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Anthropometrical indicators of non-communicable diseases for a black South African population in transition



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This was one of the toughest challenges in my life, but certainly it will not be my last challenge. The journey taught me perseverance, character and faith in the Lord Almighty.

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ANTHROPOMETRICAL INDICATORS OF NON-COMMUNICABLE DISEASES FOR A BLACK SOUTH AFRICAN POPULATION IN TRANSITION

BACKGROUND:

Non-communicable diseases (NCD) are also known as chronic diseases of lifestyle and cause the greatest burden of disease globally, whether measured as morbidity or mortality. Although there is consensus that obesity is a risk factor for NCD, differences of opinion exist as to what anthropometric measure or index of adiposity is the most effective in identifying those individuals who are at greatest risk, due to ethnic differences. Hence, uncertainty remains in the black South African population regarding the validity of different anthropometric measures and indexes and cut-off values to predict health outcomes. Africa is currently experiencing one of the most rapid demographic and epidemiological transitions in world history. Black South Africans have moved away from rural areas to more urban areas, where they are exposed to more psychosocial stress, less physical activity and adopted a more westernised diet (high in fat and has less carbohydrates and fibre), which is associated with an increased risk for the development of NCD and the metabolic syndrome (MetS). MetS is composed of a cluster of metabolic disorders associated with increased risk of cardiovascular diseases (CVD). The risk factors to define MetS include various combinations of abdominal obesity, high blood pressure, high fasting plasma glucose, dyslipidemia (increased triglycerides, low HDL cholesterol or both) and insulin resistance. There are currently three common definitions of MetS: the World Health Organization (WHO) definition, the National Cholesterol Education Program, Adult Treatment Panel III (NCEP-ATP III) definition and the International Diabetes Federation (IDF) definition. These definitions are in general agreement on the essential components of the MetS but differ in their cut-off values and method of combining the individual components. A prominent feature of the IDF definition is that abdominal obesity is a prerequisite component of the MetS, with abdominal obesity defined according to ethnic specific values of waist circumference (WC). The IDF definition suggests that sub-Saharan Africans should use the same WC cut-off values as Caucasians, derived from European data, until more specific data are available. The currently accepted WC cut-off values, might underestimate risk for metabolic syndrome risk factors in African populations, and a substantial proportion of those who would need health care advice would be missed in health screenings.

OBJECTIVES:

1. To determine the most effective anthropometric measure to indicate the presence of NCD risk factors (measures of lipids, fasting glucose, C-reactive protein, blood pressure and obesity) in a black South African population;
2. To determine the ethnically appropriate WC cut-off values for abdominal obesity in black South African men and women, to predict increased risk of metabolic syndrome risk factors (raised triglyceride, reduced HDL-cholesterol, raised blood pressure and raised fasting blood glucose), or two or more of these risk factors;
3. To determine the prevalence of the metabolic syndrome (MetS) with urbanisation, using three definitions (NCEP-ATP III, IDF, IDF with local WC cut-off values);
4. To assess the association of metabolic risk factors with abdominal obesity and raised blood pressure in a sub-Saharan African population.

STUDY DESIGN:

The study formed part of the baseline data of the South African leg of the Prospective Urban and Rural Epidemiological (PURE) study. This study had a cross-sectional design that included randomly selected participants older than 35 with no reported chronic diseases of lifestyle, Tuberculosis or HIV. A total of 2010 black Setswana speaking participants was included of which 746 were men and 1264 were women.

RESEARCH METHODS:

Data was collected by a specialised multidisciplinary team. The participants signed an informed consent form. Questionnaires were issued during individual interviews and were conducted by extensively trained fieldworkers in the language of the participant's choice. Blood pressure was measured in the sitting position on the right arm, after 5 minutes of rest, using the validated OMRON HEM-757 automatic digital blood pressure monitor. All anthropometric measurements were done using the guidelines of the International Society for the Advancement of Kinanthropometry (ISAK). Blood serum and plasma concentrations of fasting triglycerides, high-density lipoprotein cholesterol and fasting glucose was auto-analysed with a Konelab™ clinical analyser by making use of standardised enzymatic procedures. Low-density lipoprotein cholesterol was calculated.

Statistical analysis was performed using SPSS for Windows (version 16.0) performing non-parametric statistical analysis. Student T-tests, one-way ANOVA tests, ANCOVA tests and Pearsons Chi-square tests were used to compare means and percentages. Cross-tabulation was used to calculate odds ratios. Waist-circumference cut-off values were determined by ROC curve analysis. Regression models were also used to quantify the prediction of NCD risk factors

measures by all 4 anthropometric measures/indexes. Linear regression analysis with adjustments for covariates (age, urbanization, HIV, and gender) (Model 1) and (age, urbanisation, HIV, gender and BMI) (Model 2) were used to determine the association of the percentage variance, explained by risk factors, in addition to models containing covariates, with abdominal obesity (WC) and raised blood pressure. Fasting triglycerides were not normally distributed and therefore log transformed before any comparisons were made. The relationships were expressed as standardised beta (β) coefficients and the percent increase in the adjusted R^2 change when abdominal obesity (WC) or raised blood pressure was added to the model in comparison to model 1 and model 2.

RESULTS:

As assessed by the ability of the anthropometric indices, to 1) account for the variability in each risk factor and 2) correctly identify individuals with increased NCD risk factors, the predictive abilities of BMI, WC and WHtR were similar. WC was slightly better (0.01-0.08 higher R^2 value, $p < 0.05$) in predicting concentrations of total cholesterol (TC), fasting glucose (FG), triglycerides (TG), LDL-cholesterol (LDL-C), systolic blood pressure (SBP) and diastolic blood pressure (DBP) in men. BMI was slightly better in identifying men with reduced HDL-cholesterol (HDL-C) (0.03 higher R^2 , $p < 0.05$), while WHtR was slightly better (0.01-0.11 higher R^2 value, $p < 0.05$) in predicting concentrations of C-reactive protein (CRP), TG, SBP, DBP in women. WC was slightly better in identifying reduced concentrations of HDL-C (0.08 higher R^2 , $p < 0.05$) in women. On the basis of two or more metabolic risk factors, WC and BMI were equal in their predictive ability of NCD risk factors according to the receiver operating characteristic (ROC) curve analysis (AUC=0.65) in men while WHtR and WC were equal in their predictive ability (AUC=0.65) in women. For men and women combined, WHtR was the most frequent predictor for NCD risk factors (5 out of 8 risk factors) and WC (3 out of 8 risk factors) as determined by AUC. Based on the receiver operating characteristic (ROC) curve analysis the WC value for predicting metabolic risk factors in this black African population was about 80 cm for men and women. The AUC for men was 0.653 (0.611-0.695 CI) and for women it was 0.643 (0.613-0.674 CI). According to the locally determined WC criteria, the prevalence of abdominal obesity was 28.1% in the men and 52.4% in the women. The prevalence of MetS varied according to the definition used. The IDF definition with sub-Saharan Africa proposed waist circumference (WC) cut-off values (≥ 94 cm men; ≥ 80 cm women) and the IDF definition with proposed local WC cut-off values (≥ 80 cm for men and women) indicated a higher prevalence of MetS compared to the NCEP-ATP III definition. The highest prevalence of the MetS was obtained with the IDF definition with local WC cut-off values in the men (rural: 16.4%; urban: 17.6%) and women (rural: 28.4%; urban 38.2%) and the lowest with the NCEP-ATP III definition in men (rural: 2.3%;

urban: 0.8%) and women (rural: 16.3%; urban: 22.0%). Raised blood pressure ($\geq 130/85$ mmHg) was the most prevalent metabolic risk factor in both the rural (60.3-60.6%) and urban (72.0-72.6%) men and women. In the men no significant difference in the prevalence of the individual metabolic risk factors between the urban and rural groups could be found. The prevalence of most of the individual metabolic risk factors of the urban women was significantly higher compared to the rural women. The additional percentage of variance of individual continuous metabolic risk measures explained by either abdominal obesity (WC) or raised blood pressure ($\geq 130/85$ mmHg) were determined after adjusting for age, urbanisation, HIV status and gender. The standardised beta (β) coefficients and R^2 change were higher for abdominal obesity (WC) rather than for raised blood pressure, except in the case of SBP, DBP and HDL-cholesterol. The association with the metabolic risk factors (fasting glucose, triglycerides, total cholesterol and HDL-C) was slightly stronger for abdominal obesity (WC) rather than for raised blood pressure (the association of SBP and DBP will always be high with raised blood pressure). After adjusting for BMI as presented in Model 2, the associations of fasting glucose with raised blood pressure was no longer significant ($p = 0.18$).

CONCLUSIONS:

1. WC and WHtR are the strongest anthropometric indicators of non-communicable diseases in this black South African population.
2. The optimal WC cut-off values (≥ 80 cm for men and women) to predict increased risk of metabolic syndrome risk factors (raised triglyceride, reduced HDL-cholesterol, raised blood pressure and raised fasting blood glucose), or two or more of these risk factors in this black African population are lower for the men and similar for the women than the WC cut-off value proposed by the IDF (≥ 94 cm for men and ≥ 80 cm for women).
3. The prevalence of the metabolic syndrome was significantly higher in the urban groups compared to the rural groups, across the metabolic syndrome definitions. Urbanisation significantly increased the prevalence of the metabolic risk factors and metabolic syndrome (IDF definition) in the women but not in the men.
4. Both, raised blood pressure and abdominal obesity have a significant association with metabolic risk factors in this Setswana speaking South African population. The association with the metabolic risk factors was slightly stronger for abdominal obesity (WC) rather than for raised blood pressure in this population.

KEY WORDS: Non-communicable diseases, Abdominal obesity, Raised blood pressure, Waist circumference, Waist-height ratio, Black Africans, Ethnicity, Anthropometry, Urbanisation.

ANTROPOMETRIESE AANDUIDERS VAN KRONIESE LEEFSTYLSIEKTES VIR 'N SWART SUID-AFRIKAANSE POPULASIE IN 'N OORGANGSTADIUM VAN VERSTEDELIKING

AGTERGROND:

Kroniese leefstylsiektes (KLS) is tans die grootste bydraer tot morbiditeit en mortaliteit in die wêreld. Alhoewel daar ooreenstemming bestaan dat obesiteit 'n risikofaktor vir KLS is, bestaan daar kontroversie oor watter antropometriese meting of indeks die beste is om individue met verhoogde risiko te identifiseer, as gevolg van etniese verskille. Daar bestaan gevolglik onsekerheid ten opsigte van die betroubaarheid van verskillende antropometriese metings en indekse, asook afsnypunte om gesondheidsrisiko in die swart Suid-Afrikaanse gemeenskap aan te dui. Afrika is tans besig om een van die vinnigste demografiese en epidemiologiese veranderingsprosesse in wêreldgeskiedenis te ondergaan. Swart Suid-Afrikaners beweeg weg uit landelike gebiede na verstedelike gebiede, waar hulle blootgestel word aan groter psigo-sosiale stres, minder fisieke aktiwiteit en 'n westerse dieët (hoog in vet met minder koolhidrate en vesel). Verstedeliking word geassosieer met 'n verhoogde risiko vir die ontwikkeling van KLS en metabooliese sindroom (MetS). MetS bestaan uit 'n versameling metabooliese risiko faktore en siektetoestande en word geassosieer met 'n verhoogde risiko vir kardiovaskulêre siektes. Die risiko faktore wat MetS definieer sluit 'n verskeidenheid kombinasies van abdominale obesiteit, verhoogde bloeddruk, verhoogde plasma glukose en dislipidemia (verhoogde trigliseriede en/of verlaagde hoë-digtheidlipoproteïen cholesterol (HDL-C) in. Daar bestaan tans drie algemene definisies van die MetS naamlik, die Wêreld-Gesondheid-Organisasie (WGO) definisie, die "National Cholesterol Education Program, Adult Treatment Panel III" (NCEP-ATP III) definisie en dié van die Internasionale Diabetes Federasie (IDF). Hierdie definisies is in die algemeen in ooreenstemming met mekaar ten opsigte van die essensiële komponente van die metabooliese sindroom, maar verskil ten opsigte van die afsnypunte en kombinasie van die komponente. 'n Belangrike aspek van die IDF-definisie is dat abdominale obesiteit 'n voorvereiste komponent van die MetS is en volgens etnies-spesifieke maagomtrek afsnypunte geklassifiseer word. Die IDF-definisie beveel aan dat sub-Sahara Afrikane dieselfde maagomtrek afsnypunte as Kaukasiërs (verkry vanuit Europese data) moet gebruik totdat meer spesifieke data beskikbaar is. Die maagomtrek afsnypunte wat tans bestaan, mag moontlik die metabooliese risiko faktore in swart Afrikane onderskat en gevolglik daartoe lei dat 'n groot hoeveelheid individue wat gesondheidsorg benodig nie geïdentifiseer kan word tydens siftingsprosesse nie.

DOELSTELLINGS:

1. Om te bepaal watter antropometriese meting die teenwoordigheid van KLS risiko faktore (lipiede, vastende glukose, C-reaktiewe proteïen, bloeddruk en obesiteit) in 'n swart Suid-Afrikaanse populasie die beste aandui.
2. Om etnies-spesifieke afsnypunte vir maagomtrek daar te stel vir swart Suid-Afrikaanse mans en vroue, wat metaboliese sindroom risiko faktore die beste voorspel (verhoogde trigliseriede, verlaagde HDL-cholesterol, verhoogde bloeddruk, vastende glukose) of twee of meer risiko faktore.
3. Om die voorkoms van MetS te bepaal deur middel van drie definisies (NCEP-ATP III, IDF en die IDF met plaaslike afsnypunte) in 'n sub-Sahara Afrika populasie wat tans in die verstedelikingsproses is.
4. Om die verwantskap tussen metaboliese risiko faktore met abdominale obesiteit en verhoogde bloeddruk in 'n sub-Sahara Afrika populasie te bepaal.

STUDIE-ONTWERP:

Hierdie studie was deel van die basislyn data van die groter "Prospective Urban and Rural Epidemiological" (PURE) Suid-Afrika studie. PURE Suid-Afrika se basislyn data-insameling was 'n dwarsdeursnit studie van proefpersone ouer as 35 jarige ouderdom met geen gerapporteerde kroniese siektes, Tuberkulose of MIV nie. 'n Totaal van 2010 ewekansig geselekteerde swart Setswana-sprekende proefpersone, waaronder 746 mans en 1264 vroue van die Noordwes provinsie, is ingesluit in die studie.

NAVORSINGSMETODES:

Die data is deur 'n multi-dissiplinêre navorsingspan ingesamel. Proefpersone het 'n ingeligte toestemmingsvorm onderteken. Vraelyste is ingevul deur opgeleide veldwerkers tydens 'n individuele onderhoud met elke proefpersoon in die proefpersone se eie taal. Bloeddruk is gemeet deur middel van die OMRON-HEM-757 gevalideerde outomatiese digitale bloeddruk monitor. Bloeddruk is aan die regter bo-arm gemeet na 5 minute van rus, terwyl die proefpersoon regop sit. Alle antropometriese metings is gedoen volgens die riglyne van die 'International Society for the Advancement of Kinanthropometry' (ISAK). Bloed serum en plasma konsentrasies van vastende trigliseriede, HDL-C en vastende glukose is geanaliseer

met behulp van 'n Konelab™ kliniese analiseerder volgens gestandaardiseerde ensiematiese prosedures. Lae-digtheidlipoproteïen cholesterol (LDL-C) is bereken volgens die Friedewald formule.

Statistiek is deur middel van die SPSS pakket vir Windows (weergawe 16.0) verwerk. Gemiddelde en persentasies is deur middel van T-toetse, ANOVAS, ANCOVAS en Pearson Chi-kwadraat toetse vergelyk. Oor-kruis tabulering is gebruik om die voorspellingsvermoë te bepaal van die antropometriese metings om metaboliese risiko faktore te identifiseer, terwyl ROC-kurwes gebruik is om maagomtrek afsnypunte te bepaal. Stapsgewyse meervoudige regressie-analises is gebruik om die voorspellingsvermoë van al 4 antropometriese metings te toets. Liniêre regressie-analises wat gekorrigeer is vir ouderdom, verstedeliking, MIV en geslag (Model 1) en ouderdom, verstedeliking, MIV, geslag en liggaamsmassa-indeks (Model 2) is gebruik om die verband tussen abdominale obesiteit, verhoogde bloeddruk en ander metaboliese risiko faktore te bepaal. Logaritmiese transformasie van vastende trigliseriede is gedoen aangesien die data nie gelyk versprei is nie. Die verhoudings is as gestandaardiseerde beta-koëffisiënte uitgedruk asook die persentasie aangepaste korrelasie (R^2) verandering wanneer abdominale obesiteit of verhoogde bloeddruk by die bogenoemde modelle gevoeg is.

RESULTATE:

Die voorspellingsvermoë van liggaamsmassa-indeks, maagomtrek en maag-tot-lengte verhouding is ongeveer dieselfde in hulle vermoë om elke risiko faktor te voorspel en in hulle vermoë om individue wat verhoogde risiko vir KLS het, te onderskei. Maagomtrek se vermoë is egter effens beter (0.01-0.08 hoër R^2 waarde, $p < 0.05$) om totale cholesterol, vastende glukose, trigliseriede, LDL-cholesterol, sistoliese bloeddruk en diastoliese bloeddruk aan te dui. Liggaamsmassa-indeks was beter om mans met verlaagde HDL-cholesterol te voorspel (0.03 hoër R^2 waarde, $p < 0.05$) terwyl maag-tot-lengte verhouding effens beter (0.01-0.11 hoër R^2 waarde, $p < 0.05$) was om C-reaktiewe proteïen, trigliseriede, sistoliese bloeddruk en diastoliese bloeddruk in vroue te voorspel. Maagomtrek was beter om die voorkoms van verlaagde HDL-C (0.08 hoër R^2 , $p < 0.05$) in vroue te voorspel. Maagomtrek en liggaamsmassa-indeks was beter om die voorkoms van twee of meer metaboliese risiko faktore aan te dui met behulp van die ROC-kromme met 'n area onder die kromme van (0.65) in mans, terwyl maagomtrek en maag-tot-lengte verhouding dieselfde vermoë gehad het in vroue (0.65). Vir beide mans en vroue was maag-tot-lengte verhouding die mees algemene voorspeller (5 uit die 8 risiko faktore) en maagomtrek (3 uit die 8 risiko faktore) soos deur die ROC-kromme bepaal. Die afsnypunt vir hierdie populasie swart Afrikane is aangewys as (≥ 80 cm) vir mans en vroue. Hierdie waarde is laer as die IDF waarde vir mans (≥ 94 cm) maar dieselfde as die vir vroue (≥ 80 cm). Die area

onder die kromme was 0.653 (0.611-0.695 CI) vir mans en 0.643 (0.613-0.674 CI) vir vroue. Volgens die plaaslike maagomtrek afsnypunte, is die voorkoms van abdominale obesiteit (28.1%) in die mans en (52.4%) in die vroue. Die hoogste voorkoms van MetS is verkry deur die IDF-definisie met die plaaslike afsnypunte in mans (16.4% in landelike gebiede en 17.6% in verstedelike gebiede) en in vroue (28.4% in landelike gebiede en 38.2% in verstedelike gebiede). Die laagste voorkoms van die MetS is verkry deur die NCEP-ATP III definisie (2.3% in landelike gebiede en 0.8% in verstedelike gebiede) in mans en (16.3% in landelike gebiede en 22.0% in verstedelike gebiede) in vroue. Die voorkoms van MetS was aansienlik hoër in die verstedelike groepe as in die landelike groepe met die toepassing van al drie die definisies. Verhoogde bloeddruk ($\geq 130/85$ mmHg) was die risikofaktor met die hoogste voorkoms (60.3-60.6%) in die landelike groep en (72.0-72.6%) verstedelike groep mans en vroue. Geen betekenisvolle verskille het bestaan ten opsigte van die voorkoms van die individuele metaboliese risiko faktore tussen die verstedelike en landelike groepe mans nie. Die voorkoms in die verstedelike groep vroue was betekenisvol hoër as die van die landelike groep vroue. Abdominale obesiteit (maagomtrek) en verhoogde bloeddruk ($\geq 130/85$ mmHg) het 'n betekenisvolle verwantskap gehad met al die metaboliese risiko faktore, nadat daar gekorrigeer is vir verstedeliking, geslag en MIV-status. Die gestandaardiseerde beta koëffisiënte en aangepaste korrelasie (R^2) verandering was hoër vir die metaboliese risiko faktore (vastende glukose, trigliseriede, totale cholesterol) in verwantskap met abdominale obesiteit (maagomtrek) as met verhoogde bloeddruk in hierdie populasie. Die verwantskap tussen abdominale obesiteit (maagomtrek) en totale cholesterol en HDL-C was nie meer betekenisvol nadat daar gekorrigeer is vir liggaamsmassa-indeks nie. Die verwantskap tussen HDL-C en verhoogde bloeddruk het egter betekenisvol geword nadat daar vir BMI gekorrigeer is. Beide verhoogde bloeddruk en abdominale obesiteit blyk dat hulle 'n sentrale rol speel binne die MetS kriteria in swart sub-Sahara Afrikane in oorgangstadium van verstedeliking.

GEVOLGTREKKINGS:

1. Maagomtrek en maag-tot-lengte verhouding is die sterkste antropometriele aanduiders van kroniese leefstylsiektes in hierdie swart Suid-Afrikaanse populasie.
2. Die optimale maagomtrek afsnypunt (≥ 80 cm vir mans en vroue) wat MetS risiko faktore voorspel (verhoogde trigliseriede, verlaagde HDL-cholesterol, verhoogde vastende glukose of twee of meer van hierdie risiko faktore) in swart Afrikane is laer vir mans en dieselfde vir vroue as die wat deur die IDF voorgestel word.

3. Die voorkoms van MetS was aansienlik hoër in die verstedelike groepe in vergelyking met die landelike groepe met die toepassing van al die MetS definisies. Leefstyl veranderinge geassosieer met verstedeliking het 'n betekenisvolle verhoging in die voorkoms van metaboliese risiko faktore en die MetS (IDF-definisie) tot gevolg in vroue, maar nie in mans nie.
4. Beide verhoogde bloeddruk en abdominale obesiteit het 'n betekenisvolle verwantskap met metaboliese risiko faktore in hierdie swart Setswana- sprekende Suid-Afrikaanse populasie. Die verwantskap tussen metaboliese risiko faktore was sterker vir abdominale obesiteit (maagomtrek) as vir verhoode bloeddruk in hierdie populasie.

SLEUTELWOORDE: Kroniese leefstylsiektes, Abdominale obesiteit, Verhoogde bloeddruk, Maagomtrek, Maag-tot-lengte verhouding, Swart Afrikane, Etnisiteit, Antropometrie.

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A

AACE	American Association for Clinical Endocrinologists
ACSM	American College of Sports Medicine
ACTH	Adrenocorticotrophic hormone
AIDS	Acquired Immune Deficiency Syndrome
ANOVA	Analysis of variance
ATP III	Adult Treatment Panel III
AUC	Area under the curve
AUTHeR	Africa Unit for Transdisciplinary Health Research

B

BMI	Body mass index
Botsw	Botswana
BP	Blood pressure

C

CAD	Coronary artery disease
Camer	Cameroon
CD4	Cluster of differentiation-4 (Glycoprotein on surface of T-Helper cells)
CHD	Coronary heart disease
CI	Confidence interval
cm	Centimetre
cm ²	Square centimetre
CRP	C-reactive protein
CT	Computerized Tomography
CVD	Cardiovascular disease

D

DBP	Diastolic blood pressure
DEXA	Dual-Energy X-Ray Absorptiometry
DM	Diabetes Mellitus
2DM	Type 2 diabetes mellitus
DRC	Democratic Republic of Congo

E

EDTA	Ethylenediaminetetra-acetic acid
EGIR	European Group for the study of Insulin Resistance

F

F	Female
FG	Fasting glucose

G

g	Grams
GGT	Gamma-glutamyl transferase
GH	Growth hormone

H

HDL-C	High density lipoprotein cholesterol
HIV	Human Immunodeficiency Virus
HPA	Hypothalamic-pituitary-adrenal
HTGW	Hypertriglyceridemic waist

I

IAAT	Intra abdominal adipose tissue
ICO	Index of central obesity
IDF	International Diabetes Federation
IL-6	Interleukin-6
IR	Insulin resistance
ISAK	International Society for the Advancement of Kinanthropometry

K

kg/m ²	Kilogram per square meter
-------------------	---------------------------

L

L	Liter
LDL-C	Low density lipoprotein cholesterol
LPL	Lipoprotein lipase

M

M	Male
MetS	Metabolic syndrome
mg/dL	Milligrams per decilitre
MIV	Menslike Immuniteits-gebrek Virus
ml	Millilitre
mm	Millimetre
mmHg	Millimetres of mercury

mol/L	Molarities per litre
Mozam	Mozambique
MRC	Medical Research Council
MRI	Magnetic Resonance Imaging
mRNA	Messenger RNA

N

N/n	Number
Namb	Namibia
NCD	Non-communicable diseases
NCEP	National Cholesterol Education Program
N/D	No available data
Niger	Nigeria
NRF	National Research Foundation
NWU	North-West University

O

OGTT	Oral glucose tolerance test
OR	Odds ratio

P

p	Significance
PA	Physical activity
PURE	Prospective Urban and Rural Epidemiological study

R

RMR	Resting metabolic rate
ROC	Receiver operating characteristic
RSA	Republic of South Africa
RQ	Respiratory quotient

S

SAAT	Subcutaneous abdominal adipose tissue
SANPAD	South Africa-Netherlands Research Programme on Alternatives in Development
SBP	Systolic blood pressure
SD/±	Standard deviation
SE/±	Standard error
SES	Socio-economic status

SM	Skeletal muscle
SNS	Sympathetic nervous system
Swaz	Swaziland
T	
Tanz	Tanzania
TC	Total cholesterol
THUSA	Transition of Health and Urbanisation of South Africa
TG	Triglycerides
TNF- α	Tumor necrosis factor – alpha

U

USA	United States of America
-----	--------------------------

V

VAT	Visceral adipose tissue
-----	-------------------------

W

WC	Waist circumference / waist girth
WHO	World Health Organization
WHR	Waist-hip ratio / waist-to-hip ratio
WHtR	Waist-height ratio / waist-to-stature ratio

Y

Y/y	Years
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Z

Zimb	Zimbabwe
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Symbols

%	Percentage
° C	Degrees Celsius

PROBLEM STATEMENT AND AIM OF THE STUDY

1

1.1 INTRODUCTION

1.2 PROBLEM STATEMENT

1.3 RESEARCH QUESTIONS

1.4 OBJECTIVES

1.5 HYPOTHESIS

1.6 STRUCTURE OF THESIS

1.7 REFERENCES

1.1 INTRODUCTION

Non-communicable diseases (NCD) are also known as chronic diseases of lifestyle or silent killers, and are defined as diseases of long duration and slow progression (WHO, 2008b:2). NCD are defined by the Medical Research Council (MRC) of South Africa as a group of illnesses that share similar risk factors as a result of exposure, over many decades to unhealthy diets, smoking, lack of regular exercise, and possibly stress (Steyn *et al.*, 2006:iv). According to the MRC, the major risk factors for NCD are elevated blood pressure, tobacco addiction, elevated blood cholesterol, diabetes mellitus (DM) and obesity. These result in various long-term disease processes, culminating in high mortality rates attributable to strokes, heart attacks, tobacco- and nutrition-induced cancers, chronic bronchitis, emphysema, renal failure and many others (Steyn *et al.*, 2006:iv). Together these diseases represent 60% of all deaths in the world (WHO, 2008a:29). Eighty percent (80%) of mortality due to NCD occurs in low and middle income countries like South Africa, while only 20% of NCD mortality is found in high income countries (WHO, 2008b:2).

Obesity is one of the modifiable risk factors for the global NCD epidemic (WHO, 2005a:1). The risk for NCD increases progressively as body mass index (BMI) increases (WHO, 2005b:35). The overall prevalence of overweight (BMI of ≥ 25 kg/m²) and obesity (BMI of ≥ 30 kg/m²) in South Africa is high, with more than 29% of men and 56% of women being classified as overweight or obese (Puoane *et al.*, 2002:1038). Excessive calorie intake is mainly responsible for the development of obesity (Prentice, 1998:535S). South Africans in urban settings have moved away from their traditional diet and adopted a more westernized diet (high in fat and

sodium chloride and has less carbohydrates and fibre) (Van Rooyen *et al.*, 2000:785; Bourne *et al.*, 2002:157). These energy dense diets promote fat accumulation and are commonly associated with urbanization (Goedecke *et al.*, 2006:71; Vorster *et al.*, 2007:288; De Hout *et al.*, 2008:6). Urban women in South Africa were found to have a significantly higher BMI than their rural counterparts (Schutte *et al.*, 2005:61; Goedecke *et al.*, 2006:65).

The distribution of fat or abdominal fat patterning as indicated by waist circumference (WC), waist-hip ratio (WHR) and waist-height ratio (WHtR) is highly correlated with the development of NCD (Freedman *et al.*, 2007:33; Wang *et al.*, 2007:173; Lafortuna *et al.*, 2008:233). Abdominal obesity proved to be one of the most essential features of the metabolic syndrome and may be the link that unifies the syndrome (Yeater, 2000:354; Anderson *et al.*, 2001:1782; Lam *et al.*, 2004:543; Yudkin *et al.*, 2004:852; Eckel *et al.*, 2005:1417).

1.2 PROBLEM STATEMENT

The metabolic syndrome is associated with an increased risk of developing cardiovascular disease (CVD) and appears in individuals as a cluster of risk factors (abdominal obesity, raised blood pressure, raised plasma glucose, raised triglycerides and reduced HDL-cholesterol) according to the National Cholesterol Education Program, Adult Treatment Panel III (NCEP-ATP III) and International Diabetes Federation (IDF) guidelines (NCEP, 2001:2486; Zimmet *et al.*, 2005:1373-1374). Each of the risk factors directly or indirectly are thought to affect pathways leading to diabetes, coronary heart disease (CHD) and CVD (Das, 2003:560; Florez *et al.*, 2006:93).

Abdominal obesity could be the central and causal component of the metabolic syndrome (Zimmet *et al.*, 2005:1373). Research on obesity has confirmed that obesity is a state of chronic inflammation, as indicated by increased plasma concentrations of C-reactive protein (CRP) (Yudkin *et al.*, 1999:974) and interleukin-6 (IL-6) (Mohamed-Ali *et al.*, 1997:4199). Mohamed-Ali *et al.* (1997:4199) also stated that adipocytes secrete IL-6, one of the major determinants of hepatic CRP production. Rexrode *et al.* (2003:679) found that both CRP and IL-6 levels strongly correlate with BMI, not just at higher levels but also throughout the BMI spectrum. WC also had a strong association with both inflammatory markers (Rexrode *et al.*, 2003:679). According to a South African study by Slabbert *et al.* (2006:129), percentage body fat, WC, WHR and BMI were all significantly correlated with CRP throughout the anthropometric spectrum.

Cardiometabolic risks are largely a function of the severity of abdominal obesity and appropriate anthropometric cut-off values to indicate the “action level” for treatment is of great importance. There has been increasing speculation over which measure of overweight and obesity is best able to discriminate those individuals who are at increased risk for CVD (Lee *et al.*, 2008:646). The IDF urged the need for a single universally accepted diagnostic tool that was simple to use in clinical practice and did not rely upon measurements only available in research settings and that are sensitive to the race and ethnicity of a population (Al-Shaer & Abu-Sabha, 2005:820; Zimmet *et al.*, 2005:1373).

The World Health Organization (WHO) guidelines for defining the severity of obesity by body mass index (BMI) between populations are increasingly losing popularity (Lee *et al.*, 2008:646). Measures of central or abdominal obesity such as WC, WHR and WHtR have been adopted as more accurate predictors of obesity-related CVD risk and have replaced BMI in several definitions of the metabolic syndrome (Zimmet *et al.*, 2005:295; Lee *et al.*, 2008:646). Several studies have examined the ability of BMI, WC, WHR and WHtR and found that these anthropometric measures are mainly ethnicity specific in its etiology and its ability to discriminate major CVD risk factors (Al-Shaer & Abu-Sabha, 2005:820; Aekplakorn *et al.*, 2006:1782; Sakurai *et al.*, 2006:75; Schneider *et al.*, 2006:589; Onat *et al.*, 2007:183). An important unknown concern is whether the same measure of adiposity performs equally well in discriminating CVD and metabolic syndrome risk factors in all ethnic groups. This concern is also shared by other researchers that indicated that body composition and dyslipidemia criteria should be adjusted for Africans since neither definition for the metabolic syndrome seems completely suitable for Africans (Schutte *et al.*, 2009:79).

A prominent feature of the IDF definition is that abdominal obesity is a prerequisite component of the metabolic syndrome and recommends WC cut-off values that is ethnic specific (Alberti *et al.*, 2005:1060). In the IDF definition, sub-Saharan Africans should use the Caucasian (Europids) WC cut-off values of ≥ 94 cm for men and ≥ 80 cm for women until more data becomes available to determine specific cut-off values for Africans (Alberti *et al.*, 2005:1060). According to Désilets *et al.* (2006:1019), the standard anthropometric indices of obesity may not be as effective in populations of African descent compared with Caucasians, unless appropriate cut-off values are defined. Schutte and Olckers (2007:651) also showed clear differences regarding body composition between Caucasian women, who were almost 10 kg heavier and 10 cm taller than their age- and BMI-matched African counterparts.

In conclusion the literature suggest the need to employ different anthropometric measurements when diagnosing NCD, whether BMI, WC, WHR or WHtR are used. Depending on race and

ethnicity the literature also suggest that the cut-off values for these anthropometric indices should be lowered if necessary. This will eventually lead to more sensitive criteria for identification of individuals at increased risk for NCD, especially in sub-Saharan Africans.

1.3 RESEARCH QUESTIONS

The research questions that will be answered in this study are the following: Firstly, to determine the most effective anthropometric indicator of NCD risk factors in a black South African population. Secondly, to determine the ethnically appropriate WC cut-off values for abdominal obesity in black South African men and women, to predict increased risk of metabolic syndrome risk factors (raised triglyceride, reduced HDL-cholesterol, raised blood pressure and raised fasting blood glucose), or two or more of these metabolic risk factors. Thirdly, to determine the prevalence of the metabolic syndrome (MetS) with urbanisation, using three definitions (NCEP-ATP III, IDF, IDF with local WC cut-off values). Finally, to assess the association of metabolic risk factors with abdominal obesity and raised blood pressure in a sub-Saharan Africa population.

1.4 OBJECTIVES

The specific aims of this study are:

- To determine the most effective anthropometric measure that indicates the presence of NCD risk factors (measures of lipids, fasting glucose, CRP, blood pressure and obesity) in a black South African population;
- To determine the ethnically appropriate WC cut-off values for abdominal obesity in black South African men and women, to predict increased risk of metabolic syndrome risk factors (raised triglyceride, reduced HDL-cholesterol, raised blood pressure and raised fasting blood glucose), or two or more of these risk factors;
- To determine the prevalence of the metabolic syndrome (MetS) with urbanisation using three definitions (NCEP-ATP III, IDF, IDF with local WC cut-off values);
- To assess the association of metabolic risk factors with abdominal obesity and raised blood pressure in a sub-Saharan Africa population.

1.5 HYPOTHESIS

This study is based on the following hypotheses:

- WC and WHtR are the strongest anthropometric indicators of non-communicable disease risk factors in a black South African population.
- The optimal WC cut-off values to predict increased risk of metabolic risk factors (raised triglycerides, reduced HDL-cholesterol, raised blood pressure and raised fasting blood glucose), or two or more of these risk factors in this black sub-Saharan African population are lower than the WC cut-off value proposed by the IDF.
- Urbanisation may increase metabolic risk factor and metabolic syndrome prevalence as determined by the IDF definition with local WC cut-off values.
- Raised blood pressure has a stronger association with metabolic risk factors than abdominal obesity.

1.6 STRUCTURE OF THE THESIS

This thesis is presented in six main parts, namely an introduction (Chapter 1), a literature review (Chapter 2), and three research articles (Chapters 3-5). A summary with conclusions and recommendations (Chapter 6), follow after the research articles as presented in Figure 1.

Chapter 1 introduces the problem, and states the aim and hypotheses of this study. The literature review in Chapter 2 focuses on non-communicable disease and obesity related disorders, risk factors and anthropometrical measures available for diagnosis of these risk factors. Chapters 3-5 are presented in article format. Chapter 3: Anthropometric indicators of non-communicable diseases in a black South African population. Chapter 4: Optimal waist circumference cut-off values for abdominal obesity in black South African men and women. Chapter 5: Metabolic risk factors in a sub-Saharan African population in transition: Is abdominal obesity or raised blood pressure the key determinant? Chapter 6 is the final chapter and will be a collective summary with a conclusion, recommendations and limitations of the study. Chapter 6 is followed by a list of appendices.

This thesis is submitted in article format, as approved by the senate of the North-West University (NWU) (Potchefstroom Campus), according to the 2008 Guidelines for Post-Graduate Studies. Chapter 1, 2 and 6 has been written according to the prescribed standards of the NWU, Guidelines for References. The articles have been prepared for publication in accredited

peer-reviewed journals (*Atherosclerosis, Diabetes Research and Clinical Practice, Hormone and Metabolic Research*). Articles have been written according to the guidelines to authors of the various journals (see the relevant appendices). For the purpose of uniformity and examination, the font and spacing is kept the same throughout the thesis. The tables and figures are also placed in between the text and not at the end of each article. The results of the research articles in Chapters 3-5 are presented and interpreted in each chapter respectively.

The structure of the thesis is presented in **Figure 1**.

**ANTHROPOMETRICAL INDICATORS
OF NON-COMMUNICABLE DISEASES FOR A BLACK
SOUTH AFRICAN POPULATION IN TRANSITION**

CHAPTER 1

INTRODUCTION, PROBLEM
STATEMENT, OBJECTIVES, HYPOTHESIS,
STRUCTURE OF THESIS, REFERENCES

CHAPTER 2

LITERATURE REVIEW

CHAPTER 3

RESEARCH ARTICLE:
ARTERIOSCLEROSIS

ANTHROPOMETRIC INDICATORS OF NON-
COMMUNICABLE DISEASES IN A BLACK
SOUTH AFRICAN POPULATION

CHAPTER 4

RESEARCH ARTICLE:

DIABETES RESEARCH AND CLINICAL PRACTICE
OPTIMAL WAIST CIRCUMFERENCE CUT-OFF
VALUES FOR ABDOMINAL OBESITY IN
BLACK SOUTH AFRICAN MEN AND WOMEN

CHAPTER 5

RESEARCH ARTICLE:

HORMONE AND METABOLIC RESEARCH
METABOLIC RISK FACTORS IN A SUB-
SAHARAN AFRICAN POPULATION IN
TRANSITION: IS ABDOMINAL OBESITY OR
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DETERMINANT?

CHAPTER 6

SUMMARY,
CONCLUSIONS,
LIMITATIONS AND
RECOMMENDATIONS

APPENDICES

GUIDELINES TO AUTHORS
CONFERENCES
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Figure 1: Structure of the thesis

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NON-COMMUNICABLE DISEASES, OBESITY AND THE METABOLIC SYNDROME IN AFRICANS

2.1 INTRODUCTION

Non-communicable diseases (NCD) cause the greatest burden of disease globally, whether measured as morbidity or mortality (WHO, 2008a:29). In 2008 the World Health Organization (WHO) estimated that the proportion of deaths due to NCD would rise sharply within the next 25 years. Globally, deaths due to cardiovascular disease (CVD) will rise from 17.1 million in 2004 to 23.4 million in 2030 (WHO, 2008a:29). The leading cause of death in 2030 as predicted by the WHO will be ischemic heart disease, with diabetes, hypertensive heart disease and HIV/AIDS being within the top 10 causes of death (WHO, 2008a:29).

NCD are also known as chronic diseases of lifestyle or silent killers, and are defined as diseases of long duration and slow progression (WHO, 2008b:2). NCD such as heart disease, stroke, cancer, chronic respiratory disease and diabetes are by far the leading causes of mortality and morbidity and together these diseases represent 60% of all deaths in the world (WHO, 2008a:29). Eighty percent (80%) of mortality due to NCD occur in low and middle income countries like South Africa, while only 20% of NCD mortality is found in high income countries (WHO, 2008b:2).

On the African continent, NCD are projected to be liable for 23% of all deaths (WHO, 2008b:2). In 2002, NCD accounted for 28% of deaths. The WHO projects that diabetes will increase 47% on the continent. Currently, CVD kills five times as many people as do HIV/AIDS (WHO, 2008b:4). Most of the NCD share common risk factors, which includes non-modifiable risk factors (age, gender, family history and race), behavioural risk factors (physical inactivity, unhealthy diet and smoking) and physiological risk factors such as obesity, hypertension and diabetes (**Figure 2.1**). The modifiable risk factors expressed as obesity, diabetes and high lipid concentrations are the root causes of the global NCD epidemic (Wong *et al.*, 2005:92). Although the relative importance of the risk factors may vary in different populations, these conventional risk factors may explain 75% of these chronic conditions (WHO, 2005a:1).

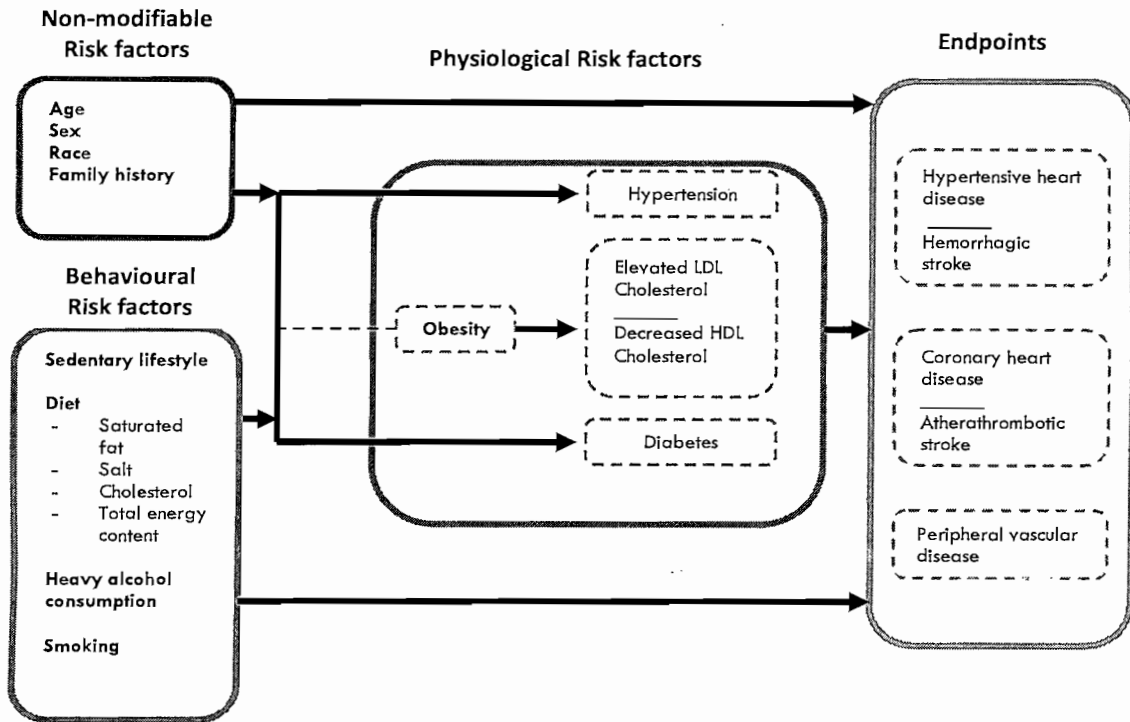


Figure 2.1: Relationships between cardiovascular risk factors and diseases

Adapted from Wong *et al.* (2005:92)

According to the WHO, obesity has reached epidemic proportions globally and projects that by 2015, approximately 2.3 billion adults will be overweight and more than 700 million will be obese (WHO, 2005b:57). The prevalence rate of obesity is a problem in both the developed and developing world (Yeater, 2000:351; Ali & Crowther, 2005:56). Obesity affects people regardless of gender across the whole life spectrum and is influenced by the lifestyle, environment and socio-economic status of an individual or population (Antipatis & Gill, 2001:3-21). Overweight and obesity lead to serious health consequences. Risk for NCD increases progressively as body mass index (BMI) increases and can be prevented by increased physical activity and a healthy diet (Antipatis & Gill, 2001:21).

It is clear that the burden of NCD and obesity is an enormous problem because of the major effects on the quality of life of the affected individuals, premature death and adverse effects on society as a whole (WHO, 2005b:35).

In this Chapter, a brief outline of obesity and anthropometric measures and its relationship with NCD, metabolic risk factors and covariates such as race or ethnicity and urbanisation are discussed.

2.2 OVERWEIGHT AND OBESITY AS RISK FACTORS

At the physiological level, obesity can be defined as a condition of abnormal or excessive fat accumulation in adipose tissue to the extent that health may be adversely affected because of a positive energy balance (WHO, 1998:2; ACSM, 2000:214; Antipatis & Gill, 2001:4). Energy balance is determined by macronutrient intake, energy expenditure, and energy or nutrient partitioning (Bouchard, 2000:214). This energy balance is disturbed against a background of progressive reduction in the energy expended during work and leisure time physical activities (Haskell, 1996:S37).

There are numerous health conditions associated with obesity and many other pathological conditions for which obesity serves as a major risk factor. According to Molarius and Seidell (1998:719), overweight, obesity and health problems associated with them are now so common that they are replacing the more traditional public health concerns such as under nutrition and infectious disease as the most significant contributors to global ill health.

The constellation of metabolic abnormalities comprising of abdominal obesity, elevated triglycerides (TG), reduced high-density lipoprotein cholesterol (HDL-C), elevated blood pressure (BP) and elevated fasting plasma glucose is referred to as the metabolic syndrome (MetS) (Eckel *et al.*, 2005:1415). The prevalence of the MetS varies according to the definition used. Many expert panels and international organizations have developed their own diagnostic criteria for the MetS. Research in numerous populations is continuously exploring gender specific guidelines and ethnicity in defining the MetS. Information on the MetS in certain African populations is scarce. Ntyintyane *et al.* (2007:12) reported that abdominal obesity as measured by waist circumference (WC) as a metabolic risk factor (International Diabetes Federation (IDF) criteria for MetS) identified more South Africans to have the MetS compared to other components of the IDF definition. Regardless of the definition used; the prevalence rate indicates that large numbers of black South Africans have the MetS (Ntyintyane *et al.*, 2007:12).

There is no consensus in the literature on the cut-off values for abdominal obesity in Africans. It is therefore the aim of this study to determine appropriate obesity cut-off values to be utilized in MetS definitions and NCD for a black Setswana speaking population of South Africa.

2.3 THE GLOBAL PROBLEM OF OBESITY

2.3.1 Statistics and recent trends

More than 1.6 billion adults are already overweight (15 years and older), at least 400 million of them obese (WHO, 2005b:57). Recent prevalence figures of obesity in Europe are around 20% in men and 15-25% in women (Coppack *et al.*, 2005:31). Results based on a Nutritional Survey conducted by the Japanese Ministry of Health & Welfare (2001:1) showed that the prevalence of obesity in this population reached almost 30% in men aged 30-60 years and women aged 50-70 years (Kanazawa *et al.*, 2005:3-9).

Future projections of overweight adults, is expected to double that of underweight adults between 1995 and 2025. This is based on crude projections from repeated national surveys (Antipatis & Gill, 2001:11).

2.3.2 Obesity in Africans

Data from almost all the countries of the industrialized world and the developing world reveal growing proportions of overweight and obesity across the lifespan (WHO, 1998:105). This trend is also true for South African adults (30-79 years) where higher BMI values was measured compared to other African countries when categorized by age and gender (Goedecke *et al.*, 2006:66). The overall prevalence of overweight and obesity in South Africa (BMI > 25 kg/m² and BMI > 30 kg/m²) is high with 29% of men and 56% of women being classified as overweight or obese (Puoane *et al.*, 2002:1038). BMI values for Seychellois and Cameroonian females show the closest association to South African trends. BMI for Seychellois females are still considerably lower, compared to South African females of the same age group (30-69 years) with mean BMI of 26.8 kg/m² and 29.1 kg/m² respectively (**Table 2.1**).

A study in the Democratic Republic of Congo with 11511 participants indicated that men had a BMI of 23.4 ± 4.7 kg/m² and females a BMI of 23.6 ± 5.3 kg/m². The mean age for participants in this study was 37 (± 16) and 36 (± 16) years for men and women respectively (On'Kin *et al.*, 2007:303). These values are comparative to the countries showing the closest relation to the high obesity rates in South Africa for the same age (Seychelles and Cameroon). According to a WHO projection into 2015, the prevalence rate of overweight adults in South Africa for both genders will be 56.5% (**Figure 2.2**). The prevalence rates for both genders of adjoining

countries of South Africa are 51.5% for Botswana, 20.0% for Mozambique and 25.0% for Namibia.

Table 2.1: Mean BMI (kg/m²) of males and females of African countries

African Country	Gender	Age in years						
		5-14	15-29	30-44	45-59	60-69	70-79	80+
Cameroon	M	N/D	23.7	24.4	24.0	N/D	N/D	N/D
	F	N/D	24.6	24.8	25.0	N/D	N/D	N/D
Ethiopia	M	14.2	17.5	18.3	18.0	18.0	17.9	19.8
	F	14.5	18.9	18.6	17.3	16.7	17.6	18.6
Gambia	M	N/D	19.6	20.5	20.9	21.0	20.0	N/D
	F	N/D	21.0	21.9	21.8	21.3	20.9	N/D
Ghana	M	N/D	N/D	N/D	N/D	N/D	N/D	N/D
	F	N/D	21.8	22.4	21.4	N/D	N/D	N/D
Kenya	M	N/D	N/D	N/D	N/D	N/D	N/D	N/D
	F	N/D	21.7	22.3	22.0	N/D	N/D	N/D
Malawi	M	N/D	N/D	N/D	19.8	19.8	19.7	N/D
	F	N/D	N/D	N/D	20.5	20.5	19.6	N/D
Mali	M	N/D	18.9	20.5	20.8	20.3	19.6	20.2
	F	N/D	19.9	21.1	20.6	20.0	19.5	20.8
Nigeria	M	N/D	19.8	20.9	21.5	N/D	N/D	N/D
	F	N/D	21.0	21.8	20.3	N/D	N/D	N/D
Senegal	M	N/D	18.2	19.9	21.0	20.7	19.8	19.2
	F	N/D	19.6	21.4	22.1	22.2	21.3	20.7
Seychelles	M	N/D	22.9	23.5	23.1	23.2	N/D	N/D
	F	N/D	23.2	25.7	27.2	27.5	N/D	N/D
South Africa	M	13.8	21.3	24.2	25.3	24.8	24.4	N/D
	F	14.0	24.4	28.5	29.9	28.8	27.7	N/D
Tanzania	M	N/D	N/D	N/D	N/D	N/D	N/D	N/D
	F	N/D	21.8	22.3	21.6	N/D	N/D	N/D
Zimbabwe	M	15.3	19.5	20.8	21.0	21.0	20.1	20.0
	F	14.4	21.3	23.0	23.5	21.8	20.5	20.3

M=Male; F=Female; N/D=No available data

Adapted from International Obesity Task Force: Global Burden of Disease Analysis 2002.

(Goedecke *et al.*, 2006:66)

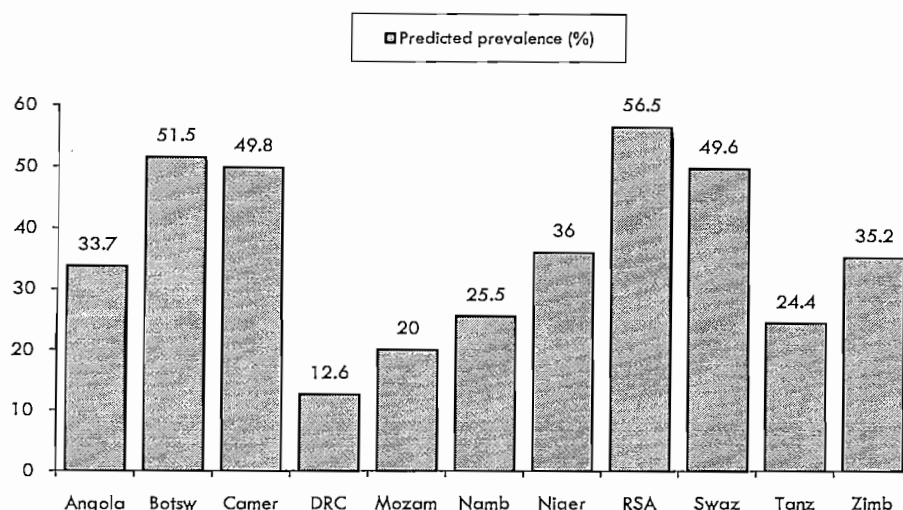


Figure 2.2: Predicted estimates for overweight (BMI ≥ 25 kg/m²) by country for ages 15-100 years, for 2015.

Botsw=Botswana; Camer=Cameroon; DRC=Democratic republic of Congo; Mozam=Mozambique; Namb=Namibia; Niger=Nigeria; RSA=Republic of South Africa; Swaz=Swaziland; Tanz=Tanzania; Zimb=Zimbabwe

(WHO: Global InfoBase BMI Country Comparison, 2008c)

2.4 FACTORS INFLUENCING OBESITY

Cossrow and Falkner (2004:2590) found significant disparities to exist in gender, ethnicity, and socio-economic status (SES) with respect to the prevalence of obesity and overweight and related co-morbidities in the USA.

There are several correlates and predictors of overweight and obesity (see **Table 2.2**). Some of these correlates are true predictors of body-fat gain and therefore can be defined as risk factors for overweight or obesity. These risk factors are associated with the metabolic effects of increased adiposity. In some cases, the relationship may be secondary to an obese state and therefore the result of being in an obese state or having excess adipose tissue (Bouchard, 2000:214; Bray, 2004:2583).

Table 2.2: Correlates of overweight and obesity

Variable	Comment
Age	▪ Childhood obesity ▪ Body-fat content increases during childhood ▪ Maximal rates of overweight and obesity are attained from 55 to 65 years
Gender	▪ Women have more body fat ▪ Gender differences in prevalence of obesity vary among ethnic groups
Socioeconomic status	▪ More obese in high-SES classes in poor countries ▪ More obese in low-SES classes in rich countries
Energy intake	▪ Overfeeding causes weight gain and leads to obesity ▪ Under nourishment in infants in utero have a greater risk to become obese adults
Dietary fat intake	▪ Dietary fat is related to prevalence of overweight in ecological studies ▪ High-fat diet causes weight gain (westernised diet) ▪ Low-fat diet reduces body weight
Resting metabolic rate	▪ A low body mass and composition-adjusted RMR is a risk factor for weight gain, but contradictory data have been found ▪ Overweight and obese people have a higher absolute RMR
Thermic response to food	▪ Obese have a depressed response in some studies, but contradictory results are abundant
Physical activity level	▪ A low level of PA is a risk factor for weight gain ▪ Level of sedentarism is higher in obese people ▪ Regular PA changes body composition ▪ High levels of PA increase SNS activity and RMR ▪ Regular PA contributes to weight loss and weight maintenance
Ethnicity	▪ Some ethnic groups are more susceptible to abdominal obesity compared to Caucasians
Smoking	▪ Smoking is associated with a lower body weight ▪ Cessation increases body weight in most people

Variable	Comment
Lipid oxidation rate	▪ Body-fat gains decrease RQ ▪ A high RQ is a risk factor for weight gain, but there are contradictory results ▪ Previously obese have a higher RQ than those who have never been obese
Blood leptin level	▪ Low leptin levels are weakly related to weight gain ▪ Most obese have high leptin levels ▪ Increased leptin levels raises BP by constricting blood vessels
SNS activity	▪ Low SNS activity could be a risk factor for weight gain ▪ SNS activity increases with overfeeding and body weight gain ▪ Raises BP by constricting blood vessels and stimulating the heart
Growth hormone level	▪ Low GH is a risk factor for weight gain ▪ Most obese have low GH levels
Insulin sensitivity	▪ Obese are often insulin resistant and hyperinsulinemic ▪ Insulin resistance protects against weight gain, but there are contradictory results
HPA axis and cortisol levels	▪ Obese have generally a hyper-responsive and hyperactive HPA axis ▪ Obese have elevated cortisol production rates, but also accelerated degradation
Sex steroid levels	▪ Obese men often have low androgen levels ▪ Obese women often have high androgen levels with further elevation upon ACTH stimulation
Adipose tissue metabolism	▪ Catecholamine-induced lipolysis is reduced in obesity ▪ Lipogenesis from glucose is increased in human fat cells from obese people ▪ Adipose tissue LPL is increased in obesity ▪ Elevated adipose LPL activity remains high in reduced obesity ▪ High adipose tissue LPL is a risk factor for weight gain

Variable	Comment
Skeletal muscle metabolism	▪ SM type 1 fiber proportion is not affected by obesity ▪ SM type IIb fiber proportion is often elevated in obesity ▪ SM oxidative enzyme markers are inversely related to obesity ▪ SM LPL activity is low in obesity
Energy and nutrient partitioning	▪ Under positive energy balance conditions, people channel more food carbons into proteins ▪ High rates of lipid accretion could be a risk for further weight gain
Environment	▪ Urban populations tend to have higher rates of obesity than rural populations ▪ Urbanisation leads to adapting a westernised diet, increased stress and decreased physical activity ▪ Rural communities eat more variety with less fat and more complex carbohydrates ▪ Urbanisation leads to a shift in patterns of disease away from infections and nutrient deficiency towards higher rates of non-communicable diseases ▪ Urbanised settings tend to have lower levels of physical activity that lead to reduced energy expenditure

SES = Socio-economic status; RMR = Resting metabolic rate; PA = Physical activity; SNS = Sympathetic nervous system; RQ = Respiratory quotient; GH = Growth hormone; HPA = Hypothalamic-pituitary-adrenal; ACTH = Adrenocorticotrophic hormone; LPL = Lipoprotein lipase; SM = Skeletal muscle.

Adapted from Bouchard (2000:214); Antipatis & Gill (2001:11); Coppack *et al.* (2005:35) and WHO (2005a:1).

2.4.1 Obesity, increased risk profiles and ethnicity

In South Africa, four major ethnic groups are recognised: black African, people of mixed origin (coloured), Indian and Caucasian (white). Several studies have reported BMI values for these groups over the past 25 years according to Van der Merwe and Pepper (2006:315). However, geographical location and other variables (age, physical activity and urbanisation) were inconsistent between the studies to perform meaningful comparisons (Van der Merwe & Pepper, 2006:315). Puoane *et al.* (2002:1038) estimated that the prevalence of obesity ($\geq 30 \text{ kg/m}^2$) in black African women was 31-34%, 18-24% in Caucasian women and 20-22% in Indian and 26-28% in coloured women. The prevalence of obesity in black, Indian and coloured men was 8%, 3-9% and 6-9% respectively, with the highest prevalence in Caucasian males 15-20%.

Some racial or ethnic groups have different risk profiles compared to Caucasians. Black Africans for example have high rates of hypertension even without considering metabolic risk factors and they may have higher disease receptiveness than other populations (Prussian *et al.*, 2007:229). In **Table 2.3** it is shown that increased hypertension (especially systolic blood pressure) and abdominal obesity as measured by WC may be the leading risk factors for NCD for black Africans. Increased risk for elevated blood pressure and waist circumference was present even in normal BMI ranges (for women in particular) as reported by Patt *et al.* (2003:660).

There has almost been a universal increase in obesity in general as well as abdominal obesity (Onat *et al.*, 2007b:182). It has been recognised that different measures of obesity and the risk of different health outcomes vary, and therefore further research is needed to understand the ethnic and racial differences in waist circumference (WC) and its association to adverse health outcomes (Wang *et al.*, 2005:555). Schutte *et al.* (2009:83) concluded that a different set of metabolic syndrome criteria in general may be needed, since criteria are firstly not designed for the African population, nor is it able to truly measure CVD risk in Africans.

Table 2.3: Differences due to African ethnicity

Author, Year	Differences in African ethnicity	Findings and conclusions
Harris <i>et al.</i> (2000) and Okosun <i>et al.</i> (2000)	↑ Hypertension	Hypertension increased at all WC quartiles Increased WC correlates with raised blood pressure
Norman <i>et al.</i> (2003)	↑ Systolic blood pressure ↑ Fasting insulin levels ↑ Increased risk profiles (women) ↑ HDL-C, ↓ LDL-C, ↓ TG (men)	Higher SBP and fasting insulin levels Increased risk factor profiles in women (except for TG) More favorable lipid profile in men
Patt <i>et al.</i> (2003)	↑ Risk profiles at normal BMI (women)	Increased risk starts in normal BMI category for women
Deurenberg <i>et al.</i> (1998)	↓ Lower body fat (BMI)	Lower body fat for the same BMI as Caucasians

All conclusions are compared to Caucasian data

WC=Waist circumference; TG=Triglycerides; BMI=Body mass index; SBP=Systolic blood pressure; HDL-C=High density lipoprotein cholesterol; LDL-C=Low density lipoprotein cholesterol
 (Prussian *et al.*, 2007:232; Deurenberg *et al.*, 1998:1164)

The International Diabetes Federation (IDF) proposed that abdominal obesity is a prerequisite risk factor for diagnosing MetS. To satisfy the diagnostic criteria, an individual must have a WC that exceeds an ethnic-specific value that is also gender specific (Alberti *et al.*, 2006:476). According to the IDF guidelines for WC to detect MetS, values have already been determined for Europeans, South Asians, Chinese and Japanese (see **Table 2.4**). At that time, no cut-off values have been proposed for ethnic South and Central Americans, Sub-Saharan Africans, East Mediterranean and Arabian populations. It was recommended that European cut-off values be used until more data became available (Alberti *et al.*, 2006:476). Recent data for WC cut-off values in an Iraq study found a WC associated with increased risk for type 2 Diabetes Mellitus (2DM) and hypertension to be (90 cm and 95 cm) in men and (91 cm and 95 cm) in women respectively (Mansour & Al-Jazairi, 2007:253). A study by Lee *et al.* (2007:72) found ethnically specific cut-off values for WC in Korean men and women to be 90 cm and 85 cm. Significantly different to the IDF guidelines of South Asians (90 cm and 80 cm), Chinese (90 cm and 80 cm) and Japanese (85 cm and 90 cm) for men and women respectively (see **Table 2.4**). A study by Nishimura *et al.* (2007:77) evaluated the previous Japanese cut-off values for optimal waist circumference in relation to the metabolic syndrome as estimated from the receiver operating

characteristic (ROC) curve to be much shorter than that was previously proposed for females in this population (80 cm for women as apposed to 90 cm according to IDF guidelines).

Table 2.4: IDF and ethnic specific guidelines for WC to determine MetS

Waist circumference cut-off values for abdominal obesity		
Ethnic group	Waist circumference	
	Male	Female
Europids [†]	≥ 94 cm	≥ 80 cm
South Asians	≥ 90 cm	≥ 80 cm
Chinese	≥ 90 cm	≥ 80 cm
Japanese§	≥ 85 cm	≥ 90 cm
Ethnic South and Central Americans	≥ 90 cm *	≥ 80 cm *
Sub-Saharan Africans	≥ 94 cm *	≥ 80 cm *
Eastern Mediterranean and Middle Eastern (Arab) populations	≥ 94 cm *	≥ 80 cm *
[†] <i>Europids: people of European descent. Note that in the USA, 102 cm for men and 88 cm for women are likely to continue to be used for clinical purposes.</i> * <i>These WC cut-off points are to be used until more specific data are available.</i> § <i>Subsequent data analyses suggest that Asian values (male 90 cm; female 80 cm) should be used for Japanese populations until more data is available.</i>		

(Alberti *et al.*, 2006:476)

This raises concern as to how WC might be utilized universally as a clinical guideline. According to the IDF, guidelines for Sub-Saharan Africans do not yet exist. However, Africans of the Sub-Saharan may in the same way be as different to each other in regards to MetS prevalence and cardiovascular disease risk as is the case in Asians, although thought to be genetically the same. The key to WC is therefore not only related to ethnicity but also to the environment that a specific population finds itself in. In contrast to this statement, the IDF guidelines are to be used for people of the same ethnic group wherever they are found (regardless of country of residence and urbanisation) (Alberti *et al.*, 2005:1060). Already contrasting studies have been found to challenge the IDF on this concept. Some studies demonstrate that metabolic risk factors may be population specific and geographical area specific (Misra *et al.*, 2005:973; Shiwaku *et al.*, 2005:52). This implicates that the simplicity of WC as a clinical guideline for detection of MetS risk may be affected and should be further studied in various minority groups.

2.4.2 Obesity and the environment (Urbanisation)

Urbanisation is associated with lifestyles that favour the development of obesity and the MetS (Fezeu *et al.*, 2007:75). Due to the widespread access to calorie richer foods in developing countries as a result of urbanisation, obesity, hypertension, MetS and type 2 diabetes mellitus has increased (Van Rooyen *et al.*, 2000:779; Dehout *et al.*, 2008:6). The adoption of a westernised diet (high in fat and sodium chloride, less fiber and carbohydrates) is especially relevant for South Africans living in urban areas (Van Rooyen *et al.*, 2000:785; Bourne *et al.*, 2002:157). Reduced leisure time physical activity, increased transportation opportunities and technology in urban settings is also a contributing factor to booming obesity rates (Popkin & Doak, 1998:112; Van Rooyen *et al.*, 2000:779; Kruger, 2001:106).

Urbanisation is associated with higher rates of MetS, insulin resistance, obesity, hypertension, fibrinogen and vascular responsiveness compared to their rural counterparts, according to sub-Saharan African studies by van Rooyen *et al.* (2000:779); Kruger (2001:104); Underhay *et al.* (2003:77); Fezeu *et al.* (2007:73) and Malan *et al.* (2007:S18). According to Sicree & Shaw (2007:75), urbanisation is reflective of a variety of lifestyle changes, which are associated with higher diabetes prevalence in developing countries, and is accounted for in these estimates by applying higher prevalence to the urban component of a population than to the rural component. Since many studies in developing countries indicate that the prevalence of diabetes is higher in urban than rural populations, urbanisation will increase the prevalence of diabetes, with some of this effect attributable to a more sedentary lifestyle and increased obesity (Sicree & Shaw, 2007:76).

Although the environment of an individual plays a major role in NCD, genetics may still be the main determinant for MetS, diabetes and obesity. It is well known that obesity is highly heritable, and it is likely that genetic factors contribute significantly to the ethnic differences in obesity related co-morbidities (Van der Merwe & Pepper, 2006:322).

2.5 ANTHROPOMETRIC INDICES OF OBESITY

In recent years, there has been increasing speculation over which measure of overweight and obesity is best able to discriminate those individuals who are at increased risk for NCD. Obesity is difficult to measure because fat is widespread and inaccessible (Toscani *et al.*, 2007:993). Whole body adiposity cannot be measured accurately or directly without invasive techniques. Therefore, anthropometry techniques to determine overweight and obesity are used, but lack in

having a “true” gold standard or reference to validate body composition analysis to (Toscani *et al.*, 2007:993). According to Han & Lean (2001:51) the most fundamental issues of using anthropometry in the assessment of body fat is that the prediction equations must be validated on a specific population level. This view was supported by research on Japanese and Asia-Oceania populations. It was determined that a lower BMI classification for obesity ($\text{BMI} \geq 25.0 \text{ kg/m}^2$ as apposed to $\text{BMI} \geq 30.0 \text{ kg/m}^2$) was more appropriate for these populations (Kanazawa *et al.*, 2005:11). This is important keeping in mind that the correlates of obesity are environmental, ethnic, age and gender specific (Wong *et al.*, 2005:92). Another key issue in anthropometry related to obesity is that different co-morbidities correlate with different anthropometric measures.

The laboratory standard methods for assessing body fat, the Dual-Energy X-ray Absorptiometry method (DEXA), Computerized Tomography (CT) and Magnetic Resonance Imaging (MRI) methods are the most reliable when considering accuracy, practicality, sensitivity to change and the ability to detect fat distribution, but are expensive (Han & Lean, 2001:52). Basic anthropometric measures such as BMI, WC, WHR and WHtR may be more appropriate, easy to administer, accessible, cost effective and reliable in epidemiological studies in South Africa.

2.5.1 Body mass index (BMI)

Clinically the prevalence of overweight and obesity is assessed by using body mass index (BMI). Although BMI is widely used in the literature to measure degree of overweight and obesity, it is not a measure of fatness, but rather a measure of heaviness (total fat) instead (WHO, 2000:2; Heyward & Wagner, 2004:67). BMI therefore does not differentiate between fat mass and lean body mass. BMI is defined as the weight in kilograms divided by the square of the height in meters (kg/m^2). Overweight as defined by the WHO is a BMI higher than 25 kg/m^2 and obesity as a BMI of 30 kg/m^2 or higher (Grundy *et al.*, 1999:S502) (see **Table 2.5**).

The BMI provides the most useful and practical population-level indicator of overweight and obesity in adults. Caution is however required when interpreting BMI measurements in certain individuals and ethnic groups. The relationship between BMI and body fat content varies according to body build and body proportion and a given BMI may not correspond to the same degree of fatness across all populations (Antipatis & Gill, 2001:4). It can be concluded that persons with a BMI in the normal range ($\text{BMI } 18.5\text{--}24.9 \text{ kg/m}^2$) can still be at increased risk of metabolic abnormalities.

The literature has proposed alternative measures to classify obesity as it is related to metabolic risk factors. Japan recently used the term pathological obesity (Kanazawa *et al.*, 2005:7) to describe obesity as it is related to disease risk. The metabolic risks associated with obesity are closely correlated with central (abdominal) rather than peripheral (gluteal-femoral) fat patterning (Smith *et al.*, 2001:425). For a comprehensive estimate of weight-related health risk, it is also desirable to assess the extent of intra-abdominal or 'central' fat accumulation (Antipatis & Gill, 2001:4) as measured by waist circumference. Lee *et al.* (2008:650) found in a meta-analysis that combining BMI with any measure of central obesity does not improve upon its discriminatory capability as previously suggested by Zhu *et al.* (2004:633). BMI should be carefully interpreted when assessed because it is a vector of several effects (Zhu *et al.*, 2004:633).

Table 2.5: Clinical guidelines for obesity classification

Body mass index classification of overweight and obesity			Waist circumference cut-off values based on BMI classifications	
Classification	BMI (kg/m ²)	Associated health risk	Level 1 (Alerting zone)	Level 2 (Action level)
Underweight	<18.5	Low (but risk of other clinical problems increased)	WC Men ≥ 94 cm Women ≥ 80 cm	WC Men ≥ 102 cm Women ≥ 88 cm
Normal range	18.5-24.9	Average	To replace BMI overweight classification	To replace BMI obesity classification (in combination with high waist-to-hip ratio)
Overweight	25.0 or higher			
Pre-obese	25.0-29.9			
Obese class I	30.0-34.9	Increased		
Obese class II	35.9-39.9	Moderately increased		
Obese class III	40.0 or higher	Severely increased Very severely increased		

(WHO, 2000:9; Deurenberg *et al.*, 1991:106)

2.5.2 Waist circumference (WC)

Analyses using computed tomography scan imaging (CT) indicate that central obesity may be classified in subcutaneous fat obesity and visceral fat obesity (Garaulet *et al.*, 2006:1181). Studies indicate that adipocytes within the deep visceral compartments are more metabolically

active than adipocytes within the superficial visceral compartment, and thus is a stronger predictor of insulin resistance (Wong *et al.*, 2003:714; Carey, 1997:1437; Pena-Gonzales *et al.*, 1997:92). Increased WC is an indicator of abdominal obesity (Grundy *et al.*, 2004b:553), and therefore predicts greater cardiovascular risk (Charlton *et al.*, 2001:142; Grundy *et al.*, 1999:S502).

A consensus statement on waist circumference and metabolic risk identified five anatomical landmarks that have been used to measure WC in clinical studies, including: 1) midpoint between the lowest rib and the iliac crest; 2) the umbilicus; 3) narrowest (minimum) or widest (maximum) WC; 4) just below the lowest rib; and 5) just above the iliac crest (Klein *et al.*, 2007:1062). It is however unclear in most studies which definition of WC was used. International standards prescribed by the International Society for the Advancement of Kinanthropometry (ISAK) defined WC as the girth taken at the visible narrowing of the waist between the costal (10th rib) border and the iliac crest (Marfell-Jones, 2006:15). The consensus statement agreed that WC should be measured with normal expiration, around the bare waist, feet touching and with no shoes. The measurement should be made with a non-elastic measuring tape and placed perpendicular to the long axis of the body in a horizontal plane (Klein *et al.*, 2007:1062). In research, this measurement should be taken three times and the median recorded to the nearest 0.1 cm (Klein *et al.*, 2007:1062).

Research reporting the difference between the diverse measuring sites is scarce. Two studies did however indicate that there was a considerable difference between the two sites mentioned, especially in women (Koda *et al.*, 1999:182; Bigaard *et al.*, 2005:2263). In a recent study minimal waist was measured in 266 overweight men and women in a randomized controlled trial. Results indicated that WC at the visible narrowing had a stronger correlation with the metabolic variables measured in the study than WC at the umbilicus site, although the statistical significance was only ($p < 0.06$) between the two sites (Willis *et al.*, 2007:753). Waist circumference should therefore be measured using international standards to make data comparable in research and therefore avoid overall confusion when interpreting data. Waist circumference correlates well with visceral fat content as determined by CT. Researchers have proposed that WC should be used instead of waist-to-hip ratio (WHR) to define abdominal obesity because of the better correlation with visceral adipose tissue (as determined by CT) (Ross *et al.*, 1992:787; Pouliot *et al.*, 1994:460; Han *et al.*, 1996:533).

2.5.3 Waist-to-hip ratio (WHR)

Traditionally, the WHR has been used as a simple method for determining body fat patterning (Bray & Gray, 1988:429). Health risks are known to increase with WHR and standards for risk vary with age and gender. Increased risk is associated at a WHR of > 0.94 for men and > 0.82 for women (ACSM, 2000:63). The focus has however shifted from WHR to using WC alone. Some studies continue to find WHR to be the best predictor for diabetes, dyslipidemia and absolute CHD risk in certain ethnic populations (Wang *et al.*, 2007:173). The main criticism of WHR is that WHR can remain the same even when there is a change in body size because WC and hip circumference can increase or decrease proportionately (Figure 2.3). The problem is then that this index may underestimate the identification of individuals at increased risk for NCD.

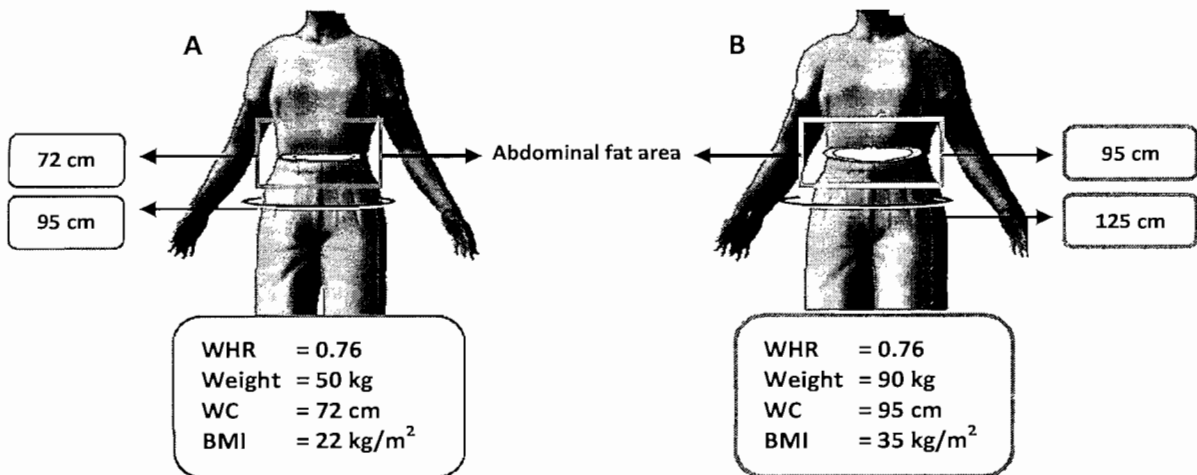


Figure 2.3: An illustration of the limits of measuring waist-to-hip ratio.

In the figure, two women (A and B) with the same WHR are presented. [A], have a smaller abdominal fat area, lower WC and lower BMI compared to [B]. Based on WHR alone, [B] would have been missed diagnosed for being at increased risk for NCD and the metabolic syndrome.

WHR=Waist-to-hip ratio; WC=Waist circumference; BMI=Body mass index

(Adapted from Désprés, 2001:5)

2.5.4 Waist-height ratio (WHtR)

Waist-height ratio (WHtR) also known as waist-to-height index, weight-to-stature ratio or index of central obesity (ICO) has been associated with CVD risk factors (Freedman *et al.*, 2007:33; Parikh *et al.*, 2007:1272). Many studies found this anthropometrical measure to be more strongly associated to CVD risk factors than BMI and WC (Parikh *et al.*, 2007:1237). WHtR takes into account the distribution of body fat in the abdominal region, which has been shown to be more associated with CVD risks than body weight (Cikim *et al.*, 2004:268). Diabetes and hypertension have also been shown to be more prevalent in short-stature subjects compared

with taller subjects after adjusting for confounders (Lara-Esqueda *et al.*, 2004:1443). A longitudinal study showed that the predictive power of WC for incident hypertension was improved when WC was corrected with height or hip circumference (Fuchs *et al.*, 2005:1515).

A universal cut-off value of 0.50 to predict CVD risk may be used in both adults and children irrespective of their age or gender. Freedman *et al.* (2007:33) found BMI-for-age and WHtR to be the same in their abilities to identify children with adverse risk factors. WHtR may however be preferred because of its simplicity and potential to be a universal parameter that can be used from child to adulthood. Results show that WHtR can be a practical anthropometrical index for the identification of higher risk for future metabolic disorders in people with normal BMI ($< 25 \text{ kg/m}^2$) and increased BMI ($\geq 25 \text{ kg/m}^2$) (Lee *et al.*, 2008:649; Skrzypczak *et al.*, 2008:338). Parikh *et al.* (2007:1275) concluded that WHtR may eliminate the confusion emanating from the lack of consensus on ethnic specific WC cut-off values for NCD and MetS and perhaps even between the genders.

Aswell and Hsieh, (2005:303) proposed six reasons for the use of WHtR (see **Table 2.6**) and proclaims that a simple public health message may be promoted if WHtR is to be used “*Keep your waist circumference to less than half your height*”.

Table 2.6: Benefits of using WHtR as a screening tool for obesity in the public health sector

6 Benefits of WHtR	
1	WHtR is more sensitive than BMI as an early warning of health risks.
2	WHtR is cheaper and easier to measure and calculate than BMI.
3	A boundary value of WHtR = 0.5 indicates increased risk for men and women.
4	A boundary value of WHtR = 0.5 indicates increased risk for people in different ethnic groups.
5	WHtR boundary values can be converted into a consumer-friendly chart.
6	WHtR may allow the same boundary values for children and adults.

(Aswell & Hsieh, 2005:303)

2.5.5 Computerized Tomography (CT) and Magnetic Resonance Imaging (MRI)

Computed tomography (CT) and magnetic resonance imaging (MRI) are considered the gold-standard methods for determining the quantity of subcutaneous abdominal adipose tissue (SAAT) and intra-abdominal adipose tissue (IAAT) (Smith *et al.*, 2001:425). According to the consensus statement on waist circumference, most CT and MRI methods, involve acquisition of

cross-sectional abdominal images, which are then analysed for fat content. Currently, there is no universally accepted site for measuring IAAT and SAAT but sites usually include either the L1-L2 or L4-L5 level (Klein *et al.*, 2007:1062).

Visceral adipose tissue (VAT) of greater than 130 cm² has been proposed to mediate the relationship between obesity and the risk for developing cardiometabolic disease (Désprés, 1997:271; Smith *et al.*, 2001:434). In Japan, however, VAT of greater than 100 cm² is considered for increased disease risk (Kanazawa *et al.*, 2005:8) however, the study sample consisted of mixed gender and did not consider that there may be differences between the genders related to MetS components. Two other studies found that differences varied between the genders as it is related to MetS and VAT in Japanese study samples (Miyawaki *et al.*, 2005:477; Hayashi *et al.*, 2007:120). These studies also challenged the 100 cm² VAT cut-off as proposed by Kanazawa *et al.* (2005:8) and the higher WC cut-off value proposed for women in the IDF definition for MetS by Alberti *et al.* (2005:1060). In 2006 the IDF expanded its definition by suggesting that Asian values (male $\geq$ 90 cm, female $\geq$ 80 cm) should be used for Japanese populations until more data become available (Alberti *et al.*, 2006:476).

Because the utility of laboratory methods is impractical for use in large field studies, the use of simple measures is more viable. There exist many constraints in the current guidelines for classification of obesity. The constraints include which guidelines to use for which population (ethnicity and urbanisation) and which method or measure to use for which purpose (different ways to measure WC for example). Therefore, researchers are continuing the search for workable guidelines in assessing obesity in clinical practice.

2.6 OBESITY AND DISEASE

The impact that obesity has on disease is not indicated by the degree of adiposity, but by the relative distribution of fat or fat patterning (Désprés *et al.*, 2001:716). The distribution of fat as indicated by WC is highly correlated with the development of NCD (Lafortuna *et al.*, 2008:233).

Abdominal obesity and its metabolic and clinical consequences have received a lot of attention by researchers globally. In a study on Turkish women, fasting insulin, CRP and (inversely) smoking are the main predictors of abdominal obesity (Onat *et al.*, 2007a:380). This study found elevated dyslipidemia, BP, MetS and CHD to rise sharply and asymptotically from quartile II (>83 cm) upwards. The risk for DM only emerged in the top quartile of this Turkish population (Onat *et al.*, 2007a:380).

A Portuguese sample population proved that WC has a significant interrelation with BP, and cardiovascular risk factors (Faleiro *et al.*, 2007:173). Although no proposed cut-off values were suggested by this study, it was clear that mean values for risk factors and their prevalence were always higher in groups with indications of visceral fat (Faleiro *et al.*, 2007:173).

Research conducted in Greece proposed cut-off values for WC that provided sensitivity and specificity for women with a cluster of metabolic abnormalities (Gazi *et al.*, 2007:173). WC of 84.5 cm was identified in this study and is referred to as the hypertriglyceridemic waist (HTGW). Additionally, fibrinogen was proposed as a clinical marker of inflammation in men with asymptomatic HTGW (Orbe *et al.*, 2007:174).

2.6.1 Stunting and obesity

Early malnutrition has been found to be significantly associated with chronic diseases, the cardiovascular risk factors tend to track into adulthood when left untreated (Török *et al.*, 2001:966; González-Barranco & Ríos-Torres, 2004:S134). Evidence points to under nutrition of the fetus during intrauterine life as a major determinant for increased risk (Yajnik, 2003:108). Childhood stunting has been suggested as a factor contributing to high rates of adult obesity among South African women (Kruger *et al.*, 2004:564), although the precise relation between stunting and obesity is unknown. Kruger *et al.* (2004:564) suggested that stunted girls may be at risk of relatively greater fat deposition, especially in the abdominal area. Similarly, Sawaya *et al.* (2003:172) found stunted girls to have higher WHR presumably influencing risk for CVD. Stunting is also related to the metabolic syndrome through obesity and relative weight gain in childhood carried over in adult life (Vanhala *et al.*, 1999:656). Van der Merwe and Pepper (2006:318) points out in a review of obesity in South Africa that as long as a (previously) stunted individual remains lean and is exposed to a non-obesigenic lifestyle, that individual can remain metabolically healthy. In addition, only when a previously undernourished individual recovers food abundance and then becomes overweight or obese, that there is an increased risk for metabolic abnormality in adulthood (Van der Merwe & Pepper, 2006:318).

2.6.2 Metabolic unhealthy lean individuals

Metabolically unhealthy normal weight individuals may represent one end of the metabolic syndrome spectrum. This additional patient group with insulin resistance in the absence of obesity (about 6% of the normal weight population) may have an increased risk of ischemic heart disease, compared to their metabolically healthy obese counterparts (Ruderman *et al.*, 1998:699; Park *et al.*, 2003:427; Kip *et al.*, 2004:709; St-Pierre *et al.*, 2005:1301). In a review by

Ruderman and colleagues (1998:700), these individuals may not be overweight or obese according to weight-height tables (BMI), but could be mildly obese especially around the midsection. Similarly, Kip *et al.* (2004:712) in a study of 780 women found that the metabolic syndrome defined by abdominal obesity (WC, WHR) and not BMI predict future cardiovascular risk in women.

2.7 OBESITY AND THE METABOLIC SYNDROME

An increase in the global epidemic of obesity (WHO, 2003:1), has led to increased prevalence of the metabolic syndrome (MetS) (Eckel *et al.*, 2005:1415) and are associated with all cardiovascular risk factors (Grundy *et al.*, 2004b:553; Janssen, 2005:1316). Obesity proved to be one of the most essential features of the metabolic syndrome and may be the link that unifies the syndrome (Yeater, 2000:354; Anderson *et al.*, 2001:1782; Lam *et al.*, 2004:543; Yudkin *et al.*, 2004:852; Eckel *et al.*, 2005:1417).

Overweight and obesity lead to adverse metabolic effects on blood pressure, cholesterol, triglycerides and insulin resistance (WHO, 1998:2). Shen *et al.* (2003:708) proposed that obesity may share a synergistic physiologic pathway with insulin resistance, manifested by abnormal metabolism (Carr *et al.*, 2004:2087; Kip *et al.*, 2004:707). In **Figure 2.4** the pathophysiology of cardiovascular disease in the metabolic syndrome originating from central adiposity and innate immunity is illustrated (Reilly & Rader, 2003:1546).

Interestingly, although most people with the metabolic syndrome are obese, some of them are of normal body weight. They do however have increased body fat, particularly around the midsection (Debè, 2002:2). Désprés (1997:271) has shown that visceral fat accumulations greater than 130 cm² as measured by computerized tomography (CT) or magnetic resonance imaging (MRI) are strongly associated with the metabolic syndrome. Relative weight gain and obesity as a child from about seven years, can predict the metabolic syndrome in adulthood (Ruderman *et al.*, 1998:699; Vanhala *et al.*, 1999:656). Therefore it is not surprising that obesity is a major target of prevention and treatment strategies, given the underlying role of altered adipose tissue metabolism in the metabolic syndrome (Robinson & Graham, 2004:809), which increases the morbidity and mortality risk of a person (Isomaa *et al.*, 2001:683; Ford & Giles, 2003:575; Kip *et al.*, 2004:706).

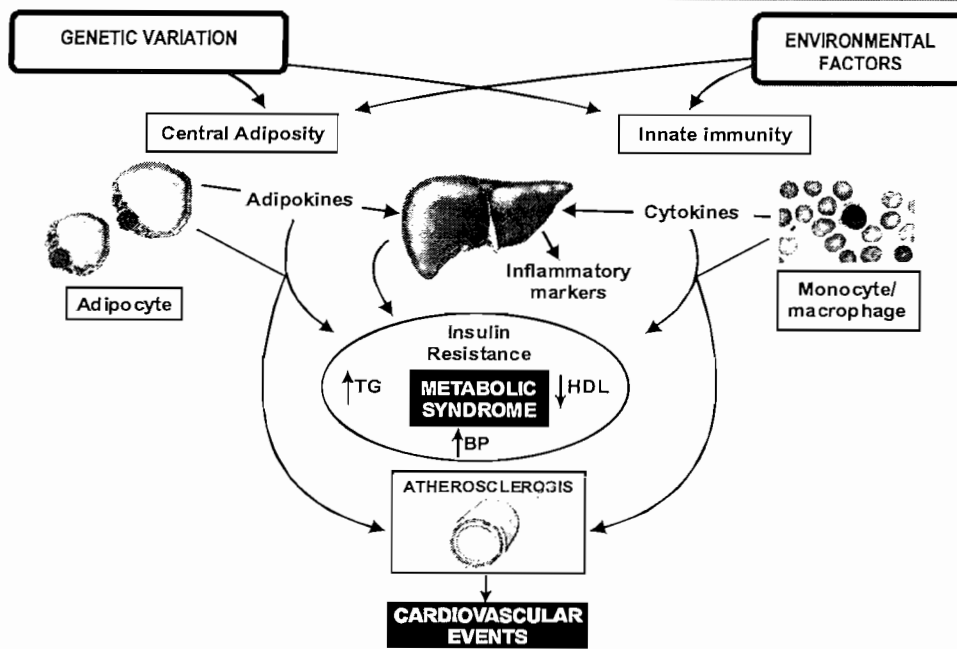


Figure 2.4: Pathophysiology of cardiovascular disease in the metabolic syndrome. Adapted with permission from Reilly and Rader (2003:1546).

The metabolic syndrome is associated with a greater risk of cardiovascular disease than any of its individual components (Hall, 2005:1). However, metabolic syndrome remains a “syndrome” and not a disease because the reasons for the clustering among the various variables are in evolution according to Hall *et al.* (2003:386). A major challenge for metabolic research according to Reilly and Rader (2003:1546) remains the identification of features of adiposity that best reflect increased risk of developing the metabolic syndrome.

2.8 OBESITY AS AN INFLAMMATORY CONDITION

Das (2001:953) proposed that obesity could be an inflammatory disorder due to low-grade systemic inflammation. This view is supported by a vast number of researchers (Weyer *et al.*, 2002:233; Ramos *et al.*, 2003:329; Dandona *et al.*, 2004:4; Nawrocki & Scherer, 2004:284; Dandona *et al.*, 2005:1452). CRP is a highly conserved molecule and a member of the pentraxin family of proteins (Du Clos, 2000:274). CRP is an acute phase reactant, synthesized primarily in hepatocytes and secreted by the liver in response to a variety of inflammatory cytokines of which IL-6 and TNF- α are the main ones involved. CRP increases rapidly in response to trauma, inflammation and infection and decreases just as rapidly with the resolution of the condition (Das, 2001:953; Heilbronn & Clifton, 2002:316). Many patients with the metabolic syndrome have a state of chronic low-grade inflammation indicated by high CRP levels, which may increase their risk for future adverse and cardiovascular events

(Ford, 2003:351; Florez *et al.*, 2006:92), even in apparently healthy individuals (Wang *et al.*, 2002:1189). Thus, the measurement of CRP can be used to monitor inflammatory states.

Abdominal obesity (indicated by elevated WC) was the single most important metabolic syndrome component associated with increased CRP levels (> 3 mg/dL) (OR= 3.1, 95% CI=1.4-10.1), followed by female gender and smoking (Florez *et al.*, 2006:92). Elevated CRP levels have been associated in cross-sectional studies with proxy indicators of elevated body fatness (body weight and BMI) and positive associations between fat-free mass, total fat mass and the intra-abdominal adipose tissue area were indicated (Tchernof *et al.*, 2002:565). In studies by Forouhi *et al.* (2001:1327) and Saijo *et al.* (2004:249), the amount of visceral fat was a better determinant of CRP levels than other levels of obesity, including fat mass. The location of the body fat, independent of the total amount, is therefore an important factor affecting chronic inflammation. There is some evidence from observational studies involving both men and women, that in addition to total body fat, visceral or abdominal body fat (measured by WC and WHR) may be an independent predictor of inflammatory markers (Bertin *et al.*, 2000:178; Barinas-Mitchell *et al.*, 2001:1099; Forouhi *et al.*, 2001:1327; Lemieux *et al.*, 2001:964; Sites *et al.*, 2002:128; Ziccardi *et al.*, 2002:806; Saijo *et al.*, 2004:249).

Several markers of inflammation correlate with indirect measures of adiposity, especially fat distribution / patterning and insulin action. Providing a possible link between obesity and insulin resistance (Pannacciulli *et al.*, 2001:1416; Weyer *et al.*, 2002:233). The synthesis of adipose tissue TNF- α could induce the production of IL-6, CRP and other acute phase reactants (Yudkin *et al.*, 1999:974), therefore contributing to the maintenance of a chronic low-grade inflammation state involved in the progression of obesity and its associated co-morbidities. Many patients with the metabolic syndrome have a state of chronic low-grade inflammation indicated by high CRP levels, which may increase their risk for future adverse and cardiovascular events (Ford, 2003:351), even in apparently healthy individuals (Wang *et al.*, 2002:1189).

2.8.1 Relationship between CRP and measures of adiposity

Evidence is strong that circulating levels of inflammatory markers are elevated with total (BMI) and abdominal obesity (WC and WHR) (Beneke *et al.*, 2007:200). This is possibly owing to a higher secretion rate of cytokines by adipose tissue in obese people (Nicklas *et al.*, 2005:1199). The relationship between CRP and abdominal obesity showed strong associations with WC, WHR and visceral fat as reported by Lemieux *et al.* (2001:961), Vikram *et al.* (2003:305), Slabbert (2004:46) and recently by Florez *et al.* (2006:92). Elevated CRP levels have been

cross-sectionally associated with proxy indicators of elevated body fatness (body weight and BMI) and positive associations between fat-free mass, total fat mass and the intra-abdominal adipose tissue area were indicated (Tchernof *et al.*, 2002:566). In studies by Forouhi *et al.* (2001:1327) and Saijo *et al.* (2004:249) the amount of visceral fat was a better determinant of CRP levels than other levels of obesity, including fat mass. The location of the body fat, independent of the total amount, is therefore an important factor affecting chronic inflammation.

Adipose tissue is known to be a secretory organ producing cytokines, acute phase reactants and other circulating factors (Ouchi *et al.*, 2003:671; Wong *et al.*, 2003:714; Kershaw & Flier, 2004:2548; Trayhurn & Wood, 2004:347). These “adipokines” are mostly not produced by the adipocyte itself but by the infiltration of macrophages into the adipocytes (Weisberg *et al.*, 2003:1796; Fain *et al.*, 2004:2273). Research by Yudkin *et al.* (1999:975) suggests that the cytokines, arising in part from adipose tissue, might be partly responsible for the metabolic, hemodynamic, and hemostatic abnormalities that cluster with insulin resistance. One of the determinants of CRP is IL-6, which is secreted by adipocytes (Mohamed-Ali *et al.*, 1997:4196; Papanicolaou *et al.*, 1998:127). In vivo release of IL-6 and TNF-soluble receptors from subcutaneous abdominal adipose tissue has been shown to correlate with BMI and body-fat proportion (Mohamed-Ali *et al.*, 1999:E971; Yudkin *et al.*, 1999:976). In one in-vitro study TNF- α release from abdominal subcutaneous adipose tissue was 7.5 fold higher in tissue from obese (BMI 30-40 kg/m²) than lean (BMI < 25 kg/m²) subjects (Kern *et al.*, 1995:2111). Ouchi and colleagues (2003:671) reported not only that CRP is expressed in adipose tissue, but also that CRP and adiponectin mRNA levels are highly inversely related. (Adiponectin is a protein with anti-inflammatory properties.) Thus, both in vivo and in vitro studies confirm that adipose tissue expression and release of cytokines are elevated in people with a higher adipose mass.

Strong associations of CRP and BMI were found in obese individuals (Hak *et al.*, 1999:1986; Lemieux *et al.*, 2001:964; Rexrode *et al.*, 2003:674; Vikram *et al.*, 2003:306; Aronson *et al.*, 2004:173; Ridker, 2004:S19), but many studies do not differentiate between android and gynoid type obesity (abdominal obesity). This complicates the interpretation of the CRP relationship to abdominal obesity and could lead to confusing assumptions in this regard. The relationship between CRP and BMI in the normal weight range has not been well characterized (Rexrode *et al.*, 2003:674). Rexrode and colleagues (2003:680) could not determine whether obesity causes elevated CRP levels directly, or whether higher CRP levels are a marker of other intermediate conditions such as atherosclerosis or insulin resistance which influence the underlying burden of inflammation among overweight and obese individuals.

The contribution of the association between abdominal obesity and metabolic risk remains the subject of considerable debate (Frayne, 2000:S72). There are however studies that indicate that adipocytes within the deep visceral compartment are more metabolically active than adipocytes within the superficial visceral compartment and thus a stronger predictor of insulin resistance (Carey, 1997:1437; Wong *et al.*, 2003:714).

2.9 DEFINITIONS OF THE METABOLIC SYNDROME

In an attempt to establish useful definitions, different international organizations and bodies have formulated various definitions for the metabolic syndrome. These include the definitions of the World Health Organization (WHO), the European Group for the Study of Insulin Resistance (EGIR), the National Education Cholesterol Program's Adult Treatment Panel III (NCEP-ATP III) and finally the International Diabetes Federation (IDF) (Schutte *et al.*, 2009:79). There are several definitions for identifying MetS and most of them are used widely in the literature. Mostly, researchers will explain why they chose to use a certain definition in a study. Since each definition has unique characteristics it should be carefully researched before being used as it may not be appropriate for all populations. The main distinguishing difference between the definitions is whether insulin resistance, obesity or abdominal obesity is considered as essential or whether all components are considered equal in the MetS. Currently no definition has been accepted as the "golden standard" and more insight to the metabolic syndrome as a whole is warranted, especially in black Africans (Schutte *et al.*, 2009:79). The most common definitions used in international research today will be briefly explained and components of these definitions are indicated in **Table 2.7**.

2.9.1 World Health Organization

The WHO's definition focused primarily on CVD as the primary outcome. In the WHO's working definition for MetS, insulin resistance is the essential required component. Insulin resistance is defined as either type 2 diabetes, impaired fasting glucose, impaired glucose tolerance or in the case of normal fasting glucose levels <6.1 mmol/L (<110 mg/dL), glucose uptake below a background population under investigation (under hyperinsulinemic and euglycemic conditions) is considered (WHO, 1999:33) (see **Table 2.7**). The presence of two other risk factors is considered essential with insulin resistance in this definition and include two of either raised BP, raised plasma triglycerides, impaired HDL cholesterol levels, obesity and elevated albumin or albumin:creatinine ratio of ≥ 30 mg/g (Grundy *et al.*, 2004a:435).

The main limitations of the WHO classification for MetS are the use of BMI and WHR as measures of obesity (Grundy *et al.*, 2004a:435). The lack to differentiate between ethnicity related dissimilarities in obesity, and the higher limitation on blood pressure compared to other definitions are the main disparity of the WHO definition to that of other international bodies. If the main outcome measure of this definition is CVD, then the primary intervention strategies such as lifestyle modification (exercise and diet) may be too late and costly interventions (therapeutic or drug therapy) required.

2.9.2 Adult Treatment Panel III

According to the NCEP-ATP III (see **Table 2.7**), the variables included in the definition are abdominal obesity, elevated triglycerides, impaired HDL cholesterol, elevated BP and fasting glucose. MetS is defined when three of the five risk factors are present in an individual and the major clinical outcome of the definition is CHD/CVD (NCEP-ATP III, 2001:16).

One of the major strengths of the NCEP-ATP III criteria is the distinction between obesity and abdominal obesity by WC and its gender specific cut-off values. The NCEP-ATP III criteria does not indicate whether this is for minimal waist, umbilical waist, or some other WC site (NCEP-ATP III, 2001:16). Strict classification of insulin resistance is not required for diagnosis of the MetS such as is needed in the WHO definition. However, most persons meeting the NCEP-ATP III criteria will be insulin resistant (Grundy *et al.*, 2004a:435).

The NCEP-ATP III received criticism from practitioners for not including a measure of insulin resistance and that the definition is not sensitive enough to detect insulin resistance in patients with normal fasting glucose levels (Appel *et al.*, 2004:24; Liao *et al.*, 2004:978). Additionally, it was proposed by researchers that the NCEP-ATP III criteria might underestimate risk in African American populations who are frequently insulin resistant, but do not have severe hypertriglyceridemia and commonly manifest higher HDL cholesterol levels (Rodriguez *et al.*, 2002:178; Solano *et al.*, 2003:82). In 2004, the NCEP-ATP III definition was updated to include the diagnostic glucose concentration (Grundy *et al.*, 2004a:433) and the cut-off value for fasting plasma glucose was changed from ≥ 6.1 mmol/L to ≥ 5.6 mmol/L (Alberti *et al.*, 2006:471).

The American Association for Clinical Endocrinologists (AACE) has similar criteria to the NCEP-ATP III definition. They however proposed lower limits for impaired fasting glucose to 100mg/dL instead of 110 mg/dL. This was due to an attempt to provide a method of earlier identification of individuals at risk for CVD (ACE, 2003:236).

Table 2.7: Clinical criteria for the diagnosis of the metabolic syndrome

WHO Criteria 1999	ATP III Criteria 2001	IDF Criteria 2005/2006
<u>Insulin resistance, identified by 1 of the following:</u> - Type 2 diabetes - Impaired fasting glucose - Impaired glucose tolerance Or for those with normal fasting glucose levels <6.1 mmol/L (<110 mg/dL), glucose uptake below the lowest quartile for background population under investigation under hyperinsulinemic, euglycemic conditions <u>Plus any 2 of the following:</u> - Anti-hypertensive medication and/or high blood pressure: ≥ 140 mmHg systolic or ≥ 90 mmHg diastolic - Plasma triglycerides: 1.7 mmol/L (≥ 150 mg/dL) - HDL-C: <1.03 mmol/L (<35 mg/dL) in men; <1.29 mmol/L (<39 mg/dL) in women - Obesity: BMI > 30 kg/m² and/or waist-to-hip ratio > 0.9 in men, > 0.85 in women - Urinary albumin excretion rate ≥ 20 μg/min or albumin:creatinine ratio ≥ 30 mg/g	<u>Risk factor</u> - Abdominal obesity, given as Waist Circumference: Male > 102 cm; Female > 88 cm - Triglycerides: ≥ 1.7 mmol/L (≥ 150 mg/dL) - HDL-C: Male < 1.03 mmol/L (<40 mg/dL); Female < 1.29 mmol/L (<50 mg/dL) - Blood pressure: $\geq 130/85$ mmHg - Fasting glucose: ≥ 6.1 mmol/L (≥ 110 mg/dL) Any 3 of the above	<u>Risk factor</u> - Central obesity: Waist Circumference*† <u>Plus any two of the following:</u> - Raised Triglycerides: - Reduced HDL-C: - Raised blood pressure: - Fasting plasma glucose: <i>Ethnicity specific values *†</i> <u>Defining level</u> ≥ 1.7 mmol/L (≥ 150 mg/dL) or specific treatment for this lipid abnormality Males < 1.03 mmol/L (<40 mg/dL); Females < 1.29 mmol/L (<50 mg/dL) or specific treatment for this lipid abnormality Systolic: ≥ 130 mmHg or Diastolic: ≥ 85 mmHg or treatment of previously diagnosed hypertension ≥ 5.6 mmol/L (≥ 100 mg/dL) or previously diagnosed Type 2 diabetes; If > 5.6 mmol/L or 100 mg/dL, oral glucose tolerance test is strongly recommended but is not necessary to define presence of the syndrome

ATP III: Adult Treatment Panel; WHO: World Health Organization; IDF: International Diabetes Federation; HDL-C: High-density lipoprotein cholesterol; BMI: Body mass index; CVD: Coronary vascular disease; WC: Waist Circumference.

*† IDF recommends the use of ethnicity-specific waist circumference cut-off values based on language spoken at home rather than country of birth. Waist circumference cut-off values for Europeans, Sub-Saharan Africans, Eastern Mediterranean and Middle East (Arab) populations: Males ≥ 94 cm, Females ≥ 80 cm, For South Asians, Chinese, Japanese, ethnic South and central Americans: Males ≥ 90 cm, Females ≥ 80 cm.

Adapted from NCEP ATP III (2001:16), Grundy *et al.* (2004b:552). & Alberti *et al.* (2006:475)

2.9.3 International Diabetes Federation

To date, the newest proposed definition was by the International Diabetes Federation (IDF) in 2005. Central obesity is essential in the IDF definition and not only classified by gender but also provides ethnic specific guidelines (**Table 2.7**). Any two of either raised triglycerides, reduced HDL- cholesterol, hypertension and fasting plasma glucose postulate MetS when abdominal obesity is present (Alberti *et al.*, 2006:475). The fact, that ethnicity is at last highlighted in a definition is a key strength in the IDF definition. Researchers have acknowledged that differences in the classification of obesity (BMI) and now WC exist in different populations.

The IDF's decision to omit the oral glucose tolerance test (OGTT) was mainly due to the difficulty of conducting this test in large numbers of subjects such as in epidemiological studies (Alberti *et al.*, 2006:475). Cameron *et al.* (2007:471) criticized the IDF criteria because this decision may be at the expense of missing individuals who would be defined as having MetS should impaired glucose tolerance (IGT) be included as a qualifying factor.

2.10 CONCLUSION

The impact of NCD globally and in South Africa particularly due to urbanisation is already substantial. Overweight and obesity need to be continually assessed so that policy makers can lower the burden of lifestyle diseases on the primary healthcare sector as well as the South African economy. South Africans may need different anthropometrical indices with population and area specific cut-off values for screening purposes, to detect risk of NCD and metabolic abnormalities. The IDF definition may be the best definition to use in a black Setswana speaking population due to its ethnic specific WC cut-off values and lower cut-off values for the remaining components of the MetS.

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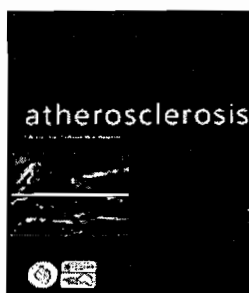
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ANTHROPOMETRIC INDICATORS OF NON- COMMUNICABLE DISEASES IN A BLACK SOUTH AFRICAN POPULATION



Left: Author with co-
author Colette Underhay in
background

Lower right:
South Africa
Country of diversity
Clear Water Gorge
(Port Edward)



This chapter is presented in article format and is written according to the referencing requirements of the journal *Atherosclerosis* to which it will be submitted. The font and spacing were kept the same throughout the thesis. All figures and tables are presented within the text rather than at the end of the article for examination purposes.

Anthropometric indicators of non-communicable diseases in a black South African population

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Abstract

Background The burden of non-communicable diseases (NCD) in sub-Saharan Africa is already substantial. Current predictions by the WHO indicate that third world countries will experience rapid increases in NCD such as diabetes and cardiovascular disease. Recently, there has been speculation over which simple anthropometric measure of obesity or abdominal obesity such as body mass index (BMI), waist circumference (WC), waist-to-hip ratio (WHR) and waist-height ratio (WHtR) is best able to discriminate those individuals who are at increased risk for NCD. **Objectives** To determine the most effective anthropometric measure that indicates the presence of NCD risk factors (measures of lipids, fasting glucose, hs-CRP, blood pressure and obesity) in black Africans. **Design and methods** Data from 2010 adults was used comprising 746 men and 1264 women (aged 35 years to 65 years), who participated in a cross sectional study that formed part of the baseline data of the South African leg of the Prospective Urban and Rural Epidemiological (PURE) study of a black Setswana speaking South African population in the North West Province. **Results** As assessed by the ability of the anthropometric indices, to 1) account for the variability in each risk factor and 2) correctly identify individuals with increased NCD risk factors, the predictive abilities of BMI, WC and WHtR were similar. WC was slightly better (0.01-0.08 higher R^2 value, $p < 0.05$) in predicting concentrations of total cholesterol (TC), fasting glucose (FG), triglycerides (TG), LDL-cholesterol (LDL-C), systolic blood pressure (SBP) and diastolic blood pressure (DBP) in men. BMI was slightly better in identifying men with reduced HDL-cholesterol (HDL-C) (0.03 higher R^2 , $p < 0.05$), while WHtR was slightly better (0.01-0.11 higher R^2 value, $p < 0.05$) in predicting concentrations of C-reactive protein (hs-CRP), TG, SBP, DBP in women. WC was slightly better in identifying reduced concentrations of HDL-C (0.03 higher R^2 , $p < 0.05$) in women. On the basis of two or more metabolic risk factors, WC and BMI were equal in their predictive ability of NCD risk factors according to the receiver operating characteristic (ROC) curve analysis (AUC=0.65) in men while WHtR and WC were equal in their predictive ability (AUC=0.65) in women. For men and women combined, WHtR was the most frequent predictor for NCD risk factors (5 out of 8

risk factors) and WC (3 out of 8 risk factors) as determined by AUC. **Conclusion** The findings showed that in black Africans living in the North West Province of South Africa BMI, WC, WHR and WHtR do not differ much in their discriminative abilities to identify adult men and women with NCD risk factors. WHtR and WC were slightly better in their predictive ability and may be preferred because of its simplicity, but additional longitudinal data is needed to examine WHtR's relation to disease in this population.

Key words: Waist circumference, Body mass index, Waist-height ratio, Waist-to-hip ratio, Metabolic syndrome, Ethnicity.

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Introduction

The burden of non-communicable diseases (NCD) in sub-Saharan Africa is already substantial, and patients with these conditions continue to challenge health care resources with the increased demand [1]. Although believed to be secondary to communicable disease in the developing world, there is a trend that diseases of lifestyle are already growing at an alarming rate in South Africa and perhaps at a greater rate compared to other developing countries [2].

The overall prevalence of overweight (Body mass index ≥ 25 kg/m²) and obesity (Body mass index ≥ 30 kg/m²) in South Africa is high with 29% of men and 56% of women being classified as overweight or obese [3]. The prevalence of obesity and its co-morbidities varies among populations, gender, socio-economic status and ethnic groups [4,5]. Abdominal obesity was identified to be one of the main modifiable risk factors associated with coronary heart disease in the INTERHEART Study [6], and is now believed to be central to identifying the metabolic syndrome (MetS).

Subsequent studies have shown that abdominal obesity, as measured by waist circumference (WC) or related indexes such as waist-to-hip ratio (WHR), is associated with the development of type 2 diabetes [7-10], ischemic heart disease [11-13], as well as cardiovascular disease (CVD) risk factors [14]. In addition, waist-height ratio (WHtR) has shown stronger associations with CVD risk factors than body mass index (BMI) [15]. It remains difficult to define obesity in Africans due to the socio-cultural context and the impact of the HIV/AIDS epidemic which causes a misconception about abdominal obesity in this population [16,17]. Hence, uncertainty remains in the South African population about the validity of anthropometric cut-off values to predict certain health outcomes [18]. The challenge however, will be in seeking simple and universally appropriate anthropometric measures to predict the absolute as well as relative risk of disease and disability of African communities. Obesity and abdominal obesity can only be defined when using relevant and population specific reference values in Africans with increasing urbanisation, and demographic and nutrition transitions [19-21].

The aims of the present study are to firstly compare the relationship of anthropometric measures (WC, WHR, BMI, and WHtR) to NCD risk factors (measures of lipids, fasting glucose, C-reactive protein, gamma-glutamyl transferase and blood pressure) among 35 to 65 year old black Setswana speaking men and women. Secondly, the study aims to examine the abilities of these anthropometric measures to correctly identify NCD risk factors in a sub-Saharan African population in the North West Province of South Africa.

1. Research Design and Methods

1.1. *Selection and Description of Participants*

This study had a cross-sectional design and formed part of the baseline data of the South African leg of the Prospective Urban and Rural Epidemiological (PURE) study which is planned to run for 12 years to investigate the health transition on chronic diseases of lifestyle in urban and rural participants. The population studied, consisted of black Setswana speaking South African men (746) and women (1264), living in either an urban or rural area in the North West Province. Participants were included in the study if they were 35 to 65 years old with no reported chronic diseases of lifestyle, Tuberculosis or HIV. The study was approved by the Ethics Committee of the North-West University (Potchefstroom Campus) in accordance with the Declaration of Helsinki revised in 2000 (Ethics nr. 04M10). Permission was also obtained from the Provincial Department of Health of the North West Province, Local Government Authorities of each town and the tribal chief of the rural communities. Participants were fully informed about the objectives and procedures of the study prior to their recruitment. Fieldworkers explained all information in the participants' own language. All participants signed an informed consent form. Full consent for voluntary testing of HIV was also given after pre-test counselling. HIV-positive participants received post-test counselling and were referred to their local clinic or hospital for further follow up. All participants identified to have hypertension, diabetes or other abnormalities were referred to a local clinic, hospital or physician.

1.2. *Technical Information*

Blood pressure was measured in the sitting position on the right upper arm, using the validated OMRON automated digital blood pressure monitor (OMRON HEM-757). The measurement was taken after 5 minutes of rest. All anthropometric measurements were done using the guidelines of the International Society for the Advancement of Kinanthropometry (ISAK) [22]. Measurements were obtained with the participant wearing minimal clothing without shoes. Maximum height and weight were measured with calibrated instruments (Precision Health Scale, A&D Company, Japan; Invicta Stadiometer, IP 1465, U.K.). The circumference was measured with a steel flexible Lufkin anthropometric tape (W606Pm) which is enclosed in a case with automatic retraction. Waist circumference was measured in cm at the narrowest point of the abdomen between the lower costal (10th rib) border and the top of the iliac crest, perpendicular to the long axis of the trunk at the end of normal expiration. Gluteal (hip) circumference was measured at the level of the greatest posterior protuberance of the buttocks, perpendicular to the long axis of the trunk. WHR was calculated by dividing waist circumference by hip circumference. BMI was calculated as weight divided by height per square meter (kg/m²). Waist-height ratio (WHtR) was calculated by dividing waist circumference (cm) by height (cm).

1.3. Blood Serum and Plasma Samples

Participants were asked to be in a fasted state of approximately 10 hours. Blood was drawn from the anti-cubital vein in the participants' right arm using a sterile butterfly infusion set (Johnson & Johnson, 21G, 19 mm). Excessive use of tourniquets was avoided as this could lead to hemo concentration and elevated results. For preparation of serum, blood was allowed to clot in glass tubes, centrifuged at 3000 rpm for 15 minutes (Universal 16R™, Hettich, with cooling facilities), and 0.5 ml transferred to 1 ml Eppendorff tubes. EDTA plasma was prepared by transferring 5 ml blood into EDTA glass tubes. Plasma was collected in EDTA tubes and centrifuged at 2000 g for 15 minutes at 4 °C (Universal 32R™, Hettich). All serum, plasma, and separated blood cells samples were immediately stored at -18 °C to -20 °C in the field for 2-4 days and afterwards at -84 °C in the laboratory.

1.4. Biochemical Analysis

Quantitative determination of the total cholesterol, HDL-cholesterol (HDL-C), triglycerides (TG), fasting glucose (FG) (GOD-POD), GGT (Gamma-glutamyl transferase) and high sensitivity C-reactive protein (hs-CRP) concentrations in the serum of the participants were done with the Konelab²⁰ⁱ™ auto analyser (Thermo Fisher Scientific Oy, Vantaa, Finland), a clinical chemistry analyser for colorimetric, immunoturbidimetric and ion-selective electrode measurements. LDL cholesterol was calculated using the Friedewald formula [23]. A rapid HIV test was done according to the National Department of Health of South-Africa protocol. First response (PMC Medical, India) rapid HIV card test was done and if positive it was repeated with the Pareeshak test (BHAT Bio-tech, India).

1.5. Questionnaires

The questionnaires used were designed for the PURE international study, adapted for the South African leg of the study and were validated with appropriate methods. Questionnaires were issued during individual interviews and were conducted by extensively trained fieldworkers in the preferred language of the participants. The comprehensive questionnaire included a demographic questionnaire and questions on the participant's health history, smoking and drinking habits and filled out by the fieldworkers. Data that was relevant to this study was utilised from the questionnaires.

1.6. Statistical Analysis

Statistical analysis was performed using SPSS for Windows (version 16.0; SPSS Inc., Chicago, IL, USA). Statistical Consultation Services of the North-West University were consulted for the analysis of this data. Student t-tests for differences in means for gender were used and $p < 0.05$ was considered statistically significant.

The ability of BMI, WC, WHR and WHtR to identify men and women with adverse measures of each NCD risk factor were examined by means of the area under the curve, as determined by the receiver operating characteristic curve (ROC-curve analysis), for each NCD risk factor. ROC analysis was used to evaluate how effectively these 4 anthropometric measurements/indexes predicted increased NCD risk factors. Sensitivity was defined as the proportion of participants with raised values for measurements of obesity together with an increased risk for NCD risk factors (range, 0-1.00). Specificity was defined as the proportion of participants with low values for measurements of obesity together with absence of NCD risk factors (range, 0-1.00). These ROC curves are constructed by plotting the sensitivity at each value of BMI, WC, WHR and WHtR compared with the corresponding 1-specificity, and the area under the curve (AUC) with its 95% confidence interval quantifies the screening performance over all cut-off values. An AUC of 0.5 indicates that the screening test is no better than chance and 1.0 indicates perfect classification. Regression models were also used to quantify the prediction of the original unadjusted measures of the NCD risk factors measures by all 4 anthropometric measures/indexes. Measures of the NCD risk factors were used as the dependant variables in these models. These analyses compared the increases in the multiple R^2 values achieved by adding either of the anthropometric measures to a model already containing age, smoking, alcohol use, HIV status and urbanisation. The statistical significance of the difference explained by the variance between the covariate measures and the 4 sets of anthropometric measures were determined [24]. High sensitivity-CRP, TG and GGT had a non-normal data distribution and therefore the data was log transformed before analysis.

In addition to determining whether differences between BMI, WC, WHR and WHtR were statistically significant, the focus was also on the magnitudes of the differences in the AUC's and R^2 values for each risk factor. It should be realised that for large data sets a small difference between the measures and indices, which indicates that their predictive abilities are similar, could be statistically significant. However, these small differences would have little practical importance [25].

2. Results

The descriptive statistics of the participants are shown in **Table 1**. A total of 2010 participants were included in the study of which 746 were men and 1264 were women. There were no significant difference between the mean ages of the men (49.7 ± 10.3 years) and women (49.1 ± 10.4 years). There were significant differences in the anthropometric measures (BMI, WC, WHR and WHtR) between the genders ($p < 0.05$). The mean BMI was (20.8 ± 4.02 kg/m²) and (26.9 ± 7.3 kg/m²) for men and women respectively. The percentage of men classified as obese

($\geq 30 \text{ kg/m}^2$) were 0.3%, overweight ($\geq 25 \text{ kg/m}^2$) were 10.3% and normal weight ($< 25 \text{ kg/m}^2$) were 86.5%. The percentage of women classified as obese ($> 30 \text{ kg/m}^2$) were 31.7%, overweight ($> 25 \text{ kg/m}^2$) were 22.1% and normal weight ($< 25 \text{ kg/m}^2$) were 46.2% (data is not presented). Women had a significant higher ($p < 0.001$) mean WC ($81.78 \pm 14.18 \text{ cm}$) and WHtR (0.52 ± 0.08), compared to the men with WC of ($76.2 \pm 9.71 \text{ cm}$) and WHtR of (0.45 ± 0.06). The blood lipids (TC, LDL-C and TG) were significantly higher ($p < 0.001$) in the women compared to the men. The men had a significantly higher SBP ($135.5 \pm 23.9 \text{ mmHg}$) and lower DBP ($86.8 \pm 14.8 \text{ mmHg}$) compared to the women.

Indicators selected to reflect behaviours of health were self reported smoking (at least one tobacco product per day) and alcohol consumption (at least one alcoholic beverage per month). In the group of men, (60.1%) were smokers and in the women (44.5%) were smokers. The percentage of men and women that reported alcohol consumption at least once a month was (63.8%) and (31.8%) respectively. The men showed significantly higher ($p < 0.001$) values in GGT ($125.33 \pm 237.82 \text{ U/L}$) compared to that of the women ($80.91 \pm 167.41 \text{ U/L}$).

The abilities of BMI, WC, WHR and WHtR to correctly identify individuals with NCD risk factors are compared in **Table 2**. The AUC varied substantially across the risk factors (smallest 0.50 to the highest 0.77), with the most accurate classification seen for triglycerides (0.77). However, for each risk factor only small differences were observed between the accuracies of BMI, WC and WHtR. The largest difference in the area under the curve (AUC), was 0.11 for hs-CRP. WHR was the weakest predictor (AUC=0.59) compared to BMI, WC and WHtR (all with AUC=0.70). WC and BMI were equal in their predictive power for reduced HDL-C (AUC=0.62; CI=0.56-0.67), raised FG (AUC=0.59, CI=0.54-0.64) and in predicting ≥ 2 metabolic risk factors (AUC=0.65, CI=0.60-0.70) in men. In the women, WC and WHtR were equal in their predictive power for raised TC (AUC=0.56, CI=0.53-0.60), raised TG (AUC=0.66, CI=0.62-0.70), raised hs-CRP (AUC=0.70, CI=0.67-0.73), and ≥ 2 metabolic risk factors (AUC=0.65, CI=0.62-0.68). WHR had the best predictive power for raised hs-CRP (AUC=0.58, CI=0.54-0.63) in men, while BMI had the best predictive power for reduced HDL-C (AUC=0.59, CI=0.55-0.62) in women. WHR did not have any superiority over the indices for any of the NCD risk factors in women.

Table 1: Descriptive statistics of the participants.

	Men [‡] N=746	Women [‡] N=1264	p	Total Group [‡] N=2010
Age (y)	49.7 ± 10.3	49.1 ± 10.4	0.147	49.4 ± 10.4
Height (cm)	169.50 ± 0.10	156.78 ± 6.43	0.082	163.14 ± 3.27
Weight (kg)	58.61 ± 12.74	66.22 ± 18.46	<0.001	62.42 ± 15.50
BMI (kg/m ²)	20.8 ± 4.0	26.9 ± 7.3	<0.001	23.9 ± 5.7
WC (cm)	76.20 ± 9.71	81.78 ± 14.18	<0.001	78.99 ± 12.26
WHR (cm:cm)	0.88 ± 0.06	0.80 ± 0.08	<0.001	0.84 ± 0.07
WHtR (cm:cm)	0.45 ± 0.06	0.52 ± 0.08	<0.001	0.49 ± 0.07
TC (mmol/L)	4.81 ± 1.33	5.13 ± 1.39	<0.001	4.97 ± 1.36
TG (mmol/L)	1.22 ± 0.85	1.35 ± 0.75	<0.001	1.29 ± 0.80
LDL-C (mmol/L)	2.68 ± 1.16	3.10 ± 1.18	<0.001	2.89 ± 1.17
HDL-C (mmol/L)	1.58 ± 0.66	1.48 ± 0.62	0.346	1.53 ± 0.64
FG (mmol/L)	5.34 ± 1.31	5.65 ± 1.71	0.005	5.50 ± 1.51
SBP (mmHg)	135.5 ± 23.9	132.3 ± 24.8	<0.001	133.9 ± 24.4
DBP (mmHg)	86.8 ± 14.8	88.2 ± 14.4	<0.001	87.5 ± 14.6
hs-CRP (mg/L)	8.32 ± 13.40	8.65 ± 11.85	0.586	8.49 ± 12.63
GGT (U/L)	125.33 ± 237.82	80.91 ± 167.41	<0.001	103.12 ± 202.62
Smoking (%)	60.1 (n=446)	44.5 (n=575)	<0.001	48.6 (n=1021)
Alcohol consumption (%)	63.8 (n=459)	31.8 (n=392)	<0.001	47.8 (n=788)

[‡]All values presented as means with standard deviation (± SD); p<0.05 was considered significant

N=Number of participants, TC=Total cholesterol, TG=Triglycerides, LDL-C=Low density lipoprotein cholesterol, HDL-C=High density lipoprotein cholesterol, FG=Fasting glucose, SBP=Systolic blood pressure, DBP=Diastolic blood pressure, hs-CRP=C-reactive protein, GGT=Gamma-glutamyl transferase, BMI=Body mass index, WC=Waist circumference, WHR=Waist-to-hip ratio, WHtR=Waist-height ratio

Table 2: Classification of adverse risk factors of NCD by means of area under the ROC curve and the 95% confidence intervals for BMI, WC, WHR and WHtR for men and women.

Adverse NCD Risk factors	Men					Women				
	N	Area under the curve				N	Area under the curve			
		BMI	WC	WHR	WHtR		BMI	WC	WHR	WHtR
Raised TC ≥5.2 mmol/L	288	0.62 (0.58-0.67)	0.62 (0.58-0.67)	0.59 (0.54-0.63)	0.63 (0.58-0.67)	487	0.55 (0.52-0.59)	0.56 (0.53-0.59)	0.54 (0.50-0.57)	0.56 (0.53-0.60)
Raised TG ≥1.7 mmol/L	94	0.76 (0.71-0.81)	0.77 (0.72-0.82)	0.70 (0.65-0.76)	0.76 (0.71-0.81)	254	0.63 (0.59-0.66)	0.66 (0.62-0.70)	0.65 (0.61-0.69)	0.66 (0.62-0.69)
Raised LDL-C ≥4.2 mmol/L	75	0.65 (0.58-0.71)	0.63 (0.56-0.70)	0.56 (0.49-0.64)	0.64 (0.57-0.70)	198	0.60 (0.55-0.64)	0.60 (0.56-0.64)	0.67 (0.53-0.61)	0.61 (0.57-0.65)
Reduced HDL-C <1.03 mmol/L Men <1.29 mmol/L Women	152	0.62 (0.57-0.67)	0.62 (0.56-0.67)	0.57 (0.52-0.63)	0.59 (0.53-0.64)	472	0.59 (0.55-0.62)	0.58 (0.55-0.62)	0.53 (0.50-0.57)	0.57 (0.54-0.61)
Raised FG ≥ 5.6 mmol/L	248	0.59 (0.54-0.66)	0.59 (0.54-0.63)	0.58 (0.53-0.62)	0.59 (0.55-0.64)	502	0.56 (0.53-0.59)	0.58 (0.54-0.61)	0.57 (0.53-0.60)	0.57 (0.54-0.61)
Raised BP ≥130/85 mmHg	448	0.58 (0.53-0.62)	0.59 (0.54-0.63)	0.56 (0.52-0.61)	0.58 (0.54-0.63)	740	0.61 (0.58-0.65)	0.64 (0.61-0.68)	0.61 (0.57-0.64)	0.65 (0.61-0.68)
Raised hs-CRP ≥3 mg/L	308	0.50 (0.46-0.55)	0.53 (0.49-0.58)	0.58 (0.54-0.63)	0.54 (0.50-0.59)	617	0.70 (0.66-0.73)	0.70 (0.67-0.73)	0.59 (0.55-0.62)	0.70 (0.67-0.73)
≥2 Risk factors IDF criteria	268	0.65 (0.60-0.69)	0.65 (0.61-0.70)	0.61 (0.57-0.66)	0.63 (0.59-0.68)	626	0.61 (0.58-0.65)	0.65 (0.62-0.68)	0.64 (0.60-0.67)	0.65 (0.62-0.68)

The 95% confidence intervals are presented inside parentheses

≥ 2 Risk factors (All metabolic risk factors defined according to IDF criteria). Raised triglycerides ≥1.7 mmol/L (≥150 mg/dL); Reduced HDL-C <1.03 mmol/L (<40 mg/dL) for men and <1.29 mmol/L (<50 mg/dL) for women; Raised blood pressure ≥130/85 mmHg or treatment for previously diagnosed hypertension; Raised fasting glucose ≥5.6 mmol/L (≥100 mg/dL) or previously diagnosed type 2DM and a combination of two or more of these metabolic risk factors

The predictive abilities of BMI, WC, WHR and WHtR for ≥ 2 metabolic risk factors by means of the ROC curve are shown in **Figure 1**. WC and BMI were equal in their predictive power in men and WC and WHtR were equal in their predictive power in the women, by AUC for two or more metabolic risk factors.

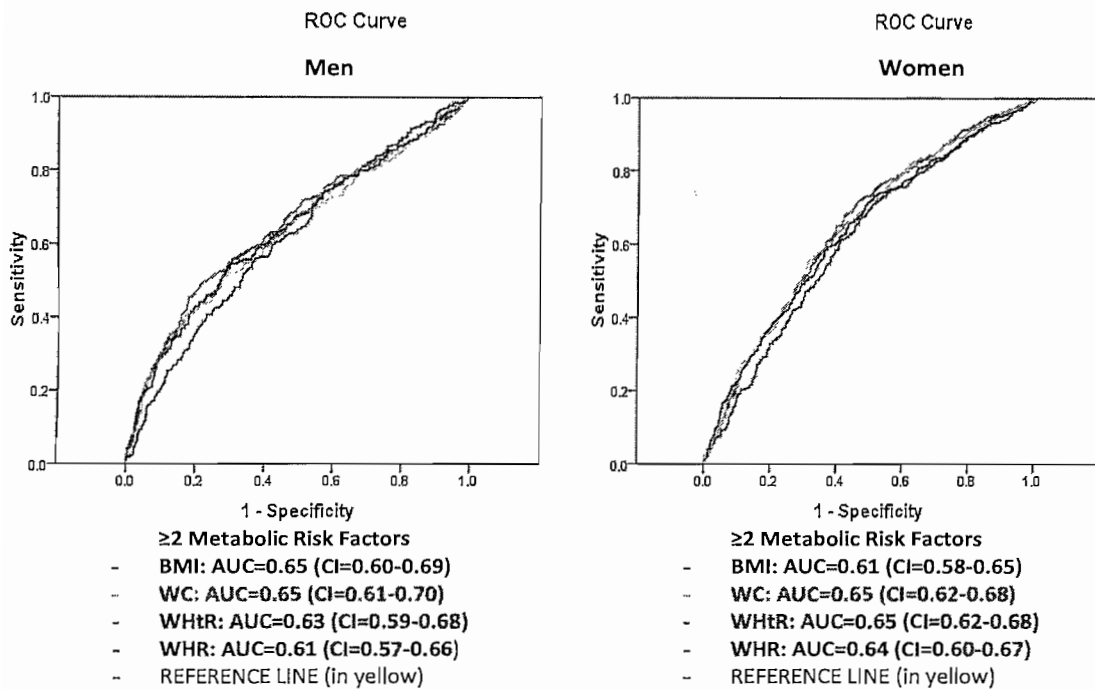


Figure 1: Receiver operating characteristic (ROC) curve for two or more NCD risk factors in men and women as indicated by four anthropometrical measures.

≥ 2 Risk factors (All metabolic risk factors defined according to IDF criteria). Raised triglycerides ≥ 1.7 mmol/L (≥ 150 mg/dL); Reduced HDL-C < 1.03 mmol/L (< 40 mg/dL) for men and < 1.29 mmol/L (< 50 mg/dL) for women; Raised blood pressure $\geq 130/85$ mmHg or treatment for previously diagnosed hypertension; Raised fasting glucose ≥ 5.6 mmol/L (≥ 100 mg/dL) or previously diagnosed type 2DM and a combination of two or more of these metabolic risk factors.

WHtR was the strongest indicator for five out of the eight NCD risk factors (raised TC, raised TG, raised LDL-C, raised FG, and raised hs-CRP) for the total group (men and women) in the present study (**Table 3**). WC was the strongest indicator for three out of the eight NCD risk factors (raised TG, raised FG, raised BP), while BMI was the strongest indicator for only one out of the eight NCD risk factors (reduced HDL-C) for the total group. WC and WHtR was equal in their ability to predict a cluster of two or more metabolic risk factors (AUC=0.66, CI=0.64-0.69). WHR was the strongest indicator for raised GGT.

Table 3: Classification of adverse risk factors of NCD by means of area under the ROC curve and the 95% confidence intervals for BMI, WC, WHR and WHtR for the total group.

NCD Risk factors	N	Total group Area under the curve			
		BMI	WC	WHR	WHtR
Raised TC ≥5.2 mmol/L	720	0.59 (0.57-0.62)	0.59 (0.56-0.62)	0.52 (0.49-0.54)	0.60 (0.57-0.63)
Raised TG ≥1.7 mmol/L	349	0.68 (0.51-0.71)	0.70 (0.67-0.73)	0.61 (0.58-0.64)	0.70 (0.67-0.73)
Raised LDL-C ≥4.2 mmol/L	273	0.63 (0.60-0.67)	0.63 (0.59-0.66)	0.52 (0.48-0.56)	0.64 (0.60-0.67)
Reduced HDL-C <1.03 mmol/L (Men) <1.29 mmol/L (Women)	625	0.64 (0.61-0.67)	0.61 (0.58-0.64)	0.48 (0.45-0.51)	0.62 (0.59-0.64)
Raised FG ≥ 5.6 mmol/L	746	0.58 (0.56-0.61)	0.59 (0.56-0.62)	0.54 (0.51-0.56)	0.59 (0.57-0.62)
Raised BP ≥130/85 mmHg	1232	0.59 (0.57-0.62)	0.64 (0.61-0.66)	0.59 (0.56-0.62)	0.63 (0.60-0.65)
Raised hs-CRP ≥3 mg/L	925	0.63 (0.61-0.66)	0.51 (0.63-0.68)	0.54 (0.51-0.57)	0.66 (0.63-0.68)
≥2 Risk factors IDF criteria	894	0.65 (0.62-0.67)	0.66 (0.64-0.69)	0.57 (0.54-0.60)	0.66 (0.64-0.69)

The 95% confidence intervals are presented inside parentheses

≥ 2 Risk factors (All metabolic risk factors defined according to IDF criteria). Raised triglycerides ≥1.7 mmol/L (≥150 mg/dL); Reduced HDL-C <1.03 mmol/L (<40 mg/dL) for men and <1.29 mmol/L (<50 mg/dL) for women; Raised blood pressure ≥130/85 mmHg or treatment for previously diagnosed hypertension; Raised fasting glucose ≥5.6 mmol/L (≥100 mg/dL) or previously diagnosed type 2DM and a combination of two or more of these metabolic risk factors.

Table 4: Increase in variance explained by risk factors of NCD that can be accounted for by anthropometrical measurements in various regression models (R^2).

<u>Men</u> NCD risk factors	Model 1	Model 2			
	Adjusted R^2	Increase in multiple R^2			
		BMI	WC	WHR	WHtR
Systolic blood pressure	0.11	0.02	0.02	0.01	0.01
Diastolic blood pressure	0.05	0.01	0.02	0.00	0.01
Total cholesterol	0.05	0.03	0.04	0.01	0.02
C-reactive protein	0.02	0.00*	0.01*	0.02	0.01*
Fasting glucose	0.02	0.02	0.04	0.03	0.03
HDL-cholesterol	0.14	0.04	0.03	0.01	0.02
Triglycerides	0.03	0.11	0.13	0.05	0.09
LDL-cholesterol	0.06	0.05	0.05	0.01	0.03
<u>Women</u> Risk factors	Adjusted R^2	Increase in multiple R^2			
		BMI	WC	WHR	WHtR
Systolic blood pressure	0.20	0.01	0.02	0.01	0.02
Diastolic blood pressure	0.09	0.03	0.04	0.01	0.04
Total cholesterol	0.07	0.01	0.01	0.01	0.01
C-reactive protein	0.02	0.11	0.12	0.02	0.13
Fasting glucose	0.01	0.02	0.02	0.01	0.02
HDL-cholesterol	0.13	0.03	0.04	0.01	0.03
Triglycerides	0.07	0.03	0.05	0.06	0.06
LDL-cholesterol	0.06	0.02	0.02	0.01	0.02

* Non-significant increase ($p > 0.05$)

R^2 values based on covariates [Covariates: Age, Gender, Smoking, Alcohol, HIV and Urbanisation] (Model 1)
Increase in multiple R^2 values for BMI, WC, WHR and WHtR (Model 2)

Significant ($p < 0.05$) difference in multiple R^2 values of a model containing either of BMI, WC, WHR and WHtR in the prediction of NCD risk factors.

The additional information was quantified by the increase in multiple R^2 , provided by BMI, WC, WHR and WHtR in predicting measures of the various risk factors (**Table 4**) in addition to covariate measures of the risk factors. Age, smoking, urbanisation, alcohol and HIV acted as covariates and could account for between 2% (hs-CRP and FG) and 14% (HDL) of the variability in the individual risk factors in men and between 2% (hs-CRP and FG) and 20% (SBP) in women. BMI, WC, WHR and WHtR could account for <0.1% (BMI predicting hs-CRP, WHR predicting DBP) and 1% (BMI predicting DBP, WC predicting hs-CRP, WHtR predicting SBP, WHtR predicting DBP and WHtR predicting hs-CRP) in the men. The biggest increase in variance was found for TG with predictors BMI (11%), WC (13%), WHR (5%) and WHtR (9%) in the men. In the women, the lowest increase in variance explained (1%) for BMI predicting TC

and SBP, WC predicting TC, WHR predicting SBP, DBP, TC, LDL-C, HDL-C and FG, WHtR predicting TC. The increase in variance was the largest in women when BMI predicted hs-CRP (11%), WC predicted hs-CRP (12%), WHR predicted TG (6%) and WHtR predicted hs-CRP (13%). Although almost all of the increases in variances explained by the anthropometric indices were statistically significant except for hs-CRP in the men, the magnitudes of all differences were of small to medium practical importance [25]. For example, although WHtR was a better predictor of TC, the difference in R^2 values were only 0.02. Similarly, WC was a better predictor of HDL-C, SBP and DBP in the men, but the largest R^2 difference was only 0.01.

3. Discussion

Current research are widely exploring increased speculation over which surface anthropometry measure of overweight and obesity is best able to discriminate between those individuals who are at increased risk for NCD in different ethnic groups [26]. The results in this study show that there is little difference in the abilities of BMI, WC, WHR and WHtR to identify African individuals with NCD risk factors. In general, WHtR and WC showed slightly stronger associations with most NCD risk factors. Although BMI is the most commonly used anthropometrical measure in epidemiologic studies, the use of BMI to assess adiposity across different populations as well as the specificity and predictive value of this measure has been questioned [27]. Mostly because of the substantial variation in abdominal fat mass that may exist between individuals with the same BMI or total body fat mass [28]. The interpretation of BMI is limited in special populations, such as the elderly and children. In the elderly a reduction in the proportion of lean body mass to fat mass with age that results in an empirical underestimation of fatness, as well an age-associated reduction in height [29] and in children BMI needs to be expressed relative to their sex and age by using Z-scores [30]. Increasingly, measures of abdominal obesity (WC and WHR) have been adopted as more accurate predictors of obesity-related cardiovascular risk and have replaced BMI in several definitions of the metabolic syndrome [8,15,31].

The current study supports the findings of previous studies that found measures of abdominal obesity to be the strongest indicators for NCD risk factors [26,32,33]. However, WHR in particular was the weakest indicator of NCD risk factors compared to the other measures of abdominal obesity (WC and WHtR) in this study. WC and WHtR were the best indicators (as shown by a larger AUC) in this black South African population. In general WHtR showed slightly stronger associations with raised TC, raised TG, raised LDL-C, raised FG, and raised hs-CRP, whereas WC showed slightly stronger associations with raised blood pressure as well as raised TG and raised FG. BMI was the best indicator for lowered HDL-C in both men and women.

However, the AUC's and multiple regression (R^2), were very similar for each risk factor. The finding of this study supports the results found in similar studies that reported differences in the discriminatory capability between different indices of obesity with cardiovascular risk factors to be small [34-36].

There has been heterogeneity in results from studies that compare associations of NCD risk factors with measures of overall obesity and abdominal obesity [27,37-40]. A meta-analysis by Lee *et al.* including data on more than 88 000 individuals from diverse populations supports the claim that measures of abdominal obesity in particularly the WHtR, provide a superior tool for discriminating obesity-related cardiovascular risk compared to BMI [26]. However, the observed differences in the discriminatory capability between BMI with each of the individual measures of abdominal obesity were observed to be small and in general statistically insignificant [27]. Charleton *et al.* reported that in Africans of mixed ancestry WHR and BMI (whether classified as a continuous variable, according to gender-specific tertiles, or using a cut-off value of 30 kg/m² or greater) was associated with a clustering of cardiovascular risk factors in either men or women [32]. In a study on an Asian (Thai) population, measures of abdominal obesity (WC, WHR, WHtR) were more strongly associated with CVD risk factors than the overall obesity measure, BMI, though the association was only slightly stronger [37]. Contrasting results were presented in another Asian (Thai) study that found BMI to be a superior CVD risk indicator in men and WHR to be the superior indicator in women of the same age group (≥ 35 years) [41].

Several other studies on different ethnic groups have reported that WC was more strongly associated with CVD risk factors than BMI [38,42]. In an Indian study, WHtR was reported to be the stronger indicator compared to BMI and WHR for predicting diabetes, hypertension and lipid abnormalities [43]. Nonetheless others have reported that WC and BMI are equally predictive of cardiovascular risk in Chinese adults [44]. The differences in the findings of studies may be attributable to ethnicity, age and gender distributions of participants across study populations [41]. A number of researchers have reported differences in the predictive value of anthropometric indicators of obesity in various ethnic groups [45-47]. It is thus clear that the same measures of adiposity do not perform equally well in discriminating NCD risk factors in all ethnic groups and therefore caution is needed when generalising results across populations. Not only is caution needed in discriminating risk factors of NCD with anthropometric indices between ethnic populations, but also that cut-off values for anthropometric indices across different ethnic populations showed great disparity both within and between ethnic groups. The optimal cut-off values used to predict NCD risk factors for the four anthropometric indices are extensive with BMI ranging from 20-30 kg/m², WC from 71-101 cm, WHtR from 0.46-0.62 and

WHR from 0.77 to 0.97 [8,48-51]. Whether universal cut-off values should be used is debatable and a matter for further expansive research which is beyond the scope of the present study.

Although there is consensus that obesity is a risk factor for NCD, differences of opinion exist as to what measure or index of adiposity is the most useful in identifying those individuals who are at greatest risk. The results of the study indicated that both WC and WHtR in this black African population could be used as indicators for NCD risk factors. The benefits of using both indices (WC and WHtR) may outweigh their individual and combined limitations. WC is a convenient and simple measurement that is unrelated to height and therefore does not have the same inherent methodological problems as BMI if measured according to internationally prescribed measuring standards [23]. WC has also been shown to be correlated with total visceral adipose tissue (VAT), measured by computed tomography (CT) [29] and is known to mediate the relationship between obesity and the risk for developing cardiometabolic disease [52,53]. Although WC is a simple measure of abdominal obesity it assumes that people with the same WC have equal NCD risk regardless of differences in height. However, this assumption is invalid as the body fat % and WHR are higher for shorter individuals compared to their taller counterparts with the same BMI [54]. The importance of the measuring site must be stressed when using WC as different measuring sites may alter associations with risk factors measures [55-57] and possible with disease risk [30]. The benefit of using WHtR in epidemiological studies may be the potential of this index to track abdominal obesity from childhood to adulthood, which would simplify the expression of obesity related disease risk regardless of age [58,59]. WHtR will only change when there is a change in height, given that height remains constant in adults. Additionally, the same cut-off value (0.5) could possibly be used to identify NCD risk factors for adults and children [58] but need to be further explored. In essence, the use of WHtR will result in a simple public health message: "Keep your waist circumference to less than half of your height" [58].

The predictive value of using two indices together for the identification of individuals at greatest risk for NCD have been identified by Sung *et al.* as having clinical importance [60]. The observation that individuals at increased risk are identified when both measures of obesity (BMI and WC) are abnormal is consistent with other studies [44,49,61,62]. However, conflicting results was presented by Lee *et al.*, where it was indicated that combining BMI with any measure of central obesity does not improve upon its discriminatory capability [26]. It was shown that the discriminatory power for NCD risk factors actually decreased when BMI was combined with either one of the three abdominal obesity measures (WC, WHR and WHtR), further supporting the use of WHtR as the sole measure of obesity in that study [26]. Although this study did not explore the discriminatory capability of using two indices together for the

identification of individuals at risk for NCD, the results did indicate that WHtR was superior to using BMI for identifying most of the NCD risk factors in this study and that by using WHtR only will identify those individuals at greatest risk.

The results from this study should be interpreted in light of several potential limitations. First, the study was conducted among a rural and urban black population in the North West Province of South Africa, and so may not necessarily be generalised to the broader black South African population. Secondly, the cross-sectional design of the study with only single measures of adiposity (taken at one point in time) may not accurately reflect participants' long-term adiposity status. The concordance of the findings with other studies, however, serves to attenuate some concerns about these potential study limitations.

In conclusion, the findings show that in this black Setswana speaking South African population, WHtR and WC are the most important indicators of NCD risk factors. These indicators have a vital public health implication for developing countries [62]. They offer the prospect of an extremely effective, simple, inexpensive and non-invasive means for first-level screening at community level to identify individuals at risk.

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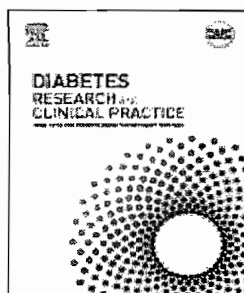
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OPTIMAL WAIST-CIRCUMFERENCE CUT-OFF VALUES FOR ABDOMINAL OBESITY IN BLACK SOUTH AFRICAN MEN AND WOMEN



Left: Parents of Author,
Patrick and Melinda
Amazing sunset over the
Indian Ocean

Lower right: Author and
Mother (Melinda)
Leaving the
Port of Maputo
(Mozambique)



This chapter is presented in article format and is written according to the referencing requirements of the journal *Diabetes Research and Clinical Practice* to which it will be submitted. The font and spacing were kept the same throughout the thesis. All figures and tables are presented within the text rather than at the end of the article for examination purposes.

Optimal waist circumference cut-off values for abdominal obesity in black South African men and women

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Abstract

Background Abdominal obesity, a fundamental component of the metabolic syndrome (MetS) as measured by waist circumference (WC) is not defined by appropriate cut-off values for sub-Saharan Africans. Current WC cut-off values are based on Caucasian data, mostly from European countries. Heterogeneity in abdominal obesity exists in different populations and the current recommended WC cut-off values by the International Diabetes Federation may not be optimal in Africans. **Aims** To investigate the ethnically appropriate WC cut-off values for abdominal obesity in black Setswana speaking South African men and women, for prediction of increased risk of raised triglyceride, reduced HDL-cholesterol, raised blood pressure and raised fasting blood glucose, or two or more of these risk factors. **Methods** Data from 2010 adults (746 men and 1264 women) aged 35-65 years, who participated in a cross sectional study that formed part of the baseline data of the Prospective Urban and Rural Epidemiological (PURE) study of a black South African population in the North West Province. **Results** The WC values where Yuden index were maximised for more than 2 metabolic risk factors was 80 cm in both men and women and for each of the individual metabolic risk factors it varied between 75-80 cm in both men and women. Based on the receiver operating characteristic (ROC) curve analysis the WC value for predicting metabolic risk factors in this black African population was about 80 cm for men and women. The AUC for men was 0.653 (0.611-0.695 CI) and for women it was 0.643 (0.613-0.674 CI). **Conclusion** According to the locally determined WC criteria, the prevalence of abdominal obesity was 28.1% in the men and 52.4% in the women. WC values of ≥ 80 cm for men and women are optimal cut-off values for abdominal obesity in this black South African population. It is recommended that these WC cut-off values be used together with the IDF diagnostic criteria. Each African country, region and ethnic group may need to establish optimal WC cut-off values before universal guidelines for sub-Saharan Africans can be accepted.

Key words: Waist circumference, Cut-off values, Abdominal obesity, Metabolic syndrome, Sub-Saharan Africans.

Introduction

The metabolic syndrome (MetS) is composed of a cluster of metabolic disorders associated with increased risk of cardiovascular diseases (CVD) [1-7], type 2 diabetes mellitus (2DM) [8-9] and subsequent premature morbidity and mortality [10-11]. Several definitions of the MetS have been developed by national and international organisations or clinical expert groups for research and/or clinical purpose to identify individuals at risk [12]. The prevalence of the MetS, as well as the characteristics of participants fulfilling the diagnostic criteria varied depending on the definitions used. In 2005, the International Diabetes Federation (IDF), in a global consensus statement, formulated a new clinically accessible worldwide definition of the MetS [13] built on earlier definitions formulated by the World Health Organisation (WHO) [14] and the National Cholesterol Education Program (NCEP) Expert panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult treatment panel, ATP III) [15].

The IDF defined MetS as abdominal obesity plus two of the following four additional factors: raised plasma triglycerides, raised blood pressure, reduced HDL cholesterol and raised fasting blood glucose [13]. A prominent feature of the IDF definition is that abdominal obesity is a prerequisite component of MetS, with abdominal obesity defined according to ethnically specific values of waist circumference (WC) [13]. According to the IDF definition, sub-Saharan Africans should use the same WC cut-off values as Caucasians (Europids) derived from European data, until more specific data is available. The cut-off point for abdominal obesity in the United States was defined as > 102 cm for men and > 88 cm for women [15], whereas, for Europids the cut-off was ≥ 94 cm for men and ≥ 80 cm for women [16,17]. Criteria for selection of cut-off values for abdominal obesity are based on data from white Caucasians, mostly from European countries [18].

Molarius et al. concluded that according to currently accepted WC cut-off values, a substantial proportion of those who would need health care advice would be missed because of higher cut-off values [19]. The WC cut-off values should be population specific [19,20]. WC was indicated to be the best indicator for non-communicable diseases (NCD) risk factors in black South Africans and should be used as a measure of abdominal obesity rather than other measures such as waist-hip ratio in this population group [21,22]. Uncertainty remains in many populations about the validity of cut-off values for WC to predict health outcomes as based on western populations, including the South African black population [23]. Schutte et al. reported that black South African women are about 10 kg lighter and 10 cm shorter than their age- and BMI-matched Caucasian counterparts and therefore suggested that when WC cut-off values are established for black Africans to fit the IDF definition a lower WC cut-off may be necessary [24,25].

The purpose of this study was to determine the optimal cut-off for WC for abdominal obesity in a black African population in the North West Province of South Africa, which could be used as a reference for the IDF definition modification for sub-Saharan Africans.

Methods

Selection and Description of Participants

The study had a cross-sectional design and formed part of the baseline data of the South African leg of the Prospective Urban and Rural Epidemiological (PURE) study which is planned to run for 12 years to investigate the health transition on chronic diseases of lifestyle in urban and rural participants. The population studied, consisted of black Setswana speaking South African men (746) and women (1264), living in either an urban or rural area in the North West Province. Participants were included in the study if they were 35-65 years old with no reported chronic diseases of lifestyle, Tuberculosis or HIV. The study was approved by the Ethics Committee of the North-West University (Potchefstroom Campus) in accordance with the Declaration of Helsinki revised in 2000 (Ethics nr. 04M10). Permission was also obtained from the Provincial Department of Health of the North West Province, Local Government Authorities of each town and the tribal chief of the rural communities. Participants were fully informed about the objectives and procedures of the study prior to their recruitment. Fieldworkers explained all information in their participant's own language. All participants signed an informed consent form. Full consent for voluntary testing of HIV was also given after pre-test counselling. HIV positive participants received post-test counselling and were referred to their local clinic or hospital for further follow up. All participants identified to have hypertension, diabetes or other abnormalities were referred to a local clinic, hospital or physician.

Technical Information

Blood pressure was measured in the sitting position on the right arm, using the validated OMRON automatic digital blood pressure monitor (OMRON HEM-757). The measurement was taken after 5 minutes of rest. All anthropometric measurements were done using the guidelines of the International Society for the Advancement of Kinanthropometry (ISAK) [26]. Measurements were obtained with the participant wearing minimal clothing without shoes. Maximum height and weight were measured with calibrated instruments (Precision Health Scale, A&D Company, Japan; Invicta Stadiometer, IP 1465, U.K.). The circumference was measured by a steel flexible Lufkin anthropometric tape (W606Pm) which is enclosed in a case with automatic retraction. Waist circumference was measured in cm at the narrowest point of

the abdomen between the lower costal (10th rib) border and the top of the iliac crest, perpendicular to the long axis of the trunk at the end of normal expiration. Gluteal (hip) circumference was measured at the level of the greatest posterior protuberance of the buttocks, perpendicular to the long axis of the trunk. BMI was calculated as weight divided by height per square meter (kg/m²). Waist-height ratio (WHtR) was calculated by dividing waist circumference (cm) by height (cm).

Blood Serum and Plasma Samples

Participants were asked to be in a fasted state of approximately 10 hours. Blood was drawn from the anti-cubital vein in the participants' right arm, using a sterile butterfly infusion set (Johnson & Johnson, 21G, 19 mm). Excessive use of tourniquets was avoided as this could lead to hemo concentration and elevated results. For preparation of serum, blood was allowed to clot in glass tubes, centrifuged at 3000 rpm for 15 minutes (Universal 16RTM, Hettich, with cooling facilities), and 0.5 ml transferred to 1 ml Eppendorff tubes. EDTA blood was prepared by transferring 5 ml blood into EDTA glass tubes. Plasma was collected in EDTA tubes and centrifuged at 2000g for 15 minutes at 4 °C (Universal 32RTM, Hettich). All serum, plasma, and separated blood cells samples were immediately stored at -18 °C to -20 °C in the field for 2-4 days and afterwards at -84 °C in the laboratory.

Biochemical Analysis

Quantitative determination of the triglycerides (TG), high-density lipoprotein cholesterol (HDL-C) and fasting glucose (FG) (GOD-POD) concentration in the serum of the participants was done with the Konelab²⁰¹ TM auto analyser (Thermo Fisher Scientific Oy, Vantaa, Finland), a clinical chemistry analyser for colorimetric, immunoturbidimetric and ion-selective electrode measurements. A rapid HIV test was done according to the National Department of Health of South-Africa protocol. First response (PMC Medical, India) rapid HIV card test was done and if positive it was repeated with the Pareeshak test (BHAT Bio-tech, India).

Questionnaires

The questionnaires used were designed for the PURE international study, adapted for the South African leg of the study and were validated with appropriate methods. Questionnaires were issued during individual interviews and were conducted by extensively trained fieldworkers in the preferred language of the participants. The comprehensive questionnaire included a demographic questionnaire and was aimed at obtaining information on the participant's health

history, smoking and drinking habits. Data that was relevant to this study was utilised from the questionnaires.

Statistical Analysis

Statistical analysis was performed using SPSS for Windows (version 16.0, SPSS Inc., Chicago, IL, USA). Statistical Consultation Services of the North West University were consulted for the analysis of this data. Age and anthropometric variables were expressed as gender-specific means and standard deviations (SD) (continuous variables), and metabolic risk factors (discrete variables) were expressed as gender-specific proportions. Receiver operating characteristic (ROC) analysis was used as a method of evaluating the accuracy of diagnostic criteria by summarising the potential of the criteria to discriminate between the absence and presence of an abnormality [27]. In the context of the present study, this diagnostic accuracy refers to the ability of an anthropometrical measurement (WC) to discriminate between participants with metabolic risk or disorders and participants who are metabolically normal or not at risk. It was proposed by researchers that the NCEP-ATP III criteria may underestimate risk for metabolic abnormalities in African populations who are frequently insulin resistant, but do not have severe hypertriglyceridemia [28,29]. The cut-off values to define and screen for multiple metabolic disorders were therefore based on the IDF diagnostic criteria. The sensitivity and specificity of each WC category in detecting the presence of reduced HDL-C, raised triglycerides, raised blood pressure, raised fasting glucose and two or more risk factors were calculated by creating dichotomous variables for each WC value. Additionally, the distance on the ROC curve for each WC value was calculated by plotting the true-positive rate (sensitivity) against the false-positive rate (1-specificity). With these diagnostic criterion values, participants deemed to have a metabolic risk /disorder and who were also classified according to anthropometric measurement as having a metabolic risk- /disorder represented the true-positive cases. Metabolic normal participants classified by the study criteria as participants without a metabolic risk/disorder represented the false positive cases. In the ROC analysis, the true-positive rate (sensitivity) is plotted against the false-positive rate (1-specificity) across a range of values from the anthropometric measurements. The decision threshold for the best trade-off is the criterion values with the highest accuracy that maximises the Yuden index or the sum of the sensitivity and specificity. An index reflecting the overall accuracy of the diagnostic test derived from an ROC analysis is known as the area under the curve (AUC). To identify the appropriate WC values for predicting metabolic risk factors in men and women, the adjusted odds ratio's (ORs) were calculated using multiple logistic regression analysis, with adjustments for age, urbanisation status and lifestyle factors (smoking and alcohol use). In all analysis, the WC values were categorised by 5 cm increments, using < 70 cm as a WC reference. The reference

value of < 70 cm was used because all WC cut-off values to identify increased metabolic risk are above 70 cm. The adjusted odds ratios (OR's) are presented together with their 95% confidence intervals (CI). All analysis was two-tailed, and $p < 0.05$ was considered statistically significant.

Results

Descriptive Statistics of the Study Participants

The descriptive statistics of the participants and the prevalence of the metabolic risk factors are shown in **Table 1**. The mean age was (49.7 ± 10.3) years in the men. According to the mean BMI $(20.8 \pm 4.0 \text{ kg/m}^2)$, the men were considered to be of normal weight ($\text{BMI} < 25 \text{ kg/m}^2$) with a WC of $(76.20 \pm 9.71 \text{ cm})$ without the presence of abdominal obesity ($\text{WC} \geq 94 \text{ cm}$). The mean systolic blood pressure was $(135 \pm 23.9 \text{ mmHg})$ and the mean diastolic blood pressure was $(86.8 \pm 14.4 \text{ mmHg})$. Raised blood pressure or previously diagnosed hypertension was present in 66.5% of the men. The results indicated that 14.5% of the men had raised triglycerides, 22.8% had reduced HDL-C and 35.8% had raised fasting glucose or previously diagnosed type 2DM. The percentage of self reported alcohol consumption were (63.8%) and (60.1%) of the men were smokers.

The mean age for the women was (49.1 ± 10.4) years. The mean BMI was $(26.9 \pm 7.3 \text{ kg/m}^2)$ in the women and is considered overweight ($\text{BMI} \geq 25 \text{ kg/m}^2$), with a mean WC of $(81.78 \pm 14.18 \text{ cm})$ that is considered as abdominal obesity ($\geq 80 \text{ cm}$) according to WHO (for obesity) and IDF (for abdominal obesity) guidelines. The mean WHtR of the women was (0.52 ± 0.08) . The women had significantly higher ($p < 0.05$) mean values for all of the metabolic risk factors compared to the men, except for raised blood pressure. The presence of raised blood pressure was present in 66% and raised fasting glucose was present in 45% of the women. The proportion of women that reported alcohol consumption (self reported intake of alcoholic beverages at least once a month) was 31.8% and 45% of them were smokers.

The mean age of the total group (men and women) was 49.4 ± 10.4 years and the mean BMI of the total group was $23.9 \pm 5.7 \text{ kg/m}^2$. Two or more metabolic risk factors (excluding abdominal obesity) were present in 38.3% of the men and 52.8% of the women. In general, the women had a significantly higher BMI, WC and percentage of metabolic risk factors compared to the men. The men presented only with raised blood pressure (similar to the women) and higher smoking and alcohol consumption.

Table 1: Descriptive statistics of the participants.

Basic characteristics	Men (n=746)	Women (n=1264)	P	Total Group (n=2010)
Age (y)*	49.7 ± 10.3	49.1 ± 10.4	0.147	49.4 ± 10.4
BMI (kg/m ²)*	20.8 ± 4.0	26.9 ± 7.3	<0.001	23.9 ± 5.7
WC (cm)*	76.20 ± 9.71	81.78 ± 14.18	<0.001	78.99 ± 12.26
Waist-height ratio (cm:cm)*	0.45 ± 0.06	0.52 ± 0.08	<0.001	0.49 ± 0.07
Systolic blood pressure (mmHg)*	135 ± 23.9	132.3 ± 24.8	<0.001	133.9 ± 24.4
Diastolic blood pressure (mmHg)*	86.8 ± 14.4	88.2 ± 14.4	<0.001	87.5 ± 14.6
Fasting glucose (mmol/L)*	5.34 ± 1.31	5.65 ± 1.71	0.005	5.50 ± 1.15
Triglycerides (mmol/L)*	1.22 ± 0.85	1.35 ± 0.75	<0.001	1.29 ± 0.80
Metabolic risk factors (%):				
Raised triglycerides	14.5 (n=102)	22.9 (n=269)	<0.001	18.4 (n=371)
Reduced HDL-C	22.8 (n=162)	42.9 (n=507)	<0.001	33.1 (n=669)
Raised blood pressure	66.5 (n=493)	66.0 (n=830)	0.819	65.4 (n=1323)
Raised fasting glucose	35.8 (n=253)	45.3 (n=533)	<0.001	38.8 (n=786)
≥ 2 metabolic risk factors §	38.3 (n=286)	52.8 (n=667)	<0.001	47.1 (n=953)
Smoking (%)	60.1 (n=446)	44.5 (n=575)	<0.001	48.6 (n=1021)
Alcohol consumption (%)	63.8 (n=459)	31.8 (n=392)	<0.001	47.8 (n=788)

*Values presented as means ± SD; p<0.05=Significance

§ Risk factors including abdominal obesity (IDF: Waist circumference cut-off value for Europeans / Sub-Saharan Africans of ≥94 cm for men and ≥80 cm for women)

All metabolic risk factors defined according to IDF criteria.

Raised triglycerides ≥1.7 mmol/L (≥150 mg/dL); Reduced HDL-C <1.03 mmol/L (<40mg/dL) for men and <1.29 mmol/L (<50 mg/dL) for women; Raised blood pressure ≥130/85 mmHg or treatment for previously diagnosed hypertension; Raised fasting glucose ≥ 5.6 mmol/L (≥100 mg/dL) or previously diagnosed type 2DM and a combination of two or more of these metabolic risk factors.

Metabolic risk factors according to waist circumference category

The mean values for metabolic risk factors are presented in **Table 2** (Men) and **Table 3** (Women) according to 5 cm WC categories (< 70 cm; 70-75 cm; 75-80 cm; 80-85 cm; 85-90 cm; 90-95 cm and > 95 cm). These categories were selected to identify the increased metabolic risk associated within each 5 cm WC increment. It is already known that metabolic risk factors are becoming more prevalent at higher WC values in Caucasians but it is not known at what WC values these metabolic risk factors are becoming more prevalent in black Africans.

In the men (**Table 2**), the mean triglycerides, SBP, DBP and FG values increased with increasing WC values. However, triglycerides showed a slight decline (1.52 ± 1.54 mmol/L; CI=1.33-1.71) within the 90-95 cm category and blood pressure (SBP, 142.9 ± 18.6 mmHg;

CI=136.7-149.2) and (DBP, 91.2 ± 12.2 mmHg; CI=87.2-95.3) showed a slight decline in the > 95 cm category. Hypertension defined as (SBP ≥ 140 ; DBP ≥ 90 mmHg) became apparent from the 85-90 cm WC category in the men, but raised blood pressure (SBP ≥ 130 ; DBP ≥ 85 mmHg) was already present from ≥ 70 cm. The mean FG (5.31 ± 1.09 mmol/L; CI=4.99-5.64) declined slightly within the 85-90 cm category, but was the highest in the > 90 cm category. HDL-C decreased considerably from WC of more than 80 cm.

Table 2: Mean values for IDF-Metabolic syndrome risk factors according to waist circumference category for black Setswana speaking South African men.

Metabolic risk factors Men	Waist circumference category (cm)						
	<70 (n=188)	70-75 (n=207)	75-80 (n=135)	80-85 (n=86)	85-90 (n=50)	90-95 (n=34)	> 95 (n=37)
Triglycerides (mmol/L)	0.79 ± 0.37	1.06 ± 0.73	1.15 ± 0.74	1.50 ± 1.67	1.75 ± 1.33	1.52 ± 1.54	1.98 ± 1.17
95% CI	0.92-1.03	0.95-1.16	1.02-1.28	1.24-1.76	1.35-2.15	1.33-1.71	1.57-2.38
HDL-C (mmol/L)	1.71 ± 0.67	1.63 ± 0.67	1.71 ± 0.70	1.48 ± 0.62	1.29 ± 0.52	1.17 ± 0.40	1.24 ± 0.47
95% CI	1.61-1.81	1.53-1.72	1.59-1.83	1.34-1.61	1.14-1.44	1.03-1.31	1.07-1.40
SBP (mmHg)	131.6 ± 24.0	132.1 ± 21.1	133.7 ± 23.3	139.3 ± 22.0	145.6 ± 23.8	152.5 ± 37.9	142.9 ± 18.6
95% CI	128.1-135.0	129.2-135.0	129.7-137.7	134.6-144.0	138.8-152.4	139.3-165.7	136.7-149.2
DBP (mmHg)	84.2 ± 15.1	85.8 ± 13.7	86.4 ± 16.0	87.4 ± 13.2	93.0 ± 14.5	93.3 ± 18.1	91.2 ± 12.2
95% CI	82.1-86.4	83.9-87.7	83.7-89.1	84.6-90.3	88.9-97.2	87.0-99.6	87.2-95.3
FG (mmol/L)	5.11 ± 1.09	5.17 ± 1.13	5.40 ± 1.38	5.54 ± 0.99	5.31 ± 1.09	5.61 ± 1.37	6.65 ± 2.61
95% CI	4.95-5.27	5.01-5.32	5.16-5.64	5.32-5.76	4.99-5.64	5.13-6.09	5.74-7.56

All values presented as means $\pm$ SD; 95% CI= 95% Confidence Interval

HDL-C=High density lipoprotein cholesterol, SBP=Systolic blood pressure, DBP=Diastolic blood pressure, FG=Fasting glucose

In the women (**Table 3**), the mean for all the metabolic risk factors (TG, SBP, DBP, FG) increased while, HDL-C decreased with increased WC categories. However, a slight decline was apparent for TG (1.40 ± 0.72 mmol/L; CI=1.29-1.51) and DBP (88.1 ± 13.0 mmHg; CI=86.2-90.0) in the 80-85 cm category and for SBP (134.0 ± 21.1 mmHg; CI=130.3-137.7) in the 85-90 cm category. Although hypertension defined as (SBP ≥ 140 ; DBP ≥ 90 mmHg) became noticeable from the 85-90 cm category in the men (for both SBP and DBP), the same was only true for DBP (90.0 ± 13.3 mmHg; CI=87.7-92.3) in the women.

Table 3: Mean values for IDF-Metabolic syndrome risk factors according to waist circumference category for black Setswana speaking South African women.

Metabolic risk factors <u>Women</u>	Waist Circumference category (cm)						
	<70 (n=293)	70-75 (n=163)	75-80 (n=140)	80-85 (n=175)	85-90 (n=131)	90-95 (n=133)	> 95 (n=218)
Triglycerides (mmol/L)	1.08 ± 0.55	1.15 ± 0.53	1.45 ± 1.09	1.40 ± 0.72	1.52 ± 0.80	1.47 ± 0.68	1.57 ± 0.79
95% CI	1.02-1.07	1.07-1.24	1.27-1.64	1.29-1.51	1.37-1.67	1.35-1.59	1.46-1.68
HDL-C (mmol/L)	1.63 ± 0.67	1.57 ± 0.77	1.60 ± 0.63	1.41 ± 0.57	1.43 ± 0.50	1.37 ± 0.50	1.29 ± 0.47
95% CI	1.55-1.71	1.45-1.69	1.49-1.71	1.32-1.50	1.33-1.52	1.28-1.46	1.22-1.35
SBP (mmHg)	125.3 ± 23.9	126.8 ± 23.4	133.0 ± 25.4	134.5 ± 23.8	134.0 ± 21.1	138.7 ± 26.0	139.0 ± 25.9
95% CI	122.6-128.1	123.2-130.5	128.7-137.2	131.0-138.1	130.3-137.7	134.2-143.1	135.5-142.4
DBP (mmHg)	84.1 ± 15.2	84.8 ± 14.7	89.0 ± 13.6	88.1 ± 13.0	90.0 ± 13.3	91.5 ± 13.5	92.8 ± 13.6
95% CI	82.4-85.9	82.5-87.1	86.8-91.3	86.2-90.0	87.7-92.3	89.1-93.8	91.0-94.7
FG (mmol/L)	5.32 ± 1.23	5.42 ± 1.33	5.51 ± 1.11	5.59 ± 1.61	5.86 ± 1.79	1.98 ± 2.34	6.12 ± 2.30
95% CI	5.18-5.45	5.20-5.63	5.32-5.70	5.35-5.83	5.53-6.19	5.57-6.40	5.80-6.45

All values presented as means ± SD; 95% CI= 95% Confidence Interval

HDL-C=High density lipoprotein cholesterol, SBP=Systolic blood pressure, DBP=Diastolic blood pressure, FG=Fasting glucose

When the metabolic risk factors were categorised according to the components of the IDF definition (reduced HDL-C, raised triglycerides, raised blood pressure, raised fasting glucose and two or more metabolic risk factors combined) these metabolic risk factors showed higher prevalence in categories of higher WC values for both genders (**Table 4**). In the men, an increase in the prevalence of metabolic risk factors according to WC category was noticeable. The prevalence of raised blood pressure was high from the WC < 70 cm to the > 95 cm category. Prevalence rates were only high from > 95 cm for raised TG (50.0%) and reduced HDL-C (47.1%), but very high from as low as 75-85 cm for raised blood pressure (60%) and raised FG (46.9%). The proportion of men with two or more metabolic risk factors was increased about three-fold from WC values of < 70 cm to > 95 cm. In the WC < 70 cm category, the prevalence of two or more metabolic risk factors was 28.3% and within the > 95 cm category the prevalence was 70.3%.

In the women (**Table 4**), an increase in the prevalence of metabolic risk factors according to WC category was also noticeable. The proportion of women with two or more metabolic risk factors

showed a two-fold increase from WC values of < 70 cm to > 95 cm. In women with a WC < 70 cm, the prevalence of two or more metabolic risk factors was 35.2% and for a WC > 95 cm the prevalence was 69.7%.

Table 4: Prevalence of metabolic risk factors according to waist circumference category among black Setswana speaking South African men and women.

Metabolic risk factors	Waist circumference category (cm)						
	<70	70-75	75-80	80-85	85-90	90-95	> 95
Men	(n=188)	(n=207)	(n=135)	(n=86)	(n=50)	(n=34)	(n=37)
Raised triglycerides	4.0	7.5	12.6	21.0	37.8	33.3	50.0
Reduced HDL-C	15.6	19.9	18.6	25.9	34.8	45.5	47.1
Raised blood pressure	58.8	63.4	60.0	73.3	86.0	88.2	83.8
Raised fasting glucose	29.6	31.8	33.1	46.9	42.2	45.5	64.7
≥ 2 risk factors	28.3	29.0	31.9	45.7	56.0	76.5	70.3
Women	(n=293)	(n=163)	(n=140)	(n=175)	(n=131)	(n=133)	(n=218)
Raised triglycerides	10.6	11.9	23.7	26.1	33.0	27.2	37.4
Reduced HDL-C	32.9	43.1	36.3	45.5	44.0	46.0	56.6
Raised blood pressure	50.3	55.6	64.3	69.5	74.6	75.8	81.5
Raised fasting glucose	37.0	39.7	45.9	42.4	51.7	52.0	55.3
≥ 2 risk factors	35.2	39.9	52.1	58.9	57.3	66.2	69.7

All values presented as percentages (%).

All metabolic risk factors defined according to IDF diagnostic criteria.

Raised triglycerides ≥1.7 mmol/L (≥150 mg/dL); Reduced HDL-C <1.03 mmol/L (<40mg/dL) for men and <1.29 mmol/L (<50 mg/dL) for women; Raised blood pressure ≥130/85 mmHg or treatment for previously diagnosed hypertension; Raised fasting glucose ≥ 5.6 mmol/L (≥100 mg/dL) or previously diagnosed type 2DM and a combination of two or more of these metabolic risk factors.

Values of waist circumference for detecting metabolic risk factors analysed by the ROC curve with the highest sensitivity and specificity

The population percentile for each WC cut-off as well as the sensitivity, specificity and Yuden index for detecting metabolic risk factors, are presented separately for men and women in (Table 5). The sensitivity, specificity and Yuden index were similar for men and women with two or more metabolic risk factors. The point at which the Yuden index were maximised, were at WC values of about 79-80 cm in the men and about 76-79 cm in the women. The WC values where sensitivity and specificity were maximised for each of the individual metabolic risk factors varied between 75-80 cm in both men and women.

Table 5: WC cut-off and sensitivity and specificity for two or more metabolic risk factors in black Setswana speaking South African men and women according to population percentiles.

≥ 2 Metabolic Risk factors				
WC Cut-off (cm)	Percentile	Sensitivity	1- Specificity	Yuden Index
Men				
60	2.4	0.99	0.98	0.01
65	9.9	0.94	0.92	0.02
70	26.6	0.81	0.70	0.11
75	53.4	0.59	0.38	0.21
80	63.2	0.45	0.18	0.27
85	76.3	0.29	0.09	0.20
90	85.8	0.18	0.04	0.14
95	92.2	0.09	0.02	0.07
100	96.2	0.05	0.01	0.04
Women				
60	4.8	0.98	0.95	0.03
65	13.5	0.94	0.84	0.10
70	25.4	0.84	0.68	0.16
75	36.0	0.74	0.52	0.22
80	46.7	0.63	0.41	0.23
85	57.9	0.48	0.29	0.19
90	68.4	0.36	0.19	0.17
95	78.5	0.22	0.12	0.10
100	85.3	0.13	0.08	0.06

Area under the ROC curve for WC with regard to combinations of two or more metabolic risk factors for men and women

The overall performance of the ROC analysis was quantified by computing area under the curve (**Figure 1**). An area under the curve of 1.0 indicated perfect performance while 0.5 indicated a performance that was not different from chance. The AUC for men was 0.650 (0.608-0.692 CI) and for women it was 0.648 (0.618-0.679 CI).

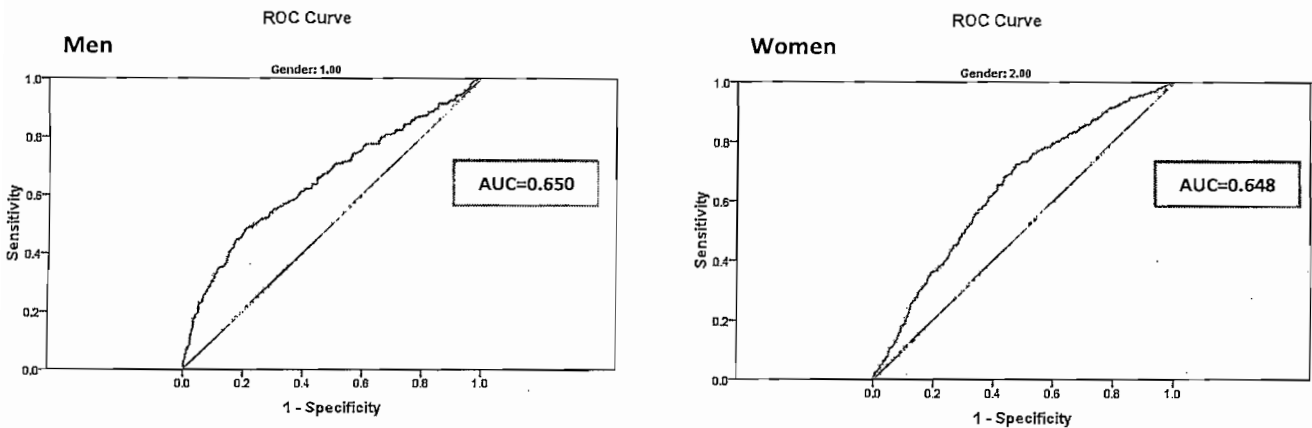


Figure 1: Area under the ROC curve for waist circumference with regard to combinations of at least two or more of the four metabolic risk factors ($n=280$) men, ($n=648$) women.

Odds ratios for different waist circumference cut-off values for predicting metabolic risk factors

The odds ratios for predicting the presence of metabolic risk factors according to WC values categorised by 5 cm increments are shown in **Figure 2** (Men) and **Figure 3** (Women). Based on a WC reference category of 70 cm the odds ratio (OR) for predicting metabolic risk factors showed a slight increase across the WC spectrum (every 5 cm) for raised glucose, reduced HDL-C and raised blood pressure but a steeper increase for raised triglycerides in the men. In the women, the OR for predicting metabolic risk factors showed a steep increase, for every 5 cm increase in WC, for raised blood pressure, raised triglycerides and two or more metabolic risk factors. Only a slight increase for raised glucose and reduced HDL-C were observed. After adjusting for age, HIV, urbanisation, smoking and alcohol use, a significant ($p < 0.05$) increase in OR's were observed for WC categories in both men and women. The OR for the presence of two or more metabolic risk factors increased abruptly in men and women at a WC of 85 cm but declined from 90 cm in the men.

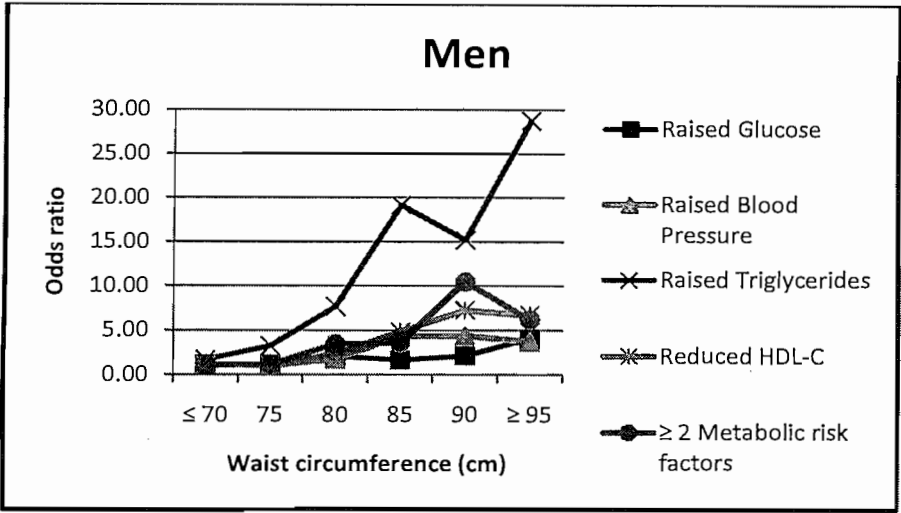


Figure 2: Odds ratios (OR) adjusted for age, urbanisation and lifestyle factors (smoking and alcohol) for predicting the presence of metabolic risk factors (raised glucose; raised blood pressure; raised triglycerides; reduced HDL-cholesterol and ≥ 2 metabolic risk factors) for men.

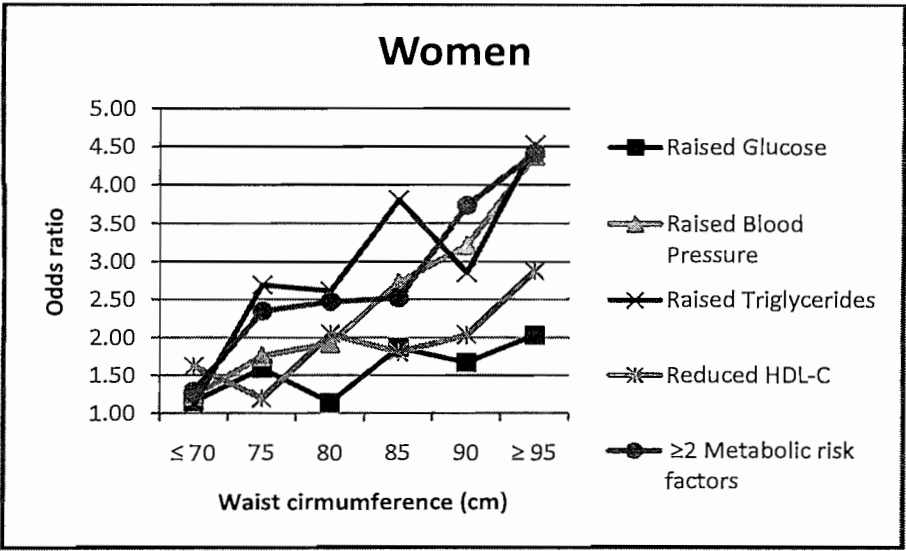


Figure 3: Odds ratios (OR) adjusted for age, urbanisation and lifestyle factors (smoking and alcohol) for predicting the presence of metabolic risk factors (raised glucose; raised blood pressure; raised triglycerides; reduced HDL-cholesterol and ≥ 2 metabolic risk factors) for women.

Discussion

Concern for a new world wide definition of the metabolic syndrome [1,13] has arose as a result of the lack of sub-Saharan Africa-specific cut-off values for WC. WC has been used as a parameter of abdominal obesity in various risk scores and definitions of the MetS [30]. Abdominal obesity has shown a strong association with type 2DM [31], insulin resistance [32], components of MetS [33,34], ischemic stroke [35] and hypertension [36]. It was proposed by researchers that the NCEP-ATP III criteria might underestimate risk for metabolic risk factors in African populations [37,38]. In this study the IDF diagnostic criteria which is known to be ethnospecific in its features and etiology because it proposes different WC cut-off values for different ethnic populations, were used.

Criteria for selection of cut-off values of abdominal obesity are based on data from white Caucasians, mostly from European countries [19]. Further, during a workshop on anthropometry by the Centers for Disease Control and Prevention, the expert panel suggested that, due to heterogeneity in average levels of measurements of obesity in different populations, the currently recommended cut-off values might not apply to all populations [39]. They concluded that there were strong indications that BMI and WC cut-off values should be set differently for Asian populations and persons of Asian ancestry living in Western countries. It was recommended that BMI and WC cut-off values be established on the basis of ethnic and racial background [39]. This might also applied for black African populations who have a different body composition than other ethnic groups [40]. According to the IDF criteria, sub-Saharan Africans should use the same WC cut-off values as Caucasians (Europids) derived from European data, until more specific data are available (≥ 94 cm in men and ≥ 80 cm in women). In this study we attempted to set local population specific WC cut-off values based on the statistical methods described by Lee et al. [41]. In agreement with the IDF definition the optimal WC cut-off values of ≥ 80 cm for men and women for identifying metabolic risk in a black South African population are proposed. In a recent study of Chinese adults aged 35-74 years similar WC cut-off values were proposed (WC ≥ 80 cm for both men and women) [42]. The findings of this study are similar to other African studies conducted in Cameroon and Nigeria which reported lower WC cut-off values than WC cut-off values used for Europids. These WC cut-off values were ≥ 76 for men and ≥ 72 cm for women and ≥ 81 cm for men and ≥ 82 cm for women for Cameroon and Nigeria respectively [43]. On'Kin et al. found that the IDF proposed WC cut-off values for abdominal obesity also underestimated rates of abdominal obesity in comparison with their local WC cut-off values in the Democratic Republic of Congo (DRC) [44]. The WC cut-off values are the same for men and women in the present study, unlike the different cut-off values for each gender proposed for other ethnic groups. Reports by other researchers have suggested a WC cut-off point near 80-85 cm for men and 75-80 cm for women, supporting a 5 cm gap between

the genders [45-47]. Other non-African studies support the ≥ 10 cm gap between men and women as proposed by the IDF, NCEP-ATP III and WHO criteria for WC [18,48,49].

According to the IDF WC cut-off values for abdominal obesity in Europids (≥ 94 cm for men and ≥ 80 cm for women), the prevalence of abdominal obesity in the present study would be 9.6 % and 52.4% for men and women respectively. Considering the actual prevalence of 28.1% in men and 52.4% in women using local WC cut-off values, the Europids WC cut-off values would have underestimated the prevalence of metabolic risk factors in black South African men of the North West Province by about 18%.

In the present study the metabolic risk factors identified by the IDF as components of the MetS were used for determining the WC cut-off values for abdominal obesity by means of a ROC curve analysis. The IDF cut-off values were derived from WC values (≥ 94 cm for men and ≥ 80 cm for women) corresponding to BMI (≥ 25 kg/m²), at those WC values prominent increases occurred in the prevalence of cardiovascular risk factors such as hypertension, hypercholesterolemia and low HDL-C [50]. Different methods were used in other studies for example in a Chinese study WC cut-off values were determined by magnetic resonance imaging techniques (MRI) at a visceral fat area larger than 100 cm² [51]. In a Canadian study WC cut-off values were determined by computerised tomogram (CT) at a visceral fat area of larger than 130 cm² [52].

A limitation of this study is its cross-sectional sample population. Another limitation was the relatively small number of participants within each WC category and the fact that this was not a representative sample of the black South African population. Although the study population was selected on the basis of "apparently healthy", the high prevalence of alcohol consumption and smoking within this population and extremely high blood pressure values raises questions about this population's perception of health. Future studies prospectively relating the suggested WC cut-off values to incidence of cardiovascular morbidity, cardiovascular mortality and all-cause mortality in a representative sample of the black adult South African population are needed. Therefore, the proposed WC cut-off values of ≥ 80 cm for men and women may not be the optimal WC cut-off for health promotion due to the study limitations, but represents values for epidemiological identification of abdominal obesity related to cardiovascular disease risk factors.

In conclusion, the analysis suggest that WC values of ≥ 80 cm for men and women are optimal cut-off values for abdominal obesity to be used together with the IDF diagnostic criteria in this black South African population group (North West Province). The high prevalence of metabolic risk factors among this population despite low WC values as shown in this study underscore the

importance of appropriate assessment of abdominal obesity in screening for MetS. In general, Africans and Europeans are not similar in comparative terms. It is therefore necessary to establish specific WC cut-off values for each African country, region and ethnic group. It is suggested that these proposed WC cut-off values be evaluated against a gold standard technique such as MRI or CT scan to determine how these cut-off values correlate with visceral fat area at 100 cm² and 130 cm² respectively.

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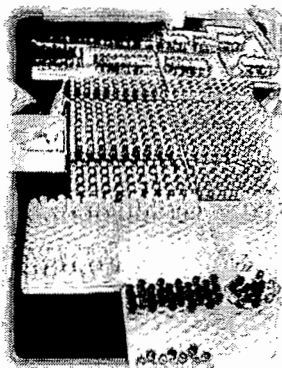
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METABOLIC RISK FACTORS IN A SUB-SAHARAN AFRICAN
POPULATION IN TRANSITION: IS ABDOMINAL OBESITY OR
RAISED BLOOD PRESSURE THE KEY DETERMINANT?



Left: Author performing an
ECG test
Below: PURE Study Participants
of Ganeysa (Rural cohort) of the
South African leg of the study



Above: Blood samples
Right: Local transport



This chapter is presented in article format and is written according to the referencing requirements of the journal *Hormone and Metabolic Research* to which it will be submitted. The font and spacing were kept the same throughout the thesis. All figures and tables are presented within the text rather than at the end of the article for examination purposes.

Metabolic Risk Factors in a Sub-Saharan African Population in Transition: Is Abdominal Obesity or Raised Blood Pressure the key determinant?

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Abstract

Background The most common definitions of metabolic syndrome today are the National Cholesterol Education Program, Adult Treatment Panel (NCEP-ATP III) and International Diabetes Federation (IDF) definitions. These definitions are similar in what they consider as essential components, but differ in their cut-off values for abdominal obesity and fasting glucose, including their perspective on what component is considered central to the definition. Currently there are no standardised criteria or definition for identifying individuals at risk for cardiometabolic diseases and opinions vary as to which definition is best to utilise in this sub-Saharan, black South African population in transition. **Objectives** The objective was to determine the prevalence of the metabolic syndrome using three definitions (NCEP-ATP III, IDF, IDF with local WC cut-off value) and to assess the association of metabolic risk factors with abdominal obesity and raised blood pressure in a sub-Saharan rural and urban population. **Methods** The study had a cross-sectional design and formed part of the baseline data of the Prospective Urban and Rural Epidemiological (PURE) study. The population studied consisted of black Setswana speaking South African men (746) and women (1264) living in either an urban or rural area in the North West Province, 35 years and older. Blood pressure and anthropometrical measures were measured according to standardised procedures. Blood samples were collected and fasting glucose and blood lipids determined. Modified NCEP-ATP III, IDF and IDF with specific local cut-off values for waist circumference were used as defining criteria for the metabolic risk factors (raised blood pressure, raised fasting glucose, raised triglycerides and reduced HDL-cholesterol). **Results** The prevalence of metabolic syndrome varied according to the definition used. The IDF definition with sub-Saharan Africa proposed waist circumference cut-off values (≥ 94 cm men; ≥ 80 cm women) and the IDF definition with proposed local waist circumference cut-off values (≥ 80 cm for men and women) indicated a higher prevalence of metabolic syndrome compared to the NCEP-ATP III definition. The highest

prevalence of the MetS was obtained with the IDF definition with local WC cut-off values in the men (rural: 16.4%; urban: 17.6%) and women (rural: 28.4%; urban 38.2%) and the lowest with the NCEP-ATP III definition in men (rural: 2.3%; urban: 0.8%) and women (rural: 16.3%; urban: 22.0%). Raised blood pressure ($\geq 130/85$ mmHg) was the most prevalent metabolic risk factor in both the rural (60.3-60.6%) and urban (72.0-72.6%) men and women. In the men no significant difference in the prevalence of the individual metabolic risk factors between the urban and rural groups could be found. The prevalence of most of the individual metabolic risk factors of the urban women was significantly higher compared to the rural women. After adjusting for age, urbanisation, HIV status and gender, abdominal obesity and raised blood pressure ($\geq 130/85$ mmHg) were significantly associated with all metabolic risk factors. The association with the metabolic risk factors was slightly stronger for abdominal obesity (WC) rather than raised blood pressure in this population. **Conclusion** The prevalence of the metabolic syndrome varied substantially between rural and urban participants across the MetS definitions. Lifestyle transitions from rural to urban significantly increased the prevalence of the metabolic risk factors and metabolic syndrome (IDF definition) in the women but not in the men. Abdominal obesity appears to be the key determinant in the presentation of the MetS in this sub-Saharan black Setswana speaking South African population in transition.

Key words: Metabolic syndrome, Urbanisation, Blood pressure, Waist circumference, Ethnicity.

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Introduction

The metabolic syndrome (MetS) is defined as a clustering of risk factors of metabolic origin [1] that are associated with a high risk for type 2 diabetes mellitus (2DM) [2,3], and cardiovascular disease (CVD) [4,5], and individuals with MetS have greater CVD mortality rates than individuals without MetS [6-12]. The risk factors to define MetS include various combinations of abdominal obesity, high blood pressure, high plasma glucose, dyslipidemia (increased triglycerides, low HDL cholesterol or both) and insulin resistance [1].

There are currently three common definitions of MetS: the World Health Organisation (WHO) [13], the National Cholesterol Education Program, Adult Treatment Panel III (NCEP-ATP III) [14] and the International Diabetes Federation (IDF) [15]. These definitions are in general agreement on the essential components of MetS but differ in their cut-off values and method of combining the individual components [16]. The WHO definition gives a central role to insulin resistance, and the NCEP-ATP III definition focuses equally on all components, while the IDF focuses on abdominal obesity and has ethnic specific waist circumference (WC) criteria. However, European cut-off values are still recommended in sub-Saharan African populations where specific data are not yet available [15]. Africa is currently experiencing one of the most rapid demographic and epidemiological transitions in world history [17]. Although a few studies have reported the prevalence of MetS in sub-populations in South Africa [18-23] and sub-Saharan Africa [24-26], this study investigated the prevalence of the MetS in black Setswana speaking South Africans of the North West Province. This study aims to assess the prevalence of MetS risk factors and the MetS in particular in a sub-Saharan African population, using three definitions of the MetS (NCEP-ATP III, IDF, IDF with local WC cut-off), and to compare the association between the main components of the MetS with abdominal obesity and raised blood pressure.

Materials and Methods

Participants and study design

The study had a cross-sectional design and formed part of the baseline data of the South African leg of the 12-year Prospective Urban and Rural Epidemiology study (PURE) which investigates the health transition in urban and rural subjects. A total of 2010 apparently healthy volunteers (35 years and older) were recruited from a sample of 6000 randomly selected households. The population studied consisted of black Setswana speaking South African men (746) and women (1264) living in either an urban or rural area in the North West Province. The

main selection criteria were that there should be migration stability within the chosen rural and urban communities. Although the participants were classified into urban and rural groups, the urban cohort was not representative of the high socio-economic class.

The study was approved by the Ethics Committee of the North-West University (Potchefstroom Campus) in accordance with the Declaration of Helsinki (Ethics nr. 04M10). Participants were fully informed about the objectives and procedures of the study prior to their recruitment. Fieldworkers explained all information in their own language. All participants signed an informed consent form. Full consent for voluntary testing for HIV was also provided after pre-test counselling. HIV-positive participants received post-test counselling and were referred to their local clinic or hospital for further follow up. All participants identified to have hypertension, diabetes, or other abnormalities were referred to a local clinic, hospital or physician.

Blood pressure was measured in the sitting position on the right arm, using the validated OMRON automated digital blood pressure monitor (OMRON HEM-757). The measurement was taken after 5 minutes of rest. All anthropometric measurements were done using the guidelines of the International Society for the Advancement of Kinanthropometry (ISAK) [27]. Measurements were obtained with the participant wearing minimal clothing without shoes. Maximum height and weight were measured with calibrated instruments (Precision Health Scale, A&D Company, Japan; Invicta Stadiometer, IP 1465, U.K.). The circumference was measured by a steel flexible Lufkin anthropometric tape (W606Pm) which is enclosed in a case with automatic retraction. Waist circumference was measured in cm at the narrowest point of the abdomen between the lower costal (10th rib) border and the top of the iliac crest, perpendicular to the long axis of the trunk at the end of normal expiration. Gluteal (hip) circumference was measured at the level of the greatest posterior protuberance of the buttocks, perpendicular to the long axis of the trunk. Waist-to-hip ratio (WHR) was calculated by dividing waist circumference by hip circumference. BMI was calculated as weight divided by height per square meter (kg/m^2). Waist-height ratio (WHtR) was calculated by dividing waist circumference (cm) by height (cm).

Participants were asked to be in a fasted state of approximately 10 hours. Blood was drawn from the anti-cubital vein in the participants' right arm, using a sterile butterfly infusion set (Johnson & Johnson, 21G, 19 mm). Excessive use of tourniquets was avoided as this could lead to hemo concentration and elevated results. For preparation of serum, blood was allowed to clot in glass tubes, centrifuged at 3000 rpm for 15 minutes (Universal 16RTM; Hettich, with cooling facilities), and 0.5 ml transferred to 1 ml Eppendorff tubes. EDTA blood was prepared by transferring 5 ml blood into EDTA glass tubes. Plasma was collected in EDTA tubes and

centrifuged at 2000g for 15 minutes at 4 °C (Universal 32R™, Hettich). All serum, plasma, and separated blood cells samples were immediately stored at -18 °C to -20 °C in the field for 2-4 days and afterwards at -84 °C in the laboratory.

The questionnaires used were designed for the PURE international study and adapted for the South African leg of the study and were validated with appropriate methods. Questionnaires were issued during individual interviews and were conducted by extensively trained fieldworkers in the preferred language of the participants. The comprehensive questionnaire included a demographic questionnaire and questions on the participant's health history, smoking and drinking habits. Data that was relevant to this study was utilised from these questionnaires.

Biochemical analysis

Quantitative determination of the concentration in the serum of the fasting triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), total cholesterol (TC) and fasting glucose (FG)(GOD-POD) was done with the Konelab™ auto analyser (Thermo Fisher Scientific Oy, Vantaa, Finland), a clinical chemistry analyzer for colorimetric, immunoturbidimetric and ion-selective electrode measurements. Low-density lipoprotein cholesterol (LDL-C) was calculated using the calculated using the Friedewald formula [28]. A rapid HIV-test was done according to the National Department of Health of South-Africa protocol. First response (PMC Medical, India) rapid HIV card test was done and if positive it was repeated with the Pareeshak test (BHAT Bio-tech, India).

Three definitions of the MetS were used. Modifications to the definitions were made because of unavailable data to fit all the definitions. Fasting glucose was not available and fasting serum glucose was therefore used in the definitions instead.

1. NCEP-ATP III definition [14]

Three or more of any of the following:

Waist circumference:	> 102 cm men and > 88 cm women
Fasting triglycerides:	≥ 1.70 mmol/L (≥ 150 mg/dL)
Systolic blood pressure:	≥ 130 mmHg and/or
Diastolic blood pressure:	≥ 85 mmHg
Fasting glucose:	≥ 6.1 mmol/L (≥ 110 mg/dL)
HDL-cholesterol:	< 1.03 mmol/L (< 40 mg/dL) for men
	< 1.29 mmol/L (< 50 mg/dL) for women

2. IDF definition with suggested WC cut-off for sub-Saharan Africans [15]

Waist circumference: ≥ 94 cm for men and ≥ 80 cm for women

Plus 2 or more of any of the following:

Fasting triglycerides: ≥ 1.70 mmol/L (≥ 150 mg/dL)
(or treatment for this lipid abnormality)

Systolic blood pressure: ≥ 130 mmHg and/or

Diastolic blood pressure: ≥ 85 mmHg
(or blood pressure lowering treatment)

Fasting glucose: ≥ 5.6 mmol/L (≥ 100 mg/dL)
(or anti-diabetic treatment)

HDL-cholesterol: < 1.03 mmol/L (< 40 mg/dL) for men
 < 1.29 mmol/L (< 50 mg/dL) for women

3. IDF definition with local WC cut-off [15,29]

Waist circumference: ≥ 80 cm for men and women

Plus 2 or more of any of the IDF definition criteria (used above) for triglycerides, blood pressure, fasting glucose and HDL-cholesterol.

Statistical procedures

Statistical analysis was performed using SPSS for Windows (version 16.0, SPSS Inc., Chicago, IL, USA). Statistical Consultation Services of the North West University were consulted for the analysis of this data. Analysis was stratified by gender and urbanisation (rural and urban). Fasting triglycerides were not normally distributed and therefore log transformed before any comparisons were made. Results are presented as means (standard error), 95% confidence intervals, percentages and adjusted odds ratio. Means and percentages of the rural and urban groups were compared by using the ANCOVA, adjusted for age after stratification for gender. Pearson Chi-square test and age adjusted ORs were used to compare prevalence between groups after stratification for gender and $p < 0.05$ was considered significant. Linear regression analysis with adjustments for covariates (age, urbanisation, HIV and gender) (Model 1) and (age, urbanisation, HIV, gender and BMI) (Model 2) were used to determine the association of the percentage variance explained by risk factors in addition to models containing covariates with abdominal obesity (WC) and raised blood pressure. The relationships were expressed as standardised beta (β) coefficients as well as the percent increase in the adjusted R^2 change when abdominal obesity (WC) or raised blood pressure was added to model 1 or model 2. The present study was an uncontrolled field study and therefore smaller effects can be expected than in controlled laboratory experiment [29]. Medium effect sizes (R^2 change of 0.1) are considered to be important in practice in this study [30].

Results

The descriptive statistics of the participants are shown in **Table 1**. There was no significant difference between the mean age of the rural and urban men. After adjustment for age, the means of BMI, WHR, blood lipids and blood pressure (SBP and DBP) were higher in the urban men compared to their rural counterparts. However, significantly higher values ($p < 0.05$) were present only for BMI, WHR, SBP and DBP in the urban men. The rural men had significantly higher abdominal obesity values (WC, WHtR) compared to the urban cohort. No significant differences between the rural and urban men were found for the metabolic risk factors, although slightly higher means for total cholesterol, triglycerides, HDL-cholesterol and LDL-cholesterol could be observed in the urban group.

The mean age of the rural women was (48.0 ± 0.38 years) and was significantly lower than the urban women (50.3 ± 0.45 years). Significantly higher values ($p < 0.05$) were present for WC, BMI, WHtR, WHR, SBP, DBP, total cholesterol and triglycerides in the urban women. The rural women had significantly higher HDL-C and LDL-C than the urban women. Mean BMI in both rural ($26.1 \text{ kg/m}^2 \pm 0.28$) and urban ($28.0 \text{ kg/m}^2 \pm 0.32$) women are considered overweight ($\geq 25 \text{ kg/m}^2$) according to World Health Organisation criteria. Total obesity (mean BMI) and abdominal obesity (mean WC, WHtR and WHR) were significantly higher ($p < 0.05$) in the urban women compared to their rural counterparts.

Lifestyle factors considered to influence health in this study was self reported alcohol consumption (at least one alcoholic beverage per month) and smoking (at least one tobacco product per day). Of the total population included in this study, 44.2% reported alcohol consumption and 52.4% were smokers. More men (60.3%) than women (28.0%) reported alcohol consumption. Smoking in the men (60.2%) was also higher than in the women (47.3%). It was observed that the urban men reported higher alcohol consumption and smoking compared to the rural men. It was interesting to note that a lower percentage of women in the urban (46.0%) areas were smokers than in the rural (48.5%) areas.

Table 1: Age adjusted gender specific rural-urban characteristics of the participants

Characteristics	Men (N=746)			Women (N=1264)		
	Rural	Urban	p	Rural	Urban	p
N	347	399	-	659	605	-
Age (years)	49.4 ± 0.55	50.1 ± 0.51	0.42	48.0 ± 0.38	50.3 ± 0.45	<0.001
BMI (kg/m ²)	20.7 ± 0.22 (20.3-21.1)	20.9 ± 0.21 (20.4-21.3)	<0.001	26.1 ± 0.28 (25.5-26.6)	28.0 ± 0.32 (27.4-28.6)	0.04
WC (cm)	76.5 ± 0.51 (75.5-77.5)	76.0 ± 0.48 (75.0-76.9)	<0.001	80.2 ± 0.55 (79.1-81.3)	83.5 ± 0.56 (82.4-84.6)	<0.001
WHtR (cm:cm)	0.46 ± 0.33 (0.44-0.47)	0.45 ± 0.33 (0.45-0.46)	<0.001	0.51 ± 0.34 (0.50-0.52)	0.53 ± 0.38 (0.52-0.54)	<0.001
WHR (cm:cm)	0.87 ± 0.003 (0.86-0.88)	0.88 ± 0.003 (0.87-0.88)	<0.001	0.80 ± 0.003 (0.79-0.81)	0.81 ± 0.003 (0.80-0.81)	<0.001
SBP (mmHg)	132.7 ± 1.23 (130.3-135.1)	138.0 ± 1.14 (135.8-140.3)	<0.001	129.3 ± 0.88 (127.6-131.0)	135.6 ± 0.92 (133.8-137.4)	<0.001
DBP (mmHg)	85.1 ± 0.79 (83.6-86.7)	88.3 ± 0.73 (86.9-89.8)	<0.001	87.1 ± 0.55 (86.0-88.2)	89.5 ± 0.57 (88.4-90.6)	<0.001
Fasting glucose (mmol/L)	5.41 ± 0.07 (5.27-5.55)	5.28 ± 0.07 (5.15-5.41)	0.14	5.68 ± 0.07 (5.55-5.82)	5.61 ± 0.07 (5.47-5.76)	0.004
Total cholesterol (mmol/L)	4.73 ± 0.07 (4.58-4.87)	4.87 ± 0.07 (4.74-5.01)	0.09	5.12 ± 0.05 (5.02-5.23)	5.13 ± 0.05 (5.01-5.24)	<0.001
Triglycerides* (mmol/L)	1.04 ± 0.01 (0.98-1.09)	1.08 ± 0.01 (1.03-1.14)	0.23	1.14 ± 0.01 (1.09-1.18)	1.25 ± 0.01 (1.20-1.30)	<0.001
HDL-cholesterol (mmol/L)	1.55 ± 0.04 (1.48-1.62)	1.61 ± 0.03 (1.54-1.68)	0.90	1.50 ± 0.03 (1.45-1.55)	1.45 ± 0.03 (1.40-1.51)	0.08
LDL-cholesterol (mmol/L)	2.67 ± 0.06 (2.55-2.80)	2.69 ± 0.06 (2.57-2.80)	0.16	3.07 ± 0.05 (2.98-3.16)	3.03 ± 0.05 (2.93-3.13)	<0.001
Smoking (%)	55.1 (n=177)	65.3 (n=269)	0.19	48.5 (n=299)	46.0 (n=266)	0.004
Alcohol (%)	52.5 (n=167)	68.0 (n=292)	<0.001	18.7 (n=115)	37.7 (n=277)	<0.001
HIV+ (%)	17.6 (n=61)	13.9 (n=55)	0.71	16.4 (n=108)	17.0 (n=101)	0.78

Age adjusted means ± Standard Error; p < 0.05 = Significant

95% Confidence intervals are presented inside parentheses

*Triglycerides have been log transformed, but back transformed to present normal interpretation.

BMI=Body mass index; WC=Waist circumference; WHtR=Waist-height ratio; WHR=Waist-to-hip ratio; SBP=Systolic blood pressure; DBP=Diastolic blood pressure; HIV+=Positive status for Human Immunodeficiency Virus.

Gender specific prevalence for the rural and urban groups with age adjusted odds ratios (OR) are presented in (**Table 2**). Higher prevalence rates of total obesity and abdominal obesity were observed for the urban men although not significant. The local WC cut-off value (≥ 80 cm) gave the highest prevalence of abdominal obesity in both the rural (27.2%) and urban (28.8%) men. The OR for WC (with rural as reference category) was (1.03) for the NCEP-ATP III definition, (1.05) for the IDF (sub-Saharan African) definition and (1.04) for the IDF definition with local WC cut-off values. No significant difference between rural and urban men was present for any of the metabolic syndrome risk factors regardless of the MetS definition used. The highest prevalence of MetS was provided by the IDF definition with local WC cut-off values.

Total obesity (BMI) and abdominal obesity (WC) prevalence were significantly higher ($p < 0.001$) in the urban (BMI=37.0%, WC=58.3%) than the rural (BMI=27.9%, WC=47.1%) women. Significantly higher means were present for total cholesterol and triglycerides, but lower means for LDL-C in the urban women. Lower means for fasting glucose and HDL-C were reported, but did not reach statistical significance in the urban women. The OR for abdominal obesity was (1.03) and (1.01) provided by the IDF and NCEP-ATP III definitions respectively.

The overall prevalence of total obesity and abdominal obesity were higher in the women than the men. The prevalence of raised blood pressure ($\geq 130/85$ mmHg) was very high in both men and women (rural and urban) ranging between 60.3-72.6%. The urban group (men and women) had a 16% higher prevalence ($p < 0.001$) of raised blood pressure compared to the rural group (men and women). The IDF definition for raised fasting glucose (≥ 5.6 mmol/L) presented a higher prevalence (35.8% in men and 45.4% in women) compared to the NCEP-ATP (≥ 6.1 mmol/L) definition (19.8% in men and 27.5% in women) due to the lower cut-off value. The rural group (men and women) had a lower prevalence of raised fasting glucose compared to the urban group (men and women) although not significant. There was no significant difference between rural (12.7%) and urban (16.0%) groups in the prevalence of raised triglycerides in men. However, a significant difference was present between the rural (18.2%) and urban (28.1%) women. Although no significant difference in the prevalence of reduced HDL-C was present between the rural and urban groups (men and women), the prevalence in the women were almost three times as high as in the men.

The NCEP-ATP definition gave the lowest prevalence for the clustering of metabolic risk factors (2.3% rural men, 0.8% urban men; 16.3% rural women, 22.0% urban women) compared to the IDF definition (4.6% rural men, 3.5% urban men; 28.4% rural women, 38.2% urban women). Regardless of the definition used, the prevalence of the clustering of metabolic risk factors was lower in the urban men than their rural counterparts except where the IDF definition with local

WC cut-off values were used where the prevalence was higher in the urban (17.6%) than the rural (16.4%) group. Women had an overall higher prevalence of the metabolic syndrome compared to men irrespective of the definition used.

Table 2: Gender specific rural and urban prevalence of metabolic risk factors with age adjusted odds ratios

Metabolic risk factors	Men			Women		
	Unadjusted prevalence Rural	Unadjusted prevalence Urban	Age adjusted OR's p	Unadjusted prevalence Rural	Unadjusted prevalence Urban	Age adjusted OR's p
Total obesity						
BMI (≥ 30 kg/m ²)	3.5	2.8	0.06	1	1.02	27.9 37.0 <0.001
Abdominal obesity						
WC ¹ (> 102 cm men; > 88 cm women)	2.6	1.3	0.19	1	1.03	28.0 36.3 0.002
WC ² (≥ 94 cm men; ≥ 80 cm women)	6.1	5.1	0.19	1	1.05	47.1 58.3 <0.001
WC ³ (≥ 80 cm for men and women)	27.2	28.8	0.63	1	1.04	47.1 58.3 <0.001
Raised Blood pressure ^{1,2,3}						
SBP/DBP ($\geq 130/ \geq 85$ mmHg)	60.3	72.0	0.001	1	1.05	60.6 72.6 <0.001
Raised fasting glucose						
Fasting glucose ¹ (≥ 6.1 mmol/L)	21.07	18.5	0.40	1	1.01	28.7 26.3 0.36
Fasting glucose ^{2,3} (≥ 5.6 mmol/L)	35.4	36.1	0.86	1	1.003	44.9 45.8 0.75
Elevated lipids						
Triglycerides ^{1,2,3} (≥ 1.7 mmol/L)	12.7	16.0	0.20	1	1.01	18.2 28.1 <0.001
Reduced HDL-cholesterol ^{1,2,3} (< 1.03 mmol/L men); (< 1.29 mmol/L women)	11.5	11.0	0.83	1	0.98	42.3 43.6 0.64
Prevalence of metabolic syndrome by definition						
NCEP-ATP III ¹	2.3	0.8	0.08	1	1.01	16.3 22.0 0.10
IDF ²	4.6	3.5	0.45	1	1.03	28.4 38.2 <0.001
IDF Local WC ³	16.4	17.6	0.67	1	1.04	28.4 38.2 <0.001

Unadjusted prevalence (%)

1 NCEP-ATP III criteria (National Cholesterol Education Panel-Adult Treatment Panel III); 2 IDF criteria with sub-Saharan Africa waist circumference cut-off (International Diabetes Federation);

3 IDF criteria with local waist circumference cut-off; Significance ($p < 0.001$)

OR=Odds ratio; BMI=Body mass index; WC=Waist circumference; SBP=Systolic blood pressure; DBP=Diastolic blood pressure; HDL-C=High density lipoprotein cholesterol.

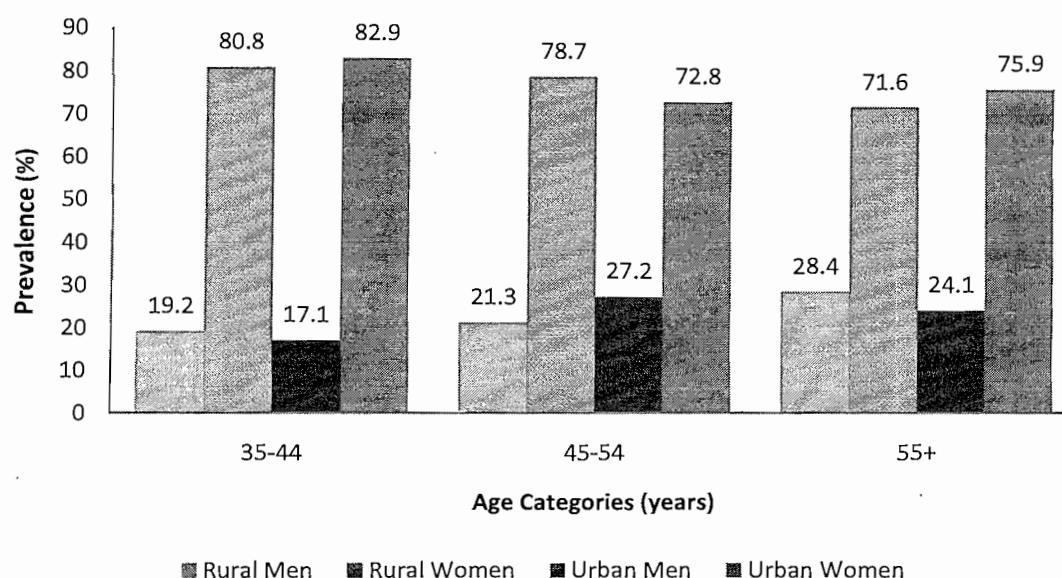


Figure 1: Prevalence of metabolic syndrome according to the IDF definition between different age categories (Stratified according to gender and urbanisation)

The prevalence of the MetS, using the IDF definition with local WC cut-off values increased with age categories in men (urban), but not in women. **Figure 1** illustrates that women in this black African population had a higher prevalence of MetS than men, regardless of age and place of residence (rural or urban). The prevalence of the MetS were obtained with the IDF definition with local WC cut-off values (women: rural 28.4% and urban 38.2%, $p < 0.001$; men: rural 16.4% and urban 17.6%, $p = 0.67$).

The percentage of variance explained by individual continuous risk measures by either abdominal obesity (WC) or raised blood pressure ($\geq 130/85$ mmHg) additional to covariates for age, urbanisation, gender and HIV is included in **Table 3**. The standardised beta (β) coefficients and R^2 change were higher for abdominal obesity (WC) rather than for raised blood pressure, except in the case of SBP, DBP. The association with the metabolic risk factors (fasting glucose, triglycerides, total cholesterol and HDL-C) were stronger for abdominal obesity (WC) rather than raised blood pressure in Model 1. After adjusting for BMI as presented in Model 2, the association of abdominal obesity with total cholesterol and HDL-C became smaller and the association of fasting glucose with raised blood pressure was no longer significant ($p = 0.18$). The variance explained by the covariates age, urbanisation, HIV and gender (Model 1) were higher than that explained by abdominal obesity for SBP ($R^2=0.16$), DBP ($R^2=0.06$) and total cholesterol ($R^2=0.07$). The percentage of variance explaining fasting glucose ($R^2=0.03$), triglycerides ($R^2=0.07$) and HDL-C ($R^2=0.06$) by abdominal obesity was similar to that explained by the covariates, with the contribution of triglycerides and HDL C probably having an effect in

practice. When BMI were added to the model (Model 2), the percentage of variance explained by abdominal obesity in Model 1 became smaller in all cases, suggesting that in practice WC does not explain additional variance about the individual risk factors to BMI. In Model 2, the additional percentage of variance explained by raised blood pressure was too small to be important in practice for all metabolic risk factors.

Table 3: Associations between observed values of each of the metabolic risk factors with abdominal obesity and raised blood pressure

Model 1 [§]	Adjusted	Abdominal obesity (WC)			Raised blood pressure		
	R ²	B	p	Δ R ²	β	p	Δ R ²
Systolic blood pressure	0.16	0.15	<0.001	0.02	-	-	-
Diastolic blood pressure	0.06	0.18	<0.001	0.03	-	-	-
Fasting glucose	0.02	0.18	<0.001	0.03	0.05	0.021	0.003
Triglycerides	0.06	0.28	<0.001	0.07	0.11	<0.001	0.01
Total cholesterol	0.07	0.11	<0.001	0.01	0.10	<0.001	0.01
HDL-cholesterol	0.05	-0.24	<0.001	0.06	0.07	0.001	0.01
Model 2 [¥]	Adjusted	Abdominal obesity (WC)			Raised blood pressure		
	R ²	B	p	Δ R ²	β	p	Δ R ²
Systolic blood pressure	0.17	0.24	<0.001	0.01	-	-	-
Diastolic blood pressure	0.07	0.25	<0.001	0.01	-	-	-
Fasting glucose	0.04	0.20	<0.001	0.01	0.03	0.18	0.001
Triglycerides	0.10	0.35	<0.001	0.03	0.07	<0.001	0.01
Total cholesterol	0.08	0.10	0.04	0.002	0.09	<0.001	0.01
HDL-cholesterol	0.11	-0.11	0.02	0.003	0.12	<0.001	0.01

§Model adjusted for age, urbanisation, HIV+ status and gender

¥Model adjusted for age, urbanisation, HIV+ status, gender and BMI

Adjusted R²= based on covariates of model 1 and model 1; β = standardised beta coefficient; p < 0.05 = statistically significant; Δ= change in R² values; WC=Waist circumference (≥ 94 cm men and ≥ 80 cm women); Raised blood pressure (≥ 130/85 mmHg)

Discussion

This was the first study comparing the prevalence of metabolic risk factors and metabolic syndrome according to the NCEP-ATP III, IDF definition and the IDF definition with local WC cut-off values for a black Setswana speaking South African population in transition. The rationale was that the NCEP-ATP III and IDF definitions differ with regard to their abdominal

obesity and raised glucose cut-off values and may therefore present very different prevalence rates within the same population. Both definitions were originally based on Caucasian cut-off values. However, the IDF proposes ethnically appropriate WC cut-off values but currently no specific cut-off values exist for ethnic black sub-Saharan Africans. The use of WC as a measure of abdominal obesity in Africans has been found to correlate with metabolic risk factors [31,32]. Local WC cut-off values for use with the IDF definition have been proposed for black South Africans in a previous study [31] and were included in this study to compare MetS prevalence between definitions (NCEP-ATP III and IDF). The prevalence of MetS varied between (2.3-16.4% in rural men; 0.8-17.6% in urban men and 16.3-28.4% in rural women; 22.0-38.2% in urban women) depending on the different definitions used. The IDF (with local WC cut-off values for men and women) were able to define the highest prevalence of MetS in this population especially in the men. The prevalence of MetS in the present study (10.4% NCEP-ATP III) were lower than that obtained in previous reports on black African populations within South Africa that reported (15.7%, 31% and 60%) when the same definition was applied [19,21,33]. When defined according to the IDF criteria, the overall prevalence was also lower (18.7%) in this study compared to (57.5%) reported by Ntyintyane et al. [19] and (24.8%) in women reported by Schutte et al. [33]. The prevalence of MetS for rural and urban men in the present study is similar to results obtained in rural (1.2%) and urban (1.2%) Cameroonian men as defined by the NCEP-ATP III criteria [17]. Compared to other ethnic groups the prevalence of MetS using the IDF criteria was comparable to that reported for Asians (15-20%) [34], higher than Australians (27.2%) [35], but lower than Chinese (46.3%) [36], Arab (45.5%) [37], Mexican (42.6%) [38] and European populations (Austria 45.5% and Greece 43.4%) [10,39]. In essence, the NCEP-ATP III gave the lowest prevalence for raised fasting glucose and abdominal obesity due the higher cut-off values compared to that of the IDF and IDF with local WC cut-off definitions. No differences between the rural and urban groups were significant for raised fasting glucose with either the NCEP-ATP III or IDF cut-off values.

Urbanisation is associated with lifestyles that favour the development of obesity, hypertension, diabetes mellitus, ischemic heart disease, stroke and the metabolic syndrome [17,40]. South Africa is a country of great diversity extending from highly industrialised cities with an urban westernised culture to rural areas with a traditional African culture [41]. Since the 1990's, black South Africans have been in a process of transition from rural to urbanized environments [42]. This process of urbanisation in South Africa is accompanied by an increase in coronary artery disease risk factors as shown by several local studies [42-45]. Results from this study confirmed that the urbanisation effect on this population leads to significant increased total and abdominal obesity, hypertension, triglycerides and metabolic syndrome prevalence, especially in the women. The higher prevalence of the metabolic syndrome in the urban area is in accordance

with other studies on metabolic risk factors [24,25]. The prevalence of total obesity (BMI ≥ 30 kg/m²) was (3.2%) in men and (32.5%) in women. In a previous representative South African study the prevalence of obesity was higher in the men (7.7%) and about the same in the women (30.5%) [25]. In the present study the prevalence of obesity was ten times higher in the rural women compared to the rural men and thirteen times higher in the urban women compared to the urban men, but the difference between the prevalence of abdominal obesity (WC: ≥ 94 cm men; ≥ 80 cm women) were only about ten times higher in the urban women compared to the urban men. This finding supports the argument that abdominal obesity (measured by WC) is important in identifying individuals who is more likely to develop hypertension, diabetes mellitus, cardiovascular disease and stroke in Africans [25]. Abdominal obesity as a metabolic risk factor therefore contributed substantially to the classification of MetS prevalence in the men and women of the study. South Africa is a country with one of the highest HIV infections in the world. The effect of HIV antiretroviral drug therapy has been shown to have side-effects that result in metabolic risk factors (triglycerides, fasting insulin and abdominal obesity) [46]. The impact of HIV on the MetS in South Africans therefore still needs to be determined [33]. Therefore results were adjusted for HIV in the present study.

Although a high prevalence of obesity was present in the women but not in the men, the high prevalence of raised blood pressure was similar in the men (66.2%) and women (66.6%). The urban group had however a significantly higher prevalence of raised blood pressure than their rural counterparts. Results from previous South African studies reported prevalence rates for hypertension between different black African groups that varies between (22.1-71.1%) in men and (24.4-80%) in women [47-51]. These variations between the black African groups may be caused by variations in levels of risk factors such as obesity (BMI and WC), sodium intake, education, social-economic status, psychological stress, smoking, alcohol use, age or unidentified factors that accompany an urban lifestyle [49-54]. It is widely recognised by researchers that black Africans present with higher prevalence rates of hypertension compared to other ethnic groups and that the urbanisation effect on the prevalence of hypertension is substantial [42,47,48].

Possible explanations have been proposed by researchers that may explain the high prevalence of raised blood pressure in this black African population. Firstly, psychosocial stressors caused by the urbanisation process may cause increased sympathetic outflow which may lead to hypertension in an individual due to damage of the endothelium by a hyperkinetic cardiovascular system and subsequent atherosclerosis [47,55]. However, it was found that endothelial dysfunction rather than atherosclerosis could be the cause for the abnormality in this population because of increased total peripheral resistance and decreased cardiac output [45].

In general it seems that a shift from a predominant cardiac output response (central effect) towards a predominant vascular resistance response (peripheral effect) is present when moving from a rural to an urban area [45,47,55]. Another possible mechanism may be due to the intake of higher calorie dense foods and the higher dietary sodium chloride content of the western diet, which form part of the urban lifestyle and may interact with obesity and the genetically determined “salt sensitivity” of black Africans [47,56]. The genetic contribution to the origin of hypertension indicated by family history of either hypertension or stroke in black Africans is also of importance [57,58]. Smoking among the men (67.3%) and women (47.3%) were extremely high. The lifestyle factors (alcohol consumption and smoking) may in part also explain the high prevalence of hypertension and metabolic syndrome in this study. Alcohol and smoking is accepted as major risk factors for CAD and previous studies argued that socio-economic classes and education have a high impact on both lifestyle factors [59,60]. However, there were no significant differences in the study between the rural and urban groups in smoking rates. The decreased smoking rates (although not significant) in the urban women may be due to the responsiveness of urban women (with a higher education and income level) to health promotion messages, since they in general have easier access to health care facilities and the media.

The results showed that raised blood pressure was clearly an important risk factor in this black African population. Abdominal obesity has been identified to be central to the IDF definition [15] and several studies confirmed the association of abdominal obesity with raised blood pressure [42,45,61]. One of the aims of this study was to determine if abdominal obesity or raised blood pressure is the key determinant of the MetS in this population. Although neither of the two metabolic risk factors proved to be superior, it was evident that both factors may be central in identifying individuals with the MetS. Supporting evidence by Schutte et al. reported that obesity ($\text{BMI} \geq 30 \text{ kg/m}^2$) and raised blood pressure ($\geq 130/85 \text{ mmHg}$) have an intertwined relationship during the development of the metabolic syndrome [22]. A study by Ntyintyane et al. explored the prevalence of a combination of metabolic risk factors for the MetS and found raised blood pressure to be the most frequent risk factor out of the five metabolic risk factors of the MetS [18]. In individuals with the MetS, the most frequent three-risk combination of risk factors included raised blood pressure and WC plus one other metabolic risk factor, suggesting that WC was the differentiating metabolic risk factor between those individuals with and without the MetS [18].

The mean triglycerides and HDL-cholesterol levels that were observed in this study were lower than the IDF and NCEP-ATP III definitions cut-off values for dyslipidaemia. It has been well documented that lower triglyceride levels and higher HDL-cholesterol levels exist in black Africans [48,62]. In general these lipid abnormalities remains strongly correlated to obesity and

CVD risk despite being lower in black Africans and have now caught up in the changes brought about by urbanisation and the HIV epidemic [63,64]. It has been suggested in a previous study that revised and modified cut-off values for lipid abnormalities due to general lower triglycerides and higher HDL-cholesterol levels in black Africans may be needed for the identification of individuals at risk for the metabolic syndrome in these populations [33].

The limitations of this study are its cross-sectional design and potential bias due to the fact that the participants were not entirely randomly selected. This study was done on a black Setswana speaking African population in the North West Province and may not be generalized to the broader black South African population. Lifestyle factors such as physical activity and dietary information did not form part of this study, but is certainly recommended to be included to understand the pathways leading to MetS and its relationship with abdominal obesity and hypertension in this population in the future.

In conclusion, this study confirmed a high prevalence of total obesity in women and in a lesser degree in men. The study demonstrated that although high prevalence of total obesity was present in the women, but not in the men the prevalence of abdominal obesity was high in both men and women (at a ≥ 80 cm cut-off for WC). A high prevalence of raised blood pressure in rural as well as urban participants was also observed in both men and women. The IDF (with local cut-off values for men and women) were able to define the highest prevalence of MetS in this study, but the lowest prevalence of MetS compared to other South African studies. Urbanisation had a significant influence on the prevalence of metabolic risk factors, especially in women. Raised blood pressure was identified to be a key determinant together with abdominal obesity as in the presentation of the MetS in this black African population.

These findings and that of other researchers indicate that the current NCEP-ATP III and IDF criteria need to be further explored in this black African population and may need to be adapted to optimally identify individuals at risk for MetS before CAD is indicated. It is thus clear that for black Africans more than only ethnic specific or population specific WC guidelines may be warranted. It's recommended that the IDF definition together with the local WC cut-off values be used in this black African population to effectively identify those individuals at risk for the MetS. The higher cut-off values used for WC and fasting glucose in the NCEP-ATP III definition could fail to identify individuals at risk and therefore delay appropriate primary intervention strategies. Prospective research will be needed to examine the predictive ability of these two definitions of the metabolic syndrome with cardiovascular disease morbidity and mortality for black South African adults.

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SUMMARY, CONCLUSIONS, LIMITATIONS AND RECOMMENDATIONS

6

6.1 SUMMARY

6.2 CONCLUSIONS

6.3 LIMITATIONS, CONFOUNDING AND CHANCE

6.4 RECOMMENDATIONS

6.1 SUMMARY

The research questions addressed in this study were the following: Firstly, to determine the most effective anthropometric indicator of NCD risk factors in a black South African population. Secondly, to determine the ethnically appropriate WC cut-off values for abdominal obesity in black South African men and women, to predict increased risk of metabolic syndrome risk factors (raised triglyceride, reduced HDL-cholesterol, raised blood pressure and raised fasting blood glucose), or two or more of these risk factors. Thirdly, to determine the prevalence of the metabolic syndrome (MetS) with urbanisation, using three definitions (NCEP-ATP III, IDF, IDF with local WC cut-off values). Finally, to assess the association of metabolic risk factors with abdominal obesity and raised blood pressure in a black sub-Saharan Africa population.

Chapter 1 provided a brief introduction and outline of the problem statement that underlies the research questions, aims and hypotheses that form the basis of this study. This thesis is submitted in article format, as approved by the Senate of the North-West University (Potchefstroom Campus) and therefore includes a literature review (Chapter 2) and three research articles (Chapters 3, 4, and 5 respectively) which will be presented to accredited peer-reviewed journals.

In order to answer the aims of this study, the current literature was investigated in Chapter 2. Firstly NCD's are discussed, together with their prevalence and impact on morbidity and mortality. The importance for appropriate and early identification, prevention and intervention were highlighted. Overweight and obesity as risk factor for NCD's and the global problem of obesity were discussed. Statistics of obesity worldwide and especially in Africans were analyzed, together with the factors that influence obesity. The importance of ethnicity as risk factor for obesity and the implication on anthropometric cut-off values to correctly identify

individuals at risk were shown. The different anthropometric indices of obesity: body mass index (BMI), waist circumference (WC), waist-hip ratio (WHR) and waist-height ratio (WHtR) together with computerized tomography (CT) and magnetic resonance imaging (MRI) were compared and discussed. The relationship between obesity and disease, especially NCD's and the metabolic syndrome, as well as the relationship between stunting and obesity were investigated. Obesity as an inflammatory condition and the relationship between CRP and measures of adiposity were highlighted. The impact of urbanisation on the prevalence of obesity and disease, especially in Africans were also discussed in Chapter 2. Finally, three of the current definitions that are used to identify individuals at risk for the metabolic syndrome, namely that of the World Health Organization, Adult Treatment Panel III and International Diabetes Federation's individual risk factors and specific cut-off values were compared and discussed.

In conclusion the literature suggest the need to employ different anthropometric measurements of obesity when diagnosing NCD, whether BMI, WC, WHR or WHtR are used. Depending on race and ethnicity the literature also suggest that the cut-off values for these anthropometric indices should be lowered if necessary. This will eventually lead to more sensitive criteria for identification of individuals at increased risk for NCD and the metabolic syndrome, especially in black sub-Saharan Africans.

In Chapter 3, the research article entitled "Anthropometric indicators of non-communicable diseases in a black South African population" by Beneke, J., De Ridder, J.H., Underhay, C., Kruger, A., Van Rooyen, J.M. and Ellis, S. will be presented for publication in *Atherosclerosis*. The main purpose of this study was to determine the most effective anthropometric measure that indicates the presence of NCD risk factors (measures of lipids, fasting glucose, CRP, blood pressure and obesity) in a black South African population.

The second article entitled "Optimal waist circumference cut-off values for abdominal obesity in black South African men and women", by Beneke J., De Ridder, J.H., Underhay, C., Kruger, A., Van Rooyen, J.M. and Ellis, S. will be presented for publication in *Diabetes Research and Clinical Practice*. This article is included in Chapter 4. The aim of this study was to determine the ethnically appropriate WC cut-off values for abdominal obesity in black South African men and women to predict increased risk of metabolic syndrome risk factors (raised triglyceride, reduced HDL-cholesterol, raised blood pressure and raised fasting blood glucose), or two or more of these risk factors.

The third article entitled “Metabolic risk factors in a sub-Saharan African population in transition: is abdominal obesity or raised blood pressure the key determinant?”, by Beneke, J., De Ridder, J.H., Underhay, C., Kruger, A., Van Rooyen, J.M. and Ellis, S. will be presented for publication in *Hormone and Metabolic Research*. The aim of this study was to determine the prevalence of the metabolic syndrome (MetS) with urbanisation, using three definitions (NCEP-ATP III, IDF, IDF with local WC cut-off values) and to assess the association of the metabolic risk factors with abdominal obesity and raised blood pressure in a black sub-Saharan African population.

All of the above mentioned articles have been written according to the referencing requirements of the journals of which it will be submitted to. The font and spacing were kept the same throughout the thesis. All figures and tables are presented within the text rather than at the end of the article for examination purposes. Each article consists of an introduction, problem statement and the resulting research questions and purposes of the study. The research methods (description and selection of the participants and data analysis) were described, after which the results were presented and discussed. Each article concluded with limitations and recommendations.

6.2 CONCLUSIONS

The conclusions that are drawn from this research are presented in accordance with the set aims from the research articles and hypothesis (Chapter 1) of this study:

AIM 1: To determine the most effective anthropometric measure that indicates the presence of NCD risk factors (measures of lipids, fasting glucose, CRP, blood pressure and obesity) in a black South African population.

HYPOTHESIS 1: WC and WHtR are the strongest anthropometric indicators of non-communicable disease risk factors in a black South African population.

As assessed by the ability of the anthropometric indices, to 1) account for the variability in each risk factor and 2) optimal identification of individuals with increased NCD risk factors, the predictive abilities of BMI, WC and WHtR were similar. WC was slightly better (0.01-0.08 higher R^2 value, $p < 0.05$) in predicting concentrations of total cholesterol (TC), fasting glucose (FG), triglycerides (TG), LDL-cholesterol (LDL-C), systolic blood pressure (SBP) and diastolic blood

pressure (DBP) in men. BMI was slightly better in identifying men with reduced HDL-cholesterol (HDL-C) (0.03 higher R^2 , $p < 0.05$), while WHtR was slightly better (0.01-0.11 higher R^2 value, $p < 0.05$) in predicting concentrations of C-reactive protein (CRP), TG, SBP, DBP in women. WC was slightly better in identifying reduced concentrations of HDL-C (0.08 higher R^2 , $p < 0.05$) in women. On the basis of two or more metabolic risk factors, WC and BMI were equal in their predictive ability of NCD risk factors according to the receiver operating characteristic (ROC) curve analysis (AUC=0.65) in men while WHtR and WC were equal in their predictive ability (AUC=0.65) in women. For men and women combined, WHtR was the most frequent predictor for NCD risk factors (5 out of 8 risk factors) and WC (3 out of 8 risk factors) as determined by AUC.

The findings showed that in black Africans living in the North West Province of South Africa BMI, WC, WHR and WHtR do not differ much in their discriminative abilities to identify adult men and women with NCD risk factors. WHtR and WC were slightly better in their predictive ability and may be preferred because of its simplicity, but additional longitudinal data are needed to examine WHtR's relation to disease in this population.

Hypothesis 1 is therefore accepted.

AIM 2: To determine the ethnically appropriate WC cut-off values for abdominal obesity in black South African men and women, to predict increased risk of metabolic syndrome risk factors (raised triglyceride, reduced HDL-cholesterol, raised blood pressure and raised fasting blood glucose), or two or more of these risk factors.

HYPOTHESIS 2: The optimal WC cut-off values to predict increased risk of metabolic syndrome risk factors (raised triglyceride, reduced HDL-cholesterol, raised blood pressure and raised fasting blood glucose), or two or more of these risk factors in this black sub-Saharan African population are lower than the WC cut-off values proposed by the IDF.

Based on the receiver operating characteristic (ROC) curve analysis the WC value for predicting metabolic risk factors in this black African population was about 80 cm for men and women. The AUC for men was 0.653 (0.611-0.695 CI) and for women it was 0.643 (0.613-0.674 CI).

According to the local determined WC criteria, the prevalence of abdominal obesity was 28.1% in the men and 52.4% in the women. WC values of ≥ 80 cm for men and women are optimal

cut-off values for abdominal obesity in this black South African population. It is recommended that these WC cut-off values be used together with the IDF diagnostic criteria. Each African country, region and ethnic group may need to establish optimal WC cut-off values before universal guidelines for sub-Saharan Africans can be accepted.

Hypothesis 2 is therefore partly accepted, since only the WC cut-off value of the men (≥ 80 cm) was lower than the IDF definition WC cut-off value (≥ 94 cm), while in the women, the WC cut-off value found in this study (≥ 80 cm) were similar to the IDF definition.

AIM 3: To determine the prevalence of the metabolic syndrome (MetS) with urbanisation using three definitions (NCEP-ATP III, IDF, IDF with local WC cut-off values).

HYPOTHESIS 3: Urbanisation may increase metabolic risk factor and metabolic syndrome prevalence as determined by the IDF definition with local WC cut-off values.

The prevalence of MetS varied according to the definition used. The IDF definition with sub-Saharan Africa proposed waist circumference (WC) cut-off values (≥ 94 cm men; ≥ 80 cm women) and the IDF definition with proposed local WC cut-off values (≥ 80 cm for men and women) indicated a higher prevalence of MetS compared to the NCEP-ATP III definition. The highest prevalence of the MetS was obtained with the IDF definition with local WC cut-off values in the men (rural: 16.4%; urban: 17.6%) and women (rural: 28.4%; urban 38.2%) and the lowest with the NCEP-ATP III definition in men (rural: 2.3%; urban: 0.8%) and women (rural: 16.3%; urban: 22.0%). Raised blood pressure ($\geq 130/85$ mmHg) was the most prevalent metabolic risk factor in both the rural (60.3-60.6%) and urban (72.0-72.6%) men and women. In the men no significant difference in the prevalence of the individual metabolic risk factors between the urban and rural groups could be found. The prevalence of most of the individual metabolic risk factors of the urban women was significantly higher compared to the rural women. The prevalence of the MetS varied substantially between rural and urban participants across the MetS definitions.

Hypothesis 3 is therefore partly accepted. Urbanization significantly increased the prevalence of the metabolic risk factors and metabolic syndrome (IDF definition) in the women but not in the men.

AIM 4: To assess the association of metabolic risk factors with abdominal obesity and raised blood pressure in a sub-Saharan Africa population.

HYPOTHESIS 4: Raised blood pressure has a stronger association with metabolic risk factors than abdominal obesity.

The additional percentage of variance of individual continuous metabolic risk measures explained by either abdominal obesity (WC) or raised blood pressure ($\geq 130/85$ mmHg) were determined after adjusting for age, urbanisation, HIV+ status and gender. The standardised beta (β) coefficients and R^2 change were higher for abdominal obesity (WC) rather than for raised blood pressure, except in the case of SBP, DBP and HDL-cholesterol. The association with the metabolic risk factors (fasting glucose, triglycerides, total cholesterol and HDL-C) were slightly stronger for abdominal obesity (WC) rather than raised blood pressure (the association of SBP and DBP will always be high with raised blood pressure). The R^2 change was very small and although statistical significance was encountered, it is of little practical importance since R^2 change of ≥ 0.1 is generally considered as an average association of practical importance. After adjusting for BMI as presented in model 2, the associations of fasting glucose with raised blood pressure was no longer significant ($p=0.18$).

Both, raised blood pressure and abdominal obesity have a significant association with metabolic risk factors in this sub-Saharan black Setswana speaking South African population. The association with the metabolic risk factors was slightly stronger for abdominal obesity (WC) rather than for raised blood pressure in this population.

Hypothesis 4 is therefore rejected.

To conclude, the findings of this study show that in this black Setswana speaking South African population, WHtR and WC are the most important indicators of NCD risk factors. These indicators have a vital public health implication for developing countries like South Africa because they offer the prospect of an extremely effective, simple, inexpensive and non-invasive means for first-level screening at community level to identify individuals at risk.

The importance of the measuring site must be stressed when using WC, as different measuring sites may alter associations with risk factors measures and possible with disease risk. The guidelines for WC measurement of "The International Society for the Advancement of Kinanthropometry" (ISAK) are recommended. The benefit of using WHtR in epidemiological

studies may be the potential of this index to track abdominal obesity from childhood to adulthood, which would simplify the expression of obesity related disease risk regardless of age. WHtR will only change when there is a change in height, given when that height remains constant in adults. Additionally, the same cut-off value (0.5) could possibly be used to identify NCD risk factors for adults and children but need to be further explored. In essence, the use of WHtR will result in a simple public health message: "Keep your waist circumference to less than half of your height."

It is suggested that WC values of ≥ 80 cm for men and women are optimal cut-off values for abdominal obesity to be used together with the IDF diagnostic criteria in this black Setswana speaking South African population group. The high prevalence of metabolic risk factors among this population despite low WC values as shown in our study underscore the importance of appropriate assessment of abdominal obesity in screening for MetS. In general, Africans and Europeans are not similar in comparative terms. It is therefore necessary to establish specific WC cut-off values for each African country, region and ethnic group. It is also suggested that these proposed WC cut-off values be evaluated against a gold standard technique such as MRI or CT scan to determine how these cut-off values correlate with visceral fat area at 100 cm^2 and 130 cm^2 respectively.

This study confirmed a high prevalence of total obesity in women and in a lesser degree in men. Although a high prevalence of total obesity was present in the women, but not in the men the prevalence of abdominal obesity was high in both men and women (at a ≥ 80 cm cut-off for WC). A high prevalence of raised blood pressure in rural as well as urban participants was also observed in both men and women. The IDF (with local cut-off values for men and women) were able to define the highest prevalence of MetS in this study, but the lowest prevalence of MetS compared to other South African studies. Urbanisation had a significant influence on the prevalence of metabolic risk factors, especially in women. Raised blood pressure was identified to be a key determinant together with abdominal obesity in the presentation of the MetS in this black African population.

6.3 LIMITATIONS, CONFOUNDING AND CHANCE

There are several limitations of this study that may have influenced the outcomes:

- 6.3.1 Due to the cross-sectional design of this sub-study, findings may not be generalised to the broader black South African population or to sub-Saharan Africans in total. The participants were selected on basis of migration stability. This study formed part of the baseline data of the "Prospective Urban and Rural Epidemiological" (PURE) study that has a longitudinal study design. Once the PURE study is completed more reliable conclusions may be drawn.
- 6.3.2 Physical activity status and dietary information were not highlighted in this study, but may in part proclaim the gender and rural-urban differences observed in this study.
- 6.3.3 Another limitation of this study is that the established waist circumference cut-off values may not as yet be appropriate for the clinical identification of individuals at risk for adverse non-communicable disease outcomes until these waist circumference cut-off values have been validated against visceral adipose fat area as measured by CT scans and mortality data for men and women.
- 6.3.4 Although the aim of the study was to determine the optimal waist circumference cut-off value for men and women in accordance with the IDF definition for the metabolic syndrome, cut-off values for the remaining components of the metabolic syndrome still need to be determined.
- 6.3.5 Confounders identified in this study were age, smoking, alcohol use, HIV, gender and urbanisation. This study included adult participants from 35 years and older and it is known that cardiovascular disease risk increases with age. Due to the high smoking and alcohol use in this population, smoking and alcohol use were included as possible confounders because it have been shown to increase cardiovascular disease risk factors. The impact of HIV on the metabolic syndrome still needs to be determined in South Africans therefore all analysis were adjusted for HIV positive status as a possible confounder in the present study. The stage of HIV/AIDS as determined by CD4 cell count was not known in this particular study and therefore the effect of muscle wasting on anthropometric data are not known either. Gender differences were taken into account when conclusions were drawn for the participants in general. Non-communicable diseases have been shown to increase in populations that are in an

urbanisation process and therefore were included as a confounder when generalised conclusions were made for men and women in particular.

- 6.3.6 Although participants had to be apparently healthy (not known to have any condition or disease) during the random selection process prior to the study, many participants reported chronic medication use during the study that was consistent with previously diagnosed diseases such as hypertension and diabetes. The reason for this could have been that some participants did not entirely understand what chronic medication use was, or what condition their chronic medication was supposed to treat. Thus, not understanding the questions asked by the fieldworkers. Another possible explanation could be that they simply were dishonest during initial interviews conducted by the fieldworkers in fear that they would have been excluded from the study if they disclosed that they have been previously diagnosed with a certain condition or disease.
- 6.3.7 The role of chance. It should be kept in mind that even if no real associations between variables exist, on average 5 out of 100 such associations will be statistically significant by chance alone. The effect of chance on associations between variables in a large sample is less than in studies with a smaller sample size. To decide whether the results obtained have occurred by chance alone, hypothesis were tested and confidence intervals determined.

6.4 RECOMMENDATIONS

The results of and recommendations made in this thesis will be disseminated to health professionals through publication in peer-reviewed research journals (*Atherosclerosis, Hormone and Metabolic Research, Diabetes Research and Clinical Practice*) and presentation of papers at the following national and international conferences:

Abstracts will be submitted to present papers at the following conferences:

- 8th International Conference on Urban Health, Nairobi, Kenya. 18 – 13 Oct 2009.
- IDF 20th World Diabetes Congress, Montreal, Canada, 18 – 22 Oct 2009.
- 7th Annual World Congress on the Insulin Resistance Syndrome, San Francisco, USA, 5-7 November 2009.
- The Asia Pacific Symposium on Controversies to Consensus in Diabetes, Obesity and Hypertension (CODHy), Shanghai, China, November 4-7, 2010.

The following recommendations are proposed:

- 6.4.1 The identification of individuals at risk for adverse non-communicable disease outcomes can be made by using appropriate identification criteria and waist circumference cut-off values to ensure early detection and prevention of progressed disease endpoints in this black African population.
- 6.4.2 Due to ethnic variety in waist circumference cut-off values it is recommended that waist-height ratio should be further explored to determine if this measure is suitable to track abdominal obesity across different ethnic populations when a universal anthropometric measure is desired. Further research will be needed to determine whether waist-height ratio is appropriate to be used to track abdominal obesity across the life spectrum (childhood to adulthood). This will give the clinician insight to the progression of non-communicable diseases through the stages of development of an individual that is currently not provided by body mass index, waist circumference or waist-hip ratio.
- 6.4.3 Waist-hip ratio is a weak indicator of non-communicable diseases in this black African population and should not be used if other anthropometric measures (such as waist circumference and waist-height ratio) can give the clinician more appropriate information about the state of health of black Africans. Due to a vast body of evidence, it is also recommended that a paradigm shift from the traditional body mass index towards more appropriate anthropometric indicators are made especially in the clinical setting for the identification of non-communicable disease risk factors.
- 6.4.4 Proper intervention programmes should be implemented to further prevent the burden of obesity related health outcomes. Screening should be an annual routine for each individual (especially 35 years and older). Those individuals identified to reach the cut-off for waist circumference should be educated about lifestyle adjustments that can be implemented to reduce their waist circumference that will lead to reduced risk for further cardiometabolic outcomes (**Figure 6.1**). When an individual fails to make the relevant lifestyle modifications, this person should enter a primary intervention programme that is properly managed by a Biokineticist. The Biokineticist will provide the necessary counselling and culturally sensitive strategies to enable a person to set reliable goals and stay motivated throughout the intervention programme. Should the individual fail to be rehabilitated within a certain time frame, the secondary intervention strategy should be implemented.

6.4.5 Additional research is needed to confirm if modifications to the metabolic syndrome definition or its components are warranted for this specific ethnic group. Thus, should abdominal obesity and raised blood pressure be central to a modified black African definition for the metabolic syndrome or should the cut-off values simply be re-evaluated for the remaining components of the metabolic syndrome?

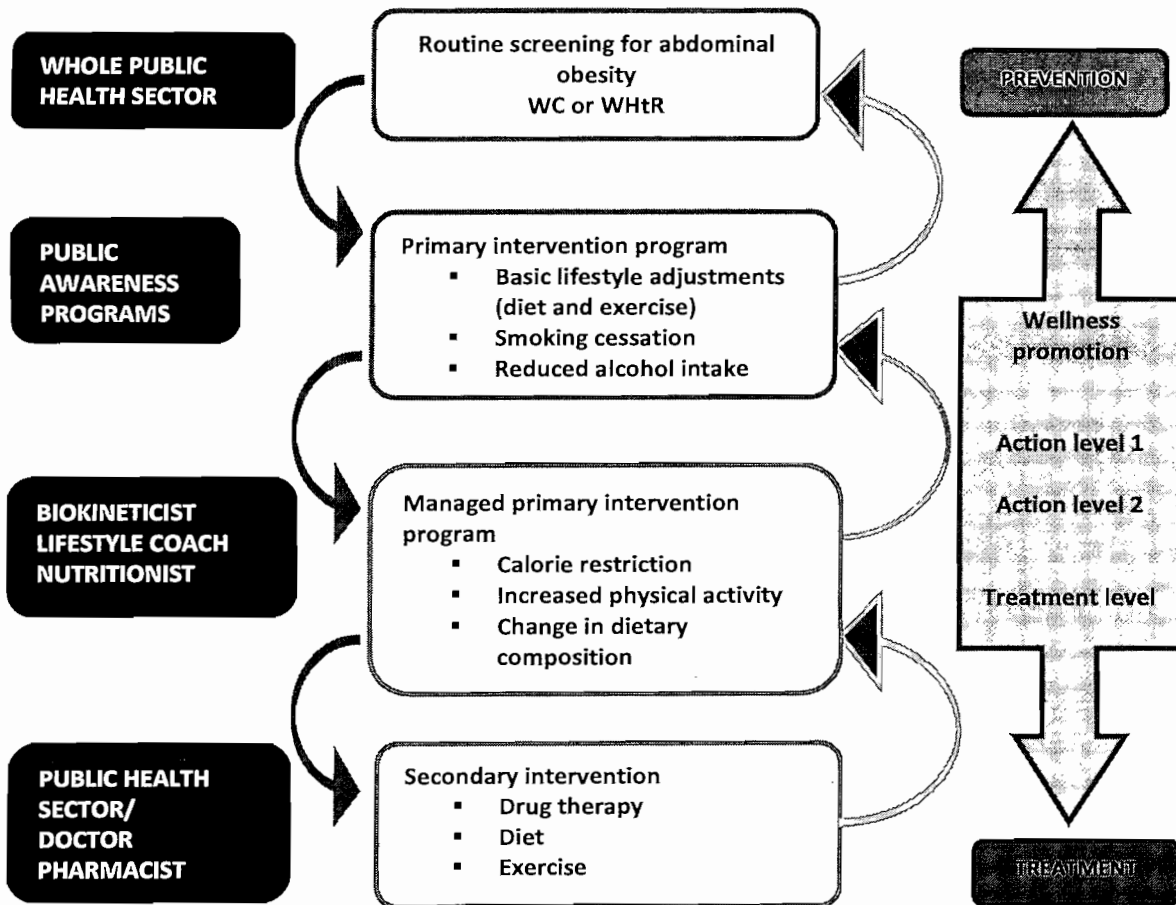


Figure 6.1: Proposed screening and intervention strategy for early management and prevention of abdominal obesity related diseases.

6.4.6 In support of the recommendations set by the IDF, 2005 for additional research in Caucasians, the following areas need to be further explored in Sub-Saharan Africans in particular:

- Insulin resistance (other than fasting glucose)
- Pro-inflammatory state (elevated CRP and TNF- α)
- Prothrombotic state (fibrinolytic and clotting factors)
- Abnormal body fat distribution (CT/MRI scan and adipose tissue biomarkers)
- Hormonal factors (pituitary-adrenal axis)

- Atherogenic dyslipidaemia (beyond raised triglycerides and lowered HDL-cholesterol)
 - Vascular dysregulation (beyond raised blood pressure)
- (Research should be population specific for black South Africans)

APPENDICES

Guidelines to Authors A

- *Atherosclerosis*
- *Diabetes Research
and Clinical Practice*
- *Hormone and Metabolic
Research*

Conferences B

PURE Study Questionnaires C

- Informed Consent Form
- Adult Questionnaire
(Demographic
questionnaire)

"Courage is reckoned the greatest of all virtues, because unless a man has that virtue, he has no security for preserving any other."

Samuel Johnson

Atherosclerosis

Guidelines for Authors

International Journal for Research and Investigation on Atherosclerosis and Related Diseases. Official Journal of the European Atherosclerosis Society affiliated with the International Atherosclerosis Society and the Society of Atherosclerosis Imaging and Prevention.

Atherosclerosis is a fully electronic journal, all manuscripts are to be submitted via the internet.

To submit your paper **online**, click on the link <https://www.editorialmanager.com/ath/>. This will take you to the *Atherosclerosis* Editorial Manager home page. The **Author Information** box to the right of the page provides relevant information, including a tutorial on how to submit your manuscript.

Authors must select an appropriate Associate Editor from the list shown on the website, the expertise terms for each Editor are shown to assist with this choice. Authors must suggest four potential reviewers for their paper, and to avoid delay in processing your submission please ensure that email addresses given for reviewers are correct. The Editorial Board reserves the right to decide whether or not the suggested reviewers are used. Please note the Associate Editors will not act as reviewers. Authors may also indicate if a particular reviewer should not be approached.

Types of papers that can be submitted for consideration by the Editorial Board include:

a) *Basic Research Papers* reporting results of original research or investigation using in vitro, cell culture, or animal models. Basic Research Papers should not exceed **4000** words (including tables, references and legends to figures).

b) *Clinical Research Papers* reporting results of original clinical research or investigation in human subjects. Clinical Research Papers should not exceed **4000** words (including tables, references and legends to figures).

Basic and Clinical Research papers must have no more than **5** figures and tables in total (e.g., 1 figure consisting of panels A and B, and 4 tables). Authors are encouraged to include additional figures and tables as supplementary appendixes, and these will be considered for Web-only publication.

Fast-track submission

For new findings of sufficient importance to justify accelerated review and publication, a fast-track submission process for original articles is available. In the submission letter, authors should explicitly request this option and provide credit card information (number, expiration date, and name as it appears on the card). If the editors agree that the manuscript is worthy of fast-track publication, the fee of 600 Euros will be automatically charged to the credit card. If accepted for fast-track submission, an article will be reviewed within 72 hours (otherwise, authors will be informed that the paper will be handled within the normal peer-review process). If accepted, a fast-track submission will appear in the first available issue of the journal.

c) *Review Articles and Mini-Reviews*, usually by invitation. Mini-Reviews should normally consist of current short reviews of topical information. Word limit: **3500** and **25** references and up to **3** tables and figures.

Full reviews may contain up to 6 tables and figures and authors are encouraged to include a "mechanism/overview" figure. Word limit **5000** and **60** references. Exceptions to these limits should be discussed with the Reviews Editor before submission. All Reviews should be submitted for handling to the Reviews Editor, Arnold von Eckardstein.

d) *Rapid Communications*. These papers should provide a brief but complete account of important new observations which merit urgent publication. The papers should be less than **5** printed pages (8-10 double-spaced typed pages) including figures and tables and should be concisely but adequately referenced. Authors should state in a covering e-mail why the paper merits urgent publication. Papers requiring revision will not be considered as Rapid Communications. The Editor-in-Chief will normally reach a decision on these papers within one month.

e) *Hypotheses and Viewpoints* of up to **1500** words are published occasionally. These contributions are subject to the normal editorial procedure. These should be submitted to the Editor-in-Chief.

f) *Letters to the Editor* are welcomed. If the letter is a commentary relating to published work in the journal, the other Author(s) will have the opportunity to reply in the same issue of the journal. Letters should not exceed **1200** words. These should be submitted to the Editor-in-Chief. Letters to the Editor that contain unpublished data or that are timely will receive a higher priority.

g) *Announcements* of meetings, workshops, courses etc. are welcomed, subject to available space.

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The official journal of the International Diabetes Federation

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9 Lowry OH, Rosebrough NJ, Farr AL, Randall RJ. Protein measurement with the Folinphenol reagent, J Biol Chem 1951; 193: 265–275

10 Kerner W, Pfeiffer EF. The artificial pancreas. In: Samols E (ed). The endocrine pancreas. New York: Raven Press, 1991: 441–456

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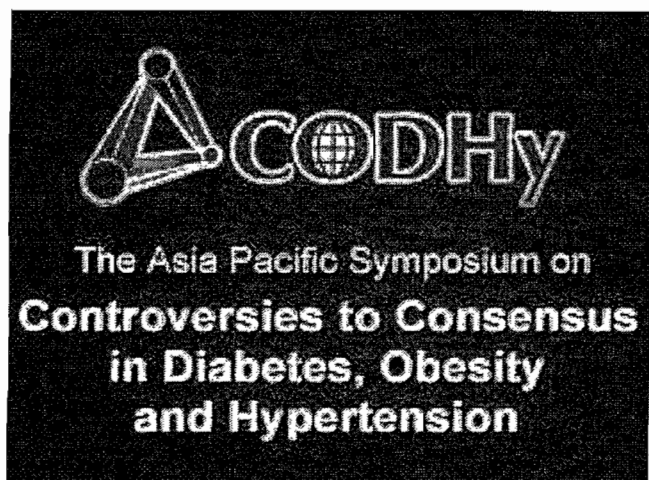
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CONFERENCES

1. The Asia Pacific Symposium on Controversies to consensus in Diabetes, Obesity and Hypertension.



The Asia Pacific Symposium on Controversies to Consensus in Diabetes, Obesity and Hypertension (CODHy)

Shanghai, China, November 4-7, 2010

We are proud to announce that the 1st Asia Pacific Symposium on Controversies to Consensus in Diabetes, Obesity and Hypertension (CODHy) will take place in Shanghai, China, November 4-7, 2010.

The 1st and the 2nd World CODHy Congresses which took place in Berlin in 2006 and in Barcelona in 2008, with the participation of 4,500 delegates all together, are the first scientific meeting of its kind focusing on hot topics facing the health professionals today.

Based on the success of the previous meetings and on feedback from the participants – the CODHy-Asia Pacific Congress is planning to include multiple controversies and debates as well as plenary sessions discussing innovations in the field.

We will also include discussions on several of the large ongoing studies that are scheduled to end during 2009-2010 in order to resolve controversies and reach a consensus.

We would be pleased to have you among the participants of this exciting congress.

Sincerely,

Prof. Sadikot M. Shaukat, Prof. Markolf Hanefeld, Prof. Guang Ning, Prof. Itamar Raz
Co-Chairpersons on behalf of the Organizing Committee

2. 13th South African Sports Medicine Association international conference 2009



Southern Sun, Elangeni Hotel, Durban, 21 – 23 October 2009

Information and Registration

21 – 23 October 2009

“Back to Basics” What is new in exercise physiology?

“Taking hands in Sports and Exercise Sciences”

Tel. 051 436 81 45 or E-mail congress@internext.co.za or Fax 051 4366 368
website www.sasma.co.za

The biennial International SASMA Conference is the highlight of the Sports Medicine calendar in South Africa. This is the one event where the whole sports medicine and exercise science community is represented, including sports physicians, orthopaedic surgeons, biokineticists, physiotherapists, chiropractors, dieticians, podiatrists, exercise scientists and other. It is also the event where these professionals assemble to sharpen up on new knowledge and new tools or products.

Focus: General Practitioners, Sport Physicians, Orthopaedic surgeons, Physiotherapists, Biokineticists, Chiropractors, Nutritionists and Dieticians, Podiatrists and other members of the multi-professional Sport Medicine team.



South African Sports Medicine Association

c/o Sports Medicine Clinic, University of the Free State, Nelson Mandela Drive, Bloemfontein, 9301

National Office Tel: (051) 4013325

Fax: (051) 444 2969

E-mail: gesal.fin@ufs.ac.za

website: www.sasma.org.za or www.sasma.co.za

28 July 2009

Dear J Beneke

NOTIFICATION OF ACCEPTANCE OF ABSTRACT: 13th BIENNIAL SASMA CONFERENCE

On behalf of the organising committee, I would like to thank you for participating in this conference.

Your abstract for a ORAL presentation has been accepted. The presentation is scheduled for:

Title: Optimal waist circumference cut-off values for abdominal obesity in black South African men and women

Date: 21 October 2009

Time: 14:15 – 14:30

Please check presentation time on the final program as small changes may be made at a late stage. Take note that paper presentations are 15 minutes in total, and not 15 plus 5 minutes as previously stated. Poster presentations will be allowed 5 minutes in a scientific session to briefly introduce the poster. A maximum of 3 Powerpoint slides may be used in a poster presentation.

Please confirm acceptance of the arrangements before 30 September by email to: gesal.fin@ufs.ac.za

Sincerely,

Dr Louis Holtzhausen

Chairperson: Scientific committee and organising committee



**YUNIBESITI YA BOKONE-BOPHIRIMA
NORTH WEST UNIVERSITY
NOORDWES UNIVERSITEIT**

POTCHEFSTROOM CAMPUS: FACULTY OF HEALTH SCIENCES

CHECK LIST

PURE-SA PROJECT

(PROSPECTIVE URBAN AND RURAL EPIDEMIOLOGY)

CHECK LIST

NAME:..... NUMBER:.....
DATE:.....

WHAT DID YOU DRINK THIS MORNING?:.....

WHAT DID YOU EAT THIS MORNING?:.....

STATION	INSTRUCTIONS	SIGNATURE
1. Recruitment	1 HIV Counselling 2 Informed consent	M Watson..... A Kruger.....
2. Blood sample	OGGT : ☐ Y ☐ N Time of sample..... ☐ Y ☐ N Problems experienced Name the problem.....	Signature:
3. Spirometry	☐ Y ☐ N	
4. Hand grip	☐ Y ☐ N	
5. Anthropometry	Weight..... Height.....	
6. ECG	☐ Y ☐ N	
7. BP	☐ Y ☐ N	
8. Urine sample	☐ Y ☐ N	
9. Physical activity	Questionnaire ☐ Y ☐ N	
10. Referral letter	☐ Y ☐ N	
11. check out		A Kruger.....



POTCHEFSTROOM CAMPUS

INFORMED CONSENT FORM

PURE-SA PROJECT

PURE-PROJECT (PROSPECTIVE URBAN AND RURAL EPIDEMIOLOGY)

INFORMED CONSENT

I, the undersigned(full names)
read/ listened to the information on the project in **PART 1** and **PART 2** of this document and I
declare that I understand the information. I had the opportunity to discuss aspects of the
project with the project leader and I declare that I participate in the project as a volunteer. I
hereby give my consent to be a subject in this project. I indemnify the University, also any
employee or student of the University, of any liability against myself, which may arise during the
course of the project.

I will not submit any claims against the University regarding personal detrimental effects due to
the project, due to negligence by the University, its employees or students, or any other
subjects.

I agree to be tested for HIV :

☐ YES☐ NO

I want to know my HIV-status:

☐ YES☐ NO

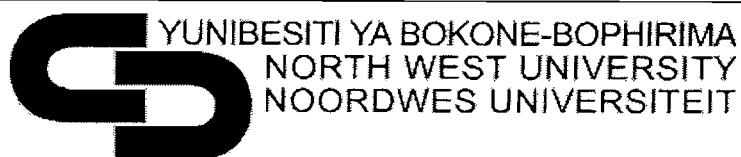
I agree to give a blood sample

☐ YES☐ NO

(The HIV testing and other measurements will only be done during September-December 2005.
You have the right to change your mind and at that time you will be asked to sign an inform
consent again on HIV testing)

.....
(Signature of the subject)

Signed at on



PART 1

School/Institute: Faculty of Health Sciences
Title of project/trial: PURE: Prospective Urban and Rural Epidemiology
Project leader: Annamarie Kruger, 4. Ph.D.(Nutrition)
Rank/position of project leader: Research Manager

1. Aim of this project

PURE's aim is that understanding the different lifestyle and health transitions of individuals in response to societal changes will elucidate societal and individual adaptive strategies that could diminish the adverse health effects of industrialization and urbanization on health, while retaining its benefits.

2. Explanation of the nature of all procedures, including identification of new procedures:

Each participant will have to fill in a number of questionnaires (Adult questionnaire, Physical activity questionnaire, Food frequency questionnaire, Health questionnaire) with the help of field workers. A blood and urine sample will be taken. Physical measures will be performed, including anthropometric measures (such as weight, height, and waist circumference), blood pressure, lung capacity and lung volume and an ECG will be performed.

3. Description of the nature of discomfort or hazards of probable permanent consequences for the subjects which may be associated with the project:

(Including possible side-effects of and interactions between drugs or radio-active isotopes which may be used.)

It will take each participant quite a while (about an hour) to complete the questionnaires and discomfort may be experienced with the taking of blood samples. No measures will have permanent damage or consequences for the participants.

4. Precautions taken to protect the subjects:

The research nurse will be present at all times, and will be responsible for the blood sampling. She is very experienced and has performed these procedures numerous times in previous studies.

5. Description of the benefits which may be expected from this project:

When measures with immediate results are taken, such as blood glucose levels or blood pressure, the information will be communicated to the individual to seek professional help. Since this study is a longitudinal study, subjects that are high at risk will be identified from the dataset and personal feedback will be given.

6. Alternative procedures which may be beneficial to the subjects:

There will be tested for HIV/AIDS, therefore pre-test counselling will be given. If the subject wants to know his/her status and he/her tests positive, post counselling will also be given.



PART 2

To the subject signing the consent:

You are invited to participate in a research project. It is important that you read/listen to and understand the following general principles, which apply to all participants in our research project:

1. Participation in this project is voluntary.
2. It is possible that you personally will not derive any benefit from participation in this project, although the knowledge obtained from the results may be beneficial to other people.
3. You will be free to withdraw from the project at any stage without having to explain the reasons for your withdrawal. However, we would like to request that you would rather not withdraw without a thorough consideration of your decision, since it may have an effect on the statistical reliability of the results of the project.
4. The nature of the project, possible risk factors, factors which may cause discomfort, the expected benefits to the subjects and the known and the most probable permanent consequences which may follow from your participation in this project, are discussed in Part 1 of this document.
5. We encourage you to ask questions at any stage about the project and procedures to the project leader or the personnel, who will readily give more information. They will discuss all procedures with you.
6. The University staff will use standardised procedures and take all possible precaution to protect the subject from risks. We require that you indemnify the University from any liability due to detrimental effects of treatment by University staff or students or other subjects to yourself or anybody else. We also require indemnity from liability of the University regarding any treatment to yourself or another person due to participation in this project, as explained in Part 1. Lastly it is required to abandon any claim against the University regarding treatment of yourself or another person due to participation in this project as described in Part 1.
8. If you are married, it is required that your spouse abandon any claims that he/she could have against the University regarding treatment or death of yourself due to the project explained in Part 1.
9. All information will be kept CONFIDENTIAL.
10. The blood samples and other measurements will only be done between September and December 2005 an appointment with yourself.



Potchefstroom Campus

THE PURE PROJECT

INFORMATION TO COMMUNITIES**Dear Participant**

Thank you for being willing to help us in this very important project. We are sure that the project will contribute to improve health of all the people of the North West Province.

The aim of the project is to get enough information regarding the development of chronic diseases like Diabetes, Stroke, Lung disease and heart disease with urbanisation to plan appropriate health and nutrition intervention strategies.

For this study we need 2 000 subjects whom we can follow for 12 years. The baseline survey will be done from April 2005 to November 2005. The subjects must be from rural as well as urban communities. Therefore, 500 subjects from 4 different levels of urbanisation will be needed. Ganyesa and Tlaskgameng were chosen for the rural and semi-rural areas because they are still under tribal law with a good infrastructure and stability. Chief M. Letlhogile and the mayor Mr E. Tladinyane are informed about the study. Ikageng and the informal Ikageng were chosen as it is convenient and near the University. Cllr GG Megalanyane and Cllr Mahesh Roopa are informed about the study.

You are one of the 2000 people (250 men and 250 women from all four sites (Ganyesa, Tlaskgameng, Ikageng, and the Informal Ikageng) that are selected from the previous questionnaires to be asked to proceed with the study. You should be

- Older than 35 years
- Healthy – which means that they must not be aware of any disease and do not take any chronic medication

You will be asked to participate voluntarily and to fill out the adult questionnaire, the food frequency questionnaire, the health questionnaire and the physical activity questionnaire. We will also make an appointment with you to take some measurements such as weight, height, skinfold thickness, ECG (test for heart abnormalities), lung functions, blood pressure, blood glucose, blood samples and a urine sample. You should understand that participation is voluntarily.

It is very important that we gather quality data and knowledge. Because HIV/AIDS is such a devastating illness and affects almost all aspects of health, it is necessary to know if HIV is absent before we analyse the data. Therefore we will ask questions about your HIV status which you are allowed not to answer.

It is also very important to us that you feel free to participate in this study and that you understand what the study is all about. The fieldworker will ask you to sign this form after you have read and understood it.

Kind regards

Dr ANNAMARIE KRUGER

Contact details:

082 7715778/ 018 2994037(W)

018 2907024(H)

PURE / SOUTH AFRICA

We are very grateful to you for your participation in this study. All information given by you will be held in strict confidence, and will be used for the purpose of this study only after removing any personal identifying information.

Adult Questionnaire

INSTRUCTIONS

Please answer EACH question by marking an
X in ONE BOX on each line:
(unless otherwise instructed)

X

OR

By writing number(s) in the spaces provided

18

OR

By specifying the answer on the line(s) provided

April 28, 2005

Adult Questionnaire

Subject Initials- F= first letter of first name
M= first letter of middle name
L= first letter of last name

3. National I.D#

If not applicable please mark the N/A box

Ethnicity Codes

- 01 - South Asian (India, Sri Lanka, Pakistan, Bangladesh)
- 02 - Chinese (China, Hong Kong, Taiwan)
- 03 - Japanese
- 04 - Malays
- 05 - Other Asian (Korea, Malaysia, Papua New Guinea, Thailand, Philippines, Indonesia, Nepal, Vietnam, Cambodia, Laos, Myanmar/Burma, Bhutan, Singapore)
- 06 - Persian
- 07 - Arab
- 08 - Black African
- 09 - Coloured African (Subsaharan African only)
- 10 - European
- 11 - Native North/South American or Australian Aborigine
- 12 - Latin American (Latino)
- 13 - Bantu/Semi Bantu
- 14 - Hemitic/Semi Hemitic
- 15 - Nilotic/Hausa
- 16 - Pygmie
- 17 - Swahili
- 18 - Other (any other ethnoracial group not listed above)

Subject ID

Centre #	Community#	Household #	Subject #		

Subject Initials

F M L

Today's date:

year month day

1. Name: _____

Given name Surname

2. Not applicable in South Africa

3. National identity # or equivalent: _____ N/A ☐

4. DOB: OR Age yrs

year month day

5. Sex: ☐ Female ☐ Male

6. Marital status: (check one only)

☐ Never married	☐ Currently married	☐ Common law/Living with partner
☐ Widowed	☐ Separated	☐ Divorced

7. Ethnicity: → (Please refer to facing page for codes)

8. Caste/Tribe: _____

9. What level of formal education have you completed? (check highest level only):

☐ None

☐ Primary

☐ Secondary/highschool/higher secondary

☐ Trade School

☐ College/University

☐ Unknown

Adult Questionnaire

11. Occupation

Group 1: Legislators, senior officials and managers

- Legislators and senior officials
- Corporate managers
- General managers
- Businessman

Group 2: Professionals

- Physical, mathematical and engineering science professionals
- Life science and health professionals
- Teaching professionals
- Other professionals

Group 3: Technicians and associate professionals

- Physical, mathematical and engineering-science associate professionals/technicians
- Life science and health associate professionals/technicians
- Teaching associate professionals/technicians
- Other associate professionals/technicians

Group 4: Clerks

- Clerks
- Customer service clerks

Group 5: Service workers and shop and market sales workers

- Personal and protective services workers
- Models, salespersons and demonstrators

Group 6: Skilled agricultural and fishery workers

- Market-oriented skilled agricultural and fishery workers
- Subsistence agricultural and fishery workers

Group 7: Craft and related trade workers

- Extraction and building trade workers
- Metal, machinery and related trades workers
- Precision, handicraft, printing and related trades workers
- Other craft and related trades workers

Group 8: Plant and machine operators and assemblers

- Stationary plant and related operators
- Machine operators and assemblers
- Drivers and mobile plant operators

Group 9: Elementary occupations

- Sales and services elementary occupations
- Agricultural, fishery and related labourers
- Labourers in mining, construction, manufacturing and transport

Group 10: Armed forces

- Armed forces

Group 11: Homemaker

- Housewife/Househusband

Subject ID

Centre #

Community#

Household #

Subject #

Subject
Initials

F M L

10. Not applicable in South Africa

11a) Not applicable in South Africa

b) Please indicate which group best describes your main occupation.
(Please refer to facing page for definitions of groups and instruction manual for detailed definitions)

☐ Group 1

☐ Group 2

☐ Group 3

☐ Group 4

☐ Group 5

☐ Group 6

☐ Group 7

☐ Group 8

☐ Group 9

☐ Group 10

☐ Group 11

c) Not applicable in South Africa

d) What is your main source of income? _____

If occupation is group 11 (homemaker) go to question 13

12. Are you currently employed?

☐ No → (answer 12a - 12b)

☐ Yes → Go to #13

a) Are you retired/stopped work from your primary occupation due to old age? ☐ No ☐ Yes

b) Have you stopped working due to illness? ☐ No ☐ Yes

Subject ID

Centre #

Community#

Household #

Subject #

Subject
Initials

F

M

L

13. CURRENT DISABILITY:

	No	Yes
a) Do you have any problems using your fingers to grasp or handle?	☐	☐
b) Do you have any trouble walking about?	☐	☐
c) Do you have any trouble bending down and picking up an object from the floor?	☐	☐
d) Do you require a walking stick cane/walker to move about?	☐	☐
e) Do you have any trouble reading or seeing the individual grains of rice/corn on your plate? (with glasses worn)	☐	☐
f) Do you have trouble seeing a person from across the room? (12 feet/3.5 meters) (with glasses worn)	☐	☐
g) Do you have trouble speaking and being understood?	☐	☐
h) Do you have any trouble hearing what is said in a normal conversation?	☐	☐

Subject Medical History

14. Have you experienced any of the following in the last six months?

	No	Yes		No	Yes
a) Chest pain or tightness with usual activity	☐	☐	i) Vomiting	☐	☐
If Yes, —————> does the pain spread to the back, neck or inner border of arm	☐	☐	j) Loss of appetite	☐	☐
b) Breathlessness with usual activity	☐	☐	k) Painful or bleeding teeth/gums	☐	☐
c) Cough for at least 2 weeks	☐	☐	l) Jaundice	☐	☐
d) Any sputum while coughing	☐	☐	m) Burning while passing urine	☐	☐
e) Blood in sputum	☐	☐	n) Swelling of feet	☐	☐
f) Wheezing or whistling in the chest	☐	☐	o) Swelling of face	☐	☐
g) Early morning cough with chest tightness	☐	☐	p) Blood in urine	☐	☐
h) Loose stools/diarrhea for at least 3 days	☐	☐	q) Involuntary weight loss of > 3kg	☐	☐

15. Not applicable in South Africa

16a) Do you use glasses/spectacles/contact lenses at present?

No

☐

Yes

☐

b) Do you use a hearing aid?

No

☐

Yes

☐

Adult Questionnaire

Cancer Sites

- 1= Mouth
- 2= Esophagus
- 3= Stomach
- 4= Small intestine
- 5= Large intestine including rectum
- 6= Pancreas
- 7= Liver
- 8= Lung
- 9= Breast
- 10= Cervical/uterine/ovarian
- 11= Prostate
- 12= Head and neck
- 13= Other, specify

Subject ID

Centre #

Community#

Household #

Subject #

Subject Initials

F

M

L

17. Have you ever been diagnosed with any of the following?(check all that apply)

	No	Yes	#of yrs since diagnosis		No	Yes	#of yrs since diagnosis
a) Diabetes	☐	☐		i) COPD	☐	☐	
b) Hypertension/ high blood pressure	☐	☐		j) Asthma	☐	☐	
c) Stroke	☐	☐		k) Tuberculosis	☐	☐	
d) Angina/heart attack/ Coronary artery disease	☐	☐		l) Malaria	☐	☐	
e) Heart failure	☐	☐		m) Chagas	☐	☐	
f) Other heart disease	☐	☐		n) HIV/AIDS	☐	☐	
g) Cancer	☐	☐					

Please refer to facing page for cancer sites

site

other, specify

18. Have you been taking any medications regularly (ie. at least once per week) in the last month? ☐ No →go to 19 ☐ Yes

a) If yes, for what conditions:

	No	Yes
Blood pressure	☐	☐
Cholesterol lowering drugs	☐	☐
Stroke	☐	☐
Diabetes	☐	☐
Asthma	☐	☐
Chinese medicine	☐	☐
Others	☐	☐
Unknown	☐	☐

If Yes, specify

Adult Questionnaire

18b) If name of medication is unknown, please list as unknown.

Subject ID

Centre #

Community#

Household #

Subject #

Subject
Initials

F M L

18b) List all the medications you are currently consuming at least once a week for the last month?

i) _____

ii) _____

iii) _____

iv) _____

v) _____

vi) _____

vii) _____

viii) _____

Men go to question #23

For Women Only (Questions 19 - 22)

19. Are you currently pregnant ? ☐ No ☐ Yes → Go to #21

20. Do you still have periods? ☐ No → (answer 20a) ☐ Yes → Go to #21

a) How many years since you stopped menstruating? years

21. Have you ever used an oral/ injectable contraceptive? ☐ No ☐ Yes

22a) How many live children have you given birth to? Boys Girls

b) Did you breast feed any of your children? ☐ No ☐ Yes

Adult Questionnaire

23. Accidents and Injuries

Location of Injury

- 1= Factory/industrial place
- 2= Office
- 3= Agriculture field/farm
- 4= Home
- 5= Road
- 6= Sport/game e.g. track, court, field, etc.
- 7= Public building
- 8= Mine/quarry
- 9= Construction site e.g. building, road-works, etc.
- 10 = Other

Type of Injury

- 1= Burns
- 2= Scalds
- 3= Fractures
- 4= Muscle and ligament sprains/tears
- 5= Cuts and lacerations
- 6= Bruises and abrasions
- 7= Suffocation
- 8= Head injury (where person did not lose consciousness)
- 9= Head injury (where person lost consciousness for some time)

Subject ID

Centre #

Community#

Household #

Subject #

Subject
Initials

F

M

L

23. During the past 12 months, have you had any injuries that were serious enough to limit your normal activities? (check all that apply)

☐ No → Go to #24

☐ Yes → (answer 23a - 23s)

If yes, please provide details:

Cause of injury

Please refer to facing page for Location and Type Codes

Location

Type

Absence from work or usual activities (Days)

a) Motor vehicle accident (as a passenger)	☐ No	☐ Yes	→			
b) Motor vehicle accident (as a pedestrian)	☐ No	☐ Yes	→			
c) Struck by an object	☐ No	☐ Yes	→			
d) Explosion	☐ No	☐ Yes	→			
e) Natural/environmental factors (gales/cyclones/lightning, etc.)	☐ No	☐ Yes	→			
f) Suffocation	☐ No	☐ Yes	→			
g) Poisoning	☐ No	☐ Yes	→			
h) Snake/scorpion bite	☐ No	☐ Yes	→			
i) Fall	☐ No	☐ Yes	→			
j) Fire/flames, resultant fumes	☐ No	☐ Yes	→			
k) Physical assault (gun, kidnapping, etc.)/violent crime	☐ No	☐ Yes	→			
l) Domestic violence (beaten by a family member)	☐ No	☐ Yes	→			
m) Drowning/submersion	☐ No	☐ Yes	→			
n) Hot or corrosive liquids/floods/substances	☐ No	☐ Yes	→			
o) Crush injuries (boulders, building materials, etc.)	☐ No	☐ Yes	→			
p) Accident caused by machinery	☐ No	☐ Yes	→			
q) Attempted suicide	☐ No	☐ Yes	→			
r) Armed conflict	☐ No	☐ Yes	→			
s) Other(specify) _____	☐ No	☐ Yes	→			

Adult Questionnaire

Location of Fractures

- 1= Hip/pelvis
- 2= Thigh
- 3= Leg
- 4= Forearm
- 5= Wrist
- 6= Hand/finger
- 7= Vertebrae (back)
- 8= Other

Fractures: In situations where subjects are in a cast and cannot differentiate between ligament tear or fracture, include as fracture only if doctor confirmed it as a broken bone

25c) Tobacco: Regular use is defined as consuming at least one tobacco product per day.

Duration of use:

For those that have consumed tobacco for <1 year, please enter "0"

Subject ID

Centre #

Community#

Household #

Subject #

Subject Initials

F

M

L

24. Have you ever fractured a bone? ☐ No (go to #25) ☐ Yes (if yes, answer a),b) and c)

a) Number of fractures

b) Years since last fracture

(yrs)

c) Bone (s) broken in the most recent fracture(if more than 3, list most severe sites)

(location)

If other, specify

Please refer to facing page for fracture locations

Tobacco

25. Which best describes your history of tobacco use?

a) ☐ Formerly used tobacco products

☐ Currently use tobacco products

☐ Never used tobacco products

Go to #26

b) At what age did you start?

yrs

c) Have you ever regularly used any of the following tobacco products? (check all that apply)

Past users only				
	Average amount/day	Duration (years)	When Stopped (years ago)	If less than 1 yr (months ago)
(i) Cigarettes (all kinds)	number			
(ii) Beedies	number			
(iii) Cigars	number			
(iv) Pipes	number			
(v) Sheesha/water pipe Hookah	# of times			
(vi) Chewing tobacco	# of times			
(vii) Snuff	# of times			
(x) Other Specify				

Subject ID

Centre #

Community#

Household #

Subject #

Subject
Initials

F M L

Question 26 to be answered by non-smokers and former smokers only

26. During the past 12 months, have you been regularly (at least once per week) exposed to other people's tobacco smoke?
("Exposed" is defined as a minimum of 5 consecutive minutes, during which you inhale other people's smoke.)

☐ No → Go to #27

☐ Yes → Please answer questions 26a

a) Over the past 12 months, what has been your typical exposure to other peoples smoke?
("Exposed" is defined as a minimum of 5 consecutive minutes, during which you inhale other peoples smoke)

Select ONE only

☐ 1-2 times/week

☐ 3-6 times/week

☐ at least once a day

☐ 2-3 times/day

☐ 4 or more times/day

27. Not applicable in South Africa

Adult Questionnaire

28c) **Alcoholic Beverage:** Regular use is defined as at least once a month.

Subject ID

Centre #

Community#

Household #

Subject #

Subject

Initials

F

M

L

28. Which best describes your history of alcohol use?

a)

☐ Formerly used alcohol products

☐ Currently use alcohol products

☐ Never used alcohol products

→ Go to #29

b) At what age did you start?

yrs

c) What forms of alcohol have you regularly used? (check all that apply)

Form of Alcohol	Approx. size of one "drink"	Frequency			Average # of drinks	Duration (years)	Past users only When Stopped (years ago)
		Daily	Weekly	Monthly			
(i) Spirits(rum,whisky, gin,vodka etc)	30ml	☐	☐	☐			
(ii) Wine	125ml	☐	☐	☐			
(vi) Beer	375ml	☐	☐	☐			
(vii) Country liquor/arrack/ sugar cane spirit	30ml	☐	☐	☐			

d) At least once a month, do you consume >5 alcoholic drinks/day?

☐ No

→ Go to #29

☐ Yes

i) How many times per month do you consume >5 alcoholic drinks in a day?

ii) What is the average number of drinks that you consume each time?

29 a) During your longest or nocturnal sleep period, what time do you normally go to bed?

:

(00:00-23:59)

b) During your longest or nocturnal sleep period, what time do you normally wake up?

:

(00:00-23:59)

c) Do you usually take naps/siestas?

☐ No

☐ Yes

→ Total nap duration

mins

Adult Questionnaire

33. **Civic organization**: are defined as non-profit, voluntary organization societies, self help groups and clubs.

Religious organization: are defined as different types of formal and informal groups set up on a religious basis.

Subject ID

Centre #

Community#

Household #

Subject #

Subject Initials

F

M

L

30. Are you a member of any of the following:

How often do you participate in the activities of this group?

Per Month

OR

Per Year

(i) Self help group, Co-operative, Social club, Sports club,

☐ No

☐ Yes

→

(ii) Religious Group (e.g: church group, etc.)

☐ No

☐ Yes

→

(iii) Other

☐ No

☐ Yes

→

Specify

31. Please answer the following: (choose only one option for each)

	Strongly Disagree	Somewhat Disagree	Somewhat Agree	Strongly Agree
(i) People are generally honest and want to help others.	☐	☐	☐	☐
(ii) If I do nice things for someone, I can anticipate that they will respect me and treat me just as well as I treat them.	☐	☐	☐	☐

32a The television, radio, newspaper or magazine advertisements help me decide to buy the type of: (choose only one option for each)

Not Applicable

	Strongly Disagree	Somewhat Disagree	Somewhat Agree	Strongly Agree	Not Applicable
(i) Cooking oil	☐	☐	☐	☐	☐
(ii) Flour	☐	☐	☐	☐	☐
(iii) Rice/ Maize meal	☐	☐	☐	☐	☐

32b The television, radio, newspaper or magazine advertisements influence whether I buy: (choose only one option for each)

	Strongly Disagree	Somewhat Disagree	Somewhat Agree	Strongly Agree	Not Applicable
(i) Soft drinks	☐	☐	☐	☐	☐
(ii) Snacks	☐	☐	☐	☐	☐
(iii) Cigarettes	☐	☐	☐	☐	☐
(iv) Alcohol	☐	☐	☐	☐	☐

33. In a difficult situation, whose help can you count on from?(Please see facing page for definitions)

(i) Civic organizations: specify

☐none

☐little

☐moderate/average

☐a great deal

(ii) Religious organizations: specify

☐none☐little☐moderate/average☐a great deal

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34. Have you experienced any of the following events during the last 12 months?

	No response	No	Yes	
(i) Loss of job	☐	☐	☐	
(ii) Retirement	☐	☐	☐	
(iii) Loss of crop/business failure	☐	☐	☐	
(iv) Household break in	☐	☐	☐	
(v) Marital separation/divorce	☐	☐	☐	
(vi) Other major intra-family conflict	☐	☐	☐	→ Please specify _____
(vii)Major personal injury or illness	☐	☐	☐	
(viii)Violence	☐	☐	☐	
(ix) Armed conflict/war	☐	☐	☐	
(x) Death of a spouse	☐	☐	☐	
(xi) Death/major illness of another close family member	☐	☐	☐	
(xii) Other major stress	☐	☐	☐	→ Please specify _____
(xiii) Wedding of family member	☐	☐	☐	
(xiv) New job	☐	☐	☐	
(xv) Birth in the family	☐	☐	☐	
(xvi) Seperation from family	☐	☐	☐	
(xvii) Unavailability of food/ food insecurity	☐	☐	☐	

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35. Please answer the following: (Choose only one option for each)

For the following question, stress is defined as feeling irritable or filled with anxiety, or as having sleeping difficulties as a result of conditions at work or at home.

	No response	Never Experienced Stress	Some Period of Stress	Several Periods of Stress	Permanent Stress
a) How often have you felt stress at work in the last 12 months? (Mark here if not applicable: i.e. no longer working ☐)	☐	☐	☐	☐	☐
b) How often have you felt stress at home in the last 12 months?	☐	☐	☐	☐	☐

36. What level of financial stress have you felt in the last 12 months?

☐ No response

☐ Little/none

☐ Moderate

☐ High/severe

37. During the past twelve months, was there ever a time when you felt sad, blue, or depressed for two weeks or more in a row?

☐ No

☐ Yes

→ If yes, during those times, did you:

	No response	No	Yes
a) Lose interest in most things like hobbies, work or activities that usually give you pleasure?	☐	☐	☐
b) Feel tired or low on energy?	☐	☐	☐
c) Gain or lose weight?	☐	☐	☐
d) Have more trouble falling asleep than you usually do?	☐	☐	☐
e) Have more trouble concentrating than usual?	☐	☐	☐
f) Think a lot about death (either your own, someone else's, or death in general)	☐	☐	☐
g) Feel down on yourself, no good or worthless?	☐	☐	☐

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38. Please answer the following: (Choose only one option for each)

	Strongly Disagree	Somewhat Disagree	Somewhat Agree	Strongly Agree
a) I can do most of my regular shopping (food, household necessities, etc.) at stores within easy walking distance (less than 15 minutes) of my home.	☐	☐	☐	☐
b) Walking or bicycling in my neighbourhood is difficult because of the speed and/or amount of traffic.	☐	☐	☐	☐
c) My neighbourhood is generally free from pollution (litter, air pollution and noise pollution).	☐	☐	☐	☐
d) My neighbourhood streets are well lit at night.	☐	☐	☐	☐
e) I can see other people when I am walking in my neighbourhood.	☐	☐	☐	☐
f) I can speak to other people when I am walking in my neighbourhood.	☐	☐	☐	☐
g) There is a high crime rate in my neighbourhood.	☐	☐	☐	☐
h) There is a problem with unattended dogs in my neighbourhood.	☐	☐	☐	☐

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38a) Please answer the following: (Please check all that apply)

i) Has your household been a victim of the following crime(s) in the last 12 months?

	No	Yes
1. Armed robbery	☐	☐
2. Violent attacks	☐	☐
3. Murder	☐	☐
4. Vehicle hijacking	☐	☐
5. House breaking	☐	☐
6. Theft	☐	☐
7. Rape	☐	☐
8. Women abuse eg. (beat,swear-words,sexual) please specify _____	☐	☐
9. Child abuse eg. (burn,swear-words,rejection) please specify _____	☐	☐
10. Child sexual abuse	☐	☐
11. Other, please specify _____	☐	☐

ii) Do you think that crime in your area has increased in the past 5 years? ☐ No ☐ Yes

if yes, which of the following crime(s)?

☐ Armed robbery

☐ Violent attacks

☐ Murder

☐ Vehicle hijacking

☐ House breaking

☐ Theft

☐ Rape

☐ Women abuse

☐ Child abuse

☐ Child sexual abuse

☐ Other, please specify _____

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38b) Questions on HIV:

i) Do you know people who have HIV/AIDS? ☐ No ☐ Yes

if yes, which of these people: (please mark all that apply)

- ☐ Your children
- ☐ Your grandchildren
- ☐ Your spouse
- ☐ Your family members
- ☐ Your friends
- ☐ People in the community

ii) What would you consider the mean age of the people who are ill/have died of HIV/AIDS?

- ☐ Younger than 10 years
- ☐ Between 11-20 years
- ☐ Between 21-30 years
- ☐ Between 31-40 years
- ☐ Between 41-50 years
- ☐ Over 50 years

iii) If someone in your household is HIV positive, who is the primary caregiver?

- ☐ Spouse
- ☐ Parents
- ☐ Family member
- ☐ Child.children
- ☐ Friends
- ☐ Volunteer

38c) Do you care for any orphans in your family? ☐ No ☐ Yes

Adult Questionnaire

40b) Health History:

Cancer Sites

- 1= Mouth
- 2= Esophagus
- 3= Stomach
- 4= Small intestine
- 5= Large intestine including rectum
- 6= Pancreas
- 7= Liver
- 8= Lung
- 9= Breast
- 10= Cervical/uterine/ovarian
- 11= Prostate
- 12= Head and neck
- 13= Other, specify

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39. How long would it take you to get from your house to the nearest facility if you walked?

	Minutes	Don't know		Minutes	Don't know
i) grocery/convenience store			iv) video store		
ii) bank			v) non-fast food restaurant		
iii) post office			vi) fast food restaurant		

40a) Total number of siblings

b) Health History: Complete for all parents and siblings, alive or dead

	Father			Mother			Siblings			# of siblings with the condition
	Unknown	No	Yes	Unknown	No	Yes	Unknown	No	Yes	
Diabetes										If yes →
Coronary Heart Disease										
High Blood Pressure										
Stroke										
Cancer										
Please refer to facing page for cancer sites										
if Yes, indicate site										
	↓			↓			↓			
	Other, Specify			Other, Specify			Other, Specify			

Adult Questionnaire

If subject refuses to provide any of the measures, enter a value of “0” into each of the boxes for that question

For more detailed instructions please refer to the instruction manual

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41. Physical Measurements

Sitting
a) Right arm
blood
pressure

#1

Systolic

Diastolic

mmHg

#2

Systolic

Diastolic

mmHg

b) Heart
Rate

#1

beats/min

#2

beats/min

c) Waist

#1

.

cm

☐ minimal/no
clothing

#2

.

cm

☐ full clothing

d) Weight

.

kg

☐ minimal/no
clothing

.

kg

☐ full clothing

e) Hip

#1

.

cm

☐ minimal/no
clothing

#2

.

cm

☐ full clothing

f) Height

.

cm (without shoes)

42a) Circumference of
mid upper right arm:

.

cm

b) Circumference of right
calf:

.

cm

c) Head Circumference:

.

cm

d) Upper flexed arm
circumference

.

cm

43a) Right arm triceps
skinfold:

#1

.

mm

#2

.

mm

#3

.

mm

b) Right calf
skinfold:

#1

.

mm

#2

.

mm

#3

.

mm

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c) Biceps skinfold

#1

.

mm

#2

.

mm

#3

mm

d) Subscapular skinfold

#1

.

mm

#2

.

mm

#3

mm

e) Supra spinal skinfolds

#1

.

mm

#2

.

mm

#3

mm

44 a) Humerous breadth

.

cm

b) Femur breadth

.

cm

45. Grip Strength (Maximal contraction):

a) Non-dominant hand:

#1

kg.

#2

kg.

#3

kg.

b) Dominant hand:

#1

kg.

#2

kg.

#3

kg.

Adult Questionnaire

If subject refuses to provide any of the measures, enter a value of “0” into each of the boxes for that question

For more detailed instructions please refer to the instruction manual

46. Spirometry:

American Thoracic Society criteria for acceptable spirograms:
Spirograms are acceptable if they are free from:

- 1. Cough during exhalation
- 2. Early termination or cut-off
- 3. Variable effort
- 4. Leaks
- 5. Obstructed mouth piece

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46. Spirometry:

a) FEV1 (Litre): #1 . #2 . #3 .

b) Does FEV1 obtained meet ATS criteria?

☐

No → (answer (i) to (iii))

☐

Yes → Go to c)

Reasons for not meeting the ATS criteria: (check all that apply)

i) Cough ☐ii) Values not within 0.2L of each other ☐iii) Less than 3 values ☐c) FVC (Litre): #1 . #2 . #3 .

d) Does FVC obtained meet ATS criteria?

☐

No → (answer (i) to (iii))

☐

Yes → Go to e)

Reasons for not meeting the ATS criteria: (check all that apply)

i) Cough ☐ii) Values not within 0.2L of each other ☐iii) Less than 3 values ☐e) PEFR (Litre/min): #1 #2 #3

f) Does PEFR obtained meet ATS criteria?

☐

No → (answer (i) to (ii))

☐

Yes → Go to Q#47

Reasons for not meeting the ATS criteria: (check all that apply)

i) Cough ☐ii) Less than 3 values ☐

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47. Not applicable in South Africa

48. ECG obtained? No ☐ —→ Go to #49 Yes ☐

a)

2

0

year

month

day

→

Place ECG :File Label Here

b) Please print ECG label #:

49 a) Blood sample obtained? No ☐ —→ Go to #50 Yes ☐

b) ☐ Fasting sample ☐ Non-fasting sample

c)

2

0

year

month

day

Time

:

→

Hours since any food/beverage consumed (excluding water)

(00:00-23:59)

d) Please print Blood label #:

Place Blood label here

50 a) Urine sample obtained? No ☐ —→ Go to #51 Yes ☐

b) ☐ Fasting sample ☐ Non-fasting sample

c) Please print Urine label #:

Place Urine label here

51. Name of Interviewer:

(please print) First Initial Last Name

Interviewer Code: