribute to the debate on the pathophysiology of hypertension especially in blacks. Longitudinal studies on the predictive value of insulin concentration on the development of hypertension in black subjects should be considered. Although an association between central obesity and glucose intolerance and between obesity and hypertension was demonstrated in FS blacks, and that black subjects with diabetes were significantly more insulin resistant than subjects with normal glucose tolerance, no link between insulin resistance and

hypertension could be demonstrated. This implies that if the metabolic syndrome does exist in black subjects, a different mechanism for the syndrome will have to be found.

Summary

The results described in the FS study are the first from a population-based study in SA and possibly in sub-Saharan Africa to contradict the hypothesis that hyperinsulinaemia is an independent determinant of hypertension in black subjects. The implication of this finding is that a different link between hypertension and the metabolic syndrome in black subjects should be looked for if this syndrome does exist in this ethnic group.

TABLE 9.8/1. Rate of Hypertension (%) in Subjects With Fasting Hyper- and Normo-insulinaemia After Controlling for BMI and Glucose Tolerance Status in the Study Populations

	Fasting Hyper-insulinaemia		Fasting Normo-insulinaemia	
	n	%	n	%
Qwaqwa				
BMI < 25 kg/m2				
Diabetic	3	66.7	11	36.4
IGT	7	28.6	41	34.2
Normal	62	12.9	258	25.6
BMI > 25 kg/m2				
Diabetic	30	56.7	7	42.9
IGT	34	61.8	23	52.2
Normal	197	39.6	163	42.3
Mangaung				
BMI < 25 kg/m2				
Diabetic	3	66.7	11	54.6
IGT	9	44.4	21	28.6
Normal	63	23.8	219	26.5
BMI > 25 kg/m2				
Diabetic	25	72	15	53.3
IGT	44	54.6	29	62.1
Normal	134	41.8	161	37.3

TABLE 9.8/2 The Relative Risk (RR) for Hypertension in Fasting Hyper-insulinaemia Compared to Normo-insulinaemic Subjects After Adjusting For BMI, Age and Glucose Tolerance: In the Total Sample and After Excluding Those on Antihypertensive Treatment (95% CI in Parenthesis)

	Compared to Normo-insulinaemic RR	Compared to Normo-insulinaemic* RR
Qwaqwa		
BMI < 25 kg/m^2		
Diabetic	1.8 (0.6-5.6)	1.8 (0.6-5.6)
IGT	0.8 (0.2-2.9)	0.7 (0.1-4.4)
Normal	0.5 (0.3-1.0)	0.5 (0.3-1.1)
BMI > 25 kg/m^2		
Diabetic	1.3 (0.5-3.3)	a
IGT	1.2 (0.7-1.9)	0.9 (0.4-1.8)
Normal	0.9 (0.8-1.2)	0.9 (0.6-1.2)
Summary RR	0.9 (0.7-1.1)	0.8 (0.6-1.0)
Mangaung		
BMI < 25 kg/m^2		
Diabetic	1.2 (0.5-3.2)	a
IGT	1.6 (0.6-4.2)	0.7 (0.1-4.7)
Normal	0.9 (0.6-1.5)	0.9 (0.5-1.6)
BMI > 25 kg/m^2		
Diabetic	1.4 (0.8-2.3)	1.9 (0.7-5.3)
IGT	0.9 (0.6-1.3)	0.7 (0.4-1.3)
Normal	1.1 (0.9-1.5)	1.1 (0.8-1.6)
Summary RR	1.1 (0.9-1.3)	1.0 (0.8-1.3)

* Excluding those subjects on antihypertensive treatment

a RR cannot be estimated

TABLE 9.8/3. Rate of Hypertension (%) in Subjects With Sum 60 and 120 Minute Hyper- and Normo-insulinaemia After Controlling for BMI and Glucose Tolerance Status in the Study Populations

	Sum 60 and 120 min Hyper-insulinaemia		Sum 60 and 120 min Normo-insulinaemia	
	n	%	n	%
Qwaqwa				
BMI < 25 kg/m^2				
Diabetic	-	-	10	50
IGT	17	17.7	30	40
Normal	76	21.1	244	23.8
BMI > 25 kg/m^2				
Diabetic	11	27.3	8	25
IGT	38	52.6	18	72.2
Normal	176	40.3	184	41.3
Mangaung				
BMI < 25 kg/m^2				
Diabetic	6	33.3	7	71.4
IGT	20	40	10	20
Normal	72	29.2	208	25
BMI > 25 kg/m^2				
Diabetic	13	69.2	14	50
IGT	50	58	21	52.4
Normal	146	44.5	146	34.9

TABLE 9.8/4 The Relative Risk of Hypertension in Hyper-insulinaemic (Sum 60 and 120 min) Compared to Normo-insulinaemic (Sum 60 and 120 min) Subjects After Adjusting For BMI, Age and Glucose Tolerance: In the Total Sample and After Excluding Those on Antihypertensive Treatment (95% CI in Parenthesis)

	Hyper-insulinaemic Compared to Normo-insulinaemic RR	Hyper-insulinaemic Compared to Normo-insulinaemic* RR
Qwaqwa		
BMI < 25 kg/m^2		
Diabetic	a	a
IGT	0.4 (0.1-1.4)	0.2 (0.03-1.4)
Normal	0.9 (0.5-1.5)	0.9 (0.5-1.6)
BMI > 25 kg/m^2		
Diabetic	1.1 (0.2-5.1)	0.8 (0.1-4.5)
IGT	0.7 (0.5-1.1)	0.4 (0.2-0.9)
Normal	0.97 (0.8-1.3)	0.9 (0.7-1.3)
Summary RR	0.9 (0.7-1.1)	0.8 (0.6-1.1)
Mangaung		
BMI < 25 kg/m^2		
Diabetic	0.5 (0.1-1.6)	0.6 (0.2-2.1)
IGT	2.0 (0.5-7.7)	a
Normal	1.2 (0.8-1.8)	1.4 (0.8-2.3)
BMI > 25 kg/m^2		
Diabetic	1.4 (0.7-2.6)	1.5 (0.6-4.1)
IGT	1.1 (0.7-1.8)	0.97 (0.5-1.7)
Normal	1.3 (0.96-1. 7)	1.1 (0.8-1.6)
Summary RR	1.2 (0.99-1.5)	1.2 (0.9-1.6)

* Excluding those subjects on antihypertensive treatment

a RR cannot be estimated

TABLE 9.8/5. Significance Levels of Analysis of Covariance for Blood Pressure and Glucose Tolerance Association (Hypertensives on treatment Excluded)

	Qwaqwa		Mangaung	
	Diastol BP	Systolic BP	Diastol BP	Systol BP
Grouping Factors				
Sex	0.64	0.32	0.01 *	0.79
Glucose tolerance (normal, IGT, diabetes)	0.26	0.86	0.18	0.06
Sex and glucose interaction	0.69	0.42	0.42	0.62
Cova riates				
BMI	< 0.01 *	< 0.01 *	0.0001 *	0.0001 *
Age	< 0.01 *	< 0.01 *	0.0001 *	0.0001 *

* Significant

TABLE 9.8/6. Significance Levels of Analysis of Covariance for Hypertension and Insulin Concentrations (Excluding Known Diabetics)

	Dependent variable			
	Sum insulin (log)		Fasting insulin (log)	
	Total group	Untreated group	Total group	Untreated group
Qwaqwa				
Grouping factors				
Sex	0.82	0.11	0.57	0.81
Hypertension[a]	0.01	0.61	0.34	0.87
Glucose tolerance[b]	0.01	<0.0001	0.41	0.45
Sex-hypertension interaction	0.09	0.01	0.53	0.52
Sex-glucose interaction	0.77	0.02	0.09	0.93
Hypertension-glucose interaction	0.01	0.02	0.06	0.14
Covariates				
BMI	<0.0001	<0.0001	<0.0001	<0.0001
Age	0.65	0.02	0.11	0.08
Mangaung				
Grouping factors				
Sex	0.03	0.11	0.48	0.81
Hypertension[a]	0.10	0.61	0.04	0.87
Glucose tolerance[b]	0.0001	0.0001	0.005	0.45
Sex-hypertension interaction	0.01	0.01	0.33	0.52
Sex-glucose interaction	0.01	0.03	0.91	0.93
Hypertension-glucose interaction	0.04	0.02	0.006	0.14
Covariates				
BMI	0.0001	0.0001	0.0001	0.0001
Age	0.02	0.02	0.10	0.08

a Hypertension in 3 categories: normotensive, untreated, treated

b Glucose tolerance in 3 categories: normal, IGT and diabetes

9.9 Relationship between oral contraceptives and hypertension

In the age range 25-44 years 55 women in the Qwaqwa sample indicated that they were using oral contraceptives at the time of the study. In Table 9.9/1 the rates of hypertension in users of oral contraceptives are shown.

TABLE 9.9/1. Rates (%) of Hypertension in Users and Non-users of Oral Contraceptives

	Users		Non-users	
	n	%	n	%
Qwaqwa				
Women 25-34 yr	40	10	9.9	9.1
Women 35-44 yr	15	26.7	94	29.8

In the Qwaqwa sample the relative risk (RR) of hypertension in users compared to non-users of oral contraceptives in the age range 25-34 years was 1.1 (95% CI 0.4-3.4). In the age range 35-44 years the RR was 0.9 (0.4-2.2). The summary RR of hypertension for both ages combined was 0.98 (0.5-2.0). No significant relationship existed between the use of oral contraceptives and hypertension in this population. The data regarding oral contraceptives and hypertension was not available for the Mangaung population.

Oral contraceptive preparations containing higher dose oestrogen-progesterone formulations are known to cause hypertension. It is, however unknown whether current lower dose formulations cause hypertension (Dluhy, 1998). Although the numbers were small in this study it is reassuring that the use of current oral contraceptives were not associated with hypertension. Studies on larger numbers of subjects are necessary to resolve this issue.

9.10 Relationship between blood pressure and anthropometrical variables

Partial correlations between blood pressure and several anthropometrical variables were calculated after excluding subjects on treatment for hypertension. Age-adjusted results for Qwaqwa subjects are presented in Table 9.10/1.

In Qwaqwa women moderate correlations existed between diastolic blood pressure and skinfold thickness as well as percentage calculated body fat, but the ratio of trunk-to-extremity skinfolds did not correlate with blood pressure. The strongest correlations were between diastolic blood pressure and triceps, sub-scapular, sum of 5 skinfolds and percentage body fat. Systolic blood pressure correlated best with triceps, sub-scapular and sum of 5 skin fold thickness. The best correlation between systolic blood pressure was however with the calculated percentage body fat. Trunk to extremity ratio of skinfolds that is also a measure of central fat distribution did not correlate well with blood pressure.

Moderate correlations were also found in Qwaqwa women between diastolic blood pressure and waist, hip, thigh and buttock circumference. systolic blood pressure was also positively correlated with all these measurements but slightly weaker. While waist circumference was positively correlated with both diastolic and systolic blood pressure no correlation existed between waist-to-hip ratio and diastolic or systolic blood pressure. These findings may be interpreted that both diastolic and systolic blood pressure in Qwaqwa women correlated best with total adiposity rather than central obesity or body fat distribution. The two strongest and most consistent correlates with both diastolic and systolic blood pressure were triceps skin fold thickness and buttock circumference. Since the risk of hypertension in this population was significantly increased with BMI $\geq$ 25 kg/m^2 it was not unexpected that percentage body fat correlated well with both systolic and diastolic blood pressure. It is of interest that waist circumference in females in both populations correlated strongest with diastolic blood pressure, and even this correlation was not very strong (r_s 0.29 and r_s 0.3 for Qwaqwa and Mangaung respectively, (Table 9.10/1 and Table 9.10/2).

In Qwaqwa males moderate correlations were also found between diastolic blood pressure and skinfold thickness with the exception of subscapular skin fold where the correlation was weak. Mean systolic blood pressure was also positively correlated with thickness off all skinfolds measured although the correlation was weak for triceps and supra-iliac skin fold thickness. Both diastolic and systolic blood pressure was positively correlated with the sum of 5 skinfolds as well as percentage body fat while no correlation existed between blood pressure and trunk-to-extremity skin fold ratio. If one measurement had to be selected for clinical practice it has to be the triceps skin fold which showed the most consistent correlation with both systolic and diastolic blood pressure. Again it may be concluded that blood pressure in Qwaqwa men correlated better with general adiposity (percentage body fat and BMI) than with any circumference or measure of central obesity.

The results for Mangaung females are shown in Table 9.10/2. The results are remarkably similar between the two groups of females and the same conclusions apply. In Mangaung men a weak and positive correlation was also evident for trunk-extremity ratio of skin fold thickness and systolic blood pressure. The correlation between percentage body fat and blood pressure was again obvious. A striking difference was, however, the positive correlation between diastolic and systolic blood pressure and waist-to-hip ratio in this group of men. It is quite possible that more advanced urbanisation of the Mangaung men was responsible for this observation. The most useful anthropometrical measurements in Mangaung men in terms of correlation with blood pressure were triceps (or parathoracic) skin fold thickness and waist-to-hip ratio.

Comparison of the FS anthropometrical data with some of the data from the Dombotombo Township in Zimbabwe is possible. In male Zimbabweans a strong correlation was found between systolic and diastolic blood pressure and BMI, waist circumference, WHR and percent fat mass. Diastolic blood pressure correlated with the same variables but the correlation was weaker. The same positive correlations but slightly weaker were also found in Zimbabwean women. The findings in Mangaung men are in keeping with these findings. In neither Qwaqwa nor Mangaung women were any associations found between central fat distribution and blood pressure when using Pearson partial correlations. This is a

very interesting observation that may mean that Zimbabwean women of Dombotombo may be more urbanized than the women from Qwaqwa or Mangaung. In rural Gambians the odds ratio for hypertension in obese subjects was 3.5 (CI 1.2-10.7) while it was not significant for urban subjects (van der Sande et al., 2000). Central obesity, however, was significantly associated with hypertension in both rural and urban Gambians. These findings and our own are not necessarily contradictory but may merely emphasize the complexity of the transition process and that the same chronic diseases do not emerge at the same rate and in the same sequence in different populations, a phenomenon that may be referred to as non-synchronised "coca-colanisation" (Koestler 1976 and Zimmet 2000). With hindsight it might have been very interesting to prospectively follow the development and emergence of the different chronic diseases in different communities and countries.

Summary

Significant urban-rural and male-female differences between the correlation of anthropometrical measurements and mean diastolic as well as systolic blood pressure were found. General adiposity rather than body at distribution correlated best with blood pressure in all subjects except Mangaung males where central adiposity also emerged as a significant anthropometrical variable. If anthropometrical measurements were to be selected for clinical use for instance in the screening and monitoring of at risk or hypertensive women, then it seems that triceps skin fold thickness and buttock circumference (or hip circumference) emerged as the most useful. In Qwaqwa men triceps skin fold thickness and in Mangaung men waist-to-hip circumference in addition to triceps skin fold thickness proved to be the most consistent measurements. In all subjects percentage body fat correlated well with both systolic and diastolic blood pressure. Since percentage body fat correlates well with BMI the latter measurement must be added to the list. Comparing the correlation between anthropometrical and blood pressure data from the FS study with that of other available studies from sub-Saharan Africa, it becomes apparent that the same chronic diseases of lifestyle do not emerge at the same rate and in the same sequence in different populations, a phenomenon that may be referred to as the emergence of non-communicable diseases during the transition (non-synchronised "coca-colanisation").

TABLE 9.10/1. Partial Correlations Between Diastolic and Systolic Blood Pressure [1], Skinfold Thickness and Calculated Percentage Body Fat and Circumferences After Adjusting for Age in the Qwaqwa Sample (Significance Levels in Parenthesis[2])

	Diastolic r	Systolic r
Males		
Skinfolds*		
Triceps	0.24 < (0.01)	0.24 < (0.01)
Biceps	0.22 < (0.01)	0.19 (0.01)
Subscapular	0.18 (0.01)	0.19 < (0.01)
Suprailiac	0.20 < (0.01)	0.17 (0.01)
Parathoracic	0.19 < (0.01)	0.18 < (0.01)
Sum of 5 skinfolds	0.22 < (0.01)	0.21 < (0.01)
Trunk/Extremity ratio	0.02 (0.70)	0.00 (1.00)
% Body fat	0.23 < (0.01)	0.21 <(0.01)
Circumferences**		
Waist	0.15 (0.01)	0.20 < (0.01)
Hip	0.08 (0.20)	0.16 (0.01)
Thigh	0.12 (0.06)	0.17 (0.01)
Buttocks	0.12 (0.05)	0.20 < (0.01)
Waist-to-hip ratio	0.16 (0.01)	0.14 (0.03)
Females		
Skinfolds*		
Triceps	0.28 < (0.01)	0.22 < (0.01)
Biceps	0.23 < (0.01)	0.19 < (0.01)
Subscapular	0.26 < (0.01)	0.21 < (0.01)
Suprailiac	0.25 < (0.01)	0.20 < (0.01)
Parathoracic	0.24 < (0.01)	0.17 < (0.01)
Sum of 5 skinfolds	0.27 < (0.01)	0.21 < (0.01)
Trunk/Extremity ratio	0.06 (0.16)	0.03 (0.57)
% Body fat	0.26 < (0.01)	0.23 < (0.01)
Circumferences**		
Waist	0.29 < (0.01)	0.20 < (0.01)
Hip	0.26 < (0.01)	0.19 < (0.01)
Thigh	0.28 < (0.01)	0.21 < (0.01)
Buttocks	0.29 < (0.01)	0.23 < (0.01)
Waist-to-hip	0.10 (0.02)	0.06 (0.22)

1 Subjects on treatment for hypertension excluded

2 p-Value testing whether correlations differ significantly from zero

* Spearman rank partial correlations

** Pearson partial correlations

TABLE 9.10/2. Partial Correlations Between Diastolic and Systolic Blood Pressure[1], Skinfold Thickness and Calculated Percentage Body Fat and Circumferences After Adjusting for Age in Mangaung Subjects (Significance Values in Parenthesis[2])

	Diastolic r	Systolic r
Males		
Skinfolds*		
Triceps	0.24 < (0.01)	0.20 < (0.01)
Biceps	0.17 < (0.01)	0.19 < (~0.01)
Subscapular	0.20 < (0.01)	0.22 < (0.01)
Suprailiac	0.18< (0.01)	0.18 < (0.01)
Parathoracic	0.22 < (0.01)	0.22 < (0.01)
Sum of 5 skinfolds	0.21 < (0.01)	0.21 < (0.01)
Trunk/Extremity** ratio	0.12 (0.05)	0.17 < (0.01)
% Body fat	0.20 < (0.01)	0.19 < (0.01)
Circumferences		
Waist	0.20 < (0.01)	0.15< (0.01)
Hip	0.12 (0.04)	0.08 (0.20)
Thigh	0.10 (0.09)	0.09 (0.12)
Buttocks	0.15 (0.01)	0.11 (0.08)
Waist-to-hip ratio	0.22 < (0.01)	0.19 < (0.01)
Females		
Skinfolds*		
Triceps	0.27 < (0.01)	0.24 < (0.01)
Biceps	0.23 < (0.01)	0.21 < (0.01)
Subscapular	0.24 < (0.01)	0.20 < (0.01)
Suprailiac	0.24 < (0.01)	0.21 < (0.01)
Parathoracic	0.26 < (0.01)	0.21 < (0.01)
Sum of 5 skinfolds	0.27 < (0.01)	0.23 < (0.01)
Trunk/Extremity ratio	-0.02 (0.75)	0.00 (0.99)
% Body fat	0.24 < (0.01)	0.23 < (0.01)
Circumferences* *		
Waist	0.30 < (0.01)	0.23 < (0.01)
Hip	0.26 < (0.01)	0.23 < (0.01)
Thigh	0.24 < (0.01)	0.20 < (0.01)
Buttocks	0.28 < (0.01)	0.24 < (0.01)
Waist-to-hip ratio	0.08 (0.11)	0.03 (0.53)

1 Subjects on treatment for hypertension excluded

2 p-Value testing whether correlations differ significantly from zero

* Spearman rank partial correlations ** Pearson partial correlations

9.11 Correlations between blood pressure and serum lipids and serum urate

Partial correlations between diastolic and systolic blood pressure on the one hand and fasting total serum cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides and urate on the other, were calculated and are presented in Table 9.11/1. In women from both populations a significant correlation was found between serum urate concentration and mean diastolic as well as systolic blood pressure although the latter correlation was weaker. Weak correlations also existed between total serum cholesterol in Qwaqwa women and diastolic blood pressure as well as between serum triglyceride concentration in Qwaqwa men and diastolic blood pressure. Uric acid has long been associated with cardiovascular disease but there is no evidence that that uric acid bears a causal or reversible relationship to vascular disease (Alderman, 2002). It is hard to explain why the correlation exists for women but not for men. Elevated serum concentration of triglycerides may interfere with the measurement of uric acid and it may be worthwhile to examine this confounding factor in more depth (Costa, 2002).

TABLE 9.11/1. Partial Correlations Between Diastolic and Systolic Blood Pressure[1] and Fasting Serum Lipids and Urate After Adjusting for Age (Significance Values in Parenthesis[2])

	Diastolic r	Systolic r
Qwaqwa		
Females		
Total Cholesterol	0.16 (< 0.01)	0.11 (0.01)
LDL -Cholesterol	0.12 (0.01)	0.10 (0.03)
HDL-Cholesterol	0.03 (0.45)	0.02 (0.70)
Triglycerides	0.13 (0.01)	0.08 (0.08)
Urate	0.21 (< 0.01)	0.13 (< 0.01)
Males		
Total Cholesterol	0.17 (0.01)	0.12 (0.05)
LDL -Cholesterol	0.12 (0.07)	0.16 (0.01)
HDL-Cholesterol	0.03 (0.69)	0.10 (0.11)
Triglycerides	0.20 (< 0.01)	0.13 (0.03)
Urate	0.15 (0.01)	0.08 (0.20)
Mangaung		
Females		
Total Cholesterol	0.11 (0.04)	0.07 (0.14)
LDL -Cholesterol	0.11 (0.04)	0.09 (0.07)
HDL-Cholesterol	0.004 (0.93)	0.04 (0.39)
Triglycerides	0.04 (0.46)	0.03 (0.54)
Urate	0.18 (< 0.01)	0.16 (< 0.01)
Males		
Total Cholesterol	0.12 (0.05)	0.05 (0.40)
LDL -Cholesterol	0.06 (0.35)	0.01 (0.82)
HDL -Cholesterol	0.04 (0.50)	0.04 (0.57)
Triglycerides	0.10 (0.10)	0.05 (0.39)
Urate	0.15 (0.01)	0.10 (0.10)

[1] Subjects on treatment for hypertension excluded

[2] p-Value testing whether Pearson correlation coefficient differs significantly from zero

9.12 Relationship between smoking and blood pressure

The rate of hypertension in smokers (current or past) and those who never smoked is shown in Table 9.12/1. Among Qwaqwa males, rates of hypertension were higher in non-smokers than in smokers with the exception of younger males. Among females rates were lower in non-smokers. In Mangaung males, rates of hypertension were also higher in non-smokers than smokers but in females it tended to be higher in smokers with the exception of middle-age females.

TABLE 9.12/1. Rate of Hypertension in Smokers[1] and Non-Smokers[2] After Controlling for Age and Sex

	Smokers		Non-smokers	
	n	%	n	%
Qwaqwa				
Males				
< 45 yr	96	19 (19.8)	28	3 (10.7)
45-64 yr	54	15 (27.8)	18	6 (33.3)
65+ yr	50	21 (42.0)	30	14 (45.5)
Females				
< 45 yr	28	7 (25.0)	219	37 (16.9)
45-64 yr	26	14 (53.9)	171	83 (48.5)
65+ yr	15	10 (66.7)	105	70 (66.7)
Mangaung				
Males				
< 45 yr	99	9 (9.1)	33	6 (18.2)
45-64 yr	86	30 (34.9)	32	15 (46.9)
65+ yr	28	15 (53.6)	12	9 (75.0)
Females				
< 45 yr	51	14 (27.5)	180	38 (21.1)
45-64 yr	37	18 (48.7)	134	81 (60.5)
65+ yr	5	4 (80.0)	59	46 (78.0)

[1] Smokers: current or past smokers

[2] Non-smokers: those who never smoked

The relative risk of hypertension in smokers versus non-smokers is shown in Table 9.12/2. In Qwaqwa non-smokers were not significantly more likely to have hypertension than smokers. In Mangaung, male smokers were significantly less likely to have hypertension than non-smokers. Smokers tend to have a lower BMI than smokers and therefore possibly lower rates of hypertension as well.

TABLE 9.12/2. Relative Risk (RR) of Hypertension in Smokers[1] Compared to Non- Smokers[2] After Controlling For Age and Sex in the Study Populations (95% CI in Parenthesis)

	Qwaqwa	Mangaung
Males		
< 45 yr	1.9 (0.6-5.8)	0.5 (0.19-1.3)
45-64 yr	0.8 (0.4-1.8)	0.74 (0.47-1.2)
65+ yr	0.9 (0.6-1.5)	0.71 (0.44-1.1)
Summary RR	1.0 (0.7-1.6)	0.69 (0.49-0.97)*
Females		
< 45 yr	1.5 (0.7-3.0)	1.3 (0.77-2.2)
45-64 yr	1.1 (0.8-1.6)	0.81 (0.56-1.2)
65+ yr	1.0 (0.7-1.5)	1.0 (0.65-1.6)
Summary RR	1.1 (0.9-1.5)	1.0 (0.86-1.2)

[1] Smokers: current or past smokers

[2] Non-smokers: those who never smoked

* Statistically significantly different from 1 at the 0.05 level

The mean diastolic and systolic blood pressure of current smokers and non-smokers and the level of significance comparing diastolic with systolic blood pressure (analysis of covariance) is shown in Table 9.12/3. Those on anti-hypertensive medication were excluded. The summary relative risk for hypertension in current smokers compared to non-smokers was 0.8 (95% CI 0.6-1.2) for males and 1.2 (95% CI 0.9-1.6) for females. It is clear that current smoking status was also not associated with blood pressure.

Table 9.12/3. Mean Diastolic and Systolic Blood Pressure (mm Hg) of Current Smokers and Non-Smokers After Adjusting for Age (excluding those on treatment) (Significance Level in Parenthesis)

	Diastolic	Systolic
Qwaqwa		
Males		
Smokers	79.4	135.2
Non-smokers	82.6	139.8
	(p = 0.06)	(p = 0.11)
Females		
Smokers	85.4	147.7
Non-smokers	82.5	141.1
	(p = 0.26)	(p = 0.10)
Mangaung		
Males		
Smokers	81.6	138
Non-smokers	83.9	138.7
	(p=0.15)	(p=0.82)
Females		
Smokers	81.7	143.7
Non-smokers	81.9	143.9
	(p=0.92)	(p=0.96)

9.13 Relationship between alcohol intake and blood pressure

The relationship between alcohol usage and hypertension is shown in (Table 9.13/1). The RR of hypertension was not increased in those subjects with a history of alcohol usage compared to those with no history of alcohol usage (Table 9.13/2). The mean DBP of Qwaqwa women who admitted to the use of alcohol was slightly but significantly increased compared to the alcohol non-users (p=0.006) (Table 9.13/3).

TABLE 9.13/1. Rate of Hypertension (%) in Alcohol-Users[1] and Non-Alcohol-Users After Controlling for Age and Sex

	Alcohol-users		Non-alcohol-users	
	n	%	n	%
Qwaqwa				
Males				
< 45 yr	85.00	16 (18.8)	39.00	6 (15.4)
45-64 yr	56.00	16 (28.6)	16.00	5 (31.3)
65+ yr	44.00	17 (38.6)	39.00	19 (48.7)
Females				
< 45 yr	52.00	13 (25)	200.00	33 (16.5)
45-64 yr	63.00	31 (49.2)	138.00	68 (49.3)
65+ yr	29.00	20 (69)	92.00	60 (65.2)
Mangaung				
Males				
< 45 yr	101.00	13 (12.9)	31.00	2 (6.5)
45-64 yr	81.00	32 (39.5)	36.00	12 (33.3)
65+ yr	28.00	17 (60.7)	11.00	7 (63.6)
Females				
< 45 yr	79.00	20 (25.3)	151.00	32 (21.2)
45-64 yr	52.00	31 (59.6)	119.00	68 (57.1)
65+ yr	16.00	13 (81.3)	48.00	37 (77.1)

[1] Any alcohol vs. no alcohol

TABLE 9.13/2. Relative Risk (RR) of Hypertension in Alcohol-Users[1] Compared to Non-Alcohol-Users For Age and Sex in the Study Populations (95% CI Parenthesis)

	Qwaqwa	Mangaung
Males		
< 45 yr	1.22 (0.52-2.89)	2.00 (0.48-8.36)
45-64 yr	0.91 (0.40-2.11)	1.19 (0.70-2.202)
65+ yr	0.79 (0.48-1.30)	0.95 (0.56-1.63)
Summary RR	0.92 (0.62 -1.35)	1.19 (0.81-1.76)
Females		
< 45 yr	1.52 (0.86-2.66)	1.20 (0.73-1.95)
45-64 yr	1.00 (0.74-1.35)	1.04 (0.79-1.37)
65+ yr	1.06 (0.79-1.41)	1.05 (0.80-1.40)
Summary RR	1.10 (0.90-1.35)	1.09 (0.89-1.33)

[1] Any alcohol vs. no alcohol

TABLE 9.13/3. Alcohol usage[1] and blood pressure (adjusting for age and excluding known hypertensives).

	Mean Diastolic BP (mm Hg)	Mean Systolic BP (mm Hg)
Qwaqwa		
Males		
Alcohol-users	76.3	126.6
Alcohol non-users	77.1	131.1
p-value	0.61	0.06
Females		
Alcohol-users	78	129.7
Alcohol non-users	74.2	126.2
p-value	0.006	0.06
Mangaung		
Males		
Alcohol-users	82.9	139.7
Alcohol non-users	80.7	133.8
p-value	0.23	0.05
Females		
Alcohol-users	83.6	146.2
Alcohol non-users	81	142.9
p-value	0.11	0.25

[1] Alcohol-users: any alcohol vs. no alcohol

9.14 Complications of hypertension

9.14.1 Electrocardiographic changes associated with hypertension

A resting electrocardiograph (ECG) was obtained from every subject. From the Qwaqwa sample, 4 ECG's got lost and 31 were of unacceptable quality. The majority of these ECG's were obtained under field conditions using a petrol-driven generator to generate power. Of the remaining 818 ECG's 52.8% were abnormal when classified according to the Minnesota coding system (Rose et al., 1968). In the Mangaung sample 758 ECG's were obtained of which 5 got lost and 3 were of poor quality. Of the remaining ECG's 435 (57.1%) were classified as abnormal. The prevalence of the most common ECG abnormalities are shown in Table 9.14.1/1. The most common finding was high amplitude R waves that were present in 33.2% of ECG's from Qwaqwa and 36.3% of of ECG's from Mangaung, followed by T wave items that were present in 15.8% and 22.1% of Qwaqwa and Mangaung subjects respectively. The prevalence of abnormal ECG'S was slightly higher in Mangaung subjects.

The prevalence of abnormal ECG's according to blood pressure status, age and sex is shown in Table 9.14.1/2. ECG abnormalities were most common in older hypertensive men from both populations (Mangaung 84.1% and Qwaqwa 76.8%).

TABLE 9.14.1/1. Prevalence of the Most Common ECG changes

According to Population

Patterns	Qwaqwa			Mangaung		
	Males	Females	Total	Males	Females	Total
Q and QS	1.6	1.5	1.6	2	2.3	2.2
QRS axis deviation	2.9	1.5	2.2	7.7	2.2	4.7
High amplitude R waves	43.7	24.6	33.2	49.2	26	36.3
S-T Junction (J) and segment depression	0	0.3	0.2	0.2	0.3	0.3
T wave items	13.3	17.7	15.8	17.3	25.8	22.1
A-V conduction defect	7.6	4.5	5.9	4.5	1.2	2.7
Ventricular conduction defects	1.3	2	1.7	0.9	0.9	0.9
Arrhythmias	11.6	4.8	7.8	7.7	6.6	7.1
Total Abnormal	62.3	44.9	52.8	66.2	49.8	57.1

TABLE 9.4.1/2. Prevalence of Abnormal ECG's According to Age, Sex and Region

	n	Abnormal ECG (%)
Qwawqa (age in yr)		
Females (< 45 yr)		
Hypertensive	45	24 (53.3)
Normotensive	194	72(37.1)
Females (≥ 45 yr)		
Hypertensive	174	108(62.1)
Normotensive	138	53(38.4)
Males (< 45 yr)		
Hypertensive	21	12(57.1)
Normotensive	97	62(63.9)
Males (≥ 45 yr)		
Hypertensive	56	43(76.8)
Normotensive	93	50(53.8)
Mangaung (age in yr)		
Females (< 45 yr)		
Hypertensive	52	25(48.1)
Normotensive	175	75 (42.9)
Females (≥45 yr)		
Hypertensive	147	99 (67.4)
Normotensive	86	41 (47.7)
Males (< 45 yr)		
Hypertensive	I5	12 (80.0)
Normotensive	117	72 (61.5)
Males (≥ 45 yr)		
Hypertensive	69	58 (84.1)
Normotensive	87	53 (60.9)

The relative risk of a hypertensive subject in Qwaqwa to have an abnormal ECG compared to a normotensive subject was significantly increased across all age and sex strata with the exception of young males (Table 9.14.1/3). The overall RR was 1.43 (95% CI 1.24; 1.64). Although the overall RR in Mangaung was also significantly increased at 1.32 (95% CI 1.13; 1.68), the RR was not significantly increased in younger males and females. In the rest of this section ECG abnormalities are discussed according to the presence or absence of hypertension (WHO, 1978 definition) in the different age and sex categories.

Q and QS patterns implicate underlying coronary heart disease (CHD) and were present (Table 9.14.1/1) in 1.6% of Qwaqwa respondents (males 1.6% and females 1.5%) and in 2.2% of Mangaung respondents (males 2 and females 2.3%). In the Qwaqwa population the highest prevalence of this abnormality was observed in older hypertensive males (5.4%) (Table 9.14.1/4). The overall RR of this type of abnormality occurring in hypertensive compared to normotensive subjects in Qwaqwa failed to reach statistical significance (Table 9.14.1/5). This finding may cautiously be interpreted that CHD does occur in this population but that hypertension is possibly not the only or main risk factor. In the Mangaung population it was surprisingly the subgroup of older hypertensive women who had the highest prevalence of Q and QS patterns (8.2%) compared to 5.8% of older males (Table 9.14.1/4). The overall RR of a Q and QS ECG pattern being present in hypertensive compared to normotensive subjects in Mangaung was 2.61 (95% CI 1.07; 6.39) (Table 9.14.1/5). It may be concluded that ECG abnormalities associated with underlying CHD are more prevalent in Mangaung than in Qwaqwa subjects and that hypertension is a risk factor for this ECG abnormality and thus possibly CHD in this urban population.

In a non-community-based sample of 297 urban blacks Seedat et al. (1992) found ECG abnormalities in 40%. In their sample large Q waves were present in 1.3% of males and in 0.7% of females. A history of chest pain was obtained on administration of the Rose questionnaire in 2.4% of the total sample of 371 subjects. However, half of them had not consulted a general practitioner. The Rose questionnaire was not used in the FS studies since it has not been validated in black South Africans. Huston et al. (1999) did not report on Q waves in their study on the prevalence of ECG left ventricular hypertrophy in civil servants.

QRS axis deviation (either left or right) occurred in 2.2% and 4.7% of subjects in Qwaqwa and Mangaung respectively (Table 9.14.1/6). Hypertension did not, as expected, increase the risk of this abnormality (Table 9.14.1/7).

High amplitude R waves were present in 33.2% of ECG's of Qwaqwa subjects (males 43.7% and females 24.6%) and in 36.3% of ECG's form Mangaung subjects (males 49.2% and females 26%). The highest prevalence of this abnormality was observed in older hypertensive males in Qwaqwa (51.8%) and Mangaung (63.3%) (Table 9.14.1/8). The overall RR of hypertensive compared to non-hypertensive subjects having this item in Qwaqwa was 1.83 (95% CI 1.46; 2.28) and in Mangaung 1.55(95% CI 1.25; 1.93). These rates are in contrast to the rates observed in Zulus (Seedat, 1992) where this abnormality occurred in 9.1% of males and 1.4% of females. In Nigerian civil servants the ECG prevalence of LV hypertrophy ranged from 3% to 29% depending on the criteria used (Huston et al., 1999). Hypertension is implicated in 49% of all cases of heart failure (Padwal et al., 2001). The high prevalence of ECG LV hypertrophy in both the Qwaqwa and Mangaung hypertensive populations predicts an increase in the future prevalence of heart failure with its associated morbidity and mortality in these populations. This is the first population-based study in SA to quantify the relative risk of hypertension-associated LV pathology. These findings have important implications since hypertension-induced heart failure is a potentially preventable condition.

S-T junction and segment depression items were very rare in both populations. In the Qwaqwa population only 2 respondents had this item, both women 45 years and older and hypertensive. In Mangaung 3 hypertensive respondents had this item, 2 females and 1 male, all in the age group 45 years and older. This abnormality was more common in the Durban study where it was reported in 1.3% of male and 2.8% of female subjects (Seedat et al., 1992).

T-wave abnormalities were common in both populations, 15.8% and 22.1% respectively in Qwaqwa and Mangaung (Table 9.14.1/1). In the former it occurred in as many as 30.4% and 23% of hypertensive men and women respectively in the age category 45 years and older. In Mangaung the highest prevalence rates

were 42% and 39.5% also occurring respectively in men and women in the 45 years and older age group (Table 9.14.1/10). The overall RR of this abnormality occurring in hypertensive compared to normotensive individuals was 1.47 (1.05; 2.06) in Qwaqwa subjects (Table 9.14.1/11). The overall RR in Mangaung subjects was not computable because of differences of the RR across the strata but in the male group 45 years and older, it was significant at a RR of 2.44 (1.42; 4.17). T-wave abnormalities have a wide differential diagnosis including hypertension and CHD (Goldberger, 2001).

A-V conduction defects were not uncommon and occurred in 5.9% and 2.7% of Qwaqwa and Mangaung subjects respectively (Table 9.14.1/1 and Table 9.14.1/12). It did not occur more frequently in hypertensive than in normotensive subjects in both populations (Table 9.14.1/13). Ventricular conduction defects were uncommon (Table 9.14.1/14 and Table 9.14.1/15).

Arrhythmias including atrial fibrillation occurred in 7.8% and 7.1% of rural and urban subjects respectively (Table 9.14.1/1). Atrial fibrillation occurred in 0.5% of subjects in Qwaqwa and in 0.1% of subjects in Mangaung. Arrhythmias was more common in all hypertensive subjects than in normotensive subjects (Table 9.14.1/16). The overall RR off this abnormality occurring more commonly in hypertensive than normotensive subjects was almost doubled at 1.90 (95% CI 1.14; 3.16) in Mangaung subjects but failed to reach significance in the Qwaqwa population. The increased risk of arrhythmias in patients with hypertension in the Mangaung population may have important implications including stroke-prevention by the early detection and optimal management of hypertension. Although the risk for arrhythmias in hypertensive subjects in Qwaqwa failed to reach significance, this combination has the potential to become an important but largely preventable health problem also in this region. No explanation is readily available to elucidate the increased risk for arrhythmias in the hypertensive population in Mangaung but not in Qwaqwa. Other causes for arrhythmias, in particular atrial fibrillation, will have to be looked into including thyroid function, chronic obstructive airways disease and valvular heart disea).

Low QRS amplitude items were uncommon (Table 9.14.1/18) and not significantly more common subjects hypertension (Table 9.14.1/19).

Summary

More than 50% of electrocardiographs obtained from both populations were abnormal in some way. High amplitude R waves followed by T wave abnormalities were the most common findings. Subjects with hypertension in both populations had a significantly increased risk of having an abnormal ECG, 43% in Qwaqwa and in 32% in Mangaung. Q and QS patterns possibly indicating coronary heart disease were present in ECG's of 1.6% and 2.2% of subjects from Qwaqwa and Mangaung respectively while as many as 5.4% of older males in Qwaqwa exhibited this ECG abnormality. The highest prevalence of this abnormality in Mangaung was 8.9% and, surprisingly, occurred in older hypertensive women. These abnormalities are suggestive that CAD does occur in significant numbers of subjects in both populations with the urban community slightly ahead of the rural community. Interestingly in the rural community the increased risk of Q and QS patterns were not significantly increased in hypertensive subjects indicating that other risk factors must be involved while in Mangaung hypertension was identified as a risk factor for these ECG abnormalities.

The RR of LV hypertrophy as indirectly indicated by high amplitude R waves was significantly increased in subjects with hypertension in both populations. LV hypertrophy is a predecessor of heart failure and therefore is this an important finding. The high prevalence of high amplitude R waves in both communities emphasizes the need for early detection and optimal management of hypertension to reduce the burden of heart failure in these communities. The FS studies are the first population-based studies of its kind in SA and possibly in sub-Saharan Africa on representative samples of black subjects that demonstrate the relationship between hypertension and LV pathology. Population-based research also needs to be done to verify the meaning of high amplitude R waves in these subjects.

Arrhythmias occurred in 7.8% and 7.1% of rural and urban subjects and the RR for this ECG abnormality was significantly increased in subjects with hypertension in Mangaung but not in Qwaqwa. This implies that other risk factors for arrhythmias especially atrial fibrillation need to be found in Qwaqwa subjects. The prevalence of atrial fibrillation in these populations was surprisingly low. However,

atrial fibrillation is an important but preventable risk factor for stroke. The early detection and proper management of hypertension may contribute to reduce the risk for catastrophes such as these. More research needs to be done in these communities to further describe the causes and complications of Arrhythmias.

TABLE 9.14.1/3. Relative Risk of ECG Abnormalities in Hypertensives

Compared to Normotensives (95% CI in Parenthesis)

Qwaqwa	
Females < 45 yr	1.44 (1.03-2.00)
Females ≥ 45 yr	1.62 (1.27-2.06)
Males < 45 yr	0.89(0.60-1.33)
Males ≥ 45 yr	1.43 (1.13-1.81)
Summary RR	1.43(1.24-1.64)
Mangaung	
Females < 45 yr	1.12(0.81-1.56)
Females ≥ 45 yr	1.41(1.10-1.81)
Males < 45 yr	1.30(0.97-1.74)
Males ≥ 45 yr	1.38(1.13-1.68)
Summary RR	1.32(1.13-1.68)

TABLE 9.14.1/4. Prevalence of a Q and QS Pattern According to Age, Sex and Region

	n	Abnormal ECG (%)
Qwaqwa (age in yr)		
Females (< 45 yr)		
Hypertensive	45	0
Normotensive	194	1(0.5)
Females (≥45 yr)		
Hypertensive	174	4(2.3)
Normotensive	138	5(3.6)
Males (< 45 yr)		
Hypertensive	21	0
Normotensive	97	1(1.0)
Males (≥ 45 yr)		
Hypertensive	56	3(5.4)
Normotensive	93	2(2.2)
Mangaung (age in yr)		
Females (< 45 yr)		
Hypertensive	52	0
Normotensive	175	0
Females (≥ 45 yr)		
Hypertensive	147	12(8.2)
Normotensive	86	3(3.5)
Males (< 45 yr)		
Hypertensive	15	1(6.7)
Normotensive	117	1(0.9)
Males (≥ 45 yr)		
Hypertensive	69	4(5.8%)
Normotensive	87	2(2.3)

TABLE 9.14.1/5. Relative Risk of Q and QS Patterns in Hypertensives Compared to Normotensives (95% CI in Parenthesis)

Qwaqwa	
Females (< 45 yr)	a
Females (≥ 45 yr)	0.63(0.17-2.32)
Males (< 45 yr)	a
Males (≥ 45 yr)	2.49(0.43-14.45)
Summary RR	1.09(0.42-2.81)
Mangaung	
Females (< 45 yr)	-
Females (≥45 yr)	2.34(0.68-8.06)
Males (< 45 yr)	7.80(0.51-118.3)
Males (≥ 45 yr)	2.52(0.48-13.4)
Summary RR	2.61(1.07-6.39)

a Cannot be calculated

TABLE 9.14.1/6. Prevalence of QRS Axis Deviation According to Age, Sex and Region

	n	Abnormal ECG (%)
Qwaqwa (age in yr)		
Females (< 45 yr)		
Hypertensive	45	1(2.2)
Normotensive	194	1(0.5)
Females (≥ 45 yr)		
Hypertensive	174	6(3.5)
Normotensive	138	1(0.7)
Males (< 45 yr)		
Hypertensive	21	0
Normotensive	97	2(2.1)
Males (≥ 45 yr)		
Hypertensive	56	5(8.9)
Normotensive	93	6(6.5)
Mangaung (age in yr)		
Females (< 45 yr)		
Hypertensive	52	0
Normotensive	175	3(1.7)
Females (≥45 yr)		
Hypertensive	147	8(5.4)
Normotensive	86	2(2.3)
Males (< 45 yr)		
Hypertensive	15	0
Normotensive	117	10(8.6)
Males (≥ 45 yr)		
Hypertensive	69	6(8.7)
Normotensive	87	7(8.1)

TABLE 9.14.1/7. Relative Risk of an QRS Axis Deviation in Hypertensives Compared to Normotensives (95% CI in Parenthesis)

	RR
Qwaqwa	
Females (< 45 yr)	4.31(0.28-67.6)
Females (≥ 45 yr)	4.76(0.58-39.1)
Males (< 45 yr)	a
Males (≥ 45 yr)	1.38(0.44-4.33)
Summary RR	1.96(0.81-4.76)
Mangaung	
Females (< 45 yr)	a
Females(≥ 45 yr)	2.34(0.51-10.8)
Males (< 45 yr)	a
Males (≥ 45 yr)	1.08(0.38-3.07)
Summary RR	1.15(0.52-2.53)

a cannot be calculated

TABLE 9.14.1/8. Prevalence of High Amplitude R Waves According to Age, Sex and Region

	n	Abnormal ECG (%)
Qwaqwa (age in yr)		
Females < 45 yr		
Hypertensive	45	17(37.8)
Normotensive	194	34(17.5)
Females ≥45 yr		
Hypertensive	174	68(39.1)
Normotensive	138	24(17.4)
Males < 45 yr		
Hypertensive	21	9(42.9)
Normotensive	97	43(44.3)
Males ≥ 45 yr		
Hypertensive	56	29(51.8)
Normotensive	93	28(30.1)
Mangaung (age in yr)		
Females < 45 yr		
Hypertensive	52	14(26.9)
Normotensive	175	36(20.6)
Females ≥ 45 yr		
Hypertensive	147	55(37.4)
Normotensive	86	19(22.1)
Males < 45 yr		
Hypertensive	15	8(53.3)
Normotensive	117	58(49.6)
Males ≥ 45 yr		
Hypertensive	69	43(62.3)
Normotensive	87	30(34.5)

TABLE 9.14.1/9. Relative Risk of High Amplitude R Waves in Hypertensives Compared to Normotensives (95% CI in Parenthesis)

	RR
Qwaqwa	
Females < 45 yr	2.16 (1.33-3.50)
Females ≥45 yr	2.25 (1.49-3.38)
Males < 45 yr	0.97 (0.56-1.66)
Males ≥ 45 yr	1.72 (1.15-2.57)
Summary RR	1.83 (1.46-2.28)
Mangaung	
Females < 45 yr	1.31 (0.77-2.23)
Females ≥ 45 yr	1.69 (1.08-2.65)
Males < 45 yr	1.08 (0.65-1.79)
Males ≥ 45 yr	1.81(1.28-2.55)
Summary RR	1.55 (1.25-1.93)

TABLE 9.14.1/10. Prevalence of abnormal T waves According to Age, Sex and Region

	n	Abnormal ECG (%)
Qwaqwa (age in yr)		
Females < 45 yr		
Hypertensive	45	7 (15.6)
Normotensive	194	34 (17.5)
Females ≥ 45 yr		
Hypertensive	174	40 (23.0)
Normotensive	138	17 (12.3)
Males < 45 yr		
Hypertensive	21	1 (4.8)
Normotensive	97	12 (12.4)
Males ≥ 45 yr		
Hypertensive	56	17 (30.4)
Normotensive	93	15 (16.1)
Mangaung (age in yr)		
Females < 45 yr		
Hypertensive	52	7 (13.5)
Normotensive	175	40 (22.9)
Females ≥ 45 yr		
Hypertensive	147	58 (39.5)
Normotensive	86	23 (26.7)
Males < 45 yr		
Hypertensive	15	4 (26.7)
Normotensive	117	12 (10.3)
Males ≥ 45 yr		
Hypertensive	69	29 (42.0)
Normotensive	87	15 (17.2)

TABLE 9.14.1/11. Relative Risk of Abnormal T Waves in Hypertensives Compared to Normotensives (95% CI in Parenthesis)

	RR
Qwaqwa	
Females < 45 yr	0.89 (0.42-1.87)
Females ≥45 yr	1.87 (1.11-3.14)
Males < 45 yr	0.39 (0.05-2.80)
Males ≥ 45 yr	1.88 (1.02-3.46)
Summary RR	1.47 (1.05-2.06)
Mangaung	
Females < 45 yr	0.59 (0.28-1.24)
Females ≥ 45 yr	1.48 (0.99-2.21)
Males < 45 yr	2.60 (0.96-7.04)
Males ≥ 45 yr	2.44 (1.42-4.17)
Summary RR	a

a cannot be calculated

TABLE 9.14.1/12. Prevalence of a-v Conduction Defects According to Age, Sex and Region

	n	Abnormal ECG (%)
Qwaqwa (age in yr)		
Females < 45 yr		
Hypertensive	45	1 (2.2)
Normotensive	194	11 (5.7)
Females ≥ 45 yr		
Hypertensive	174	8 (4.6)
Normotensive	138	5 (3.6)
Males < 45 yr		
Hypertensive	21	2 (9.5)
Normotensive	97	6 (6.2)
Males ≥ 45 yr		
Hypertensive	56	7 (12.5)
Normotensive	93	5 (5.4)
Mangaung (age in yr)		
Females < 45 yr		
Hypertensive	52	1 (1.9)
Normotensive	175	1 (0.6)
Females ≥ 45 yr		
Hypertensive	147	2 (1.4)
Normotensive	86	2 (2.3)
Males < 45 yr		
Hypertensive	15	1 (6.7)
Normotensive	117	6 (5.1)
Males ≥ 45 yr		
Hypertensive	69	0
Normotensive	87	5 (5.8)

TABLE 9.14.1/13. Relative Risk of A-V Conduction Defects in Hypertensives Compared to Normotensives (95% CI in Parenthesis)

	RR
Qwaqwa	
Females < 45 yr	0.39 (0.05-2.96)
Females ≥ 45 yr	1.27(0.43-3.79)
Males < 45 yr	1.54 (0.33-7.11)
Males ≥ 45 yr	2.33 (0.78-6.98)
Summary RR	1.33 (0.70-2.50)
Mangaung	
Females < 45 yr	3.37 (0.21-52.9)
Females ≥ 45 yr	0.59 (0.08-4.08)
Males < 45 yr	1.30 (0.17-10.1)
Males ≥ 45 yr	a
Summary RR	0.55 (0.19-1.57)

a cannot be calculated

TABLE 9.14.1/14. Prevalence of Ventricular Conduction Defects According to Age, Sex and Region

	n	Abnormal ECG (%)
Qwaqwa (age in yr)		
Females < 45 yr		
Hypertensive	0	0
Normotensive	0	0
Females ≥ 45 yr		
Hypertensive	174	9 (5.2)
Normotensive	138	5 (3.6)
Males < 45 yr		
Hypertensive	21	0
Normotensive	97	1 (1.0)
Males ≥ 45 yr		
Hypertensive	56	4 (7.1)
Normotensive	93	0
Mangaung (age in yr)		
Females < 45 yr		
Hypertensive	52	0
Normotensive	175	0
Females ≥ 45 yr		
Hypertensive	147	4 (2.7)
Normotensive	86	2 (2.3)
Males < 45 yr		
Hypertensive	15	0
Normotensive	117	0
Males ≥ 45 yr		
Hypertensive	69	2 (2.9)
Normotensive	87	2 (2.3)

TABLE 9.14.1/15. Relative Risk of Ventricular Conduction Defects in Hypertensives Compared to Normotensives (95% CI in Parenthesis)

	RR
Qwaqwa	
Females < 45 yr	-
Females ≥ 45 yr	1.43 (0.49-4.16)
Males < 45 yr	a
Males ≥ 45 yr	a
Summary RR	1.85 (0.71-4.81)
Mangaung	
Females < 45 yr	-
Females ≥ 45 yr	1.17 (0.22-6.26)
Males < 45 yr	-
Males ≥ 45 yr	1.26 (0.18-8.72)
Summary RR	1.21 (0.34-4.29)

a cannot be calculated

TABLE 9.14.1/16. Prevalence of Arrhythmias According to Age, Sex and Region

	n	Abnormal ECG (%)
Qwaqwa (age in yr)		
Females < 45 yr		
Hypertensive	45	4 (8.9)
Normotensive	194	6 (3.1)
Females ≥ 45 yr		
Hypertensive	174	11 (6.3)
Normotensive	138	7 (5.1)
Males < 45 yr		
Hypertensive	21	4 (19.1)
Normotensive	97	11 (11.3)
Males ≥ 45 yr		
Hypertensive	56	9 (16.1)
Normotensive	93	1 (11.8)
Mangaung (age in yr)		
Females < 45 yr		
Hypertensive	52	5 (9.6)
Normotensive	175	9 (5.1)
Females ≥ 45 yr		
Hypertensive	147	16 (10.9)
Normotensive	86	6 (7.0)
Males < 45 yr		
Hypertensive	15	3 (20.0)
Normotensive	117	6 (5.1)
Males ≥ 45 yr		
Hypertensive	69	9 (13.0)
Normotensive	87	6 (6.9)

TABLE 9.14.1/17. Relative Risk of Arrhythmias in Hypertensives Compared to Normotensives (95% CI in Parenthesis)

	RR
Qwaqwa	
Females < 45 yr	2.87 (0.85-9.76)
Females ≥ 45 yr	1.25 (0.50-3.13)
Males < 45 yr	1.68 (0.59-4.77)
Males ≥ 45 yr	1.36 (0.60-3.07)
Summary RR	1.53 (0.94-2.48)
Mangaung	
Females < 45 yr	1.87 (0.66-5.34)
Females ≥ 45 yr	1.56 (0.63-3.84)
Males < 45 yr	3.90 (1.09-14.0)
Males ≥ 45 yr	1.89 (0.71-5.06)
Summary RR	1.90 (1.14-3.16)

TABLE 9.14.1/18. Prevalence of Low QRS Amplitude According to Age, Sex and Region

	n	Abnormal ECG (%)
Qwaqwa (age in yr)		
Females < 45 yr		
Hypertensive	44	1 (2.3)
Normotensive	194	1 (0.5)
Females ≥ 45 yr		
Hypertensive	169	4 (2.4)
Normotensive	136	1 (0.7)
Males < 45 yr		
Hypertensive	21	0
Normotensive	97	1 (1.0)
Males ≥ 45 yr		
Hypertensive	53	4 (7.6)
Normotensive	93	5 (5.4)
Mangaung (age in yr)		
Females < 45 yr		
Hypertensive	52	0
Normotensive	175	2 (1.1)
Females ≥ 45 yr		
Hypertensive	144	7 (4.9)
Normotensive	85	2 (2.4)
Males < 45 yr		
Hypertensive	15	0
Normotensive	117	3 (2.6)
Males ≥ 45 yr		
Hypertensive	68	3 (4.4)
Normotensive	85	5 (5.9)

TABLE 9.14.1/19. Relative Risk of Low QRS Amplitude in Hypertensives Compared to Normotensives (95% CI in Parenthesis)

	RR
Qwaqwa	
Females < 45 yr	4.41 (0.28-69.1)
Females ≥ 45 yr	3.22 (0.36-28.5)
Males < 45 yr	a
Males ≥ 45 yr	1.40 (0.39-5.00)
Summary RR	1.88 (0.71-5.02)
Mangaung	
Females < 45 yr	a
Females ≥ 45 yr	2.07 (0.44-9.72)
Males < 45 yr	a
Males ≥ 45 yr	0.75 (0.19-3.03)
Summary RR	1.11 (0.44-2.8)

a cannot be calculated

9.14.2 Relationship between hypertension and renal function

An unexpectedly high proportion of subjects in each age and sex category in Qwaqwa had dipstix positive proteinuria (Table 9.14.2/1). Proteinuria was more common in hypertensive than in normotensive subjects in all age and sex categories. The same observation held true for Mangaung subjects with the exception of young males, although the prevalence of proteinuria was much less in this population. In the study of hypertension in rural Zulus, (Seedat et al., 1982) proteinuria was found in 5.5% of subjects with no difference between normotensive and hypertensive subjects. In the same study the prevalence of proteinuria in the urban sample was less than 1% with no difference between hypertensive and normotensive subjects. This discrepancy was explained by the possible presence of endemic schistosomiasis in rural KwaZulu Natal. In the Qwaqwa study urinalysis with Multistix® was performed on all samples by the same experienced staff nurse except for a short period when she went on leave and was replaced by another experienced staff nurse. In the Mangaung sample experienced staff from the diabetes clinic performed the urinalysis also using Multistix®. The only reasonable explanation for this discrepancy in the FS studies, is that proteinuria was systematically over-diagnosed in the Qwaqwa samples.

The overall RR (Table 9.14.2/2) of proteinuria in hypertensive compared to normotensive subjects in Qwaqwa was 1.71 (95% CI 1.33; 2.21) and in Mangaung 1.97 (95% CI 1.03; 3.78). In spite of the higher prevalence of proteinuria in the former population the impact of hypertension on kidney function was greater in the urban sample. It must be considered that renal disease may be the cause of hypertension as in secondary hypertension and that hypertension may cause nephrosclerosis and proteinuria. Due to the high prevalence of ECG changes associated with hypertension in both populations, it can be assumed that hypertension was the cause of proteinuria in the majority of the respondents. Ideally, diabetic subjects should have been removed from the calculations. Due to relative small number of diabetic subjects compared to those with hypertension, it is expected that the difference would have been minimal.

Hypertension is the most common cause of end-stage renal disease (ESRD) in black patients and blood pressure control particularly in black patients does not

always prevent progression of renal failure (Seedat, 1999). Rostand et al. (1989) reported that the RR of ESRD in hypertensive blacks compared with hypertensive whites was 17.7 (95% CI 5.2; 31.3) in the U.S. The same authors speculated that blacks, especially older blacks, have a greater susceptibility to ESRD than whites. Other factors implicated in the higher prevalence of ESRD in blacks include socio-economic status, physiological differences and inadequate blood pressure control (Seedat, 1999). The findings that hypertension in FS blacks is associated with proteinuria is the first in a population-based study in S.A. to show this relationship and is in line with the findings of Rostand et al. (1989). At present the only modifiable risk factors to decrease the prevalence of ESRD in black South Africans is the early detection and tight control of hypertension and improvement in socio-economic status. A dedicated programme for the early detection and effective control of hypertension is long overdue in the Free State.

The prevalence of raised serum urea concentrations are shown in Table 9.14.2/3. The RR of an increased serum urea concentration in hypertensive compared to normotensive subjects was significantly elevated in both populations, 2.14 (95% CI 1.01; 4.52) in Qwaqwa and 4.6 (1.9; 10.9) in Mangaung subjects (Table 9.14.2/4). These results are in keeping with the proteinuria findings.

The results for serum creatinine concentrations are shown in Table 9.14.2/5 and Table 9.14.2/6). The RR of increased serum creatinine concentrations in subjects with hypertension compared to normotensive individuals was not significantly increased in any of the populations. This negative finding is unexpected in view of the proteinuria and serum urea findings. The cut-point for raised serum creatinine was the upper limit of normal for the population (115 μmol/l).

Summary

The significantly increased relative risks for proteinuria as well as raised serum urea levels in hypertensive compared to normotensive subjects in the FS studies are most likely due to early hypertensive nephrosclerosis. The fact that serum creatinine concentrations did not support the proteinuria and serum urea findings need to be studied in more depth including further analysis of the data using a higher cut-point. The incidence and rate of progression of early hypertensive nephrosclerosis to ESRD in the SA black population is not known and remains an

important area for further study. Programmes for the early detection and tight control of blood pressure in FS communities to decrease the burden of ESRD are highly recommended. It is noteworthy that the RR of both proteinuria and raised serum urea levels in hypertensive subjects in Mangaung exceeded that of subjects in Qwaqwa. A possible explanation might be that the burden of hypertension is higher in the urban group.

TABLE 9.14.2/1. Prevalence of Proteinuria[1] According to Hypertension by Age, Sex and Region

	Total	Total Affected
	n	n (%)
Qwaqwa (age in yr)		
Females < 45 yr		
Hypertensive	45	15 (33.3)
Normotensive	202	33 (16.3)
Females ≥ 45 yr		
Hypertensive	162	50 (30.9)
Normotensive	128	21 (16.4)
Males < 45 yr		
Hypertensive	22	9 (40.9)
Normotensive	102	31 (30.4)
Males ≥ 45 yr		
Hypertensive	49	19 (38.8)
Normotensive	92	24 (26.1)
Mangaung (age in yr)		
Females < 45 yr		
Hypertensive	50	5 (10)
Normotensive	174	2 (1.2)
Females ≥ 45 yr		
Hypertensive	127	11 (8.7)
Normotensive	75	5 (6.7)
Males < 45 yr		
Hypertensive	14	1 (7.1)
Normotensive	115	8 (7.0)
Males ≥ 45 yr		
Hypertensive	59	4 (6.8)
Normotensive	84	3 (3.6)

1 Dipstix positive

TABLE 9.14.2/2. Relative Risk of Proteinuria [1]

in Hypertensives Compared to Normotensives (95% CI in Parenthesis)

	RR
Qwaqwa	
Females < 45 yr	2.04 (1.22-3.42)
Females ≥ 45 yr	1.88 (1.19-2.96)
Males < 45 yr	1.35 (0.75-2.41)
Males ≥ 45 yr	1.49 (0.91-2.43)
Summary RR	1.71 (1.33-2.21)
Mangaung	
Females < 45 yr	8.70 (1.74-43.50)
Females ≥ 45 yr	1.30 (0.90-1.06)
Males < 45 yr	1.03 (0.14-7.61)
Males ≥ 45 yr	1.90 (0.44-8.17)
Summary RR	1.97 (1.03-3.78)

1 Dipstix positive

TABLE. 9.14.2/3. Prevalence of Elevated Serum Urea[1] According to Age, Sex and Region

	Total	Total Affected
	n	n (%)
Qwaqwa (age in yr)		
Females < 45 yr		
Hypertensive	45	45 (4.4)
Normotensive	205	205 (1.5)
Females ≥ 45 yr		
Hypertensive	143	143 (5.6)
Normotensive	178	178 (1.4)
Males < 45 yr		
Hypertensive	22	22 (4.6)
Normotensive	101	101 (3.0)
Males ≥ 45 yr		
Hypertensive	57	57 (7.0)
Normotensive	97	97 (6.2)
Mangaung (age in yr)		
Females < 45 yr		
Hypertensive	52	1 (0.6)
Normotensive	179	2 (3.9)
Females ≥ 45 yr		
Hypertensive	149	15 (10.1)
Normotensive	85	2 (2.4)
Males < 45 yr		
Hypertensive	15	0
Normotensive	117	5 (4.3)
Males ≥ 45 yr		
Hypertensive	68	8 (11.8)
Normotensive	88	1 (1.1)

1 Serum Urea ≥ 6.7 mmol/l

TABLE 9.14.2/4. Relative Risk of Elevated Serum Urea[1] in Hypertensives Compared to Normotensives (95% CI in Parenthesis)

	RR
Qwaqwa	
Females < 45 yr	3.04 (0.52-17.5)
Females ≥ 45 yr	4.02 (0.89-18.2)
Males < 45 yr	1.53 (0.17-14.1)
Males ≥ 45 yr	1.14 (0.33-3.85)
Summary RR	2.14 (1.01-4.52)
Mangaung	
Females < 45 yr	6.9 (0.64-76.9)
Females ≥ 45 yr	4.3 (1.0-18.2)
Males < 45 yr	a
Males ≥ 45 yr	10.3 (1.3-83.3)
Summary RR	4.6 (1.9-10.9)

[1] Serum Urea ≥ 6.7 mmol/l

TABLE 9.14.2/5. Prevalence of Elevated Serum Creatinine[1] According to Age, Sex and Region

	Total	Total Affected
	n	n (%)
Qwaqwa (age in yr)		
Females < 45 yr		
Hypertensive	45	45 (2.2)
Normotensive	205	205 (0.5)
Females ≥ 45 yr		
Hypertensive	178	178 (3.4)
Normotensive	143	143 (0.7)
Males < 45 yr		
Hypertensive	22	22(9.1)
Normotensive	101	101 (5.0)
Males ≥ 45 yr		
Hypertensive	57	57 (10.5)
Normotensive	97	97 (10.3)
Mangaung (age in yr)		
Females < 45 yr		
Hypertensive	52	2 (3.9)
Normotensive	179	4 (2.2)
Females ≥ 45 yr		
Hypertensive	149	9 (6.0)
Normotensive	85	2 (2.4)
Males < 45 yr		
Hypertensive	15	2 (13.3)
Normotensive	117	11 (9.4)
Males ≥ 45 yr		
Hypertensive	68	8 (11.8)
Normotensive	88	6 (6.8)

1 Serum Serum Creatinine > 115 umol/l

TABLE 9.14.2/6. Relative Risk of Elevated Serum Creatinine [1]

in Hypertensives Compared to Normotensives (95% CI in Parenthesis)

	RR
Qwaqwa	
Females < 45 yr	4.55 (0.29-71.4)
Females 45+ yr	4.83 (0.59-40)
Males < 45 yr	1.83 (0.38-8.85)
Males > 45+ yr	1.02 (0.39-2.66)
Summary RR	1.67 (0.82-3.39)
Mangaung	
Females < 45 yr	1.7 (0.32-9.2)
Females 45+ yr	2.6 (0.57-11.6)
Males < 45 yr	1.4 (.035-5.8)
Males > 45+ yr	1.7 (0.63-4.7)
Summary RR	1.8 (0.95-3.50)

[1] Serum Creatinine > 115 umol/l

9.14.3 Hypertension and hypertensive retinopathy

Fundoscopy through dilated pupils were attempted on each subject. The presence or the absence of hypertensive retinopathy was recorded and graded according to the Keith-Wagener-Barker classification (Table 9.14.3/1). No cases of grade IV retinopathy (papiloedema) were encountered. Hypertensive changes were more common in older than in younger subjects and, as expected, were grade III changes less common than grade II changes and the latter less common than grade I changes. Hypertensive changes were more common in hypertensive than in normotensive subjects in all age and sex categories in the both populations (9.14.3/2). The RR of hypertensive retinopathy in hypertensive compared to normotensive subjects in Qwaqwa was 1.94 (95% CI 1.70; 2.22). The risk of hypertensive retinal end-organ damage was significantly increased in hypertensive subjects (Table 9.14.3/3).

TABLE 9.14.3/1. Prevalence of Hypertensive Retinopathy[1] by Age, Sex and Region

	Grade[2]			
	Normal	I	II	III
	n (%)	n (%)	n (%)	n (%)
Qwaqwa (age in yr)				
Females < 45 yr	195 (81.9)	37 (15.6)	6 (2.52)	0
Females ≥ 45 yr	87 (31.3)	157 (56. 5)	26 (9.4)	8 (2.9)
Males < 45 yr	93 (80.2)	22 (19.0)	1 (0.7)	0
Males ≥ 45 yr	41 (34.5)	72 (60.5)	5 (4.2)	1 (0.8)
Mangaung (age in yr)				
Females < 45 yr	192 (84.3)	34 (14.9)	2 (0.9)	0
Females ≥ 45 yr	65 (29.7)	127 (58.0)	25 (11.4)	2 (0.91)
Males < 45 yr	109 (86.5)	16 (12.7)	0	1 (0.8)
Males ≥ 45 yr	60 (42.0)	78 (54.6)	5 (3.5)	0

1. Trough dilated pupils

2. Keith-Wagener-Barker classification (Williams 2001a)

No cases of Grade IV hypertensive retinopathy were encountered

TABLE 9.14.3/2. Prevalence of Hypertensive Retinopathy[1] by Age, Sex and Region

	n	Grades I-III %
Qwaqwa (age in yr)		
Females < 45 yr		
Hypertensive	41	53.7
Normotensive	197	10.7
Females ≥ 45 yr		
Hypertensive	150	84
Normotensive	128	50.8
Males < 45 yr		
Hypertensive	21	42.9
Normotensive	95	14.7
Males ≥ 45 yr		
Hypertensive	40	90
Normotensive	79	53.2
Mangaung (age in yr)		
Females < 45 yr		
Hypertensive	50	44
Normotensive	178	7.9
Females ≥ 45 yr		
Hypertensive	138	81.2
Normotensive	79	53.2
Males < 45 yr		
Hypertensive	15	26.7
Normotensive	111	11.7
Males ≥ 45 yr		
Hypertensive	59	88.1
Normotensive	84	36.9

[1] Keith-Wagener-Barker classification (Williams 2001a)

TABLE 9.14.3/3. Relative Risk of Hypertensive Retinopathy[1]

in Hypertensives Compared to Normotensives (95% CI in Parenthesis)

	RR
Qwaqwa	
Females < 45 yr	5.03 (3.07- 8.26)
Females ≥ 45 yr	1.65 (1.38-1.99)
Males < 45 yr	2.91(1.46-5.81)
Males ≥ 45 yr	1.69 (1.34-2.13)
Summary RR	1.94 (1.70-2.22)
Mangaung	
Females < 45 yr	
Females ≥ 45 yr	
Males < 45 yr	
Males ≥ 45 yr	
Summary RR	

[1] Composite of grades 1-3

Summary

Sufficient evidence was collected in this rural-urban study of a representative sample of the populations of Qwaqwa and Mangaung to conclude that hypertension is a frequent occurrence, that the risk of hypertensive complications is significantly increased including LV hypertrophy, CAD, hypertensive nephrosclerosis and hypertensive retinopathy. More information is needed to determine the actual incidence and rate of progression of target organ damage in these populations. A programme should be established for the early identification and effective treatment of hypertension according to existing guidelines (Milne, 2001), in FS communities to reduce the burden of this common chronic condition with potentially devastating complications.

10 Overweight and obesity

10.1 Descriptive data on height, weight and body mass index

A positive secular trend for mean height appears to be present in both sexes and in both samples (Table 10.1/1). In the Qwaqwa sample, men 25-34 years old were 2 cm taller than 55-64 year-old men, while the corresponding figure for men in the Mangaung sample was 5 cm. The corresponding figure for women in the Qwaqwa sample was 3 cm while it was 4 cm for women in the Mangaung sample. However, after correcting the mean height of subjects with a correction factor of 6 mm per decade for height lost after the age of 30 years (Tobias, 1990), most of the observed differences disappeared (Fig.10.1/1). For women in the Qwaqwa sample a positive secular trend was present for those born between c. 1925 and c. 1945 where after the trend was reversed for a decade just to become positive again for those born in c. 1965. Overall, a positive secular trend was present for women in Qwaqwa. The corrected heights for men in Qwaqwa showed no clear trend with increasing age and even moved up and down between the age groups. This was interpreted as an absent trend. The maximum corrected height for Women from Mangaung was recorded in the group born c. 1945. Corrected heights for women born before and after that date were shorter. This was again interpreted as an absent secular trend. The pattern for men was erratic again but the youngest generation born in c. 1965 was conspicuously taller than any other group of men born before them.

In a study of 5018 adult and sub-adult male black subjects from Johannesburg, Tobias (1990) showed that these men had not been subject to a secular trend towards increased adult mean stature over the period c. 1919 - c. 1950. Slome et al. (1960) found that the heights of adult Zulu men were the same than that of men studied in 1940-1945 but were significantly lower than that of Zulu men studied in 1927. Further analysis of the FS data will have to be done before a firm conclusion concerning any secular trend can be reached.

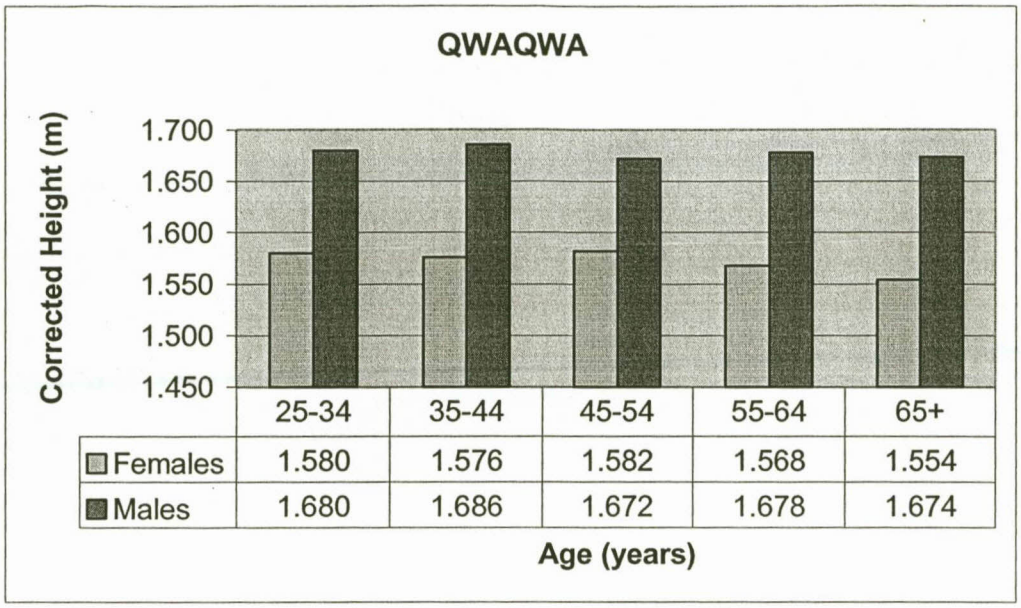
The mean BMI of men (Table 10.1/1 and Fig. 10.1/2) in both samples changed very little with increasing age and remained within the normal range (20-25 kg/m^2). In both samples and in every age group the mean BMI for women

exceeded that for men and increased with age until age 64 years. In the Qwaqwa sample the mean BMI of all women fell within the pre-obesity range except women in the 55-64 year age group whose mean BMI fell within the obesity, class 1 range. In the Mangaung sample mean BMI for all women also fell within the pre-obesity category except women in the age range 45-64 years whose BMI was in class 1 obesity range. Overall, the BMI of women in both studies were very similar in the different age groups. Young men in Qwaqwa (mean BMI 24.0 kg/m^2) were clinically significantly heavier than their counterparts in Mangaung (mean BMI 22.3 kg/m^2). The mean BMI of elderly subjects was lower than that of the preceding age group for both sexes and in both samples.

The mean BMI of Cape Peninsula black men and women (Steyn et al., 1991) in the age group 15-64 years were 23.4 kg/m^2 and 27.8 kg/m^2 respectively. Overall the BMI of both sexes in the BRISK study exceeded that of FS black men and women. The mean BMI of FS and Cape Peninsula black men were less that that for US black men (26.4 kg/m^2) while the mean BMI of black women in the FS and Cape Peninsula were very similar to that of US black women (28.2 kg/m^2) (Kuczmarski et al., 1994).

TABLE 10.1/1. Mean Height (m), Weight (kg) and BMI (kg/m^2) of Study Subjects by Age, Gender and Region (Standard Deviation in Parenthesis)

	n	Height (m)	Weight (kg)	BMI
Qwaqwa				
Males (age in yrs)				
25-34	55	1.68 (0.07)	68.40 (16.4)	24.0 (4.7)
35-44	68	1.68 (0.07)	69.39 (15.3)	24.7 (5.3)
45-54	27	1.66 (0.06)	64.61(15.5)	23.6 (5.8)
55-64	45	1.66 (0.07)	65.74 (15.5)	23.6 (4.6)
65+	81	1.65 (0.06)	62.71 (14.2)	22.9 (4.5)
Females (age in yrs)				
25-34	142	1.58 (0.06)	67.48 (15.0)	27.1 (5.5)
35-44	110	1.57 (0.06)	72.67 (17.4)	29.4 (6.6)
45-54	99	1.57 (0.06)	73.93 (21.0)	29.8 (7.8)
55-64	102	1.55 (0.06)	73.40 (17.7)	30.5 (7.3)
65+	121	1.53 (0.06)	64.67 (19.0)	27.8 (8.0)
Mangaung				
Males (age in yrs)				
25-34	67	1.70 (0.07)	64.56(10.0)	22.3 (3.2)
35-44	64	1.67 (0.07)	67.58 (14.00)	24.2 (4.5)
45-54	64	1.68 (0.06)	66.24 (16.2)	23.5 (5.7)
55-64	54	1.65 (0.06)	66.47 (17.1)	24.5 (6.3)
65+	40	1.66 (0.07)	65.21 (17.6)	23.6 (5.4)
Females (age in yrs)				
25-34	103	1.57 (0.06)	67.58 (16.0)	27.2 (6.2)
35-44	126	1.56 (0.06)	71.85 (17.3)	29.5 (7.0)
45-54	105	1.57 (0.06)	76.92 (19.1)	31.1 (7.2)
55-64	68	1.53 (0.07)	72.02 (21.4)	30.6 (9.0)
65+	64	1.53 (0.06)	68.98 (19.4)	29.5 (7.7)



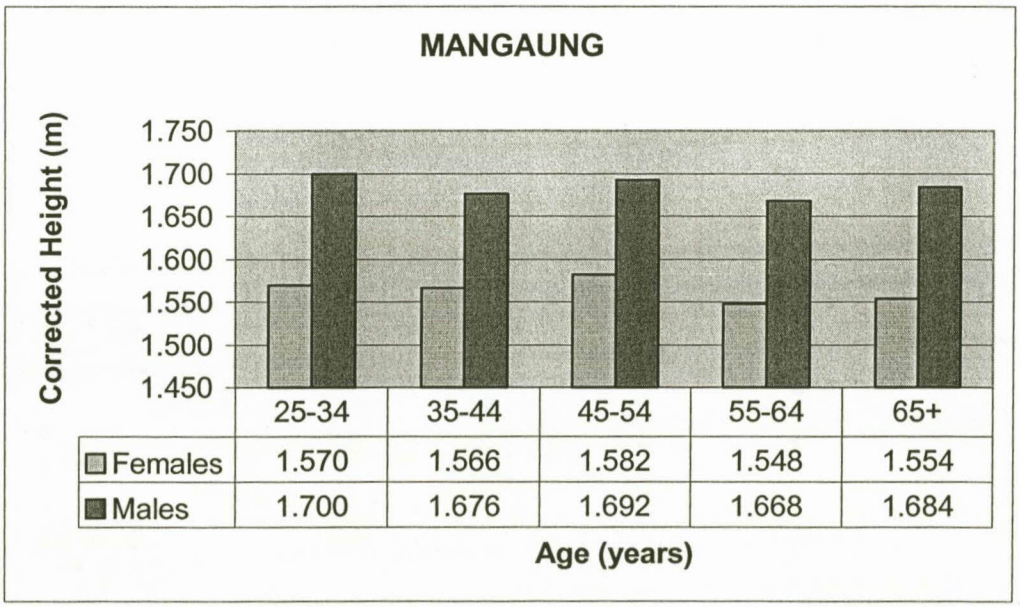
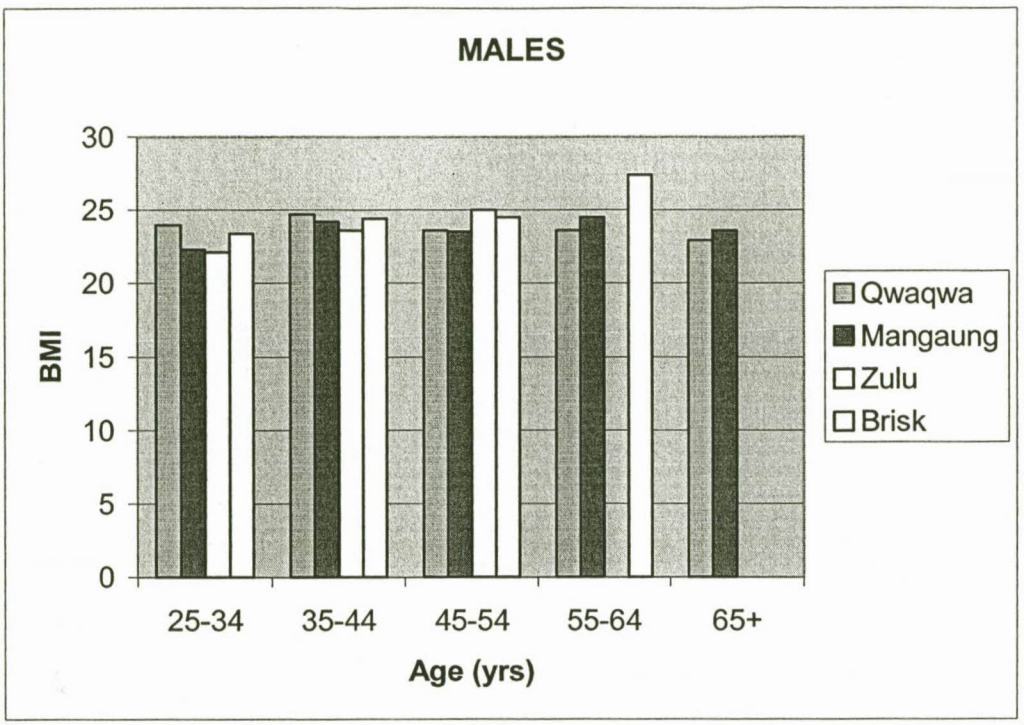


Fig. 10.1/1. Height (corrected for shrinkage) and age for both sexes and populations.



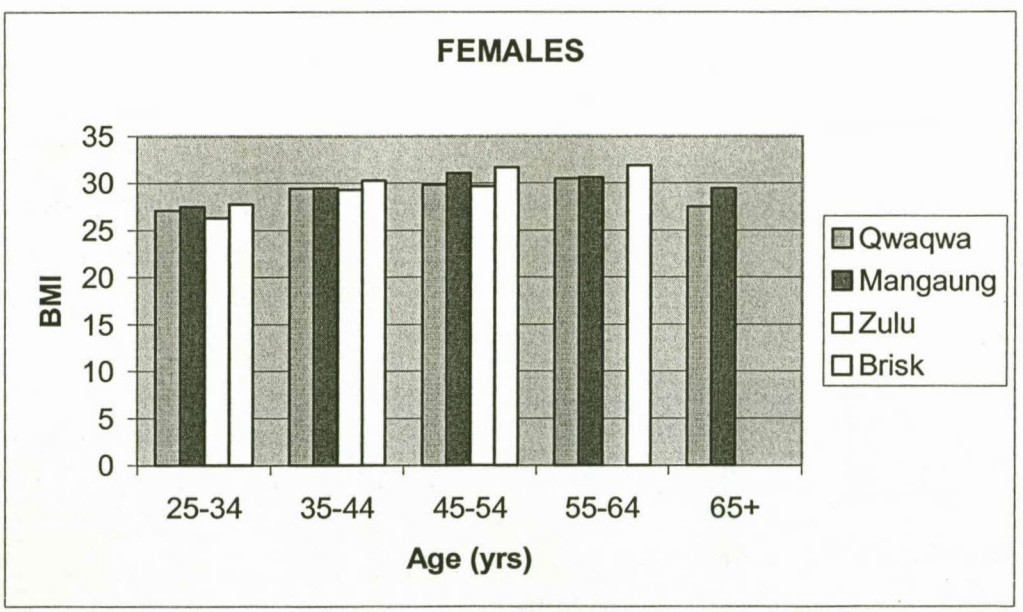


Fig. 10.1/2. Comparison of Mean BMI (kg/m^2) for Selected Populations in S.A.
(Zulu: Seedat et al., 1992, BRISK: Steyn et al., 1991)

10.2 Prevalence of overweight and obesity

The age- and sex-specific and age-standarised prevalence rates of overweight (pre-obesity and obesity combined) are shown in Table 10.2/1. In both populations the majority of females were overweight and twice as many females than males were overweight. The age-standardised prevalence of overweight in Qwaqwa and Mangaung males was 31.3% and 29.7% respectively while the corresponding rates for females were 65.5 and 69.2%. The highest prevalence of overweight (35.3%) in Qwaqwa males was present in the 35-44 year age group while the highest prevalence in Mangaung males was in the 55-64 year age group. The highest prevalence of overweight in Qwaqwa females (78.4%) was present in the 55-64 year age group while the highest prevalence for females in Mangaung was in the 45-54 year age group (81.9%).

The overall prevalence of obesity (BMI $\geq$ 30 kg/m^2) was very similar between the two populations and was 2.1% more common in Mangaung (Table 6.2/1). In Qwaqwa obesity was three times as common in females (36.6%) than in males (12.2%) while in Mangaung four times as many females (41.1%) were obese than males (10.9%). The highest prevalence of obesity (49%) in Qwaqwa occurred in the 55 to 64 year old group of women while in Mangaung the peak prevalence (54.3%) occurred in females in the 45 to 54 year old group. The prevalence of obesity in FS black men exceeded that reported for black men in Cape Town (7.9%) but was slightly less in FS black women than in Cape Town black women (44.4%) (Steyn et al., 19 91). The prevalence of overweight and obesity in Mangaung was 51.1% and 27.7% respectively after sex- and age-standardisation of the sample to the population structure of Qwaqwa. The differences in prevalence were not statistically significant (Table 10.2/1).

There are few African countries or populations for which trends in obesity have been documented (WHO, 1997). Since the FS studies were concluded at least 6 years prior to the SADHS an opportunity arose to compare data from the earlier FS studies with data from the SADHS (Table 10.2/2 and Fig. 10.2/1.) In 1996 84.4% of the FS population was black (www.stats.gov.census96). Therefore, the results of the SADHS for the FS is mostly applicable to black subjects. The prevalence of obesity in 1997 in male subjects in the FS was 8% for all ethnic

groups (SADHS, 1998). The latter prevalence was somewhat less than that observed in Qwaqwa and Mangaung during 1990-1991 (12.2% and 10.9% respectively). The difference observed for females was much more pronounced: 30% in 1997 during the SADHS compared to 36.6% and 41.1% for Qwaqwa and Mangaung respectively during 1990-1991. Possible explanations for this apparent decrease in the prevalence of obesity among males and especially among females over a 6 year period include methodological differences, the HIV/AIDS epidemic and a true natural decline in prevalence. The sampling procedure followed for the Qwaqwa and Mangaung studies allowed the drawing of a representative sample in each region. It is therefore unlikely that the difference in prevalence can be attributed only to differences in sampling procedures. At the time the FS studies were conducted the HIV/AIDS epidemic had hardly taken off. A retrospective analysis of stored frozen serum samples from the Qwaqwa and Mangaung populations produced only three positive HIV test results for Qwaqwa (unpublished). The HIV prevalence in South Africa in 1999-2000 was estimated to be 14-15% in the age group 20-64 years (van Rensburg, 2002). It is possible to hypothesise that the HIV/AIDS epidemic did have a negative effect on the prevalence of obesity in the FS during the previous decade. The only other possibility, a true natural decline in the prevalence of obesity over such a short period, is unlikely since no national intervention campaign had been launched and the nutrition transition is still in progress (Bourne et al., 20 02).

The prevalence of obesity in FS blacks and especially in black women reached an alarmingly high rate and exceeded that of black women in other Sub-Saharan countries (Bovet et al., 20 02, Zinyowera et al.1994). The prevalence of obesity in women in the age group 25-55 years is already exceeding that of American black women (Luke et al., 20 01). Walker et al. (2001) attributed the increased prevalence to an increase in the intake of dietary fat, and a decrease in the intake of dietary fibre. Walker still has the opinion that the health disadvantages of obesity in black women are less than that in white women. Evidence is accumulating that obesity in black women is already contributing to non-communicable diseases in this group (Kruger et al., 20 01 and Levitt et al., 19 93).

Obesity and its co-morbidities are preventable (WHO, 2000). Greater awareness should be created for the existing co-morbidities of obesity as well as the potential contribution of obesity in black women to the emergence of non-communicable diseases.

TABLE 10.2/1. Prevalence (%) of Overweight[1] and Obesity[2] According to Age Group, Sex and Population

	Qwaqwa			Mangaung		
	n	Overweight	Obesity	n	Overweight	Obesity
Males (age in yrs)						
25-34	55	30.9	10.9	67	19.4	3
35-44	68	35.3	19.1	64	37.5	12.5
45-54	27	29.6	7.4	64	29.7	15.6
55-64	45	28.9	13.3	54	40.7	20.4
65+	81	28.4	7.4	40	35	17.5
Total						
Age-standardised	276	31.3	12.2	289	29.7	10.9
Females (age in yrs)						
25-34	142	57.8	27.5	103	61.2	31.1
35-44	110	73.6	41.8	126	73.8	42.9
45-54	99	67.7	42.4	105	81.9	54.3
55-64	102	78.4	49	68	64.7	47.1
65+	121	56.2	31.4	64	67.2	42.2
Total						
Age-standardised	574	65.5	36.6	466	69.2	41.1
Total						
Age- and sex standardised	850	50	25.6	755	51.6	27.7
Sex- and age-standardised to the Qwaqwa population strucure		50	25.6		51.1a	27.7b

BMI ≥ 25 kg/m2

BMI ≥ 30 kg/m2

[a] 95% CI for the difference Qwaqwa-Mangaung: -8.3;6.1

[b] 95% CI for the difference Qwaqwa-Mangaung: -7.1;2.9

TABLE 10.2/2. Comparison of Prevalence (%) Obesity[1] in FS Studies and SADHS

	Qwaqwa	Mangaung	SADHS				
			S.A. Total	African NU[2]	African U[3]	Afr. Total	FS
Males (age in yrs)							
25-34	10.9	3.0	7.6				
35-44	19.1	12.5	12.6				
45-54	7.4	15.6	16.7				
55-64	13.3	20.4	14.2				
65+	7.4	17.5	13.2				
Total			9.1	5.4	9.4	7.7	8.(
Age-standardised	12.2	10.9					
Females (age in yrs)							
25-34	27.5	31.1	26.3				
35-44	41.8	42.9	38.7				
45-54	42.4	54.3	44.3				
55-64	49.0	47.1	45.1				
65+	31.4	42.2	32.0				
Total			29.4	24.6	35.7	30.5	29
Age-standardised	36.6	41.1					
Total Age- and sex standardised	25.6	27.7					

[1] Obesity= BMI ≥ 30 k/m2

[2] NU=Non-urban

[3] U=Urban

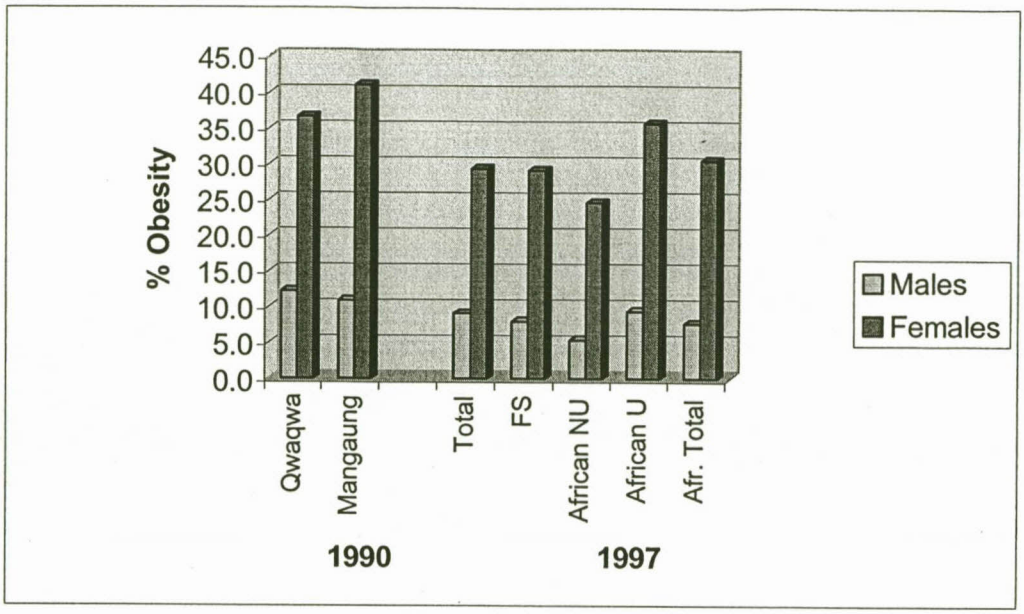


Fig. 10.2/1. Comparison of prevalence (%) obesity between FS studies and SADHS reflecting the time-trend. (Total=total population for S.A., NU=Non-urban, U=Urban, FS=Total for FS: all ethnic groups included, African total = whole country: all ethnic groups included).

10.3 Anthropometry

10.3.1 Circumferences

In both samples mean waist, hip, buttock and thigh circumferences for females in the age categories were very similar (Table 10.3.1/1). The same was true for male subjects. In both samples the mean buttock circumference exceeded the mean hip circumference in each age and sex category. A highly significant correlation existed between mean hip and buttock circumferences among female subjects in the Qwaqwa sample (r_s = 0.92, $p < 0.01$). Among male subjects the correlation was also highly significant (r_s = 0.87, $p < 0.01$). In the Mangaung sample the corresponding correlations were r_s = 0.95 ($p < 0.01$) for females and r_s = 0.96 ($p < 0.01$) for males.

The sexual dimorphism of fat distribution is clearly visible in Table 10.3.1/1. The waist circumferences of males and females were fairly comparable with subjects of the same sex in both populations. Hip, buttock and thigh circumferences for females in both studies were conspicuously greater than that of male subjects. Fatness, and particularly peripheral body fat, is the most dimorphic of the morphological variables (Brown, 1992 p 321) and was also true for these populations. Males in both studies exhibited healthy mean waist circumferences < 94 cm but the mean waist circumference of most women exceeded the lower healthy cut-point of 80 cm (WHO, 1997).

TABLE 10.3.1/1. Mean Waist, Hip, Buttocks and Thigh Circumference (cm) by Age, Gender and Study Population (Standard Deviation in Parenthesis).

	n	Waist	Hip	Buttock	Thigh
Qwaqwa					
Men (age in yr)					
25-34	56	82.6 (13.2)	88.2 (10.4)	92.7 (10.0)	51.2 (5.9)
35-44	68	85.0 (12.5)	87.7 (10. 0)	93.0 (9.1)	50.4 (6.1)
45-54	27	83.7 (13.4)	86.5 (11.4)	91.8 (11.2)	48.5 (6.5)
55-64	45	84.8 (12.0)	85.9 (10.1)	90.9 (9.8)	47.8 (6.1)
65+	82	83.3 (12.3)	84.4 (9.0)	90.0 (8.9)	47.1 (6.6)
Women (age in yr)					
25-34	141	80.2 (10.7)	98.4 (12.6)	102.4 (11.4)	56.7 (7.5)
35-44	110	85.4 (13.4)	101.7 (12.9)	105.6 (13.2)	58.6 (8.5)
45-54	98	87.5 (16.1)	100.7 (12.7)	105.8 (14.4)	58.5 (9.5)
55-64	102	88.8 (13.3)	99.0 (11.4)	105.1 (11.8)	57.5 (8.0)
65+	121	82.9 (13.7)	93.2 (12.9)	99.4 (16.1)	52.9 (9.2)
Mangaung					
Men (age in yr)					
25-34	67	79.3 (7.7)	86.3 (6.7)	91.0 (6.4)	50.0 (4.9)
35-44	65	84.7 (11.5)	87.5 (9.3)	93.1 (8.4)	50.6 (6.7)
45-54	64	85.3 (13.9)	84.1 (10.4)	90.8 (11.3)	48.0 (7.4)
55-64	54	86.9 (16.2)	84.1 (9.8)	91.4 (10.7)	47.7 (7.0)
65+	40	86.7 (14.4)	83.6 (9.6)	91.3 (10.7)	47.3 (6.9)
Women (age in yr)					
25-34	105	77.5 (10.7)	98.6 (12.0)	102.3 (11.6)	57.3 (8.7)
35-44	126	84.2 (11.5)	100.0 (13.8)	104.9 (12.6)	58.0 (8.9)
45-54	105	88.1 (13.3)	100.3 (13.6)	107.0 (13.8)	59.1 (9.9)
55-64	68	85.7 (14.0)	97.4 (15.7)	105.3 (17.9)	57.8 (11.5)
65+	64	85.7 (13.0)	94.7 (14.5)	103.6 (15.9)	55.9 (10.9)

10.3.2 Circumference ratios

In both populations and in both sexes mean waist-to-hip circumference ratio increased across the age deciles with the exception of elderly women in Qwaqwa (Table 10.3.2/1). Among men, mean waist-to-hip circumference ratios in all age groups exceeded that of women in corresponding age groups reflecting the more central pattern of fat distribution in men. The mean waist-to-hip circumference ratio among males in the 45-year and older age group in the Mangaung sample exceeded that for corresponding males in the Qwaqwa sample. The mean WHR of females in both samples with the exception of the two younger age deciles in Qwaqwa and the youngest age decile in Mangaung, exceeded 0.85 indicating abdominal fat accumulation. The mean WHR for men in Qwaqwa was just below 1.00 while the WHR of men 45-years and older in the Mangaung sample exceeded 1.00 also indicating abdominal obesity according to Caucasian standards. These cut-points have, however, not yet been validated in black South Africans.

In the Mangaung sample a highly significant correlation existed between the mean waist-to-hip circumference ratio and mean waist-to-buttock circumference ratio in both females ($rs = 0.91$, $p < 0.01$) and males ($rs = 0.90$, $p < 0.01$). The corresponding correlations in the Qwaqwa sample were $rs = 0.89$ ($p < 0.01$) for females and $rs = 0.75$ ($p < 0.01$) for males.

Since the correlation between WHR and WBR was excellent it may suffice to calculate only WHR in future. At the time of the initiation of these studies no consensus existed as to the definitions of hip- and waist-circumference. Furthermore, waist circumference has been accepted to provide the same information as WHR and is recommended as the only measurement necessary to define central adiposity in clinical practice (WHO, 2000).

According to Caucasian standards most women in both studies exhibited an unfavourable body fat distribution while half of the men in Mangaung had a predominantly central fat distribution. Since WHO cut-points were not previously validated in black men and women, median WHR values were used for men and women to calculate excessive risk for glucose intolerance, hypertension and

dyslipidaemia. Since excessive risk was demonstrated by using these cut-points and since the median WHR in both sexes (the median WHR for males was 0.97 in Qwaqwa and 0.98 in Mangaung while the median WHR for females was 0.85 in both populations) were either identical or very close to the WHO cut-points, it is suggested that the WHO cut-points (1.0 for males and 0.85 for females) also be accepted for our local black population.

TABLE 10.3.2/1. Mean Waist-to-Hip (WHR) Waist-to-Buttock (WBR) Circumference Ratios by Age, Gender and Study Population (Standard Deviation in Parenthesis).

	n	WHR	WBR
Qwaqwa			
Men (age in yr)			
25-34	55	0.94 (0.07)	0.89 (0.06)
35-44	68	0.97 (0.07)	0.91 (0.05)
45-54	27	0.97 (0.07)	0.91 (0.05)
55-64	45	0.99 (0.07)	0.93 (0.05)
65+	80	0.99 (0.11)	0.93 (0.07)
All ages	275	0.97 (0.09)	0.91 (0.06)
Women (age in yr)			
25-34	141	0.82 (0.09)	0.78 (0.06)
35-44	110	0.84 (0.10)	0.81 (0.08)
45-54	97	0.86 (0.10)	0.82 (0.08)
55-64	102	0.90 (0.09)	0.84 (0.07)
65+	121	0.89 (0.09)	0.84 (0.10)
All ages	571	0.86 (0.10)	0.82 (0.08)
Mangaung			
Men (age in yr)			
25-34	67	0.92 (0.05)	0.87 (0.04)
35-44	64	0.97 (0.07)	0.91 (0.06)
45-54	64	1.01 (0.08)	0.94 (0.07)
55-64	54	1.03 (0.10)	0.94 (0.08)
65+	40	1.03 (0.08)	0.95 (0.06)
All ages	289	0.99 (0.09)	0.92 (0.07)
Women (age in yr)			
25-34	105	0.79 (0.06)	0.76 (0.05)
35-44	126	0.85 (0.09)	0.80 (0.07)
45-54	105	0.88 (0.10)	0.83 (0.08)
55-64	68	0.89 (0.09)	0.82 (0.08)
65+	64	0.90 (0.09)	0.82 (0.07)
All ages	468	0.85 (0.10)	0.80 (0.07)

10.3.3 Skinfold thickness

The mean age- and sex-specific skinfold thickness from five different sites (biceps, triceps, suprailiac, sub-scapular and parathoracic) for the two samples are shown in Table 10.3.3/1 and Fig. 10.3.3/1 and Fig. 10.3.3/2. Skinfold thickness from all sites were consistently greater in females in all age categories than males in corresponding age groups for both samples. This illustrates the sexual dimorphism of fatness (Brown, 1992). With the exception of the young male group in the Qwaqwa sample, skinfolds were thinner in the youngest age group. Overall, skinfold measurements of male subjects in Qwaqwa differed from their female counterparts as well as from Mangaung subjects since skinfold thickness were thickest in these young men. In Mangaung males skinfold thickness increased from the first to the second age decile where after it tended to plateau. Skinfold thickness in Mangaung females showed a clear pattern of progressively increasing from the youngest age group, reaching a peak in the 45-54 year age decile and then declining progressively with increasing age. Skinfold thickness in Qwaqwa women followed a different pattern in that skinfold thickness increased progressively to reach a peak decade later than in Mangaung females and then declined. This phenomenon was most obvious for suprailiac and subscapular skinfold thickness. Suprailiac skinfold thickness in women from both samples was considerably thicker than in their male counterparts. This observation is at odds with other populations (Brown, 1992).

The mean triceps skinfold thickness of males and females in Qwaqwa and Mangaung was considerably thicker than that reported for Zulu males and females 3 decades earlier (Table 4.3.1/1). The mean triceps skinfold thickness of urban and rural Venda males were also much thinner compared to male subjects from both FS populations (Table 4.3.1/2). These findings support the observation that overnutrition is becoming the pattern of malnutrition in SA rather than undernutrition (Bourne et al., 20 02).

No entirely satisfactory explanation is available for the observed "population dimorphism" of skinfold thickness. An observation made in Qwaqwa was that manual labour was frequently performed by women e.g. digging of ditches with picks and shovels. Since validated physical activity questionnaires were not

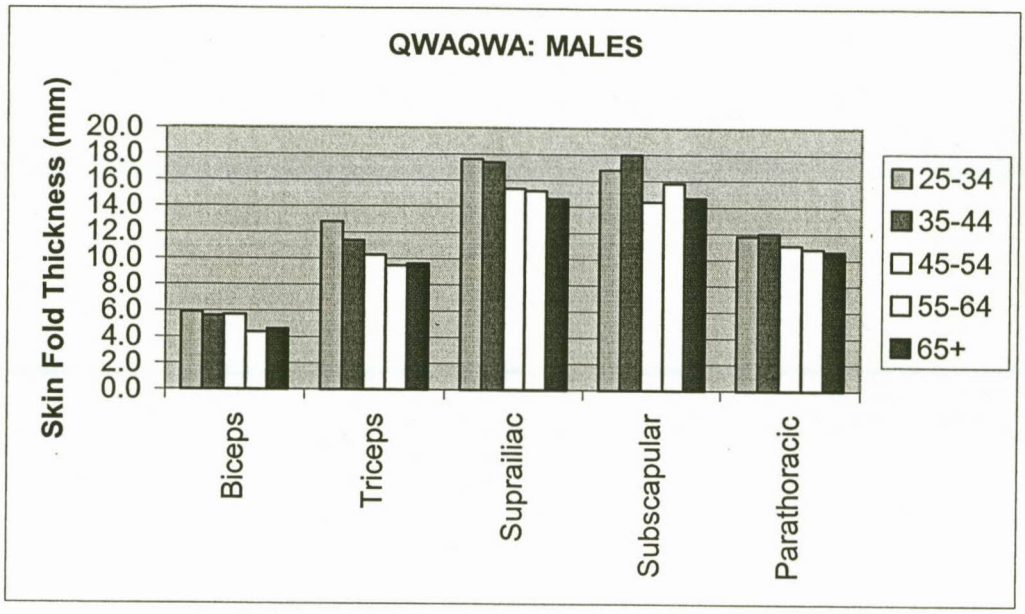
completed in this survey, the contribution of physical activity to body composition in the populations is not known.

The mean sum of five skinfolds decreased with increasing age in male subjects in the Qwaqwa sample while no consistent pattern was noted in males from the Mangaung sample (Table 10.3.3/2). The mean sum of five skinfolds for female subjects tended to increase with increasing age up to 64 years in the Qwaqwa sample and up to 54 years in the Mangaung sample where after it declined sharply. A remarkable similarity was noted in the sum of five skinfolds for females in the two samples in the different age groups.

Overall, the ratio of trunk-to-extremity skinfold thickness tended to increase with increasing age in both samples and both sexes (Table 10.3.3/2). This was most distinct for females in the Qwaqwa sample and males in the Mangaung sample. In spite of the lesser thickness of skinfolds in males, the ratio of trunk-to-extremity skinfold thickness in males from both samples exceeded that for females in all corresponding age groups indicating the sexual dimorphism of body fat distribution. The sexual dimorphism in body build for the two populations is shown in Fig. 10.3.3/3. Adult Caucasian men are 8% taller than women while women have more subcutaneous fat (Brown, 1992). Adult limb fatness is much more dimorphic than trunk fatness, a finding that appears to be universal (Brown, 1992). The findings depicted in Fig. 10.3.3/3 for these black populations are in keeping with the latter observations.

TABLE 10.3.3/1. Mean Skinfold Measurements from Five Sites by Age, Gender and Study population (Standard Deviation in Parenthesis).

	n	Biceps	Triceps	Suprailiac	Subscapular	Parathoracic
Qwaqwa						
Men (age in yr)						
25-34	56	5.9 (3.4)	12.8 (8.1)	17.6 (12.1)	16.8 (10.3)	11.8 (9.5)
35-44	68	5.6 (4.3)	11. 4 (6.8)	17.4 (12.1)	18.0 (10.9)	12.0 (8.1)
45-54	27	5.7 (6.5)	10.3 (7.3)	15.4 (11.5)	14.4 (10.5)	11.1 (9.4)
55-64	45	4.4 (2.5)	9.5 (5.9)	15.2 (9.9)	15.8 (8.9)	10.8 (8.4)
65+	83	4.6 (2.2)	9.6 (5.9)	14.6 (9.8)	14.7 (8.7)	10.6 (7.5)
Women (age in yr)						
25-34	142	11.1(6.7)	24.6 (9.6)	23.1(11.0)	26.5 (10.9)	20.0 (10.7)
35-44	110	12.5 (6.9)	26.8 (9.4)	26.8 (11.8)	29.7 (11.3)	22.1 (10.5)
45-54	99	12.8 (8.2)	26.7 (10.5)	27.2 (11.6)	30.6 (10.3)	22.8 (9.8)
55-64	102	12.2 (6.5)	26.1(9.3)	27.9 (10.8)	31.7 (10.0)	22.6 (8.9)
65+	121	9.4 (5.7)	20.5 (9.5)	21.1(11.0)	26.4 (11.3)	17.8 (8.8)
Mangaung						
Men (age in yr)						
25-34	67	4.3 (1.6)	9.7 (4.8)	16.0 (9.6)	13.3 (7.0)	9.3 (6.0)
35-44	65	5.1(2.7)	11.9 (6.7)	19.6 (12.0)	16.3 (9.9)	12.7 (8.8)
45-54	64	4.5 (2.4)	10.3 (6.1)	18.1(11.5)	15.5 (10.5)	12.7 (10.0)
55-64	54	4.8 (2.8)	11. 4 (8.0)	18.4(12.2)	16.9 (11.1)	13.6 (10.4)
65+	40	4.5 (2.9)	10.3 (6.7)	17.5 (11.3)	16.3 (10.6)	13.2 (9.1)
Women (age in yr)						
25-34	105	9.6 (5.1)	24.2 (9.1)	23.6 (10.9)	25.3 (11.0)	18.5 (9.6)
35-44	126	11.6 (7.0)	26.0 (10.0)	27.0 (10.6)	28.6 (10.4)	22.7 (10.1)
45-54	105	12.6 (6.9)	28.1(10.1)	28.1 (10.5)	31.4 (10.2)	24.0 (9.5)
55-64	68	12.0 (7.5)	26.2 (10.1)	25.6 (11.2)	28.6 (10.6)	21.3 (9.4)
65+	64	10.6 (6.5)	24.2 (9.6)	24.4 (10.9)	28.1 (11.0)	20.3 (8.6)



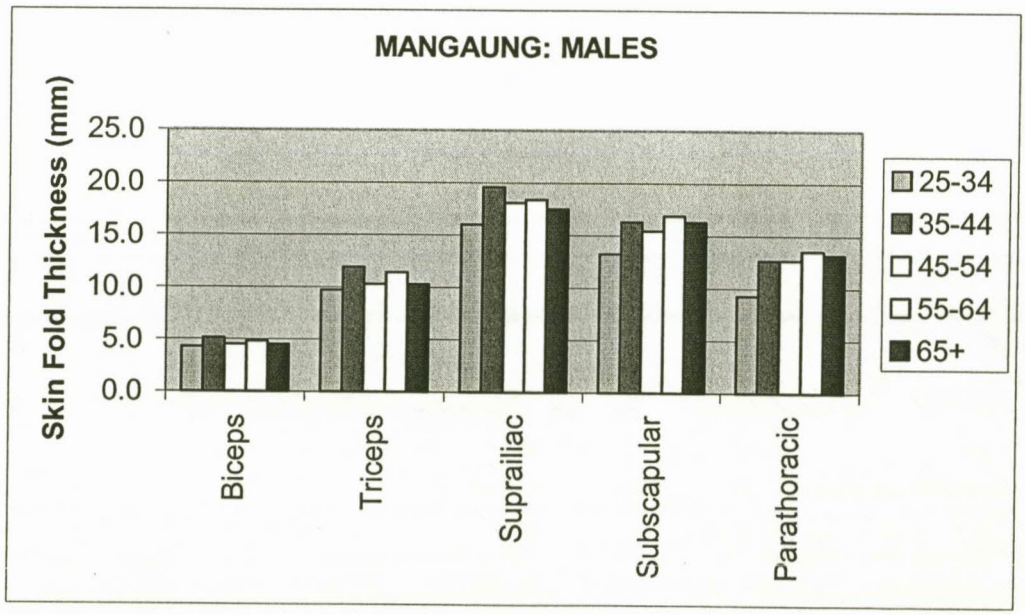
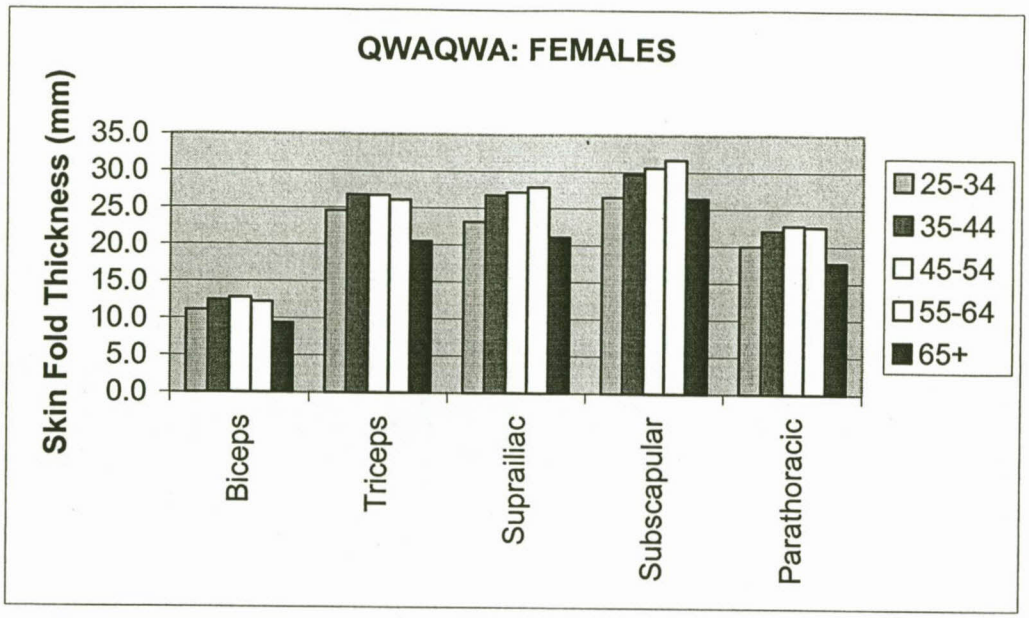


Fig. 10.3.3/1. Skinfold thickness from 5 sites for males by age (yr) and population.



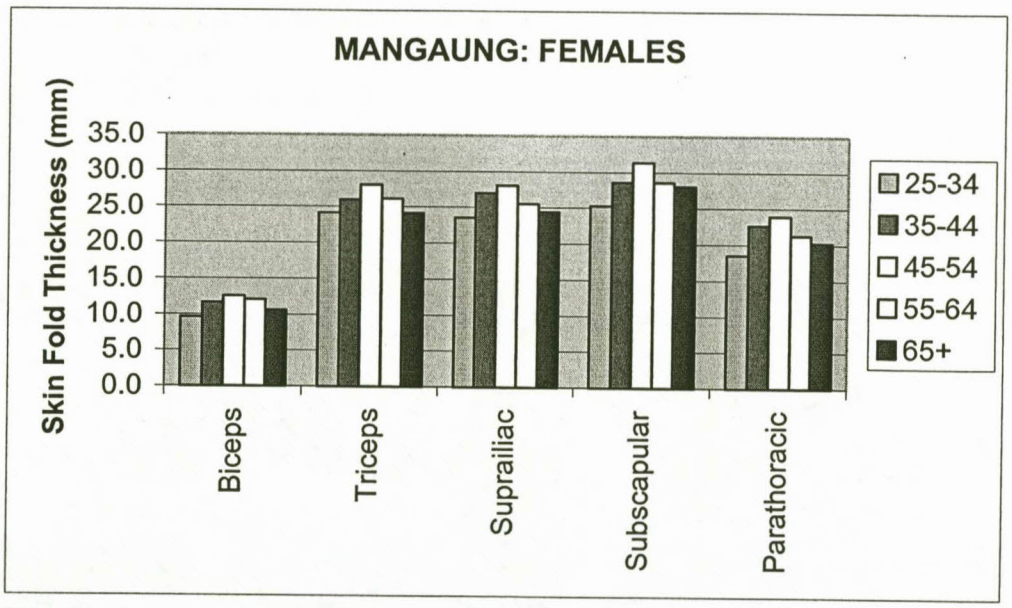


Fig. 10.3.3/2. Skinfold thickness from 5 sites for females by age (yr) and population.

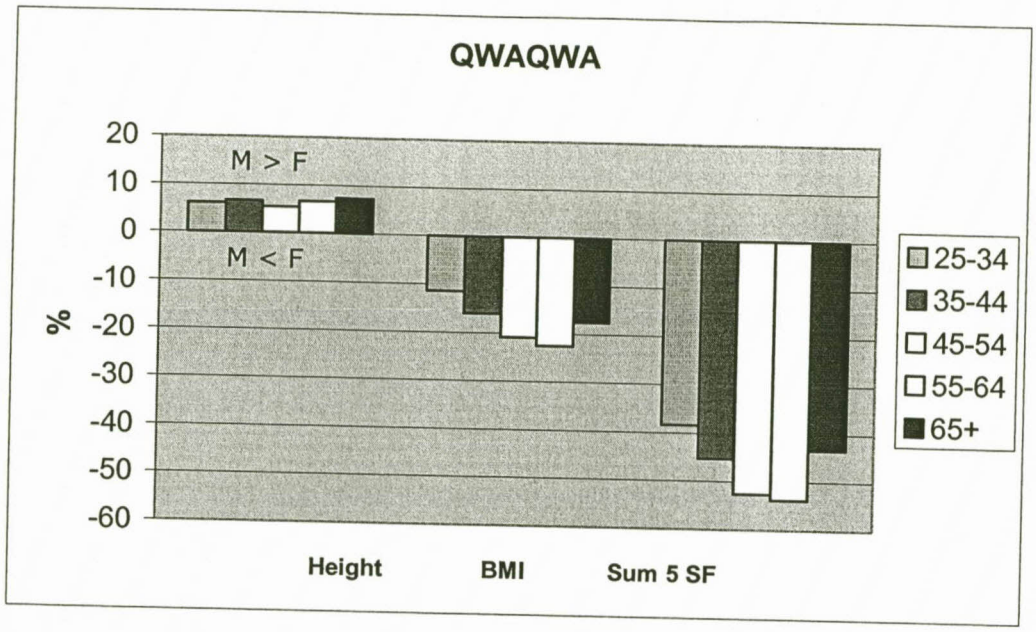
TABLE 10.3.3/2. Mean Sum of Five Skinfolds[1] (mm) and Ratio of Trunk to Extremity Skinfold Thickness (Standard Deviation)

	n	Sum of 5 Skinfolds	Ratio Trunk-to[2] Extremity Skinfolds[3]
Qwaqwa			
Men (age in years)			
25-34	56	64.9 (41.4)	2.41 (0.55)
35-44	68	64.4 (39.0)	2.76 (0.75)
45-54	27	56.9 (42.1)	2.58 (0.75)
55-64	45	55.8 (33.3)	2.97 (0.95)
65+	83	54.0 (32.2)	2.73 (0.69)
Females (age in years)			
25-34	141	105.2 (44.8)	1.98 (0.55)
35-44	109	117.6 (45.8)	2.02 (0.49)
45-54	99	120.1 (45.6)	2.16 (0.65)
55-64	102	120.4 (40.0)	2.25 (0.69)
65+	120	95.3 (42.9)	2.24 (0.66)
Mangaung			
Men (age in years)			
25-34	67	52.6 (27.1)	2.72 (0.73)
35-44	65	65.6 (37.9)	2.77 (0.71)
45-54	64	61.1 (37.5)	2.98 (0.99)
55-64	54	65.0 (42.7)	2.93 (0.85)
65+	40	61.8 (38.3)	3.15 (0.97)
Females (age in years)			
25-34	105	101.3 (42.1)	2.01 (0.58)
35-44	126	115.8 (43.7)	2.18 (0.61)
45-54	105	124.1 (42.7)	2.13 (0.60)
55-64	68	113.6 (43.6)	2.08 (0.67)
65+		107.5 (45.7)	2.2 (0.54)

[1] Biceps-, triceps-, suprailiac-, sub-scapular-, and parathoracic-skinfolds

[2] Sub-scapular-, parathoracic-, and suprailiac-skinfolds

[3] Triceps- and biceps-skinfolds



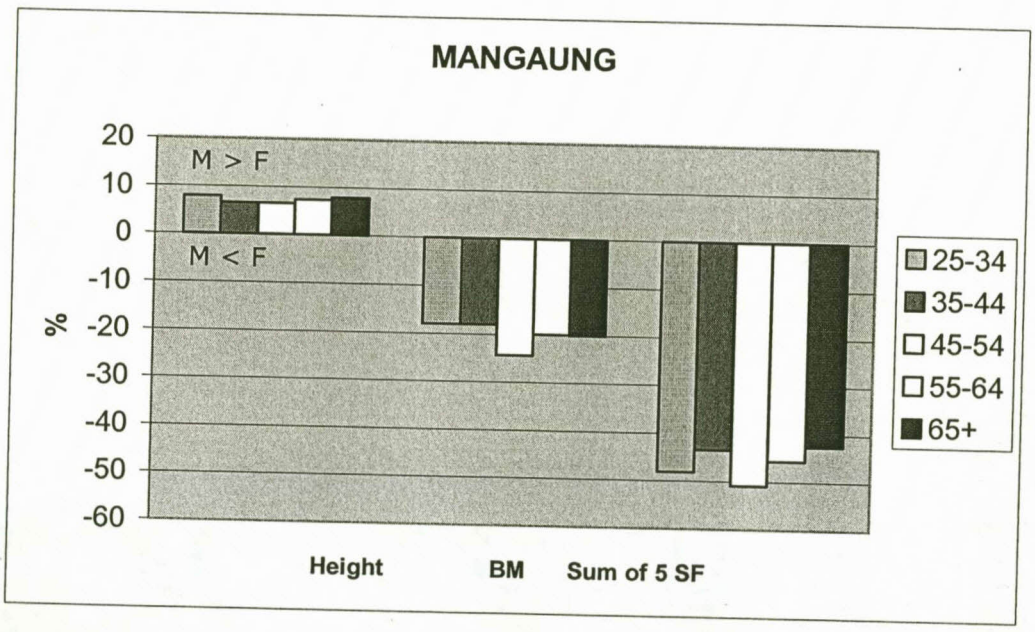


Fig. 10.3.3/3. Sexual dimorphism in stature, BMI and sum of 5 skinfolds by age, sex and population.

10.3.4 Percentage body fat

The age- and sex-specific percentage body fat as predicted from skinfold measurements for the two samples is shown in Table 10.3.4/1 and Fig.10.3.4/1. The sexual dimorphism in body fat (Brown, 1992) is again obvious. Percentage body fat increased with increasing age from 25 years to 64 years in both sexes and both samples (45-54 year-old males in the Qwaqwa sample was the only exception). A sharp decline in percentage body fat was noted in elderly subjects in both samples. The percentage body fat for females exceeded that for males in both samples. The difference in percentage body fat between females and males ranged between 8.7% and 15.8% (Table 10.3.4/1). Percentage body fat in Mangaung women peaked a decade earlier (45-54 years) than was the case for Qwaqwa women and was very similar in both populations (38% and 38.1% for Mangaung and Qwaqwa women respectively). The maximum % body fat in men was reached in the age group 55-64 years and was 24% and 23.1% respectively for Mangaung and Qwaqwa respondents. The 25-34 year old male subgroup in Mangaung was the leanest (18.1% body fat). The percentage body fat of subjects in the 25-34 year subgroup of both sexes and in both populations exceeded that for young adults in an affluent society where adipose tissue accounts for 15% and 27% of body weight in males and females respectively (Brown, 1992).

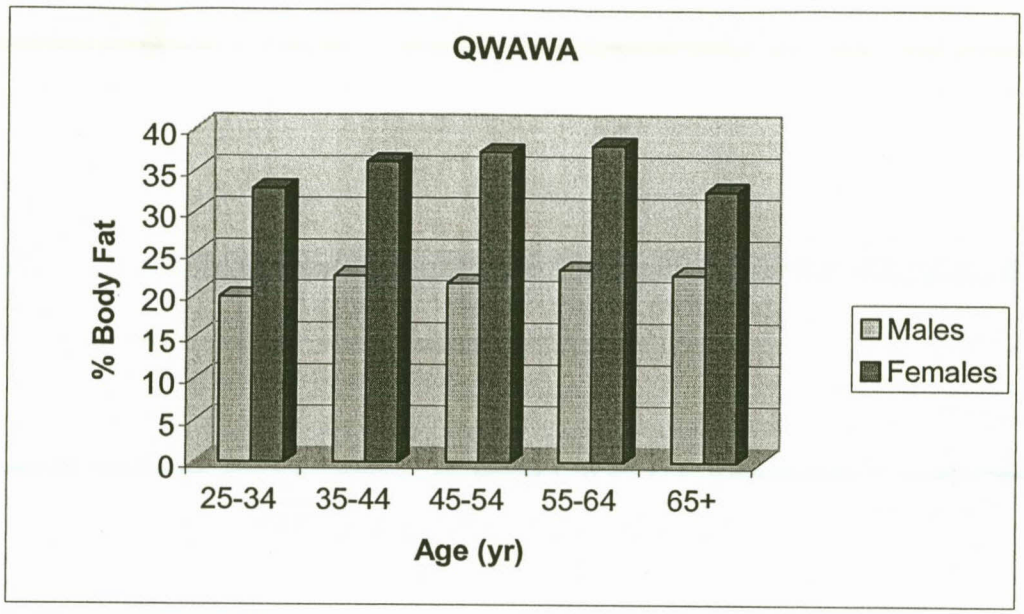
TABLE 10.3.4/1. Percentage Body Fat as Predicted by Skinfold Thickness[1] by Age, Gender and Sample[2] (Standard Deviation in Parenthesis)

	n	% Body fat
Qwaqwa		
Males (age in years)		
25-34	56	19.8(8.1)
35-44	68	22.4 (7.9)
45-54	27	21.5 (8.6)
55-64	45	23.1 (6.7)
65+	63	22.5 (7.5)
Females (age in years)		
25-34	141	32.9 (6.6)
35-44	109	36.1 (5.9)
45-54	99	37.3 (6.2)
55-64	102	38.1 (6.0)
65+	24	32.6(7.1)
% BF females -%BF males[3]		
25-34		13.1
35-44		13.7
45-54		15.8
55-64		15
65+		10.1
Mangaung		
Males (age in years)		
25-34	67	18.1 (5.8)
35-44	65	22.4 (7.5)
45-54	64	22.9 (8.1)
55-64	54	24.0 (8.3)
65+	32	23.5 (8.0)
Females (age in years)		
25-34	105	32.4 (6.7)
35-44	126	35.9 (5.4)
45-54	105	38.0 (5.8)
55-64	68	37.0 (6.6)
65+	17	32.2 (4.8)
% BF females -%BF males3		
25-34		14.3
35-44		13.5
45-54		15.1
55-64		13
65+		8.7

1 Females < 69 years, Males < 77 years

2 Durnin and Womersley, 1973

3 BF=Body Fat



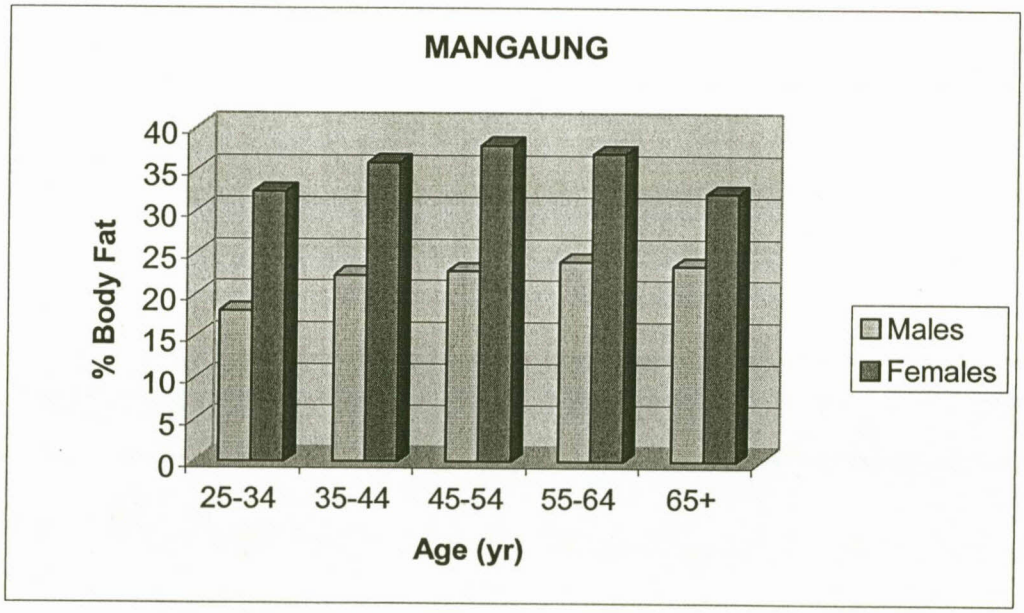


Fig. 10.3.4/1. Percentage body fat by age, gender and population.

10.4 Association between overweight and selected variables

The association between overweight (BMI > 25 kg/m^2) and glucose intolerance, hyperinsulinaemia and hypertension was already dealt with in Chapters 8 and 9. The association between overweight (BMI > 25 kg/m^2) and dyslipidaemia is dealt with in Chapter 11. The main findings in this regard is summarised in Table 10.4/1.

Hypertension as well as borderline hypertension were significantly associated with overweight in the Qwaqwa sample but in the Mangaung sample overweight was only associated with hypertension and not with borderline hypertension (Table 9.5/2). The relationship between overweight and dyslipidaemia was inconsistent. In the Qwaqwa sample only hypercholesterolaemia, and in the Mangaung sample only hypertriglyceridaemia was significantly associated with overweight. No association was found between overweight and non-protective levels of HDL-cholesterol in either sample (Table 10.4/1).

Logistic regression analysis also identified overweight as a predictor of glucose intolerance in the Mangaung sample (odds ratio 1.8 (95% CI 1.2-2.8)) but overweight was not retained in the model for the Qwaqwa sample (Table 8.15/1). Overweight was also a predictor of impaired glucose tolerance in the Mangaung sample (odds ratio 1.8 (95% CI 1.1-2.9)) but not in the Qwaqwa sample (Table 8.15/2).

Among females in the Qwaqwa sample weak but significant partial correlations were found between percentage body fat and diastolic blood pressure ($r = 0.26$, $p < 0.01$) as well as between percentage body fat and systolic blood pressure ($r = 0.23$, $p < 0.01$) (Table 10.4/2). For males the respective partial correlations were $r = 0.23$ ($p < 0.01$) and $r = 0.21$ ($p < 0.01$). For females in the Mangaung sample the corresponding partial correlations were $r = 0.24$ ($p < 0.01$) and $r = 0.23$ ($p < 0.01$) for diastolic and systolic blood pressure respectively (Table 10.4/3). For males the respective partial correlations were $r = 0.20$ ($p < 0.01$) and $r = 0.19$ ($p < 0.01$). The sum of five skinfolds' thickness was also positively but weakly associated with both systolic and diastolic blood pressure in both sexes and in both samples.

TABLE 10.4/1. Association Between Overweight (BMI > 25 kg/m^2) and Glucose Tolerance, Hyperinsulinaemia, Hypertension and Dyslipidaemia after Adjusting for Age and Sex (95% Confidence Intervals in Parenthesis)

	Qwaqwa Relative risk	Mangaung Relative risk
Glucose intolerance	1.3 (0.93-1.7)	1.9 (1.4-2.5)
IGT	1.0 (0.7-1.5)	1.8 (1.3-2.7)
Diabetes	2.4 (1.3-4.7)	2.2 (1.2-4.0)
Borderline hypertension	1.5 (1.2-1.9)	1.4 (1.0-1.9)
Hypertension	1.7 (1.4-2.0)	1.4 (1.1-1.7)
Hypercholesterolaemia [1]	1.6 (1.3-1.9)	a
Non-protective levels of HDL-cholesterol	a	a
Hypertriglyceridaemia	a	2.2 (1.4-3.5)

[1] Total cholesterol ≥ 5.2 mmol/I

a Cannot be calculated

* Statistically significantly different from 1 at the 0.05 level

TABLE 10.4/2. Partial Correlations Between Diastolic and Systolic Blood Pressure[1], Skinfold Thickness and Calculated Percentage Body Fat and Circumferences After Adjusting for Age in Qwaqwa Subjects (Significance Values in Parenthesis[2])

	Diastolic r	Systolic r
Females		
Skinfolds*		
Triceps	0.28 < (0.01)	0.22 < (0.01)
Biceps	0.23 < (0.01)	0.19 < (0.01)
Subscapular	0.26 < (0.01)	0.21 < (0.01)
Suprailiac	0.25 < (0.01)	0.20 < (0.01)
Parathoracic	0.24 < (0.01)	0.17 < (0.01)
Sum of 5 skinfolds	0.27 < (0.01)	0.21 < (0.01)
Trunk/Extremity ratio	0.06 (0.16)	0.03 (0.57)
% Body fat	0.26 < (0.01)	0.23 < (0.01)
Circumferences**		
Waist	0.29 < (0.01)	0.20 < (0.01)
Hip	0.26 < (0.01)	0.19 < (0.01)
Thigh	0.28 < (0.01)	0.21 < (0.01)
Buttocks	0.29 < (0.01)	0.23 < (0.01)
Waist-to-hip	0.10 (0.02)	0.06 (0.22)
Males		
Skinfolds*		
Triceps	0.24 < (0.01)	0.24 < (0.01)
Biceps	0.22 < (0.01)	0.19 (0.01)
Subscapular	0.18 (0.01)	0.19 < (0.01)
Suprailiac	0.20 < (0.01)	0.17 (0.01)
Parathoracic	0.19 < (0.01)	0.18 < (0.01)
Sum of 5 skinfolds	0.22 < (0.01)	0.21 < (0.01)
Trunk/Extremity ratio	0.02 (0.70)	0.00 (1.00)
% Body fat	0.23 < (0.01)	0.21 <0.01)
Circumferences**		
Waist	0.15 (0.01)	0.20 < (0.01)
Hip	0.08 (0.20)	0.16 (0.01)
Thigh	0.12 (0.06)	0.17 (0.01)
Buttocks	0.12 (0.05)	0.20 < (0.01)
Waist-to-hip ratio	0.16 (0.01)	0.14 (0.03)

1 Subjects on treatment for hypertension excluded

2 p-Value testing whether correlations differ significantly from zero

* Spearman rank partial correlations

** Pearson partial correlations

TABLE 10.4/3. Partial Correlations Between Diastolic and Systolic Blood Pressure1, Skinfold Thickness and Calculated Percentage Body Fat and Circumferences After Adjusting for Age in Mangaung Subjects (Significance Values in Parenthesis2)

	Diastolic r	Systolic r
Females		
Skinfolds*		
Triceps	0.27 < (0.01)	0.24 < (0.01)
Biceps	0.23 < (0.01)	0.21 < (0.01)
Subscapular	0.24 < (0.01)	0.20 < (0.01)
Suprailiac	0.24 < (0.01)	0.21 < (0.01)
Parathoracic	0.26 < (0.01)	0.21 < (0.01)
Sum of 5 skinfolds	0.27 < (0.01)	0.23 < (0.01)
Trunk/Extremity ratio	-0.02 (0.75)	0.00 (0.99)
% Body fat	0.24 < (0.01)	0.23 < (0.01)
Circumferences* *		
Waist	0.30 < (0.01)	0.23 < (0.01)
Hip	0.26 < (0.01)	0.23 < (0.01)
Thigh	0.24 < (0.01)	0.20 < (0.01)
Buttocks	0.28 < (0.01)	0.24 < (0.01)
Waist-to-hip ratio	0.08 (0.11)	0.03 (0.53)
Males		
Skinfolds*		
Triceps	0.24 < (0.01)	0.20 < (0.01)
Biceps	0.17 < (0.01)	0.19 < (~0.01)
Subscapular	0.20 < (0.01)	0.22 < (0.01)
Suprailiac	0.18< (0.01)	0.18 < (0.01)
Parathoracic	0.22 < (0.01)	0.22 < (0.01)
Sum of 5 skinfolds	0.21 < (0.01)	0.21 < (0.01)
Trunk/Extremity** ratio	0.12 (0.05)	0.17 < (0.01)
% Body fat	0.20 < (0.01)	0.19 < (0.01)
Circumferences		
Waist	0.20 < (0.01)	0.15< (0.01)
Hip	0.12 (0.04)	0.08 (0.20)
Thigh	0.10 (0.09)	0.09 (0.12)
Buttocks	0.15 (0.01)	0.11 (0.08)
Waist-to-hip ratio	0.22 < (0.01)	0.19 < (0.01)

1 Subjects on treatment for hypertension excluded

2 p-Value testing whether correlations differ significantly from zero

* Spearman rank partial correlations ** Pearson partial correlations

10.5 Association between central obesity and selected variables

Subjects with central obesity were significantly more likely to have glucose intolerance, IGT, diabetes and fasting hyperinsulinaemia (Table 10.5/1). Post-glucose load hyperinsulinaemia was only significantly associated with central obesity among subjects in the Qwaqwa sample. Hypertension, but not borderline hypertension, was also significantly more frequent in subjects with central obesity in both samples. In neither of the samples was hypercholesterolaemia significantly associated with central obesity, while non-protective levels of HDL-cholesterol in both samples were significantly more common in subjects with central obesity. Hypertriglyceridaemia in both samples was also significantly more common in subjects with central obesity.

In both samples neither the trunk-to-extremity-skinfold thickness ratio nor the waist-to-hip-circumference ratio correlated significantly with diastolic or systolic blood pressure (Table 10.4/2 and Table 10.4/3). The exception was males in the Mangaung sample where a weak but significant correlation between blood pressure and waist-to-hip-circumference ratio was noted.

TABLE 10.5/1. The Association Between Central Obesity [1] and Glucose Intolerance, Hyperinsulinaemia, Hypertension and Dyslipidaemia after Adjusting for Age and Sex (95% Confidence Intervals in Parenthesis)

	Qwaqwa Relative risk	Mangaung Relative risk
Glucose intolerance	2.3 (1.7-3.2)*	2.8 (2.0-3.8)*
IGT	2.1 (1.4-3.0)*	2.4 (1.6-3.5)*
Diabetes	3.9 (2.0-7.3)*	5.0 (2.5-10.1)*
Fasting hyperinsulinaemia	1. 7 (1.4-2.0)*	1.4 (1.2-1.7)*
Sum of 60+120 min hyperinsulinaemia	1.5 (1.2-1.8)*	a
Borderline hypertension	1.1 (0.9-1.5)	1.3 (0.98-1.7)
Hypertension	1.5 (1.2-1.8)*	1.5 (1.2-1.8)*
Hypercholesterolaemia[2]	1.2 (0.98-1.4)	a
Non-protective levels of HDL-cholesterol[3]	2.0 (1.6-2.6)*	2.2 (1.6-2.9)*
Hypertriglyceridaemia4	4.0 (2.4-6.8)*	3.1 (1.9-5.0)*

[1] WHR > median (females median WHR = 0.85, males median WHR = 0.97)

a Cannot be calculated

[2] Total serum cholesterol ≥ 5.2 mmol/L

[3] HDL-cholesterol < 20% of total cholesterol

[4] Serum triglycerides ≥ 2.3 mmol/L

10.6 Macro and micronutrient intake of a representative sample of the Mangaung Population

A 10% subset of respondents was selected from the Mangaung population for nutrient intake assessment that was carried out by registered dieticians from the University of Potchefstroom using the 24 hour recall method. After random selection of the first respondent every 10th respondent was identified and invited to participate. If that particular respondent was not available or refused, the next respondent on the list was invited. From Mangaung 75 respondents were identified of whom 56 turned up for assessment. The dietary data from three of the respondents was considered to be unreliable or deemed to be outliers, and their data was not used. A final response rate of 70% was thus achieved. The results of the Mangaung diet survey are shown in Table 10.6/1 and Table 10.6/2.

TABLE 10.6/1. Mean daily nutrient intake of Mangaung subjects (Macronutrients) (Standard Deviations inParenthesis)

Nutrient	Males	Females	Group
	n=18	n=32	n=50
MACRONUTRIENTS			
Total energy (MJ)	9.88(3.34)	9.36(2.73)	9.55(2.94)
Total protein (g)	80.49(30.15)	76.66(30.47)	78.04(30.10)
animal protein (g)	45.70(25.47)	47.04(27.69)	46.56(26.66)
plant protein (g)	34.18(11.89)	29.27(8.12)	31.04(9.82)
total protein	13.88(2.34)	14.05(3.13)	13.99(2.85)
%E: animal protein	7.72(3.09)	8.57(3.39)	8.26(3.28)
plant:animal ratio	0.95(0.55)	0.74(0.34)	0.81(0.43)
Total fat (g)	80.73(35.02)	79.20(27.14)	79.75(29.87)
saturated fat (S)	25.08(11.98)	24.84(9.45)	24.92(10.31)
monounsaturated fat	25.83 (11.28)	25.69(9.92)	25.74(10.31)
polyunsaturated (P)	21.61(11.84)	20.67(8.90)	21. 01 (9.95)
P:S ratio	0.90(0.32)	0.87(0.33)	0.88(0.33)
%E: fat	30.28(7.91)	32.37(6.49)	31. 62 (7.03)
Cholesterol (mg)	463.55(284.65)	413.00(229.76)	431.20(249.22)
(mg/1000 kJ)	44.90(20.25)	45.76(26.10)	45.45(23.94)
Total carbohydrate (g)	286.77(107.44)	285.68(99.88)	286.08 (101. 57)
%E: carbohydrate	49.33(8.28)	51. 74 (7.29)	50.88(7.66)
Sucrose (g)	60.41(51.91)	73.36(54.17)	68.70(53.21)
%E: sucrose	9.40(6.50)	12.92(7.12)	11.65(7.05)
Total fibre (g)	20.69(6.89)	19.33(5.78)	19.82(6.17)
fibre (g/1000 kJ)	2.17(0.69)	2.11(0.45)	2.13(0.54)

TABLE 10.6/2. Mean daily nutrient intake of Mangaung subjects (Micronutrients) (Standard Deviations in Parenthesis)

Nutrient	Males n=18	Females n=32	Group n=50
MICRONUTRIENTS			
Calcium (mg)	652.28(438.98)	766.44 (799.93)	725.34(689.02)
Iron (mg)	14.45(4.34)	12.47(3.29)	13.18(3.78)
Magnesium (mg)	380.94(124.76)	319.37(107.14)	341.54(116.42)
Phosphorus (mg)	1372.5(565.5)	1270.8(667.4)	1307.4(628.6)
Potassium (mg)	2704.8(904.9)	2618.6(1267.9)	2649.7(1141.4)
Sodium (mg)	1609.3(706.9)	1520.8(651.4)	1552.7(666.1)
Zinc (mg)	11.51(4.15)	10.49(3.85)	10.86(3.95)
Copper (mg)	1.43(0.67)	1.32(0.52)	1.36(0.58)
Selenium (mg)	24.44(22.43)	25.52 (21. 91)	25.13(21.87)
Vitamin A (IU)	9568.8(6055.2)	9693.1(4315.3)	9648.3(4950.3)
Vitamin (RE)	1271.9(786.5)	1321.7(659.0)	1303.8(699.9)
Thiamine (mg)	1.33(0.36)	1.28(0.46)	1.30(0.43)
Riboflavin (mg)	1.51(0.58)	1.55(0.99)	1.54(0.85)
Nicotinic acid (mg)	18.80(7.79)	14.82(4.88)	16.25(6.31)
Vitamin B6 (mg)	1.27(0.45)	1.15(0.40)	1.19(0.42)
Folic acid (u.g)	240.44(107.93)	227.72(99.79)	232.30(101.88)
Vitamin B12 (ug)	7.29(7.30)	5.70(3.29)	6.27(5.09)
Ascorbic acid (mg)	49.83(30.78)	69.12(60.85)	62.18(52.52)
Vitamin D (mg)	3.98(4.49)	2.96(4.88)	3.33(4.73)
Vitamin E (mg)	20.00(13.30)	21.01(12.39)	20.65(12.60)
Pantothenic acid (mg)	4.17(1.70)	4.31(2.41)	4.26(2.16)
Biotin (μg)	25.45(14.70)	23.79(15.23)	24.39(14.91)

Summary

A small positive secular trend in mean adult stature was observed for women in Qwaqwa. For Qwaqwa males the trend was absent. The mean height of Qwaqwa males born in c. 1965 was 6 mm taller than men born 40 years earlier. To put this into perspective, the expected increase in early adult life was 0.6 cm per decade (Tobias, 1990). Men and women in Mangaung exhibited an absent secular trend but the youngest generation of men born in c. 1965 was conspicuously taller than any other group of men born before them. The most obvious explanation for the absence of a secular trend in mean adult stature in both populations is poor socio-economic circumstances and nutrition spanning over at least 4 decades.

The sexual dimorphism in terms of BMI was conspicuous for both populations. Mean BMI for women was excessive in all age categories and increased over the age deciles. The mean BMI of men in the two populations were very similar and appropriate. The prevalence of obesity in women ranged between 37% and 41% exceeding the national prevalence by 10%. The prevalence of obesity in SA black women is among the highest recorded in Africa. An interesting but macabre observation was the decline in the prevalence of obesity during the period 1991-1997 possibly due to the HIV/AIDS epidemic. The implication is that a bimodal distribution in BMI may develop characterising two populations of women, one with and the other without HIV/AIDS.

Most women in both studies exhibited an unfavourable body fat distribution while half of the men in Mangaung had a predominantly central fat distribution. The latter was associated with excessive risk of glucose intolerance, hypertension and dyslipidaemia in both sexes and both populations. The WHO definitions of central adiposity were also shown to be applicable to both these populations. Although skinfold thickness is rarely measured in daily clinical practice it was useful not only to demonstrate the degree of adiposity and body fat distribution in both sexes but the sum of five skinfolds was an excellent indicator of sexual dimorphism of fatness. Percentage body fat calculated from skinfold thickness measurements, increased with age in both sexes and both populations but peaked a decade later in Qwaqwa women than in Mangaung women. The meaning of this phenomenon is

not clear but differences in physical activity and or nutrient intake may be responsible.

Overweight and obesity and thus generalized adiposity were associated with glucose intolerance, hypertension and dyslipidaemia in both populations especially in the Mangaung population. The risk of these abnormalities was especially pronounced in subjects of both sexes with features of central obesity. It is clear that "healthy obesity" is an outdated concept and should be abandoned. (One would not think of hypertension in terms of "healthy hypertension" in the absence of target-organ damage).

11 Dyslipidaemia

11.1 Descriptive data

The fasting serum total cholesterol, HDL-cholesterol, LDL-cholesterol and triglyceride concentrations for both study samples are shown in Table 11.1/1. The mean fasting TC concentration for males between 25-34 years in Qwaqwa was 4.7 mmol/L and changed very little with increasing age. The peak TC concentration was 4.9 mmol/L in the 35-54 year old group of males. The mean fasting TC concentration in Mangaung men in the age group 25-34 years was also 4.7 mmol/L but increased with age to a maximum level of 5.3 mmol/L in the 65-year and older group of males. The TC concentration in the latter group was clinically significantly higher than the mean 4.7 mmol/L present in elderly Qwaqwa men and exceeded the 5.2 mmol/L desirable cut-point (ATP III, 2001). Mean TC concentrations of males in both populations exceeded that for black males of corresponding age in the Cape Peninsula (the only exception was Qwaqwa males in the age group 55 to 64 years who had a mean TC concentration of 4.6 mmol/L compared to 4.7 mmol/L in Cape Peninsula black males in the same age group) (Steyn et al., 1991).

In women from both populations TC concentrations increased with increasing age from a mean of 4.4 mmol/L in young women in both populations to a mean of 5.3 mmol/L and 5.7 mmol/L in Qwaqwa and Mangaung elderly females respectively (Table 11.1/1). In the Qwaqwa sample the mean TC level of all women 55 years and older exceed the desirable level while in Mangaung, the mean TC of all women 45 years and older exceeded the desirable level (ATP, 2001). TC concentrations of women in both samples exceeded most of the corresponding levels for men in both populations. The same phenomenon was also present in the BRISK study (Steyn et al., 1991).

There is a paucity of studies describing lipid abnormalities in sub-Saharan black Africans. In one small study 75% of Nigerian subjects between 50 and 54 years had TC levels below 4.4 mmol/L and 2% had TC levels above 6.2 mmol/L (Kadiri et al., 1997).

Mean LDL-C concentrations in Qwaqwa males fluctuated between 2.4 and 2.9 mmol/L and did not rise with increasing age. Only in the age group 55-64 years was the mean LDL-C concentration below the optimal level of 2.6 mmol/L. In Mangaung male subjects mean LDL-C concentration increased across the age deciles from 2.8 mmol/L in the 25-34 year old group to 3.2 mmol/L in elderly subjects (Table 11.1/1). The mean LDL-C concentration in all Mangaung male subgroups were within the 2.6 to 3.3 mmol/L range defining the near or above optimal range (ATP III, 2001). LDL-C levels were not reported separately in the Cape Peninsula study making direct comparison with that sample impossible.

A clear increase in LDL-C concentration across age deciles was noted for both Qwaqwa and Mangaung women (Table 11.1/1). LDL-C concentration rose in the former from 2.8 mmol/L in the youngest to 3.3 mmol/L in the oldest group. The corresponding concentrations for Mangaung women were 2.7 mmol/L to 3.7 mmol/L. The latter level fell within the 3.4mmol/L - to 4.1 mmol/L borderline high category (ATP III, 2001).

Serum TG concentrations in both populations and both sexes showed an inconsistent tendency to rise with increasing age (Table 11.1/1). Serum TG levels did not clinically differ much between the same sexes in the two studies.

Overall, Mangaung subjects tended to have higher lipid levels in all categories compared to the same age group in the Qwaqwa sample. Again, this may point towards more advanced urbanisation of the former and possibly also a higher dietary fat intake. Overall, women also tended to have higher lipid levels than men. A possible explanation may be the greater prevalence of obesity in females (Kruger et al., 2001). Mean TC levels for both sexes and both samples were lower than that previously reported for white South Africans while HDL-C levels in black men were more favourable than that of white South African males (Rossouw et al., 1983).

The ratio of protective HDL-C to TC ranged between 0.26 and 0.31 in Qwaqwa males with the lowest level present on young men and the highest in the 55-64 year age group (Table 11.1/1). A clear increase over the age deciles was present

followed by a sharp decline in elderly men (Fig. 11.1/1). Although TC concentrations were similar in young men from both populations, the level of protective HDL-C to TC ratio in Mangaung subjects (0.30) was much more favourable than that of their peer group in Qwaqwa. Less fluctuation was also noted in these levels in Mangaung men.

The protective levels of HDL-C to TC in women in both populations declined over the age deciles with age and were very similar for the two populations Table 11.1/1 and Fig. 11.1/1).

The protective ratio of HDL-C to TC ratio for different South African studies are shown in Fig. 11.1/2 and Fig. 11.1/3. Favourable ratios of HDL-C:TC were lower in Qwaqwa and Mangaung males and females especially in the two younger age deciles compared to other black SA subjects. These ratios were, however, still considerably more favourable than that of white South African subjects reported in the CORIS study (Rossouw et al., 1983).

Summary

Mean TC concentrations increased slightly across the age deciles for Mangaung males and females and Qwaqwa females but changed very little in Qwaqwa men. Mean TC levels were overall higher in females than males in most but not all of the age categories. Mangaung subjects in most of the age categories had higher TC levels than Qwaqwa subjects possibly indicating that the former population consumed a diet higher in saturated animal fat than the latter. Mean TC for both males and females in both populations also exceeded that of blacks in the Cape Peninsula. In a significant proportion of subgroups in the Mangaung sample the mean TC level exceeded the desirable level of 5.2 mmol/L. Favourable ratios of HDL-C:TC were present in both sexes in both populations and in all age groups. Protective HDL-C to TC ratios were somewhat lower in FS blacks than Cape Peninsula blacks but were still much more favourable than ratios reported for white South Africans.

TABLE 11.1/1. Mean Fasting Serum Lipid Concentrations (mmol/L) and HDL-C to TC Ratio by Age, Gender, Population and Region (Standard Deviation in Parenthesis)

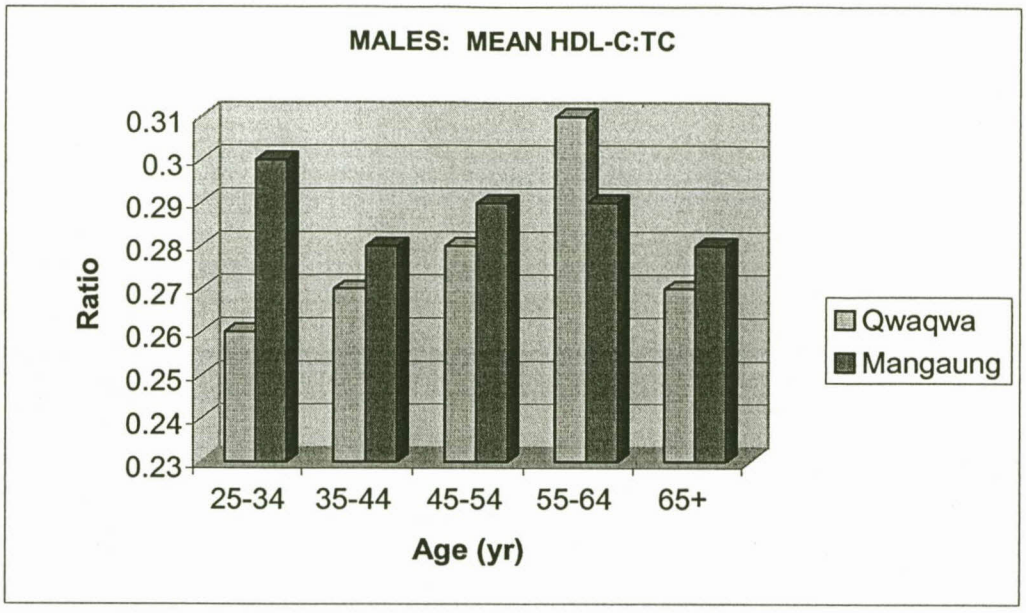
	TC[1]	HDL-C[2]	LDL-C[3]	HDL-C:TC	TG[4]
Qwaqwa					
Males					
25-34 yr	4.7 (1.2)	1.2 (0.4)	2.9 (1.1)	0.26 (0.09)	1.3 (0.9)
35-44 yr	4.9 (1.2)	1.3 (0.5)	2.9 (1.0)	0.27 (0.11)	1.7 (1.4)
45-54 yr	4.6 (1.0)	1.2 (0.4)	2.7 (1.0)	0.28 (0.11)	1.5 (1.0)
55-64 yr	4.6 (1.5)	1.3 (0.6)	2.4 (0.8)	0.31 (0.12)	1.5 (1.0)
65+ yr	4.7 (0.9)	1.2 (0.5)	2.9 (0.9)	0.27 (0.11)	1.4 (0.7)
Females					
25-34 yr	4.4 (1.0)	1.2 (0.3)	2.8 (1.0)	0.28 (0.08)	0.9 (0.4)
35-44 yr	4.6 (1.0)	1.2 (0.4)	2.8 (0.9)	0.27 (0.09)	1.1 (0.6)
45-54 yr	4.8 (1.1)	1.2 (0.4)	3.0 (1.1)	0.25 (0.1)	1.4 (0.7)
55-64 yr	5.4 (1.3)	1.2 (0.3)	3.5 (1.2)	0.23 (0.08)	1.5 (0.8)
65+ yr	5.2 (0.9)	1.2 (0.3)	3.3 (0.9)	0.25 (0.08)	1.4 (0.6)
Mangaung					
Males					
25-34 yr	4.7 (0.9)	1.4 (0.4)	2.8 (0.9)	0.30 (0.09)	1.3 (0.9)
35-44 yr	4.9 (1.1)	1.3 (0.5)	2.9 (1.1)	0.28 (0.12)	1.5 (1.3)
45-54 yr	5.1 (1.3)	1.4 (0.6)	2.9 (1.3)	0.29 (0.12)	1.8 (1.8)
55-64 yr	5.1 (1.1)	1.4 (0.5)	3.0 (0.9)	0.29 (0.11)	1.4 (0.7)
65+ yr	5.3 (1.7)	1.4 (0.5)	3.2 (1.6)	0.28 (0.13)	1.6 (1.1)
Females					
25-34 yr	4.4 (0.9)	1.3 (0.4)	2.7 (0.7)	0.30 (0.08)	0.8 (0.4)
35-44 yr	4.9 (1.0)	1.4 (0.5)	3.1 (0.9)	0.29 (0.1)	1.1 (0.6)
45-54 yr	5.5 (1.3)	1.3 (0.4)	3.4 (1.3)	0.26 (0.09)	1.5 (1.5)
55-64 yr	5.3 (0.9)	1.4 (0.5)	3.3 (0.9)	0.27 (0.1)	1.3 (0.6)
65+ yr	5.7 (1.2)	1.4 (0.4)	3.7 (1.1)	0.25 (0.09)	1.5 (0.9)

[1] TC = Total cholesterol (mmol/L)

[2] HDL= High density lipoprotein cholesterol

[3] LDL C = Low density lipoprotein cholesterol

[4]TG = Triglycerides



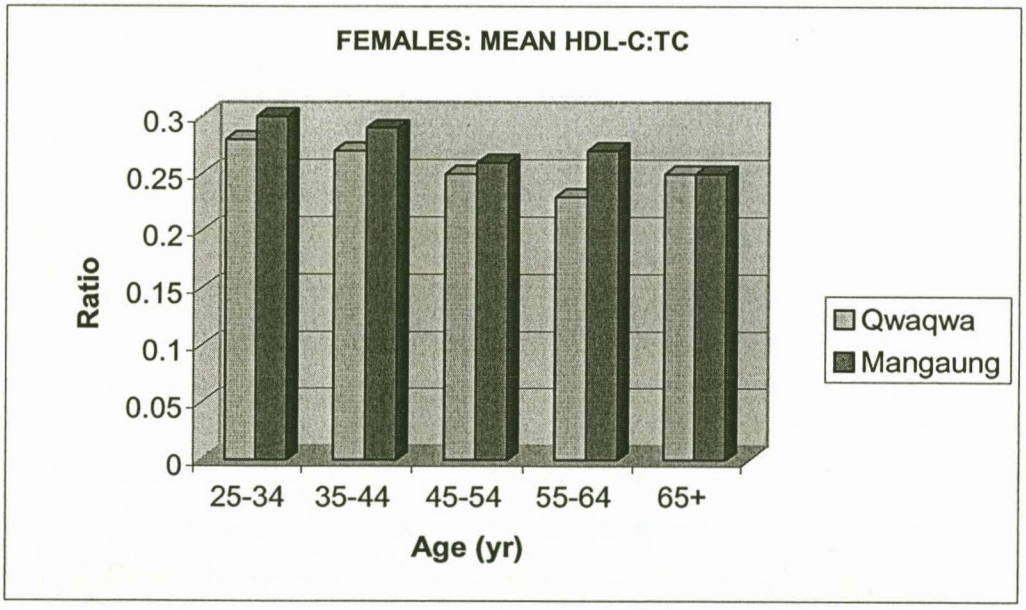
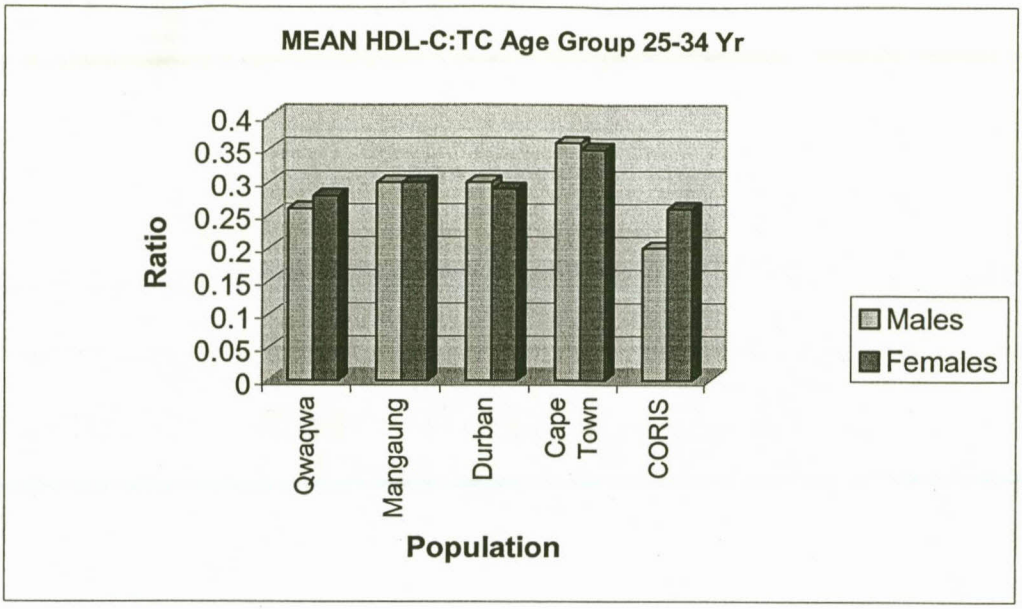


Fig. 11.1/1. Mean HDL-C:TC Ratio for two populations by age and gender.



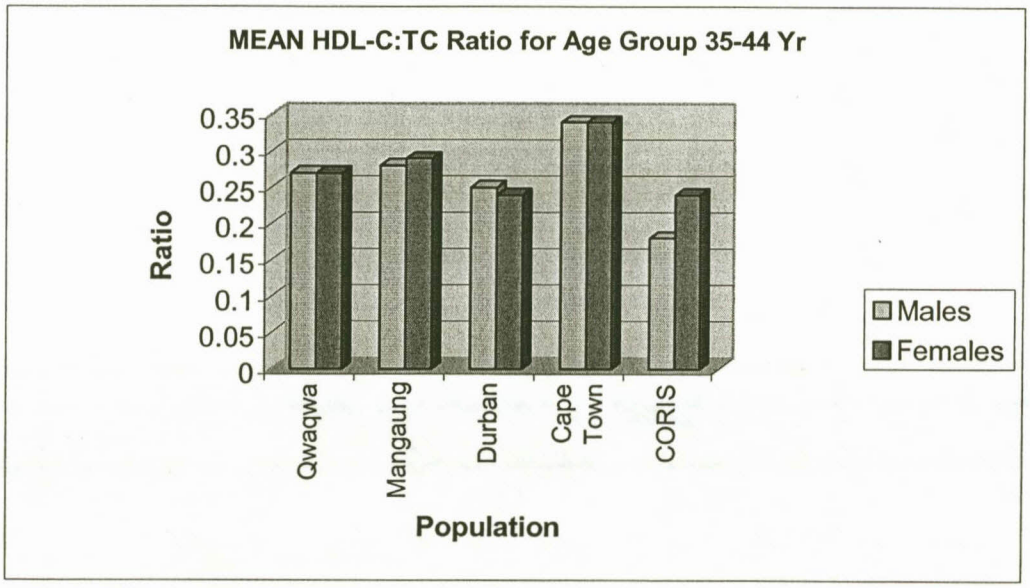
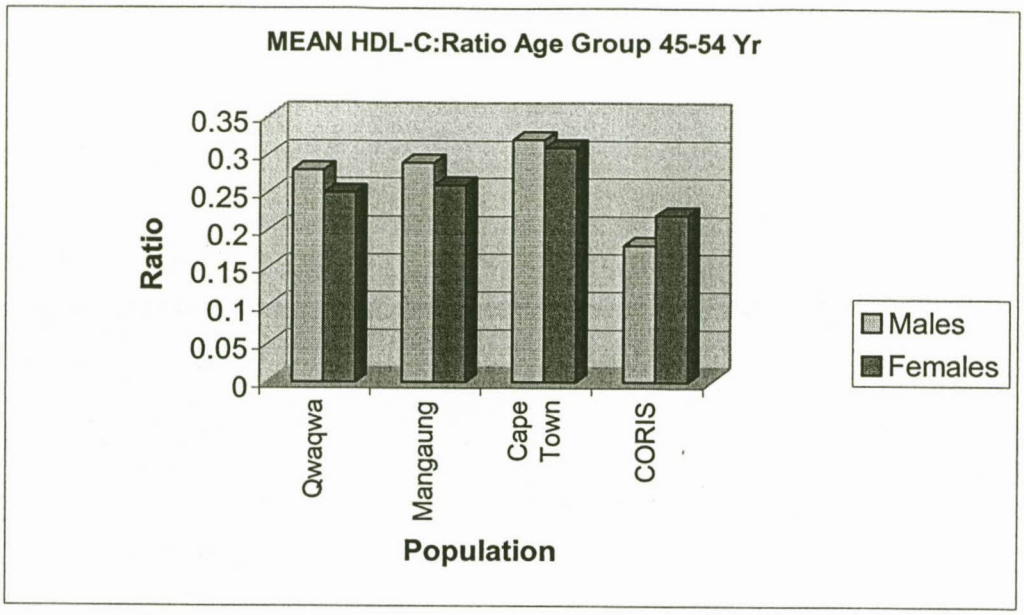


Fig. 11.1/2. Mean HDL-C:TC Ratio for black subjects from different ethnic groups and age groups compared to a Caucasian population (CORIS: Rossouw et al., 1983).



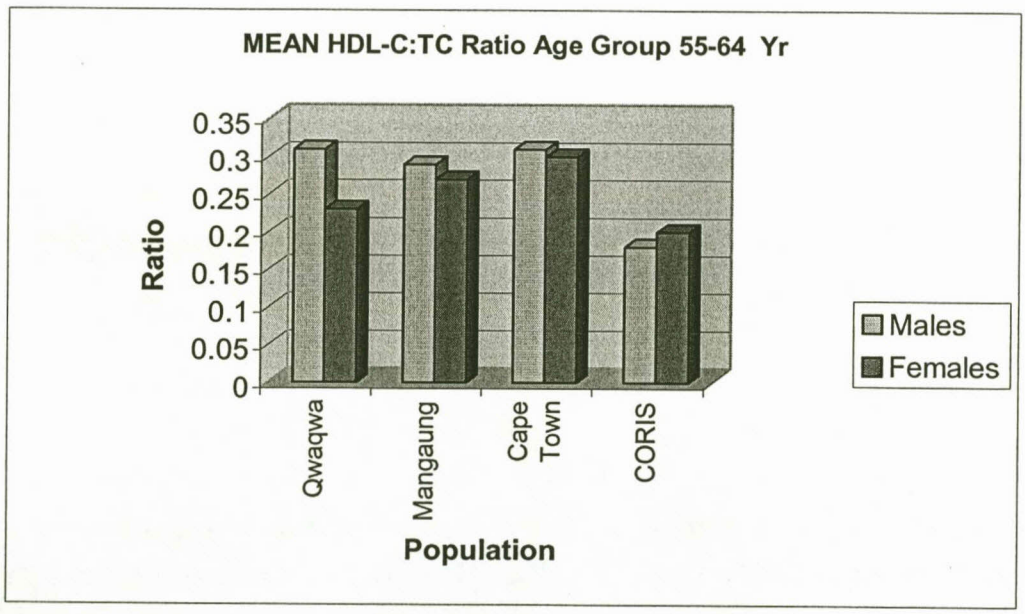


Fig. 11.1/3. Mean HDL-C:TC Ratio for black subjects from different ethnic groups and age groups compared to a Caucasian population (CORIS: Rossouw et al., 1983).

11.2 The prevalence of lipid abnormalities

The prevalence rates of lipid abnormalities in the Qwaqwa population are shown in Table 11.2/1. The age-standardised prevalence of borderline high (TC=5.2-6.21 mmol/L) and high cholesterol concentrations (≥ 6.21 mmol/L) combined in Qwaqwa males was 32.7%. Fewer males in the age groups 25-34 years (62.5%) and 35-44 years (64.2%) had desirable levels of TC compared to older males. Two to three times more males in the age group 25-54 years had high levels of TC compared to males in the age group 55-65 years and older. This difference may reflect an unhealthy lifestyle in the younger group compared to their elders. The percentage of women with high levels of TC increased from 4.3% in the 25-34 year old group to 24.5% 55-64 year old group and declined again in the 65 year and older group. The percentage of middle-aged and older women with high TC levels exceeded the percentage of males with high TC levels several-fold.

The age-adjusted prevalence of borderline high and high cholesterol concentrations in Mangaung males was 38.5% (Table 11.2/2). After the age and sex structure of the Mangaung sample was adjusted to the age and sex structure of the Qwaqwa population, the prevalence of borderline high and high TC levels combined in the Mangaung sample was 38.5% compared to 32.7% in the Qwaqwa sample (Table 11.2/2). This difference in prevalence rates between the two samples was not significant (95% CI −12.1;0.05).

The percentage of male and females subjects with desirable levels of TC in this sample declined as expected with aging across the age deciles. This decline was accompanied by an increase in the percentage of subjects of both sexes with high levels of TC with increasing age. The exception was women in the age group 55-64 years where 16.2% had high levels of TC. A considerable greater percentage of women in the age group 45 years and older had high levels of TC compared to men in the same age group.

In the BRISK study (1991) subjects were categorised for hypercholesterolaemia according to the action limits of the Heart Foundation of Southern Africa. These action limits are no longer in use (Berger et al., 2000 and ATP III, 2001). Direct

comparison between the FS and Cape Peninsula studies of the prevalence rates of hypercholesterolaemia was therefore not possible.

The percentage of subjects of both sexes in the Qwaqwa sample with favourable HDL-C:TC ratios fluctuated between the different age deciles and was overall lower compared to Mangaung subjects (Table 11.2/1 and Table 11.2/2). The age-standardised prevalence of males and females in the Qwaqwa sample with a favourable ratio of HDL-C:TC was 74.6% and 76.6% respectively (Table 11.2/1). The corresponding prevalence rates in the Mangaung sample were 78.3% for males and 80.1% (Table 11.2/2). The percentage of subjects in Mangaung with a favourable HDL-C:TC ratio declined from 90.9% in males in the youngest decile to 63.2% in subjects 65 years and older. For women, the corresponding prevalence rates declined from 90.5% to 65.1% (Table 11.2/2). After the age and sex structure of the Mangaung sample was adjusted to the age and sex structure of the Qwaqwa population, the prevalence of HDL-C < 20% of TC levels in the Mangaung sample was 79.1% compared to 75.7% in the Qwaqwa sample (Table 11.2/2). This difference in prevalence rates between the two samples was not significant (95% CI –13.0; 6.2).

The prevalence of hypertriglyceridaemia (TG ≥ 1.7 mmol/L) in both populations are shown in Table 11.2/1, Table 11.2/2. The age-standardised prevalence of hypertriglyceridaemia in Qwaqwa males (21.5%) was higher than in females (15.9%) (Table11.2/1). The total age- and sex- standardised prevalence of hypertriglyceridaemia for this sample was 18.4%. In Qwaqwa males the prevalence ranged between 16.1% and 29.6%. The latter occurred in men in the age group 45-54 years. In Qwaqwa females the prevalence ranged between 3.6% and 29.6% and increased with increasing age until 45-54 years. In both males and females the prevalence of hypertriglyceridaemia increased with age until the age decile 45-54 years was reached where-after the prevalence declined somewhat across the remaining age deciles.

In the Mangaung sample, the age-standardised prevalence of hypertriglyceridaemia in males (23.8%) was also higher than in females (14.8%) (Table 11.2/2). The total age- and sex-standardised prevalence for the Mangaung sample was 18.8%. The prevalence of hypertriglyceridaemia in

Mangaung subjects was 19.7% after the structure of this sample was age- and sex- standardised to the population structure of the Qwaqwa sample (Table 11.2.2). The difference in the prevalence of hypertriglyceridaemia between the two samples was not significant (95% CI –5.9;3.3).

The lower cut-point for fasting triglyceride levels (≥ 1.7 mmol/L) as proposed by the ATP III has important implications for the study populations: hypertriglyceridaemia is now regarded as more deleterious than previously accepted (ATP III, 2001), and since the abnormality is so frequent in these populations (18.4% to 19.7%), routine screening may have to considered with the ensuing cost-implications including the possibility of drug treatment.

SUMMARY

Hypercholesterolaemia at a high level of risk was already present in a significant percentage of males and females in all the age groups in both populations. This is one of the major CV risk factors that had a low prevalence until 2 decades ago (Seftel, 1978). A finding of some concern was the group of young males in Qwaqwa who had high TC levels. Fortunately these younger subjects still had higher levels of protective HDL-C to TC ratios than older subjects. No previous studies using the recent ATP III cut-points for dyslipidaemia in blacks are available to compare these results with. The abnormalities described warrant a follow-up study in this region to establish trends of lipid levels during the period of nutrition transition. Due to the potential serious long-term CV complications of these prevalent dyslipidaemias, the health authorities should seriously consider a screening and life-style intervention programme.

TABLE 11.2/1. Age-Standardised Prevalence (%) of Lipid Abnormalities by Age and Gender for Qwaqwa Population

	n	TC < 5.2 mmol/L	≥ 5.2 TC <6.21 mmol/L	TC≥5.2 mmol/L	TC ≥ 6.21	HDL-C > 20% TC	TG > 1.7 mmol/L
Males							
25-34 yr	56	62.5	23.2		14.3	78.6	16.1
35-44 yr	67	64.2	26.9		9.0	71.7	23.9
45-54 yr	27	77.8	11.1		11.1	70.4	29.6
55-64 yr	45	75.6	20.0		4.4	75.0	22.7
65+ yr	82	73.2	23.2		3.7	74.4	20.7
All ages	277					74.3	
Age-standardised prevalence				32.5		74.6	21.5
Females							
25-34 yr	141	77.3	18.4		4.3	86.4	3.6
35-44 yr	109	76.2	15.6		8.3	84.3	13.0
45-54 yr	98	65.3	21.4		13.3	64.3	29.6
55-64 yr	102	53.9	21.6		24.5	63.7	26.5
65+ yr	121	47.9	38.8		13.2	68.3	23.3
All ages	571					74.3	
Age-standardised prevalence				32.8		76.6	15.9
Total	848					74.3	
Age- and sex-standardised				32.7		75.7	18.4

TC = Total cholesterol

HDLC = High density lipoprotein cholesterol

TABLE 11.2/2. Age-Standardised Prevalence (%) of Lipid Abnormalities by Age and Gender for Mangaung Population

	n	TC < 5.2 mmol/L	≥ 5.2 TC < 6.21 mmol/L	TC≥5.2 mmol/L	TC ≥ 6.21 mmol/L	HDL-C > 20% TC	TG > 1.7 mmol/L
Males							
25-34 yr	67	73.1	22.4		4.5	90.9	19.4
35-44 yr	65	58.5	27.7		13.9	70.8	24.6
45-54 yr	64	62.5	18.8		18.8	74.6	29.7
55-64 yr	54	55.6	29.6		14.8	68.5	22.2
65+ yr	38	52.6	29.0		18.4	63.2	29.0
All ages Age-standardised prevalence				36.3		78.3	23.8
Females							
25-34 yr	105	84.8	12.4		2.9	90.5	4.8
35-44 yr	126	57.9	33.3		8.7	81.0	13.5
45-54 yr	104	45.2	31.7		23.1	68.3	25.0
55-64 yr	68	44.1	39.7		16.2	75.0	20.6
65+ yr	64	35.9	32.8		31.3	65.1	31.3
All ages Age-standardised prevalence				38.3		80.1	14.8
Total Age- and sex-standardised				37.4		79.3	18.8
Age- and Sex-standardised to the Qwaqwa population structure						79.1a	19.7b

TC = Total cholesterol, TG = Triglycerides, HDLC = High density lipoprotein cholesterol

Prevalence of TC > 5.2% = 38.5% (Age- and sex-standardised to the structure of the Qwaqwa population). The Qwaqwa-Mangaung difference was not significant (95% CI -12.1;0.5)

a Qwaqwa-Mangaung difference not significant: 95% CI -13.0;6.2

b Qwaqwa-Mangaung difference not significant: 95% CI -5.9;3.3.

11.3 Association between obesity and dyslipidaemia

11.3.1 Obesity and serum cholesterol

The relationship between overweight (pre-obesity and obesity) and elevated cholesterol concentrations (≥ 5.2 mmol/L) is shown in Table 11.3.1/1 and Table 11.3.1/2. The overall risk of overweight subjects in Qwaqwa having TC levels in the borderline high category compared to non-overweight subjects was significantly increased at a RR of 1.6 (95% CI:1.3;1.9). Relative risks were also separately calculated for age groups (below 45 years and 45 years and above) according to sex. The highest RR of 1.9 (95% CI 1.2; 3.0) was present in young males in Qwaqwa. The RR in all the other subgroups just failed to reach statistically significant levels. It was also the same group of young males that had an exceptionally high prevalence of borderline high and high TC levels.

The overall or summary RR of overweight compared to non-overweight subjects in Mangaung to have elevated TC levels could not be calculated due to differences between the strata. The RR's in both male subgroups, however, were significantly increased (Table 11.3.1/2). It is interesting that the RR's of overweight females in both age categories to have borderline high TC levels were not significantly increased. It is understandable that a single observation like this may lead to the conclusion that a "healthy" subset of obesity exists in black females. This finding is in line with the THUSA study where no association was found between BMI and total serum cholesterol (Kruger et al., 2001). In the latter study total fat intake was also not a significant predictor of total serum cholesterol concentration.

In the NHANES II study, overweight (men BMI ≥ 27.8 kg/m^2, women BMI ≥ 27.3 kg/m^2) increased the risk of elevated serum cholesterol in both black males and females but more so in the former (van Italie, 1985). The risk of elevated cholesterol levels was highest in black men who fell under the poverty line. It is striking that overweight was generally associated with an increased risk of

elevated cholesterol levels in Qwaqwa respondents but not in Mangaung respondents with the exception of the subgroup of young males. It can be hypothesised that this difference is attributable to the obvious greater poverty that existed in the Qwaqwa area.

Although the prevalence of CHD is still low in this rural and urban population it is reasonable to expect that the prevalence of CHD will increase in the near future since no population with increased levels of TC is indefinitely immune to its effects (Verschuren et al., 1995). In the Seven-Countries study an increase in TC of 0.50 mmol/L was associated with an increase of 17% in long-term CHD mortality (Verschuren et al., 1995).

TABLE 11.3.1/1. Relationship Between Overweight[1] and Elevated Total Serum Cholesterol Concentrations After Adjusting for Age and Sex in Two Populations

		TC ≥ 5.2	
	n	n	%
Qwaqwa			
Males (age in yr)			
< 45			
BMI 25+	41	22	53.7
BMI < 25	81	23	28.4
45+			
BMI 25+	44	16	36.4
BMI < 25	108	23	21.3
Females (age in yr)			
< 45			
BMI 25+	161	44	27.3
BMI < 25	89	14	15.7
45+			
BMI 25+	214	105	49.1
BMI < 25	107	39	36.5
Mangaung			
Males (age in yr)			
< 45			
BMI 25+	37	18	48.7
BMI < 25	94	26	27.7
45+			
BMI 25+	54	31	57.4
BMI < 25	102	36	35.3
Females (age in yr)			
< 45			
BMI 25+	156	44	28.2
BMI < 25	73	24	32.9
45+			
BMI 25+	172	95	55.2
BMI < 25	64	41	64.1

[1] Overweight = BMI ≥ 25 kg/m^2

TABLE 11.3.1/2. The Relative Risk (RR) of Elevated Total Cholesterol Concentrations[1] in Overweight Compared to Non-Overweight Subjects After Adjusting for Age and Sex (95% Confidence Interval in Parenthesis)

	RR Borderline High TC[1]
Qwaqwa (age in yr)	
Males < 45	1.9 (1.2-3.0)
Males 45+	1.7 (1.0-2.9)
Females < 45	1.7 (1.0-3.0)
Females 45+	1.3 (1.0-1.8)
Summary RR	1.6 (1.3-1.9)
Mangaung (age in yr)	
Males < 45	1.8 (1.1-2.8)
Males 45+	1.6 (1.1-2.3)
Females < 45	0.86 (0.57-1.3)
Females 45+	0.86 (0.69-1.1)
Summary RR	a

a Cannot be calculated

[1] TC ≥ 5.2 mmol/L

11.3.2 Overweight and non-protective HDL-C levels

The relationship between overweight and the risk of non-protective levels of HDL-C (< 20% of TC) is shown in Table 11.3.2/1 and Table 11.3.2/2. In both populations and in all subgroups with the exception of young females in Mangaung the RR's of non-protective HDL-C:TC ratios were several fold increased in overweight compared to non-overweight subjects. Due to the large CI in some of the subgroups a summary RR could not be calculated. In the THUSA study a negative correlation was also found between BMI and HDL-C levels.

An escalating risk of having non-protective HDL-C levels emerged where older females tended to have the lowest risk and young males the highest risk (Table 11.3/4). Mangaung women < 45 years were the only subgroup where overweight was neither associated with an increased risk of increased TC levels nor of increased risk of having non-protective HDL-C levels. This advantage was no longer present in women 45 years and older. The concept of "healthy obesity" in females is no longer justified – neither in this rural nor in the more urbanised Mangaung population.

TABLE 11.3.2/1. Relationship Between Overweight and Non-Protective Levels of HDL-Cholesterol

		HDL-C < 20% TC	
	n	n	%
Qwaqwa			
Males (age in yr)			
< 45			
BMI 25+	41	25	61
BMI < 25	81	6	7.4
45+			
BMI 25+	44	26	59.1
BMI < 25	107	13	12.2
Females (age in yr)			
< 45			
BMI 25+	159	31	19.5
BMI < 25	89	5	5.6
45+			
BMI 25+	213	91	42.7
BMI < 25	107	19	17.8
Mangaung			
Males (age in yr)			
< 45			
BMI 25+	37	16	43.2
BMI < 25	93	8	8.6
45+			
BMI 25+	54	30	55.6
BMI < 25	101	17	16.8
Females (age in yr)			
< 45			
BMI 25+	156	27	17.3
BMI < 25	73	7	9.6
45+			
BMI 25+	171	61	35.7
BMI < 25	64	11	17.2

TABLE 11.3.2/2. The Relative Risk (RR) of Non-Protective HDL-C Concentrations[1] in Overweight Compared to Non-Overweight Subjects After Adjusting for Age and Sex

(95% Confidence Interval in Parenthesis)

	RR HDL-C < 20% TC
Qwaqwa (age in yr)	
Males < 45	8.2 (3.7-18.5)
Males 45+	4.9 (2.8-8.6)
Females < 45	3.5 (1.4-8.6)
Females 45+	2.4 (1.6-3.7)
Summary RR	a
Mangaung (age in yr)	
Males < 45	5.0 (2.4-10.7)
Males 45+	3.3 (2.0-5.4)
Females < 45	1.8 (0.83-4.0)
Females 45+	2.1 (1.2 -3.7)
Summary RR	a

a Cannot be calculated

[1] HDL-C < 20% of TC

11.3.3 Overweight and serum triglycerides

The relationship between overweight and serum TG levels is shown in Table 11.3.3/1 and Table 11.3.3/2. In the Qwaqwa sample the RR of hypertriglyceridaemia in overweight compared to non-overweight subjects was significantly increased in all the age and sex subgroups with the exception of females < 44 years. The summary RR of hypertriglyceridaemia in overweight subjects compared to subjects of normal weight was significantly increased at 3.02 (95% CI 2.18-4.20). In the Mangaung sample, the RR of hypertriglyceridaemia in young overweight women was also not significantly increased. The RR was, however, significantly increased in all remaining subgroups with a summary RR of 2.03 (95% CI 1.48-2.79) (Table 11.3.3/2).

Apart from obesity other contributing factors to hypertriglyceridaemia include excessive consumption of simple sugars and saturated fats, inactivity, alcohol consumption and insulin resistance (Ginsberg and Goldberg, 2001). In the THUSA study BMI also correlated positively with serum TG levels (Kruger et al., 2001) in women, a finding which is in keeping with the FS populations. Although the association between hypertriglyceridaemia CHD is weaker than for LDL-C, hypertriglyceridaemia is associated with low HDL-C levels and small dense LDL particles (Ginsberg and Goldberg, 2001).

TABLE 11.3.3/1. Relationship Between Overweight[1] and High Serum Triglyceride[2] Concentrations

		TG ≥ 1.7 mmol/L	
	n	n	%
Qwaqwa			
Males (age in yr)			
< 45			
BMI 25+	41	18	43.9
BMI < 25	81	7	8.6
45+			
BMI 25+	44	20	45.5
BMI < 25	107	15	14
Females (age in yr)			
< 45			
BMI 25+	159	16	10.1
BMI < 25	89	3	3.4
45+			
BMI 25+	213	69	32.4
BMI < 25	107	15	14
Mangaung			
Males (age in yr)			
< 45			
BMI 25+	37	14	37.8
BMI < 25	94	15	16
45+			
BMI 25+	54	24	44.4
BMI < 25	102	18	17.7
Females (age in yr)			
< 45			
BMI 25+	156	15	9.6
BMI < 25	73	7	9.6
45+			
BMI 25+	172	51	29.7
BMI < 25	64	9	14.1

[1] BMI ≥ 25 kg/m^2

[2] TG ≥ 1.7 mmol/L

TABLE 11.3.3/2. The Relative Risk (RR) of High Serum Triglyceride Concentrations[1] in Overweight[2] Compared to Non-Overweight Subjects After Adjusting for Age and Sex (95% Confidence Interval in Parenthesis)

Qwaqwa (age in yr)	
Males < 45	5.08 (2.31-11.17)
Males 45+	3.24 (1.83-5.73)
Females < 45	2.99 (0.89-9.97)
Females 45+	2.31 (1.39-3.84)
Summary RR	3.02 (2.18-4.20)
Mangaung (age in yr)	
Males < 45	2.37 (1.27-4.41)
Males 45+	2.52 (1.51-4.21)
Females < 45	1.00 (0.43-2.35)
Females 45+	2.11 (1.10-4.03)
Summary RR	2.03 (1.48-2.79)

[1] Serum TG ≥ 1.7 mmol/L

[2] BMI ≥ 25 kg/m^2

11.4 Association between central obesity and dyslipidaemia

11.4.1 Central obesity and total cholesterol

The association between elevated serum TC levels (≥ 5.2 mmol/L) central obesity is shown in Table 11.4.1/1. The summary RR of elevated serum TC levels in subjects with central obesity compared to subjects with peripheral fat distribution in the Qwaqwa sample was 1.2 (95% CI 0.98-1.4) (Table 11.4.1/2). Central obesity was also not significantly associated with hypercholesterolaemia in any of the subgroups. In the Mangaung sample, however, the summary RR of hypercholesterolaemia in subjects with central obesity compared to subjects with peripheral fat distribution was significantly increased at 1.43 (95% CI 1.20-1.70) while in the subgroups the only significant association was seen in the younger group of women where it was particularly strong with a RR of 2.45 (95% CI 1.67-3.60).

TABLE 11.4.1/1. Relationship Between WHR and Elevated Total Serum Cholesterol Levels in Two Populations After Adjusting for Age and Sex

		TC ≥ 5.2 mmol/L	
	n	n	%
Qwaqwa			
Males (age in yr)			
< 45			
WHR Below median	66	21	31.8
WHR Above median	56	24	42.9
45+			
WHR Below median	72	20	27.8
WHR Above median	79	19	24
Females (age in yr)			
< 45			
WHR Below median	171	35	20.5
WHR Above median	78	23	29.5
45+			
WHR Below median	115	47	40.9
WHR Above median	204	96	47.1
Mangaung			
Males (age in yr)			
< 45			
WHR Below median	95	29	30.5
WHR Above median	36	16	44.4
45+			
WHR Below median	47	16	34
WHR Above median	109	50	45.9
Females (age in yr)			
< 45			
WHR Below median	157	32	20.4
WHR Above median	74	37	50
45+			
WHR Below median	77	42	54.6
WHR Above median	159	94	59.1

Qwaqwa: Sex-specific median WHR: females = 0.85, males = 0.97

Mangaung: Sex-specific median WHR: females = 0.85, males 0.98

TABLE 11.4.1/2. The Relative Risk (RR) of Elevated Total Serum Cholesterol[1] Concentrations in Subjects With Central Obesity Compared to Subjects Without Central Obesity After Adjusting for Age and Sex (95% Confidence Interval in Parenthesis)

	RR TC ≥ 5.2 mmol/L
Qwaqwa (age in yr)	
Males < 45	1.3 (0.85-2.1)
Males 45+	0.87 (0.50-1.5)
Females < 45	1.4 (0.92-2.3)
Females 45+	1.2 (0.88-1.5)
Summary RR	1.2 (0.98-1.4)
Mangaung (age in yr)	
Males < 45	1.46 (0.91-2.34)
Males 45+	1.35 (0.86-2.11)
Females < 45	2.45 (1.67-3.60)
Females 45+	1.08 (0.85-1.38)
Summary RR	1.43 (1.20-1.70)

[1] TC ≥ 5.2 mmol/L

11.4.2 Central obesity and non-protective HDL-C levels

The association between non-protective levels of HDL-C and central obesity is shown in Table 11.4.2/1. The summary RR of subjects with central obesity to have non-protective levels of HDLC was 2.0 (95% CI 1.6-2.6) in the Qwaqwa sample and 2.22 (95% CI 1.62-3.05) in the Mangaung sample (Table 11.4.2/2). The increased RR was present in all the subgroups with the exception of females < 45 years in Qwaqwa and males < 45 years in Mangaung. Low HDLC levels are considered as one component of the "lipid triad" which is associated with the metabolic syndrome and increased risk for CVD (Grundy, 1998).

TABLE 11.4.2/1. The Prevalence of Non-Protective Levels of HDL-C[1] in Subjects With Central Obesity Compared to Subjects Without Central Obesity After Adjusting for And Sex for Two Populations

		HDL-C < 20% TC	
	n	n	%
Qwaqwa			
Males (age in yr)			
< 45			
WHR Below median	66	11	16.7
WHR Above median	56	20	35.7
45+			
WHR Below median	71	9	12.7
WHR Above median	79	29	36.7
Females (age in yr)			
< 45			
WHR Below median	169	21	12.4
WHR Above median	78	15	19.2
45+			
WHR Below median	114	25	21.9
WHR Above median	204	84	41.2
Mangaung			
Males (age in yr)			
< 45			
WHR Below median	94	15	16
WHR Above median	36	9	25
45+			
WHR Below median			
WHR Above median	47	6	12.8
Females (age in yr)			
< 45			
WHR Below median	157	14	8.9
WHR Above median	77	15	19.5
45+			
WHR Below median	158	56	35.4
WHR Above median			

[1] HDLC < 20% of TC [2] Qwaqwa: Sex-specific median WHR: females = 0.85, males = 0.97, Mangaung: Sex-specific median WHR: females = 0.85, males 0.98

TABLE 11.4.2/2. The Relative Risk (RR) of Non-Protective Levels of HDL-C[1] in Subjects With Central Obesity Compared to Subjects Without Central Obesity After Adjusting for Age and Sex (95% Confidence Interval in Parenthesis)

	RR Non-Protective HDL-C
Qwaqwa (age in yr)	
Males < 45	2.1 (1.1-4.1)
Males 45+	2.9 (1.5-5.7)
Females < 45	1.5 (0.84-2.8)
Females 45+	1.9 (1.3-2.8)
Summary RR	2.0 (1.6-2.6)
Mangaung (age in yr)	
Males < 45	1.57 (0.75-3.26)
Males 45+	2.97 (1.36-6.52)
Females < 45	3.03 (1.62-5.66)
Females 45+	1.82 (1.10-3.00)
Summary RR	2.22 (1.62-3.05)

[1] HDL-C < 20% TC

11.4.3 Central obesity and elevated serum triglycerides

The association between central obesity and hypertriglyceridaemia is shown in Table 11.4.3/1. The RR of hypertriglyceridaemia (Table 11.4.3/2) was significantly elevated in subjects with central obesity compared to subjects with peripheral fat distribution in both populations and in both sexes as well in all the subgroups with the exception of the older group of men in Mangaung. The summary RR for hypertriglyceridaemia in subjects with central obesity compared to subjects with peripheral obesity in Qwaqwa was significantly increased at 2.34 (95% CI 1.70-3.22). The summary RR could not be calculated for the Mangaung sample due to differences between the strata.

Hypertriglyceridaemia is associated with increased levels of small dense LDL cholesterol and reduced levels of HDL cholesterol. The latter two variables form the other components of the "lipid triad" (Grundy, 1998). It is evident that this component of the metabolic syndrome is also highly prevalent in black subjects from both populations.

TABLE 11.4.3/1. The Prevalence of High Serum Triglyceride[1] Concentrations in Subjects With Central Obesity[2] Compared to Subjects Without Central Obesity After Adjusting for Age and Sex for Two Populations (95% CI Between Brackets)

		TG ≥ 1.7 mmol/L	
	n	n	%
Qwaqwa			
Males (age in yr)			
< 45			
WHR Above median	56	18	32.1
WHR Below median	66	7	10.6
45+			
WHR Above median	79	24	30.4
WHR Below median	71	9	12.7
Females (age in yr)			
< 45			
WHR Above median	78	12	15.4
WHR Below median	169	7	4.1
45+			
WHR Above median	204	64	31.4
WHR Below median	114	19	16.7
Mangaung			
Males (age in yr)			
< 45			
WHR Above median	36	15	41.7
WHR Below median	95	14	14.7
45+			
WHR Above median	109	30	27.5
WHR Below median	47	12	25.5
Females (age in yr)			
< 45			
WHR Above median	74	17	23
WHR Below median	157	5	3.2
45+			
WHR Above median	159	47	29.6
WHR Below median	77	13	16.9

[1] TG ≥ 1.7; [2] Qwaqwa: Sex-specific median WHR: females = 0.85, males = 0.97, Mangaung: Sex-specific median WHR: females = 0.85, males 0.98

TABLE 11.4.3/2. The Relative Risk (RR) of High S-Triglyceride Concentrations[1] in Subjects With Central Obesity Compared to Subjects Without Central Obesity After Adjusting for Age and Sex (95% Confidence Interval in Parenthesis)

	RR
Qwaqwa (age in yr)	
Males < 45	3.03 (1.37-6.73)
Males 45+	2.40 (1.20-4.81)
Females < 45	3.71 (1.52-9.07)
Females 45+	1.88 (1.19-2.98)
Summary RR	2.34 (1.70-3.22)
Mangaung (age in yr)	
Males < 45	2.83 (1.52-5.25)
Males 45+	1.08 (0.61-1.92)
Females < 45	7.21 (2.77-18.80)
Females 45+	1.75 (1.10-3.04)
Summary RR	a

[1] TG ≥ 1.7 mmol/L

[a] Cannot be calculated

11.5 Other factors associated with high triglyceride concentrations

11.5.1 Fasting hyperinsulinaemia (Table 11.5.1/1 and Table 11.5.1/2)

The summary RR of fasting hypertriglyceridaemia in subjects with fasting hyperinsulinaemia compared to subjects with normal fasting insulin concentrations in the Qwaqwa sample was 2.37 (95% CI 1.79-3.12). The RR of hypertriglyceridaemia in fasting hyperinsulinaemic subjects was significantly increased in all the age subgroups and in both sexes in the Qwaqwa sample. Although the summary RR of hypertriglyceridaemia in fasting hyperinsulinaemic subjects compared to normo-insulinaemic subjects in Mangaung was significantly increased at 1.67 (95% CI 1.27-2.19), the association in the subgroups was significant for male subjects only. Insulin resistance may be an important contributing factor to these findings (Reaven 1988).

11.5.2 Sum of 60 min and 120 min post-glucose load hyperinsulinaemia (Table 11.5.2/1 and Table 11.5.2/2)

The summary RR of fasting hypertriglyceridaemia in subjects with post-glucose load hyperinsulinaemia in the Qwaqwa sample compared to those subjects with normal post-glucose load serum insulin levels could not be calculated. In the age and sex subgroups the RR of hypertriglyceridaemia was significantly increased in all the subgroups with the exception of young females. The summary RR of fasting hypertriglyceridaemia in subjects with post-glucose load hyperinsulinaemia in the Mangaung sample was, however, significantly increased.

11.5.3 Alcohol use (Table 11.5.3/1 and Table 11.5.3/2)

In both samples the RR of fasting hypertriglyceridaemia was significantly increased (Qwaqwa: RR =1.41 (95% CI 1.06-1.87) and Mangaung: RR=1.42 (95% CI 1.06-1.91)) in subjects who used any alcohol compared to subjects who denied the use of any alcohol.

11.5.4 Elevated serum GGT concentration (Table 11.5.4/1 and Table 11.5.4/2)

Although mildly elevated γ-glutamyl transferase (GGT) levels may be used as a proxy for excessive alcohol use (Schuckit, 2001) non-alcoholic steato-hepatitis (NASH) commonly associated with obesity (Podolsky, 2001) may also cause raised GGT levels. The summary RR of fasting hypertriglyceridaemia in subjects with elevated s-GGT levels could not be calculated for the Qwaqwa sample. The RR were, however, calculated for the subgroups and was significantly increased in all the categories except in older males. In the Mangaung sample the summary RR for fasting hyperinsulinaemia in subjects with elevated GGT levels was significantly increased at 1.94 (95% CI 1.45-2.60). In the Mangaung sample the RR was significantly increased in both male subgroups.

TABLE 11.5.1/1. The Prevalence of Fasting Hypertriglyceridaemia[1] in Subjects With Fasting Hyperinsulinaemia[2] Compared to subjects With Normal Fasting Insulin Levels After Adjusting for Age And Sex for Two Populations (95% CI Between Brackets)

		TG ≥ 1.7 mmol/L	
	n	n	%
Qwaqwa			
Males (age in yr)			
< 45			
High fasting s-insulin	37	13	35.1
Normal fasting s-insulin	86	12	14.0
45+			
High fasting s-insulin	39	16	41.0
Normal fasting s-insulin	114	19	16.7
Females (age in yr)			
< 45			
High fasting s-insulin	124	16	12.9
Normal fasting s-insulin	123	3	2.4
45+			
High fasting s-insulin	136	50	36.8
Normal fasting s-insulin	184	34	18.5
Mangaung			
Males (age in yr)			
< 45			
High fasting s-insulin	39	14	35.9
Normal fasting s-insulin	93	15	16.1
45+			
High fasting s-insulin	40	19	47.5
Normal fasting s-insulin	116	23	19.8
Females (age in yr)			
< 45			
High fasting s-insulin	103	13	12.6
Normal fasting s-insulin	128	9	7.0
45+			
High fasting s-insulin	104	28	26.9
Normal fasting s-insulin	131	31	23.7

[1] Fasting TG ≥ 1.7 mmol/L

[2] Fasting hyperinsulinaemia: S-Insulin ≥ 75th Percentile of fasting s-insulin concentrations in non-obese, NGT and normotensive subjects.

TABLE 11.5.1/2. The RR of Fasting Hypertriglyceridaemia[1] in Subjects With Fasting Hyperinsulinaemia[2] Compared to Subjects With Normal Fasting Insulin Levels After Adjusting for Age and Sex.

	RR TG ≥ 1.7 mmol/L
Qwaqwa (age in yr)	
Males < 45	2.52 (1.27-4.99)
Males 45+	2.46 (1.41-4.30)
Females < 45	5.29 (1.58-17.70)
Females 45+	1.99 (1.37-2.90)
Summary RR	2.37 (1.79-3.12)
Mangaung (age in yr)	
Males < 45	2.23 (1.19-4.16)
Males 45+	2.40 (1.47-3.91)
Females < 45	1.80 (0.80-4.03)
Females 45+	1.14 (0.73-1.77)
Summary RR	1.67 (1.27-2.19)

[1] Fasting TG ≥ 1.7 mmol/.

[2] Fasting Insulin ≥ 75th percentile of fasting s-insulin concentrations in non-obese, NGT and normotensive subjects.

TABLE 11.5.2/1. The Prevalence of Fasting Hypertriglyceridaemia[1] in Subjects With Hyperinsulinaemia[2] (Sum 60 and 120 min) Compared to subjects With Normal Insulin Levels (sum 60 and 120 min) After Adjusting for Age And Sex For Two Populations (95% CI Between Brackets)

		TG ≥ 1.7 mmol/L	
	n	n	%
Qwaqwa			
Males (age in yr)			
< 45			
High sum 60 and 120 min insulin	34	15	44.1
Normal sum 60 and 120 min insulin	89	10	11.2
45+			
High sum 60 and 120 min insulin	42	16	38.1
Normal sum 60 and 120 min insulin	101	13	12.9
Females (age in yr)			
< 45			
High sum 60 and 120 min insulin	110	9	8.2
Normal sum 60 and 120 min insulin	133	10	7.5
45+			
High sum 60 and 120 min insulin	129	40	31.0
Normal sum 60 and 120 min insulin	174	36	20.7
Mangaung			
Males (age in yr)			
< 45			
High sum 60 and 120 min insulin	40	13	32.5
Normal sum 60 and 120 min insulin	90	16	17.8
45+			
High sum 60 and 120 min insulin	60	23	38.3
Normal sum 60 and 120 min insulin	93	18	19.4
Females (age in yr)			
< 45			
High sum 60 and 120 min insulin	96	11	11.5
Normal sum 60 and 120 min insulin	128	10	7.8
45+			
High sum 60 and 120 min insulin	119	33	27.7
Normal sum 60 and 120 min insulin	102	83	18.6

[1] Serum TG ≥ 1.7 mmol/L; [2] Sum of 60+120 min post-glucose load S-insulin ≥ 75th percentile of that in non-obese, NGT and normotensive subjects.

TABLE 11.5.2/2. The Relative Risk (RR) of Fasting Hypertriglyceridaemia[1] in Subjects With Hyperinsulinaemia[2] (Sum 60 and 120 min) Compared to Subjects With Normal Insulin Levels (Sum 60 and 120 min) After Adjusting for Age and Sex (95% Confidence Interval in Parenthesis)

	RR TG ≥ 1.7 mmol/L
Qwaqwa (age in yr)	
Males < 45	3.93 (1.96-7.87)
Males 45+	2.96 (1.56-5.60)
Females < 45	1.09 (0.46-2.58)
Females 45+	1.50 (1.02-2.21)
Summary RR	a
Mangaung (age in yr)	
Males < 45	1.83 (0.97-3.43)
Males 45+	1.98 (1.17-3.35)
Females < 45	1.47 (0.65-3.31)
Females 45+	1.49 (0.90-2.45)
Summary RR	1.68 (1.25-2.25)

[1] TG > 1.7

[2] Sum of 60+120 min post glucose load s-insulin : ≥ 75th Percentile of that in non-obese, NGT and Normotensive subjects.

[a] Cannot be calculated: Strata estimates significantly different

TABLE 11.5.3/1. The Prevalence of Fasting Hypertriglyceridaemia[1] in Alcohol-Users[2] Compared to Non-Alcohol-Users[3] (95% CI Between Brackets)

		TG ≥ 1.7 mmol/L	
	n	n	%
Qwaqwa			
Males (age in yr)			
< 45			
History of Alcohol	84	20	23.8
No History of Alcohol	39	5	12.8
45+			
History of Alcohol	99	22	22.2
No History of Alcohol	54	13	24.1
Females (age in yr)			
< 45			
History of Alcohol	52	7	13.5
No History of Alcohol	196	12	6.1
45+			
History of Alcohol	92	31	33.7
No History of Alcohol	228	53	23.3
Mangaung			
Males (age in yr)			
< 45			
History of Alcohol	101	21	20.8
No History of Alcohol	31	8	25.8
45+			
History of Alcohol	108	32	29.6
No History of Alcohol	46	10	21.7
Females (age in yr)			
< 45			
History of Alcohol	79	12	15.2
No History of Alcohol	151	10	6.6
45+			
History of Alcohol	68	23	33.8
No History of Alcohol	168	37	22

[1] Fasting TG ≥ 1.7 mmol/L

[2] History of any alcohol use

[3] Denied the use of any alcohol

TABLE 11.5.3/2. The Relative Risk (RR) of Fasting Hypertriglyceridaemia[1] in Alcohol-Users[2] Compared to Non-Alcohol-Users[3] After Adjusting for Age and Sex (95% Confidence Interval in Parenthesis)

	RR TG ≥ 1.7 mmol/L
Qwaqwa (age in yr)	
Males < 45	1.86 (0.75-4.58)
Males 45+	0.92 (0.51-1.68)
Females < 45	2.20 (0.91-5.30)
Females 45+	1.45 (1.00-2.10)
Summary RR	1.41 (1.06-1.87)
Mangaung (age in yr)	
Males < 45	0.81 (0.40-1.64)
Males 45+	1.36 (0.73-2.54)
Females < 45	2.29 (1.04-5.07)
Females 45+	1.54 (0.99-2.38)
Summary RR	1.42 (1.06-1.91)

1 TG ≥ 1.7 mmol/L

TABLE 11.5.4/1. The Prevalence of Fasting Hypertriglyceridaemia[1] in Subjects With Increased S-GGT[2] Levels Compared to Subjects With Normal S-GGT Levels After Adjusting for Age and Sex in Two Populations (95% CI Between Brackets)

		TG ≥ 1.7 mmol/L	
	n	n	%
Qwaqwa			
Males (age in yr)			
< 45			
GGT ≥ median	67	22	32.8
GGT < median	56	3	5.4
45+			
GGT ≥ median	69	19	27.5
GGT < median	84	16	19.1
Females (age in yr)			
< 45			
GGT ≥ median	101	15	14.9
GGT < median	147	4	2.7
45+			
GGT ≥ median	177	58	32.8
GGT < median	143	26	18.2
Mangaung			
Males (age in yr)			
< 45			
GGT ≥ median	58	14	24.1
GGT < median	74	2	2.7
45+			
GGT ≥ median	85	18	21.2
GGT < median	70	8	11.4
Females (age in yr)			
< 45			
GGT ≥ median	104	6	5.8
GGT < median	126	1	0.8
45+			
GGT ≥ median	120	19	15.8
GGT < median	115	7	6.1

1 Serum TG ≥ 1.7 mmol/L

2 Mangaung : Median S-GGT for males = 40 IU/L and for females = 25 IU/L

Qwaqwa: Median S-GGT for males = 36 IU/L and for females = 20 IU/L

TABLE 11.5.4/2. The Relative Risk (RR) of Hypertriglyceridaemia[1] in Subjects With Elevated S-GGT Levels Compared to Subjects with Normal S-GGT Levels After Adjusting for Age and Sex (95% Confidence Interval in Parenthesis)

	RR High S-TG
Qwaqwa (age in yr)	
Males < 45	6.13 (1.94-19.41)
Males 45+	1.45 (0.81-2.59)
Females < 45	5.46 (1.87-15.97)
Females 45+	1.80 (1.20-2.71)
Summary RR	a
Mangaung (age in yr)	
Males < 45	3.35 (1.60-7.01)
Males 45+	1.48 (0.86-2.56)
Females < 45	3.23 (1.31-7.96)
Females 45+	1.54 (0.98-2.43)
Summary RR	1.94 (1.45-2.60)

[1] TG ≥ 1.7

[2] Mangaung : Median S-GGT for males = 40 IU/L and for females = 25 IU/L

[2] Qwaqwa: Median S-GGT for males = 36 IU/L and for females = 20 IU/L

[a] Cannot be calculated since the strata estimates were significantly different

Summary

Obesity was associated with a significantly increased risk of elevated total cholesterol in the Qwaqwa sample mostly due to a greater risk in male subjects. In the Mangaung sample the risk was only significantly increased in males. Although the risk of CHD is still low in SA blacks with increased levels of TC, it may be predicted on the grounds of other studies that the risk of CHD will not remain low indefinitely. The contribution of poverty to elevated TC levels in the FS populations also warrants investigation. The prevalence rates of unfavourable HDL-C:TC ratios were significantly increased in overweight compared to non-overweight subjects in both populations and in both sexes with the exception of young black women in Mangaung. An interesting pattern of escalating risk for unfavourable HDLC:TC ratios emerged from both studies, with the lowest RR in young women and the highest RR in younger males in Qwaqwa. The risk of elevated TG levels in overweight compared to non-overweight subjects was significantly increased in both samples. Apart from obesity other contributing factors for elevated TG levels should also be considered including alcohol, diet and lack of exercise.

Central obesity was significantly associated with hypercholesterolaemia in Mangaung subjects and this association was particularly strong in young women. This association was absent in the Qwaqwa sample, emphasising the complexity of central obesity and its co-morbidities in epidemiological studies. Care must be exercised to extrapolate results from one population to another. The association between central obesity and unfavourable HDLC to TC ratios was particularly strong in both samples. This was a consistent finding in all the subgroups with the exception of young females in Qwaqwa and young males in Mangaung. Central obesity as an important feature of the metabolic syndrome was overall strongly associated with hypertriglyceridaemia in both samples.

Overall, no significant differences were found between the two samples in the prevalence rates of any of the lipid abnormalities that were described. It can therefore be concluded that the urbanisation process in the rural and semi-rural areas of Qwaqwa were as far advanced, as was the case in the urban area of Mangaung.

Significant other associations between fasting hypertriglyceridaemia and hyperinsulinaemia, a history of alcohol use, and raised levels of s-GGT were found in this study. Most of the factors that were associated with increased fasting TG levels are interrelated and it is therefore not possible to hypothesise on the contribution of each. A healthy lifestyle including weight loss if overweight, moderate daily exercise such as brisk waking, and limited use of alcohol are all inexpensive measures that may improve most of these metabolic abnormalities (WHO, 2001).

A follow-up study to monitor the possible future changes in lipid levels and abnormalities as a result of the nutrition transition is not only warranted but also essential. Lifestyle intervention at the community level should already be regarded as a priority considering the unfavourable lipid profile that emerged from in these populations this study.

12 Clustering of cardiovascular risk factors

12.1 The deadly quartet in black dwellers in Qwaqwa and Mangaung

The clustering of one or more of the components of the Kaplan's deadly quartet (1989) in the same individual for both study populations is shown in Table 12.1/1. After adjusting for age and sex 35.2% of the Qwaqwa population harboured at least one the components of the deadly quartet, 23.6% two components, 9.3% three components and 2.2% all four components. The rates for Mangaung were very similar (30.5%, 21%, 12.1% and 2.2% respectively). This means that only 29.7% of the population 25 years and older in Qwaqwa and 34.2% the population in Mangaung were metabolically healthy and free from hypertension.

Hyperinsulinaemia was not associated with hypertension (see 9.8) but was associated with the other components of the deadly quartet in both populations. The mechanism linking hypertension to the other components of the quartet in these black populations is not known. Although clustering of cardiovascular risk factors was demonstrated in both these black populations sufficient evidence linking the clustering of risk factors to cardiovascular disease is still needed. Since the prevalence of CAD is still regarded as low in black populations (Seftel, 1978) prospective study is needed to demonstrate the impact of the Deadly Quartet on the incidence of cardiovascular disease in black populations. A different approach would be to identify a subgroup of subjects who has all the components of the syndrome for a longitudinal study. Such a subgroup could easily be identified at low cost from a diabetes clinic.

To obtain evidence from these cross-sectional studies about the deleterious cardiovascular effects of the deadly quartet the ECG's of subjects who had all four components of the deadly quartet were analysed (Table 12.1/3). In the Qwaqwa sample 10 out of the 22 subjects (48%) had an abnormal ECG. In the Mangaung sample, however, 15 out of 22 subjects with the Quartet (71%) had an abnormal ECG. In this subset of respondents two had Q-waves compared to only one in the Qwaqwa sample. Although the numbers were small, this is

probably the first epidemiological study in SA providing evidence that the clustering of cardiovascular risk factors not only exists, but also may be causally related to cardiovascular pathology. It should, however, be remembered that the prevalence of ECG abnormalities were overall very high, for example 52.8% of Qwaqwa subjects had an abnormal ECG.

TABLE 12.1/1. The Age- and Sex-Specific Prevalence (%) of the Deadly Quartet[1] and its Components in Qwaqwa and Mangaung

	None	One[a]	Two[b]	Three[c]	Four[d]
Qwaqwa					
Males (age in yrs)					
25-34	43.6	38.2	10.9	7.3	-
35-44	29.9	29.9	25.4	11.9	3
45-54	25.9	33.3	37	-	3.7
55-64	19.1	38.1	31	7.1	4.8
65+	10.3	41	26.9	19.2	2.6
Age-standardised prevalence	30.6	35.7	22.9	8.9	2.1
Females (age in yrs)					
25-34	56.5	35.5	5.8	2.2	-
35-44	28.3	48.1	17	5.7	0.9
45-54	14.7	29.5	36.9	17.9	1.1
55-64	11	24		19	7
65+	5	29.2	46.7	14.2	5
Age-standardised prevalence	29.4	34.8	24	9.6	2.2
Total (age-standardised)	29.7	35.2	23.6	9.3	2.2
Mangaung					
Males (age in yrs)					
25-34	58.5	26.2	10.8	3.1	1.5
35-44	44.4	23.8	22.2	9.5	-
45-54	15.6	34.4	26.6	20.3	3.1
55-64	7.7	36.5	36.5	17.3	1.9
65+	7.9	18.4	42.1	21.1	10.5
Age-standardised prevalence	37.2	27.8	22	11	2.1
Females (age in yrs)					
25-34	62.1	30.1	5.8	1.9	-
35-44	27.6	39.8	20.3	11.4	0.8
45-54	8	39	26	21	6
55-64	7.5	25.4	40.3	23.9	3
65+	1.6	16.1	43.6	32.3	6.5
Age-standardised prevalence	31.9	32.5	20.3	13	2.2
Total (age- and sex-standardised)	34.2	30.5	21	12.1	2.2

[1] Kaplan, 1989

(a,b,c and d: see Table 12.1/2 for legend to Table 12.1/1 on next page)

TABLE 12.1/2. Legend to Table 12.1/1.

One
Only WHR > median for specific sex or
Only raised serum triglycerides (≥ 2.3 mmol/L) or
Only hypertension (SBP ≥140 and or DBP ≥ 90 mmHg) or
Only diabetes or IGT
Two
Any two of:
Diabetes or IGT
Raised serum triglycerides (≥ 2.3 mmol/L) or
Hypertension (SBP ≥140 and or DBP ≥ 90 mmHg) or
WHR> media n for specific sex
Three
Any three of the above
Four
All 4 components

TABLE 12.1/3. Abnormal ECG's in patients with all four components of the Deadly Quartet

	n	n Available ECG's	% Abnormal ECG's	Q-1 code	Q-2 code
Qwaqwa	22	21	10 (48%)	1 (5%)	-
Mangaung	21	21	15 (71%)	1 (5%)	1 (5%)

12 .2 The metabolic syndrome in black dwellers in Qwaqwa and Mangaung

12.2.1 Prevalence of the Metabolic Syndrome

The WHO criteria (Alberti et al., 1998) without microalbuminuria were used to calculate the prevalence of the metabolic syndrome in the two populations (Table 12.2/1). The age-standardised prevalence of the metabolic syndrome (without microalbuminuria) in Qwaqwa was 30.7% (males 28.1% and females 32.8%) and in Mangaung 30.5% (males 26.3% and females 33.9%) (Table 12.2/1). After adjusting the Mangaung sample to the population structure of Qwaqwa, the prevalence of the metabolic syndrome in the Mangaung was 32.4%. The difference in the prevalence of the metabolic syndrome between the two regions was not significant (95% CI −7.7; 4.0).

12.2.2 The relative risk of abnormal ECG's in subjects with the metabolic syndrome

The RR of significant ECG abnormalities in those subjects with the metabolic syndrome are shown in Tables 12.2.2/1-4. The RR of subjects with the metabolic syndrome having a Q-wave abnormality , an R-wave abnormality, a T-wave abnormality or any of these abnormalities were not increased compared to subjects without the metabolic syndrome. These findings must be interpreted against the background of a high prevalence of ECG abnormalities in both populations (Chapter 9). It may be concluded that although two or more of the components of the metabolic syndrome were present in 30.7% and 30.5% of subjects in Qwaqwa and Mangaung respectively, no ECG evidence of an increased risk of CHD could be found. This does not mean that these populations are immune against the atherosclerotic effects of the metabolic syndrome. Since the incubation period of CV disease in a population exposed to major CV risk factors may be 30-40 years, it may be hypothesised that the two study populations are merely still in a process of transition.

TABLE 12.2.2/1. The Age-Standardised Prevalence (%) of the Metabolic Syndrome[1] by Sex and Population

	Qwaqwa		Mangaung	
	n	%	n	%
Males (age in yr)				
25-34	56	21.4	65	16.9
35-44	68	26.5	63	25.4
45-54	27	37.0	64	31.3
55-64	42	31.0	53	34.0
65+	80	36.3	39	51.3
Total	273		284	
Age-standardised prevalence		28.1		26.3
Females (age in yr)				
25-34	140	15.0	101	17.8
35-44	108	32.4	122	29.5
45-54	97	40.2	103	53.4
55-64	101	55.5	67	44.8
65+	120	42.5	63	58.7
Total	566		456	
Age-standardised prevalence		32.8		33.9
Total All ages Age- and sex-standardised prevalence		30.7		30.5
Adjusted to the Qwaqwa population structure		30.7		32.4[a]

[1] Alberti et al., 1998

[a] 95% CI for the difference between Qwaqwa and Mangaung: -1.7;5.7

TABLE 12.2.2/1. The Relative Risk of Q-Wave ECG Abnormalities in Subjects With, Compared to Subjects Without the Metabolic Syndrome (95% Confidence Interval in Parenthesis)

	With MS[1]		Without MS[1]		
	n	% Q-abn.	n	% Q-Abn.	RR
Qwaqwa (age in yr)					
Males < 45	30	0.0	94	3.2	a
Males 45+	52	11.5	97	10.3	1.12 (0.43;2.91)
Females < 45	56	1.8	192	1.0	1.71 (0.16;18.56)
Females 45+	146	4.8	172	5.2	0.92 (0.35;2.40)
Summary RR					0.96 (0.50;1.83)
Mangaung (age in yr)					
Males < 45	27	3.7	101	9.9	0.37 (0.05-2.80)
Males 45+	58	19.0	98	8.0	2.32 (0.99-5.44)
Females < 45	54	0.0	169	1.8	a
Females 45+	122	10.7	111	7.2	1.48 (0.64-3.43)
Summary RR					1.39 (0.80-2.41)

[1] MS = Metabolic Syndrome

a Cannot be calculated

TABLE12.2.2/2. The Relative Risk of R-Wave ECG Abnormalities in Subjects With, Compared to Subjects Without the Metabolic Syndrome (95% Confidence Interval in Parenthesis)

	With MS[1]		Without MS[1]		
	n	% R-abn.	n	% R-Abn.	RR
Qwaqwa (age in yr)					
Males < 45	30	36.7	94	43.6	0.84 (0.50;1.42)
Males 45+	52	32.7	97	40.2	0.81 (0.51;1.29)
Females < 45	56	19.6	192	20.3	0.97 (0.53;1.76)
Females 45+	146	28.1	172	28.5	0.99 (0.69;1.40)
Summary RR					0.91 (0.72;1.14)
Mangaung (age in yr)					
Males < 45	27	33.3	101	55.5	0.60 (0.34-1.05)
Males 45+	58	44.8	98	46.9	0.96 (0.67-1.36)
Females < 45	54	13.0	169	23.7	0.55 (0.26-1.15)
Females 45+	122	32.0	111	28.8	1.11 (0.75-1.64)
Summary RR					0.85 (0.68-1.07)

[1] MS=Metabolic Syndrome

TABLE12.2.2/3. The Relative Risk of T-Wave ECG Abnormalities in Subjects With, Compared to Subjects Without the Metabolic Syndrome (95% Confidence Interval in Parenthesis)

	With MS1		Without MS1		
	n	% T-Abn.	n	% T-Abn.	RR
Qwaqwa (age in yr)					
Males < 45	30	0	94	13.8	a
Males 45+	52	25	97	18.6	1.35 (0.72;2.53)
Females < 45	56	8.93	192	18.8	0.48 (0.20;1.16)
Females 45+	146	19.2	172	16.9	1.14 (0.71;1.82)
Summary RR					a
Mangaung (age in yr)					
Males < 45	27	18.5	101	9.9	1.87 (0.70-5.01)
Males 45+	58	36.2	98	22.5	1.61 (0.98-2.66)
Females < 45	54	18.5	169	20.1	0.92 (0.49-1.74)
Females 45+	122	36.1	111	31.5	1.14 (0.80-1.64)
Summary RR					1.24 (0.96-1.60)

1 MS=Metabolic Syndrome

a cannot be calculated

TABLE12.2.2/4. The Relative Risk of Any[1] ECG Abnormality in Subjects With, Compared to Subjects Without the Metabolic Syndrome (95% Confidence Interval in Parenthesis)

	With MS2		Without MS2		
		%		%	
	n	Abn. ECG.	n	Abn. ECG.	RR
Qwaqwa (age in yr)					
Males < 45	30	36.7	94	54.3	0.68 (0.41;1.12)
Males 45+	52	53.9	97	52.6	1.02 (0.75;1.40)
Females < 45	56	30.4	192	35.4	0.86 (0.55;1.32)
Females 45+	146	41.1	172	40.7	1.01 (0.77;1.32)
Summary RR					0.93 (0.78 ;1.11)
Mangaung (age in yr)					
Males < 45	27	44.4	101	66.3	0.67 (0.43-1.04)
Males 45+	58	67.2	98	60.2	1.12 (0.88-1.42)
Females < 45	54	29.6	169	42	0.71 (0.45-1.10)
Females 45+	122	56.6	111	52.3	1.08 (0.85-1.37)
Summary RR					0.94 (0.81-1.10)

1 Any = Q-wave, R-wave or T-wave abnormality

2 MS=Metabolic Syndrome

12.3 Framingham CVD Risk Profiles

The Framingham prediction equations were used to calculate for both sexes and both populations the 5- and 10- year risk of CHD, myocardial infarction, CHD death, stroke, CVD, and CVD death (Anderson et al., 1991). The results are presented in Tables 12.3/1-12 and Fig.12.3/1-16. Five- and ten-year risk was categorised into 6 categories (<2.5%, 2.5%-<5%, 5%-<10%, 10-<15%, 15-<20%, and >20%). The actual systolic or diastolic blood pressure of the individual subjects was used to calculate these risks. Although these equations have not been validated in black South Africans, they do provide an estimate of risk and therefore a departing point for the management of risk reduction, possibly by prioritising a particular condition e.g. stroke.

Stroke is a major health problem in SA (Fritz, 1995) and was the cause of death of approximately 7622 black males and 9752 black females in SA during 1996 (Bradshaw, 2002). The number of survivors must be approximately twice as many since 30% of stroke victims die within the first month (Joubert, 1991). 17.1% of male subjects 45-74 years old in Qwaqwa had a 5-10% risk of developing a stroke within 5 years according to their SBP levels (Table 12.3/2). This figure went up from 17.1% to 24.8% after 10 years (Table 12.3/2). The corresponding percentages for diastolic blood pressure for the same group of men were 5.1% (within 5-years) and 30.8% (within 10-year) (Table 12.3/5). Adequate BP control is no guarantee that none of these subjects will sustain a stroke since other CV risk factors are also important. However, by reducing the mean diastolic BP by 5 mmHg over 5 years reduced the number of strokes in this period by at least 35% in a meta-analysis of blood pressure-lowering trials (Collins et al., 1990). The actual reduction in risk by lowering the DBP by 5 mm Hg for a particular patient can be calculated using the Framingham formulae.

In Table 12.3/9 it can be seen that 68.5% of men in the Mangaung sample in the age group 45-74 years had a greater than 20% risk of developing CV disease including heart failure in the next 10 years due to their levels of SBP. Targeting these men and improving their BP control should contribute substantially to lower this risk.

These are a few examples of how the Framingham prediction formulae could be used to allocate scare resources to improve disease outcome.

TABLE 12.3/1. Cardiovascular Disease Risk Profiles for Qwaqwa According to Framingham Prediction Equations Using Systolic Blood Pressure: For CHD and Myocardial Infarction

5 Year CHD Risk

		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20%
Qwaqwa	n	%	%	%	%	%	%
Males (age yr)							
30-44	100	51	28	14	4	2	1
45-74	117	12.8	14.5	21.4	17.1	13.7	20.5
Females (age in yr)							
30-44	173	87.9	8.7	2.9	0.58	0	0
45-74	283	22.6	25.4	28.3	11.7	5.7	6.4

10 Year CHD Risk

		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20%
Qwaqwa	n	%	%	%	%	%	%
Males (age yr)							
30-44	100	20	22	28	17	6	7
45-74	117	0.85	6	17.1	12.8	11.1	52.1
Females (age in yr)							
30-44	173	66.5	17.3	10.4	4.1	1.2	0.6
45-74	283	5	10.3	26.5	20.5	13.43	24.4

5 Year MI Risk

		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20%
Qwaqwa	n	%	%	%	%	%	%
Males (age yr)							
30-44	100	84	12	3	1	0	0
45-74	117	35.9	17.1	24.8	11.1	9.4	1.7
Females (age in yr)							
30-44	173	99.4	0.6	0	0	0	0
45-74	283	72.1	18.7	6.4	2.5	0.4	0

10 Year MI Risk

		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20%
Qwaqwa	n	%	%	%	%	%	%
Males (age yr)							
30-44	100	50	28	16	3	2	1
45-74	117	15.4	16.2	18.8	15.4	15.4	18.8
Females (age in yr)							
30-44	173	96.6	2.3	1.2	0	0	0
5-74	283	41	23.7	25.1	6	2.1	2.1

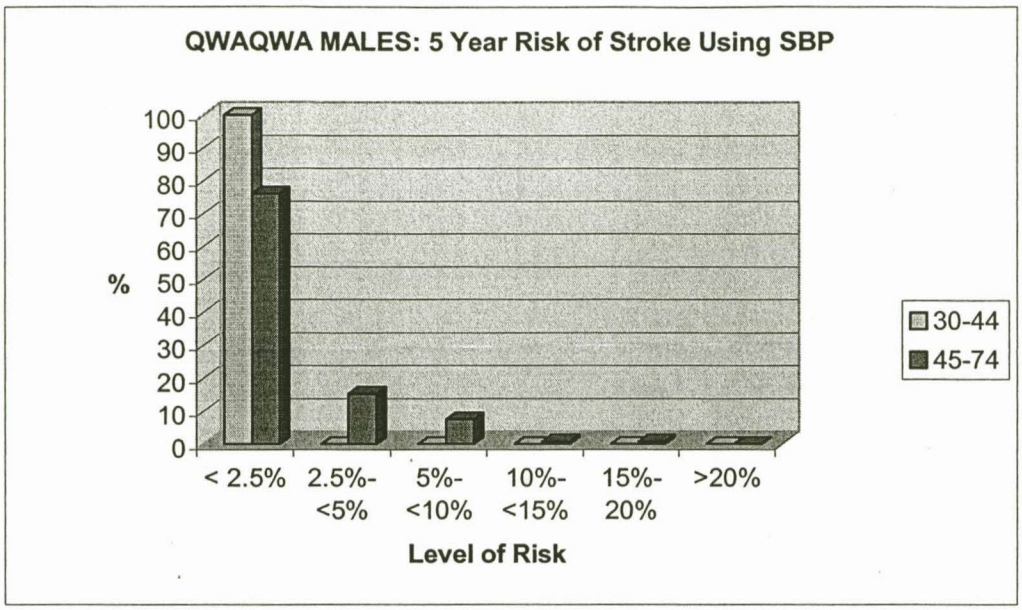
TABLE 12.3/2. Cardiovascular Disease Risk Profiles for Qwaqwa According to Framingham Prediction Equations Using Systolic Blood Pressure: For CHD Death and Stroke

		5 Year CHD Death Risk					
		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20%
Qwaqwa	n	%	%	%	%	%	%
Males (age yr)							
30-44	100	100	0	0	0	0	0
45-74	117	61.5	18	19.7	0.9	0	0
Females (age in yr)							
30-44	173	100	0	0	0	0	0
45-74	283	88.7	6.4	3.9	1.1	0	0

		10 Year CHD Death Risk					
		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20%
Qwaqwa	n	%	%	%	%	%	%
Males (age yr)							
30-44	100	94	5	1	0	0	0
45-74	117	15.4	21.4	12	13.7	2.6	0
Females (age in yr)							
30-44	173	100	0	0	0	0	0
45-74	283	65	15.9	11.7	4.6	1.8	1.1

		5 Year Risk For Stroke					
		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20%
Qwaqwa	n	%	%	%	%	%	%
Males (age yr)							
30-44	100	100	0	0	0	0	0
45-74	117	64.1	18.8	17.1	0	0	0
Females (age in yr)							
30-44	173	100	0	0	0	0	0
45-74	283	76	15.2	7.4	0.7	0.7	0

		10 Year Risk For Stroke					
		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20%
Qwaqwa	n	%	%	%	%	%	%
Males (age yr)							
30-44	100	97	3	0	0	0	0
45-74	117	30.8	20.5	24.8	8.6	9.4	
Females (age in yr)							
30-44	173	94.8	5.2	0	0	0	0
45-74	283	44.9	21.2	18	7.8	5	3.2



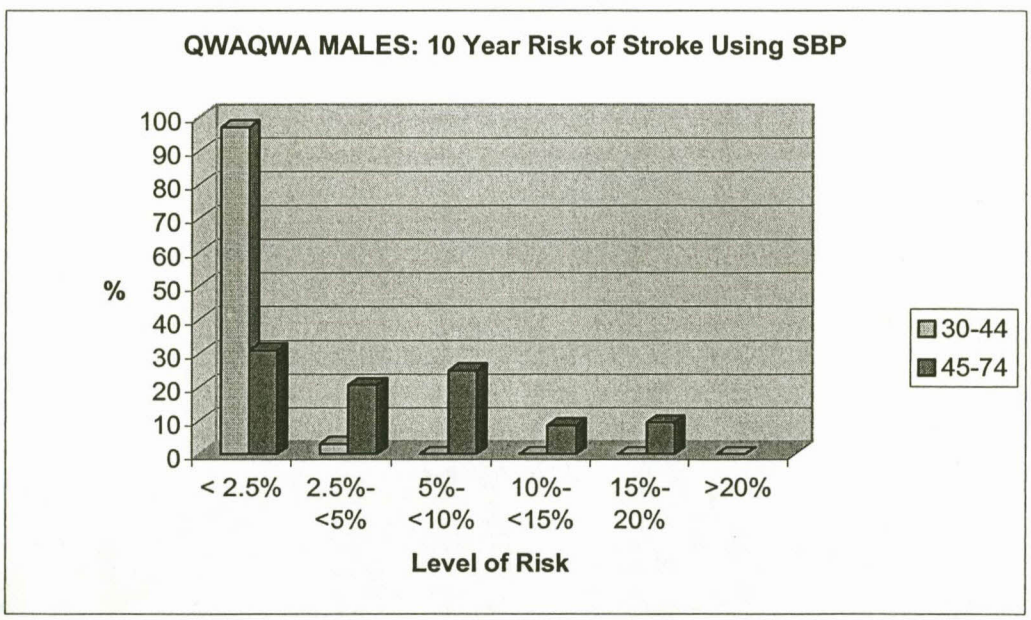
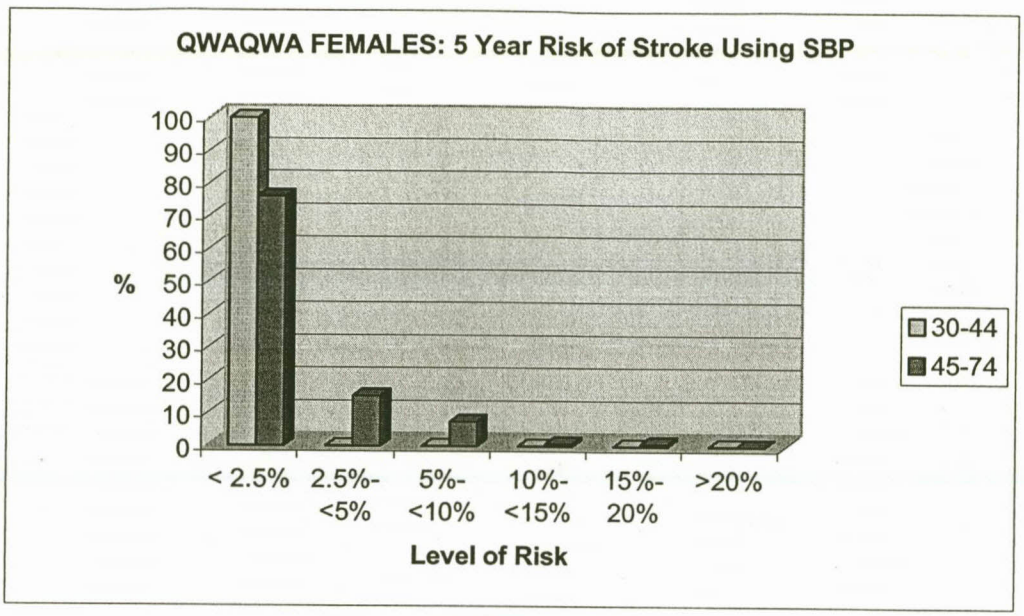


Fig 12.3/1. Prediction of 5- and 10-year risk of stroke in Qwaqwa males by using SBP



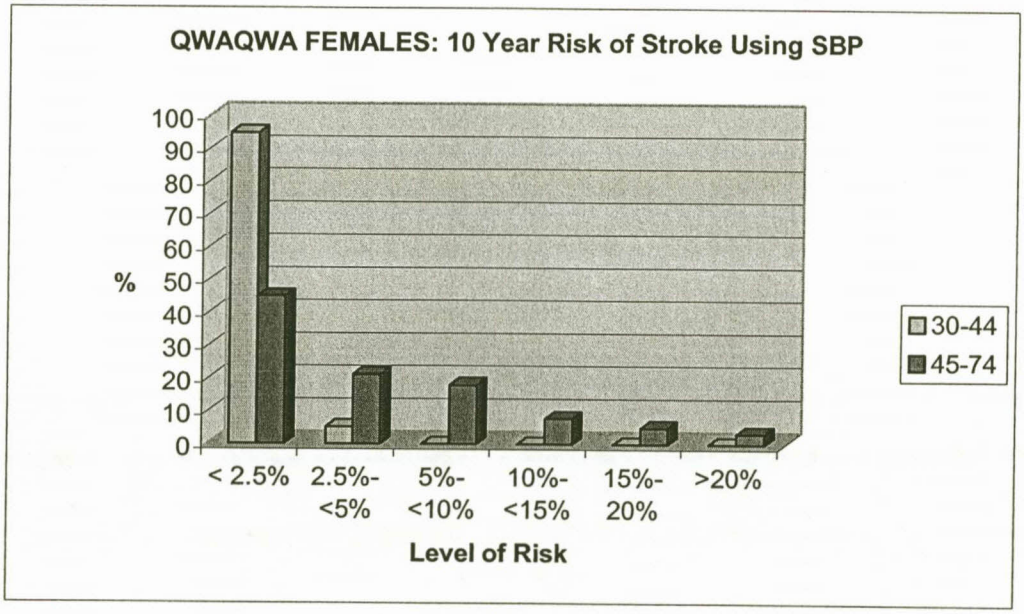
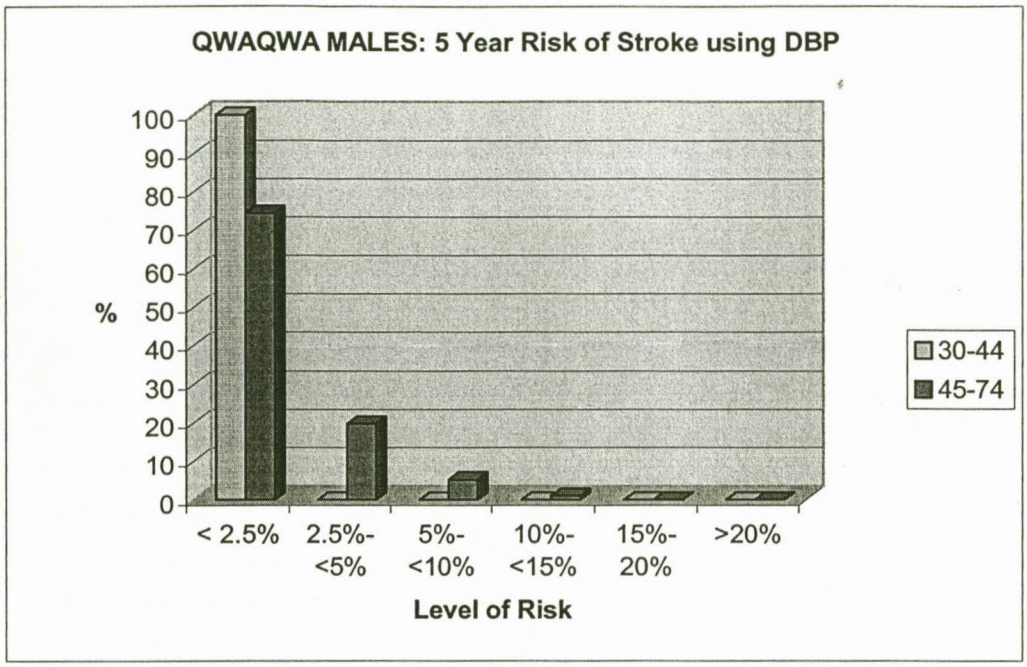


Fig.12.3/2. Prediction of 5- and 10-year risk of stroke in Qwaqwa females Using SBP



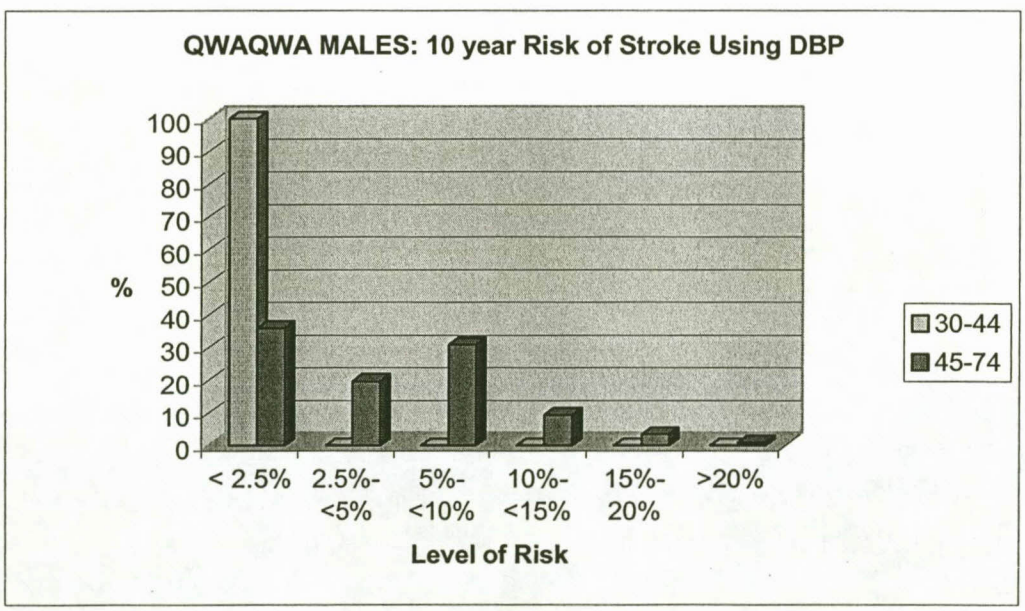
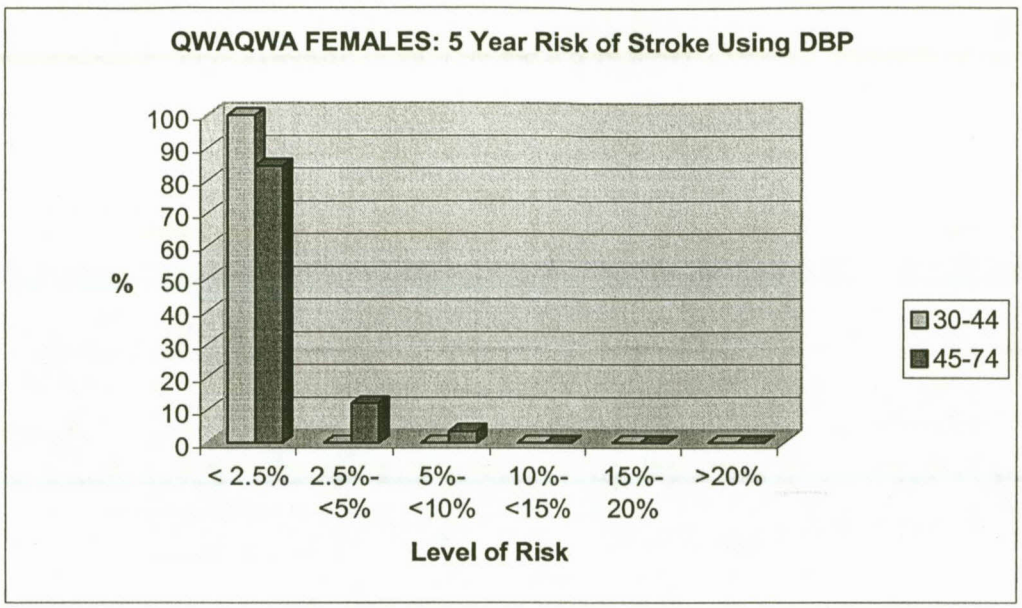


Fig. 12.3/3. Prediction of 5- and 10-year risk of stroke in Qwaqwa males using DBP



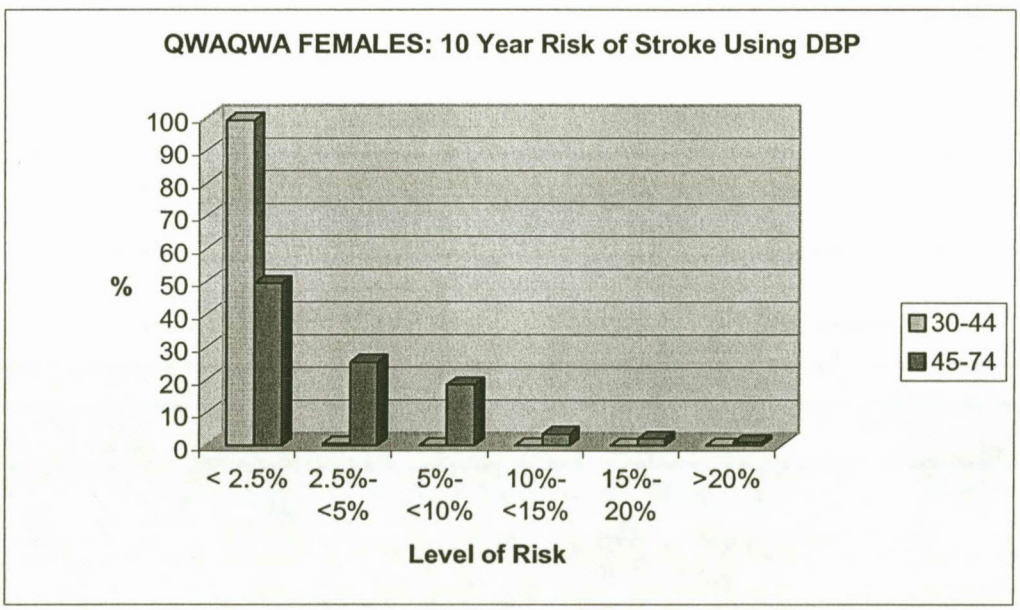


Fig. 12.3/4. Prediction of 5- and 10-year risk of stroke in Qwaqwa females according to DBP

TABLE 12.3/3. Cardiovascular Disease Risk Profiles for Qwaqwa According to Framingham Prediction Equations Using Systolic Blood Pressure: For CVD and CVD Death

		5 Year Risk For CVD					
		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20%
Qwaqwa	n	%	%	%	%	%	%
Males (age yr)							
30-44	100	52	33	10	4	1	0
45-74	117	5.2	12	21.4	14.5	12.8	34.2
Females (age in yr)							
30-44	173	80.9	11.6	7	0.6	0	0
45-74	283	11.7	20.5	28	19.4	6.4	14.1

		10 Year Risk For CVD					
		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20%
Qwaqwa	n	%	%	%	%	%	%
Males (age yr)							
30-44	100	19	10	36	14	6	6
45-74	117	0	1.7	9.4	14.5	12.8	61.5
Females (age in yr)							
30-44	173	48.6	24.9	16.2	5.8	2.9	1.73
45-74	283	2.47	5	16.3	20.1	11.7	44.5

		5 Year Risk of CVD Death					
		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20%
Qwaqwa	n	%	%	%	%	%	%
Males (age yr)							
30-44	100	100	0	0	0	0	0
45-74	117	58.1	12.82	18	10.3	0.9	0
Females (age in yr)							
30-44	173	100	0	0	0	0	0
45-74	283	79.2	10.3	6.7	3.9	0.4	0

		10 Year Risk of CVD Death					
		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20%
Qwaqwa	n	%	%	%	%	%	%
Males (age yr)							
30-44	100	83	11	6	0	0	0
45-74	117	25.6	16.2	17.1	9.4	9.4	22.2
Females (age in yr)							
30-44	173	97.7	2.3	0	0	0	0
45-74	283	44.5	20.1	15.2	7.8	4.2	8.1

TABLE 12.3/4. Cardiovascular Disease Risk Profiles for Qwaqwa According to Framingham Prediction Equations Using Diastolic Blood Pressure: For CHD and Myocardial Infarction

	5 Year Risk for CHD						
		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20
Qwaqwa	n	%	%	%	%	%	%
Males (age yr)							
30-44	100	60	15	16	3	5	1
45-74	117	11.1	16.2	22.2	18.8	9.4	22.2
Females (age in yr)							
30-44	173	87.7	9.3	2.3	0	0.6	0
45-74	283	23.3	27.2	23	14.1	5.7	6.7

	10 Year Risk for CHD						
		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20
Qwaqwa	n	%	%	%	%	%	%
Males (age yr)							
30-44	100	24	22	24	17	4	9
45-74	117	0.9	3.4	20.5	10.3	13.7	51.3
Females (age in yr)							
30-44	173	69.4	14.5	12.1	1.7	1.7	0.6
45-74	283	5	10.3	26.5	20.5	11.3	26.5

	5 Year Risk for MI						
		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20
Qwaqwa	n	%	%	%	%	%	%
Males (age yr)							
30-44	100	89	7	4	0	0	0
45-74	117	38.5	16.2	28.2	10.2	4.27	2.56
Females (age in yr)							
30-44	173	99.4	0.58	0	0	0	0
45-74	283	77.4	14.3	6.7	1.4	0	0

	10 Year Risk for MI						
		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20
Qwaqwa	n	%	%	%	%	%	%
Males (age yr)							
30-44	100	60	23	12	4	1	0
45-74	117	17.1	12.8	22.2	18	16.2	13.7
Females (age in yr)							
30-44	173	1.2	0.6	0	0	0	0
45-74	283	41.7	27.9	21.2	6	1.8	1.4

TABLE 12.3/5. Cardiovascular Disease Risk Profiles for Qwaqwa According to Framingham Prediction Equations Using Diastolic Blood Pressure: For CHD Death and Stroke

		5 Year Risk for CHD Death					
		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20%
Qwaqwa	n	%	%	%	%	%	%
Males (age yr)							
30-44	100	100	0	0	0	0	0
45-74	117	65	20.5	12.8	1.7	0	0
Females (age in yr)							
30-44	173	100	0	0	0	0	0
45-74	283	91.9	5	2.8	0.4	0	0

		10 Year Risk for CHD Death					
		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20%
Qwaqwa	n	%	%	%	%	%	%
Males (age yr)							
30-44	100	95	5	0	0	0	0
45-74	117	32.5	18.8	23.9	16.2	6.8	1.7
Females (age in yr)							
30-44	173	100	0	0	0	0	0
45-74	283	68	17	9.5	3.9	1.4	0.4

		5 Year Risk of Stroke					
		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20%
Qwaqwa	n	%	%	%	%	%	%
Males (age yr)							
30-44	100	100	0	0	0	0	0
45-74	117	74.4	19.7	5.1	0.9	0	0
Females (age in yr)							
30-44	173	100	0	0	0	0	0
45-74	283	84.5	12	3.5	0	0	0

		10 Year Risk of Stroke					
		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20%
Qwaqwa	n	%	%	%	%	%	%
Males (age yr)							
30-44	100	100	0	0	0	0	0
45-74	117	35.9	19.7	30.8	9.4	3.4	0.9
Females (age in yr)							
30-44	173	99.4	0.6	0	0	0	0
45-74	283	49.5	25.4	18.4	3.5	2.1	1

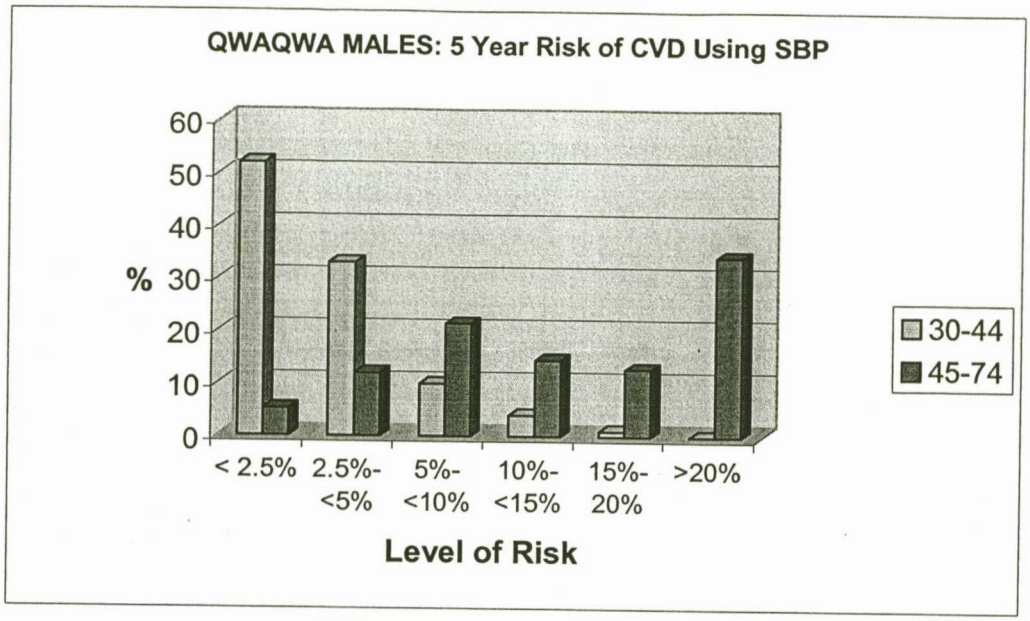
TABLE 12.3/6 Cardiovascular Disease Risk Profiles for Qwaqwa According to Framingham Prediction Equations Using Diastolic Blood Pressure: For CVD and CVD Death

	5 Year Risk of CVD						
		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20
Qwaqwa	n	%	%	%	%	%	%
Males (age yr)							
30-44	100	60	28	8	3	1	0
45-74	117	2.6	14.5	22.2	15.3	15.4	30
Females (age in yr)							
30-44	173	86.7	10.4	2.3	0	0.6	0
45-74	283	11	20.9	33.9	16.6	7.8	9.9

	10 Year Risk of CVD						
		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20
Qwaqwa	n	%	%	%	%	%	%
Males (age yr)							
30-44	100	26	23	34	8	3	6
45-74	117	0.9	0	10.3	14.5	10.3	64.1
Females (age in yr)							
30-44	173	57.8	23.7	13.3	4.6	0	0.9
45-74	283	1.77	6.4	17.7	17	17.7	40

	5 Year Risk of CVD Death						
		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20
Qwaqwa	n	%	%	%	%	%	%
Males (age yr)							
30-44	100	100	0	0	0	0	0
45-74	117	57.3	16.2	18	7.7	0.9	0
Females (age in yr)							
30-44	173	100	0	0	0	0	0
45-74	283	81.9	9.5	7.4	1.1	0	0

	10 Year Risk of CVD Death						
		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20
Qwaqwa	n	%	%	%	%	%	%
Males (age yr)							
30-44	100	90	4	6	0	0	0
45-74	117	24.8	13.7	20.5	12.9	12	16.3
Females (age in yr)							
30-44	173	99.4	0	0.6	0	0	0
45-74	283	44.2	24	14.1	8.1	3.9	5.7



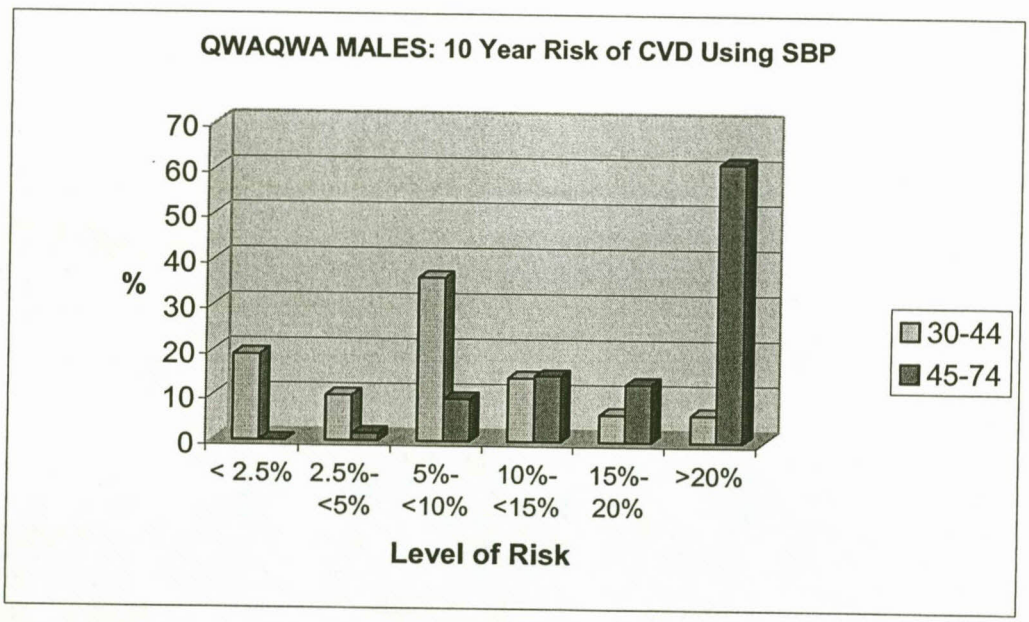
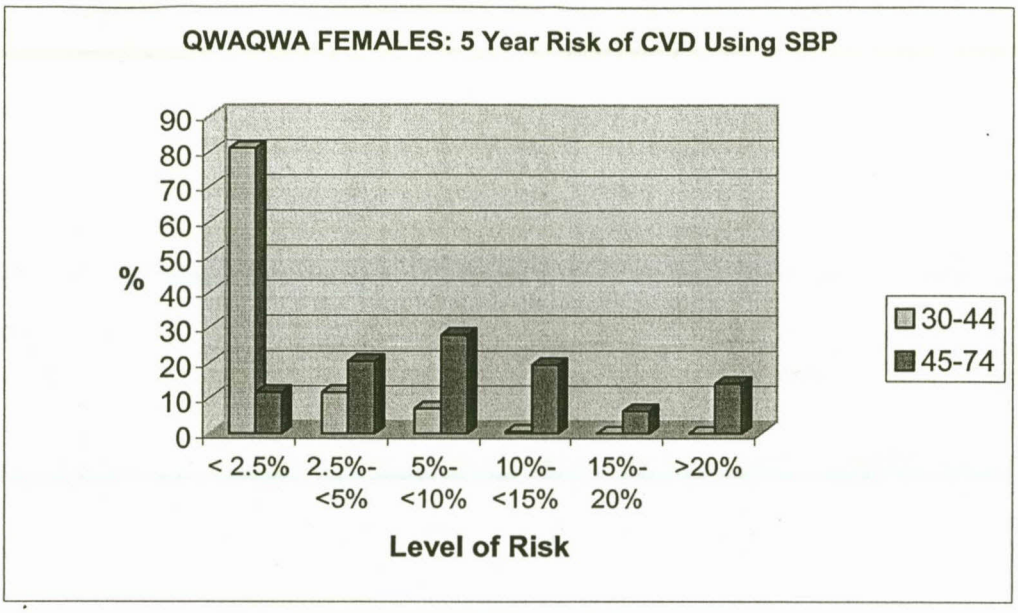


Fig. 12.3/5. Prediction of 5-and 10-year risk of CVD in Qwaqwa males by age using SBP.



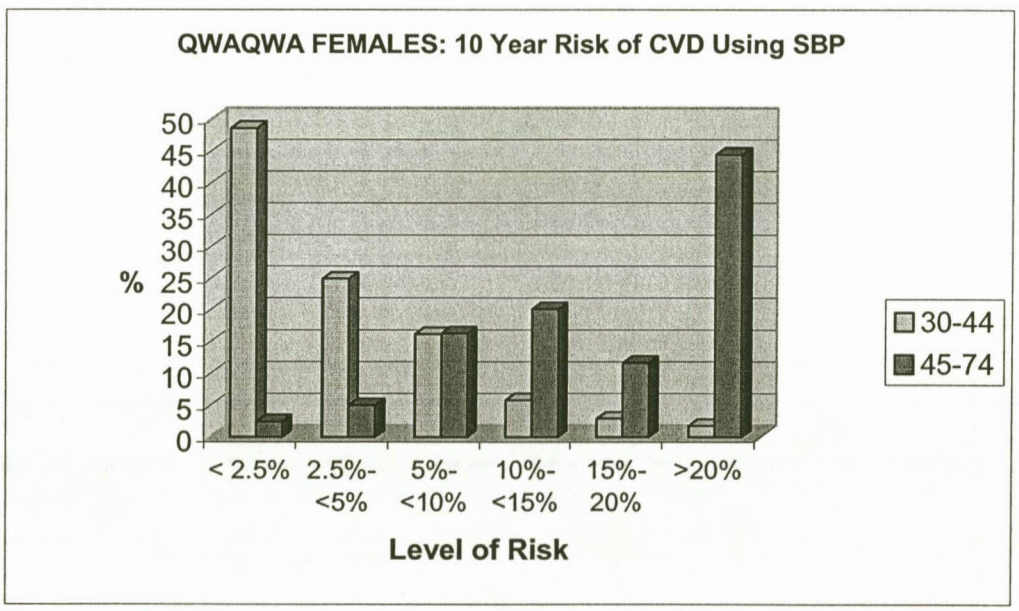
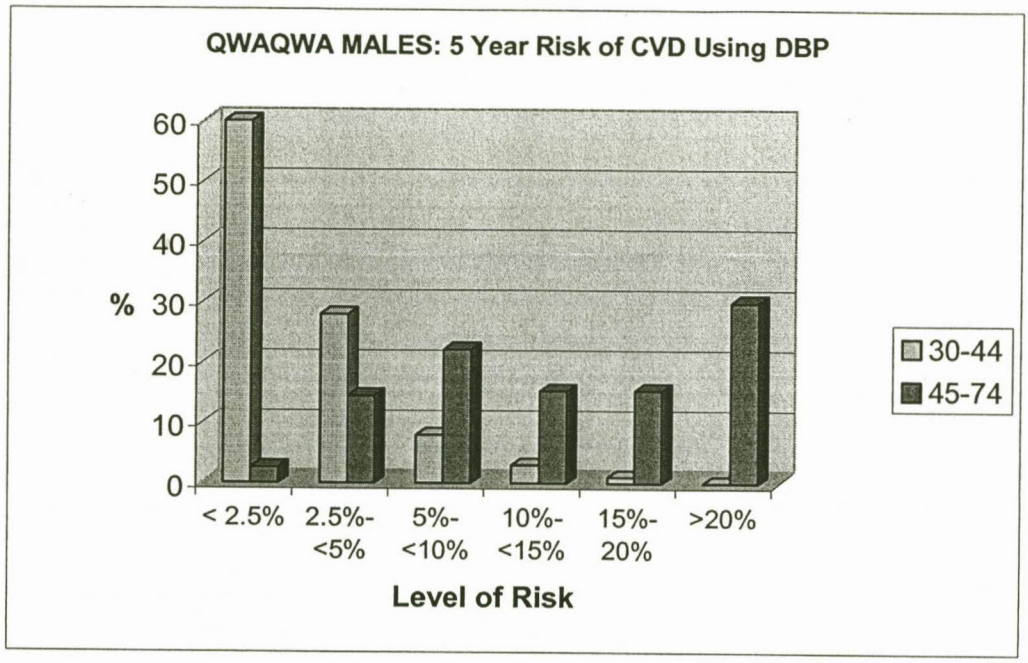


Fig. 12.3/6. Prediction of 5-year risk of CVD in Qwaqwa females by age using SBP



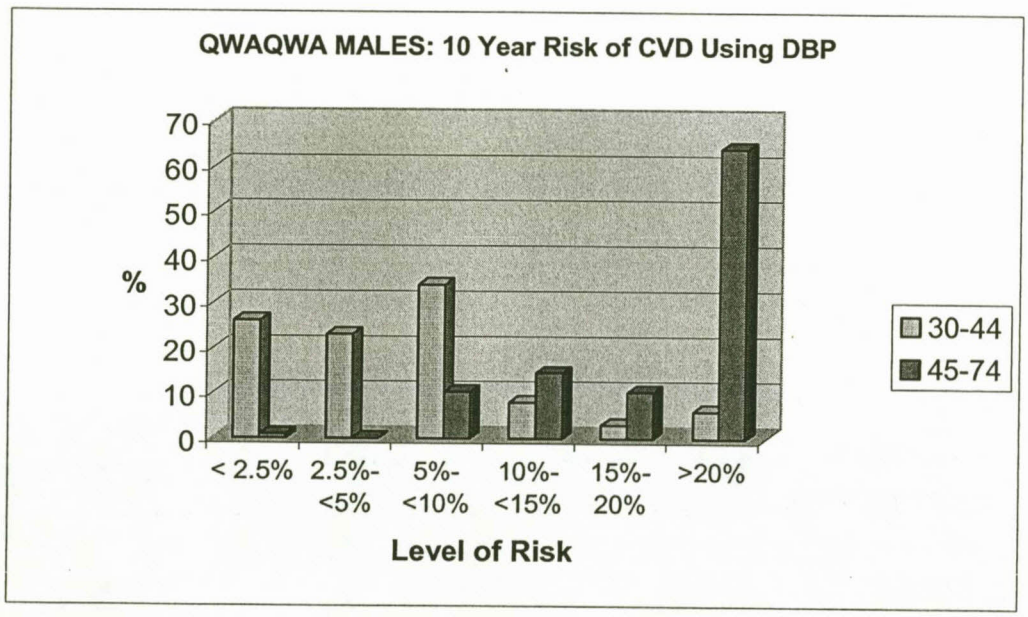
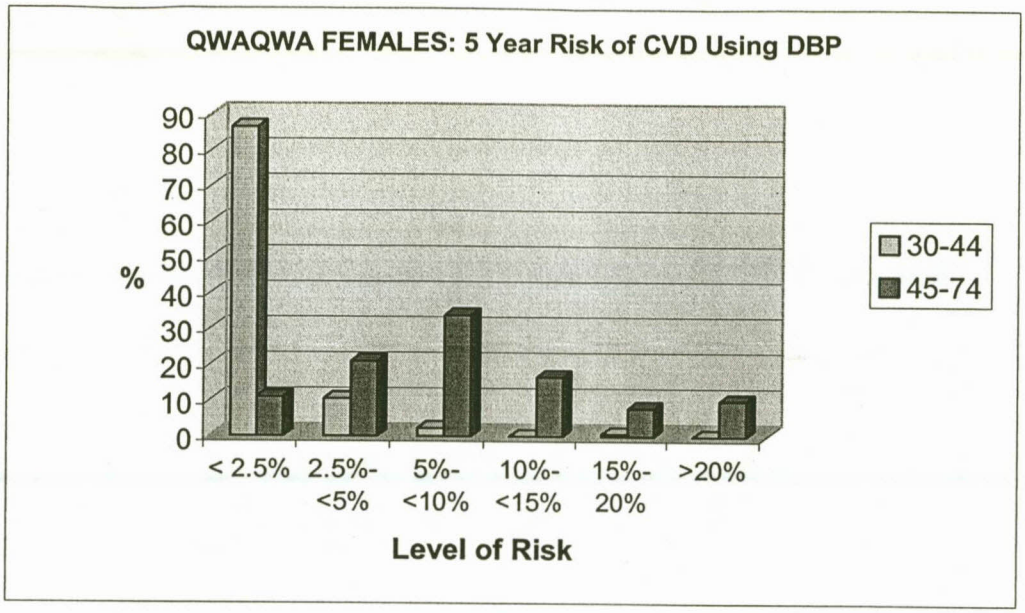


Fig. 12.3/7. Prediction of 5- and 10-year risk of CVD for Qwaqwa males Using DBP



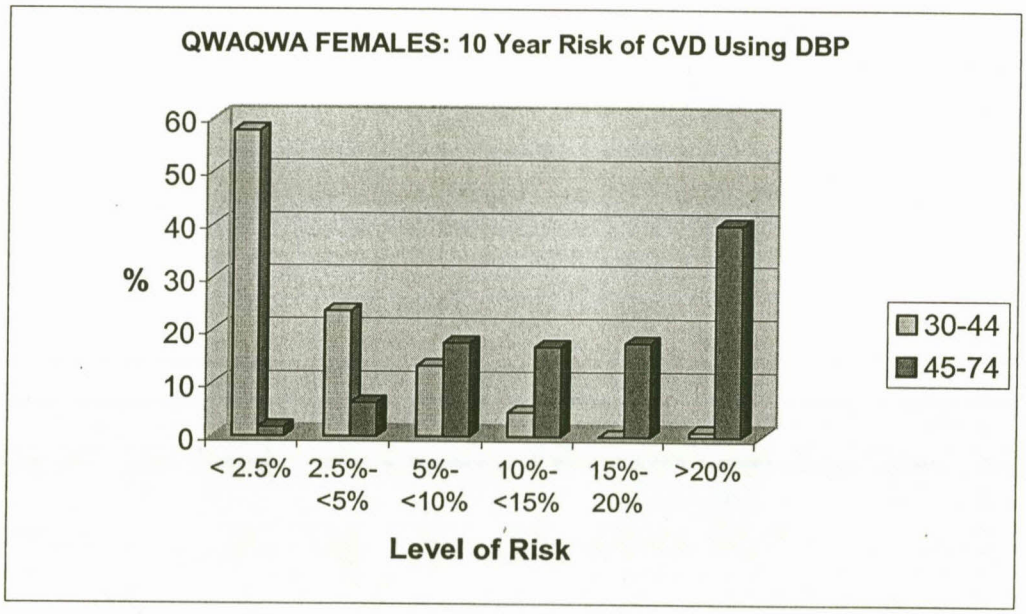


Fig. 12.3/8. Prediction of 5- and 10-year risk of CVD for Qwaqwa females using DBP

TABLE 12.3/7. Cardiovascular Disease Risk Profiles for Mangaung According to Framingham Prediction Equations Using Systolic Blood Pressure: For CHD and Myocardial Infarction

5 Year CHD Risk

		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20%
Mangaung	n	%	%	%	%	%	%
Males (age yr)							
30-44	99	52.5	23.2	16.2	7.1	1	0
45-74	143	9.8	13.3	26.6	15.4	17.5	17.5
Females (age in yr)							
30-44	165	90.3	4.9	4.2	0.6	0	0
45-74	214	21.5	25.2	28.5	11.2	5.1	8.4

10 Year CHD Risk

		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20%
Mangaung	n	%	%	%	%	%	%
Males (age yr)							
30-44	99	17.2	25.3	30.3	11.1	8.1	8.1
45-74	143	0.7	5.59	14.7	14.7	14	50.4
Females (age in yr)							
30-44	165	69.7	14.6	9.1	4.2	1.8	0.6
45-74	214	4.7	10.3	27	18.2	14.5	25.2

5 Year Risk of MI

		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20%
Mangaung	n	%	%	%	%	%	%
Males (age yr)							
30-44	99	83.8	12.1	4	0	0	0
45-74	143	29.4	20.3	27.3	15.4	4.9	2.8
Females (age in yr)							
30-44	165	98.2	1.8	0	0	0	0
45-74	214	67.8	19.4	10.3	1.4	0.5	0.5

10 Year Risk of MI

		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20%
Mangaung	n	%	%	%	%	%	%
Males (age yr)							
30-44	99	53.5	23.2	18.2	4	1	0
45-74	143	8.4	13.3	26.6	19.6	11.9	20.3
Females (age in yr)							
30-44	165	90.3	6.7	1.8	1.2	0	0
45-74	214	37.9	24.8	21	9.8	4.2	2.3

TABLE 12.3/8. Cardiovascular Disease Risk Profiles for Mangaung According to Framingh Prediction Equations Using Systolic Blood Pressure: For CHD Death and Stroke

5 Year Risk of CHD Death

		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20%
Mangaung	n	%	%	%	%	%	%
Males (age yr)							
30-44	99	100	0	0	0	0	0
45-74	143	71.3	14.7	11.9	0.7	1.4	0
Females (age in yr)							
30-44	165	100	0	0	0	0	0
45-74	214	86.9	9.8	2.8	0.5	0	

10 Year Risk of CHD Death

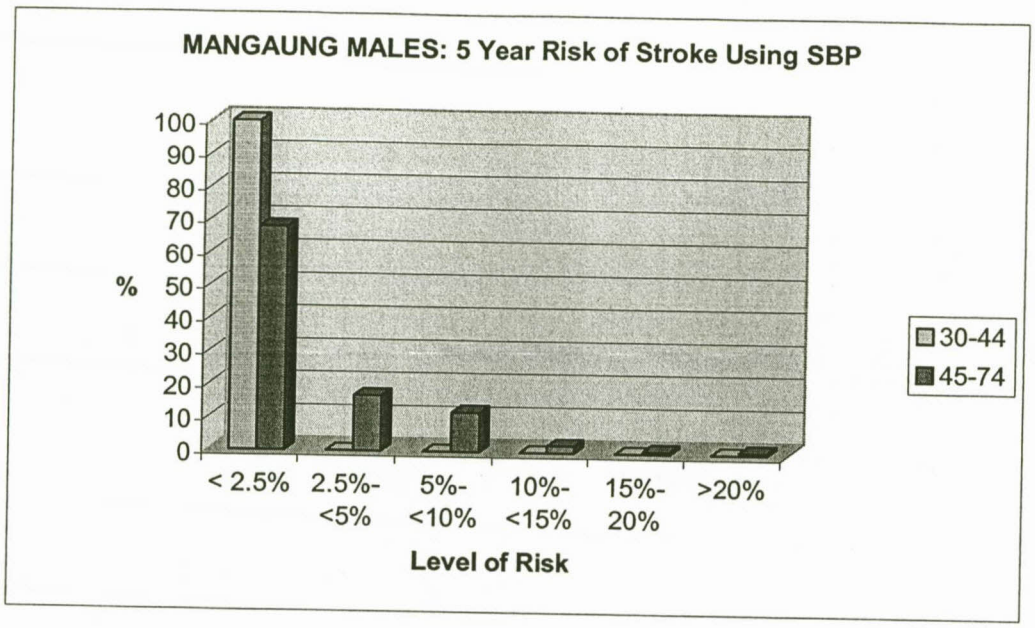
		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20%
Mangaung	n	%	%	%	%	%	%
Males (age yr)							
30-44	99	95	5.1	0	0	0	0
45-74	143	32.9	23.1	22.4	13.3	4.9	3.5
Females (age in yr)							
30-44	165	99.4	0.6	0	0	0	0
45-74	214	67.8	11.7	14	3.3	1.9	1.4

5 Year Risk of Stroke

		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20%
Mangaung	n	%	%	%	%	%	%
Males (age yr)							
30-44	99	100	0	0	0	0	0
45-74	143	67.8	16.8	11.9	2.1	0.7	0.7
Females (age in yr)							
30-44	165	100	0	0	0	0	0
45-74	214	76.2	12.6	6.1	2.8	1.4	0.9

10 Year Risk of Stroke

		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20%
Mangaung	n	%	%	%	%	%	%
Males (age yr)							
30-44	99	96	4	0	0	0	0
45-74	143	28	30.8	17.5	9.8	6.3	7.7
Females (age in yr)							
30-44	165	97.6	1.8	0.6	0	0	0
45-74	214	39.3	24.8	18.7	7	3.7	6.5



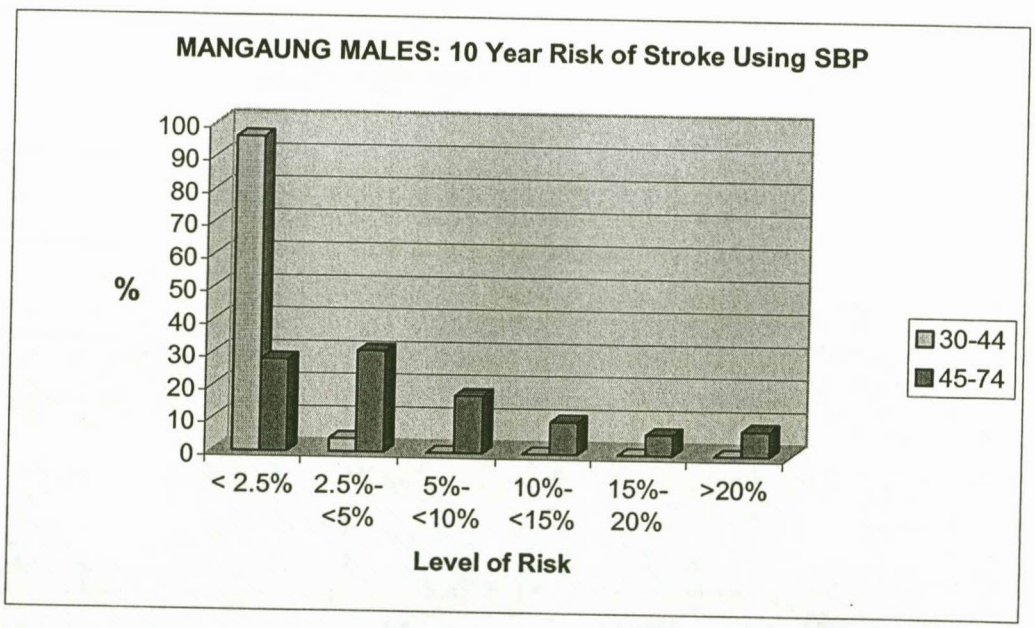
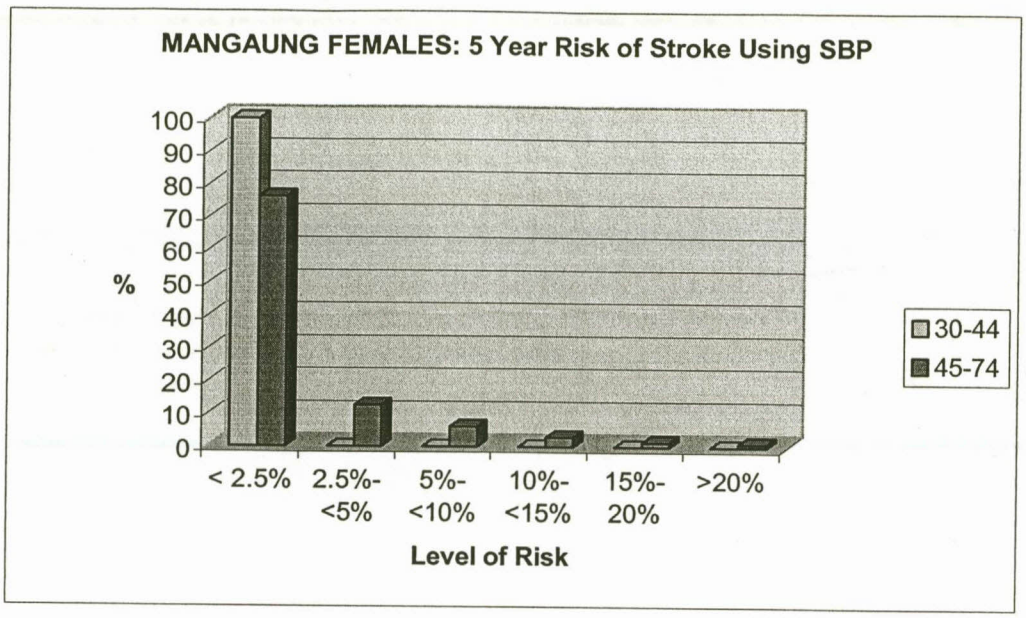


Fig. 12.3/9. Prediction of risk 5- and 10- year risk of stroke in Mangaung males Using SBP



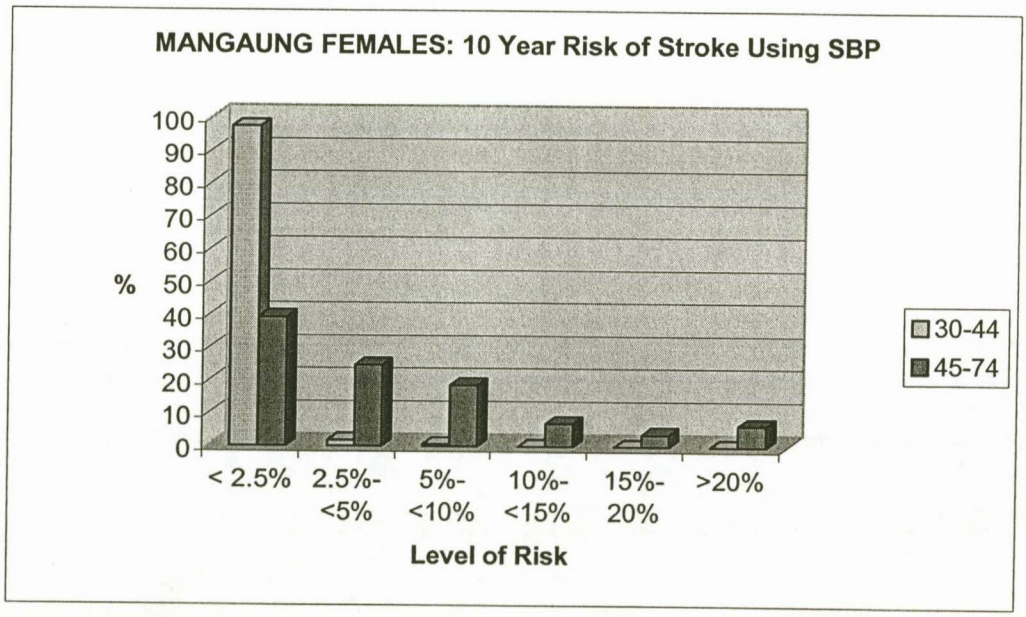


Fig. 12.3/10. Prediction of 5- and 10-year risk of stroke in Mangaung females Using SBP

TABLE 12.3/9. Cardiovascular Disease Risk Profiles for Mangaung According to Framingham Prediction Equations Using Systolic Blood Pressure: For CVD and CVD Death

	5 Year Risk of CVD						
		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20%
Mangaung	n	%	%	%	%	%	%
Males (age yr)							
30-44	99	51.2	30.3	14.1	3	1	0
45-74	143	2.8	9.8	23.1	18.9	16.1	29.4
Females (age in yr)							
30-44	165	77.6	13.3	6.7	2.4	0	0
45-74	214	9.8	22.4	27.6	15.4	8.4	16.4
	10 Year Risk of CVD						
		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20%
Mangaung	n	%	%	%	%	%	%
Males (age yr)							
30-44	99	14.1	25.3	34.3	13.1	9.1	4
45-74	143	0	1.4	7.7	8.4	14	68.5
Females (age in yr)							
30-44	165	44.2	25.5	18.8	5.5	3	3
45-74	214	1.4	4.7	16.8	17.3	15.9	43.9
	5 Year Risk of CVD Death						
		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20%
Mangaung	n	%	%	%	%	%	%
Males (age yr)							
30-44	99	100	0	0	0	0	0
45-74	143	67.1	13.3	11.2	5.6	1.4	1.4
Females (age in yr)							
30-44	165	100	0	0	0	0	0
45-74	214	79.4	9.4	8.4	1.9	0.9	0
	10 Year Risk of CVD Death						
		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20%
Mangaung	n	%	%	%	%	%	%
Males (age yr)							
30-44	99	83.8	12.1	4	0	0	0
45-74	143	24.5	20.3	23.1	9.1	8.4	14.7
Females (age in yr)							
30-44	165	97	3	0	0	0	0
45-74	214	47.2	19.2	13.6	6.1	5.6	8.4

TABLE 12.3/10. Cardiovascular Disease Risk Profiles for Mangaung According to Framingha

Prediction Equations Using Diastolic Blood Pressure: For CHD and Myocardial Infarction

	5 Year CHD Risk						
		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20
Mangaung	n	%	%	%	%	%	%
Males (age yr)							
30-44	99	54.6	17.2	19.2	8.1	1	0
45-74	143	8.4	16.8	21.7	16.8	13.3	23.1
Females (age in yr)							
30-44	165	90.9	4.9	3.6	0.6	0	0
45-74	214	23.4	28.5	22.9	8.4	7.9	8.9

	10 Year CHD Risk						
		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20
Mangaung	n	%	%	%	%	%	%
Males (age yr)							
30-44	99	24.2	20.2	25.3	12.1	9.1	9.1
45-74	143	2.1	2.1	17.5	9.8	15.4	53.2
Females (age in yr)							
30-44	165	67.9	18.2	8.5	2.4	2.4	0.6
45-74	214	3.7	14.5	29.4	15	11.7	25.7

	5 Year Risk of MI						
		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20
Mangaung	n	%	%	%	%	%	%
Males (age yr)							
30-44	99	85.9	11.1	3	0	0	0
45-74	143	32.9	19.6	30.1	10.5	4.9	2.1
Females (age in yr)							
30-44	165	98.2	1.8	0	0	0	0
45-74	214	77.6	15.2	4.7	2.3	0	0

	10 Year Risk of MI						
		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20
Mangaung	n	%	%	%	%	%	%
Males (age yr)							
30-44	99	60.6	19.2	17.2	3	0	0
45-74	143	5.6	15.4	28	23.8	13.3	14
Females (age in yr)							
30-44	165	94	4.2	1.8	0	0	0
45-74	214	44	24.8	22.9	5.1	1.4	1.9

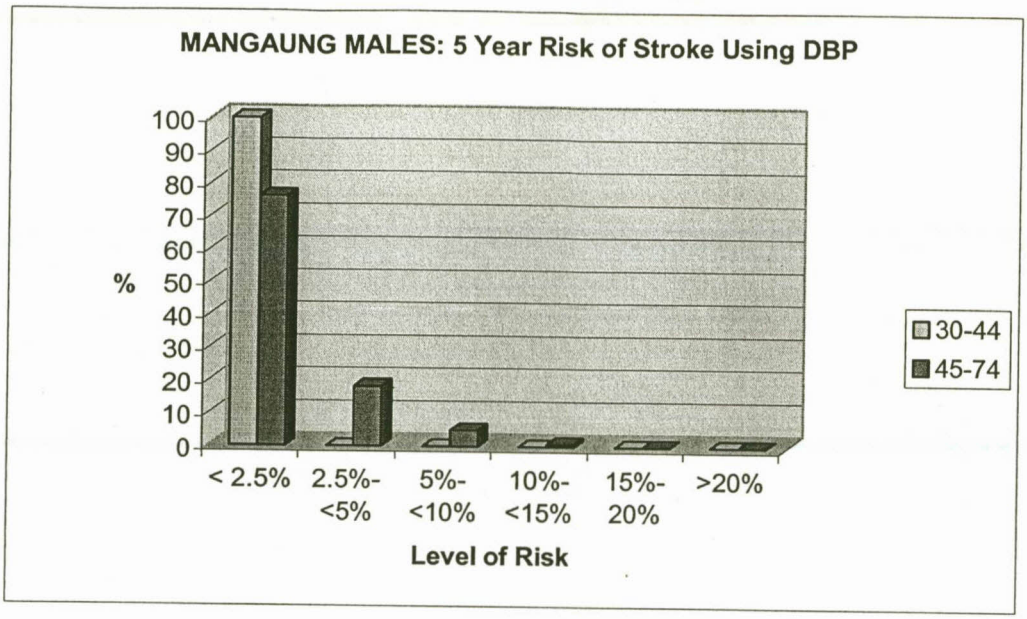
TABLE 12.3/11. Cardiovascular Disease Risk Profiles for Mangaung According to Framingham Prediction Equations Using Diastolic Blood Pressure: For CHD Death and Stroke

	5 Year Risk of CHD Death						
		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20%
Mangaung	n	%	%	%	%	%	%
Males (age yr)							
30-44	99	100	0	0	0	0	0
45-74	143	75.5	14.7	7	2.1	0.7	0
Females (age in yr)							
30-44	165	100	0	0	0	0	0
45-74	214	93.5	5.1	1.4	0	0	0

	10 Year Risk of CHD						
		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20%
Mangaung	n	%	%	%	%	%	%
Males (age yr)							
30-44	99	98	2	0	0	0	0
45-74	143	37.1	22.4	23.8	10.5	2.8	3.5
Females (age in yr)							
30-44	165	99.4	0.6	0	0	0	0
45-74	214	70.6	15	10.8	2.3	0.9	0.5

	5 Year Risk of Stroke						
		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20%
Mangaung	n	%	%	%	%	%	%
Males (age yr)							
30-44	99	100	0	0	0	0	0
45-74	143	76.2	18.2	4.9	0.7	0	0
Females (age in yr)							
30-44	165	100	0	0	0	0	0
45-74	214	84.6	13.1	1.4	0.9	0	0

	10 Year Risk of Stroke						
		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20%
Mangaung	n	%	%	%	%	%	%
Males (age yr)							
30-44	99	99	1	0	0	0	0
45-74	143	30.8	32.2	23.8	7.7	2.1	3.5
Females (age in yr)							
30-44	165	99.4	0.6	0	0	0	0
45-74	214	56.1	22.4	13.1	6.5	0.5	1.4



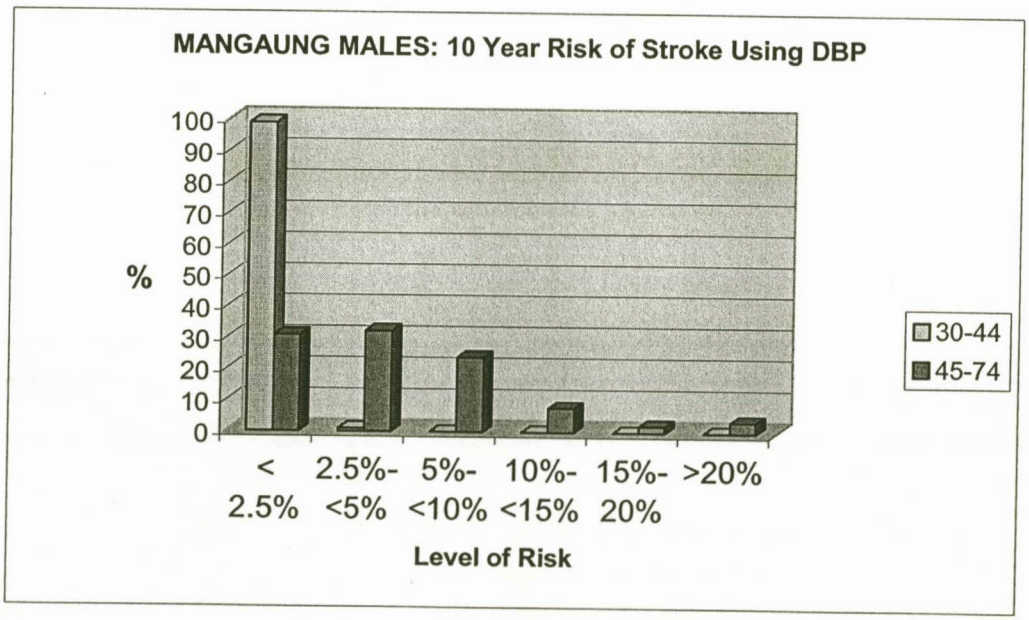
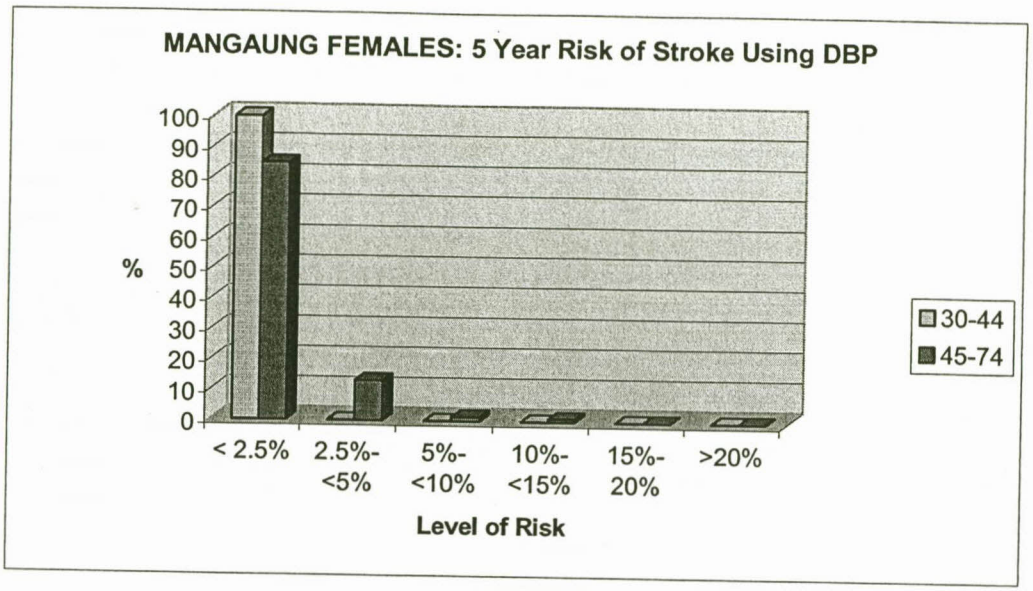


Fig. 12.3/11. Prediction of 5- and 10-year risk of stroke in Mangaung Using DBP



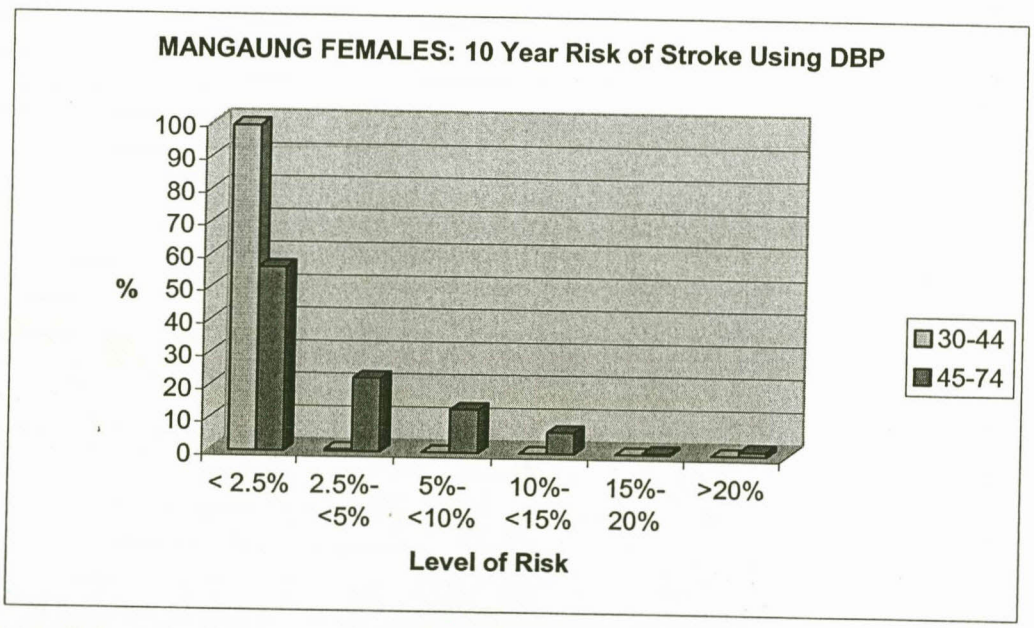
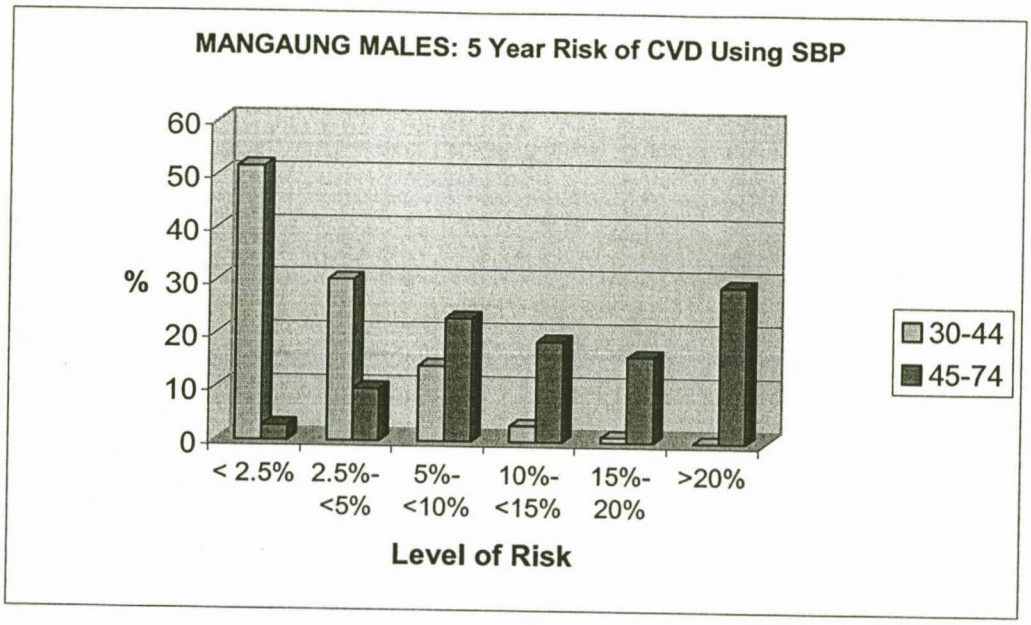


Fig.12.3/12. Prediction of 5- and 10-year risk of stroke in Mangaung females Using DBP

TABLE 12.3/12. Cardiovascular Disease Risk Profiles for Mangaung According to Framingham Prediction Equations Using Diastolic Blood Pressure: For CVD and CVD Death

	5 Year Risk of CVD						
		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20%
Mangaung	n	%	%	%	%	%	%
Males (age yr)							
30-44	99	58.6	26.3	12.1	3	0	0
45-74	143	2.8	6.3	26.6	23.1	16.1	25.2
Females (age in yr)							
30-44	165	85.5	9.7	3.6	1.2	0	0
45-74	214	12.6	23.8	29.9	15.4	8.4	9.8
	10 Year Risk of CVD						
		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20%
Mangaung	n	%	%	%	%	%	%
Males (age yr)							
30-44	99	19.2	26.3	30.3	12.2	9.1	3
45-74	143	0	2.1	4.9	11.2	15.4	66.4
Females (age in yr)							
30-44	165	55.8	19.4	18.2	3	1.8	1.8
45-74	214	1.4	6.5	18.2	21.5	15.9	36.5
	5 Year Risk of CVD Death						
		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20%
Mangaung	n	%	%	%	%	%	%
Males (age yr)							
30-44	99	100	0	0	0	0	0
45-74	143	70.6	13.3	10.5	2.8	2.1	0.7
Females (age in yr)							
30-44	165	100	0	0	0	0	0
45-74	214	84.6	8.4	5.6	1.4	0	0
	10 Year Risk of CVD Death						
		< 2.5%	2.5%-<5%	5%-<10%	10%-<15%	15%-20%	>20%
Mangaung	n	%	%	%	%	%	%
Males (age yr)							
30-44	99	85.9	13.1	1	0	0	0
45-74	143	24.5	20.3	26.6	9.8	7	11.9
Females (age in yr)							
30-44	165	99.4	0.6	0	0	0	0
45-74	214	54.2	15	17.3	4.7	6.1	2.8



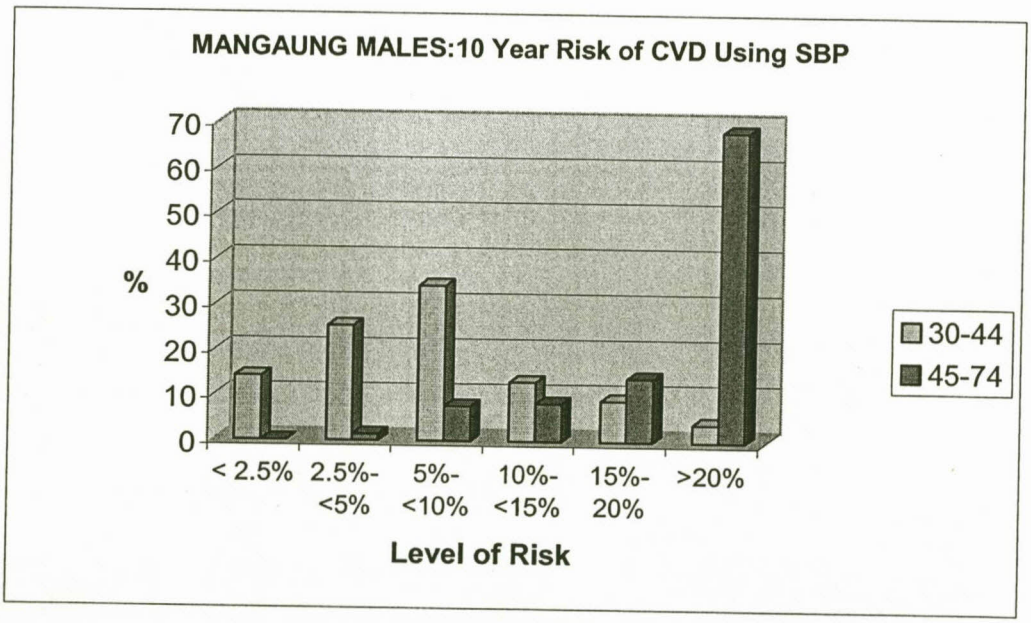
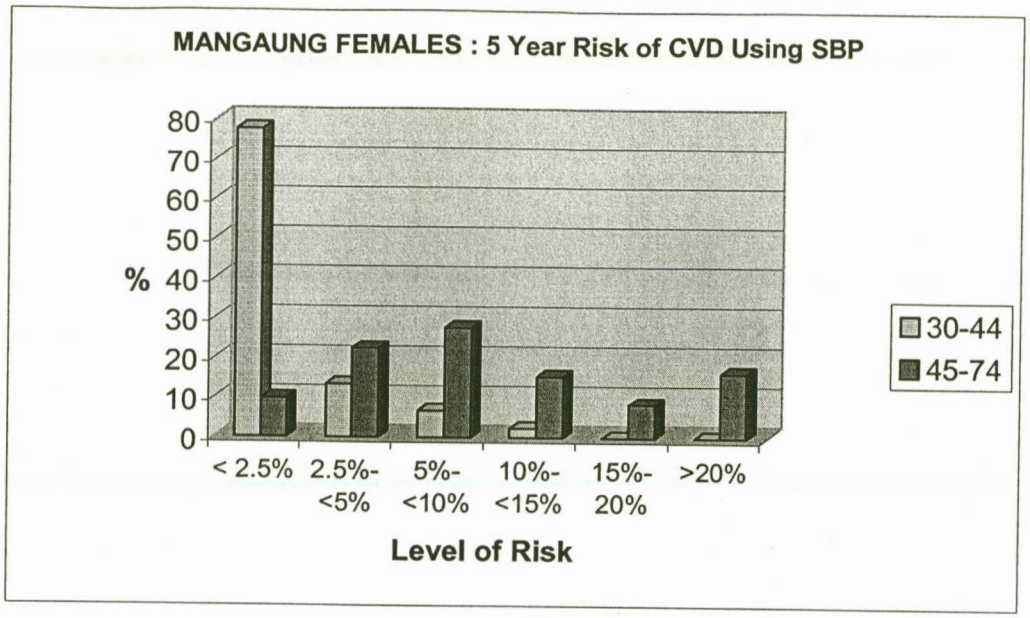


Fig. 12.3/13. Prediction of 5- and 10-year risk of CVD for Mangaung males using SBP.



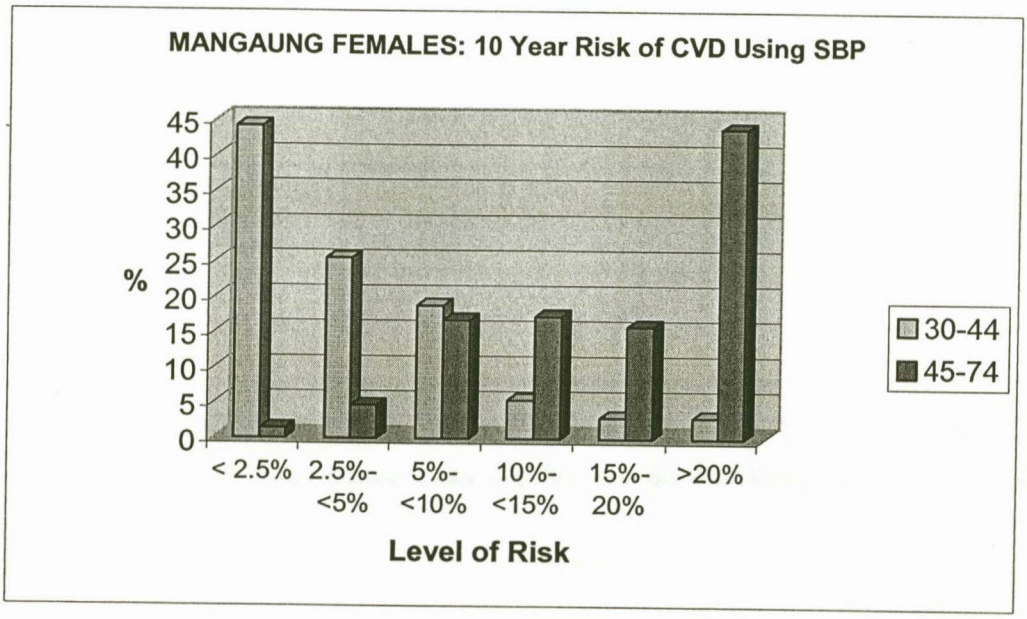
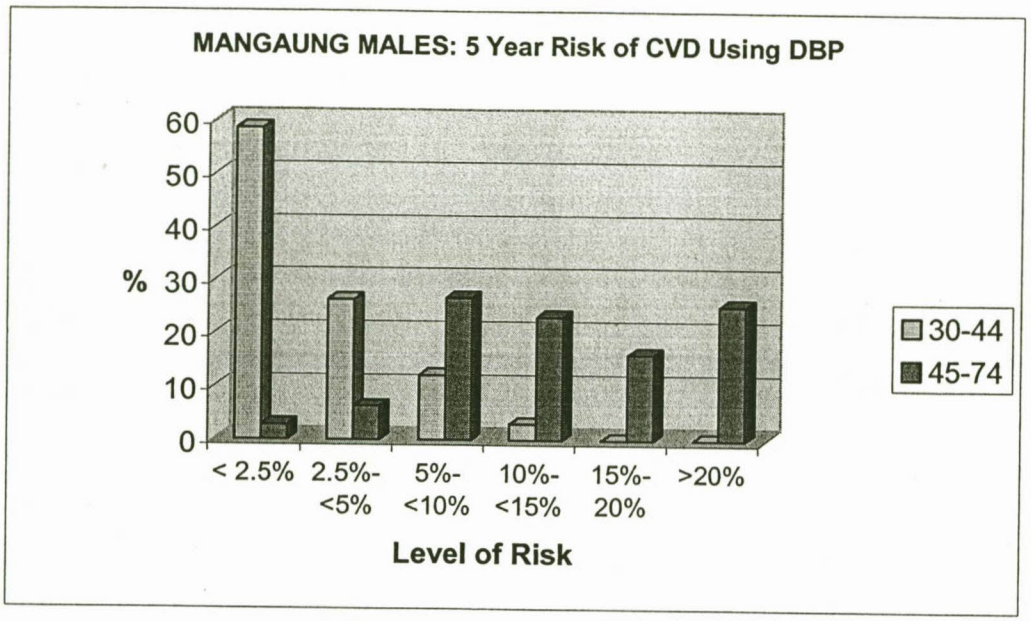


Fig. 12.3/14. Prediction of 5- and 10-year risk of CVD for Mangaung females using SBP.



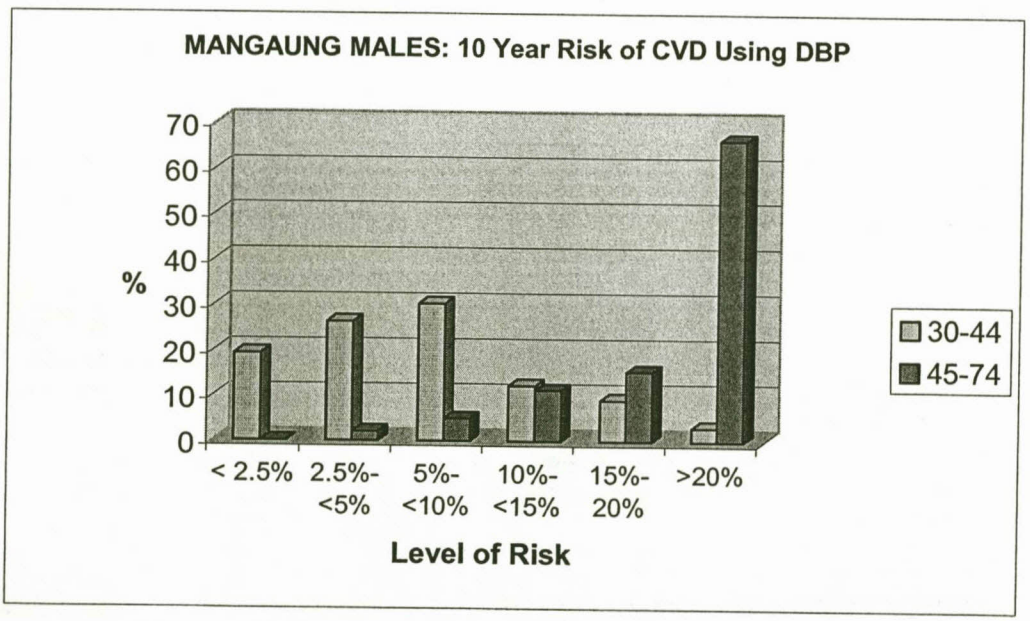
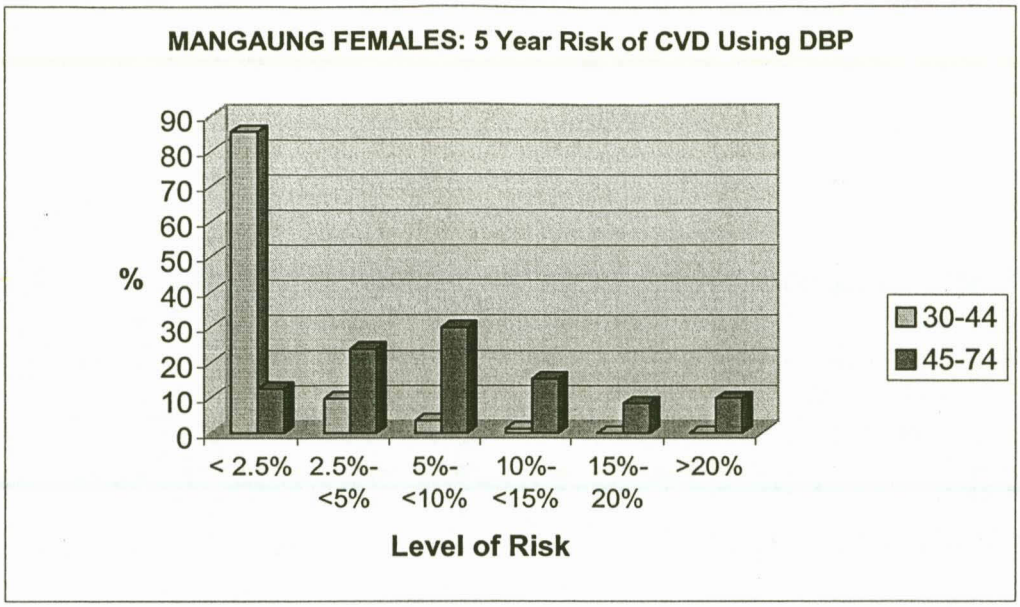


Fig. 12.3/15. Prediction of 5- and 10-year risk of CVD for Mangaung males using DBP



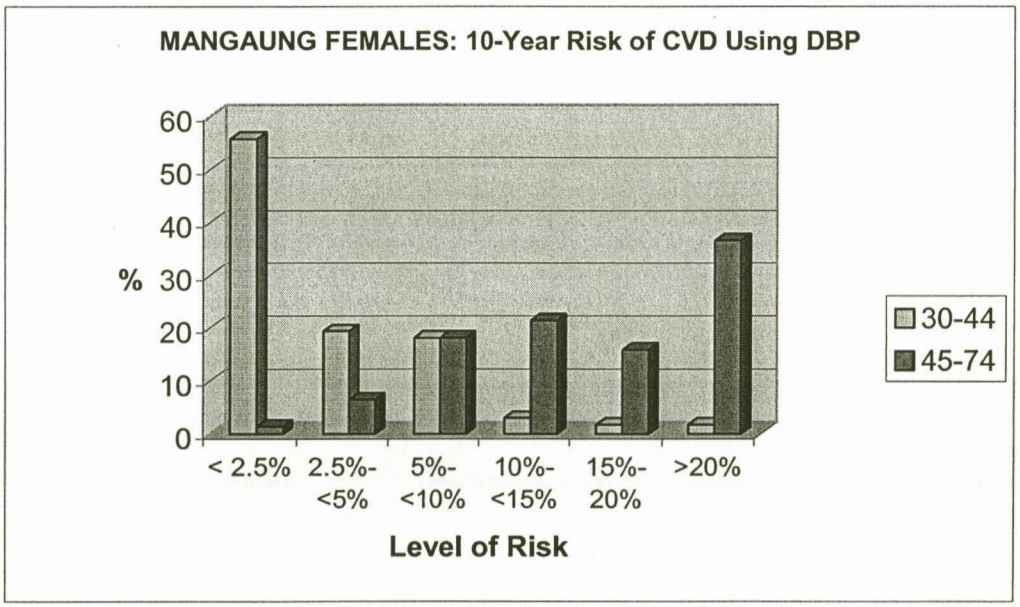


Fig. 12.3/15. Prediction of 5- and 10-year risk of CVD for Mangaung females using to DBP.

Summary

The clustering of two or more CV risk factors occurred frequently in both males and females in both samples. Although 21% to 23.6% of both samples harboured at least two components of the deadly quartet, no ECG evidence of an increased risk of CHD in those with the quartet compared to those without the quartet could be found. This is possibly the first time that the proposed WHO criteria of the metabolic syndrome were applied to a black African population. The prevalence of the metabolic syndrome without microalbuminuria, was 30.7% and 30.5% in Qwaqwa and Mangaung. ECG abnormalities frequently associated with CHD were not more common in those with the metabolic syndrome compared to those without the metabolic syndrome. It can be concluded that although the metabolic syndrome was present in more than thirty percent of the subjects, the syndrome has not yet resulted in an increase in CHD as judged from resting ECG's. These subjects, however, remain at increased future risk of CHD.

Although the prevalence of CHD was not increased in subjects with features of the metabolic syndrome, stroke and cardiac failure are not uncommon in the black communities and both contribute substantially to morbidity and mortality in blacks. The Framingham prediction equations were useful to calculate increased risk for these common conditions and may be useful in identifying subjects who might benefit from more intensive risk factor management.

The high prevalence of the metabolic syndrome in the study populations may be the forerunner of a sharp increase in the prevalence of CHD in the black population in the near future. Time for preventative measures is running out. Health policy makers are advised to recognise the importance of these findings and to start planning and implementing preventative strategies. The promotion of a healthy lifestyle and public awareness of the features of the metabolic syndrome should form the heart of such a programme. Continued research in this field is necessary to measure the outcomes of any intervention programme and to monitor the prevalence and impact of the components of the metabolic syndrome in the black communities.

SECTION D

Summary, conclusions and recommendations

13 Summary, conclusions and recommendations

13.1 Summary and conclusions

The prevalence of diabetes and IGT did not differ significantly between the rural and the urban samples indicating that the rural community is possibly already well advanced in the transition process. Similarly, the prevalence of diabetes and IGT also did not differ significantly between males and females and was more common in subjects older than 45 years. The age-adjusted prevalence rates of diabetes in black subjects in two FS populations are somewhat lower than that of blacks from a Cape Town urban area but are several fold higher than in black African subjects in Cameroon and Tanzania. The prevalence rates of IGT in the FS studies are the highest recorded for any population in SA thus far. A potential implication of this finding is that the prevalence of diabetes may increase in these populations in the near future. The poor glycaemic control in known diabetics in both samples is a matter of concern but it has to be kept in mind that due to the small number of subjects in this category this observation needs to be investigated further. Measures to prevent an increase in the prevalence of diabetes and to improve the quality of health care for those already affected, should be taken urgently in these communities.

Fasting as well as 2-hour plasma glucose concentrations increased in both samples with age with the exception of the elderly group of women in Qwaqwa. The increase in 2-hour glucose concentrations with aging may result in an underestimation of the prevalence of diabetes should ADA diagnostic criteria be used instead of WHO criteria in FS black populations. This may also possibly be true for other black populations in South Africa as well as in other Sub-Saharan African populations.

The revised ADA criteria (1997) should not be accepted unconditionally at this stage. The concordance between the proposed ADA criteria and the tried and trusted WHO 1985 criteria is far from perfect and is especially poor between subjects with IFG and IGT. Since IGT as such has not been properly studied in black subjects in South Africa, it would be premature to abandon the 1985 WHO criteria at this stage. Both sets of criteria should be used and compared until

criteria at this stage. Both sets of criteria should be used and compared until greater clarity emerges as to the prognosis of subjects falling outside either the one or the other set of criteria.

An important finding was that even a mild excess in body fat as indicated by pre-obesity was associated with diabetes in both the FS populations. Pre-obesity was also associated with IGT in the urban sample. The relationship between pre-obesity and glucose intolerance was more consistent in the subgroups in the urban sample than in the rural group. Enough epidemiological evidence has been accumulated to challenge the concept of "healthy obesity" in both urban and rural black South Africans.

Central obesity was significantly associated with diabetes in both the urban and rural samples while central obesity was associated with IGT only in the urban sample. It may be hypothesized that the urban group might be more urbanized than the rural group. In the populations studied the RR for diabetes associated with central obesity was higher than that for pre-obesity. Enough epidemiological evidence has been accumulated to satisfy the first WHO criterion for the existence of the metabolic syndrome in black South Africans.

A positive association was found between the pharmacological management of hypertension and glucose intolerance in Qwaqwa but not in Mangaung except when treated hypertensives were compared to normotensive subjects in the latter population. The possibility exists that high dose thiazide therapy was used more frequently in Qwaqwa than in Mangaung. The situation might have changed since the introduction of a primary health care Essential Drug List and hypertension management guidelines since 1994. However, it is recommended that this association warrant further investigation.

This study provided for the first time serum insulin measurements as part of the 75g OGTT test in the epidemiological study of diabetes and IGT in black South Africans or possibly even in Sub-Saharan Africa. No direct comparisons were therefore possible with other African subjects. Overall, mean serum insulin levels tended to be somewhat lower in Qwaqwa subjects than in urban subjects but

levels were fairly comparable. When median insulin values were examined, this difference almost disappeared. Technical reasons like the transport of specimens may contribute to this mild difference. Fasting, 60 min and 120 min serum insulin concentrations post-glucose load were higher in subjects with diabetes and even still higher in subjects with IGT than in subjects with normal glucose tolerance. The decrease in serum insulin concentrations at 60 and 120 minutes in diabetic subjects compared to subjects with IGT in the face of higher plasma glucose levels supports also in these populations the concept of a Starling curve for the β-cell. Diabetic subjects older than 45 years secreted relatively less insulin in the fasting state (relative to the fasting hyperglycaemia) and absolutely less insulin at 120 min than normal subjects indicating β-cell failure. The HOMA model assessment supported this observation. It also showed that older diabetic subjects were particularly insulin resistant compared to normal subjects, again supporting De Fronzo's (1988) previous observations in older subjects in both these populations. The HOMA model is a very useful epidemiological tool but deserves to be evaluated and validated in the South African black population as well. Urban subjects tended to be more insulin resistant than rural subjects, but more statistical analysis will have to done to explore this possibility. The positive association between WHR and serum insulin levels demonstrated for both males and females in both populations supports the importance of central obesity in the development of insulin resistance and glucose intolerance. These observations provide more evidence to challenge the concept of healthy obesity in black females. A possible mechanism for the association between central obesity and diabetes also in black South Africans is thus provided by these population-based studies. Since central obesity is potentially preventable as well as reversible, these findings provide epidemiological support for these efforts.

Fasting serum C-peptide concentrations < 300 pmol/l were present in 11.2% of normal subjects. Fasting C-peptide concentrations in subjects with IGT were significantly higher than in normal subjects while in diabetics it did not differ significantly from normal although fasting plasma glucose levels were higher in diabetics. This observation supports a diagnosis of Type 2 diabetes in the vast majority of cases. This observation is also indicative of failing β-cell function. An unexpected decrease in C-peptide levels was observed in men in the age-group

55-64 years that corresponded to a similar decrease in insulin concentrations. This phenomenon was unrelated to renal function. Overall, C-peptide concentrations provided much the same information than serum insulin concentrations with the exception that no obvious age-related decline in C-peptide concentrations could be detected.

Proinsulin levels appeared higher in urban than in rural subjects. Again one may speculate that the difference is due to more advanced urbanisation of the former. A unique finding was that fasting and 60 min proinsulin concentrations increased with aging in normal subjects in the face of unchanged β-cell function and increased insulin resistance while corresponding insulin concentrations (and fasting C-peptide concentrations) nearly remained the same. This finding is in accordance with the concept that altered β-cell pathways of insulin secretion may operate in glucose intolerance and possibly also in the aging process. This hypothesis deserves further investigation.

In neither of the two FS populations was any correlation found between plasma glucose concentrations and final adult height. Adult height was the only available variable to examine the foetal origins hypothesis in the pathogenesis of Type 2 diabetes these communities. The contribution of the foetal origins hypothesis in the pathophysiology of Type 2 diabetes in FS communities deserves further study.

The traditional risk factors for diabetes namely age, WHR and pre-obesity were also identified as risk factors for glucose intolerance (IGT + diabetes) in both the FS populations studied. Other additional unique risk factors for Africans were also identified namely hypercholesterolaemia and treated hypertension in the Qwaqwa population and hypertriglyceridaemia, treated hypertension and pre-obesity in the Mangaung population. A clustering of cardiovascular risk factors was observed with regression analysis in patients with glucose intolerance. With regression analysis pre-obesity emerged as a risk factor, only in Mangaung subjects, while the odds ration (OR) for WHR was also higher in Mangaung subjects. It may be hypothesised that urbanisation is more advanced in Mangaung than in Qwaqwa.

The FS populations had the highest prevalence rates for IGT in South Africa as well as in Sub-Saharan Africa. For the first time were modifiable risk factors for IGT in black South Africans identified. These were WHR for subjects in both studies as well as hypercholesterolaemia in Qwaqwa subjects and pre-obesity and hypertriglyceridaemia in Mangaung subjects.

Since IGT as such has not been properly studied in black subjects in South Africa, it would be premature to abandon the 1985 WHO criteria at this stage. Both sets of criteria should be used and compared until greater clarity emerges as to the prognosis of subjects falling outside either the one or the other set of criteria. This is especially important for subjects diagnosed with IGT.

The expected rise in mean diastolic and systolic blood pressure with age was observed for both sexes and populations. This rise was more pronounced for systolic blood pressure in both populations. The increase in mean diastolic as well as mean systolic blood pressure across the age centiles for men as well as for mean systolic blood pressure for women was more pronounced in the urban than in the rural group. This important observation should be explored further to establish whether this was a true difference possibly attributable to a more advanced urbanisation process in the Mangaung population.

Application of a reasonably strict definition of hypertension such as a systolic blood pressure equal to or exceeding 140 mm Hg and / or a diastolic blood pressure equal to or exceeding 90 mm Hg, resulted in an age-standardised prevalence of hypertension of 48.4% (44.3% in males and 51.3% in females) in Qwaqwa and 47.3% (43.4% in males and 50.4% in females) in Mangaung. These rates are considerably higher than that reported for black subjects in the Cape Peninsula or in Zimbabwe.

By applying the more conservative WHO definition, the age- and sex-adjusted prevalence of hypertension was 29.2% (22.1% in males and 34.5% in females) in Qwaqwa and 30.3% (22.8% in males and 36.3% in females) in Mangaung. Up to 14% of subjects in the young age group of 25-34 years had hypertension according to this definition. These rates are higher than that previously reported for urban and rural Zulus as well as for Cape Peninsula blacks. The SADHS

reported much lower rates for hypertension in the FS although these rates were also among the highest in the SA. Methodological differences such as the sampling procedure, technique of BP measurement and the place where BP was measured (community health centre vs. home) may account for some of the difference. It is interesting that the prevalence of hypertension in FS blacks are very similar to that reported for Afro-Caribbean subjects in Birmingham. Up to 83% of elderly subjects was hypertensive while isolated systolic hypertension was present in up to 25% of the elderly. Overall, these rates are unacceptably high and calls for action not only to detect and aggressively manage hypertension at an earlier stage but also to implement preventative measures.

The prevalence of hypertension was no different between subjects living in semi-rural and rural areas of Qwaqwa possibly indicating that those living in the former areas have attained the same level of urbanization as those living in the semi-rural areas.

After adjusting for age and sex, the risk of hypertension was clearly increased in obese (BMI $\geq$ 25 kg/m^2) subjects in both Qwaqwa and Mangaung. This finding is agreement with other studies in black populations in SA, in Africa and in the UK Overall this increased risk was higher in Qwaqwa subjects than Mangaung subjects and cannot be explained on the grounds of urbanisation. Other factors such as family history of hypertension, physical activity and dietary factors need to be investigated in an attempt to explain this paradox. The confirmation of obesity as a risk factor for hypertension in the FS populations supports the call for weight management programmes also in the FS.

In both the FS populations WHR was significantly associated with increased risk of hypertension, a risk that was particularly high for young male subjects. A second criterion to satisfy the WHO definition for the existence of the metabolic syndrome in FS blacks has been established.

The results described in the FS study are the first from a population-based study in SA and possibly in sub-Saharan Africa to contradict the hypothesis that hyperinsulinaemia is an independent determinant of hypertension in black subjects. The implication of this finding is that a different link between

hypertension and the metabolic syndrome in black subjects should be looked for if this syndrome does exist in this ethnic group.

The findings of this study on a limited number of users of current oral contraceptives were that these agents are not associated with hypertension. Studies on larger numbers of subjects are necessary to resolve this issue.

Significant urban-rural and male-female differences between the correlation of anthropometrical measurements and mean diastolic as well as systolic blood pressure were found. General adiposity rather than body fat distribution correlated best with blood pressure in all subjects except Mangaung males where central adiposity also emerged as a significant anthropometrical variable. If anthropometrical measurements were to be selected for clinical use for instance in the screening and monitoring of at risk or hypertensive women, then it seems that triceps skin fold thickness and buttock circumference (or hip circumference) emerged as the most useful. In Qwaqwa men triceps skin fold thickness and in Mangaung men waist-to-hip circumference in addition to triceps skin fold thickness proved to be the most consistent measurements. In all subjects percentage body fat correlated well with both systolic and diastolic blood pressure. Since percentage body fat correlates well with BMI the latter measurement must be added to the list. Comparing the correlation between anthropometrical and blood pressure data from the FS study with that of other available studies from sub-Saharan Africa, it becomes apparent that the same chronic diseases of lifestyle do not emerge at the same rate and in the same sequence in different populations, a phenomenon that may be referred to as the emergence of non-communicable diseases during the transition (non-synchronised "coca-colanisation").

More than 50% of electrocardiographs obtained from both populations were abnormal in some way. High amplitude R waves followed by T wave abnormalities were the most common findings. Subjects with hypertension in both populations had a significantly increased risk of having an abnormal ECG, 43% in Qwaqwa and in 32% in Mangaung. Q and QS patterns possibly indicating coronary heart disease were present in ECG's of 1.6% and 2.2% of subjects from Qwaqwa and Mangaung respectively while as many as 5.4% of older males in

Qwaqwa exhibited this ECG abnormality. The highest prevalence of this abnormality in Mangaung was 8.9% and, surprisingly, occurred in older hypertensive women. These abnormalities are suggestive that CAD does occur in significant numbers of subjects in both populations with the urban community slightly ahead of the rural community. Interestingly in the rural community the risk of Q and QS patterns were not significantly increased in hypertensive subjects indicating that other risk factors must be involved while in Mangaung hypertension was identified as a risk factor for these ECG abnormalities.

The RR of LV hypertrophy as indirectly indicated by high amplitude R waves was significantly increased in subjects with hypertension in both populations. LV hypertrophy is a predecessor of heart failure and therefore is this an important finding. The high prevalence of high amplitude R waves in both communities emphasizes the need for early detection and optimal management of hypertension to reduce the burden of heart failure in these communities. The FS studies are the first population-based studies of its kind in SA and possibly in sub-Saharan Africa on representative samples of black subjects that demonstrate the relationship between hypertension and LV pathology. Population-based research also needs to be done to verify the meaning of high amplitude R waves in these subjects.

Arrhythmias occurred in 7.8% and 7.1% of rural and urban subjects and the RR for this ECG abnormality was significantly increased in subjects with hypertension in Mangaung but not in Qwaqwa. This implies that other risk factors for arrhythmias need to be found in Qwaqwa subjects. Arrhythmias, including atrial fibrillation, are important risk factors for stroke. The early detection and proper management of hypertension can also reduce the risk for catastrophes such as these – at least in the urban population. More research needs to be done in these communities to further describe the causes and complications of atrial fibrillation.

The significantly increased relative risks for proteinuria as well as raised serum urea levels in hypertensive compared to normotensive subjects in the FS studies are most likely due to early hypertensive nephrosclerosis. The fact that serum creatinine concentrations did not support the proteinuria and serum urea

findings, need to be studied in more depth. The incidence and rate of progression of early hypertensive nephrosclerosis to ESRD in the SA black population is not known and remains an important area for further study. Programmes for the early detection and tight control of blood pressure in FS communities to decrease the burden of ESRD are highly recommended. It is noteworthy that the RR of both proteinuria and raised serum urea levels in hypertensive subjects in Mangaung exceeded that of subjects in Qwaqwa. A possible explanation might be that the burden of hypertension is higher in the urban group.

Sufficient evidence was collected in this rural-urban study of a representative sample of the populations of Qwaqwa and Mangaung to conclude that hypertension is a frequent occurrence, that the risk of hypertensive complications is significantly increased including LV hypertrophy, CAD, hypertensive nephrosclerosis and hypertensive retinopathy. More information is needed to determine the actual incidence and rate of progression of target organ damage in these populations. A programme should be established for the early identification and effective treatment of hypertension according to existing guidelines (Milne, 2001), in FS communities to reduce the burden of this common chronic condition with potentially devastating complications.

A small positive secular trend in mean adult stature was observed for women in Qwaqwa. For Qwaqwa males the trend was absent. The mean height of Qwaqwa males born in c. 1965 was 6 mm taller than men born 40 years earlier. To put this into perspective, the expected increase in early adult life was 0.6 cm per decade (Tobias, 1990). Men and women in Mangaung exhibited an absent secular trend but the youngest generation of men born in c. 1965 was conspicuously taller than any other group of men born before them. The most obvious explanation for the absence of a secular trend in mean adult stature in both populations is poor socio-economic circumstances and nutrition spanning over at least 4 decades.

The sexual dimorphism in terms of BMI was conspicuous for both populations. Mean BMI for women was excessive in all age categories and increased over the age deciles. The mean BMI of men in the two populations were very similar and

appropriate. The prevalence of obesity in women ranged between 37% and 41% exceeding the national prevalence by 10%. The prevalence of obesity in SA black women is among the highest recorded in Africa. An interesting but macabre observation was the decline in the prevalence of obesity during the period 1991-1997 possibly due to the HIV/AIDS epidemic. The implication is that a bimodal distribution in BMI may develop characterising two populations of women, one with and the other without HIV/AIDS.

Most women in both studies exhibited an unfavourable body fat distribution while half of the men in Mangaung had a predominantly central fat distribution. The latter was associated with excessive risk of glucose intolerance, hypertension and dyslipidaemia in both sexes and both populations. The WHO definitions of central adiposity were also shown to be applicable to both these populations. Although skin fold thickness is rarely measured in daily clinical practice it was useful not only to demonstrate the degree of adiposity and body fat distribution in both sexes but the sum of five skin folds was an excellent indicator of sexual dimorphism of fatness. Percentage body fat calculated from skin fold thickness measurements, increased with age in both sexes and both populations but peaked a decade later in Qwaqwa women than in Mangaung women. The meaning of this phenomenon is not clear but differences in physical activity and or nutrient intake may be responsible.

Overweight and obesity and thus adiposity in general were associated with glucose intolerance, hypertension and dyslipidaemia in both populations especially in the Mangaung population. The risk of these abnormalities was especially pronounced in subjects of both sexes with features of central obesity. It is clear that "healthy obesity" is an outdated concept and should be abandoned. (One would not think of hypertension in terms of "healthy hypertension" in the absence of target-organ damage).

Mean TC concentrations increased slightly across the age deciles for Mangaung males and females and Qwaqwa females but changed very little in Qwaqwa men. Mean TC levels were overall higher in females than males in most but not all of the age categories. Mangaung subjects in most of the age categories had higher TC levels than Qwaqwa subjects possibly indicating that the former population

consumed a diet higher in saturated animal fat than the latter. Mean TC for both males and females in both populations also exceeded that of blacks in the Cape Peninsula. In a significant proportion of subgroups in the Mangaung sample the mean TC level exceeded the desirable level of 5.2 mmol/L. Protective ratios of HDL-C:TC were present in both sexes in both populations and in all age groups. Protective HDL-C to TC ratios were somewhat lower in FS blacks than Cape Peninsula blacks but were still much more favourable than ratios reported for white South Africans.

Hypercholesterolaemia at a high level of risk was already present in a significant percentage of males and females in all the age groups in both populations. This is one of the major CV risk factors that had a low prevalence until 2 decades ago (Seftel, 1978). A finding of some concern was the group of young males in Qwaqwa who had high TC levels. Fortunately these younger subjects still had higher levels of protective HDL-C to TC ratios than older subjects. The abnormalities described warrant a follow-up study in this region to establish trends of lipid levels during the period of nutrition transition. Due to the potential serious long-term CV complications of these prevalent dyslipidaemias, the health authorities should seriously consider a screening and life-style intervention programme.

The risk of elevated TG levels in overweight compared to non-overweight males was significantly increased in all male subjects in both samples. This was also the case for most females in both populations. Central obesity as an important feature of the metabolic syndrome was overall strongly associated with hypertriglyceridaemia in both populations. Apart from obesity other contributing factors to elevated TG levels should also be considered including alcohol, diet and lack of exercise.

Lifestyle intervention at the community level should be undertaken to try and improve these metabolic abnormalities. The impact of such an intervention should be closely monitored in a follow-up study to observe possible changes in lipid levels and patterns associated the nutrition transition.

Obesity was associated with a significantly increased risk of elevated total cholesterol in the Qwaqwa sample mostly due to a greater risk in male subjects. In the Mangaung sample the risk was only significantly increased in males. Although the risk of CHD is still low in SA blacks with increased levels of TC, it may be predicted on the grounds of other studies that the risk of CHD will not remain low indefinitely. The contribution of poverty to elevated TC levels in the FS populations also warrants investigation. The prevalence rates of unfavourable HDL-C:TC ratios were significantly increased in overweight compared to non-overweight subjects in both populations and in both sexes with the exception of young black women in Mangaung. An interesting pattern of escalating risk for unfavourable HDLC:TC ratios emerged from both studies, with the lowest RR in young women and the highest RR in younger males in Qwaqwa. The risk of elevated TG levels in overweight compared to non-overweight subjects was significantly increased in both samples. Apart from obesity other contributing factors for elevated TG levels should also be considered including alcohol, diet and lack of exercise.

Central obesity was significantly associated with hypercholesterolaemia in Mangaung subjects and this association was particularly strong in young women. This association was absent in the Qwaqwa sample, emphasising the complexity of central obesity and its co-morbidities in epidemiological studies. Care must be exercised to extrapolate results from one population to another. The association between central obesity and unfavourable HDLC to TC ratios was particularly strong in both samples. This was a consistent finding in all the subgroups with the exception of young females in Qwaqwa and young males in Mangaung. Central obesity as an important feature of the metabolic syndrome was overall strongly associated with hypertriglyceridaemia in both samples.

Overall, no significant differences were found between the two samples in the prevalence rates of any of the lipid abnormalities that were described. It can therefore be concluded that the urbanisation process in the rural and semi-rural areas of Qwaqwa were as far advanced, as was the case in the urban area of Mangaung.

Significant other associations between fasting hypertriglyceridaemia and hyperinsulinaemia, a history of alcohol use, and raised levels of s-GGT were found in this study. Most of the factors that were associated with increased fasting TG levels are interrelated and it is therefore not possible to hypothesise on the contribution of each. A healthy lifestyle including weight loss if overweight, moderate daily exercise such as brisk waking, and limited use of alcohol are all inexpensive measures that may improve most of these metabolic abnormalities (WHO, 2001).

A follow-up study to monitor the possible future changes in lipid levels and abnormalities as a result of the nutrition transition is not only warranted but also essential. Lifestyle intervention at the community level should already be regarded as a priority considering the unfavourable lipid profile that emerged from in these populations this study.

The clustering of two or more CV risk factors occurred frequently in both males and females in both samples. Although 21% to 23.6% of both samples harboured at least two components of the deadly quartet, no ECG evidence of an increased risk of CHD in those with the quartet compared to those without the quartet could be found. This is possibly the first time that the proposed WHO criteria of the metabolic syndrome were applied to a black African population. The prevalence of the metabolic syndrome without microalbuminuria, was 30.7% and 30.5% in Qwaqwa and Mangaung. ECG abnormalities frequently associated with CHD were not more common in those with the metabolic syndrome compared to those without the metabolic syndrome. It can be concluded that although the metabolic syndrome was present in more than thirty percent of the subjects, the syndrome has not yet resulted in an increase in CHD as judged from resting ECG's. These subjects, however, remain at increased future risk of CHD.

Although the prevalence of CHD was not increased in subjects with features of the metabolic syndrome, stroke and cardiac failure are not uncommon in the black communities and both contribute substantially to morbidity and mortality in blacks. The Framingham prediction equations were useful to calculate

increased risk for these common conditions and may be useful in identifying subjects who might benefit from more intensive risk factor management.

The high prevalence of the metabolic syndrome in the study populations may be the forerunner of a sharp increase in the prevalence of CHD in the black population in the near future. Time for preventative measures is running out. Health policy makers are advised to recognise the importance of these findings and to start planning and implementing preventative strategies. The promotion of a healthy lifestyle and public awareness of the features of the metabolic syndrome should form the heart of such a programme. Continued research in this field is necessary to measure the outcomes of any intervention programme and to monitor the prevalence and impact of the components of the metabolic syndrome in the black communities.

13.2 Recommendations

The World Health Organization's recommendations regarding the prevention and management of the global epidemic of obesity (WHO, 2000) should be adapted to develop strategies for the prevention and management of chronic diseases of lifestyle in the Free State.

13.2.1 Prevention strategies

The prevention of weight gain and thus overweight and obesity at population level will have a significant negative impact on the development of insulin resistance, type 2 diabetes, hypertension, dyslipidaemia and the metabolic syndrome.

The development of strategies for the prevention of chronic diseases of lifestyle requires action at three levels:

- the public health level (directed at everyone in the population)
- selective prevention (directed at subgroups of the population with an above average risk of developing chronic diseases of lifestyle e.g. those with a sedentary life-style, a family history of hypertension, diabetes and obesity)

- targeted prevention (directed at high risk individuals e.g. with existing weight problems but who are not yet obese)

Small-scale pilot projects should be carried out to determine the practicality and appropriateness of specific intervention strategies. The following variables should be measured at baseline and periodically after an intervention programme: the prevalence of obesity, body fat distribution, glucose tolerance status, blood pressure, lipid levels, nutrient intake and levels of physical activity.

13.2.2 Improving physical activity levels and healthy eating

The WHO emphasized that prevention of chronic diseases of lifestyle should start early in life (WHO, 2000). The development and maintenance of life-long healthy eating and physical activity patterns will also prevent the development of glucose intolerance, dyslipidaemia, hypertension and the metabolic syndrome to a large extent.

- Schools should promote physical activity by incorporating a variety of recreational activities into teaching curricula. Learners should be empowered to obtain the necessary knowledge and food skills to encourage healthy eating.
- Community facilities should be designed and traffic and town planning policies should be developed to facilitate everyday walking and exercise in children and adults. It is important to prevent a decline in physical activity in developing communities where physical activity still forms part of a traditional lifestyle.
- Workplaces should provide facilities for the evaluation of employees for the presence of chronic diseases of lifestyle and to educate workers about management and prevention of these conditions. Workplaces should also promote physical activity by providing exercise and changing facilities.
- Consumers should be empowered to interpret food labels, to demand and to recognise food products of high nutritional quality. Novel ways of food labelling should be developed to empower subjects in communities where literacy rates are still low.

13.2.3 Public health strategies

Multi-sectoral public health strategies aimed to reduce the obesity-promoting aspects of the environment and to improve a population's knowledge about obesity and other chronic diseases of lifestyle and their management should be developed. Stakeholders in such programmes include central, provincial and local government, communities, consumers, the food industry and the media.

13.2.4 Improving the quality of primary health care

A great need exists for the development of infrastructure and capacity to diagnose and manage chronic diseases of lifestyle effectively at primary care level in the Free State.

- Pilot projects should be planned to examine the basic infrastructure at randomly selected primary health care facilities and to determine the capacity and skills of staff to effectively diagnose and manage chronic diseases of lifestyle before and after the implementation of well-designed and appropriate intervention programmes and treatment protocols.
- Communities should be involved to increase awareness of chronic diseases of lifestyle and to educate and empower individuals to assume greater responsibility for their own health.
- The efficacy of management protocols should be evaluated over a period of at least one year and preferably 2- 5 years.

13.2.5 The need for evaluation

Regular surveys such as the ones that formed the basis for this thesis should be conducted in the Free State to determine time-trends in the prevalence of the chronic diseases of lifestyle described in this work. The establishment of a research centre to initiate, implement and co-ordinate such surveys should be considered. Such a research centre should also assume responsibility for the regular auditing of the quality of care that patients who suffer from chronic diseases of lifestyle receive at the different levels of health care in the Free State.

References

Abate N, Vega GL, Grundy SM. (1993). Variability in cholesterol content and physical properties of lipoproteins containing apolipoprotein B-100. *Atherosclerosis* 104:159-171.

Adult Treatment Panel III. (2001). Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive summary of the third report of the National Cholesterol Education Program (NCEP) Expert Panel on detection, evaluation, and treatment of high blood cholesterol in adults. *Journal of the American Medical Association.* 285:2486-2497.

Adult Treatment Panel II. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (1994). National Cholesterol Education Program. Second report of the expert panel on detection, evaluation, and treatment of high blood cholesterol in adults. Circulation 89:1333-1445.

Agostino RB, Grundy S, Sullivan L, et al. (2001). Validation of the Framingham coronary heart disease prediction scores. *Journal of the American Medical Association* 286:180-187.

Ahrén B and Corrigen CB. (1984). Prevalence of diabetes mellitus in North-Western Tanzania. *Diabetologia* 26:333-336.

Akinkugbe Oo and Ojo OA. (1969). Arterial Pressures in Rural and Urban Populations in Nigeria. *British Medical Journal* 2:222-224.

Akinkugbe OO. (1985a). *Hypertension in blacks. Year Book Medical Publishers*, Chicago, pp. 3-5.

Akinkugbe OO. (1985b). *Hypertension in Blacks. Year Book Medical Publishers*, Chicago, p8.

Alberti KGMM and Zimmet PZ. (1998). Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: Diagnosis and classification of diabetes mellitus. Provisional report of a WHO consultation. *Diabetic Medicine* 15:539-553.

Alderman MH. (2002). Uric acid and cardiovascular risk. *Current Opinion in Pharmacology* 2(2):126-130.

Altshuler D, Hirschhorn J, Klannemark M, et al. (2000). The common PPARγ Pro12Ala polymorphism is associated with decreased risk of type 2 diabetes. *Nature Genetics* 26:76-80.

American Diabetes Association. (2000). Type 2 diabetes in children and adolescents. *Diabetes Care* 23:381-389.

American Diabetes Association. (2002). Clinical Practice Recommendations. www.diabetes.org

Amoah AGB, Owusu SK, Adjei S. (2002). Diabetes in Ghana: a community based prevalence study in Greater Accra. *Diabetes Research and Clinical Practice* 56:197-205.

Amos AF, McCarty DJ, Zimmet PZ. (1997). The rising global burden of diabetes and its complications: Estimates and projections to the year 2010. *Diabetic Medicine* 14:S7-S84.

Anderson KM, Odell PM, Wilson PWF et al. (1991). Cardiovascular disease risk profiles. *American Heart Journal* 121:293-8.

Antonis A and Bersohn I. (1960). Serum triglyceride levels in South African Europeans and Bantu and in ischaemic heart disease. *The Lancet* :998-1002.

Antonis A, Bersohn I. The influence of diet on serum triglycerides in South African white and Bantu prisoners. *The Lancet* 1961; 1 :3-9.

Argyropoulos G, Brown A, Willi SM, et al. (1998). Effects of mutations in the human uncoupling protein 3 gene on the respiratory quotient and fat oxidation in severe obesity and type 2 diabetes. *Journal of Clinical Investigation* 102:1345-51.

Assmann G and Shulte H. (1992). Relation of high-density lipoprotein cholesterol and triglycerides to incidence of atherosclerotic coronary artery disease (the PROCAM experience). *American Journal of Cardiology* 70:733-737.

ATP III Panel. (2001). Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. National Cholesterol Education Program (NCEP). Adult Treatment Panel III (ATP III). www.nhlbi.nih.gov.

Austin M, Hokanson JE, Edwards KL. (1998). Hypertriglyceridemia as a cardiovascular risk factor. *American Journal of Cardiology* 81:(4A)7B-12B.

Avogaro P, Cazzolato G, Bon GB. et al. (1979). Are apolipoproteins better discriminators than lipids for atherosclerosis? . *The Lancet* :901-903.

Bachman MO, Eachus J, Hopper CD, et al. (2001). Socio-economic inequalities in diabetes complications, control, attitudes and health service use: a cross-sectional study. (In press).

Barker DJP, Osmond C, Golding J, et al. (1986). Growth in utero, blood pressure in childhood and adult life, and mortality from cardiovascular disease. *British Medical Journal* 298:564-7

Barker DJP, Winter PD, Osmond C. (1989). Weight in infancy and death from ischaemic heart disease. *The Lancet ii*:577-580.

Barker DJP, Bull AR, Osmond C, (1990). Fetal and placental size and risk of hypertension in adult life. *British Medical Journal* 301:259-262.

Barker DJP, Hales CN, Fall CHD, et al. (1993). Type 2 (non-insulin-dependent) diabetes mellitus, hypertension and hyperlipidaemia (Syndrome X): relation to reduced fetal growth. *Diabetologia* 36:62-67.

Barker DJP. (2001). The malnourished baby and infant. *British Medical Bulletin* :60:69-88.

Barrett-Conner EL, Cohn BA, Wingard DL, et al. (1991). Why is diabetes mellitus a stronger risk factor for fatal ischaemic heart disease in women than in men? The Rancho Bernardo Study. *Journal of the American Medical Association* 265:627-631.

Blair D, Habicht JP, Sims EAH, et al. (1984). Evidence for an increased risk for hypertension with centrally located body fat, and the effect of race and sex on this risk. *American Journal of Epidemiology* 119:526-540.

Beck-Nielsen H and Groop L. (1994). Metabolic and genetic characterization of prediabetic states. Sequence of events leading to non-insulin-dependent diabetes mellitus. *Journal of Clinical Investigation* 94:1714-1721.

Bengtsson K, Orho-Melander M. Melander O, et al. (2001a). Beta-2-adrenergic receptor gene variations and hypertension in subjects with type 2 diabetes. *Hypertension* 37: 1807-8.

Bengtsson K, Melander O, Orho-Melander M et al. (2001). Polymorphism in the beta- 1-adrenergic receptor and hypertension. Circulation 104:187-190.

Bennet PH. (1991). Classification and diagnosis of diabetes mellitus and impaired glucose tolerance. In: Pickup JC and Williams G, eds. *Textbook of Diabetes*, Blackwell Scientific Publishers, Oxford, pp. 37-44.

Berger GMB and Marais AD. (2000). Diagnosis, management and prevention of the common dyslipidaemias in South Africa – Clinical Guideline, 2000. South African Medical Association and Lipid and Atherosclerosis Society of Southern Africa Working Group. *South African Medical Journal* 90:164-178.

Bersohn I and Wayburne S. (1956). Serum cholesterol concentration in new-born African and European infants and their mothers. *American Journal of Clinical Nutrition* 4:117-123.

Bester FCJ and Weich DJV. (1991). Prevalence of hypertension among elderly blacks in the Orange Free State. *Cardiovascular Journal Of Southern Africa* 2:154-156.

Bertrand E. (1995). Coronary heart disease in black Africans: an overview. *East African Medical Journal* 72:37-41.

Björntorp P. (1985). Regional fat distribution. *Annals of Internal Medicine* 103(6):994-995.

Björntorp P. (1992). Regional fat distribution - implications for type II diabetes. *International Journal of Obesity* 16(S4):819-827.

Björntorp P, Holm G and Rosmond R. (1999). Hypothalamic arousal, insulin resistance and Type 2 diabetes mellitus. *Diabetic Medicine* 16:373-383.

Björntorp P, and Rosmond R. (1999). Visceral obesitv and diabetes. *Drugs* 58(S1):13-18.

Bouchard C. Genetic aspects of human obesity. (1992). In: Björntorp P and Brodoff BN, eds. *Obesity*. JB Lippincott Company, Philadelphia, pp. 343-351.

Bourne LT, Lambert EV and Steyn K. (2001). Where does the black population of South Africa stand on the nutrition transition? *Public Health Nutrition* 5(1A):157-162.

Bovet P, Ross AG, Gervasoni JP, et al. (2002). Distribution of blood pressure, body mass index and smoking habits in the urban population of Dar es Salaam, Tanzania, and associations with socio-economic status. *International Journal of Epidemiology* 31:240-247.

Bradshaw D, Schneider M, Dorrington R, et al. (2002). South African cause-of-death profile in transition - 1996 and future trends. *South African Medical Journal* 92:618-623.

Bradshaw D, Bourne D, Schneider, et al. (1995). Mortality patterns of chronic diseases of lifestyle in South Africa. In: Fourie J and Steyn K, eds. *Chronic Diseases of Lifestyle in South Africa, MRC Technical Report,* Tygerberg, pp 5-36.

Brand E, Chatelain N, Mulatero P, et al. (1998). Structural analysis and evaluation of the aldosterone synthase gene in hypertension. *Hypertension* 32(2):198-204.

Bransome ED. (1992). Financing the care of diabetes mellitus in the US: Background, Problems, and Challenges. *Diabetes Care* 15(S1):1-5.

Bray GA. (1990). Obesity and diabetes. *Acta Diabetologia Latina* 27:81-88.

Briggs BA, Jackson WPU, du Toit ED, et al. (1980). The histocompatibilty (HLA) antigen distribution in Southern African blacks (Xhosa). Diabetes 29:68-70.

Bronte-Stewart B, Budtz-Olsen OE, Hickley JM, et al. (1960). The Kung Bushmen: Purpose, itinerary and methods. *South African Journal of Laboratory and Clinical Medicine* 6:188-202.

Brown DC, Byrne CD, Clark PMS, et al. (1991). Height and glucose tolerance in adult subjects. *Diabetologia* 34:531-533.

Brown PJ. (1992). The biocultural evolution of obesity: An anthropological view. In: Björntorp P and Brodoff BN, eds. *Obesity*. JB Lippincott Company, Philadelphia, pp320-327.

Brown WCB, Kennedy S, Inglis GC, et al. (1997). Mechanisms by which the Hawksley random zero sphygmomanometer underestimates blood pressure and produces a non-random distribution of RZ values. *Journal of Human Hypertension* 111:75-93.

Burkitt DP. (1973). Some Diseases Characteristic of Modern Western Civilization. *British Medical Journal* 1:274-278.

Burkitt DP. (1994). Western diseases and what they encompass. In: Temple NJ and Burkitt DP, eds. *Western Diseases: Their Dietary Prevention and Reversibility*. Humana Press, Totowa, New Jersey, pp.15-27.

Campbell GD. (1960). Incidence of diabetes mellitus in one district of Basutoland. *South African Medical Journal* 34:332.

Campbell GD. (1963). Diabetes in Asians and Africans in and around Durban. *South African Medical Journal* 37:1195-1208.

Campese VM. (1994). Salt sensitivity in hypertension. Renal and cardiovascular implications [clinical conference] Hypertension Apr;23(4):531-50:

Candy G, Samania N, Norton G, et al. (2000). Association analysis of β_2 adrenoceptor polymorphisms with hypertension in a black African population. *Journal of Hypertension* 18:167-172.

Carlsson M, Orho-Melander M, Hedenbro J, et al. (2000). The T 54 allele of the intestinal fatty acid-binding protein 2 is associated with a parental history of stroke. *Journal of Clinical Endocrinology and Metabolism* 85:2801-2804.

Carlsson M, Orho-Melander M, Hedenbro J, et al. (2001). Common variants in the β_2-(Gln27Glu) and β_3-(Trp4Arg)-adrenoceptor genes are associated with elevated NEFA levels and type II diabetes. *Diabetologia* 44:629-636.

Central Statistical Services Report. (1990). *Deaths of blacks: 1990.* Report No. 03-10-01. Central Statistical Services, Pretoria.

Chagnon Y, Chen W, Perusse L, et al. (1997). Linkage and association studies between the melanocortin receptor-4 and receptor-5 genes and obesity-related phenotypes in the Quebec family study. Mollecular Medicine 3:663-73.

Chale SC, Swai ABM, Mujinja PGM, et al. (1992). Must diabetes be a fatal disease in Africa? Study of costs of treatment. *British Medical Journal* 304:1215-1218.

Chan JM, Stampfer M, Rimm EB, et al (1994). Obesity, fat distribution, and weight gain as risk factors for clinical diabetes in men. Diabetes Care 17:961-969.

Charlton KE, Schloss I, Visser M, et al. (2001). Waist circumference predicts clustering of cardiovascular risk factors in older South Africans. *Cardiovascular Journal Of South Africa* 12:142-150.

Clausen JO, Hansen T, Bjoerbaek C, et al. (1995). Insulin resistance: interactions between obesity and a common variant of the insulin receptor substrate-1. *The Lancet* 346:397-402.

Clement K, Vaisse C, Manning B, et al. (1995). Genetic variation in the β_3-adrenergic receptor and an increased capacity to gain weight in patients with morbid obesity. *New England Journal of Medicine* 333:352-354.

Clement K, Ruiz J, Cassard-Doulcier A. (1996). Additive effect of A-G (-3826) variant of the uncoupling protein gene and the Trp64Arg mutation of the beta-3-adrenergic receptor gene on weight gain in morbid obesity. *International Journal of Obesity* 1996: 20: 1062-6.

Clément K, Vaisse C, Lahlou N, et al. (1998). A mutation in the leptin receptor gene causes obesity and pituitary dysfunction. *Nature* 392: 398-401.

Colditz GA, Willett WC, Stampfer MJ, et al. (1990). Weight as a risk factor for clinical diabetes in women. *American Journal of Epidemiology* 132:501-513.

Collins V, Dowse GK, Finch CF, et al. (1990). An inconsistent relationship between insulin and blood pressure in three pacific island pulations. *Journal of Clinical Epidemiology* 43:1369-1378.

Collins R, Peto R, MacMahon S, et al. (1990). Blood pressure, stroke, and coronary heart disease. *The Lancet* 335:827-838.

Comuzzie AG, Hixson JE, Almasy L, et al. (1997). A major quantitative trait locus determining serum leptin levels and fat mass is located on human chromosome 2. *Nature Genetics* 15:273-276.

Cooper ES. (1985) Cerebrovascular disease in blacks. In: Hall WD, Saunders E and Shulman NB, eds. *Hypertension In Blacks: Epidemiology, Pathophysiology and Treatment.* Year Book Medical Publishers, Chicago, pp 83-105.

Cooper ES and Caplan LR. (1991). Cerebrovascular disease in hypertensive blacks. In: Saunders E and Brest AN, eds. *Cardiovascular disease in blacks. Cardiovascular Clinics*, F.A. Davis Company, Philadelphia, p. 145-155.

Cooper R, Rotimi C, Ataman S, et al. (1997). The prevalence of hypertension in seven populations of West African origin. *American Journal of Public Health* 87:160-168.

Cooper RS, Xiuqing G, Rotimi CN, et al. (2000). Heritability of angiotensin-converting enzyme and angiotensinogen a comparison of US blacks and Nigerians. *Hypertension* 35:1141-1147.

Cosnett JE. (1957). Illness among Natal Indians: A survey of hospital admissions. South African Medical Journal 31:1109-1115.

Costa A, Iguala I, Bedini J, et al. (2002). Uric acid concentration in subjects at risk of type 2 diabetes mellitus: relationship to components of the metabolic syndrome. Metabolism 51:372-375.

Coresh J, Klag MJ, Whelton PK, et al. (1991). Left Ventricular Hypertrophy and Skin Color among American Blacks. *American Journal of Epidemiology* 134:129-36.

Coutinho M, Wang Y, Gerstein HC, et al. (1999). The relationship between glucose and incident cardiovascular events. A metaregression analysis of published data from 20 studies of 95 783 individuals followed for 12.4 years. *Diabetes Care* 22:233-240.

Cowie CC, Port FK, Wolfe RA, et al. (1989). Disparities in incidence of diabetic end-stage renal disease according to race and type of diabetes. *The New England Journal Of Medicine* 321:1074-1079.

Crowther NJ, Cameron N, Trusler T, et al. (1998). Association between poor glucose tolerance and rapid post natal weight gain in seven-year-old children. *Diabetologia* 41:1163-1167.

Cruickshank JK, Cooper J, Burnett M, et al. (1991). Ethnic differences in fasting plasma C-peptide and insulin in relation to glucose tolerance and blood pressure. *The Lancet* 338:842-847.

Cruickshank JK, Mbanya JC, Wilks R, et al. (2001). Hypertension in four African-origin populations: current 'Rule of Halves', quality of blood pressure control and attributable risk of cardiovascular disease. *Journal of Hypertension* 19:41-46.

Cusi D, Bassina C, Azzani T, et al. (1997). Polymorphisms of alpha-adducin and salt sensitivity in patients with essential hypertension. *The Lancet* 349:1353-1357.

Cui Y, Blumenthal RS, Flaws JA, et al. (2001). Non-high-density lipoprotein cholesterol level as a predictor of cardiovascular disease mortality. *Archives of Internal Medicine* 161:1413-1419.

Cutler JA, Follmann, D, Allender, PS. (1997). Randomised trials of sodium reduction: an overview. *American Journal of Clinical Nutrition* 1997 :643S-651S.

Daniels A, Biesma R, Otten J, et al. (2000). Ambivalence of primary health care professionals towards the South African guidelines for hypertension and diabetes. *South African Medical Journal* 90:1206-1211.

DECODE Study Group on behalf of the European Diabetes Epidemiology Study Group. (1998). Will new diagnostic criteria for diabetes mellitus change phenotype of patients with diabetes? Re-analysis of the European epidemiological data. *British Medical Journal* 317:371-375.

Deeb SS, Fajas L, Nemoto M, et al. (1998). A Pro12Ala substitution in PPARγ2 associated with decreased receptor activity, lower body mass index and improved insulin sensitivity. *Nature Genetics* 20:284-7.

DeFronzo RA, Cooke CR, Andres R, et al. (1975). The effect of insulin on renal handling of sodium, potassium, calcium, and phosphate in man. *Journal of Clinical Investigation* 55:845-855.

DeFronzo RA. (1981). Glucose intolerance and aging. *Diabetes Care* 4:493-501.

DeFronzo RA. (1988). The Triumvirate: β-Cell, Muscle, Liver. A collusion responsible for NIDDM. Lilly Lecture 1987. *Diabetes* 37:667-686.

Delplanque J, Barat-Houari M, Dina C, et al. (2000). Linkage and association studies between the proopiomelanocortin (POMC) gene and obesity in caucasian families. *Diabetologia* 43: 1554-1557.

De Vegt F, Dekker JM, Cooen DA, et al. (1998). The 1997 American Diabetes Association criteria versus the 1985 World Health Organization criteria for the diagnosis of abnormal glucose tolerance. Diabetes Care 21:1686-1690.

Dietz WH. (2001). The obesity epidemic in young children (Editorial). Reduce television viewing and promote playing. *British Medical Journal* 322:313-314.

Dluhy RG and Williams GH. (1998). In: Wilson, Foster, Kronenberg and Larson, eds. *Williams Textbook of Endocrinology*, 9th Edition, W.B. Saunders, Philadelphia, p745.

Donahue RP, Bloom E, Abbott RD, et al. (1987). Central obesity and coronary heart disease men. *The Lancet* 821-824.

Donahue RP, Skyler JS, Schneiderman N, et al. (1990). Hyperinsulinemia and elevated blood pressure: cause, confounder, or coincidence? *American Journal of Epidemiology* 132:827-836.

Donnison CP. (1929). Blood pressure in the African native. Its bearing upon the aetiology of hyperpiesia and arterio-sclerosis. *The Lancet* :6-7.

Dowse GK and Zimmet PZ. (1989). The prevalence and incidence of non-insulin-dependent diabetes mellitus. In: Alberti KGGM and Mazze R, eds. *Frontiers of diabetes research: current trends in non-insulin-dependent diabetes mellitus.* Elsevier Science Publishers B.V. (Biomedical Division), pp37-59.

Dowse GK, Zimmet PZ, Finch CF, et al. (1991a). Decline in incidence of epidemic glucose intolerance in Nauruans: implications for the "thrifty genotype". *American Journal Epidemiology* 133:1093-104.

Dowse GK, Zimmet PZ, Gareeboo H, et al. (1991b). Abdominal obesity and physical inactivity as risk factors for NIDDM and impaired glucose tolerance in Indian, Creole, and Chinese Mauritians. *Diabetes Care* 14:271-82.

Drewnowski A and Popkin BM. (1997). The Nutrition Transition: New trends in the Global Diet. *Nutrition Reviews* 55:31-43.

Durnin JVGGA and Womersley J. (1973). Body fat assessed from total body density and its estimation from skinfold thickness: measurements 481 men and women aged from 16 to 72 years. *British Journal of Nutrition* 32: 77-97.

Dustan HP. (1991). Obesity and hypertension. *Diabetes Care* 14:488-504.

Eaton SB, Konner M and Shostak M. (1988). Stone agers in the fast lane: Chronic degenerative diseases in evolutionary perspective. *The American Journal of Medicine* 84:739-749.

Edginton ME, Hodkinson J and Seftel HC. (1972). Disease patterns in a South African rural Bantu population. So*uth African Medical Journal* 46:968-976.

Editorial (1977). The epidemiological transition. *The Lancet ii*:670.

Editorial (1998). The hidden epidemic of cardiovascular disease. *The Lancet* 352:1795.

Edwards R, Unwina N, Mugusi F, et al. (2000). Hypertension prevalence and care in an urban and rural area of Tanzania. *Journal of Hypertension* 18:145-152.

Ekoé JM. (1988). Life expectancy in diabetes mellitus. In: Ekoé JM ed. *Diabetes Mellitus-Aspects of the world-wide epidemiology of Diabetes Mellitus and its long-term complications.* Elsevier, Amsterdam, p237.

Elamin A. (1989). Prevalence of IDDM in schoolchildren in Khartoum, Sudan. *Diabetes Care* 12:430-432.

Elbein SC, Chu W, Ren Q, et al. (2002). Role of Calpain-l0 Gene Variants in Familial Type 2 Diabetes in Caucasians. *Journal of Clinical Endocrinology and Metabolism* 87:650-654.

Epstein FH and Higgins M. (1992). Epidemiology of Obesity. In: Björntorp P and Brodoff BN, eds. *Obesity.* JB Lippincott Company, Philadelphia, pp330-342.

Erasmus RT, Blanco Blanco E, Okesina AB, et al. Prevalence of diabetes mellitus and impaired glucose tolerance in factory workers from Transkei, South Africa. *South African Medical Journal* 91:157-160.

Evans DJ, Hoffmann RG, Kalkhoff RK, et al. (1983). Relationship of androgenic activity to body fat topography, fat cell morphology, and metabolic aberrations in premenopausal women. *Journal of Clinical Endocrinology and Metabolism* 57:304-310.

Evans JMM, Newton RW, Ruta DA, et al. (2000). Socio-economic status, obesity and prevalence of Type 1 and Type 2 diabetes mellitus. *Diabetic Medicine* 17:478-480.

Expert Committee on the Diagnosis and Classification of Diabetes Mellitus (From the American Diabetes Association) (1997). Report of the Expert Committee on the diagnosis and classification of diabetes mellitus. *Diabetes Care* 20:1183-1197.

Ezenwaka CE, Abayomi O, Akanji, et al. (1997). The prevalence of insulin resistance and other cardiovascular disease risk factors in healthy elderly southwestern Nigerians. *Atherosclerosis* 128 (1997) 201-211.

Fagot-Campagna A, Narayan KMV and Imperatore G. (2001). Type 2 diabetes in children exemplifies the growing problem of chronic diseases (Editorial). *British Medical Journal* 322:377-378.

Farooqi IS, Yeo GSH, Keogh JM, et al. (2000). Dominant and recessive inheritance of morbid obesity associated with melanocortin 4 receptor deficiency. *Journal of Clinical Investigation* 106:271-279.

Ferrannini E, Buzzigoli G, Bonadonna R, et al. (1987). Insulin resistance in essential hypertension. *New England Journal of Medicine* 317:350-357.

Finnerty FA. (1971). Hypertension is different in blacks (Editorial). *Journal of the American Medical Association* 216:1634-1635.

Fitzgerald AP and Jarrett RJ. (1991). Are conventional risk factors for mortality relevant in Type 2 diabetes? *Diabetic Medicine* 8:475-480.

Ford ES and DeStefano F. (1991). Risk factors for mortality from all causes and from coronary heart disease among persons with diabetes. Findings from the National Health and Nutrition Examination Survey I. Epidemiologic Follow-up Study. *American Journal of Epidemiology* 33:1220-1230.

Forsblom C, Kanninen T, Lehtovirta T, et al. (1999). Albumin excretion is an inherited trait in families with NIDDM? *Diabetologia* 42:1359-1366.

Fowden AL. (1995). Endocrine regulation of fetal growth. Reprod Fertil Dev 3:351-63.

Fraze E, Donner CC, Swislocki AL, et al. (1985). Ambient plasma free fatty acid concentrations in non-insulin dependent diabetes mellitus: evidence for insulin resistance. *Journal for Clinical Endocrinology and Metabolism* 61:807-811.

Fritz V. (1995). Stroke, including rehabilitation. In: Fourie J and Steyn K, eds. *Chronic Diseases of Lifestyle in South Africa, MRC Technical Report,* Tygerberg, pp161-175.

Fritz V. (2000). Stroke therapy clinical guideline. *South African Medical Journal* 90:276-306.

Fuller JH. (1980). Coronary heart disease risk and impaired glucose tolerance. The Whitehall Study. *The Lancet* :1374-1376.

Garn SM, Rosen NN, McCann MB. (1971). Relative values of different fat folds in a nutritional survey. *American Journal of Clinical Nutrition* 24:1380-1381.

Garrrow JS and Webster J. (1985). Quetelet's index (W/H^2) as a measure of fatness. *International Journal of Obesity* 9:147-153.

Gavin JR and Goodwin N. (1990). Diabetes in black populations: Current state of knowledge. Introduction. *Diabetes Care* 11: (S4)1140-1142.

Gill GV. (1991). Morbidity and mortality of diabetes. In: Pickup JC and Williams G, eds. *Textbook of Diabetes*, Blackwell Scientific Publishers, Oxford, p27.

Gill GV and Huddle KR. (1991). Patterns of insulin dependence in an African diabetic clinic. *Quarterly Journal of Medicine* 294:829-835.

Gill GV, Rolfe M, MacFarlane IA, et al. (1996). Smoking habits of black South African patients with diabetes mellitus. *Diabetic Medicine* 13:996-999.

Ginsberg HN and Goldberg IJ. (2001). Disorders of intermediary metabolism. In: Braunwald E, Fauci AS, Kasper DL, et al., eds. *Harrison's Principles of Internal Medicine*, 15th Edition, McGraw-Hill, New York, p. 2250.

Goldberg MD, Marine N, Ribeiro F, et al. (1968). Prevalence of glycosuria and diabetes among Indians and Bantu. *South African Medical Journal* 43:733-738.

Goldberger AL. (2001). Electrocardiography. In: Braunwald E, Fauci AS, Kasper DL, et al., eds. *Harrison's Principles of Internal Medicine*, 15th Edition, McGraw-Hill, New York, pp. 1262-1271.

Gordon DJ, Probstfield JL, Garrison R. et al. (1989). High- density lipoprotein cholesterol and cardiovascular disease –four prospective American studies. Circulation 79:8-15

Gottdiener JS. (1991). Hypertensive heart disease in blacks. In: Saunders E and Brest AN, eds. *Cardiovascular disease in blacks. Cardiovascular Clinics*, F.A. Davis Company, Philadelphia, p. 133-143.

Gray DS, Bray GA, Bauer M, et al. (1990). Skinfold thickness measurements in obese subjects. American Journal of Clinical Nutrition 51:571-577.

Grimm CE, Wilson TW, Nicholson GD, et al. (1990). Blood pressure in blacks twin studies in Barbados. *Hypertension* 15:803-809.

Groop L, Ekstrand A, Forsblom C, et al. (1993). Insulin resistance, hypertension and micro-albuminuria in patients with Type 2 diabetes mellitus. *Diabetologia* 36:642-647.

Groop LC, Kankuri M, Schalin-Jäntti C, et al. (1993). Association between polymorphism of the glycogen synthase gene and non-insulin-dependent diabetes mellitus. *New England Journal of Medicine* 328:10-14.

Groop L and Orho-Mehlander M. (2001). The dysmetabolic syndrome. *Journal of Internal Medicine* 250:105-120.

Groop L. (2001). Pathogenesis of type 2 diabetes: the relative contribution of insulin resistance and impaired insulin secretion. International Journal of Clinical Practice 113:(S)3-13.

Grundy SM. (1998). Hypertriglyceridemia, atherogenic dyslipidaemia, and the metabolic syndrome. *American Journal of Cardiology* 81:18B-25B.

Guidelines Subcommittee. (1999). World Health Organization–International Society of Hypertension Guidelines for the Management of Hypertension. *Journal of Hypertension* 17:151-183.

Guo X, Rotimi C, Cooper R, et al. (1999). Evidence of a major gene effect for angiotensinogen among Nigerians. *Annals of Human Genetics* 63:293-300.

Guzzetti S, Mayet J, Shahi M, et al. (2000). Absence of sympathetic overactivity in Afro-Caribbean hypertensive subjects studied by heart rate variability. *Journal of Human Hypertension* 14:337-342.

Haffner SM, Lehto S, Rönnemaa T, et al. (1998). Mortality from coronary heart disease in subjects with Type 2 diabetes and in non-diabetic subjects with and without prior myocardial infarction. *New England Journal of Medicine* 339:229-234.

Haffner SM, Fong D, Hazuda HP, et al. (1988). Hyperinsulinemia, upper body adiposity, and cardiovascular risk factors in non-diabetics. Metabolism 37:338-45.

Haffner SM, Valdez, RA, Hazuda HP, et al. (1992). Prospective analysis of the insulin-resistance syndrome (Syndrome X). *Diabetes* 41:715-722.

Hales CN, Barker DJP, Clark PMS, et al. (1991). Fetal and infant growth and impaired glucose tolerance at age 64. *British Medical Journal* 303:1019-1022.

Hales CN and Barker DJP. (1992). Type 2 (non-insulin-dependent) diabetes mellitus: the thrifty phenotype hypothesis. *Diabetologia* 35:595-601.

Hales CN and Barker DJP. (2001). The thrifty phenotype hypothesis. *British Medical Bulletin* 60:605-620.

Hanis CL, Boerwinkle E, Chakraberty R, et al. (1996). A genome-wide search for human non-insulin-dependent (type 2) diabetes genes reveals a major susceptibility locus on chromosome 2. *Nature Genetics* 13:161–166.

Harris MI, Hadden WC, Knowler WC, et al. (1987). Prevalence of diabetes and impaired glucose tolerance and plasma glucose-levels in US population aged 20-74 yr. *Diabetes* 36:523-534.

Harris MI, Goldstein DE, Flegal KM, et al. (1998). Prevalence of diabetes, impaired fasting glucose, and impaired glucose tolerance in US Adults. The Third National Health and Nutrition Examination Survey, 1988-1994. *Diabetes Care* 21:518-524.

Hartz AJ, Rupley DC, Rimm AA. (1984). The association of girth measurements with disease in 32 856 women. *American Journal of Epidemiology* 119:71-80.

Harris MI, Klein R, Cowie CC, et al. (1998). Is the risk of diabetic retinopathy greater in non-Hispanic blacks and Mexican Americans than in non-Hispanic whites with Type 2 Diabetes? A US population study. *Diabetes Care* 21:1230-1235.

Helmrich SP, Ragland DR, Keung RW, et al. (1991). Physical activity and reduced occurrence of non-insulin-dependent diabetes mellitus. *New England Journal of Medicine* 325:147-152.

Herlitz J, Karlson BW, Lindqvist J, et al. (1998). Mode of death during five years of follow-up among patients with acute chest pain with and without a history of diabetes mellitus. *Diabetic Medicine* 15:308-314 .

Himsworth HP. (1936). Diabetes mellitus its differentiation into insulin-sensitive and insulin-insensitive types. *The Lancet* i:127-130.

Hinchliffe SA, Lynch MR, Sargent PH. (1992). The effect of intrauterine growth retardation on the development of renal nephrons. *British Journal of Obstetrics and Gynaecology* 99:296-301.

Hinney A, Becker I, Heibult O, et al. (1998). Systematic mutation screening of the pro-opiomelanocortin gene: identification of several genetic variants including three different insertions. One nonsense and two missense point mutations in probands of different weight extremes. *Journal of Clinical Endocrinology and Metabalism* 83:3737-3741.

Hinney A, Schmidt A, Nottebom K, et al. (1999). Several mutations in the melanocortin-4 receptor gene including a nonsense and a frameshift mutation associated with dominantly inherited obesity in humans. *Journal of Clinical Endocinology and Metabolism* 84:1483-1486.

Hixson JE, Almasy L, Cole S, et al. (1999). Normal variation in leptin levels is associated with polymorphisms in the proopiomelanocortin gene, POMC. *Journal of Clinical Endocrinology and Metabolism* 84:3187-3191.

Hoosen S, Seedat YK, Bhigjee AI, et al. (1985). A study of urinary sodium and potassium excretion rates among urban and rural Zulus and Indians. *Journal of Hypertension* 3:351-358.

Hopper J.L. (1999). Is Type II (non-insulin-dependent) diabetes mellitus not so "genetic" after all? *Diabetologia* 42:125-127.

Huddle KRL. (1995). Diabetes care in South Africa: Present and future (Editorial). *Diabetic Medicine* 12: 737-738.

Hypertension Detection And Follow-Up Program Cooperative Group. (1977). Race, education and prevalence of hypertension. *American Journal of Epidemiology* 106:351-361.

Hypertension Detection And Follow-Up Program Cooperative Group. (1979a). Five-year findings of the hypertension detection and follow-up program. I. Reduction in mortality of persons with high blood pressure, including mild hypertension. *JAMA* 242(23):2562-2571.

Hypertension Detection And Follow-Up Program Cooperative Group. (1979b). Five-year findings of the hypertension detection and follow-up program. II. Mortality by Race-sex and age. *JAMA* 242(23):2572-2577.

Hypertension Detection And Follow-Up Program Cooperative Group. (1982). Five-year findings of the hypertension detection and follow-up program. III. Reduction in stroke incidence among persons with high blood pressure. *JAMA* 247(5):633-638.

Hong Y, Rice T, Gagnon J, et al. (1998). Familial clustering of insulin and abdominal visceral fat: The HERITAGE Family Study. *Journal of Endocrinology and Metabolism* 83:4239-4245.

Huang ES, Meigs JB, Singer D, et al. (2001). The effect of interventions to prevent cardiovascular disease in patients with type 2 diabetes mellitus. *American Journal of Medicine* 111:633-642.

Huston SL, Bunker CH, Ukoli FA, et al. (1999). Electrocardiographic left ventricular hypertrophy by five criteria among civil servants in Benin City, Nigeria: prevalence and correlates. *International Journal of Cardiology* 70:1-14.

Idahosa PE. (1987). Hypertension: an ongoing health hazard in Nigerian workers. *American Journal of Epidemiology* 125:85-91.

International Diabetes Federation. (2002). Press release, 17 July 2002. www.idf.org.

Intersalt Cooperative Research Group. (1988). Intersalt: an international study of electrolyte excretion and blood pressure. Results for 24 hour urinary sodium and potassium excretion. *British Medical Journal* 297:319-328.

Isaacson C. (1977). The changing pattern of heart disease in south African Blacks. *South African Medical Journal* 52:793-798.

Isomaa B, Almgren P, Tuomi T, et al. (2001). Cardiovascular morbidity and mortality associated with the metabolic syndrome. *Diabetes Care* 24:683-689.

Jackson WPU. (1978). Epidemiology of diabetes in South Africa. *Advances in Metabolic Disorders* 9:111-146.

Jackson RS, Creemers JWM, Ohagi S, et al. (1997). Obesity and impaired prohormone processing associated with mutations in the human prohormone convertase 1 gene. *Nature Genetics* 16:303-306.

Jarrett RJ, Keen H, Fuller JH, et al. (1979). Worsening to diabetes in men with impaired glucose tolerance ("Borderline Diabetes"). *Diabetologia* 16:25-30.

Jarrett RJ. (1984). Type 2 (non-insulin-dependent) diabetes mellitus and coronary heart disease – chicken, egg or neither? *Diabetologia* 26:99-102.

Jarrett RJ. (1987). Do we need IGT? *Diabetic Medicine* 4:544-545.

James SA, Strogatz DS, Wing SB, et al. (1987). Socio-economic status, John Henryism, and hypertension in blacks and whites. *American Journal of Epidemiology* 126:664-673.

Jebb SA. (1998). Measuring body composition. In: Kopelman PG and Stock MJ eds. *Clinical Obesity*, Blackwell Science, Oxford, p. 29.

Joffe BI, Panz VR, Wing JR, et al. (1992). Pathogenesis of non-insulin-dependent diabetes mellitus in the black populations of Southern Africa. *The Lancet* 340:460-462.

Joffe BI and Seftel HC. (1994). Diabetes mellitus in the black communities of Southern Africa. *Journal of Internal Medicine* 235:137-142.

Joint National Committee. (1997). The sixth report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure. *Archives of Internal Medicine* 157:2413-2446.

Jönsson B. (1998). The economic impact of diabetes. *Diabetes Care* 21(S3):C7-C10.

Joubert J. (1991).The MEDUNSA stroke data bank. An analysis of 304 patients seen between 1986 and 1987. *South African Medical Journal* 80:567-570.

Joubert J, McLean CA, Reid CM, et al. (2000). Ischemic heart disease in black South African stroke patients. *Stroke* 31:1294-1298.

Kadiri S and Salako BL. (1997). Cardiovascular risk factors in middle aged Nigerians. *East African Medical Journal* 74:303-306.

Kalk WJ, Huddle KRL, Raal FJ. (1993). The age of onset and the sex distribution of insulin-dependent diabetes mellitus in Africans in South Africa. *Postgraduate Medical Journal* 69:552-556.

Kaminer B and Lutz WPW. (1960). Blood pressure in Bushmen of the Kalahari Desert. *Circulation* 22:289-295.

Kannel WB, Dawber T, Kagan A, et al. (1961). Factors of risk in the development of coronary heart disease six - year follow-up experience. The Framingham Study. *Annals of Internal Medicine* 55:33-50.

Kannel WB. (1996). Blood pressure as a cardiovascular risk factor. Prevention and treatment. *Journal of the American Medical Association* 275:1571-1576.

Kaplan NM. (1989). The Deadly Quartet. Upper-body obesity, glucose intolerance, hypertriglyceridaemia, and hypertension. *Archives of Internal Medicine* 149:1514-1520.

Kaplan NM. (2002a). Salt intake and hypertension. *UpToDate* 10:2. www.uptodate.com

Kaplan NM. (2002b). Genetic factors in the pathogenesis of essential hypertension. *UpToDate* 10:2. www.uptodate.com.

Keen H, Jarrett RJ, McCartney P. (1982). The ten-year follow-up of the Bedford Survey (1962-1972): Glucose tolerance and diabetes. *Diabetologia* 22:73-78.

Keen H. (1998). Impact of new criteria for diabetes on pattern of disease (Editorial). *The Lancet* 352:1000-1001.

Keys A, Fidanza F, Karvonen MJ, et al. (1972). Indices of relative weight and obesity. *Journal of Chronic Diseases* 25:329-343.

Khaw KT and Barrett-Connor E. (1987). Dietary potassium and stroke-associated mortality. A 12-Year prospective population study. *New England Journal of Medicine* 316:235-240.

King H and Rewers M. (1991). Diabetes in adults is now a Third World problem. *Bulletin of the World Health Organization* 69:643-648.

King H. Study in Tanzania of IGT. (1992). Effect of regression to the mean. *Diabetes Care* 15:1114-1115.

Kissebah AH, Vydelingum N, Murray R, et al. (1982). Relation of Body Fat Distribution to Metabolic Complications of Obesity. *Journal of Clinical Endocrinology and Metabolism* 54:254-260.

Klag MJ, Paul K, Whelton , et al. (1991). The Association of skin colour with blood pressure in US blacks with low socio-economic status. *Journal of the American Medical Association* 265:599-602.

Klannemark M, Suurinkeroinen L, Orho-Melander M, et al. (2000). Interaction between the Asn291Ser variant or the LPL gene and insulin resistance on dyslipidaemia in high risk individuals for Type 2 diabetes mellitus. *Diabetic Medicine* 17:599-605.

Klatsky AL, Friedman GD, Siegelaub AB, et al. (1977). Alcohol consumption and blood pressure. Kaiser-Permanente Multiphasic Health Examination Data. *The New England Journal Of Medicine* 296:1194-1200.

Knowler WC, Pettitt DJ, Savage PJ, et al. (1981). Diabetes incidence in Pima Indians: Contributions of obesity and parental diabetes. *American Journal of Epidemiology* 113:144-156.

Knudsen P, Murtomäki S, Antikainen M, et al. (1997). The Asn291Ser and Ser-477-stop mutations of the lipoprotein lipase gene and their significance for lipid metabolism in patients with hypertriglyceridemia. *European Journal Clinical Investigation* 27:928-935.
Koestler A. (1976). The Call-Girls. A tragic-comedy with prologue and epilogue. Pan Books Ltd., London, p. 80.

Kohno M, Yasunari K, Murakawa KI, et al. (1990). Plasma immunoreactive endothelin in essential hypertension. *The American Journal of Medicine* 88: 614-618.

Kreisberg RA. (1998). Diabetic dyslipidaemia. *American Journal Cardiology* 17:82:67U-73U.

Kriska AM, Alberti KGMM, Pereira MA, et al. (2001). Association of physical activity and serum insulin concentrations in two populations at high risk for type 2 diabetes but differing by BMI. *Diabetes Care* 24:1175-1180.

Krotkiewski M, Björntorp P, Sjöström L, et al. (1983). Impact of obesity on metabolism in men and women. Importance of regional adipose tissue distribution. *Journal of Clinical Investigation* 72:1150-1162.

Kruger HS, Venter CS, and Vorster H. (2001). Obesity in African women in the North West Province, South Africa is associated with an increased risk of non-communicable diseases: the THUSA study. *British Journal of Nutrition* 86:733-740.

Krude H, Biebermann H, Luck W, et al. (1998). Severe early-onset obesity, adrenal insufficiency and red hair pigmentation caused by POMC mutations in humans. *Nature Genetics* 19:155-157.

Krop JS, Shaffer TH, Powe N, et al. (1998). Patterns of expenditures and use of services among older adults with diabetes. Implications for the transition to capitated managed care. *Diabetes Care* 21:747-752.

Kuczmarski RJ, Flegal KM, Campbell SM, et al. (1991). Increasing prevalence of overweight among US adults. The National Health and Nutrition Examination Surveys, 1960 to 1991. *Journal of the American Medical Association* 272:205-211.

Kurtz TW, Al-Bander HA, Morris RC. (1987). "Salt-sensitive" essential hypertension in men. Is the sodium ion alone important? *New England Journal of Medicine* 317:1043-1048.

Lapidus L, Bengtsson, C, Larsson B, et al. (1984). Distribution of adipose tissue and risk of cardiovascular disease and death: a 12 year follow up of participants in the population study of women in Gothenburg, Sweden. *British Medical Journal* 289:1257-1261.

Larsson B, Svärdsudd K, Welin L, et al. (1984). Abdominal adipose tissue distribution, obesity, and risk of cardiovascular disease and death: 13 year follow up of participants in the study of men born in 1913. *British Medical Journal* 288:1401-1404.

Law MR. (1999). Lowering heart disease risk with cholesterol reduction: evidence from observational studies and clinical trials. *European Heart Journal* 1(Suppl S): S3-S8.

Leger J, Levy-Marchal C, Bloch J, et al. (1997). Reduced final height and indications for insulin resistance in 20 year olds born small for gestational age: regional cohort study. *British Medical Journal* 315:341-347.

Lehtovirta M, Kaprio J, Forsblom C. (2000). Insulin secretion and insulin sensitivity in monozvgotic and dizygotic twins. *Diabetologia* 43:285-293.

Lemieux S, Prud'homme D, Bouchard C, et al. (1993). Sex differences in the relation of visceral adipose tissue accumulation to total body fatness. *American Journal of Clinical Nutrition* 58:463-467.

Levitt NS, Katzenellenbogen JM, Bradshaw D, et al. (1993). The prevalence and risk factors for NIDDM in urban Africans in Cape Town, South Africa. *Diabetes Care* 16:601-607.

Levitt NS, Zwarenstein MF, Doepfmer S, et al. (1996). Public sector primary care of diabetics – a record review of quality of care in Cape Town. *South African Medical Journal* 86:1013-1017.

Levitt NS, Bradshaw D, Zwarenstein MF, et al. (1997). Audit of public sector primary diabetes care in Cape Town, South Africa: High prevalence of complications, uncontrolled hyperglycaemia, and hypertension. *Diabetic Medicine* 14:1073-1077.

Levitt NS, Steyn K, Lambert EV, et al. (1999). Modifiable risk factors for Type 2 diabetes mellitus in a peri-urban community in South Africa. *Diabetic Medicine* 16:946-950.

Levitt NS, Lambert EV, Woods D, et al. (2000). Impaired glucose tolerance and elevated blood pressure in low birth weight, non-obese, young South African adults: Early programming of cortisol axis. *Journal of Clinical Endocrinology & Metabolism* 85:4611-4618.

Levitt NS, Unwin NC, Bradshaw D, et al. (2000). Application of the new ADA criteria for the diagnosis of diabetes to population studies in sub-Saharan Africa. *Diabetic Medicine* 17:381-385.

Levy D, Anderson KM, Savage DD, et al. (1988). Echocardiographically detected left ventricular hypertrophy: Prevalence and risk factors. The Framingham Heart Study. *Annals of Internal Medicine* 108:7-13.

Levy D, Larson MG, Vasan RS, et al. (1996). The proqression from hvpertension to conqestive heart failure. *Journal of the American Medical Association* 275:1557-1562.

Levy D, DeStefano AL, Larson MG. (2000). Evidence for a gene influencing blood pressure on chromosome 17. Genome scan linkage results for longitudinal blood pressure phenotypes in subjects from the Framingham Heart Study. *Hypertension* 36:477-483.

Levy SB, Lilley JJ, Frigon RP, et al. (1977). Urinary kallikrein and plasma renin activity as determinants of renal blood flow. The influence of race and dietary sodium intake. *The Journal of Clinical Investigation* 60:129-138.

Lew EA and Garfinkel L. Variations in mortality by weight among 750,000 men and women. *Journal of Chronic Diseases* 32;563-576.

Lewis CE, Raczynski JM, Oberman A, et al. (1991). Risk factors and the natural history of coronary heart disease in blacks. In: Saunders E and Brest AN, eds. *Cardiovascular disease in blacks. Cardiovascular Clinics*, F.A. Davis Company, Philadelphia, p. 29-45.

Lloyd-Jones DM, Larson MG, Beiser A, et al. (1999) Lifetime risk of developing coronary heart disease. *The Lancet* 353:89-92.

Lillioja S, Mott DM, Howard BV, et al. (1988). Impaired glucose tolerance as a disorder of insulin action. Longitudinal and cross-sectional studies in Pima Indians. *New England Journal of Medicine* 318:1217-1225.

Linas SL. (1991). The role of potassium in the pathogenesis and treatment of hypertension *Kidney International* 39:771-786.

Lönnqvist F, Thörne A, Nillsell K, et al. (1995). A pathogenetic role of visceral fat β_3-adrenoreceptors in obesity. *Journal of Clinical Investigation* 95:1109-1116.

Loots JM and Lamprecht De V. (1971). A comparative study of rural and urban Venda males. Anthropometrical evaluation. *South African Journal of Nutrition* 7:1284-1288.

Lubbe, 1971 (1971). A comparative study of rural and urban Venda males. Dietary evaluation. *South African Journal of Nutrition* 7:1289-1296

Luft FC, Grim CE, Weinberger MH. (1985). Electrolyte and volume homeostasis in blacks. In: Hall WD, Saunders E and Shulman NB, eds. *Hypertension In Blacks: Epidemiology, Pathophysiology and Treatment*. Year Book Medical Publishers, Chicago, pp 115-131.

Luft FC. (1989). Salt and hypertension: Recent advances and perspectives. *Journal for Laboratory and Clinical Medicine*. 114:215-221.

Luke A, Cooper RS, Prewitt TE, et al. (2001). Nutritional consequences of the African diaspora. *Annual Reviews of Nutrition* 21:47-71.

MacMAhon S, Peto R, Cutler J, et al. (1990). Blood pressure, stroke, and coronary heart disease. Part 1, prolonged differences in blood pressure: prospective observational studies corrected for the regression dilution bias. *The Lancet* 1990 335;765-774.

Mahley RW, Weisgraber KH, and Farese RV. (1998). Disorders of lipid metabolism. In: Wilson JD, Foster DW, Kronenberg HM, and Larson PR, eds. *Williams Textbook of Endocrinology*, 9th Edition. W.B. Saunders Company, Philadelphia, pp. 1099-1153.

Mahtani MM, Widen E, Lehto M, et al. (1996). Nature Genetics 14(1):90-4.
Marine N, Vinik AI, Edelstein I. (1969). Diabetes, hyperglycemia and glycosuria among Indians, Malays and Africans (Bantu) in Cape Town, South Africa. *Diabetes* 18:840-857.

Master AM, Garfield CI and Walters MB. (1952). Presentation of new limits of normal blood pressure. In: *Normal blood pressure and hypertension*, Lea Febiger, Philadelphia, pp. 86-114.

Mathews DR, Hosker JP, Rudenski AS, et al. (1985). Homeostasis model assessment: insulin resistance and β-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia* 28:412-419 .

Mbanya JC, Thomas TH, Wilkinson R, et al. (1988). Hypertension and hyperinsulinaemia: a relation in diabetes but not essential hypertension. *The Lancet* :733-734.

Mbanya JCN, Ngogang J, Salah JN, et al. (1997). Prevalence of NIDDM and impaired glucose tolerance in a rural and an urban population in Cameroon. *Diabetologia* 40:824-829.

Mbanya JCN, Minkoulou EM, Salah JN, et al. (1998). The prevalence of hypertension in rural and urban Cameroon. *International Journal of Epidemiology* 27:181-185.

Mbanya JCN, Riste L, Cruickshank K, et al. (1999). Standardized comparison of glucose intolerance in West African-origin populations of rural and urban Cameroon, Jamaica, and Caribbean Migrants to Britain. *Diabetes Care* 22:434-440.

Mbanya JCN, Mbanya DNS, Pani LN, et al. (2000). Reduced insulin secretion in offspring of African Type 2 Diabetic Parents. *Diabetes Care* 23:1761-1765.

McCarthy M and Menzel S. (2001). The genetics of type 2 diabetes. *British Journal of Clinical Pharmacology* 51:195-199.

McLarty DG, Swai ABM, Kitange HM, et al. (1989). Prevalence of diabetes and impaired glucose tolerance in rural Tanzania. *The Lancet* i:871-875.

McLarty DG, Pollitt C, Swai ABM. (1990). Diabetes in Africa. *Diabetic Medicine* 7:670-684.

McLarty DG, Unwin N, Kitange HM, et al. (1996). Diabetes mellitus as a cause of death in sub-Saharan Africa: Results of a community-based study in Tanzania. *Diabetic Medicine* 13:990-995.

Medici F, Hawa M, Ianari A, et al. (1999). Concordance rate for Type II diabetes mellitus in monozygotic twins: actuarial analysis. *Diabetologia* 42:146-150.

Melander O, Orho M, Fagerudd J, et al. (1998). Mutations and variants of the epithelial sodium channel gene in Liddle's syndrome and primary hypertension. *Hypertension* 31:1118-1124.

Midgley JP, Matthew AG, Greenwood CMT. (1996). Effect of reduced dietary sodium on blood pressure. A meta-analysis of randomized controlled trials. *Journal of the American Medical Association* 275:1590-1597.

Milne FJ. (2000). Hypertension Clinical Guideline. *South African Medical Journal* 91:163-172.

Milne J and Pinkney-Atkinson V (2002). Hypertension clinical guidelines. Benefits and risks to patients.

Mitchell B, Blangero J, Comuzzie A, et al. (1998). A paired sibling analysis of the beta-3 adrenergic receptor and obesity in Mexican Americans. *Journal of Clinical Investigation* 101: 584-587.

Modan M, Halkin H, Almog S, et al. (1985). Hyperinsulinemia: A link between hypertension, obesity and glucose intolerance. *Journal of Clinical Investigation* 75:809-817.

Mollentze WF, Stulting AA, Steyn AF. (1990). Ophthalmoscopy versus non-mydriatic fundus photography in the detection of diabetic retinopathy in black patients. South African Medical Journal 78:248-250.

Montague C, Farooqi S, Whitehead J, et al. (1997). Congenital leptin deficiency is associated with severe early-onset obesity in humans. *Nature* 387: 903-908.

Morris , Sebastian A, Forman A, et al. (1999). Normotensive salt sensitivity: effects of race and dietary potassium. *Hypertension* 33:18-23.

Morrish NJ, Stevens LK, Head J, et al. (1990). A prospective study of mortality among middle-aged diabetic patients (the London cohort of the WHO Multinational Study of vascular disease in diabetics) I: causes and death rates. *Diabetologia* 33:538-541.

Moss SE, Klein R, Klein B. (1991). Cause-specific mortality in a population-based study of diabetes. *American Journal of Public Health* 81:1158-1162.

Motala AA, Pirie FJ, Gouws E, et al. (2001). Microvascular complications in South African patients with long duration diabetes mellitus. *South African Medical Journal* 91:987-992.

Mufunda J, Scott LJ, Chifamba J, et al. (2000). Correlates of blood pressure in an urban Zimbabwean population and comparison to other populations of African origin. *Journal of Human Hypertension* 14: 65-73

Mulrow CD, Cornell JA, Herrera CR. (1994). Hypertension in the elderly. Implications of randomised trials. *Journal of the American Medical Association* 272:1932-1938.

Must A, Jaques PF, Dallal GE, et al. (1992). Long-term morbidity and mortality of overweight adolescents. A follow-up of the Harvard Growth Study of 1929 to 1935. *The New England Journal of Medicine* 327:1350-5.

Mykkänen L, Zaccaro D, Wagenknecht L, et al. (1998). Microalbuminuria is associated with insulin resistance in non-diabetic subjects. *Diabetes* 47:703-800.

Nakajime H. (1991). Epidemiology and the future of world health – The Robert Cruickshank Lecture. *International Journal of Epidemiology* 20:589-594.

National Diabetes Data Group. (1979). Classification and diagnosis of diabetes mellitus and other categories of glucose intolerance. Diabetes 28:1039-57.

Neel V. (1962). Diabetes mellitus: a "thrifty" genotype rendered detrimental by progress? *American Journal of Human Genetics* 14:352-362.

Nilsson PM. (1997). Hypertension and diabetes mellitus. In: Pickup JC and Williams G, eds. *Textbook of Diabetes*, 2nd edition. Blackwell Science, Oxford, p. 56.2.

Nissinen A, Böthig S, Granroth H, et al. (1988). Hypertension in developing countries. *World Health Statistical Quarterly* 41:141-154.

Njelekela M, Negishi H, Nara Y, et al. (2001). Cardiovascular risk factors in Tanzania: a revisit. *Acta Tropica* 79:231-239.

Norgan NG. (1994). Population differences in body composition in relation to the body mass index. *European Journal Clinical Nutrition* 48: (S1)3:S10-27.

O'Brien E, Mee F, Atkins N, et al. (1990). Inaccuracy of the Hawksley random zero sphygmomanometer. *The Lancet* i(336):1465-1468.

Ohlson LO, Larsson B, Svärdsudd K, et al. (1985). The Influence of body fat distribution on the incidence of diabetes mellitus. 13.5 years of follow-up of the participants in the study of men born in 1913. *Diabetes* 34:1055-1058.

Okesina AB,Oparinde DP, Akindoyin KA, et al. (1999). Prevalence of some risk factors of coronary heart disease in a rural Nigerian population. *East African Medical Journal* 76:212-216.

Olatunbosun ST and Bella AF. (2000). Relationship between height, glucose intolerance, and hypertension in an urban African black adult population: a case for the "thrifty phenotype" hypothesis? *Journal of Natural Medical Association* 92:265-268.

Omar MAK, Seedat MA, Motala AA, et al. (1993). The prevalence of diabetes mellitus and impaired glucose tolerance in a group of urban South African blacks. *South African Medical Journal* 83:641-643.

Omar MAK, Motala AA, Seedat MA, et al. (1994). South African Indians show a high prevalence of NIDDM and bimodality in plasma plucose distribution patterns. *Diabetes Care* 17:70-73.

O'Rahilly SP. (1999). The metabolic syndrome: all in the mind? *Diabetic Medicine* 16:355-357.

Orho-Melander M, Almgren P, Kanninen T, et L. (1999). A paired sibling analysis of the XbaI polymorphism in the muscle glycogen synthase gene. *Diabetologia* 42:1138-1145.

Padwal R, Straus SE, McAlister FA. (2001). Cardiovascular risk factors and their effects on the decision to treat hypertension: evidence based review. *British Medical Journal* 322:977-980.

Pan XR, Li GW, Hu YH, et al. (1997). Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance. The Da Qing IGT and Diabetes Study. *Diabetes Care* 20:537-44

Panz VA, Raal FJ, Joffe BI, et al. (1992). Insulin-receptor activity in non-diabetic and diabetic urbanised South African black women. *Diabetes Care* 15:277-281.

Patel S, Unwin N, Bhopal R, et al. (1999). A comparison of proxy measures of abdominal obesity in Chinese, European and South Asian adults. *Diabetic Medicine* 16:853-860.

Peiris AN, Mueller RA, Smith GA, et al. (1986). Splanchnic insulin metabolism in obesity influence of body fat distribution. *Journal of Clinical Investigation* 78:1648-1657.

Pestana JAX, Steyn K, Leiman A, et al. (1996). The direct and indirect costs of cardiovascular disease in South Africa in 1991. *South African Medical Journal* 86:79-684.

Pickering G. (1968). The concept. In: Pickering G, ed. *High blood pressure*, Second Edition, J and A Churchill Ltd, London, pp. 2-5.

Pickup JC, Crook MA. (1998). Is Type II diabetes mellitus a disease of the innate immune system? *Diabetologia* 41:1241-1248.

Pobee JOM, Larbi EB, Belcher DW, et al. (1977). Blood pressure distribution in a rural Ghanaian population. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 71:66-72.

Podolski DK. (2001). Infiltrative, genetic, and metabolic diseases affecting the liver. In: Braunwald E, Fauci AS, Kasper DL, et al., eds. *Harrison's Principles of Internal Medicine*, 15th Edition, McGraw-Hill, New York, p. 1767.

Politzer WM and Schneider T. (1962). Diet and diabetes mellitus: possible relationships. A comparative study in a rural and urban community. *South African Medical Journal* 36:608-610.

Poulsen P, Kyvik O, Vaag A, et al. (1999). Heritability of Type 2 (non-insulin-dependent) diabetes mellitus and abnormal glucose tolerance – a population-based twin study. *Diabetologia* 42;139-145.

Poulter N, Khaw KT, Hopwood BEC, et al. (1984). Blood pressure and its correlates in an African tribe in urban and rural environments. *Journal of Epidemiology and Community Health* 38:181-186.

Prineas RJ and Gillum R. (1985). US Epidemiology of hypertension in blacks. In:Hall WD, Saunders E, Shulman N, eds. *Hypertension in Blacks*. Year Book Medical Publishers, Chicago, p. 17-36.

Pÿoräla K, Savolainen E, Kaukola S, et al. (1979). Plasma insulin as coronary heart disease risk factor: Relationship to other risk factors and predictive value during 9½ year follow-up of the Helsinki Policemen Study Population. *Acta Medica Scandinavia* 701:38-52.

Qualheim RE, Rostand SG, Kirk KA, et el. (1990). Changing patterns of end-stage renal disease due to hypertension. *Kidney International* 37:244.

Ralph L and Sacco MS. (1995). Risk factors and outcomes for ischaemic stroke. *Neurology* 45:S10-S14.

Reaven GM. (1988). Role of insulin resistance in human disease. *Diabetes* 37:1595-1607.

Reaven GM. (1995). The fourth Musketeer – from Alexandre Dumas to Claude Bernard. *Diabetologia* 38:3-13.

Regan TJ. (1990). Alcohol and the cardiovascular system. *Journal of the American Medical Association* 264:377-381.

Reisin E, Abel R, Modan M, et al. (1978). Effect of weight loss without salt restriction on the reduction of blood pressure in overweight hypertensive patients. *New England Journal of Medicine* 298:1-6.

Reymer P, Gagné E, Groenemeyer B. (1995). A lipoprotein lipase mutation (Asn291Ser) is associated with reduced HDL cholesterol levels in premature atherosclerosis. *Nature Genetics* 10:28-34.

Ristow M, Mueller-Wieland D, Pfeiffer A. (1998). Obesity associated with a mutation in a genetic regulator of adipocytes differentiation. *New England Journal of Medicine* 339:953-959.

Robinson R. (2001). The fetal origins of adult disease - No longer just a hypothesis and may be critically important in south Asia (Editorial). *British Medical Journal* 322:375-376.

Rolland-Cachera MF, Cole TJ, Sempe M, et al. (1991). Body mass index variations: centiles from birth to 87 years. *European Journal of Clinical Nutrition* 45:13-21.

Roper NA, Bilous RW, Kelly WF, et al. (2001). Mortality in a population with diabetes and the impact of material deprivation: longitudinal, population based study. *British Medical Journal* 322:1389-1393.

Rose GA, Blackburn H. Cardiovascular Survey Methods. World Health Organization, Geneva, 1968.

Rose GA and Blackburn H. (1968). *Cardiovascular survey methods*. World Health Organization, Geneva.

Rose GA. (1985). Hypertension in the community. In: Bulpitt CJ, ed. *Handbook of hypertension, Volume 6, Epidemiology of hypertension*, Elsevier Science, Amsterdam, pp. 1-14.

Rosman KD. The profile of strokes among the urban black population of Pretoria. Ph.D. thesis, University of Pretoria, 1989.

Rossouw JE, Du Plessis JP, Benade AJS, et al. (1983). Coronary risk factor screening in three rural communities. *South African Medical Journal* 64:430-436.

Rostand SG, Kirk KA, Rutsky EA, et al. (1982). Racial differences in the incidence of treatment for end-stage renal disease. *The New England Journal of Medicine* 306:1276-1279.

Rostand SG. (1989). Diabetic renal disease in blacks - inevitable or preventable? *The New England Journal of Medicine* 321:1121-1122.

Ruderman NB, Schneider SH, Berchtold P. (1981). The "metabolically-obese", normal-weight individual. *American Journal of Clinical Nutrition* 34:1617-1621.

Rwiza HT, Swai ABM, McLarty DG. (1986). Failure to diagnose diabetic ketoacidosis in Tanzania. *Diabetic Medicine* 3:181-183.

Saad MF, Knowler WC, Pettitt DJ, et al. (1988). The natural history of impaired glucose tolerance in the Pima Indians. *New England Journal of Medicine* 319:1500-1506.

Saad MF, Lillioja S, Nyomba BL, et al. (1991). Racial differences in the relation between blood pressure and insulin resistance. *New England Journal of Medicine* 324:733-739.

Sagnella GA. (2001). Why is plasma renin activity lower in populations of African origin? *Journal of Human Hypertension* 15:17-25.

Sako Y and Grill VE. (1990). A 48-hour lipid infusion in the rat time-dependently inhibits glucose-induced insulin secretion and B-cell oxidation through a process likely coupled to fatty acid oxidation. *Endocrinology* 127: 1580-1589.

Samaras K, Spector T, Nguyen T, et al. (1997). Independent genetic factors determine the amount and distribution of fat in women after the menopause. *Journal Clinical Endocrinology and Metabolism* 82:781-785.

Sanders S. (1960). Incidence of diabetes mellitus in one district of Basutoland. *South African Medical Journal* 34:248.

Schuckit MA. (2001). Alcohol and alcoholism. In: Braunwald E, Fauci AS, Kasper DL, Hauser SL, Longo DL and Jameson JL eds. *Harrison's Principles of Internal Medicine*, 15th Edition, McGraw-Hill, New York, p. 2564.

Seedat YK. (1977). Myocardial infarction in the African hypertensive patient. *American Heart Journal* 94:388-389.

Seedat YK, Seedat MA, Reddy K. (1978). The prevalence of hypertension in the Indian population of Durban. *South African Medical Journal* 54:10-15.

Seedat YK, Seedat MA, Veale MT. (1980). The prevalence of hypertension in urban whites. *South African Medical Journal* 57:1025-1030.

Seedat YK, Seedat MA, Hackland DBT.(1982). Prevalence of hypertension in the urban and rural Zulu. *Journal of Epidemiology and Community Health* 36:256-261.

Seedat YK, Seedat MA, Hackland DBT. (1982). Biosociaial factors and hypertension in urban and rural Zulus. *South African Medical Journal* 61:999-1002.

Seedat YK. (1990). Perspectives on dialysis and transplantation in South Africa. *South African Medical Journal* 77:549-550.

Seedat YK, Mayet FGH, Latiff GH, et al. (1992). Risk factors and coronary heart disease in Durban blacks – the missing links. *South African Medical Journal* 82:251-256.

Seedat YK. (1999). Improvement in treatment of hypertension has not reduced incidence of end-stage renal disease. *Journal of Human Hypertension* 13:747-751.

Seedat YK, Bhoola KD, Muller R, et al. (1999). Urinary levels of tissue kallikrein in the South African black and Indian hypertensives. *Journal of Human Hypertension* 13:771-775.

Seftel HC and Abrams GJ. (1960). Diabetes in the Bantu. *British Medical Journal* 16:1207-1208.

Seftel HC and Schultz E. (1961). Diabetes mellitus in the urbanized Johannesburg African. *South African Medical Journal* :66-70

Seftel HC, Keeley KJ, Walker ARP. (1963). Studies in glycosuria and diabetes in non-white populations of the Transvaal. *South African Medical Journal* 37:1213-1216.

Seftel HC. (1978a). Eidemiology of hypertension in developed and developing populations. *South African Medical Journal* 54:957-959.

Seftel HC. (1978b). The rarity of coronary heart disease in South African blacks. *South African Medical Journal* 54:99-105.

Seftel HC, Johnson S, Muller EA. (1980). Distribution and biosocial correlations of blood pressure levels in Johannesburg backs. *South African Medical Journal* 57:313-320.

Seftel HC, Asvat MS, Joffe BI, et al. (1993). Selected risk factors for coronary heart disease in male scholars from the major South African population groups. *South African Medical Journal* 83:891-897.

Seftel HC, Raal D, Joffe B, (1995). Dyslipidaemia in South Africa. In: Fourie J and Steyn , eds. Chronic Diseases of Lifestyle in South Africa. MRC Technical Report, Parrow.

Seidell JC. (1998). Epidemiology: Definition and Classification of Obesity. In: Kopelman PG and Stock MJ eds. *Clinical Obesity*. Blackwell Science, Oxford, p103.

Selby JV, Friedman GD, Quesenberry CP. (1989). Precursors of essential hypertension: The role of body fat distribution pattern. *American Journal Of Epidemiology* 129:43-53.

Sever PS, Gordon D, Peart WS, et al. (1980). Blood pressure and its correlates in urban and tribal Africa. *The Lancet* :60-64.

Shaper AG and Saxton GA. (1969). Blood pressure and body build in a rural community in Uganda. *East African Medical Journal* 46:228-245.

Shaper AG, Leonard PJ, Jones KW, et al. (1969). Environmental effects on the body build, blood pressure and blood chemistry of nomadic warriors serving in the army in Kenya. *East African Medical Journal* 46:281-289.

Shaper AG, Wright DH, Kyobe J. (1969). Blood pressure and body build in three nomadic tribes of Northern Kenya. *East African Medical Journal* 46:273-281.

Shaw JE, De Courten M, Boyko EJ, et al. (1999). Impact of new diagnostic criteria for diabetes on different populations. *Diabetes Care* 22:762-766.

Shires R, Joffe BI, Seftel HC. (1978). Hormonal and metabolic responses to an oral glucose load in obese black diabetics. *South African Medical Journal* 53:446-448.

Shires A, Joffe BI, Seftel HC. (1985). Maximal pancreatic beta-cell stimulation and the counter-regulatory hormonal responses in South African black and white obese subjects. *South African Medical Journal* 67:845-847.

Shuenyane E, Mashigo S, Eyberg C, et al. (1977). A socio-economic, health and cultural survey in Soweto. *South African Medical Journal* 51:495-500.

Shulman NB. (1985). Renal disease in hypertensive blacks. In: Hall WD, Saunders E, Shulman NB, eds. *Hypertension in Blacks*: Epidemiology, Pathophysiology and Treatment. Hall, Saunders and Shulman. P. 110.

Shulman NB. (1991). Economic issues relating to access to medications. In: Saunders E and Brest AN, eds. *Cardiovascular disease in blacks. Cardiovascular Clinics*, F.A. Davis Company, Philadelphia, pp.75-82..

Siffert W, Dusing R. (1995). Sodium-proton exchange and primary hypertension. An update. *Hypertension* 26:649-55.

Simmons D, Barbour G, Congleton J, et al. (1986). Blood pressure and salt intake in Malawi: an urban rural study. *Journal of Epidemiology and Community Health* 40:188-192.

Sjöström L. (1993) In: Stunkard and Wadding, eds. *Obesity: Theory and Therapy*, Second Edition, Raven Press New York. p13.

Slome C, Gampel B, Abrahamson JH, et al. (1960). Weight, height and skinfold thickness of Zulu adults in Durban. *South African Medical Journal* :505-509.

Somova LI, Connolly C, and Diara K. (1995). Psychosocial predictors of hypertension in Black and White Africans. *Journal of Hypertension* 13:193-199.

South Africa Demographic and Health Survey. (1998). *Preliminary Report*, MRC / Department of Health.

South African Medical Association Heart Failure Working Group. (1998). Heart Failure Clinical Guideline. *South African Medical Journal* 88:1135-1155.

Stallones R. (1985). Epidemiologic studies of obesity. *Annals of Internal Medicine* 103:1003-1005.

Stamler J, Wentworth D, Neaton JD, et al. (1986). Is the relationship between serum cholesterol and risk of premature death from coronary heart disease continuous and graded? Findings in 356 222 primary screenees of the Multiple Risk Factor Intervention Trial. *Journal of the American Medical Association* 256:2823-2828.

Stamler R, et al. (1978). Weight and blood pressure: Findings in hypertension screening of 1 million Americans. Journal of the American Medical Association 240:1607-1610.

Steppan C, Bailey S, Bhat S, et al. (2001). The hormone resistin links obesity to diabetes. *Nature* 409:307-312.

Steyn K, Jooste PL, Fourie JM, et al. (1986). Hypertension in the coloured population of the Cape Peninsula. *South African Medical Journal* 69:165-169.

Steyn K, Jooste PL, Bourne L, et al. (1991). Risk factors for coronary heart disease in the black population of the Cape Peninsula. The BRISK study. *South African Medical Journal* 79:480-485.

Steyn K, Katzenellenbogen JM, Lombard CJ, et al. (1997). Urbanization and the risk for chronic diseases of lifestyle in the black population of the Cape Peninsula, South Africa. Journal of Cardiovascular Risk 4:135-142.

Steyn K, de Wet T, Richter L, et al. (2000). Cardiovascular disease risk factors in 5- year-old urban South African children - the Birth to Ten Study. *South African Medical Journal* 90:719-725.

Steyn K, Gaziano T, Bradshaw D, et al. (2001). Hypertension in South African adults: results from the Demographic and Health Survey. *Journal of Hypertension* 19:1717-1725.

Stoker DJ. (1977). Statistiese Tabelle, Academica, Pretoria and Cape Town.

Stratton IM, Adler AI, Neil HAW. (2000). Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *British Medical Journal* 321:405-412.

Strobel A, Issad T, Camoin L, et al. (1998). A leptin missense mutation associated with hypogonadism and morbid obesity. *Nature Genetics* 18:213-215.

Swai ABM. (1990). Diabetes in tropical Africa: a prospective study, 1981-7. I.Characteristics of newly presenting patients in Dar es Salaam, Tanzania. *British Medical Journal* 300:1103-1106.

Swai ABM, McLarty DG, Kitange HM, et al. (1991). Study in Tanzania of impaired glucose tolerance. Methodological myth? *Diabetes* 40:516-520.

Swai ABM, Lutale JL, McLarty DG. (1993). Prospective study of incidence of juvenile diabetes mellitus over 10 years in Dar es Salaam, Tanzania. *British Medical Journal* 306:1570-1572.

Swai ABM, Mclarty DG, Kitange HM, et al. (1993). Low prevalence of risk factors for coronary heart disease in rural Tanzania. *International Journal of Epidemiology* 22:651-659.

Swislocki AL, Chen YD, Golay A, et al. (1987). Insulin suppression of plasma-free fatty acid concentration in normal individuals and patients with type 2 (non-insulin dependent) diabetes. *Diabetologia* 30:622-626.

Tahvanainen E, Syvänne M, Frick M, et al. (1998). Association or variation in hepatic lipase activity with promoter variation in the hepatic lipase gene. *Journal of Clinical Investigation* 101:956-960.

Tchernof A and Després JP. (1998). Obesity and lipoprotein metabolism. In: Kopelman PG and Stock MJ, eds. *Clinical Obesity*, Blackwell Science, Oxford, pp. 176-204.

Telmer S, Christiansen JS, Anderson AR, et al. (1984). Smoking habits and prevalence of clinical diabetic microangiopathy in insulin-dependent diabetics. Acta Medica Scandinavica; 215;63-68.

Temple R, Clark PMS, Hales CN. (1989). Measurement of insulin secretion in type 2 diabetes: pitfalls and problems. *Diabetic Medicine* 9:503-512.

Tiret L, Blanc H, Ruidavets JB, et al. (1998). Gene polymorphisms of the renin-angiotensin system in relation to hypertension and parental history of myocardial infarction and stroke: the PEGASE study. *Journal of Hypertension* 16:37-44.

Touyz RM, Rathakrishnan S, Reinach SG, et al. (1989). Hypertension, alcohol, and cations in urban black and coloured South Africans. *South African Medical Journal* 75:109-113.

Tripodi G, Valtorta F, Torielli L, et al. (1996). Hypertension-associated point mutations in the adducin α and β subunits affect actin cytoskeleton and ion transport. *Journal of Clinical Investigation* 97:2815-2822.

Truswell AS, Kennelly BM, Hansen JDL, et al. (1972). Blood pressures of !Kung Bushmen in Northern Botswana. *American Heart Journal* 84:5-12.

Trowell HC and Burkitt DP. (1981a). Preface. In: Trowell HC and Burkitt DP eds. *Western Diseases: their emergence and prevention*. Edward Arnold, London, p. xiv.

Trowell HC and Burkitt DP. (1981b). Preface. In: Trowell HC and Burkitt DP eds. *Western Diseases: their emergence and prevention*. Edward Arnold, London, p. xiii.

Tobias PV. (1990). Adult stature in southern African Negroes—further evidence on the absence of a positive secular trend. *South African Medical Journal* 78:97-101.

Tuch PS, Gill GV and Huddle KRL. (1994). Autonomic neuropathy in African diabetic patients. *Postgraduate Medical Journal* 70:188-191.

Tuomi T, Carlsson A, Haiyan L, et al. (1999). Clinical and genetic characteristics of type 2 diabetes with and without GAD antibodies. *Diabetes* 48:150-157.

Turner RC, Millns H, Neil HAW, et al. (1998). Risk factors for coronary artery disease in non-insulin dependent diabetes mellitus: United Kingdom prospective diabetes study (UKPDS:23). *British Medical Journal* 316:823-828.

Turner R. (1998). U.K. Prospective Diabetes Study. *Diabetes Care* 21:C35-C38.

UK Prospective Diabetes Study Group. (1998). Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. *British Medical Journal* 317:703-713.

Unger R and Foster DW. (1998). Diabetes mellitus. In: Wilson JD, Foster DW, Kronenberg HM, and Larsen PR, eds. *Williams Textbook of Endocrinology*, W.B. Saunders Company, Philadelphia, p. 985.

Unwin N, Alberti KGGM, Bhopal R, et al. (1998). Comparison of the current WHO and new ADA criteria for the diagnosis of diabetes mellitus in three ethnic groups in the UK. *Diabetic Medicine* 15:554-557.

Vaccarino V, Berger AK, Abramson J, et al. (2001). Pulse pressure and risk of cardiovascular events in the Systolic Hypertension in the Elderly Program. *American Journal of Cardiology* 88:980-986.

Vague J. (1956). The degree of masculine differentiation of obesities: A factor determining predisposition to diabetes, atherosclerosis, gout, and uric calculous disease. *The American Journal of Clinical Nutrition* 4:20-34.

Vaisse C, Clement K, Durnad E, et al. (2000). Melanocortin-4 receptor mutations are a frequent and heterogeneous cause of morbid obesity. *The Journal of Clinical Investigation* 106:253-262.

Van Gaal LF and Mertens IL. (1998a). Effects of obesity on the cardiovascular system. In: Kopelman PG and Stock MJ. *Clinical Obesity.* Blackwell Science, London, p. 212.

Van Gaal LF and Mertens IL. 1998b Effects of obesity on the cardiovascular system. *Clinical Obesity.* PG Kopelman and MJ Stock. Blackwell Science. London.p207.

Van Italie TB. (1985). Health implications of overweight and obesity in the United States. *Annals of Internal Medicine* 103:983-988.

van der Sande MAB, Milligan PJM, Nyan OA, et al. (2000). Blood pressure patterns and cardiovascular risk factors in rural and urban Gambian communities. *Journal of Human Hypertension* 14:489-496

Van Rensburg D, Friedman I, Ngwena C, et al. (2002). Strengthening local government and Civic responses to the HIV / AIDS epidemic in South Africa. Centre for Health Systems Research & Development, pp xvi.

Vaughan JP. (1979). Blood pressure and heart murmurs in a rural population in the United Republic of Tanzania. *Bulletin of the World Health Organization* 57:89-97.

Vermaak WJH, Steyn K, Rossouw JE, et al. (1988). Towards standardisation of pre- and post-analytical variables in the assessment of lipid risk factors for ischaemic heart disease. *South African Medical Journal* 74:485-490.

Verschuren WMM, Jacobs DR, Bloemberg BPM, et al. (1995). Serum Total Cholesterol and Long-term Coronary Heart Disease Mortality in Different Cultures. Twenty-five-Year Follow-up of the Seven Countries Study. Journal of the American Medical Association 274:131-136.

Veterans Administration Cooperative Study Group. (1967). Effects of treatment on morbidity in hypertension. Results in patients with diastolic blood pressure averaging 115 through 129 mm Hg. JAMA 202:1028-1034.

Veterans Administration Cooperative Study Group on Antihypertensive Agents. (1970). Effects of treatment on morbidity in hypertension (II). Results in patients with diastolic blood pressure averaging 90 through 114 mm Hg. JAMA 213:7:1143-1152.

Veterans Administration Cooperative Study Group on Antihypertensive Agents. (1987). Urinary and serum electrolytes in untreated black and white hypertensives. *Journal of Chronic Diseases* 40:839.

Vorster HH, Wissing MP, Venter CS, et al. (2000). The impact of urbanization on physical, physiological and mental health of Africans in the North West Province of South Africa: the THUSA study. *South African Journal of Science* 96:505-514.

Vorster HH. (2002). The emergence of cardiovascular disease during urbanisation of Africans. *Public Health Nutrition* 5(1A):239-243.

Wahl PW, Savage PJ, Psaty BM, et al. (1998). Diabetes in older adults: comparison of 1997 American Diabetes Association classification of diabetes mellitus with 1985 WHO classification. *The Lancet* 352:1012-1015.

Walker ARP. (1973). Studies bearing on coronary heart disease in South African populations. *South African Medical Journal* 47:85-90.

Walker ARP. (1975). The epidemiological emergence of ischaemic arterial diseases. *American Heart Journal* 89:133-136.

Walker ARP. (1981). South African black, Indian and coloured populations. In: Trowell HC and Burkitt DP, eds. *Western Diseases: their emergence and prevention*. Edward Arnold, London, p. p303.

Walker ARP and Walker BF. (1985). Coronary disease in blacks in underdeveloped populations (Letter). *American Heart Journal* :1410.

Walker ARP, Walker BF, Manetsi B, (1990). Obesity in black women in Soweto, South Africa: Minimal effects on hypertension, hyperlipidaemia and hyperglycaemia. *Journal of the Royal Society of Hypertension* 3:101-103.

Walker ARP, Walker BF, Manetsi B. (1991). Obesity in indigent elderly rural African women: effects on hypertension, hyperlipidaemia and hyperglycaemia. *International Journal of Vitamin and Nutrition Research* 61:244-250.

Walker ARP, Adam A, Kustner HGV. (1993). Changes in total death rate and in ischaemic heart disease death rate in interethnic South African populations, 1978- 1989. *South African Medical Journal* 83:602-605.

Walker AR, Adam F, Walker BF. (2001). World pandemic of obesity: the situation in Southern African populations. *Journal of Public Health* 115:368-372.

Walston J, Silver K, Bogardus C, et al. (1995). Time of onset of non-insulin dependent diabetes mellitus and genetic variation in the β_3-adrenergic-receptor gene. *New England Journal of Medicine* 333:343-347.

Watt GC, Harrap SB, Foy CJW, et al. (1992). Abnormalities of glucocorticoid metabolism and the renin-angiotensin system: a four-corners approach to the identification of genetic determinants of blood pressure. *Journal of Hypertension* 10:473-482.

Weiner JS, Lourie JA. (1969). Human Biology. International Biological Programme Handbook No 9. Blackwell, Scientific Publications, Oxford.

Weir MR and Hise MK. (1991). Hypertensive renal damage. In: Saunders E and Brest AN, eds. *Cardiovascular disease in blacks. Cardiovascular Clinics*, F.A. Davis Company, Philadelphia, p. 115-132.

West K. (1978). Factors associated with occurrence of diabetes. In: West Kelly M. *Epidemiology of Diabetes and Its Vascular Lesions*. Elsevier, New York, p. 232.

Weyer C, Pratley RE, Tataranni A, et al. (2002). Role of insulin resistance and insulin secretory dysfunction in the pathogenesis of type 2 diabetes mellitus: lessons from cross-sectional, prospective, and longitudinal studies in Pima Indians. *Current Opinion in Endocrinology & Diabetes* 9:130-138.

Widén E. Ekstrand A. Saloranta C. et al. (1992). Insulin resistance in Type 2 diabetic patients with hypertriglyceridemia. *Diabetologia* 35:1140-1145.

Widén E, Lehto M, Kanninen T, et al. (1995). Association of a polymorphism in the β_3-adrenergic-receptor gene with features of the insulin resistance syndrome in Finns. *New England Journal of Medicine* 333:348-51.

WHO Expert Committee. (1978). *Report of a WHO Expert Committee on arterial hypertension. World Health Organization*, Technical Report Series 628, World Health Organization, Geneva.

WHO Expert Committee (1980). *Report of a WHO Expert Committee on diabetes mellitus. Second report*. World Health Organization, Technical Report Series 646, World Health Organization, Geneva.

WHO Study Group. (1985). *Report of a WHO Expert Committee on diabetes mellitus*. World Health Organization, Technical Report Series 727, World Health Organization, Geneva.

WHO Consultation. (2000). *Obesity: Preventing the epidemic*. World Health Organization, Technical Report Series 894, World Health Organization, Geneva.

Williams AW. (1969). Blood pressure differences in Kikuyu and Samburu communities in Kenya. *East African Medical Journal* 46:262-272.

Williams R. (1997). Public health problems of diabetes mellitus and its cost to the community. In: Pickup JC and Williams G, eds. *Textbook of Diabetes*. Blackwell Science, Oxford, pp. 4.1-4.4.

Williams G. (2001). Diabetes black spots and death by postcode. The incidence, and inequity, of diabetes are likely to be worsened by obesity (Editorial). *British Medical Journal* 322:1375-1376.

Williams GH. (2001a). Approach to the patient with hypertension. In: Braunwald E, Fauci AS, Kasper DL, et al., eds. *Harrison's Principles of Internal Medicine*, 15th Edition, McGraw-Hill, New York, pp. 212-213.

Williams GH. (2001b). Hypertensive vascular disease. In: Braunwald E, Fauci AS, Kasper DL, et al., eds. *Harrison's Principles of Internal Medicine*, 15th Edition, McGraw-Hill, New York, p. 1414.

Williams GH. (2002c). Hypertensive vascular disease. In: Braunwald E, Fauci AS, Kasper DL, et al., eds. *Harrison's Principles of Internal Medicine*, 15th Edition, McGraw-Hill, New York, p. 1415

Wilson FH, Disse-Nicodème S, Choate KA, et al. (2001). Human hypertension caused by mutations in WNK kinases. *Science* 293:1107-1112.

Wilson PWF, D'Agostino RBD, Levy D, et al. (1998). Prediction of coronary heart disease using risk factor categories. *Circulation* 97:1837-1847.

Wing JR, Panz VA, Joffe BI, et al. (1993). Changes in glucose disposal and cellular insulin binding in obese black Southern African patients with Type 2 diabetes mellitus before and after sulphonylurea therapy. *Diabetic Medicine* 10:50-55.

Wolf PA, D'Agostino RB, O'Neal A, et al. (1992). Secular trends in stroke incidence and mortality. The Framingham Study. *Stroke* 23:1551-1555.

Wong ND, Wilson PWF, Kannel WB. (1991). Serum cholesterol as a prognostic factor after myocardial infarction: The Framingham Study. Annals of Internal Medicine 115:687-693.

Wong ZY, Stebbing M, Ellis JA, et al. (1999). Genetic linkage of beta and gamma subunits of epithelial sodium channel to systolic blood pressure. *The Lancet* :1222-5.

World Health Organization. (1994). *1993 World Health Statistical Annual.* Geneva, World Health Organisation p.xxxiv.

Yanagisawa M, Kurihara H, Kimura S, et al. (1988). A novel potent vasoconstrictor peptide produced by vascular endothelial cells. *Nature* 332:411-415.

Yeo GSH, Farooqi IS, Aminian S, et al. (1998). A frameshift mutation in MCR4R associated with dominantly inherited human obesity. *Nature Genetics* 20:111-112.

Yudkin JS. (1990). Impaired glucose tolerance. Is it a risk factor for diabetes or a diagnostic ragbag? *British Medical Journal* 301:397-402.

Zhou Y-P, Grill VE. (1994). Long-term exposure of rat pancreatic islets to fatty acids inhibits glucose-induced insulin secretion and biosynthesis through a glucose fatty acid cycle. Journal of Clinical Investigation 93:870—876

Zimmet PZ. (1982). Type 2 (non-insulin-dependent) diabetes - an epidemiological overview. *Diabetologia* 22:399—411.

Zimmet PZ. (1989). Non-insulin-dependent (Type 2) diabetes mellitus: Does it really exist? *Diabetic Medicine* 6:728-735.

Zimmet PZ. (2000). Globalization, coca-colonization and the chronic disease epidemic: can the Doomsday scenario be averted? *Journal of Internal Medicine* 247:301-310.

Zimmet P, Alberti KGMM and Shaw J. (2001). Global and societal implications of the diabetes epidemic. *Nature* 414:782-787.

Zinyowera T and Msamati BC. (1994). Obesity: is it a problem in black Africans in Zimbabwe? *Central African Journal of Medicine* 40:33-38.

ANNEX 1

Data collecting sheet and informed consent

UOFS, DEPT. OF INTERNAL MEDICINE: MANGAUNG DIABETES AND HYPERTENSION PROJECT

DATA COLLECTING SHEET :

Name: _____ Subject No: [ ][ ][ ][ ][ ]

Address: _____ Interviewer: [ ]

_____

_____

Nature of region: [1] (City = 1 Semi – rural = 2 Rural = 3)

Date of Examination: [ ][ ][ ][ ][ ][ ]

Date birth: [ ][ ][ ][ ][ ][ ] Age [ ][ ][ ] yr

Place of birth: (Town or district): _____

Sex (M,F): [ ]

Weight: [ ][ ][.][ ] kg
Height: [ ][.][ ][ ] m BMI [ ][ ][.][ ]
Protein in urine? Y = Yes N = No

Proturine [ ]

Glucose in urine? Y = Yes N = No

Glucosurin [ ]

Temperature [ ][ ][.][ ]

Is the respondent fasting? Y = Yes N = No

Fasting [ ]

Have you been sick lately? Y = Yes N = No
Na o kile wa kula morao tje?

Sicklately [ ] Specify: .....

Are you taking any drugs or medication regularly?

Na o nwa dipidisi kapa meriana kamehla?

Drugsregul ☐ Y = Yes N = No

Specify/ ha ho le jwalo, nehana ka hlaloso hore ke eng le hore hobaneng:

Have you ever been told by a doctor that you are suffering from diabetes?
Na o kile wa bolellwa ke ngaka hore tshwerwe ke bohloko ba tswekere (diabetes)?

Hxdiabetes ☐ Y = Yes N = No

Have you ever been told by a doctor that you are suffering from hypertension?
Na o kile wa bolellwa ke ngaka hore o tshwerwe ke bohloko ba kgatello e phahameng ya madi (high blood)?

Hxhyperten ☐ Y = Yes N = No

Since when are you living in Mangaung?
Ke ho tloha neng o dula Mangaung?

LiveMangaung | 1 | 9 | | |

What language do you most often speak at home? ☐
(only ONE language allowed)
Ke puo efe yeo o e buang haholo lapeng?

S. Sotho	1	English	5
Tswana	2	Afrikaans	6
Xhosa	3	Other	7
Zulu	4	Specify/Hlalosa	

EMPLOYMENT

Are you presently employed?
Na o ya sebetsa ha jwale?

Employed ☐ Y = Yes N = No

If no, are you a: ☐

Housewife?	1	unemployed	5
student	2	Other? (specify)	6
pensioner	3		
disabled	4		

Occupation (most of your workinglife): _____
(Describe)
Ke mofuta ofe wa mosebetsi oo o o entseng boholo ba bophelo ba hao ba ho sebetsa?

Occupation ☐☐ [for office use only]

Do you work in Bloemfontein? ☐ Y=Yes N=No
Na o sebetsa hona Bloemfontein?

PHYSICAL ACTIVITY

Does your work involve:
Na mosebetsi wa hao o o Qosa:

sitting and standing (minimal walking)
Ho dula le ho ema (no tsamaya ho honyenyane)

minimal walking ☐ Y = Yes N = No

or a lot of walking
kapa ho tsamaya haholo

lot of walking ☐ Y = Yes N = No

or hard physical word (sweat work)
kapa ho sebetsa haholo ka matla (ho fufuletsang)

sweat work ☐ Y = Yes N = No

Do you get any regular exercise outside working hours? (eg walking/cycling to and from work, gardening, sport, etc)
Na ho nale boikwetliso ba ka mehla boo o bo etsang ntle ho dihora ts mosebetsi e.g. ho tsamaya/ho palama baesekele, garden, sport

Regular exercise ☐ Y = Yes N = No

If yes: is it light exercise eg. gardening, walking, homework?
Ha karabo e le "E" na ke boikwetliso bo bobebe jwaloka toene (gardening) ho tsamaya kapa mosebetsi: wa lelapa?

Lightexercise ☐ Y = Yes N = No

or is it strenuous exercise eg. jogging, cycling, soccer, boxing etc.
Kapa ke boikwetliso bo matla jwaleka ho matha, ho palama baesekele, ho bapala bolo.

Strenuous exercise ☐ Y = Yes N = No

SMOKING HABITS/HO TSUBA

Do you smoke at present?
Na o motho ya tsubang kwae (ha jwale)?

Smokenow ☐ Y = Yes N = No

Do you use snuff? Y = Yes N = No

Snuff ☐

What do you smoke?
O tsuba mofuta ofe wa kwae?

Cigarettes ☐ Y, N, Blank

Pipe ☐ Y, N, Blank

Roll – up ☐ Y, N, Blank

Cigars ☐ Y, N, Blank

Give amounts/Bolela bongata ba kwae yeo o e tsubang. (per day) ka letsatsi.

Cigarettes ☐☐ per day

Pipe ☐☐ grams tabacco per day

Roll – up ☐☐ grams tabacco per day

Cigars ☐☐ per day

Snuff ☐☐ grams per day

At what age did you start smoking?
O qadile ho tsuba o na le dilemo tse kae?

Startsmoke ☐☐ yrs.

Have you ever tried to stop smoking?
Na o kile wa leka ho tlohela ho tsuba?

Try to stop ☐ Y = Yes N = No

If you do not smoke now have you ever?
Haeba ha o tsube hajwale na o kile wa tsuba pele?

Smokebefor ☐ Y=Yes N=No

Age when you began smoking:
O ne o le dilemo tse kae ha o qala ho tsuba?

Startsmoke ☐☐ yrs

Age when stopped smoking:
O ile wa tlohela ho tsuba ha ona le dilemo tse kae?

Stopsmoke ☐☐ yrs

DYSPNOEA/LETSHOEYA (HO FELLWA KE MOYA)

If disabled from walking by any other condition than heart or lung disease (eg amputation or stroke), mark "1" here and leave remaining questions unanswered.
O hlolwa ke tsamaya ka mabaka a mang ntle le ho bohloko ba pelo kapa matshwafo (eg jwaloka ho kgaoha leoto/ maoto kapa stroke)

Anyother ☐ Specify:

1. Are you troubled by shortness of breath when hurrying on level ground or walking up a slight hill? (If No, stop here)
Na o kgathatswa ke letshoeya (ho fellwa ke moya) ha o phakisa o tsamaya moo ho lekanang kapa ha o tsamaya o ehlwa lerallanyana?

Slight hill ☐ Y=Yes N=No

2. Do you get short of breath walking with other people of your own age on level ground? (If No, stop here)
Na o kgathatswa ke letshoeya (ho fellwa ke moya) ha o tsamaya le batho ba bang bao e leng dithaka le wena moo ho lekanang (ho sa nyolohe kapa ho theohela)?

own age ☐ Y = Yes N = No

3. Do you have to stop for breath when walking at your own pace on level ground? (If No, stop here)
Na o tlameha ho ema hore o kge moya ha o tsamaya o iketlile moo ho lekanang (ho sa nyolohe ho theohela)?

own pace ☐ y = yes N = No

4. Are you short of breath on washing or dressing?
Na o fellwa ke moya ha hlapa kapa o apara?

Washndress ☐ Y=Yes N=No

RESPIRATORY

Use the actual wording of each question. When in doubt, record No.

Cough/ Ho hohlela

1. Do you usually cough first thing in the morning in the winter?

(Count a cough with first smoke or on "first going out of doors". Exclude clearing throat or single cough.)
Na o tlwaetse ho hohlela hoseng feela ha o tsoha mariha (balla sehohlela se bang teng ha o qala ho tsuba hoseng kapa ha o tswela kantle) o se balle ho tletha sehohlela kapa sehohlela se le seng.

Coughearly ☐ Y=Yes N=No

2. Do you usually cough during the day or at night in the winter
(Ignore an occasional cough.)
Na o tlwaetse ho hohlela hara motshere kapa bosiu ha e le mariha. (Lebala ka sehohlela sa mohlang oo/ka sewelo).

Coughday ☐ Y=Yes N=No

3. Do you cough like this on most days for as much as 3 months each year?
Na o tlwaetse ho hohlela jwalo ka matsatsi a mangata hoo o ka a lekanyang le kgwedi tse kabang tharo selemong?

Coughmonth ☐ Y=yes N=No

Phlegm/Sekgohlela

4. Do you usually bring up any phlegm from your chest first thing in the morning in the winter?

Na o ntsha sekgohlela ho tswa ka sefubeng hoseng feela ha o tsoha mariha?

Phlegmfirst ☐ Y=Yes N=No

5. Do you usually bring up any phlegm from your chest during the day or at night. in the winter? (Accept twice or more.)
Na o tle o ntshe sekgohlela ho tswa ka sefubeng hara motsheare kapa bosiu mariha?(Amohela habedi kapa hofeta).

Phlegmday ☐ Y=Yes N=No

If yes to 4 and 5 ask:
Ha karabo e le "E" ho 4 kapa 5:

6. Do you bring up phlegm like this on most days for as much as three months each year?
Na o tle o ntshe sekgohlela hangata hoo o ka ho lekanyang kgwedi tse 3 selemong se seng le se seng?

Phlegmyear ☐ Y=Yes N=No

7. Since when are you bringing up phlegm on most days for as much as three months each year?
Ke ho tloha neng (selemo) o ntsha sekgohlela nako e ka etsang kgwedi tse tharo selemong, ka selemo le selemo?

each year | 1 | 9 | | |

8. Do you suffer from tuberculosis at present or have you ever suffered from tuberculosis in the past?

Tuberculosis ☐ Y = Yes N = No

HEALTH PERCEPTION/KA MOO O BANANG BOPHELO KATENG

Do you think to be obese could be harmful to one's health?
Na o nahana hore ho nona ho kaba le kotsi bophelong ba motho?

Obesity ☐ Yes = 1 No=2 Uncertain = 3

Do you think smoking is harmful to one's health?
Na o nahana hore ho tsuba ho kotsi bopheleng ba motho?

Harmful ☐ Yes = 1 No = 2 Uncertain = 3

Have you consulted a private doctor during the past 12 months?
Na o kile wa ya ngakeng ya Private dikgweding tse 12 tse?

Doctor ☐ Y = Yes N = No

Have you attended a hospital or clinic during the past 12 months?
Na o kile wa ya sepetlete dikgweding tse 12 tse fetileng?

Hospital ☐ Y = yes N = No

Have you consulted a traditional healer during the past 12 months?
Na o kile wa ya ngakeng ya sesotho dikgweding tse 12 tse fetileng?

TradHeal ☐ Y = yes N = No

MARITAL STATUS/TSA LENYALO

Are you married?(Legally or according to custom)
A o nyetse/nyetsoe?

married ☐ Y = Yes N = No

Do you live together?
O dula mmoho le motswalle jwaleka monna le mosadi?

livtogether ☐ Y = Yes N = No

Are you widowed?
O mohlolohadi?

widowed ☐ Y = Yes N = No

Are you divorced?

O hladile ka molao kapa le kgaohane feela?

divorced ☐ Y = Yes N = No

SOCIO – ECONOMIC

How many years of formal schooling have you completed? (including technicon and university)
O kene sekolo dilemo tse kae? (Balella le tsa technicon le hae le university)

Schooling ☐☐ yrs

Can you read in your home language?
Na o ka bala ka puo ya hao?

Read ☐ Y = Yes N = No

Can you write in your home language?
Na o ka ngola ka puo ya hao?

Write ☐ Y = Yes N = No

How many persons in this household earn money?
Na ke batho ba bakae lelapeng mo ba fumanang moputso?

earn money ☐

How many people are dependent on this money?
(Including those who live elsewhere?)
Ke batho ba bakae lapeng ba phelang ka moputso o (balella le batho ba s
duleng moo empa ba ja moputsong oo).

dependent ☐☐

Type of housing: ☐
Mofuta wa ntlo:

Council house 1
Thlo ya masepala

Core house/ 2

Private (western)House 3
Ntlo ya

Hostel 4
Hostele

Shack 5
Mokhukhu wa masenke

Tent 6
Tente

Hut 7
Mohlomafatshe

Traditional house 8

Other 9

Do you have electricity available inside your house?

Na mothlakase o teng ntlong ya hao?

electricity ☐ Y = Yes N = No

Water supply: ☐
Metsi mohlodi

Tap in house 1
Pompo ka hara ntlo

Tap outside house 2
Pompo e ka ntle

Shared tap 3
Pompo e kopanetsoeng

Communal tap 4
Pompo ya seterateng

Other (describe) 5
Mohlodi o mong (Hlalosa) _____

What do you use for cooking? Y = Yes N = No
O sebedisa eng bakeng sa ho pleha?

Electricity Motlakase	☐	Wood Patsi	☐
Gas Gase	☐	Coal Mashala	☐
Paraffin Paraffin	☐	Open fire Leifo	☐
Other Ho hong, hlalosa	☐	_____ (SPECIFY)	

Does any one or more persons in your house own a motorcar?
Na hona le motho kapa batho lapeng la hao ba nang le makoloi?

Motorcar ☐ Y = Yes N = No

Do you have a radio in your house?
Na o na le radio/wireless lapeng la hao?

Radio ☐ Y = Yes N = No

Do you have a TV set in your house?
Na o na le Television lapeng la hao?

TV ☐ Y = Yes N = No

Have you read a newspaper yesterday or today?
Na o kile wa bala koranta kajeno?

Newspaper ☐ Y = Yes N = No

Number of rooms in house?
(Excluding kitchen and bathroom)
Ntlo e, e na le dikamoro tse kae? (O seke wa bala kitchen kapa bathroom)

Rooms ☐☐

Number of people living under the same roof:
Ke batho ba bakae ka palo ba dulang lapeng le?

Sameroof ☐☐

Did you breastfeed your children? (females only)
Na o ne o nyantsha bana ha ba le banyenyane?

Brestfed ☐ Y = Yes N = No

FAMILY HISTORY/ BOPHELOBA FAMILY (LESIKA)

Do any of your relatives suffer from hypertension?
Na ho nale e mong wa lesika la hao ya tshwerweng ke bohloko ba kgatell phahameng ya madi?

Family1 ☐ Y=Yes N=No

If Yes, specify:
Ha karabo e le E hlalosa ka botlalo:

Family2 ☐

Mother = 1 Brother/Sister = 3
Mme Oubuti/Ousi

Father = 2 Other = 4 .....
Ntate Ba bang

Do any of your relatives suffer from diabetes?
Na ho nale e mong wa lesika la hao ya tshwerweng ke bohloko tswekere(diabetes)?

Family3 ☐ Y = Yes N = No

Ha karabo e le E hlalosa ka bothlalo:

Family4 ☐

Mother = 1 Brother/Sister = 3
Mme Oubuti/Ousi

Father = 2 Other = 4 .....
Ntate Ba bang

ALCOHOL/JWALA

Do you drink alcoholic beverages?
Na o nwa dino tse tahang?

DrinkAlcol ☐ Y = Yes N = No

If Yes, when do you drink – during the week or over week-ends?
Ha karabo e le "E" o nwa hara beke kapa mafelong a beke?

During the week ☐ Y = Yes N = No
Hara beke

Over week-ends ☐ Y = Yes N = No
Ka mafelo a beke

Occasionally only ☐ Y = Yes N = No
Mohlang oo/ka sewelo

Do you brew your own beer? ☐ Yes N = No
Na o iketsetsa jwala?

What do you usually buy/drink?

Home-brewed beer ☐ Y = Yes N = No
Mqombothi

Beer ☐ Y = Yes N = No

Wine ☐ Y = Yes N = No

Hot stuff ☐ Y = Yes N = No
(Brandy, whisky, gin, cane, vodka)

Skonfana ☐ Y = Yes N = No

How much do you usually buy per week?
(Number of bottles, cans, litres)
O reka jwala bo bokae ka beke?
(Bolela palo ya dibotlolo, dikane, dilitara)

Beer ☐☐.☐ litre
Wine ☐☐.☐ litre
Hot stuff ☐☐.☐ litre
Skonfana ☐☐.☐ litre

GYNAECOLOGIC QUESTIONNAIRE

Have you or your husband had any of the following?
Na oena kapa monna wa hao o kile a ba le engwe ya tse latelang?

Contra1 ☐ Y = Yes N = No

If you haven't had a sterilisation or hysterectomy, are you using a contraception now?
Haeba ha wa ikwala kapa ha wa ntsha popela, na o sebedisa tekanyo malapa?

Contra2 ☐

Pill/ Pilisi = 1 Injection = 2

"Loop" = 3 Condom (Husband) = 4

Other = 5

How many children did you deliver?
O pepile bana ba bakae?

Children ☐

Year of menopause: 19☐☐

PHYSICAL EXAMINATION;

Skinfolds to the nearest 0,2 mm:

Midarm ☐☐.☐ cm Waistcirc ☐☐☐.☐ cm

Triceps ☐☐.☐ mm Hipcirc ☐☐☐.☐ cm

Biceps ☐☐.☐ mm Buttocks ☐☐☐.☐ cm

Subscap ☐☐.☐ mm Thigh circ ☐☐.☐ cm

Parathor ☐☐.☐ mm

Suprailil ☐☐.☐ mm

Clubbing present ☐ Y = Yes N = No

Anaemic ☐ Y = Yes N = No

Koilonychia ☐ Y = Yes N = No

Skin: Y = Yes N = No

Pellagrous dermatoses ☐

Naso – labial dyssebacea ☐

Xerosis ☐

Parotid enlargement ☐ Y = Yes N = No

Mouth: Y = Yes N = no

Angular stomatitis ☐

Glossitis ☐

Depigmentation of lips ☐

Thyroid 1 = Normal 2 = Enlarged ☐

Trachea 1 = Central 2 = Displaced ☐

Gynecomastia 1 = Abscent 2 = Present ☐

Hirsutism 1 = Abscent 2 = Present ☐

Bloodpressure:

Systolic1 ☐☐☐ mm Hg

Systolic2 ☐☐☐ mm Hg

Diastolic1 ☐☐☐ mm Hg

Diastolic2 ☐☐☐ mm Hg

Phase IV and V differ more than 10 mm Hg ☐ Y = Yes N = No

Apex Beat: ☐

Absent = 1

Inside MCL = 2

Outside MCL = 3

Interspace ☐

Murmers: Y = Yes N = No ☐

MI present = Y Absent = N ☐

MS present = Y absent = N ☐

AI present = Y absent = N ☐

AS present = Y absent = N ☐

Other present = Y absent = N ☐

Chest findings:

Normal Y = Yes N = No ☐

COAD Y = Yes N = No ☐

Pleureffus Y = Yes N = No ☐

Pneumonia Y = Yes N = No ☐

Other Y = Yes N = No ☐

Fundus Right:

KW Grade ☐ 5 = normal 6 = cannot examine

Fundus Left:

KW Grade ☐ 5 = normal 6 = cannot examine

Arcus cornealis ☐ 1 = abscent 2 = Present

Did he/she take the glucose solution? ☐ Y = Yes N = No

Untoward effects of glucose solution? ☐ Y = Yes N = No

Describe: _____

Was it necessary to refer the respondent? ☐ Y = Yes N = No

ECG ☐ Y = Yes N = No

Resp. Function ☐ Y = Yes N = No

REPEAT SKINFOLD MEASUREMENTS FOR EVERY 20TH RESPONDENT

Midarm2 ☐☐.☐ Waistcirc2 ☐☐☐.☐

Triceps2 ☐☐.☐ Hipcirc2 ☐☐☐.☐

Biceps2 ☐.☐ Buttocks2 ☐☐☐.☐

Subscapula2 ☐.☐ Thigh circ2 ☐☐.☐

Parathorac2 ☐☐.☐

Suprailiac2 .☐☐

/qwaqwa.dia

CONSENT FORM/FOROMO YA TUMELLO

I, ... hereby declare that I participate out of my ow
free will in the Mangaung diabetes and hypertension study. I agree to take th
glucose solution and give my consent to the taking of blood samples a
explained to me.

Nna, ... ke tsebisa mona hore ke na le kabelo k
boithaopo morerong wa Mangaung twantsho ya bohloko ba tswekere le b
kgatello e phahameng ya madi a yang hloohong le mahloko a mang a pelo. K
dumela le ho nwa mokedikedi wa tlulukose mme ke dumela hape le hore h
nkuwe disampule tsa madi a ka jwalo ka ha ke se ke hlaloseditswe.

I have been fully informed by ..... regarding the detail of th
study as well as the possible untoward effects of the abovementioned tests.

Ke se ke hlaloseditswe ka botlalo tsa morero wona ekasitana le dipheto tsa k
hlahelang hamarao tsa diteko tsa boletsweng ka hodimo.

_____ _____

Volunteer/Moithaopi Date/Mohla

_____

Person who informed participant
Motho ya haloseditseng ya bileng le kabelo

_____

Person in charge of the project
Motho ya ikarabellang mabapile morero

ANNEX 2

Repeat measurements

Table A.2/1. Mean difference between first and second skinfold and circumference measurement

	Both observers				First observer				Second observer			
	n	Difference	SD	p	n	Difference	SD	p	n	Difference	SD	p
Midarm (cm)	54	0.47	0.97	0.00	44	0.51	1.06	0.00	10	0.28	0.42	0.07
Waist (cm)	54	0.48	1.78	0.07	43	0.46	1.83	0.13	11	0.55	1.61	0.44
Triceps (mm)	55	0.11	1.06	0.15	44	0.11	1.18	0.29	11	0.11	0.26	0.21
Hip (cm)	55	-0.42	3.70	0.98	44	-0.03	1.82	0.95	11	-1.96	7.60	0.86
Biceps (mm)	55	-0.20	3.06	0.73	44	-0.42	3.36	0.49	11	0.70	0.99	0.03
Buttock (cm)	54	0.89	5.08	0.15	43	1.01	5.70	0.36	11	0.40	0.99	0.19
Subscapular (mm)	55	0.52	3.51	0.34	44	0.67	3.90	0.33	11	-0.11	0.75	0.64
Thigh (cm)	55	-0.69	5.00	0.81	44	-0.88	5.56	0.30	11	0.10	0.51	0.76
Parathoracic (mm)	55	0.79	3.73	0.18	44	0.73	4.04	0.29	11	1.02	2.20	0.54
Suprailiac (mm)	55	0.08	3.31	0.55	44	0.05	3.70	0.59	11	0.20	1.16	0.58

Table A.2/2. Mean difference between first and second skinfold and circumference measurement (after correction)

	Both observers				First observer				Second observer			
	n	Difference	SD	p	n	Difference	SD	p	n	Difference	SD	p
Midarm (cm)	52	0.32	0.60	0.07	42	0.33	0.66	0.00	10	0.28	0.42	0.07
Waist (cm)	53	0.49	1.79	0.07	42	0.47	1.86	0.13	11	0.55	1.62	0.44
Triceps (mm)	54	0.09	1.06	0.20	43	0.09	1.18	0.38	11	0.11	0.26	0.21
Hip (cm)	54	-0.29	3.63	0.80	43	0.14	1.44	0.72	11	-1.96	7.60	0.86
Biceps (mm)	54	-0.34	2.92	0.90	43	-0.60	3.14	0.33	11	0.70	0.99	0.03
Buttock (cm)	53	0.94	5.11	0.09	42	1.08	5.73	0.23	11	0.40	0.99	0.19
Subscapular (mm)	54	0.84	4.10	0.22	43	1.08	4.60	0.20	11	-0.11	0.75	0.64
Thigh (cm)	54	-0.69	5.05	0.72	43	-0.89	5.65	0.90	11	0.10	0.51	0.76
Parathoracic (mm)	54	0.82	3.76	0.13	43	0.77	4.08	0.22	11	1.02	2.20	0.54
Suprailiac (mm)	54	-0.08	3.13	0.70	43	-0.14	3.47	0.77	11	0.20	1.16	1.00

ANNEX 3

Study protocol

Diabetes mellitus, hypertension and related factors in black subjects residing in Qwaqwa and Mangaung

SUMMARY

Urbanisation as well as internal and external migration may profoundly influence the health of a population. Specific lifestyle-interventions may prevent or attenuate the development of typical Western diseases. The purpose of this proposed study is to determine the prevalence of hypertension and diabetes as well as some other cardiovascular risk factors in a rural and urban black population. The possible contribution of external factors to the development of these diseases will be examined as well as the relationship between insulin levels, blood pressure and body fat distribution. A further objective is to determine the prevalence of chronic bronchitis and abnormal respiratory function tests in the same communities. This study could also pave the way for future longitudinal studies to examine the impact of modernization on the health patterns of a rapidly urbanizing society.

BACKGROUND

Epidemiological studies have shown that Type 2 or non-insulin dependent diabetes (NIDDM) has a global distribution and its prevalence varies from country to country, in different ethnic groups in the same country, and between the same ethnic group undergoing internal or external migration[1]. The impact that an uncontrolled and rapid urbanization process has on all aspects of health is of great concern[2]. Furthermore, there is already evidence of the black people now sharing what are for them new diseases but which are long-established in Western communities e.g. ischaemic heart disease and hypertension[2]. To this can also be added diabetes mellitus. By the year 2000 more than 75% of all people living in South Africa will be urbanised[2].

Information is particularly scarce regarding the occurrence of NIDDM in African blacks[3]. Prevalence rates of diabetes are also generally lower in rural than in urban populations[3]. A study conducted in Cape Town during 1969 found the prevalence of diabetes amongst Blacks to be 3.6%[4]. This is also the figure officially recognized by the World Health Organization (WHO) for both Caucasians and Blacks in this country[5]. The Cape Town study however, was biased towards the age group 25 - 44 years. An unusual finding of this study was the fact that the prevalence of diabetes did not increase with increasing age above 35 years. This finding was never substantiated by other studies since the Cape Town study was the only well-

planned study ever done to assess diabetes prevalence amongst Blacks in this country.

Although obesity is a recognized risk factor for NIDDM, the susceptibility to diabetes is also unmasked by environmental factors such as a sedentary life-style, dietary factors, stress, urbanization and acculturation[4].

Diabetes mellitus is associated with accelerated atherosclerosis: It doubles the risk for stroke, increases the risk for myocardial infarction 2- to 3-fold and for peripheral vascular problems 50-fold. Diabetes is also the most common cause of blindness in the Western world today as well as a leading cause of end stage renal disease. Today NIDDM is being viewed as a possible preventable disease and programmes for prevention are receiving attention[5].

Modernization of lifestyle of a population in situ as well as rural to urban shifts of traditional populations provide the opportunity to study the influence of urbanization on the development of diseases such as diabetes and hypertension[1]. Since 1985 a more rational classification and definition of diabetes and impaired glucose tolerance has emerged thus obviating many of the earlier problems in the study of the epidemiology of diabetes[5].

The prevalence of hypertension in a sample population of rural and urban Zulus was found to be 10.5% and 25% respectively[6]. The most common clinical complication longstanding hypertension in Blacks is some form cardiovascular disease developing in 38.5%[7].

There is also substantial evidence that insulin resistance, glucose intolerance and hyperinsulinaemia exist in subjects with high blood pressure[8,9]. A central pattern of fat distribution was postulated to be of cardinal importance in the development of these metabolic abnormalities as well as dyslipidaemia[10]. Since hypertension in blacks differ in several respects from hypertension in Caucasians the relationship between hypertension, serum lipids, body fat distribution, carbohydrate tolerance and serum insulin (and related peptides) should also be examined in this group. It was also postulated that a reduced urinary excretion of potassium and a high urinary sodium / potassium ratio might be contributory to the development of hypertension in blacks[11].

HYPOTHESIS

Hyperinsulinaemia, insulin resistance and a central pattern of fat distribution is associated with essential hypertension and dyslipidaemia in blacks.

AIM OF STUDY

The objectives of this study are as follows:

1. To determine and compare the prevalence of the following variables in urban and rural blacks: hypertension, diabetes mellitus and glucose intolerance, dyslipidaemia, and obesity.
2. To evaluate the relationships between serum insulin levels, body fat distribution and the aforementioned variables.
3. To study the possible association of some external factors with these variables. E.g.: Age, physical activity, dietary factors, socio-economic status, parity, alcohol and psycho-social stress due to modernization and urbanization.
4. To evaluate the possible association between a low potassium intake and urinary excretion and essential hypertension in blacks.
5. A secondary objective will be to determine the prevalence of chronic bronchitis and abnormal respiratory function tests in a black community.

BASIC ORGANIZATION

Prof. D.J.V. Weich will act as overall supervisor of this study. The study will be conducted in the field by dr. W.F. Mollentze assisted by health care workers and a research assistant. We plan on starting the study at the beginning of May 1990, and to conduct it in two phases of 25 weeks each, starting at Qwaqwa. A third phase of 25 weeks is planned for analysis and reporting of data.

This study will also be conducted with close liaison between ourselves, the Dept. ot Community Health, UOFS and the South African Medical Research Council's Centre for Epidemiological Research and Institute for Biostatistics.

MATERIALS AND METHODS

Sampling:

a). Qwaqwa: According to the Human Sciences Research Council[12] Qwaqwa can socio-economically be divided into 3 regions: The first being the capital Phuthaditjhaba which is a rapidly growing city, secondly the remote areas where a traditional lifestyle still prevails and thirdly a transitional zone which lies in between. The population registry of the Dept. of Development Aid of 1986/87 will be used for sampling purposes. The estimated sample size is 1900 and subjects will be selected proportional to the population of the 12 regions of the area. The sample will be stratified according to sex and age in decades from 25 years and older. Those older than 65 years will be treated as one stratum. The method of systematic sampling

will be used to select dwellings once the area of interest has been identified. Two persons (a male and a female) will be selected per dwelling and the subjects will be interviewed to explain the proposed study. Those who are willing to participate in the study will constitute the actual sample. Previously diagnosed cases of hypertension and diabetes will be noted. The sampling procedure was designed by prof. Stoker of the Human Sciences Research council. b). Mangaung: A similar sampling procedure will be followed in this area. Should difficulties be encountered to find and interview a specific subject, two more attempts at later dates will be made before abandoning the recruiting process. The response rate will be noted.

Exclusion criteria:

Pregnancy, being bedridden, mental retardation, known malignancies, anti-tuberculous drug therapy and hospitalization of more than 1 week in the previous 3 months. Those who are unwilling will also be excluded.

Anthropometric measurements:

All subjects will be examined in the morning and all skinfold measurements will be performed in the standing position. Height will be recorded and subjects will be weighed dressed in underwear only with the aid of a Seca beam scale and measuring column. Body mass will be rounded of to the nearest 0.5 kg. The scale will be standardized weekly during the study. Skinfold measurements will be made on the left side of the body with a Harpenden skinfold caliper as described by Weiner and Lourie[13]. The instrument will be calibrated monthly. Triceps skinfold: The subject must be standing, left arm relaxed but flexed 90^0 at the elbow. A horizontal mark will be made with a black "koki" pencil half way (measured) between the inferior border of the acromial process and the tip of the olecranon process. (Acromion: The inferior edge of the most external border of the acromion process.) The arm will now be allowed to hang down just away from the body. The skinfold will be picked up between the thumb and the forefinger at the back of the arm about 1 cm above the level marked on the skin with the skinfold directly in line with the olecranon process. The caliper jaws will be applied at exactly the level marked. The measurement is read 2 seconds after the full pressure of the calliper jaws is applied to the skinfold. The biceps skinfold: The skinfold will be picked up at the front of the arm, with the arm still in the hanging position, directly above the center of the cubital fossa, at the same level as that at which the triceps skinfold is measured. Upper arm circumference: A steel tape will be used. The subject's arm hangs relaxed, just away from his side, and the circumference is taken horizontally at the marked level. The subscapular skinfold: The skinfold will be picked up under the angle of the left scapula with the crest at 450 to the vertical. Parathoracic skinfold: The skinfold will be picked up midway between the axilla and iliac crest. Suprailiac skinfold: Will be picked up just above the iliac crest in the mid-

axillary line. Abdominal circumference: (Umbilical level) The subject will be standing erect with his abdomen relaxed and breathing normally. The circumference will be recorded to the nearest 0.5 cm at the end of normal expiration. The tape will be held behind the subject with one edge in the horizontal plane through the center of the umbilicus. The tape will then be wrapped carefully around the subject's torso. The skin should not be pressed inwards. Hip circumference will be measured to the nearest cm at the iliac crest level. The maximum circumference over the buttocks will also be recorded. Thigh circumference: Thigh length will first be measured. The subject must stand with the left knee slightly flexed, leg abducted and with the left foot remaining on the floor. A skin mark will be made halfway between the greater trochanter and the inferior border of the lateral epicondyle of the femur. Thigh circumference will be measured at this level, care will be taken that the tape remains horizontally and that the tape does not indent the skin. Elbow breadth: The subject's left arm will be extended forward perpendicular to the body. With the arm bent so the angle at the elbow forms 90^0 with the fingers pointing up and the dorsal part of the wrist toward the examiner, the greatest breadth across the elbow joint will be measured with a sliding caliper along / the axis of the upper arm. Skinfold and circumference measurements will be made in duplicate in every 20th subject after random selection of the first subject.

Blood glucose and insulin levels:

Subjects will be requested to fast overnight after an early dinner (not later than $\pm$ 20h00) and to report early in the morning. Drinking of water will be allowed. The subject's oral temperature will be recorded and if the subject is pyrexial the test will be postponed. Prior dietary preparation will not be requested but the following questions will be put to the respondent: 1. Have you been on a diet lately? 2. Have you lost any weight recently? 3. Have you cut down lately on starches and sugars? If the answer is affirmative to any of these questions a preparatory diet containing at least 300g of carbohydrate will be prescribed for 3 days before doing the test. As regards possible underlying illness, the following questions will also be put to the subject and the answers recorded: 1. Have you been sick lately? 2. Are you taking birth control pills (females)? 3. Are you taking any drugs or medication regularly (including herbal/tribal medicines)? The test will not be cancelled should the answers be affirmative, but it will be considered when interpreting the results. Subjects will be allowed to lie down after the oral glucose tolerance test (OGTT) has started. Known diabetics will not be submitted to an OGTT. However, fasting plasma glucose and serum fructosamine levels will be determined. The OGTT will be started between 08h00 and 09h00. Five ml clotted venous blood will be collected as well as 2 ml blood in a NaF container for fasting insulin and plasma glucose estimations respectively. Seventy-five grams of glucose will be dissolved in 250 ml water

(30% solution) and the subject will be instructed to drink the mixture in 5 min. Nausea and vomiting will be noted. One and two hours later blood samples will again be obtained for glucose and insulin measurements. Additional blood samples will be obtained at 30 min from every 10th patient.

Other biochemical parameters:

Fasting blood specimens will also be collected for the following measurements: 10 ml clotted blood for total cholesterol, HDL-cholesterol and triglycerides; 5ml clotted blood for a biochemical profile; 5ml clotted blood for thyroid function tests from every 10th subject; 5ml clotted blood for serum iron measurement; 5ml clotted blood for serum zinc, chromium and copper measurements; 5ml clotted blood for serum fructosamine measurement. All blood specimens will be centrifuged on site within 5 hours and where necessary the serum/plasma stored at -20°C until the appropriate analysis can be performed. The diagnosis of diabetes and impaired glucose tolerance will be made according to the 1985 WHO criteria[5].

Urine specimens:

One and a half hours after the glucose load the subject will be asked to empty his bladder. At 2 hours post glucose load a second urine specimen will be obtained and tested semi-quantitatively with Labstix for glucose and protein. An aliquot of this specimen will be frozen for the later biochemical determination of sodium, potassium, calcium and creatinine. A Micro-Bumintest examination will also be performed on the urine of all diabetic and hypertensive subjects whose urine is dipstick negative for albumin. This will be done at a later date as a sensitive semi-quantitative measure of protein excretion. The test material will be provided free of charge by Ames laboratories.

Habitual physical activity:

Occupation and habitual physical activity will be recorded according to the data collecting sheet.

Socio-economic status:

The number of rooms in the dwelling with the exception of the bathroom and kitchen will be recorded as well as the number of people living together. It will be recorded whether the subject is employed and whether he works in Qwaqwa or not. The kind of employment will also be noted. The dependent-to-worker ratio will be determined.

Parity:

The parity of each female subject as well as a history of breastfeeding will be recorded.

Alcohol:

The type, amount and frequency of alcoholic beverages consumed will be recorded for all subjects.

Smoking:

A detailed smoking history will also be obtained for all subjects.

A Dyspnoea and respiratory questionnaire will also be completed (data collecting sheet).

Electrocardiograph:

A 12 lead resting electrocardiograph will be obtained with a Mac PC electrocardiograph machine. The recordings and interpretations will be performed by the same person. The electrodes will be placed according to the "classic" positions described[14]. The actual procedure will be conducted as prescribed and the ECG's interpreted independently by two separate observers according to a revised Minnesota coding system[15]. Where agreement between the two observers cannot be reached a third person's opinion will be sought.

Respiratory function tests will be performed with a dry rolling spirometer with a pulmonary analysis computor (Vica Test®). The following parameters will be measured: Vital capacity, peak flow, forced expiratory volume in 1 second FEV1, FEV25%, FEV50% and FEV 75%. The best of 3 measures will be recorded.

Dietary factors:

A standardized food frequency questionnaire will be completed for every tenth person after random selection of the first person. A pilot study will be done to assess local food predilection as well as methods of preparation. This questionnaire will be completed by trained dieticians from the Department of Dietetics, Potchefstroom University for higher Christian Education. Portion sizes will be established by weighing. Respondents will also be requested to bring their eating utensils along to assist us with portion sizes.

Physical Examination:

Every subject will be examined according to the attached data collecting sheet with emphasis on the cardiovascular and respiratory systems.

Blood pressure:

It will be documented whether the respondent is a known hypertensive and whether he is or was on therapy in the past. Blood pressure will be measured 2 times in the supine position in the right arm after 5 min rest with a random zero sphygmomanometer and will be recorded to the nearest 2 mm Hg. These values will be averaged[16]. A cuff with a standard bladder size will be used (12.5x23 cm). The center of the bladder will be placed over the brachial artery. Should it be necessary to use an obese cuff, it will be noted. Every endeavor will be made to use the standard cuff throughout. The method described by Maxwell[17] will be used to correct BP for arm circumference. The 1st and 5th phase Korotkoff sounds will be used to record systolic and diastolic BP respectively. Should the difference between the 4th and 5th Korotkoff phases exceeds 10 mmHg it will also be noted. Some patients will be examined while the

OGTT is still in progress.

Direct funduscopy will be performed on each subject trough a dilated pupil. Dilatation will be performed by the installation of 2 drops of tropicamide into each eye after clinically excluding a shallow anterior chamber. The Keith-Wagener-Barker grading system will be used to grade abnormalities. Should diabetic retinopathy be present, it will be recorded separately.

ETHICAL CONSIDERATIONS:

Approval for the conduction of the study will be obtained from the ethics committee of the Medical Faculty of the UOFS[18] and the researchers will also comply with the Declaration of Helsinki as adopted by the World Medical Assembly 1964 and amended in 1975 and 1983. Informed and signed consent will be obtained from each subject and the consent of the head of the household will also be obtained where applicable. In case of illiteracy the subject's right thumb print will be accepted as a signature after careful explanation in his own language. In cases where subjects are found to be suffering from diseases specifically screened for or any other disease, they will be referred in writing to the nearest hospital/doctor of choice.

BUDGET:

Personnel: Dr. W. F. Mollentze will be seconded by the Dept of Internal Medicine to complete the study. Health care workers: Will be provided by the local authority or homeland-government. Research assistant: (Std. 10 and from same ethnic group) : R10,000 p.a. for one year. Transportation: An equipped vehicle will be provided by a private company (negotiations under way). Running costs are estimated as follows: 1st phase: Qwaqwa: 25000 km @ 35c: R8750. 2nd phase - Mangaung: 10000 km @ 35c: R3500 TOTAL: R12250

Accommodation: The Qwaqwa government will provide us with accommodation. The 2nd phase will be conducted from Bloemfontein on a daily basis. The Qwaqwa government will also supply the necessary fuel for travelling in that area. Food models:Will be provided by the Department of Dietetics, UOFS. Stationary and consumables: Will be supplied by the Dept. of Internal Medicine, UOFS. Laboratory tests: All analytical work will be done by the Dept. of Chemical Pathology, UOFS at an all inclusive fee of R24 per subject. Total estimate for laboratory work: R96000. Total cost for project: R118250.

Pilot study: We plan to do a pilot study on 20 subjects scheduled for April 1989.

DATA CAPTURING AND ANALYSIS:

The Epi Info Version 3 software program for personal computers will be used for construction of the questionnaires as well as for storing of data. The association of hypertension and glucose (fasting, 1 hour and 2 hours), serum insulin levels (fasting, 1 hour and 2 hours) and

BMI will be submitted to regression and correlation analysis. The association of body fat distribution and blood pressure, insulin levels and blood glucose will be examined by Chi-square analysis of contingency tables. Nutrient analysis will be carried out by computer using a programme based on local food tables (NRIND). Data collecting sheets are attached.

This draft protocol was prepared by dr. W.F. Mollentze and prof. D.J.V. Weich, Department of Internal Medicine (G73), University of the Free State, P.O. Box 339, Bloemfontein, 9300.

REFERENCES:

1. Zimmet P. Type 2 (Non-Insulin-Dependent) Diabetes - An Epidemiological Overview. Diabetologia 1982;22:399-411.
2. Brink AJ. The challenges for the supply of research manpower in South Africa. People for research and development 1988; Proceedings of Conference held in the CSIR Conference Center, Pretoria, 23-24 August 1988.
3. Marble A, Krall LP, Bradley RF, et al. Joslin's Diabetes Mellitus. 12th ed. Philadelphia: Lea and Febiger, 1985.
4. Marine N, Vinik AI, Edelstein I, et al. Diabetes, Hyperglycemia, and Glucosuria Among Indians, Malays and Africans (Bantu) in Cape Town, South Africa. Diabetes 1969;8:840-857.
5. Report of a WHO Study Group. World Health Organization Technical Report Series 727, 1985.
6. Seedat YK, Seedat MA, Hackland DBT. Biosocial factors and hypertension in urban and rural Zulus. S Afr Med J 1982; 61: 999-1002.
7. Mokhobo KP. Aspects of hypertension among Blacks. S Afr Med J 1982;61:929-930.
8. Modan M, Halkin H, Almog S, et al. Hyperinsulinemia: A link between hypertension, obesity and glucose intolerance. J Clin Invest 1985;75:809-817.
9. Reaven GM, Hoffman BB. A role for insulin in the aetiology and course of hypertension. Lancet 1987:435-436.
10. Kaplan MN. The deadly quartet. Arch Intern Med 1989;149:1514-1520.
11. Barlow RJ, Connell MA, Levendig BJ, et al. A comparative study of urinary sodium and potassium excretion in normotensive urban Black and White South African males. S Afr Med J 1982; 62: 939-941.
12. Prof. Stoker, personal communication.
13. Weiner JS, Lourie JA. Human Biology - A guide to field methods. London: Blackwell, 1969;
14. Meyer BJ. Die Fisiologiese basis van geneeskunde. 2e uitgawe. Pretoria: Haum, 1979;32.3-32.5.
15. Rose GA, Blackburn H. Cardiovascular survey methods. Geneva: World Health

Organization, 1968.
16. Frohlich ED, Grim C, Labarthe DR, et al. Recommendations for human blood pressure determination by sphygmomanometers. Dallas: American Heart Association, 1987.
17. Maxwell MH, Waks AU, Schroth PC, Karam M, et al. Error in blood-pressure measurement due to incorrect cuff size in obese patients. Lancet 1982;33-36.
18. ETOVS NO: 28/89

Abstract

Uittreksel

Abstract

BACKGROUND

The black population of South Africa underwent rapid urbanisation during the last century. This process was accompanied by major changes in lifestyle including less physical activity, the moving away from traditional low-fat diets to diets high in saturated fat, and the acquiring of unhealthy habits such as the smoking of cigarettes. Previously rare chronic diseases of lifestyle such as diabetes mellitus, hypertension, obesity, dyslipidaemia and atherosclerotic cardiovascular disease started to emerge during this period.

AIMS

The primary aims of the study were to determine the prevalence of diabetes mellitus, hypertension, obesity, and dyslipidaemia, in a partly rural and an urban black community. The secondary objectives were to investigate the hypotheses that the metabolic syndrome existed in the black population and that hypertension was associated with hyperinsulinaemia in the study populations.

STUDY DESIGN

A cross-sectional study

SETTING:

The study was conducted in the semi-rural area of Qwaqwa and in Mangaung, the main black residential area of Bloemfontein.

METHODS

A representative sample of 853 subjects 25 years and older (279 males and 574 females) was selected from Qwaqwa, a partly rural community in the Free State, and a similar sample of 758 subjects (290 males and 468 females) from Mangaung, the black residential area of Bloemfontein, as the urban sample for comparison. After informed consent, the prevalence of the following conditions was determined according to standardised procedures: diabetes mellitus, impaired glucose tolerance, impaired fasting glucose, hypertension, dyslipidaemia, and overweight and obesity. In addition, anthropometrical measurements including the measurement of selected skinfold thickness and body circumferences were measured. A 12-lead resting electrocardiograph was obtained from each subject and blood specimens were collected for the measurement of insulin, proinsulin and C-peptide. A trained nurse

administered a questionnaire to each respondent in his or her own language to obtain demographic and biosocial information.

RESULTS

The response rates were 68% in Qwaqwa and 62% in Mangaung. The age-standardised prevalence rates for the chronic diseases that were studied, are provided in the Table S1.

TABLE A1. The Age- and Sex-Standardised Prevalence of Cardiovascular Risk Factors in Two Free State Populations

	Qwaqwa			Mangaung		
	Males n=274 %	Females n=566 %	Total n=840 %	Males n=284 %	Females n=457 %	Total n=741 %
Diabetes	3.5	5.7	4.8	5.0	6.8	6.0
IGT[a]	9.9	11.3	10.7	10.0	14.0	12.2
Hypertension[b]	22.1	34.5	29.2	22.8	36.3	30.3
Obesity[c]	12.2	36.6	25.6	10.9	41.1	27.7
TC ≥ 5.2 mmol/L	32.5	32.8	32.7	36.3	38.3	37.4
HDLC> 20% TC	74.6	76.6	75.7	78.3	80.1	79.3
TG≥1.7 mmol/L	21.5	15.9	18.4	23.8	14.8	18.8
Metabolic syndrome[d]	28.1	32.8	30.7	26.3	33.9	30.5

[a] IGT=Impaired glucose tolerance

[b] BP >160/95 mm Hg

[c] BMI > 30 kg/m2

[d] WHO Definition

The prevalence rates of the risk factors that were studied did not differ significantly between the Qwaqwa and Mangaung samples. Although the metabolic syndrome was present in 31% of subjects in both samples, no electrocardiographic evidence of an increased prevalence of coronary heart disease was found in subjects with the metabolic syndrome. Hyperinsulinaemia and thus insulin resistance was not associated with hypertension in any of these two black populations with a high prevalence of obesity and hypertension. It is unlikely that a population with such a clustering of cardiovascular risk factors can much longer escape the emergence of coronary artery disease as an important public health problem.

CONCLUSION

The black populations of Qwaqwa and Mangaung are well advanced on the road of urbanisation and the nutrition transition. Chronic diseases of lifestyle are as prevalent in these communities as elsewhere in the Western world. Coronary artery disease is usually the last of the typical Western diseases to emerge in a population in transition and it is unlikely that these black populations will escape this disease much longer.

KEY WORDS

diabetes mellitus, type 2
hypertension
hyperinsulinaemia
obesity
dyslipidaemia
metabolic syndrome
blacks
chronic diseases of lifestyle

Uittreksel

AGTERGROND

Die swart bevolking van Suid-Afrika het gedurende die vorige eeu 'n proses van vinnige verstedeliking ondergaan. Hierdie proses het gepaard gegaan met belangrike veranderinge in lewensstyl insluitende 'n afname in fisiese aktiwiteit, die wegbeweeg van 'n tradisionele dieet laag in vet na 'n dieet hoog in versadigde vette tesame met die aanvaarding van ongesonde gewoontes soos die rook van sigarette. Die chroniese siektes van lewensstyl soos diabetes mellitus, hipertensie, obesiteit, dislipiedemie en aterosklerotiese kardiovaskulêre siekte wat voorheen skaars was onder swart mense, het gedurende hierdie periode na vore getree.

DOELWITTE

Die primêre doelwitte van hierdie studie was om die voorkomssyfer van diabetes mellitus, hipertensie, obesiteit en dislipiedemie in 'n gedeeltelike landelik en in 'n stedelike swart bevolking te bepaal. Die sekondêre doelwitte was om die hipoteses te ondersoek dat die metaboliese sindroom wel voorkom in die swart bevolking en dat hipertensie geassosieer is met hiperinsulinemie in hierdie bevolkings.

STUDIE ONTWERP

'n Deursneestudie.

OMGEWING

Die studie was uitgevoer in die deels landelike Qwaqwa en in Mangaung die hoof swart residensiële gebied van Bloemfontein.

METODES

'n Verteenwoordigende steekproef van 853 vrywilligers 25 jaar en ouer (279 mans en 574 vroue) was lukraak geselekteer in Qwaqwa, 'n deels landelike gebied in die Vrystaat, en 'n soortgelyke steekproef van 758 vrywilligers (290 mans en 468 vroue) in Mangaung, die swart residensiële gebied van Bloemfontein, as die stedelike steekproef vir vergelykende doeleindes. Na ingeligte toestemming is die voorkomssyfer van die volgende toestande bepaal volgens gestandariseerde prosedures: diabetes mellitus, versteurde glukose toleransie, versteurde vastende glukose, hipertensie, dislipiedemie, oorgewig en obesiteit. Bykomstig is antropometriese metings insluitende die meting van geselekteerde velvoudiktes en liggaamsomtrekke gedoen. 'n 12-Afleiding rustende elektrokardiogram was by elke vrywilliger

verkry en bloedmonsters was versamel vir die bepaling van serum insulien, pro-insulien en C-peptiedvlakke. 'n Opgeleide verpleegkundige het 'n vraelys by elke vrywilliger in sy/haar eie taal afgeneem om demografiese en maatskaplike inligting te bekom.

RESULTATE

Die responssyfer was 68% in Qwaqwa en 62% in Mangaung. The ouderdoms aangepaste voorkomssyfer vir die chroniese siektes wat bestudeer is, word aangedui in Tabel U1.

TABEL U1. Die Ouderdoms- en Geslagsaangepaste Voorkomssyfer van Kardiovaskulêre Risikofaktore in Twee Vrystaatse Populasies

	Qwaqwa			Mangaung		
	Mans	Vroue	Totaal	Mans	Vroue	Totaal
	n = 274	n = 566	n = 840	n = 284	n = 457	n = 741
	%	%	%	%	%	%
Diabetes	3.5	5.7	4.8	5.0	6.8	6.0
VGT[a]	9.9	11.3	10.7	10.0	14.0	12.2
Hipertensie[b]	22.1	34.5	29.2	22.8	36.3	30.3
Obesiteit[c]	12.2	36.6	25.6	10.9	41.1	27.7
Totale Cholesterol > 5.2 mmol/L	32.5	32.8	32.7	36.3	38.3	37.4
HDL-Cholesterol > 20%	74.6	76.6	75.7	78.3	80.1	79.3
Trigliseriedvlakke > 1.7 mmol/L	21.5	15.9	18.4	23.8	14.8	18.8
Metaboliese Sindroom[d]	28.1	32.8	30.7	26.3	33.9	30.5

[a] VGT = Versteurde Glukose Toleransie

[b] Bloeddruk > 160/95 mm Hg

[c] LMI > 30 kg/m2

[d] WGO definisie

Die voorkomssyfer van die risikofaktore wat bestudeer is, het nie betekenisvol verskil tussen die Qwaqwa en Mangaung steekproewe nie. Alhoewel die metaboliese sindroom teenwoordig was in 31% van vrywilligers in beide steekproewe, kon geen elektrokardiografiese bewys van 'n verhoogde voorkomssyfer van koronêre vatsiekte in vrywilligers met die metaboliese

sindroom aangetoon word nie. Hiperinsulinemie en dus insulienweerstandigheid was nie geassosieer met hipertensie in enige van die twee swart bevolkings met 'n hoë voorkomssyfer van obesiteit en hipertensie wat ondersoek is nie. Dit is onwaarskynlik dat 'n bevolking waarin daar so 'n mate van saambondeling van kardiovaskulêre risikofaktore teenwoordig is veel langer die ontstaan van koronêre vatsiekte as 'n belangrike openbare gesondheidsorgprobleem sal kan ontsnap.

SAMEVATTING

Die swart bevolking van Qwaqwa en Mangaung het reeds ver gevorder op die weg van verstedeliking en die nutrisionele oorgang. Chroniese siektes van lewensstyl is net so algemeen in hierdie gemeenskappe as elders in die Westerse wêreld. Koronêre vatsiekte is gewoonlik die laaste van die tipiese Westerse toestande wat ontstaan in 'n bevolking in oorgang en dit is onwaarskynlik dat hierdie swart bevolkings hierdie toestande veel langer sal kan ontsnap.

SLEUTELWOORDE

diabetes mellitus, tipe 2
hipertensie
hiperinsulienemie
obesiteit
dislipiedemie
metaboliese sindroom
swart mense
chroniese siektes van lewensstyl

U.O.V.S. BIBLIOTEEK