RELATIONSHIPS BETWEEN PHYSICAL ACTIVITY, CARDIORESPIRATORY FITNESS AND SEDENTARY BEHAVIOUR, AND RISK FACTORS FOR CARDIOVASCULAR DISEASE AND TYPE 2 DIABETES, IN BLACK SOUTH AFRICAN WOMEN

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DECLARATION

I, Kasha Dickie, hereby declare that the work on which this thesis is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is submitted for another degree in this or any other university.

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ABBREVIATIONS

ACSM - American College of Sports Medicine
AFM - Appendicular Fat Mass
AHA - American Heart Association
AIDS - Acquired Immunodeficiency Syndrome
ARV - Anti-retroviral drug
BMI - Body Mass Index
BP - Blood Pressure
CDC - Centers for Disease Control and Prevention
CFM - Central Fat Mass
cm - centimetres
cm^2 - centimetres squared
CRF - Cardiorespiratory Fitness
CT - Computerised Tomography
CVD - Cardiovascular Disease
CV% - Coefficient of Variance
counts/min - counts per minute
DBP - Diastolic Blood Pressure
DSAT - Deep Subcutaneous Adipose Tissue
DSTV - Digital Satellite Television
DXA - Dual-energy X-ray Absorptiometry
FFSTM - Fat-free Soft Tissue Mass
FM - Fat Mass
GLUT4 - Glucose transporter type 4
GPAQ - Global Physical Activity Questionnaire
HDL-C - High-density Lipoprotein Cholesterol
HEPA - Health-enhancing physical activity
HICs - High-Income Countries
HIV - Human Immunodeficiency Virus
HR - Heart Rate
HR_{max} - Maximum Heart Rate
HOMA-IR - Homeostatic Model of Insulin Resistance
hr/day - hours per day
IR - Insulin Resistance
IPAQ - International Physical Activity Questionnaire
kg - kilograms
kg/m^2 - kilograms per metre squared
LDL-C - Low-density Lipoprotein Cholesterol
LPL - Lipoprotein Lipase
LMICs - Low- to Middle-Income Countries
m - metres
m^2 - metres squared
METs - Metabolic Equivalents

METmin/week - Metabolic Equivalents per minute per week
min/week - minutes per week
mmol/L - millimoles per Litre
MNET - Electronic Media Network
MVPA - Moderate- to Vigorous-intensity Physical Activity
mU/L - milliunits per Litre
NCDs - Non-communicable Diseases
OGTT - Oral Glucose Tolerance Test
PA - Physical Activity
SA - South Africa
SAT - Subcutaneous Adipose Tissue
SBP - Systolic Blood Pressure
SES - Socio-economic Status
SSA - Sub-Sahara Africa
SSAT - Superficial Subcutaneous Adipose Tissue
STEPS - The WHO STEPwise approach to Surveillance
Steps/day - Steps per day
T2D - Type 2 diabetes
TC - Total Cholesterol
TC/HDL-C – Total Cholesterol to High-density Lipoprotein Cholesterol ratio
TG/HDL-C - Triglyceride to High-density Lipoprotein Cholesterol ratio
VO_{2max} - Maximal Oxygen Consumption
WHO - World Health Organisation
yrs - years

ABSTRACT

Introduction: Non-communicable diseases (NCDs), including cardiovascular disease (CVD) and type 2 diabetes (T2D), constitute the second highest cause of mortality in South Africa (SA) and seem to be exacerbated by the high prevalence of obesity, particularly amongst black SA women. Although the aetiology of obesity is complex, common antecedents for its development include a sedentary lifestyle and poor nutrition.

Aims: The overall aim of this thesis was to examine the association between physical activity (PA) and risk factors for CVD and T2D in a sample of apparently healthy black SA women. The aims of this thesis were addressed in two separate studies with the following objectives: Study 1: i) to compare body composition and metabolic risk factors for CVD and T2D between active and inactive groups classified according to international PA recommendations for health (Part 1, cross-sectional analysis) and ii) to determine whether PA level predicts changes in body composition and metabolic risk factors for CVD and T2D over a 5.5-year follow-up period (Part 2, longitudinal analysis); Study 2: to examine the independent effects of PA, cardiorespiratory fitness (CRF) and sedentary time on body composition and metabolic risk factors for CVD and T2D (cross-sectional analysis).

Methods: In part 1 of study 1, a sample of 240 apparently healthy black SA women (26±7 years) underwent the following measurements in 2005/6: PA (Global Physical Activity Questionnaire (GPAQ)), body composition (dual-energy x-ray absorptiometry and computerised tomography), blood pressure, fasting glucose, insulin and lipid concentrations. Thereafter (part 2), a sub-sample of women (*n*=57) underwent follow-up testing after a 5.5-year follow period (2010/11), which included additional measurements of objective PA (accelerometry) and CRF (VO_{2max}, ml/kg/min) measured during a submaximal step-test. Study 2 included women from the follow-up subsample and 19 additional women (*n*=76). Cross-sectional comparisons of objective PA, CRF and sedentary time with body composition and metabolic risk factors for CVD and T2D were examined.

Results: Study 1: Using the GPAQ, the majority (61%) of women were sufficiently active, meeting the guidelines for moderate- to vigorous-intensity physical activity (MVPA) according to international criteria. Women who were active had significantly lower body weight ($p<0.001$), measures of body fat (BMI, fat mass, %body fat, waist circumference, central and appendicular fat mass, $p<0.001$), and measures of insulin resistance (fasting serum insulin, $p=0.010$ and HOMA-IR, $p=0.010$, respectively), and higher high-density lipoprotein cholesterol (HDL-C, $p=0.041$) compared to the inactive group. At follow-up, bodyweight increased from 82.0±19.6 kg to 89.5±19.2 kg ($p<0.001$) in the active group, and from 91.0±15.6 kg to 98.3±13.2 kg ($p<0.001$) in the inactive group, whereas serum lipid concentrations remained unchanged ($p>0.05$), and diastolic blood pressure decreased significantly in those who were active (78±7 vs. 74±14 mmHg, $p=0.039$). Study 2: Using

accelerometry as an objective measure of PA, more than half (51.3%) of the women met international MVPA criteria and the goal of ≥10 000 steps per day (55.3%). Greater light PA and steps per day, but not MVPA, were associated with lower trunk (central) fat mass (r=-0.25, p=0.03, r=-0.31, p=0.01 and r=-0.09, p=0.42, respectively). Conversely, greater sedentary time was associated with higher TG and TG/HDL-C (r=0.36, p=0.01 and r=0.34, p=0.04, respectively), and these relationships were independent of body fat. In addition, higher CRF was associated with reduced body fat% (r=-0.34, p=0.02) and central fat mass (r=-0.31, p=0.03), as well as reduced insulin resistance (HOMA-IR; r=-0.41, p=0.01). These associations were independent of body fat and PA, but not VAT. CRF was inversely associated with sedentary time (r=-0.31, p=0.03) and not with any of the PA variables (p>0.05).

Conclusion: Both PA and CRF level were associated with reduced total and central fat mass, and reduced metabolic risk for CVD and T2D amongst a sample of apparently healthy black SA women. Promotion of increasing daily PA, including light-intensity and MVPA, whilst reducing sedentary time, and increasing CRF should be encouraged to reduce levels of obesity and risk factors for CVD and T2D.

CHAPTER ONE

LITERATURE REVIEW

1.1 Introduction

Non-communicable diseases (NCDs), including type 2 diabetes (T2D) and cardiovascular disease (CVD), are a large global problem in low- to middle-income (LMICs) and high-income countries (HICs) [1]. In 2000, they constituted the second highest cause of mortality in South Africa (SA), accounting for an estimated 36% of all deaths [2]. Risk factors for CVD include hypertension, dyslipidaemia, tobacco-use, impaired fasting glucose, obesity and physical inactivity [3].

Data from SA population-based surveys, from as early as 1990, continue to show the high prevalence of CVD (14-33%) and diabetes (5-6%) [4,5], with 13-31% of the adult population between 1997-2004 reported to have at least one risk factor for CVD. However, evidence shows that the prevalence of CVD varies according to ethnicity in SA, with the risk of CVD shown to be lower, possibly due to the low prevalence of dyslipidaemia [5,6], in the black population compared to other ethnic groups [7,8,9]. Despite this, recent evidence highlights an increase in the prevalence of T2D [10,11] and CVD-risk [9,12], with the epidemiological transition, which is characterised by rapid urbanisation. Lifestyle and behavioural changes associated with increased urbanisation include decreased physical activity energy expenditure and changes in dietary intake, both of which have contributed to the significant progression of the obesity epidemic, particularly in the urban black population [13,14]. Recent findings from Peer et al. (2012) [11] suggest that the rapid rise in T2D prevalence is strongly related to higher adiposity level, as more than 80% of the black (urban) diabetic study participants were either overweight (Body Mass Index (BMI): ≥25-29.9 kg/m^2) or obese (BMI: ≥30 kg/m^2), and also had higher measures of central (abdominal) adiposity compared to their black (urban) non-diabetic counterparts.

Data from the most recent (2003) South African Demographic Health Survey [15] (SADHS) reported that the overall prevalence of overweight and obesity is high in women (15-65+ years), with more than 54.9% of SA women being classified as overweight or obese (BMI ≥25 kg/m^2). Black urban women (60.9%) had the highest prevalence of overweight and obesity compared to their black rural (49.6%), mixed ancestry (52.2%), white (38.0%) and Asian (59.2%) counterparts (Figure 1.1).

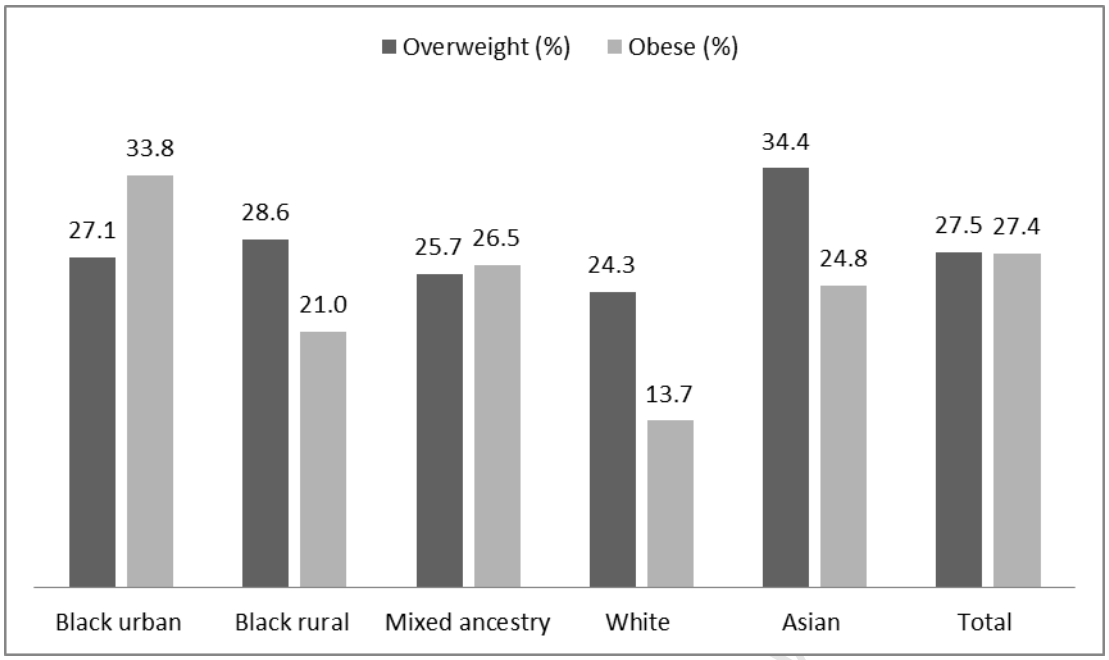

Figure 1.1 Prevelance (%) of overweight and obese SA adult women (SADHS, 2003)[15].

The clustering of CVD risk factors including obesity, dyslipidaemia, hypertension and impaired glucose tolerance, is commonly referred to as the metabolic syndrome. Numerous studies have explored relationships between central adiposity and metabolic risk for CVD, amongst women [16,17,18]. Components of abdominal adiposity include both visceral adipose tissue (VAT) and subcutaneous adipose tissue (SAT). Although both VAT and SAT have previously been shown to be individually associated with components of the metabolic syndrome, VAT showed a stronger association, highlighting its detrimental role in the development of CVD. To date, studies by Jennings et al. (2008 and 2009) [19,20] and Goedecke et al. (2009 and 2010) [21,22] describe an atypical presentation of CVD-risk factors amongst black urban SA women. When compared to their age-matched white counterparts, black women have lower levels of VAT and a favourable lipid profile, but are more insulin resistant.

It is clear that obesity, as well as the association of obesity with disease risk is complex, and may be affected by many factors, including ethnicity [23], genetics [24], socioeconomic status [25,26] and lifestyle factors [27], some of which are particularly unique to black SA women. The major focus of this review will be on the relationships between physical activity (PA), cardiorespiratory fitness (CRF) and sedentary behaviour, and risk factors for CVD and T2D, in black SA adult women. In addition, the review will focus on South African studies, with comparison from other Sub-Saharan African (SSA) countries, non-African LMICs as well as HICs, where

available. While important, other factors such as genetics and dietary factors fall outside the scope of this thesis.

Prior to examining these relationships I have defined PA, CRF and sedentary behaviour, and discuss the methods used to measure each of them.

1.2 Physical activity, cardiorespiratory fitness and sedentary behaviour

1.2.1 Definitions

Habitual physical activity (PA) is defined as body movements resulting from skeletal muscle contractions resulting in energy expenditure [28], and can also be referred to as 'physical activity energy expenditure' (PAEE). 'Exercise', on the other hand, is a component of PA and defined as planned or structured PA [29]. Cardiorespiratory fitness (CRF), can be defined as a physiologic state of well-being that allows one to meet the demands of daily living [34], and perform dynamic, large muscle, moderate- to vigorous-intensity (MVPA) exercise for prolonged periods [29].

Collectively, PA and exercise are termed 'activity energy expenditure' (AEE), a component of total energy expenditure (TEE). Other components of TEE include: basal metabolic rate (BMR) described as the energy needed to sustain vital functions, and diet-induced thermogenesis (DIT), the amount of energy required to digest, store and utilise sources of food.

Methodologies used to measure different intensities of PA and exercise include the use of maximal heart rate (HR_{max}), maximal oxygen consumption (VO_{2max}), and metabolic equivalents (METs) [29]. Maximal oxygen consumption (VO_{2max}) is defined as the product of maximal cardiac output (litre of blood per minute) and arterial-venous oxygen difference (millilitres of oxygen per litre of blood), and is commonly measured during a maximal exercise test to exhaustion together with HR_{max}. However, a more convenient method to measure PA and exercise intensities includes the use of METs. A MET, is a physiological measure and expression of the energy cost of physical activities and is defined as the ratio of metabolic rate (and therefore the rate of energy consumption) during a specific PA to a reference metabolic rate, set by convention to 3.5 ml/kg/·min of oxygen consumed whilst sitting relatively still [30]. In accordance with public health PA recommendations published by the American College of Sports Medicine (ACSM) and Centers for Disease Control

and Prevention (CDC) [31], light PA is defined as requiring <3 METs, moderate activities 3-6 METs, and vigorous activities >6 METs. Overall, these can be used to calculate AEE in MET-minutes per week (METmin/week), but excludes 'incidental' activity (non-purposeful activity related to activities of daily living [32,33]). As an example, an individual walking at a moderate-intensity level (~4 METs) for a total of 150 minutes per week, would expend a total of 600 METmin/week, and derive PA health-related benefits. However, ≥3000 METmin/week is recommended for health-enhancing benefits (HEPA, defined as ≥5 days of walking, moderate and/vigorous activities achieving ≥3000 METmin/week), most notably an improvement in cardiorespiratory fitness (CRF), including participation in structured exercise and/or sport at higher intensities (>6 METs) [29].

As an entirely separate entity, not the converse of PA, is 'sedentary behaviour', and refers to any activity characterised by an energy expenditure ≤1.5 METs, including time spent seated or in a reclined posture [33,35,36,37,38], excluding sleeping. Common sedentary behaviours include screen time (television and computer use), driving and reading.

1.2.2 Measurement methodologies

1.2.2.1 Physical activity

Activity energy expenditure (AEE) is a complex and multidimensional behaviour that is challenging to measure accurately [39]. Figure 1.2 highlights the different methodologies used to measure PA, as a component of AEE, including their respective degrees of difficulty and precision (Ekelund, unpublished).

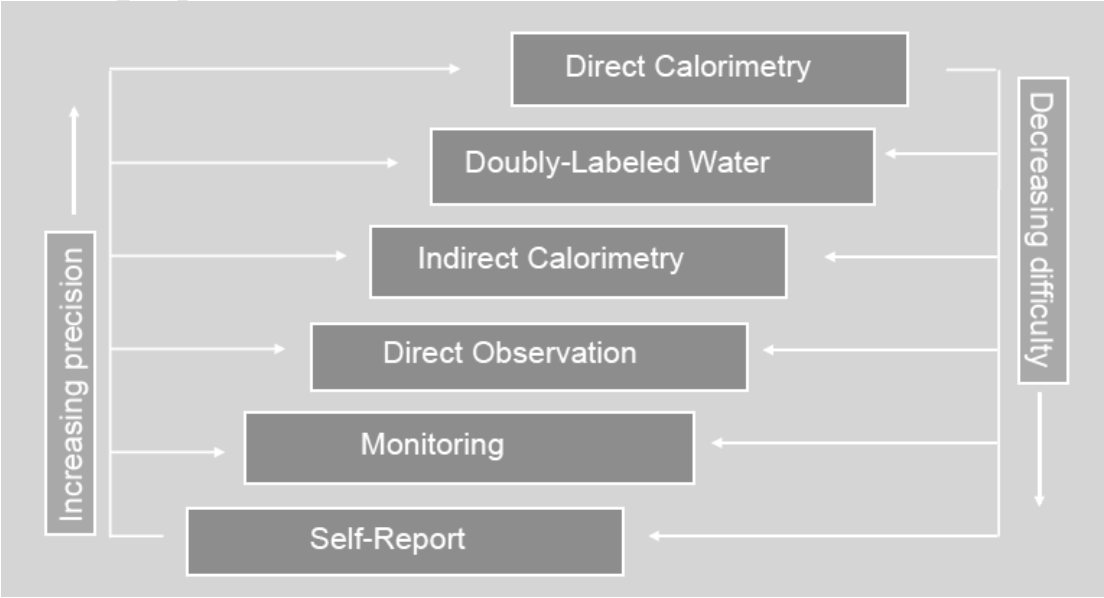

Figure 1.2 The physical activity measurement cascade (Ekelund, unpublished).

The criterion methods (direct calorimetry) used to measure TEE include room calorimetry (using a respiration or metabolic chamber) and the doubly-labeled water technique [40]. Alternatively, the use of indirect calorimetry, which includes the use of a ventilated hood system to measure BMR, can be used in addition to AEE. However, these methodologies are difficult, time-consuming and expensive. Thus, the use of less sophisticated methods including objective monitoring devices (combined heart rate and movement sensors, accelerometers and pedometers) and self-report tools (questionnaires and activity diaries) are easy alternatives to use.

Examples of self-report questionnaires that have been validated in multiple countries (both LMICs and HICs) include the International Physical Activity Questionnaire (IPAQ) [41,42] and the Global Physical Activity Questionnaire (GPAQ) [43]. The IPAQ was developed in 1998 by an International Consensus Group [41], as a means to standardise the capturing of PA surveillance data across different countries. Physical activity frequency, intensity (METs) and duration (minutes) over a 7-day period is captured, and used to calculate total METmin/week by multiplying 3.3, 4.0 and 8.0 METs for walking, moderate- and vigorous-intensity, respectively [30], by the number of minutes accumulated in minimum bouts of 10 minutes. Similarly, the GPAQ which forms part of the WHO STEP-wise approach to chronic disease risk factor surveillance (STEPS) is also used for PA surveillance [43]. The GPAQ provides an overall measure of PA on the basis of intensity (moderate and/or vigorous) and duration (min/wk and/or METmin/week), and also measures PA within specific domains (work-, travel- and leisure-time). Strengths related to the use of questionnaires such as the IPAQ and GPAQ include cost-effectiveness, ease of administration and low participant burden [44]. Conversely, a key limitation includes the potential problem of subjective recall, which objective monitoring devices can eliminate.

There are many different objective measurement tools available, including pedometers, accelerometers, as well as combined heart rate monitoring and movement sensing devices. Pedometers are small, portable devices which provide valuable feedback including the number of steps taken, distance covered, activity time and estimates of PAEE [45]. However, pedometers are not able to quantify intensity, which is important for chronic disease risk surveillance. On the other hand, accelerometers such as the ActiGraph MTI 7164, contain a motion sensor which measures the frequency and amplitude of acceleration of the individual, and

generates the information in the form of movement 'counts' measured per minute (counts/min) [44]. The intensity of PA is then determined using a set of predetermined cut-points that have been devised to quantify intensity levels [46]. The most frequently used cut-points in adult studies [47,48,49] include those derived by Freedson et al. (1998) [50]. The Freedson cut-points define and divide PA into four sub-categories, namely light-intensity (100-1951 counts/min), moderate-intensity (1952-5724 counts/min), vigorous-intensity (5725-9498 counts/min) and very vigorous-intensity (≥9499 counts/min). A clear advantage of using accelerometry lies in its ability to capture low movement counts which constitute light-intensity PA or 'incidental' activity (>1.5 to <3 METs), as well as time spent involved in sedentary behaviours (≤1.5 METs). However, a key limitation when using accelerometers relates to the wide range of proposed cut-points [46,50,51] and the different thresholds employed to characterise PA intensities. As an example, the cut-points employed for light-intensity differ greatly, with the widest range and highest threshold (100-2019 counts/min) reported by Troiano (2008) [51], compared to the smallest range and lowest threshold (100-759 counts/min) reported by Matthew (2005) [46]. This highlights the difficulty when comparing results from adult studies using different cut-points.

Lastly, the use of combined heart rate monitoring and movement sensing devices, for example the Actiheart (Cambridge Neurotechnology), provide a more accurate and individualised measure of AEE. The device converts minute-by-minute HR data into energy expenditure using pre-established calibration curves determined during an exercise test [52]. When the HR exceeds a pre-determined 'flex-HR point', defined as the mean of the highest HR during rest and the lowest HR during the lightest imposed exercise, the device is able to differentiate between periods of PA and rest, during free-living conditions (≥24-hour period).

1.2.2.2 Cardiorespiratory fitness

Maximal oxygen consumption (VO_{2max}) is accepted as the criterion measure of cardiorespiratory fitness (CRF) [29]. Whilst exercising to exhaustion on either a motorised treadmill- or mechanically-braked cycle ergometer, VO_{2max} can be measured using indirect calorimetry methods, and is commonly represented relative to bodyweight in millilitres of oxygen per kilogram per minute (ml/kg/min). However, the equipment required to complete this procedure is costly, thus a submaximal step-test can be used to estimate VO_{2max} using HR_{max}. For example, the 8-minute graded step-test (Medical Research Council (MRC), Cambridge, United Kingdom

(UK)) requires participants to increase their step frequency progressively on a 20cm high step, guided by an audible metronome at a rate of change of 2.5 body lifts per minute squared [53,54]. Throughout the test HR, measured in beats per minute, is captured using a HR monitor. After the test is terminated, seated recovery HR is monitored and recorded at the end of a 2-minute period. Thereafter, VO_{2max} was calculated for each participant using mathematical calculations inclusive of HR and PA intensity as described by Brage et al. (2005 and 2006) [53,54]. Firstly, the time data and step height were used to calculate power at each time point and subsequently the PA intensity (PAI) at each time point (PAI_step). Alpha step and beta step were then calculated from the slope and the gradient of the PAI_step against HR curve, during the stepping part of the test. These were both then used to calculate PAI_walk_run_max_ which in turn is used with resting metabolic rate (Oxford equation as described by Henry, 2005) [197] to calculate VO_{2max}.

1.2.2.3 Sedentary behaviour (time)

Methods used to characterise (measure) sedentary behaviour (time) are similar to those used for PA and thus include subjective (questionnaires and diaries) and objective tools (accelerometers). Examples of self-report measures include the capturing of television viewing time as a proxy measure of overall sedentary behaviour [55]. However, its application is limited as it excludes the measurement of other common sedentary behaviours which include time spent sitting or using a computer [56]. Alternatively, the GPAQ captures total sitting time over the course of a typical day, however similar to television viewing time, questionnaires have yet to report levels of reliability and validity [55].

The use of objective measurement methods to measure sedentary behaviour may help to address some of the limitations of self-report questionnaires [44]. For example, accelerometry can be used to estimate time spent in sedentary behaviour and does so by recording the total number of low movement counts at a specific cut-point (<100 counts/min) [46,50,51]. It also allows for short incidental breaks in sedentary time to be detected, either above or below the specified thresholds [44]. However, a key limitation of the traditional accelerometer such as the ActiGraph MTI 7164 is its lack of ability to distinguish different postures, for example standing, sitting or lying, an important component of sedentary behaviour. More recent and advanced models made by the same manufacturer include the ActiGraph GT3X and ActiGraph GT3X+. Both include an inclinometer function, which classify posture according to

four categories namely standing, sitting, lying and/or whether the device has been removed [44].

1.3 Physical activity

1.3.1 International physical activity recommendations for health

Novel studies published in 1958 [57] and 1978 [58], laid the foundation for the well-established relationship between PA and health, which has since generated an extensive body of evidence [59,60,61,62,63,64]. Since then several international PA recommendations for health have been published in order to raise public awareness of the importance of PA and health-related benefits [29].

The ACSM partnered by the American Heart Association (AHA) and other national organisations, issued the first PA recommendation to the public in the mid 1970's [65]. Based on scientific evidence highlighting the fitness-enhancing benefits associated with exercise and sports participation, its primary focus was to enhance cardiorespiratory endurance, and thus specified exercises (vigorous-intensity) involving large muscle groups, for at least 20 minutes on 3 or more days of the week. Following on from this, the understanding of the benefits associated with less intense (moderate-intensity) PA grew. By 1995 the ACSM, AHA, together with the CDC and the President's Council on Physical Fitness and Sports [66], recommended regular, moderate-intensity PA as an option, and individuals were 'active' if they engaged in aerobic activity in 10 minute bouts at,

i) a moderate-intensity for a minimum of 30 minutes, on at least 5 days of the week; or
ii) vigorous-intensity for a minimum of 20 minutes for three days of the week.

Since then, the guidelines have been revised using more recent clinical data and advice from a panel of medical and exercise experts [31]. The current ACSM/AHA guidelines published in 2007 [31] are age-group specific, and include guidelines for adults (18-65 years). An adult is referred to as 'active' if they engage in aerobic activity in 10 minute bouts at,

i) a moderate-intensity for a minimum of 150 minutes per week, and muscle-strengthening activities that require the functioning of all

major muscle groups (legs, hips, back, abdomen, chest, shoulders, and arms) on 2 or more days; or

ii) vigorous-intensity for a minimum of 75 minutes per week, and muscle-strengthening activities that require the functioning of all major muscle groups (legs, hips, back, abdomen, chest, shoulders, and arms) on 2 or more days; or

iii) a combined equivalent (both moderate- and vigorous-intensity), and muscle-strengthening activities that require the functioning of all major muscle groups (legs, hips, back, abdomen, chest, shoulders, and arms) on 2 or more days.

In addition the ACSM/AHA recommend that individuals exceed the aerobic activity guidelines and aim to double the duration of moderate-intensity (≥300 min/week) and/or vigorous-intensity (≥150 min/week) PA, in order to increase CRF and gain greater health-enhancing benefits [67,68].

More recent international criteria for PA and health using self-report tools such as the IPAQ [41] and GPAQ [43], have been developed and categorise individuals according to the following criteria:

i) inactive (<600 METmin/week),
ii) minimally/sufficiently active (600-2999 METmin/week) and
iii) HEPA active (≥3000 METmin/week).

In addition, the GPAQ uses its own specified cut-offs inclusive of frequency (days) [69], to distinguish participants as either 'active' or 'inactive'. Meeting GPAQ 'active' criteria requires engagement in aerobic activity for a minimum of 10 minutes per bout and for at least,

i) 30 minutes of moderate-intensity activity (or walking per day), on at least 5 days in a typical week; or
ii) 20 minutes of vigorous-intensity activity per day on at least 3 days in a typical week; or
iii) 5 days of any combination of walking and MVPA achieving a minimum of at least 600 METmin/week (calculated by multiplying the

number of minutes reported for moderate- and vigorous-intensity PA in the various domains by 4 and 8 METs [30], respectively).

With the launch of commercially sold step counters (pedometers and accelerometers), recommendations for the number of steps required per day to improve health, have also been developed. The guideline of ≥10 000 steps/day has been accepted by both the media and commercial entities and is linked to government agencies and/or professional organisations from various HICs (Australia, Japan, Northern Ireland, UK and the USA). However, in 2004 Tudor-Locke and Bassett proposed preliminary pedometer-determined PA cut-points for healthy adults [70], based on published literature, which include the following categories:

i) sedentary (<5 000 steps/day),
ii) low-active (5 000-7 499 steps/day),
iii) somewhat active (7 500-9 999 steps/day),
iv) active (≥10 000-12 499 steps/day), and
v) highly active (≥12 500 steps/day).

Furthermore, it is suggested that these recommendations supplement the more recent PA recommendations from the World Health Organisation (WHO) [71,72], released in 2010 (referred to as the WHO global standard), which classify individuals as 'active' if they engage in aerobic activity for a minimum of,

i) 150 minutes of moderate-intensity activity per week (min/week); or
ii) 75 minutes of vigorous-intensity activity min/week; or
iii) an equivalent combination of moderate- and vigorous-intensity activity (MVPA).

An increase in weekly volume, in order to derive additional health benefits (≥300 min/week of moderate-intensity activity or ≥150 min/week of vigorous-intensity activity; or an equivalent combination of min/week of MVPA) is recommended.

The numerous PA guidelines/recommendations for health have been formulated in an effort to guide and promote the importance of PA for public health. Despite differences in the frequency and the requirements for MVPA, there is a general consensus with regard to the type of activity required (aerobic), and that the higher

the volume of PA the greater the health benefit. Indeed, PA recommendations for health are important benchmarks (criteria) to determine PA and physical inactivity prevalences, and to examine their association with CVD-risk and health outcomes in different population groups.

1.3.2 Physical activity levels of SA adult women

To date, numerous small-scale SA studies have measured and characterised PA levels in adult women of different ethnicities [19,21,22,73,74,75,76,77], in relation to body composition [11,78,79,80,81,82], and metabolic risk factors for CVD and T2D [80,83]. In addition, data from two large SA population-based surveys [15,84] provide PA prevalence estimates between 2002-2004. According to IPAQ criteria, results from the World Health Survey in 2003 (WHO, 2005) [84] highlighted that 49% of a representative sample of SA adult women (urban and rural) were inactive (Figure 1.3).

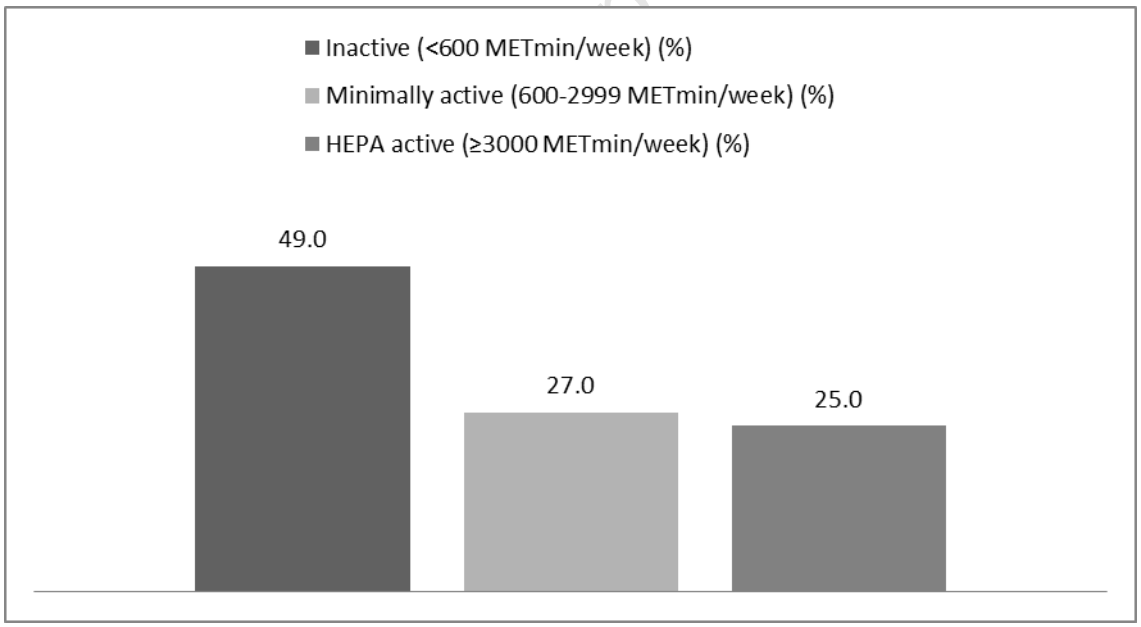

Figure 1.3 Prevalence (%) of physical activity in a representative sample of adult SA women from the World Health Survey in 2003 (WHO, 2005) [84].

In comparison, PA GPAQ data from the SADHS [15], report a higher prevalence of physical inactivity (63.2%) among adult women (15-65+ years) (*n*=4 131) as shown in Figure 1.4.

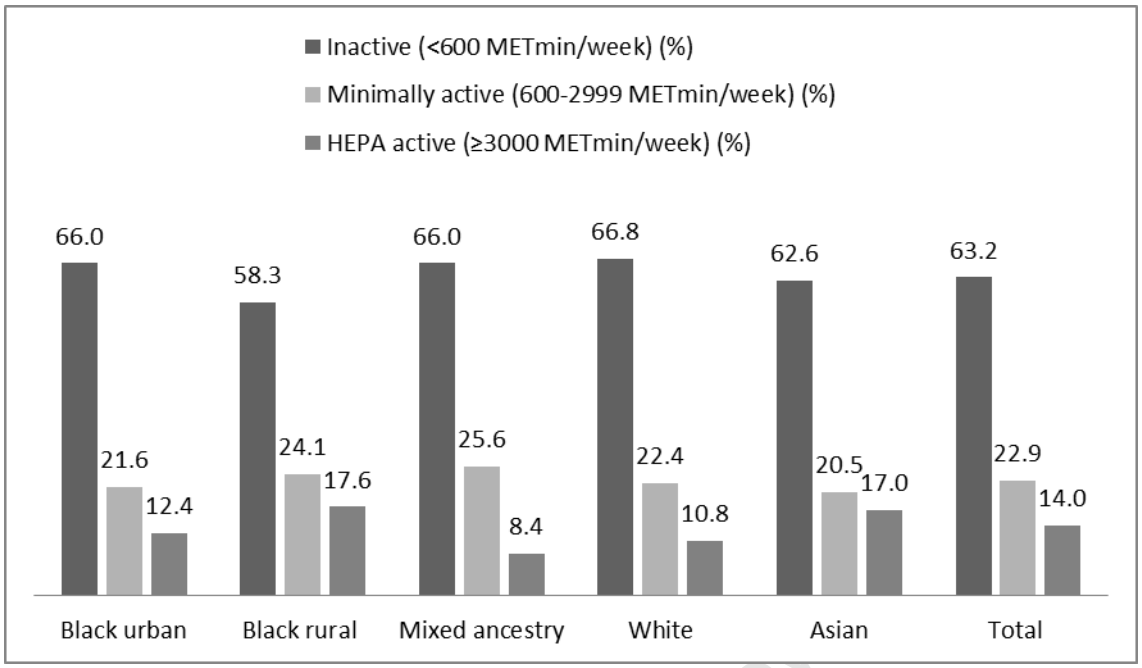

Figure 1.4 Prevalence (%) of physical activity in a representative sample of adult SA women from the South African Demographic Health Survey (2003) [15].

One of the benefits of using the GPAQ includes collecting data within three PA domains, namely work-, transport- and leisure-time. Based on the GPAQ data from the SADHS [15], the majority of PA, irrespective of female ethnic group, was achieved during leisure-time (53.9%), with a 13.1% difference shown between urban (49.8%) and rural (62.9%) groups. The contribution of work- and transport-related PA to overall PA (18.4% and 27.6%, respectively) were lower than leisure-time PA, with smaller differences between urban and rural groups (5.1% and 8.1%, respectively). In addition, women with no formal education were the most inactive (68%). In contrast, smaller studies in SA have shown black rural women accumulate more activity than black women living in urban settings [74,75,80]. Further, a small study from our laboratory has previously shown that black urban women accumulate less leisure-time activity and more transport-related activity than their white counterparts [21]. Differences in the findings may relate to the different questionnaires used, as well as subjective error and for example misinterpretation of PA domains (language and cultural differences [85,86]) when using the GPAQ. For instance, when comparing black urban to white women, leisure-time PA is lowest in white (39%) compared to black urban (49.8%), and thus highlights the possibility of these results confounded by the subjective PA tool used. While the smaller studies did not characterise sedentary behaviour or physical inactivity, the findings from the SADHS [15] highlight the likely contribution of physical inactivity to the increased risk of CVD and T2D in SA adult women.

1.3.3 Physical activity levels of adult women from other countries

As part of the WHO Stepwise approach to Surveillance (STEPS), a PA survey of 22 African countries (SA excluded) using the GPAQ, was recently completed [43]. Results from the study highlight the wide range of prevalence estimates for physical inactivity amongst adult women in Africa. On the extremes, adult women from Mali were reported to be the most inactive (66.6%), while women from Mozambique were the least inactive (6.6%). However, unlike SA, the study showed that leisure-time PA was consistently low (5%), compared to work- and transport-related PA (49% and 46%). Possible explanations for this finding may relate to the rapid rate of epidemiological transition in SA compared to other Sub-Saharan Africa (SSA) countries like those involved in the 22 African countries survey [43], as well as the possibility of misinterpretation of the GPAQ PA domains questioned. Nevertheless, these findings are in contrast to those from the SADHS [15] but not the smaller SA studies [21,77], and thus highlights the need for objective measures of PA.

On the other hand, PA prevalence estimates derived from the IPAQ among adult women from other countries outside of Africa, highlight the disparity in PA level between HICs and LMICs [87]. As shown in Figure 1.5, physical inactivity among adult women living in HICs (Australia, Canada and the USA) was lower compared to those living in LMICs (Argentina, Colombia and India).

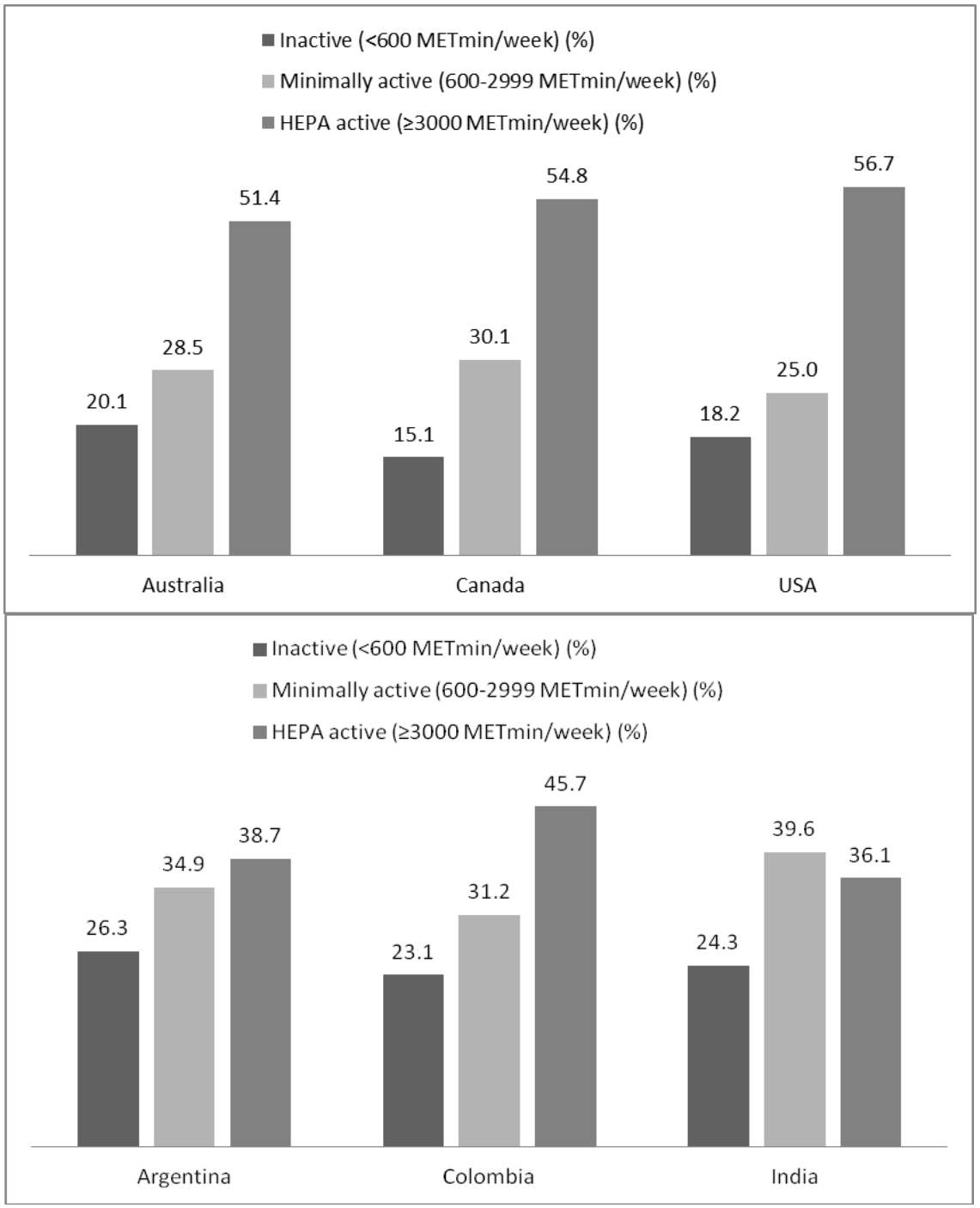

Figure 1.5 Prevalence (%) of physical activity in adult women (15-65 years) from 'The International Prevalence Study on Physical Activity' (2002-2004) [87].

Differences in patterns of PA among adult populations from HICs and LMICs were also highlighted in the study. Similar to the PA patterns described by Guthold et al. (2011) [43] in the African survey, the majority of PA performed in LMICs was for transport (walking) and typically performed at lower intensities. In contrast, the predominant PA domain in HICs was during leisure-time, with PA performed at higher intensities [88].

Overall, the results from these PA surveillance studies show how greatly PA level and PA patterns, both vary among different countries across the globe. More importantly, the results highlight the low levels of PA, particularly among women from LMICs such as SA and Mali. The reasons for the low level of PA may relate to limited access to exercise facilities and issues of safety [89]. Further, the negative influence of socio-cultural beliefs including weight-loss and the perception of illness, as well as the social stigma surrounding participation in sport and leisure-time activities perceived by the community as neglecting family and/or community responsibility (Brangan, unpublished). g

1.3.4 Relationships between physical activity and body fat distribution in adult women

International observational studies highlight the inverse association between PA and adiposity (body fat mass and its distribution) [90,91], which has also been shown to occur in a dose-response manner [92]. Prospective results from large international studies (VITAL Study [94] and Canadian Physical Activity Longitudinal Study [93]) show a tendency for adult women with higher PA levels (moderate-intensity) to report lower weight gain over time [93,94]. However, these results are not entirely consistent due to limitations in both study design (cross-sectional vs. longitudinal) and measurement methodology (subjective vs. objective), and thus it remains unknown whether an increase in adiposity is the consequence or cause of decreased PA levels [95].

Invariably, methodological measurement issues exist when measuring obesity and body fat distribution. To date, BMI is the standard measure of obesity and has been used to assess the global burden of disease [96]. Relationships between PA and BMI [97,98], as well as waist circumference (WC) [99], have previously been examined. However, studies reporting the use of higher precision body composition methods (dual-energy x-ray absorptiometry (DXA) and computerised tomography (CT)), which include relative and absolute body fat measurements and its distribution, may strengthen the associations previously found when using proxy measures of adiposity such as BMI, WC, and waist:hip ratio (WHR). Results from a multi-country study highlight the differences in body fatness and its distribution (using DXA), between women of five different ethnicities [100]. The study showed ethnic differences in the relationship between BMI and adiposity (%BF), as well as differences in central and peripheral fat depots. This study highlights the importance of using a

more accurate measure of body fat and its distribution when examining the relationship between obesity, PA and disease risk in different ethnic groups.

There is a paucity of data from SSA examining the relationship between PA and measures of adiposity. While many studies have reported the use of questionnaire-derived PA measures [11,19,21,22,74,76,77,83], objective PA measures [75,76,77,81], or both [77,81], none of them have directly investigated the association between PA and measures of obesity.

Of the few studies from SSA that have examined the relationship between PA and measures of adiposity, a cross-sectional study from Cameroon reported an inverse association between PAEE, measured using accelerometry, and %BF, measured using bioelectrical impedance [101]. Although few participants took part in the study (*n*=34), the study was able to describe free-living energy expenditure (TEE and AEE) using a direct calorimetry method (doubly-labeled water technique), and included both rural and urban, men and women. A number of small-scale SA studies [78,79,80,81,82] have explored the relationship between PA and measures of obesity (BMI, WC and %BF) in adult women, as summarised in Table 1.1.

Table 1.1 Summary of SA studies examining the relationship between physical activity and obesity, in black adult women (15-70 years), 2001-2012.

Reference	Study design (name of study)	*n*	Mean age (range)	Location (urban/rural)	Measures of physical activity (PA)	Measures of obesity	Findings
Tshabangu et al. 2001[74]	Cross-sectional	226	(18-70 yrs)	Gauteng Province (urban)	Subjective (Lifestyle questionnaire) (PA, min/day)	BMI & WHR	Did not explore any relationships between PA & BMI and WHR Majority were overweight (61%) Mean MVPA: 180 min/day
Kruger et al. 2002[78]	Cross-sectional (THUSA)	530	(15-70 yrs)	North West Province (urban)	Subjective (*Baecke* short questionnaire) (PA Index score (PAI)	BMI & WC	**Inverse relationship reported between PAI & BMI and WC** Fewer women in the highest PAI-tertile were obese compared to those in the lowest- & middle PAI-tertiles
Kruger et al. 2003[83]	Cross-sectional (THUSA)	530	~39 yrs	North West Province (urban)	Subjective (*Baecke* short questionnaire) (PA Index score)	BMI	Did not explore a relationship between PAI & BMI Majority of women were overweight (53.8%)
Cook et al. 2007[75]	Cross-sectional (DHDSS)	160	~34 yrs	Limpopo Province (rural)	Objective (Accelerometry) (PA, min/day)	BMI	Did not explore a relationship between PA & BMI Majority of the women were overweight Mean BMI: 26.6 kg/m^2 Mean MVPA: 247 min/day
Cook et al. 2008[79]	Cross-sectional (DHDSS)	121	~33 yrs) (15-55 yrs)	Limpopo Province (rural)	Objective (Pedometry) (PA, Steps/day)	BMI, WC & BF% (sum of 4 skinfolds)	**Inverse relationships reported between Steps/day & measures of obesity *(only BMI remained significant after adjusting for age)*** Majority of the women were overweight Mean BMI: 26.0 kg/m Mean BF%: 31.2 % Mean Steps/day: 9 085
Jennings et al. 2008[19]	Cross-sectional	223	(18-45 yrs)	Western Cape Province (urban)	Subjective (GPAQ) PAEE (METmin/week)	BMI & WC, BF% (DXA), VAT & SAT (CT)	Did not explore any relationships between PA & BMI and WC, BF%, VAT & SAT

Reference	Study design (name of study)	*n*	Mean age (range)	Location (urban/rural)	Measures of physical activity (PA)	Measures of obesity	Findings
Cook et al. 2009[80]	Cross-sectional (DHDSS)	206 [1997]	~44 yrs	Limpopo Province (rural)	Subjective [1997 & 2003/4] (PA Index level)	BMI & WC	**Inverse relationships between PAI level & both measures of obesity**
		138 [2003/4]	~36 yrs		Objective [only 2003/4] (Accelerometry) (counts-, Steps- & min/day)	BF% (sum of 4 skinfolds)	Linear relationships reported between PAI level & Accelerometry outputs **Inverse relationship between PAI level & BF% *(remained significant after adjusting for age)* however only tendencies reported with the other obesity measures**
							% of women meeting ACSM/ CDC physical activity guidelines [66]: 96.4%
Dugas et al. 2009[76]	Cross-sectional	20	~30 yrs	Western Cape Province (urban)	Subjective (self-report questionnaire) (PAEE, kJ/day)	BMI, WHR & BF% (DXA)	Did not explore any relationships between PAEE & BMI, WHR and BF%
					Objective (Respiration chamber) (PAEE, kJ/min)		Did not explore any relationships between PAEE & BMI, WHR and BF%
Dugas et al. 2009[81]	Cross-sectional	20	~23 yrs	Western Cape Province (urban)	Objective (Doubly-labeled water) (AEE, kJ/min)	BMI & BF% (isotope dilution method)	Non-significant relationships were reported between AEE & obesity measures Majority of the women were obese Mean BMI: 31.0 kg/m^2 Mean BF%: 43.5 %
					Objective (Accelerometry [*n*=13]) (PA, min/day & % awake time)		Non-significant relationships between % of awake time spent in vigorous-intensity PA & obesity measures
Goedecke et al. 2009[21]	Cross-sectional	29	~26 yrs	Western Cape Province (urban)	Subjective (GPAQ) (PAEE, METmin/wk)	BMI & WC, BF% (DXA), VAT & SAT (CT)	Did not explore any relationships between PAEE & BMI and WC, BF%, VAT & SAT

Reference	Study design (name of study)	*n*	Mean age (range)	Location (urban/rural)	Measures of physical activity (PA)	Measures of obesity	Findings
Cook et al. 2010[82]	Cross-sectional survey (DHDSS)	516	~41 yrs	Limpopo Province (rural)	Objective (Pedometry) Steps per day	BMI, WC	**Inverse relationship between steps/day & obesity measures *(remained significant after adjusting for age)***
Goedecke et al. 2010[22]	Cross-sectional	28	~26 yrs	Western Cape Province (urban)	Subjective (GPAQ) (PAEE, METs/day)	BMI & WC, BF% (DXA), VAT & SAT (CT)	Did not explore any relationships between PAEE & BMI and WC, BF%, VAT & SAT
Walter et al. 2011[77]	Cross-sectional study	180	(18-45 yrs)	Eastern Cape Province (urban)	Subjective[*n*=146] (GPAQ) (PAEE, METmin/week)	BMI	Did not explore any relationships between PAEE & BMI
					Objective[*n*=69] (Accelerometry) (PAEE-, steps-, MET- & min/day [Moderate & Vigorous])		Did not explore any relationships between PAEE & BMI
Peer et al. 2012[11]	Cross-sectional study	707	(25-74 yrs)	Western Cape Province (urban)	Subjective (GPAQ) (PA, min/week)	BMI, WC & WHR	No relationships were reported between PA & BMI, WC and WHR
							Significantly higher % of physical inactivity amongst those who were diabetic (11.6%) compared to those who were non-diabetic (6.1%) (p=0.035)

BMI, body mass index; WHR, waist:hip ratio; WC, waist circumference; %BF, percentage of body fat; VAT, visceral adipose tissue; SAT, subcutaneous adipose tissue

Results from the Transition and Health during Urbanisation of South Africans (THUSA) study of black urban women living in the North West Province (*n*=530), found an inverse association between subjectively measured PA level and BMI (r=-0.14; p=0.001) and WC (r=-0.15; p<0.001) [78]. When PA level was categorised according to tertiles, those in the highest tertile were less likely to be obese compared to those in the lowest tertile (OR=0.38; 95% CI: 0.22-0.66). Similarly, those in the middle PA tertile had approximately half the risk of obesity, compared to those in the least active tertile. Notably, the women at the highest risk of obesity were from higher income categories, with low PA.

Similarly, Cook et al. (2008 and 2010) [79,82] has shown that steps/day, measured using pedometers, is associated with a reduced risk of obesity, in a dose-dependent manner, in black rural women from the Limpopo Province (*n*=121). Results from their first study [79] showed that measures of obesity (BMI and WC), were significantly lower (52%) in those who reported ≥10 000 steps/day compared to those who were classified as sedentary (<5 000 steps/day) (p=0.028). This was confirmed by results from their second study, using a larger sample size (*n*=516) [82]. In another study using objectively measured PA (accelerometry), Dugas et al. (2009) [81] reported non-significant relationship between higher PA, and in particular vigorous-intensity PA, with lower BMI and %BF measured using the isotope dilution method. In addition, when examining relationships with AEE and TEE, measured using indirect calorimetry in a respiration chamber, with adiposity (BMI and %BF), neither were found to be significant. As mentioned, the failure to show an association between PA and BMI was likely due to the relatively small sample size (*n*=20).

The findings of these studies confirm the association between PA and obesity in black rural and urban SA adult women. However, to my knowledge, there are no studies that have determined whether urban black women meeting PA public health guidelines are indeed, less likely to be overweight or obese, and therefore at reduced risk for CVD and T2D. Thus, in this context it is important to investigate, quantify and characterise PA level according to international PA criteria, and determine if urban black women who are sufficiently 'active' have lower adiposity and metabolic risk for CVD and T2D, compared to their inactive counterparts.

1.3.5 Relationships between physical activity and metabolic risk factors for cardiovascular disease and type 2 diabetes in adult women

Metabolic risk factors for CVD and T2D include hypertension, dyslipidaemia, impaired glucose tolerance and insulin resistance [102], all of which are strongly associated with obesity [103,104] and when clustered together are referred to as the metabolic syndrome [105]. Epidemiological studies from HICs have shown that PA, and in particular leisure-time MVPA, is associated with a reduced risk of the metabolic syndrome in adults [106,107]. Results from the Canadian Heart Health Surveys completed from 1986-1992 [106], categorised adult participants according to PA criteria, and after adjusting for age and other behaviour/lifestyle factors, found that those who engaged in a minimum of 30 minutes per week of vigorous-intensity PA were less likely to have metabolic syndrome, compared to those who were inactive (failed to complete one session of PA for a minimum of 30 minutes continuous over a period of one week). Further, studies by Franks et al. (2004) [108] and Ekelund et al. (2005) [47] showed an inverse association between objectively measured AEE and clustered metabolic risk, which was independent of adiposity. Moreover, results from a longitudinal cohort study, showed that an increase in PAEE over 5.6-year period was associated with improvements in insulin sensitivity, glucose tolerance, fasting triglycerides, and a reduction in clustered metabolic risk score, that were all independent of change in adiposity (Ekelund et al., 2007) [48]. However, the application of these results are limited to white women living in a HICs, as women from other ethnic groups were excluded from the study. Nonetheless, in agreement with these studies in HICs, two cross-sectional studies of Cameroonian adults [101,109,110] showed a positive association between PAEE and improved metabolic outcomes. Using precise PAEE measures (doubly-labeled water technique), an inverse association was shown between PAEE and 2-hour plasma glucose concentration ($r=-0.43$; $p=0.01$), before and after adjusting for adiposity (BMI, WC or %BF). In a larger study (n=552), using objectively measured free-living energy expenditure, Assah et al. (2011) [110] found lower PAEE (44.2 ± 21.0 vs. 59.6 ± 23.7 kJ/kg/day; $p<0.001$) and a higher prevalence of metabolic syndrome (17.7 vs. 3.5%; $p<0.001$) in the urban compared to the rural Cameroonian adults. Overall, the study highlights the disparity in PAEE between rural and urban groups, and the increasing presence of physical inactivity linked to the increased prevalence of metabolic syndrome linked to urbanisation. The findings from small-scale cross-sectional SA studies [80,83] are summarised in Table 1.2.

Table 1.2 Summary of small-scale SA studies examining the relationship between physical activity and metabolic risk factors for CVD and T2D, in black adult women (15-70 years), 2003-2012.

Reference	Study design (name of study)	*n*	Mean age (range)	Location (urban/rural)	Measures of physical activity (PA)	Metabolic risk factors for CVD & T2D	Finding
Kruger et al. 2003[83]	Cross-sectional (THUSA)	530	~39 yrs	North West Province (urban)	Subjective (*Baecke* short-questionnaire) (PA Index score)	SBP, DBP TC, LDL-C, HDL-C, TG, GLU& INS (fasting)	**Most active women (highest PA tertile) (Mean BMI, 25.3 kg/m^2) had significantly higher mean HDL-C, lower mean TG & higher fasting GLU concentrations, compared to the less active & overweight counterparts** Lowest PA tertile group, had the highest mean: BMI: 28.7 kg/m^2 SBP: 128 mmHg TC: 4.2 mmol/L LDL-C: 2.8 mmol/L
Jennings et al. 2008[19]	Cross-sectional	223	(18-45 yrs)	Western Cape Province (urban)	Subjective (GPAQ) PAEE (MET/min/week)	SBP, DBP, TC, LDL-C, HDL-C, TG, GLU& INS (fasting)	Did not explore any relationships between PAEE and any of the metabolic risk factors for CVD & T2D
Cook et al. 2009[80]	Cross-sectional (DHDSS)	206 [1997] 138 [2003/4]	~44 yrs ~36 yrs	Limpopo Province (rural)	Subjective [1997 & 2003/4] (PA Index level (PAI))	SBP & DBP measured in 1997 & 2003/4 TC, LDL-C, HDL-C, TG & GLU (fasting), only measured in 1997	No association between PA Index level and hypertensive state ((≥140/90 mmHg) **Inverse relationship between PAI level & fasting plasma GLU** No association between PA Index level and diabetic state (Fasting GLU ≥7.0 mmol/L)
					Objective [only 2003/4] (Accelerometry) (counts-, steps- & min/day)		No relationships between objective PA measures & any of the metabolic outcomes were found and thus reported

Reference	Study design (name of study)	*n*	Mean age (range)	Location (urban/rural)	Measures of physical activity (PA)	Metabolic risk factors for CVD & T2D	Finding
Goedecke et al. 2009[21]	Cross-sectional	29	~26 yrs	Western Cape Province (urban)	Subjective (GPAQ) PAEE (MET/min/wk)	GLU& INS (fasting)	Did not explore any relationships between PAEE & fasting GLU and INS
Goedecke et al. 2009[111]	Cross-sectional	28	~26 yrs	Western Cape Province (urban)	Subjective (GPAQ) PAEE (MET/day)	SBP, DBP, TC, LDL-C, HDL-C, TG, GLU& INS (FSIGT)	Did not explore any relationships between PAEE and any of the metabolic risk factors for CVD & T2D
Peer et al. 2012[11]	Cross-sectional study	707	(25-74 yrs)	Western Cape Province (urban)	Subjective (GPAQ) (PA, min/week)	SBP, DBP, TC, LDL-C, HDL-C, TG, GLU& INS (OGTT)	No relationships were reported Significantly higher % of physical inactivity amongst those who were diabetic (11.6%) compared to those who were non-diabetic (6.1%) (p=0.035)

SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triglyceride; GLU, fasting plasma glucose; INS, fasting serum insulin; FSIGT, frequently sampled intravenous glucose tolerance test [111]; OGTT, oral glucose tolerance test [111]

Results from the THUSA study in black rural women (*n*=530) [83], showed that women who were most active had significantly higher mean HDL-C concentration and significantly lower mean TG, compared to women in the inactive group. Furthermore, the most active group also had significantly higher fasting plasma glucose concentrations, compared to the moderately active group. More importantly, the most active and overweight (BMI ≥25 kg/m^2) women had significantly lower mean LDL-C concentration, LDL-C:HDL-C ratio and fasting serum insulin concentrations, compared to women who were also overweight but inactive. Similarly, Cook et al. (2009) [80] using a 4-item PA index, showed a significant and inverse relationship between PA level, and fasting plasma glucose concentrations ($p<0.0001$), and a tendency for higher levels of PA level to be associated with lower blood pressure and serum lipid concentrations in a sample of rural women. To date, only a few SA studies have measured the relationship between PA and measures of insulin sensitivity and ß-cell function in black urban adult women using robust methods [104,112,113,107], namely the frequently sampled intravenous glucose tolerance test (FSIGT) [111] and the oral glucose tolerance test (OGTT) [12,16]. Peer et al. (2012) [11] found no association between PA levels (using the GPAQ) and prevalence of T2D, among black urban adults in the Western Cape. However, they did show a higher prevalence of physical inactivity (11.6%) in women with T2D compared those who were non-diabetic (6.1%) ($p= 0.035$). Although, the application of these results are limited by their use of subjectively measured PA. The possibility of over-reporting PA when using the GPAQ especially among women with known T2D was likely and may have confounded their overall findings. Thus, the results from all of these small-scale SA studies highlight the need for an objective measure of PA.

Overall, the data presented highlight the importance of increasing PA to reduce the risk for CVD and T2D. However, the use of subjectively measured PA in relation to overall disease risk is limited by the possibility of subjective error inclusive of language and cultural differences [85,86], which may influence study results. Thus, the investigation of the relationship between objectively measured PA and metabolic risk outcomes for CVD and T2D is needed in SA, and in particular in black urban women. Furthermore, it is not known whether PA level is associated with changes in metabolic risk for CVD and T2D over time, and whether a change in risk is independent of adiposity, especially in adult women who are already overweight or obese.

1.4 Cardiorespiratory fitness

1.4.1 Cardiorespiratory fitness, obesity and body fat distribution, in adult women

There is a growing body of evidence highlighting the health-related benefits associated with higher levels of CRF [59,60,61]. Furthermore, CRF is associated with higher levels of habitual PA, which in turn are associated with the reduction in all-cause and CVD mortality [114,115]. In addition, several studies have shown that it is a better indicator of health compared to measures of PA and obesity (BMI) [116]. Large-scale prospective studies examining CRF in relation to CVD risk factors in adult women, report similar findings [60,61]. For example, a study by Stevens et al. (2002) showed that CVD-risk was lower in women with high CRF and a high BMI, compared to women with low BMI and low CRF, after adjusting for potential confounding [60].

Several studies have examined the association between CRF and body fat distribution measures [117,118]. Data from a large observational survey (Canadian Fitness Survey) showed that when participants were matched for BMI, those with higher CRF had significantly lower WC measures compared to those with lower CRF[117]. Similar findings, between CRF and WC levels, as well as other more precise CT-derived body fat distribution measurements have also been reported [118,119]. Notably, results from the Dallas Cooper Clinic (USA) [214, 215] highlight significant and inverse associations (for a given BMI) between high CRF and lower abdominal adiposity (total-, VAT and SAT depots) and WC levels in men. Subsequently, Arsenault et al. (2007) [119], showed a similar relationship between higher CRF and lower VAT accumulation in adult men. The differences in abdominal adiposity between CRF groups provide insight into the possible mechanisms by which CRF attenuates the health-related risks attributed to obesity. However, all of these studies involved male participants.

To my knowledge, only one study has examined the relationship between CRF and CT-derived VAT in adult women (21-46 years) [120]. Maximal oxygen consumption (VO_{2max}) was determined during a maximal exercise motorised treadmill-test, in African-American (AA) and European-American (EA) women. Although matched for age, BMI and %BF, VAT was significantly lower in the AA compared to EA group

(64.4 ± 26.2 cm^2 vs. 94.5 ± 28.5 cm^2, p<0.01). In addition, women in the highest CRF tertile groups had significantly lower VAT compared with women in the lowest CRF tertile groups. Future studies are needed to determine whether these associations are present in other populations, and in women of different ethnicities and whether increased CRF is associated with reduced metabolic risk in these populations.

1.4.2 Cardiorespiratory fitness and metabolic risk for cardiovascular disease and type 2 diabetes, in adult women

Previous intervention [121] and cross-sectional [122] studies have examined the relationship between CRF and CVD-risk, and have shown that independent of weight status, high CRF attenuates overall CVD-risk. Furthermore, results from other cross-sectional studies [123] as well as data from the Aerobics Center Longitudinal Study (ACLS) [124,125], report an inverse association between CRF and metabolic syndrome prevalence, in adult men [124] and women [125]. Although, prospective data is limited [123,126,127] more recent results from the ACLS report important findings highlighting that low CRF is a strong and independent predictor of incident metabolic syndrome, in both adult men and women [128].

Numerous SSA studies have measured CRF [129,130,131] and/or CVD-risk [9,11,78] however, to my knowledge none have examined the relationship between the two. Studies by Assah et al. (2009) [109] and Cook et al. (2009) [80] reported the use of different submaximal step-test protocols, to determine CRF, as well as metabolic CVD-risk factor measurements, but neither examined the association between CRF and CVD risk. Although, results from Cook et al. (2009) [80] report a significant and positive relationship between CRF and PA Index (PAI) level, as well as an inverse association between PAI level and fasting plasma glucose level (p<0.0001), however relationships between CRF and other metabolic CVD-risk factors were not significant.

Interestingly, despite the majority (96.4%, *n*=138) of women in the study by Cook et al. (2009) [80], being classified as sufficiently 'active' according to public health guidelines [66], they were shown to have relatively poor CRF (mean: 26.7; range: 25.6- 27.7 ml/kg/min) compared with international age- and gender-ratings [29]. This would suggest that meeting PA guidelines is not associated with improved CRF, and therefore raises the question whether CRF and PA, in particular MVPA, are related.

These relationships, as well as those between CRF and metabolic risk factors for CVD and T2D need to be examined, and in particular among black urban SA adult women at high risk for CVD and T2D.

1.5 Sedentary behaviour

1.5.1 Sedentary behaviour, obesity and body fat distribution, in adult women

Recent evidence suggests that time spent in sedentary behaviours is associated with adverse health-related outcomes [132,133], and that these effects are often independent of PA [134,135,136]. However, it is important to note that the strength of these relationships are indeed, highly dependent on the methodologies used to measure both sedentary behaviour and health-related outcomes.

To date, the vast majority of sedentary data that exists is based on subjective measures, including self- and proxy-report. Examples include questionnaires on sitting- [137,138] and screen-time [139,140], and limitations similar to self-report PA measures need to considered. The use of objectively measured sedentary time, using accelerometry [139,134], limits potential self-report problems.

Cross-sectional studies by Brown et al. (2003) [138] and Rastogi et al. (2004) [141] have shown a significant and positive relationship between BMI and time spent sitting. Both studies investigated these relationships in a work environment, and showed that full-time [138] and higher occupation status (non-manual labour) employees [141] had a higher BMI than part-time and lower occupation status (manual labour) employees who spent less time sitting.

Other cross-sectional studies, and prospective studies, from both LMICs [142] and HICs [139,140,143,144,145,146] have examined the relationship between BMI and sedentary behaviour. Notably, results from the larger prospective studies [139,143,145] demonstrate positive associations for higher BMI and higher television screen-time. In contrast, results from the Health Professionals Follow-up study showed that changes in television screen-time over a 5-year period were not significantly associated with changes in BMI, but rather with changes in WC levels [147]. A possible explanation for this finding, may relate to the greater absolute change in WC level as compared to absolute change in BMI, measured over the 5-year period. Other studies examining the association between general screen-time (television-, computer- and video

game-use) and BMI [148], confirm the findings shown with television screen-time only [144,146].

Few studies have used objective measures of sedentary time to explore the relationship with obesity. Cross-sectional results from the National Health and Nutrition Examination Survey (NHANES) in the USA, failed to show a relationship between total sedentary time (<100 counts/min) measured using accelerometry and BMI, however higher BMI was associated with greater television screen-time [139]. Similarly, other cross-sectional studies from HICs [146,149] in which sedentary time was measured with accelerometry, also failed to show an association with BMI [146] and WC [149]. The lack of finding relationships, may in part relate to the misclassification of sedentary vs. activity time, when using older accelerometer devices without inclinometers. Therefore, more research on sedentary behaviour is required, as is the possibility of using newer measurement tools which may assist in refining our ability to measure this complex behaviour.

When examining the relationship between sedentary time and more precise measures of body fat distribution, specifically VAT, results from the Quebec Family study highlight relationships between sitting-time, VAT and changes in VAT over a 6-year period, in a large sample of adults [150]. After adjustment for possible covariates, the relationship between sedentary time and VAT, as well as change in VAT over the 6-year period, were not significant. However, results from the logistic regression analysis showed that the increase in sedentary time from baseline to follow-up was significantly associated with increase in WC. Overall, the results from the study showed that neither baseline or change in sedentary behaviour were associated with longitudinal changes in VAT, however sedentary time was significantly associated with WC. These findings suggest that other adipose tissue depots, such as SAT, may be more closely associated with sedentary behaviour.

The results of these studies provide evidence for the relationship between sedentary behaviour and obesity. Although the association seems less robust with objective measures of sedentary time, and shows WC and not VAT to be associated with sedentary behaviour, these relationships have not been investigated in SA population groups, and in particular in black SA women who have less VAT and more SAT [21,22] .

1.5.2 Sedentary behaviour and metabolic risk for cardiovascular disease and type 2 diabetes, in adult women

In contrast to the data for body composition, recent epidemiological studies have reported consistent and significant associations between sedentary behaviour and metabolic risk for CVD and T2D, in adults [49,134,136,151,152], using both self-reported screen-time [151] and accelerometer measured sedentary time [136]. Longitudinal data collected from the NHANES show an inverse relationship between sedentary behaviour and the metabolic syndrome [136,151]. Further results from numerous cross-sectional studies [49,134,153] show significant relationships between sedentary behaviour and serum lipid concentrations (TC, LDL-C and TG) [49,134,152,154], fasting plasma glucose concentrations [49,134,152,154], 2-hour plasma glucose concentrations [49,134,152], fasting serum insulin levels [49,134,154], resting blood pressure measures [49,134,154] and with reduced HDL-C serum concentrations [49,134,154], in adult women. However, only some of these associations remained significant after adjusting for WC, [152] [134].

Overall, these studies demonstrate the adverse relationship between higher sedentary behaviour and metabolic risk factors for CVD and T2D. However, all the participants in these studies are representative of adults (Caucasian) living in HICs. Thus, it remains unknown whether the same relationships between sedentary behaviour and risk factors for CVD and T2D will be found in adults from LMICs such as SA, inclusive of black population groups.

1.6 Literature conclusions

The prevalence of obesity amongst black urban SA adult women is disproportionately high and exceeds that of all other ethnic groups [155]. This may, in part, be explained by the high prevalence of physical inactivity in this population group [15].

Physical activity can be measured using numerous methods which vary according to level of difficulty and precision. Although criterion methods are expensive and not always practical for epidemiological research investigations, questionnaires such as the GPAQ can provide valid and reliable measures. Research using GPAQ have highlighted the beneficial relationship between high PA levels and health outcomes. Accordingly, numerous PA recommendations for health exist, including most recent

guidelines from the ACSM/AHA [31] and WHO [72]. However, to my knowledge, there have been no studies in South Africa, in particular in urban black women who are at increased risk for obesity, to show that women who meet the PA cut-points are less likely to be obese and are at reduced risk for CVD and T2D, compared to women who are inactive. Furthermore, it is unknown whether women who meet the criteria for sufficient PA will remain weight stable over time and have a lower risk for CVD and T2D.

However, the GPAQ is only able to characterise activities of MVPA and therefore unable to quantify 'light' or 'incidental' activity. Accelerometers are able to quantify intensity, as well as reduce subjective bias associated with questionnaire data. They also have the added advantage of quantifying steps/day and sedentary time. Numerous large studies from HICs [90,91,92,93,94,97,98,99], as well as smaller studies from SSA [101] and SA [78,79,80,81,82,83] demonstrate inverse associations between PA (PAEE, MVPA and/or Steps/day) and obesity, body fat distribution measures, and metabolic risk factors for CVD and T2D. Conversely, sedentary behaviour has been shown to have an independent (of PA) and positive association with obesity and metabolic risk. Furthermore, high CRF, independent of PA [134,135,136], is associated with reduced adiposity and improved metabolic profile.

There are a dearth of studies that have examined these relationships in urban black SA women, who are at increased risk for obesity and the associated co-morbidities. Thus, it is important to determine the influence of either: PA level and/or sedentary time, as well as CRF, on the development of obesity and risk of CVD and T2D, in black SA urban women. This information can be used to guide recommendations for PA to reduce obesity and risk for CVD and T2D in black SA populations.

1.7 Aims and objectives

The overall aim of this thesis is to examine the association between PA and risk factors for CVD and T2D in a sample of apparently healthy black SA women. Therefore, the aims of this thesis will be addressed in two separate studies with the following objectives:

Study 1:

i) to compare body composition and metabolic risk factors for CVD and T2D between active and inactive groups classified according to international PA recommendations for health [72] (Part 1, cross-sectional analysis), and
ii) to determine whether PA level at baseline predicts changes in body composition and metabolic risk factors for CVD and T2D over a 5.5-year follow-up period (Part 2, longitudinal analysis);

Study 2:

i) to examine the independent effects of PA, CRF and sedentary time on body composition and metabolic risk factors for CVD and T2D (cross-sectional analysis).

CHAPTER TWO

RELATIONSHIPS BETWEEN PHYSICAL ACTIVITY, OBESITY AND RISK FACTORS FOR CARDIOVASCULAR DISEASE AND TYPE 2 DIABETES, IN BLACK SOUTH AFRICAN WOMEN

2.1 Introduction

Non-communicable diseases, including T2D and CVD were the second highest cause of mortality in SA in 2000 [2]. This is exacerbated by the high prevalence of obesity in SA women, in particular black urban women [155]. Although the aetiology of NCDs is complex, common antecedents include a sedentary lifestyle and poor nutrition [156].

Data from longitudinal cohort studies conducted in HICs have shown that when PA is promoted, it has a positive impact by reducing the overall risk of most NCDs [157,158]. Subsequently, the WHO has implemented several public health recommendations to increase PA, in an attempt to reduce disease risk. Accordingly, those who meet the global recommendations of PA for health are referred to as 'active' and, engage in at least 150 minutes of moderate-intensity activity per week; or 75 minutes of vigorous-intensity activity per week; or an equivalent combination of MVPA [72].

To date, a wide range of methods have been used to measure PA in adults. These include self-report methods such as questionnaires, activity logs and/or diaries. The WHO Stepwise approach to chronic disease risk factor surveillance (STEPS) was initiated in 2000, and uses the GPAQ to collect PA data in both HICs and LMICs [43,159]. Although there are limited studies investigating PA levels in SA populations, a recent study conducted in a black population in the Eastern Cape of SA found that 59% of black apparently healthy adult women (18-45 years) were inactive according to the ACSM/CDC recommendations for health-enhancing PA (to accumulate 30 minutes of moderate-intensity activity on most, preferably all, days of the week) [77]. These results support findings from earlier small-scale studies [78,83] and national surveys [15] (Tshabangu, unpublished), highlighting black SA women as a particularly vulnerable group for low levels of habitual PA.

Although previous SA studies have examined the association between PA, body composition and body fat distribution measures [78,83], most have used BMI as a measure of body fatness and WC as a measure of body fat distribution. To date, studies from our laboratory have used more precise body composition and body fat distribution measures such as DXA and CT [19,21,22], but have never explored their association with PA. This is important as PA has been shown to differentially alter

body composition within the adipose tissue depots, with some studies showing greater relative changes in VAT compared to SAT in response to exercise interventions [160,161], but this has not been consistently shown across studies [162]. Inconsistencies in these findings may be related to the ethnicity of the participants tested as when matched for BMI, black women have significantly less VAT and more abdominal SAT than white women, despite being more insulin resistant [21,163,164].

Cross-sectional data from studies in SSA [80,109] support evidence from larger international prospective female cohort studies [165,166] showing an inverse association between MVPA and metabolic disease risk. Results from both the small-scale SA and Cameroonian adult women studies showed similar inverse associations between higher PAEE and lower fasting plasma glucose levels [80], and 2-hour plasma glucose levels [109]. However, it remains unknown if being physically active (meeting global PA recommendations for health) [72] will reduce the risk and onset of CVD and T2D over time, particularly among female population groups living in LMICs such as SA.

To my knowledge there are no longitudinal studies that have examined the association between PA and changes in body composition and metabolic risk factors for CVD and T2D in SA women. Therefore, the aims of this chapter are to:

1. compare body composition measures and metabolic risk factors for CVD and T2D between active and inactive groups classified according to the global PA recommendations for health (WHO, 2010) (cross-sectional analysis);
2. determine whether PA level at baseline predicts changes in body composition and metabolic risk factors for CVD and T2D over a 5.5-year follow-up period (longitudinal analysis).

2.2 Materials and methods

2.2.1 Participants

Participants included a convenience sample of 240 apparently healthy premenopausal black SA women who were tested in 2005/6 as previously described [19,167]. The women were recruited from church groups, community centers, and universities and through the local press, and were included in the study if they were

i) 18-45 years old; ii) had no known diseases and were not taking medications for T2D, hypertension, HIV/AIDS, or any other metabolic diseases; iii) were not pregnant, lactating or postmenopausal (self-reported); and iv) of SA ancestry (self-reported). For the purposes of this study, 9 women were excluded from the original cohort based on invalid PA data in 2005/6 (Figure 2.1) as instructed by the GPAQ Analysis Guide [69].

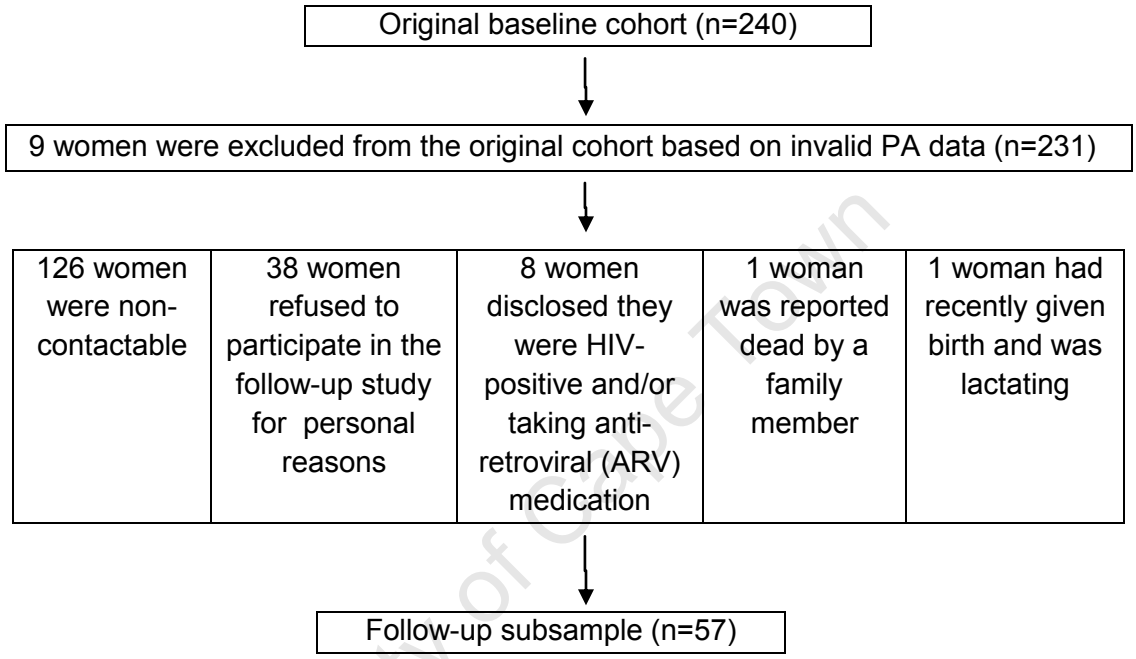

Figure 2.1 Original baseline cohort and follow-up subsample after the 5.5-year period.

The original cohort of women were contacted and invited to participate in the longitudinal follow-up study in 2010/11. Participants that were pregnant, lactating or HIV positive were excluded. In addition, voluntary HIV screening was performed and participants were further excluded on the basis of a confirmed positive test (Sanitests Home Test Kits, SA). Those who declined HIV screening were not excluded from the sample. The same Xhosa speaking fieldworker involved in the original baseline study assisted with the participant recruitment and testing for follow-up. Of the original baseline sample, only 57 women underwent follow-up testing and were included in the longitudinal follow-up subsample analysis (Figure 2.1). Testing procedures were identical to those at baseline as described by Jennings et al. (2008) [19] and as detailed above.

2.2.2 Socio-economic status and behaviour/lifestyle factors

At baseline and follow-up, a socio-demographic questionnaire was administered that included measures of socio-economic status (SES), family history of CVD and T2D (first degree relatives), and behaviour/lifestyle factors. Four indicators of SES were used: education (completion of grade 12), employment, housing density and asset index. An asset index score was based on 14 items reflecting individual and household wealth and resources, as described by Jennings et al. (2008) [19]. This included electricity in the home, ownership of a television, radio, motor vehicle, fridge, stove/oven, washing machine, telephone, video machine, microwave, computer, cellular telephone and paid television channels (MNET or DSTV). Participants were categorised as employed or unemployed. Those who were studying (students) were categorised as unemployed. Housing density was defined as the number of persons in the household divided by the number of rooms. Behaviour/lifestyle factors included self-reported indicators of current smoking status (categorised as smoker or non-smoker), alcohol consumption based on average weekly intake of alcohol (categorised as non drinker or drinker (≥1 drink per day)), and hormonal contraceptive use (oral or injectable).

2.2.3 Body composition assessment

2.2.3.1 Anthropometry

Weight and height, in light-weight clothing without shoes, were measured using a standard scale and stadiometer, respectively (Detecto, Model UWE BW-150, Cardinal Scale Manufacturers, Webb City, Missouri, USA). Body mass index was calculated as weight in kilograms divided by height in metres squared. Waist circumference at the level of umbilicus, and hip circumference at the largest part of hips, were both measured. Waist to hip ratio was also calculated.

2.2.3.2 Dual-energy x-ray absorptiometry

Whole body composition including fat mass (FM) and fat-free soft tissue mass (FFSTM), was measured by dual-energy x-ray absorptiometry (DXA) (Discovery-W®, software version 12.7.3.7; Hologic, Bedford, MA) according to standard procedures. In vivo precision (CV) was 0.7% and 1.67% for FFSTM and FM, respectively. Regional body fat distribution (FM) was further divided into central fat mass (CFM) and appendicular fat mass (AFM). AFM was calculated as fat mass from the limbs and CFM was calculated as total FM minus AFM, as previously

described [100]. Those participants whose body proportions exceeded the DXA scanning area were analysed using the arm-replacement method which replaces the data obtained for the left arm with the data obtained for the right arm [168].

2.2.3.3 Computerised tomography

A single-slice computerised tomography (CT) (Toshiba X-press Helical Scanner®; Toshiba Medical Systems, Tokyo, Japan) scan was taken at the level of the L4-L5 lumbar vertebrae to determine VAT area and SAT area. Furthermore, SAT was divided into two sub-compartments; deep subcutaneous adipose tissue (DSAT) and superficial subcutaneous adipose tissue (SSAT) which were differentiated by the fascia superficialis [169].

2.2.4 Metabolic risk factors for cardiovascular disease and type 2 diabetes

2.2.4.1 Blood pressure

After at least 5 minutes of seated rest, blood pressure (BP) was measured three times at 1-minute intervals using an appropriate-sized cuff and an automated BP monitor (Omron® 711; Omron Health Care, Hamburg, Germany). An average of the last two readings was used for analyses.

2.2.4.2 Blood sampling and analysis

Blood samples were drawn after an overnight fast (10-12 hours) at baseline and follow-up for the subsequent measurements of plasma glucose and serum insulin, TC, TG, HDL-C and LDL-C.

Fasting plasma glucose levels at baseline and follow-up were measured using the glucose oxidase method [(Baseline: Glucose Analyzer 2, Beckman Instruments, Fullerton, CA, USA with intra-assay CV: 0.67%)] [Follow-up: YSI 2300 STAT PLUS, YSI Life Sciences, Yellow Springs, OH with intra-assay CV: 1.17% and inter-assay CV: 2.29%)]. An inter-method comparison was performed and yielded an inter-assay CV of 1.53%. Serum insulin levels were measured by a Micro-particle Enzyme Immunoassay (MEIA) (AxSym Insulin Kit, Abbot, IL, USA) [Baseline: intra-assay CV: 2.3% and inter-assay CV: 3.2%)] [Follow-up: intra-assay CV: 3.28% and inter-assay CV: 5.45%)] in 231 women at baseline and 57 women at follow-up.

Insulin sensitivity was estimated using the homeostasis model of insulin resistance (HOMA-IR) [170] at baseline and follow-up. The subsample of 57 women also

underwent a standard 2-hour (2-hr) oral glucose tolerance test (OGTT) at follow-up. After an overnight fast, participants ingested 75 g glucose diluted in 250ml of water. Blood samplings were taken at 30-minute intervals (0, 30, 60, 90 and 120 minutes) to measure plasma glucose and serum insulin levels, respectively. The Matsuda insulin sensitivity index [171] was calculated from the OGTT in the follow-up subsample.

Serum TC (intra-assay %CV: 0.4%), TG (intra-assay %CV: 0.6%), and HDL-C (intra-assay %CV: 0.55%) concentrations were measured on the Roche Modular Auto Analyzer (Roche/ Hitachi Cobas C System from Roche Diagnostics GmbH, D-68298, Mannheim) using enzymatic colorimetric assays. LDL-C was calculated using the Friedewald equation [172].

2.2.4.3 Physical activity

Physical activity (PA) was assessed using the Global Physical Activity Questionnaire (GPAQ) [69,173] which is largely based on the International Physical Activity Questionnaire [41] and have been shown to be similarly reliable and valid for use in SA (Tshabangu, unpublished data). GPAQ 1, the first version of the questionnaire, was administered by the same Xhosa speaking fieldworker during each interview. An introductory text explaining which activities to consider for each of the different domains, as well as the definitions of moderate-intensity and vigorous-intensity PA, were read out to each participant. The domains investigated were: work-, transport- (including walking) and leisure-related physical activities. Total PA time recorded in minutes per week (min/week) according to intensity bands (total moderate, total vigorous and total moderate- to vigorous-intensity (MVPA)) were calculated for each of the three domains.

2.2.4.4 Criteria for active vs. inactive groups

The WHO STEPwise approach to chronic disease risk factor surveillance (STEPS) uses the GPAQ and GPAQ Analysis Guide criteria to categorise active and inactive groups [69]. The large baseline cohort (*n*=231) was categorised into the two activity groups. The physical activity data for 9 participants was excluded from the original baseline cohort for reporting time values higher than 16 hours of physical activity in a 24-hour period. Those who met the following criteria were defined as active: 30 minutes of moderate-intensity activity or walking per day, on at least 5 days in a typical week; or 20 minutes of vigorous-intensity activity per day on at least 3 days in a typical week; or 5 days of any combination of walking and moderate- or vigorous-

intensity activities achieving a minimum of at least 600 MET-minutes per week. Those who did not meet these criteria were classified as inactive.

For the purposes of this chapter the GPAQ Analysis Guide criteria were used to categorise participants into inactive and active groups. For comparison purposes, the new WHO global standard PA recommendation [72] was also used. Participants were referred to as 'WHO active' if they engaged in at least: 150 minutes of moderate-intensity activity per week; or 75 minutes of vigorous-intensity activity per week; or an equivalent combination of moderate- and vigorous-intensity activities. Participants who failed to meet these criteria were referred to as 'WHO inactive'.

2.2.5 Statistical analysis

Data are presented as means ± standard deviations or percentages (n). Chi-squared tests were used to examine differences between categorical data (behaviour/lifestyle factors) at baseline and follow-up. Non-normally distributed variables (PA, HDL-C, TG and serum insulin levels) were normalized by log transformation for parametric analyses.

Two-way analysis of covariance (ANCOVA) adjusting for differences in age was used to compare body composition and body fat distribution measures between active and inactive groups. The unadjusted mean values and age-adjusted p values are presented in the table. Furthermore, an ANCOVA, adjusting for age, as well as age and weight, was used to compare metabolic outcomes measured between the two activity groups. The unadjusted values together with the age-adjusted and; age- and weight-adjusted p values are presented in the table.

Changes in body composition, body fat distribution and metabolic outcomes measurements over the 5.5-year follow-up period were assessed using repeated measures ANOVA, adjusting for age (for body composition outcomes), and age and weight (for metabolic outcomes), with Tukey post-hoc analyses to explore the effect of activity group over time. The unadjusted mean values as well as age-adjusted and age- and weight-adjusted p values are presented in the table. Lastly, multiple logistic regression and odd ratio analyses were performed to determine how increasing PA changes both body composition and metabolic outcome measurements. Statistical significance was based on a $p<0.05$. All data were analysed using STATISTICA version 10 (StatsoftInc. Tulsa, OK).

2.3 Results

2.3.1 Physical activity

There was no significant difference in the proportion of women classified as active or inactive according to the GPAQ Analysis Guide criteria (61 vs. 39%) and the WHO PA 2010 recommendation [72] (71.4 vs. 28.6%). For the purpose of this study, all further classifications of active and inactive were based on the GPAQ criteria, in accordance with the criteria used in several multi-country surveys [43]. The raw PA data (min/week) for the active and inactive groups, broken down into the various intensity bands (total moderate, total vigorous and total moderate-vigorous) and domains (work-, transport- and leisure-time) according to the GPAQ criteria are presented in Table 2.1 and Figure 2.2. As expected, women classified as active by definition reported more minutes per week (min/week) in all PA domains. Notably, the majority of PA time recorded by both groups was reported for transport (domain) and performed at a moderate-intensity (walking).

Table 2.1 Comparison of physical activity time measured using the GPAQ between active and inactive groups.

PHYSICAL ACTIVITY TIME	**active (*n*=141)**	**inactive (*n*=90)**	**p value**
Total vigorous (min/week)	0 (0 - 90)	0 (0 - 0)	<0.001
Total moderate (min/week)	540 (300 - 1080)	60 (0 - 140)	<0.001
Total MVPA (min/week)	610 (360 - 1200)	60 (0 - 180)	<0.001
WORK			
Total work (min/week)	0 (0 - 30)	0 (0 - 0)	<0.001
TRANSPORT			
Total travel (min/week)	360 (160 - 840)	45 (0 - 140)	<0.001
LEISURE			
Total leisure (min/week)	0 (0 - 180)	0 (0 - 0)	<0.001

Values are medians with inter-quartile range in parenthesis. MVPA, moderate- to vigorous-intensity physical activity. PA time (work, transport and leisure) were normalized by log transformation for parametric analyses (ANOVA).

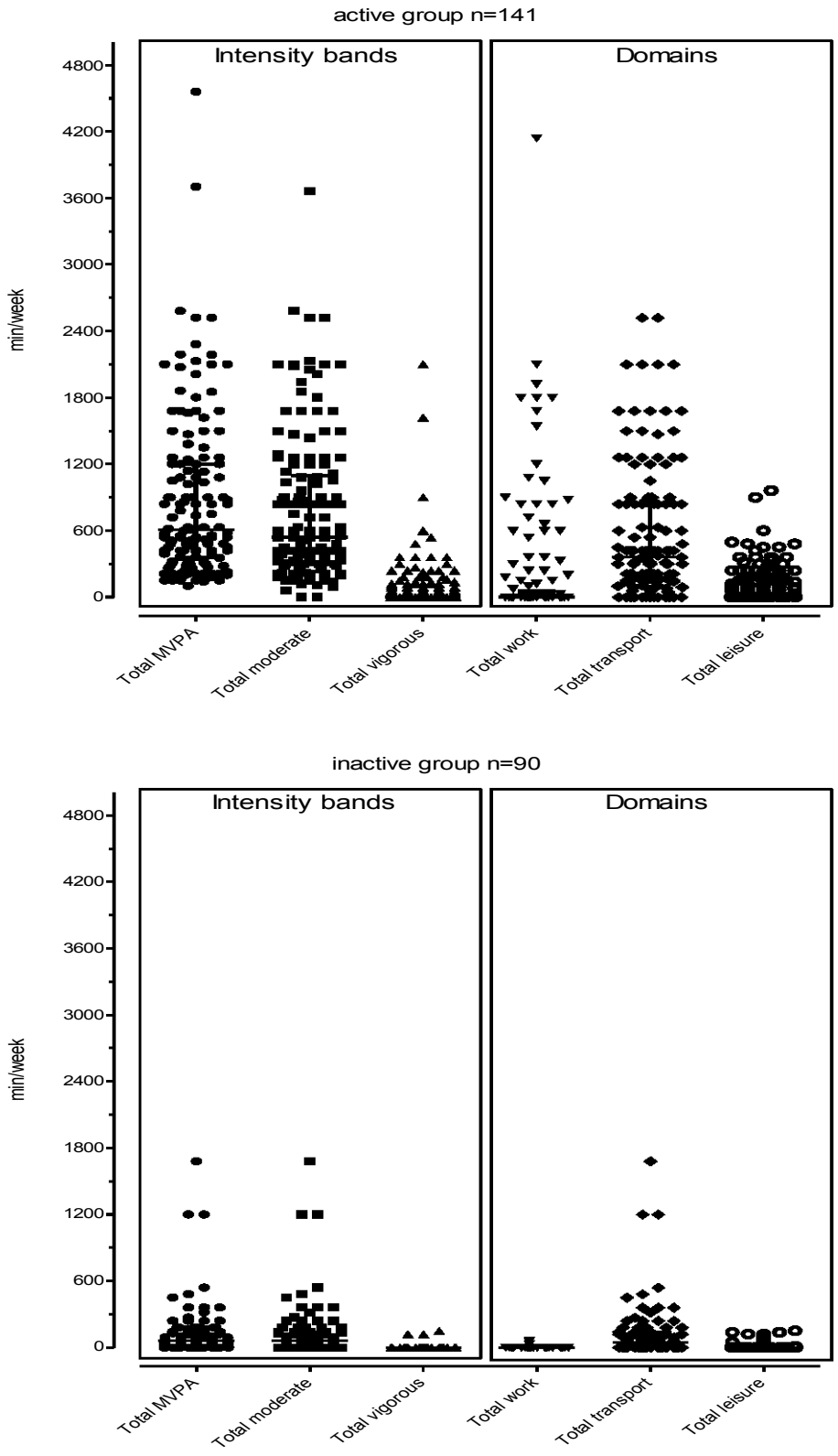

Figure 2.2 A diagrammatic comparison of weekly physical activity time between active and inactive groups.

2.3.2 Baseline socio-demographic, body composition and body fat distribution characteristics according to physical activity groups

Baseline characteristics (socio-economic status and behaviour/lifestyle factors), body composition and body fat distribution measurements of the PA groups are presented in Table 2.2. There were no differences in level of education between activity groups, however a larger proportion of women from the inactive group were employed (p=0.008). Few women smoked (12.2%) and there were no differences in alcohol consumption or hormonal contraceptive use between the activity groups.

The active group were significantly younger than their inactive counterparts (p=0.019); as a result all subsequent analyses comparing body composition and body fat distribution were adjusted for age. There was no difference in height between the activity groups however all other measures of whole body composition were significantly lower in the active compared to the inactive group. All absolute measures of body fat distribution including waist and hip circumferences, CFM and AFM were also significantly lower in the active group compared to their inactive counterparts. When expressed as a % of total fat mass neither CFM nor AFM, were different between activity groups. In addition, abdominal SAT was significantly lower in the active compared to the inactive group however there was no significant difference in VAT or VAT/SAT.

2.3.3 Baseline metabolic outcomes according to physical activity groups

Baseline metabolic characteristics of the two PA groups are presented in Table 2.3. As previously reported the inactive group were significantly older (p=0.019) and heavier (p<0.001) than their active counterparts, therefore all subsequent analyses were adjusted for age, as well as, weight and age, respectively. The active group had significantly higher HDL-C concentrations, lower fasting serum insulin concentrations and lower HOMA-IR values compared to their inactive counterparts, before and after adjusting for age. However, none of these differences in metabolic outcomes remained significant after adjusting for age and weight (p>0.05). There were no differences in resting BP or any of the other serum lipid concentrations (TC, LDL-C and TG) between activity groups.

Table 2.2 Baseline socio-demographic, body composition and body fat distribution characteristics according to physical activity groups.

	n	**active**	***n***	**inactive**	**p values**
Age (years)	*141*	26 ± 7	*90*	28 ± 8	***0.019***
Behaviour/ lifestyle factors					
Education: completed grade 12 % (*n*)	*133*	62.4 (*83*)	*89*	59.5 (*53*)	*0.669*
Employment % (*n*)	*133*	20.3 (*27*)	*88*	36.3 (*32*)	***0.008***
Housing density (persons/room)	*138*	1.1 ± 0.8	*90*	1.1 ± 0.7	*0.858*
Asset index	*133*	7 ± 3	*89*	7 ± 3	*0.682*
Smokers % (*n*)	*137*	8.0 (*11*)	*90*	4.4 (*4*)	*0.287*
Consumers of alcohol % (*n*)	*136*	37.5 (*51*)	*87*	25.2 (*22*)	*0.057*
Hormonal contraceptive use % (*n*)	*117*	33.3 (*39*)	*82*	43.9 (*36*)	*0.129*
Body composition					**age-adjusted p values**
Height (m)	*141*	1.60 ± 0.1	*90*	1.60 ± 0.1	*0.463*
Weight (kg)	*141*	71.7 ± 19.1	*90*	83.9 ± 20.6	***<0.001***
BMI (kg/m^2)	*141*	28.0 ± 7.5	*90*	32.7 ± 8.0	***<0.001***
Fat-free soft tissue mass (kg)	*126*	40.9 ± 5.9	*74*	43.1 ± 6.6	***0.025***
Fat-free soft tissue mass (%)	*126*	61.0 ± 7.9	*74*	56.3 ± 6.9	***<0.001***
Fat mass (kg)	*126*	26.0 ± 12.5	*74*	33.2 ± 12.6	***<0.001***
Body fat (%)	*126*	35.8 ± 8.5	*74*	40.8 ± 7.3	***<0.001***

	n	active	*n*	inactive	age-adjusted p values
Body fat distribution					
Waist circumference (cm)	*141*	86.2 ± 17.0	*90*	95.3 ± 18.2	***0.001***
Hip circumference (cm)	*141*	109.0 ± 15.4	*90*	117.4 ± 14.8	***<0.001***
Waist:Hip	*141*	0.79 ± 0.1	*90*	0.80 ± 0.1	*0.296*
CFM (kg)	*124*	11.5 ± 6.4	*74*	14.9 ± 6.5	***0.001***
CFM (% FM)	*124*	42.0 ± 7.8	*74*	43.9 ± 4.6	*0.091*
AFM (kg)	*124*	14.5 ± 6.3	*74*	18.3 ± 6.4	***<0.001***
AFM (% FM)	*124*	56.4 ± 8.8	*74*	55.9 ± 4.6	*0.855*
Total VAT (cm^2)	*84*	50.0 ± 39.4	*53*	65.8 ± 36.5	*0.088*
Total SAT (cm^2)	*84*	331.6 ± 204.5	*53*	429.8 ± 188.5	***0.044***
VAT/SAT	*84*	0.15 ± 0.1	*53*	0.16 ± 0.1	*0.700*

Values are unadjusted mean ± standard deviation or percentage (n). p values for body composition and body fat distribution variables are adjusted for age (p<0.05). BMI, body mass index; FM, fat mass; CFM, central fat mass; AFM, appendicular fat mass; VAT, visceral adipose tissue; SAT, subcutaneous adipose tissue.

Table 2.3 Baseline metabolic outcomes according to physical activity groups.

	n	active	*n*	inactive	Normal range	p values	
						age-adjusted	age and weight-adjusted
Resting blood pressure							
SBP (mmHg)	*141*	109.6 ± 16.6	*90*	111.3 ± 14.0	100 - 140	*0.682*	*0.389*
DBP (mmHg)	*141*	74.0 ± 11.9	*90*	76.0 ± 9.9	70 - 90	*0.797*	*0.275*
Lipid profile							
Total cholesterol (mmol/L)	*135*	3.9 ± 0.8	*86*	4.1 ± 0.9	3.1 - 5.2	*0.711*	*0.240*
LDL-C (mmol/L)	*135*	2.2 ± 0.7	*86*	2.3 ± 0.8	1.0 - 3.0	*0.307*	*0.373*
HDL-C (mmol/L)	*135*	1.3 ± 0.4	*86*	1.2 ± 0.4	1.2 - 1.7	***0.041***	*0.409*
Triglycerides (mmol/L)	*135*	0.7 ± 0.3	*86*	0.8 ± 0.4	0.5 - 2.0	*0.229*	*0.925*
TC/HDL-C	*135*	3.5 ± 3.8	*86*	3.7 ± 3.7	-	*0.870*	*0.815*
Insulin sensitivity							
Fasting plasma glucose (mmol/L)	*136*	4.5 ± 0.4	*85*	4.4 ± 0.5	3.1 - 5.5	*0.673*	*0.626*
Fasting serum insulin (mU/L)	*138*	10.1 ± 6.8	*89*	12.4 ± 8.7	-	***0.010***	*0.353*
HOMA-IR	*129*	2.1 ± 1.4	*84*	2.6 ± 2.0	-	***0.010***	*0.332*

Values are unadjusted mean ± standard deviation. p values are age-adjusted and age- and weight-adjusted (p<0.05). SBP, systolic blood pressure; DBP, diastolic blood pressure; LDL-C, low-density lipoprotein cholesterol, HDL-C, high-density lipoprotein cholesterol; TC/HDL-C, total cholesterol to high-density lipoprotein cholesterol ratio; HOMA-IR, homeostasis assessment model of insulin resistance. Normal range values highlighted according to the WHO/International Society for Hypertension (ISH) statement for the management of hypertension [174] and Adult Treatment Panel (ATP) III criteria (2001) [175].

2.3.4 Original baseline cohort vs. follow-up subsample according to physical activity groups

Similar to the original baseline cohort, in the subsample of women (*n*=57) who were followed up after 5.5 years, 61.4% (*n*=35) of the women were classified as active according to the GPAQ criteria, and 38.6% (*n*=22) of the women were classified as inactive. As with the baseline cohort, the majority of PA time was spent in active commuting (transport domain of the GPAQ) particularly walking.

2.3.5 Changes in socio-demographic, body composition and body fat distribution characteristics between baseline and follow-up (5.5-years) according to physical activity groups

Changes in socio-demographic (SES and behaviour/lifestyle factors), body composition and body fat distribution characteristics between baseline and follow-up for the two activity groups are presented in Table 2.5. Socio-economic status (education, employment and asset index) increased significantly in both groups between baseline and follow-up. Although housing density remained unchanged in the active group it increased significantly in those who were inactive. There was a significant increase in smoking and alcohol consumption between baseline and follow-up amongst the active participants, while smoking did not change and alcohol consumption decreased in their inactive counterparts. At follow-up significantly less of the women in both groups were using hormonal contraceptives. Overall, changes in SES and lifestyle did not differ when comparing the two activity groups.

Body weight and all measures of body fatness (BMI, fat mass, % body fat, waist circumference, central and appendicular fat mass) except waist to hip ratio (WHR), VAT and VAT/SAT ratio, increased significantly in both activity groups over the 5.5 year follow-up period. The changes in body composition did not differ by activity group. For both activity groups, CFM (mean % change) increased to the greatest extent over the 5.5-year period (28.1% and 25.1% for active and inactive groups, respectively), which was mirrored by increases in CT-derived measures of central fat (SAT) (mean % change: 22.7% and 16.6% for active and inactive groups, respectively). Notably, the relative increase in CFM was greater than that of peripheral fat mass (AFM) (mean % change: 14.8% and 11.4% for active and inactive groups, respectively) in both groups.

When dividing the 5.5-year follow-up sample (*n*=57) into two groups based on a median split of %bodyweight change:

- Those who have gained ≥10% bodyweight over the 5.5-year follow-up period and,
- those that gained <10% bodyweight over the 5.5-year follow-up period.

Based on logistic regression (Table 2.4), I found that women who were active at baseline were less likely to gain ≥10% bodyweight over the 5.5-year follow-up period compared to those who were inactive (odds ratio 0.21; 95% CI: -0.50 to 0.92, P=0.032), after adjusting for age, BMI and socioeconomic status (housing density).

Table 2.4 Logistic regression

	Odds ratio	**(95% CI)**	**p value**
Intercept	0.000	-4.968; 4.969	0.002
Active at baseline	0.210	-0.506; 0.926	0.032
Age at baseline	1.072	0.973; 1.172	0.166
BMI at baseline	1.189	1.071; 1.307	**0.003**
Housing density at baseline	0.707	-0.187; 1.602	0.448

95% CI, confidence intervals.

Table 2.5 Changes in socio-demographic, body composition and body fat distribution characteristics between baseline and follow-up (5.5-years) according to physical activity groups.

	Active			inactive					
	N	**baseline**	**follow-up**	***n***	**baseline**	**follow-up**			
Age (years)	*35*	25 ± 6 [a]	31 ± 6 [a]	*22*	28 ± 7 [b]	34 ± 7 [b]			
Behaviour/ lifestyle factors									
Education completed grade 12 % (*n*)	*34*	41.1 (*14*) [a]	48.6 (*17*) [a]	*22*	36.3 (*8*) [b]	45.4 (*10*) [b]			
Employment % (*n*)	*34*	11.8 (*4*) [a]	51.4 (*18*) [a]	*22*	31.8 (*7*) [b]	40.9 (*9*) [b]			
Housing density (persons/room)	*35*	1.3 ± 1.1	1.3 ± 0.9	*22*	1.1 ± 0.4 [b]	1.4 ± 1.6 [b]			
Asset index	*35*	6 ± 3 [a]	9 ± 3 [a]	*22*	7 ± 3 [b]	9 ± 3 [b]			
Smokers % (*n*)	*35*	11.4 (*4*) [a]	17.1 (*6*) [a]	*22*	9.1 (*2*)	9.1 (*2*)			
Consumers of alcohol % (*n*)	*35*	34.3 (*12*) [a]	57.1 (*20*) [a]	*22*	36.4 (*8*) [b]	27.3 (*6*) [b]			
Hormonal contraceptive-use % (*n*)	*35*	40.0 (*14*) [a]	25.7 (*9*) [a]	*22*	50.0 (*11*) [b]	27.3 (*6*) [b]			
							age-adjusted p values		
Body composition							**time**	**group**	**interaction**
Height (m)	*35*	1.59 ± 0.1	1.59 ± 0.1	*22*	1.60 ± 0.1	1.60 ± 0.1	-	*0.328*	-
Weight (kg)	*35*	82.0 ± 19.6 [a]	89.5 ± 19.2 [a]	*22*	91.0 ± 15.6 [b]	98.3 ± 13.2 [b]	***<0.001***	*0.087*	*0.730*
BMI (kg/m^2)	*35*	32.4 ± 7.5 [a]	35.4 ± 7.6 [a]	*22*	35.4 ± 5.9 [b]	38.3 ± 6.1 [b]	***<0.001***	*0.181*	*0.732*
FFSTM (kg)	*35*	44.4 ± 6.5 [a]	45.4 ± 6.5 [a]	*22*	47.3 ± 5.7 [b]	48.0 ± 4.6 [b]	***0.051***	*0.127*	*0.825*
Fat mass (kg)	*35*	34.2 ± 14.0 [a]	38.9 ± 13.9 [a]	*22*	39.5 ± 11.0 [b]	44.7 ± 10.3 [b]	***<0.001***	*0.135*	*0.490*
Body fat (%)	*35*	40.7 ± 8.6 [a]	43.9 ± 6.4 [a]	*22*	43.5 ± 6.3 [b]	46.7 ± 5.3 [b]	***0.001***	*0.166*	*0.823*

							age-adjusted p values		
	n	**Baseline**	**follow-up**	***n***	**baseline**	**follow-up**	**time**	**group**	**interaction**
Body fat distribution									
Waist circumference (cm)	*35*	97.1 ± 17.9 [a]	105.1 ± 17.5 [a]	*22*	102.4 ± 15.3 [b]	113.6 ± 13.3 [b]	***0.001***	*0.323*	*0.181*
Hip circumference (cm)	*35*	116.5 ± 16.2	119.4 ± 14.9	*22*	122.3 ± 10.3	123.7 ± 9.3	***0.001***	*0.185*	*0.856*
Waist:Hip	*35*	0.83 ± 0.1 [a]	0.87 ± 0.1 [a]	*22*	0.83 ± 0.1 [b]	0.91 ± 0.1 [b]	*0.104*	*0.455*	*0.117*
CFM (kg)	*34*	15.9 ± 7.3 [a]	18.7 ± 7.0 [a]	*21*	18.9 ± 6.6 [b]	22.2 ± 6.3 [b]	***<0.001***	*0.104*	*0.359*
CFM (% FM)	*34*	37.3 ± 11.1 [a]	41.6 ± 10.4 [a]	*21*	42.3 ± 10.6 [b]	47.1 ± 9.5 [b]	***<0.001***	*0.083*	*0.492*
AFM (kg)	*34*	18.2 ± 7.0 [a]	20.1 ± 7.2 [a]	*21*	20.6 ± 5.0 [b]	22.4 ± 5.2 [b]	***0.001***	*0.704*	*0.217*
AFM (% FM)	*34*	43.4 ± 9.4	44.9 ± 10.1	*21*	46.7 ± 7.3	47.8 ± 7.6	***0.014***	*0.239*	*0.997*
Total VAT (cm^2)	*25*	58.6 ± 36	75.2 ± 41	*14*	80.8 ± 51	89.1 ± 48	*0.563*	*0.316*	*0.452*
Total SAT (cm^2)	*25*	418.7 ± 214	472.5 ± 187	*14*	478.0 ± 142	511.7 ± 122	***0.004***	*0.464*	*0.541*
VAT/SAT	*25*	0.14 ± 0.1	0.16 ± 0.1	*14*	0.16 ± 0.1	0.18 ± 0.1	*0.764*	*0.785*	*0.876*

Values are unadjusted mean ± standard deviation or percentage (n). Matching superscript letters represent significant difference (p<0.05) between age-adjusted baseline and follow-up values for each activity group. BMI, body mass index; FM, fat mass; CFM, central fat mass; AFM, appendicular fat mass; VAT, visceral adipose tissue; SAT, subcutaneous adipose tissue.

Table 2.6 Changes in metabolic outcomes between baseline and follow-up (5.5-years) according to physical activity groups.

	Active			Inactive			p values					
	n	baseline	follow-up	*n*	baseline	follow-up	age-adjusted			age- & weight-adjusted		
							time	group	interaction	time	group	interaction
Resting blood pressure												
SBP (mmHg)	*35*	112 ± 14	110 ± 17	*22*	113 ± 13	115 ± 19	*0.135*	*0.831*	*0.479*	*0.483*	*0.990*	*0.446*
DBP (mmHg)	*35*	79 ± 8 [a]	73 ± 13 [a]	*22*	79 ± 7	81 ± 9	*0.081*	*0.276*	***0.039***	*0398*	*0.288*	***0.035***
Lipid profile												
TC (mmol/L)	*35*	3.8 ± 0.9 [a]	4.1 ± 0.9 [a]	*22*	3.6 ± 0.6	3.9 ± 0.9	*0.384*	*0.296*	*0.870*	*0.198*	*0.380*	*0.733*
LDL-C (mmol/L)	*35*	2.3 ± 0.8	2.5 ± 0.9	*22*	2.0 ± 0.5 [b]	2.4 ± 0.8 [b]	*0.661*	*0.210*	*0.244*	*0.334*	*0.309*	*0.185*
HDL-C (mmol/L)	*35*	1.1 ± 0.3	1.2 ± 0.3	*22*	1.0 ± 0.4 [b]	1.2 ± 0.3 [b]	***0.004***	*0.918*	*0.165*	*0.067*	*0.965*	*0.194*
Triglycerides (mmol/L)	*35*	0.7 ± 0.3 [a]	0.9 ± 0.4 [a]	*22*	0.7 ± 0.3	0.9 ± 0.3	*0.307*	*0.581*	*0.827*	*0.279*	*0.361*	*0.918*
TC/HDL-C	*35*	3.6 ± 1.4	3.5 ± 1.0	*22*	3.3 ± 0.7	3.3 ± 0.9	*0.441*	*0.910*	*0.110*	*0.919*	*0.670*	*0.152*
Insulin sensitivity												
Fasting plasma glucose (mmol/L)	*35*	4.5 ± 0.4 [a]	5.2 ± 1.7 [a]	*22*	4.6 ± 0.7 [b]	5.1 ± 0.8 [b]	*0.849*	*0.654*	*0.821*	*0.402*	*0.720*	*0.402*
Fasting serum insulin (mU/L)	*35*	14.0 ± 7.8	12.4 ± 6.0	*22*	17.8 ± 11	16.4 ± 10.5	*0.125*	***0.020***	*0.707*	*0.655*	***0.045***	*0.408*
HOMA-IR	*34*	3.1 ± 1.7	2.8 ± 1.5	*21*	3.7 ± 2.7	3.7 ± 2.1	*0.145*	***0.036***	*0.904*	*0.950*	*0.081*	*0.664*
Matsuda index	*34*	-	4.0 ± 2.1	*21*	-	3.5 ± 2.6	-	*0.233*	-	-	*0.193*	-

Values are unadjusted mean ± standard deviation. All p values are adjusted for age (p<0.05). Matching superscript letters represent significant difference (p<0.05) between age- and weight-adjusted baseline and follow-up values for each activity group. SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol, HDL-C, high-density lipoprotein cholesterol; TC/HDL-C, total cholesterol to high-density lipoprotein cholesterol ratio; HOMA-IR, homeostasis assessment model of insulin resistance; Matsuda index, measure of insulin sensitivity [171].

2.3.6 Changes in metabolic outcomes between baseline and follow-up (5.5-years) according to physical activity groups

Changes in the metabolic characteristics of the two activity groups between baseline and follow-up, adjusting for age, and age and body weight, are presented in Table 2.6. There was a significant group x time interaction for DBP when adjusting for differences in age, and age and body weight, such that DBP decreased in the active group, but not in the inactive group. Although TC, LDL-C and TG serum lipid concentrations did not change in both activity groups, HDL-C concentrations increased significantly in the inactive group and showed a similar tendency in the active group. Fasting plasma glucose levels remained the same over the 5.5-year follow-up period in both activity groups, however significant age-adjusted group differences were found for both fasting serum insulin levels and HOMA-IR values, both of which were lower in the active group compared to the inactive group.

Lastly, when dividing the 5.5-year follow-up sample into two groups based on a median split according to % fasting serum insulin change and %HOMA-IR change. Significant differences were not found when comparing women who were active to those who were inactive at baseline.

2.4 Discussion

2.4.1 Part 1, cross-sectional study

The main findings of the cross-sectional study were that the majority (61%) of black apparently healthy women in the cohort were sufficiently active according to current GPAQ criteria. Compared to those who failed to meet GPAQ criteria, the active women had lower body weight and body fat, as well as higher serum HDL-C concentrations, and were more insulin sensitive (based on lower fasting serum insulin concentrations and HOMA-IR). However the differences in these metabolic variables were mediated via differences in body weight.

Based on the GPAQ criteria, 61% of the women were active, whereas 71.4% of women were classified as active using the WHO guidelines [72]. This is in accordance with studies from developed countries [176], as well as a survey of 22 African countries [43] in which they showed that the prevalence of subjects classified as active were

approximately 5-10% lower using the GPAQ [69] compared to the WHO criteria [72]. Similar to the findings from other African countries, we showed that PA both at work and for transport (bouts of ≥ 10 min of walking at a time) contributed mostly to overall activity time, while leisure-time PA was less common.

Notably, the study showed that women who were active were lighter and had less body fat compared to their less active counterparts. Although international intervention studies have shown that a significant increase in PAEE is associated with a loss of fat mass from both the VAT and SAT regions [161,162], we found that VAT was not different between the groups, whereas SAT was significantly lower in the active women. Results from studies completed in the USA and SA have previously shown that despite having the same level of adiposity, black women have significantly less VAT and more SAT compared to their white counterparts [21,163,164]. Although results from Goedecke et al. (2009) [21] showed that both VAT and SAT were associated with reduced insulin sensitivity, SAT was more closely related to insulin sensitivity than VAT. Thus, it seems plausible that a significantly lower SAT in black women may be linked to an improvement in their overall metabolic profile.

Indeed, those who were classified as active had higher HDL-C and lower fasting serum insulin levels and HOMA-IR values than their less active counterparts. These differences were largely mediated by differences in body weight between the groups. These findings have important practical applications, especially with the majority of black South African women being overweight and/or obese, and suggest that being active is associated with a lower body weight which consequently is associated with an improved metabolic profile. Thus, the cross-sectional data provides support for the current MVPA guidelines and the health-derived benefits (reduction in body fat and improved measures of insulin sensitivity) amongst women who met PA criteria. However, one cannot assume a cause-effect relationship and thus longitudinal studies are needed to better understand these relationships between PA level and measures of body composition and metabolic risk for CVD and T2D.

2.4.2 Part 2, longitudinal (5.5-year) follow-up study

Irrespective of activity group, body weight and fat mass increased significantly over the 5.5-year follow-up period. Although women who met the MVPA guidelines at

baseline had significantly less body fat compared to those who did not, being active at baseline did not translate into a reduction (or attenuated the increase, or aid in weight maintenance) in body fat at the 5.5-year follow-up. Possible explanations for failing to show an effect includes the reliability and validity of subjective recall (GPAQ) in determining an accurate measure of PA level (time) and in particular the different intensities at which it is documented. Another difficulty includes the ability to track the changes in PA over an extended period of time (5.5-years). Unfortunately, I was only able to measure PA at baseline and did not measure the subjective changes in PA over the 5.5-year period. Further, evidence from large international prospective cohort studies [177,178,179] suggest that weight gain is due in part to aging, changes in PA levels, as well as other lifestyle changes, all of which are difficult to characterise [180]. Future studies should use objective PA measures to broaden our knowledge of the relationship between PA at different intensities, and changes in body composition and metabolic outcomes captured over time, particularly in black SA women.

Despite an increase in body weight in both activity groups, the study's results show some metabolic benefits in the previously active group including a significant decrease in DBP (p=0.004) that remained significant after adjusting for age and weight (p=0.026). Potential mechanisms for this finding include sympathetic neural stimulation in response to PA, which results in increased blood flow and vasodilation due to nitric oxide release that provides a stimulus for both acute and chronic changes in vascular function [181]. However, irrespective of activity group, both systolic and DBP remained within a normal range after the 5.5-year period and may be due to the relatively young age of the participants. Future prospective studies are needed to track possible age-related changes in BP as well as lifestyle and environmental factors known to effect vascular health [182], in this population.

Serum lipid concentrations remained relatively low, despite large increases in body weight amongst the women in both activity groups over the 5.5-year follow-up period. These findings support evidence from international and other SA studies showing a more favourable lipid profile in black compared to white women [22,183,184], which may be explained, in part, by genetic differences [185,186,187] . For example, a recent gene-association study amongst black and white SA women (Ellman, unpublished) highlighted a number of 'protective' single nucleotide polymorphisms (SNPs) within the cholesteryl ester transfer protein (*CETP B1/B2*), lipoprotein lipase (*LPL S/X*) and proprotein convertase subtilisin/kexin type 9 (*PCSK9 C/X*) genes,

which were all found to be associated with reduced serum lipid concentrations (LDL-C, TG, TC/HDL-C and TG/HDL-C ratios) in black, but not white women. Other behaviour/lifestyle factors, including smoking, dietary intake and alcohol consumption, could also account for the ethnic differences in serum lipid concentrations.

The strengths of the study include the state-of-the-art measures of body fat and its distribution (DXA and CT). In addition, this is the first SA study to examine PA as a determinant of change in body composition and metabolic risk for CVD and T2D over time. However, numerous limitations need highlighting and include the use of a convenient sample and the difference in starting age between activity groups. However, differences in age between the groups could reflect changes in activity with age, i.e. showing that as women get older they become less active. Secondly, the blood samples for the longitudinal study were not analysed at the same time and using the same assay, which could have increased the variability between measures. Although the intra-assay variability was relatively low, we cannot exclude the possibility that the changes in circulating levels could be due to inter-assay variability. Thirdly, the change in PA level over the 5.5-year follow-up period was not measured. Future studies should consider the advantages of using more robust PA measurements such as accelerometry as suggested by Swartz et al. (2000) [188]. This will offer an opportunity to objectively characterise both PA (time, intensity and steps per day) and sedentary behaviour to investigate how these variables relate to obesity and metabolic risk factors for CVD and T2D amongst young black SA women.

In conclusion, the findings of this study highlight that meeting PA guidelines is associated with lower total and central fat mass and reduced metabolic risk for CVD and T2D when compared to not meeting PA guidelines. Importantly, the majority of PA reported in both activity groups was for travel-purposes (walking), whereas more structured, leisure-time activity was low in this population group. Despite these cross-sectional findings, the study showed that baseline PA level was not associated with a reduction or attenuated increase in body weight (fat mass) over the 5.5-year follow-up period, however, some metabolic benefits, notably a significant reduction in DBP was still present at follow up. Barriers and determinants of leisure-time PA amongst young black women in SA need to be identified.

Furthermore, public health interventions aimed at promoting daily PA to reduce the burden of obesity and its associated morbidities in SA should be designed, implemented and their effectiveness measured.

CHAPTER THREE

LIGHT-INTENSITY PHYSICAL ACTIVITY AND CARDIORESPIRATORY FITNESS ARE INDEPENDENTLY ASSOCIATED WITH REDUCED BODY FAT AND METABOLIC RISK FACTORS FOR CARDIOVASCULAR DISEASE AND TYPE 2 DIABETES, IN BLACK SOUTH AFRICAN WOMEN

3.1 Introduction

To date large SA population-based surveys [15] (WHO, 2005) (Tshabangu, unpublished data) and numerous small-scale research studies have used self-report tools such as questionnaires to characterise and measure PA [19,21,22,74,77] in relation to body composition [78,80] and metabolic risk factors for CVD and T2D [80,83]. In chapter 2 of this thesis, using the GPAQ I found that women who were sufficiently active according to the WHO Global Recommendations for PA and Health [69] had lower body weight, body fat, serum lipid concentrations (HDL-C) and measures of insulin sensitivity (fasting serum insulin and HOMA-IR, respectively) compared to their inactive counterparts, although the metabolic differences were not independent of body fat. Further, I showed that similar changes in body composition and metabolic outcomes over a 5.5-year period in the active and inactive groups. The use of subjective measurement tools such as the GPAQ are limited as they do not include all PA intensities, most notably light-intensity. Additional sources of error occur when using subjectively measured PA data, including subjective recall, definitions of desired variables (intensities), failure to account for seasonal and weekday versus weekend variations, as well as language and cultural differences [85,86]. In contrast, objective measurement of PA may counter these sources of subjective error as they provide objective information on the duration, intensity and frequency of PA [188], irrespective of differences in season, language and/or day of the week. Measurement tools such as accelerometers and heart rate monitoring devices can be used to measure PA and CRF levels. Thus, the additional data derived from the Actigraph MTI 7164 can be used to examine the associations between PA and CRF levels, and their relationships with metabolic risk factors for CVD and T2D in black SA women.

A small number of studies have examined the association between PA and body composition variables [79,80,81,82]. One particular study of black SA adult women found an inverse association between the number of steps per day (steps/day), using pedometers, and level of adiposity (BMI, WC and %BF) [79]. Notably, the study showed that overall obesity risk decreased with increasing ambulation, while access to motor vehicles was associated with greater adiposity. In another SA study, Dugas et al. (2009) [81] found that greater vigorous-intensity (≥7 METs) PA minutes per day, measured using accelerometers, was associated with lower levels of adiposity in a sample of black women of which 50% were obese. However, results from a more

recent meta-analysis concluded that objectively measured PA had no impact on body composition amongst adults from both HICs and LMICs [189].

Cross-sectional data from SSA countries such as Cameroon [109] show that higher levels of PA energy expenditure are associated with lower 2-hour plasma glucose levels, independent of adiposity or CRF level in non-diabetic adult women. To date, only one SA study has used objective methods to examine the association between PA and metabolic risk for CVD and T2D [80] and found an inverse relationship between PA Index level and fasting plasma glucose.

Recent evidence suggests that an increase in time spent in sedentary behaviours and decreased time spent in MVPA are independently associated with an increased risk of metabolic syndrome and its components [49,134,136,151,152,190]. Indeed, a large prospective adult study showed that increased sedentary behaviour was associated with elevated risks of CVD and all-cause mortality independent of PA level, BMI, smoking status and alcohol consumption [135]. Sedentary behaviour refers to any waking activity characterised by an energy expenditure ≤1.5 METs including time spent seated or in a reclined posture [35,37,38,191], excluding sleeping. Common sedentary behaviours include television and computer use (screen-time), driving or as a motor vehicle passenger, and reading. The sedentary and PA results from many of these studies have been reported for populations from HICs with few from LMICs [109,192] such as SA (Brangan, unpublished data).

In contrast to PA, which is defined as any body movement produced by skeletal muscle that requires energy expenditure [28], CRF refers to a physiologic state of well-being that allows one to meet demands of daily living [34]. Few researchers have reported similar relationships between levels of PA and CRF, in relation to body composition measures and metabolic risk factors for CVD and T2D [193,194], and a recent review [195] concluded that only CRF and not PA level consistently reduced obesity-related risk. To our knowledge, there is only one SA study that has examined CRF level in adult women and showed a positive association with level of PA derived from a 4-item PA index score [80].

Findings from my previous chapter showed that the majority of PA was performed for transport, which is typically performed at low intensities, which contrasts to that in HICs in which the predominant PA domain is leisure-time activity, performed at higher intensities [87,196]. Thus, I hypothesise that CRF is not associated with PA

(time, intensity and steps/day) or sedentary behaviour in this population and that all three entities have independent effects on body composition measures and metabolic risk factors for CVD and T2D. Therefore, the aim of this chapter is to examine the independent associations between CRF, PA and sedentary time, and body composition measures and metabolic risk factors for CVD and T2D, in a sample of apparently healthy black SA women.

3.2 Materials and methods

The study consisted of a subsample (*n*=76) from the original cohort of premenopausal black SA women. Further details of their recruitment and selection, as well as detailed methods, are presented in Chapter 2 of this thesis. In brief, age and socioeconomic status (SES) were assessed using questionnaires. In addition, data on 'motor vehicle ownership' defined as owning or having the use of a motor vehicle was also collected. Radiological scanning techniques (DXA and CT) were used to measure body composition (fat mass, %BF and fat-free soft tissue mass) and body fat distribution (VAT, SAT and trunk fat mass (TFM), defined as CFM minus the head). The women were classified according to WHO BMI categories namely: normal weight (18.5-24.9 kg/m^2), overweight (25-29.9 kg/m^2) and obese (≥30 kg/m^2). Metabolic outcomes that were measured included resting blood pressure, fasting serum lipid levels; fasting plasma glucose levels and fasting serum insulin concentrations.

3.2.1 Measurements of physical activity

Physical activity (PA) was measured using accelerometry. The uniaxial ActiGraph MTI 7164 accelerometer (ActiGraph LLC, Pensacola, Florida) was worn for 7 consecutive days by each participant. Recording of PA began on the first day, 2 hours after the monitor was received, and was completed when returned 8 days later. Participants were instructed to wear the accelerometer on their right hip, attached by an elastic belt during waking hours. As the monitors were not waterproof, the women were asked to remove the belt while bathing, showering or swimming. The time sampling interval was set at 60 second epochs. The original ActiGraph data files (*.dat) were downloaded onto a personalised computer and processed on a Microsoft Excel spreadsheet using a custom-written program ('MAHUFFE', http://www.mrc-epid.cam.ac.uk). Data from each participant was included if they met the minimum requirement of 10 hours or more of monitor wear

time on 4 or more days of the week. Wear time was determined by subtracting non-wear time from 24-hours, where non-wear time was defined as an interval of ≥60 consecutive minutes with zero activity counts allowing for intervals of 1-2 minutes of relatively low activity counts per minute (<100).

Freedson cut-points [50] were used to convert the accelerometer counts measured per minute into intensity bands. Sedentary behaviour (time) was defined as <100 counts/min. Active activity (≥100 counts/min) was divided into 4 sub-categories according to intensity level namely: light (100-1951 counts/min), moderate (1952-5724 counts/min), vigorous (5725-9498 counts/min) and very vigorous (≥9499 counts/min). Average daily time in minutes per day (min/day) was used to summarise both sedentary time and PA time (light- and MVPA-intensity).

3.2.2 Cardiorespiratory fitness

A submaximal step-test (MRC Step-test, Cambridge, UK) was used to determine CRF. A total of 51 participants were tested. Forty-two completed the total 8-minute duration of stepping, whereas 4 participants completed only 6-minutes, but still managed to reach 90% of their age-predicted HRmax and were therefore included in the final group analysis (*n*=46). Overall, 5 participants were excluded as they i) failed to reach 90% of their age-predicted HRmax, ii) experienced lower limb orthopaedic discomfort and/or pain whilst stepping and stopped before they reached 90% of their age-predicted HRmax, or iii) chose not to participate in the step-test.

The test required participants to increase their step frequency progressively on a 20 cm high step, guided by an audible metronome (rate of change: 2.5 body lifts/min^2) (MRC step-test, Cambridge, UK) [53]. The step-test was terminated early if HR exceeded 90% of age-predicted maximum HR, or if the participant was unable to maintain the prescribed step frequency, even after verbal encouragement from the test administrator. Throughout the test a HR monitor (SUUNTO, T6 Heart Rate Monitor; Finland) was used to capture HR measured in beats per minute for each participant. After the test was terminated, seated HR recovery was monitored and recorded at the end of a 2 minute period. Predicted maximal oxygen consumption (VO_{2max}) was calculated for each participant using mathematical calculations inclusive of HR and PA intensity as described by Brage et al. (2005 and 2006) [53,54]. Firstly, the time data and step height were used to calculate power at each time point and subsequently the PA intensity (PAI) at each time point (PAI_step). Alpha

step and beta step were then calculated from the slope and the gradient of the PAI_step against HR curve, during the stepping part of the test. These were both then used to calculate PAI_walk_run_max_ which in turn is used with resting metabolic rate (Oxford equation as described by Henry, 2005) [197] to calculate VO_{2max}.

3.2.3 Statistical analysis

Data are presented as means ± standard deviations or percentages (*n*). PA data (accelerometry) as well as measures of CRF are presented as medians (inter-quartile range). Non-normally distributed variables (HDL-C, TG, TC/HDL-C ratio, TG/HDL-C ratio, fasting serum insulin levels, 2-hour plasma glucose levels, sedentary time and MVPA) were normalized by log transformation for parametric analyses. Student t-tests and Chi-squared tests were used to determine if there were any differences (age, SES, body composition and metabolic outcomes) between the whole sample and subsample (who completed the CRF submaximal step-test). One-way ANOVA was used to determine if CRF, PA and sedentary time were different between SES and behaviour/lifestyle factors. Pearson product-moment correlation coefficients were used to evaluate the associations between CRF and measures of PA, sedentary time, body composition and metabolic outcomes. Multiple logistic regression and odd ratio analyses were performed to determine how PA level (active vs. inactive) relates to differences in both body composition and metabolic outcome measurements. Multivariate regression analyses were performed to explore the independent associations between CRF, PA and sedentary time, and measures of body composition and metabolic outcomes. Statistical significance was based on a $p<0.05$. All data were analysed using STATISTICA version 10 (StatsoftInc. Tulsa, OK).

3.3 Results

3.3.1 Age, socio-demographic, body composition and body fat distribution characteristics

The mean age of the women in this study was 34 ± 7 years. Less than a third (22.3%) had completed Grade 12 and/or tertiary education, and 50.0% were employed. The majority of women consumed alcohol (78.9%) and 14.4% reported smoking currently.

Table 3.1 Body composition and body fat distribution characteristics (*n*=76).

	Mean ± SD	***Range***
Body composition		
Height (m)	1.61 ± 0.1	(1.46 - 1.73)
Weight (kg)	93.8 ± 17.8	(54.8 - 132.6)
BMI (kg/m^2)	35.9 ± 7.0	(23.7 - 53.4)
Fat-free soft tissue mass (kg)	47.0 ± 6.5	(30.9 - 65.5)
Fat mass (kg)	42.3 ± 12.7	(18.2 - 76.1)
% Body fat	45.5 ± 5.8	(31.9 - 58.0)
Body fat distribution		
Waist circumference (cm)	107.0 ± 15.5	(78.5 - 146.8)
Trunk fat mass (kg)	19.9 ± 6.6	(8.3 - 34.3)
Trunk fat mass (% FM)	46.8 ± 5.0	(35.9 - 58.5)
Appendicular fat mass (kg)	21.4 ± 6.7	(9.1 - 41.6)
Appendicular fat mass (% FM)	50.8 ± 6.6	(39.3 - 61.3)

Values are mean ± standard deviation. m, metres; kg, kilograms; kg/m^2, kilograms per metre squared; BMI, body mass index; %FM, percentage of fat mass.

The majority of women had one child or more (87.1%) and 32.8% of women reported current use of hormonal contraceptives (including oral and injectable contraceptives). Body composition and body fat distribution of the women are presented in Table 3.1. A small proportion of women were normal weight (3.9%) and overweight (17.1%) while the majority (79.0%) were obese.

When comparing the subsample of women who performed the submaximal step-test (*n*=46) to the whole sample (*n*=76), there were no differences in age, SES, height or measures of body composition (weight, BMI, fat mass and %BF). Furthermore, CT-

derived measures of central fat (VAT and SAT) were not different between the subsample and whole sample.

3.3.2 Physical activity, sedentary time and CRF measurements

Measures of PA, sedentary time and CRF are presented in Table 3.2. The majority of time during waking hours was spent in sedentary behaviours (~8.5hrs/day) (Figure 3.1).

Table 3.2 Sedentary time, physical activity and cardiorespiratory fitness.

Accelerometry data (n=76)	
Number of activity days measured	6 (4 - 7)
Non-wear time (min/day)	582 (526 - 668)
Wear time (min/day)	858 (771 - 914)
Sedentary time (min/day)	511 (423 - 569)
Total physical activity (min/day)	348 (275 - 436)
- Light-intensity physical activity (min/day)	318 (259 - 407)
- Moderate-intensity physical activity (min/day)	30 (14 - 42)
MVPA (min/day)	31 (15 - 43)
Steps per day	10 459 (8 152 - 13 021)
Cardiorespiratory fitness (n=46)	
Predicted VO_{2max} (ml/kg/min)	25.1 (22.8 - 28.4)

Values are presented as median (inter-quartile range). min/day, minutes per day; MVPA, moderate- to vigorous-intensity physical activity; VO_{2max}, maximal oxygen consumption; ml/kg/min, millilitres per kilogram per minute.

When engaged in PA, most time was spent in light-intensity activity with no vigorous- or very vigorous-intensity activity being recorded for any of the participants. A median of 31 min/day of MVPA was recorded, with just over half of the women (51.3%) meeting the global recommendations on PA for health (WHO, 2010) of at least 150 minutes of moderate-intensity activity per week; or 75 minutes of vigorous-intensity activity per week; or an equivalent combination of MVPA. A median of 10 459 daily steps was accumulated by all of the women who took part in the study with 55.3% (*n*=42) achieving an average of ≥10 000 steps per day

(steps/day), whereas the median for predicted VO_{2max} was rated as being 'very poor' [29] and falls below the 5th percentile for females aged 30-39 years.

CRF was inversely associated with sedentary time (*r*=-0.31, p=0.031; Figure 3.2), however, no associations were found between CRF and any of the PA measures.

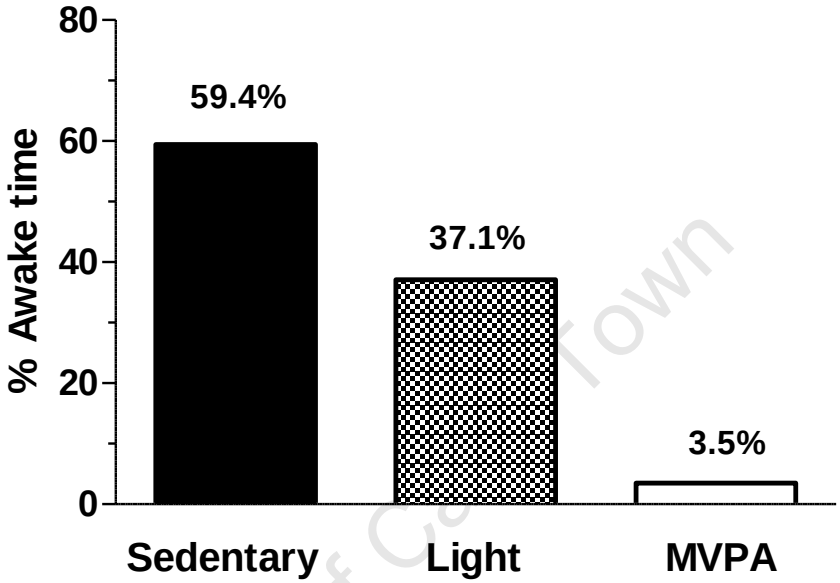

Figure 3.1 Percent of awake time spent at different activity in the sample of apparently healthy black SA women (*n*=76).

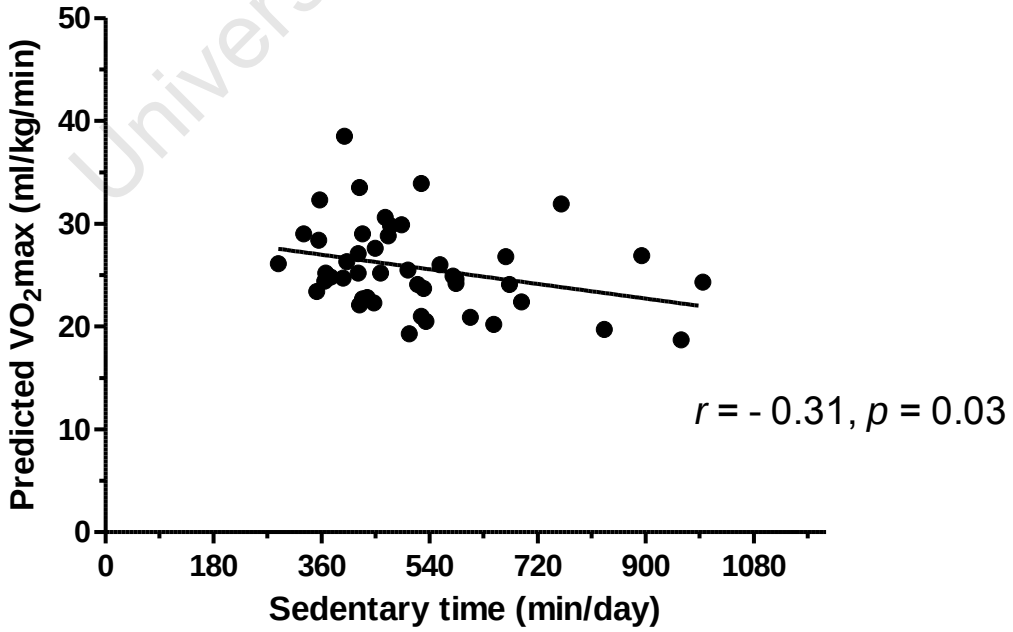

Figure 3.2 Relationship between sedentary behaviour measured in min/day and cardiorespiratory fitness as predicted VO_{2max} (ml/kg/min) in a subsample apparently healthy black SA women (*n*=46).

3.3.3 Metabolic outcomes

The metabolic characteristics of the women are presented in Table 3.3. According to the WHO/International Society of Hypertension statement for the management of hypertension (2003) [174], 12% (*n*=9) of the women were hypertensive (blood pressure, BP ≥140/90 mmHg). Although the mean serum lipid concentrations for all participants were within the desired normal range, 14.5% (*n*=11) had elevated TC, 6.6% (*n*=5) had elevated TG levels, 50.0% (*n*=38) had elevated LDL-C and 36.8% (*n*=28) had low HDL-C levels, according to the Adult Treatment Panel III criteria (ATP III, 2001) [175]. The majority (85.3%, *n*=58) of women were normoglycemic, whereas 14.7% (*n*=10) had impaired fasting plasma glucose (IFG ≥5.6 mmol/L).

Table 3.3 Metabolic outcomes.

	n	Mean ± SD	***Range***
Resting blood pressure			
SBP (mmHg)	*76*	111.8 ± 17.1	(78.5 - 166.5)
DBP (mmHg)	*76*	76.6 ± 12.0	(50.0 - 112.0)
Lipid profile			
Total cholesterol (mmol/L)	*76*	4.2 ± 0.9	(2.3 - 6.7)
LDL-C (mmol/L)	*76*	2.5 ± 0.8	(0.8 - 4.7)
HDL-C (mmol/L)	*76*	1.2 ± 0.3	(0.7 - 2.2)
Triglycerides (mmol/L)	*76*	0.9 ± 0.4	(0.4 - 2.9)
TC/HDL-C	*76*	3.7 ± 1.1	(1.7 - 6.1)
TG/HDL-C	*76*	0.9 ± 0.5	(0.2 - 3.3)
Insulin sensitivity			
Fasting plasma glucose (mmol/L)	*68*	5.2 ± 1.2	(4.0 - 14.3)
2-hour plasma glucose (mmol/L)	*65*	6.2 ± 2.1	(2.7 - 18.6)
Fasting serum insulin (mU/L)	*68*	14.1 ± 8.3	(4.0 - 44.7)
HOMA-IR	*68*	3.2 ± 1.1	(0.9 - 9.2)
Matsuda index	*69*	3.7 ± 2.2	(0.9 - 12.2)

mmol/L, millimoles per Litre; SBP, systolic blood pressure; DBP, diastolic blood pressure; LDL-C, low-density lipoprotein cholesterol, HDL-C, high-density lipoprotein cholesterol; TC/HDL-C, total cholesterol to high-density lipoprotein cholesterol ratio; TG/HDL-C, triglycerides to high-density lipoprotein cholesterol ratio; mU/L, milliunits per Litre; HOMA-IR, homeostasis assessment model of insulin resistance; Matsuda index, measure of insulin sensitivity [171].

Results from the 2-hr oral glucose tolerance test (OGTT) identified 2 women (3.1%, *n*=2) with impaired glucose tolerance (IGT, 2-hour OGTT plasma glucose level: 7.8-11.0 mmol/L) and another 2 women diagnosed with T2D (2-hour OGTT plasma glucose level: >11.0mmol/L) (WHO Technical Report, 2006).

3.3.4 Associations between PA, sedentary time, CRF, SES and lifestyle factors

Women who had not completed Grade 12 accumulated significantly more light-intensity PA than those who had completed Grade 12 and/or tertiary education (346 ± 12 vs. 283 ± 23 min/day, p=0.01). Women who reported having one child or more accumulated significantly more light-intensity PA (341 ± 12 vs. 272 ± 30 min/day, p=0.039) and more steps/day (11 292 ± 464 vs. 8 535 ± 1 192 steps/day, p=0.03) than those who did not have children. There was a tendency for those who did not own or use a motor vehicle to accumulate more moderate-intensity PA (30 ± 2 vs. 19 ± 5 min/day, p=0.08) than those who used and/or owned a private motor vehicle for transport.

Women who had completed Grade 12 and/or tertiary education tended to be fitter (28.2 ± 1.4 vs. 25.2 ± 1.0 ml/kg/min, p=0.06) than those with a lower level of education. Neither CRF nor sedentary time, were different between SES variables or lifestyle factors including hormonal contraceptive use, smoking and alcohol consumption.

3.3.5 Associations between PA, sedentary time and CRF and body composition measures

The associations between PA, sedentary time, CRF and body composition measures are presented in Table 3.4. Light-intensity PA was inversely correlated with WC, TFM and %TFM, while steps/day was inversely correlated with all measures of body composition and body fat distribution, except %TFM and %AFM. Neither MVPA nor sedentary time, were associated with any of the body composition measurements. Predicted VO_{2max} (ml/kg/min) was inversely associated with %BF and measures of centralisation of body fat including TFM, %TFM, as well as VAT (r=-0.47, p< 0.01) and VAT/SAT (r=-0.43, p<0.01).

Table 3.4 Associations between sedentary time, physical activity, cardiorespiratory fitness and body composition measurements.

	Weight (kg)	BMI (kg/m^2)	FM (kg)	% BF	WC (cm)	TFM (kg)	% TFM	AFM (kg)	% AFM
Sedentary time (min/day)	*r* = 0.03	*r* = -0.03	*r* = -0.01	*r* = -0.02	*r* = -0.07	*r* = 0.02	*r* = 0.11	*r* = -0.03	*r* = -0.10
Light-intensity PA (min/day)	*r* = -0.21	*r* = -0.17	*r* = -0.20	*r* = -0.17	***r* = -0.24***	***r* = -0.25***	***r* = -0.25***	*r* = -0.12	*r* = 0.23
MVPA (min/day)	*r* = -0.16	*r* = -0.15	*r* = -0.14	*r* = -0.11	*r* = -0.07	*r* = -0.09	*r* = 0.09	*r* = -0.18	*r* = -0.11
Steps per day	***r* = -0.35****	***r* = -0.27***	***r* = -0.33****	***r* = -0.25***	***r* = -0.24***	***r* = -0.31****	*r* = -0.08	***r* = -0.31****	*r* = 0.04
Predicted VO_{2max} (ml/kg/min)	*r* = -0.23	*r* = -0.26	*r* = -0.27	***r* = -0.34***	*r* = -0.20	***r* = -0.31***	***r* = -0.30***	*r* = 0.13	*r* = 0.24

Values are Pearson product-moment correlation coefficients. min/day, minutes per day; PA, physical activity; MVPA, moderate- to vigorous-intensity physical activity; VO_{2max}, maximal oxygen consumption; ml/kg/min, millilitres per kilogram per minute; kg, kilograms; BMI, body mass index; kg/m^2, kilogram per metre squared; FM, fat mass; %BF, percentage of body fat; WC, waist circumference; cm, centimetres; TFM, trunk fat mass, %TFM, percentage of trunk fat mass; AFM, appendicular fat mass; %AFM, percentage of appendicular fat mass. p<0.05; ** p<0.01*

To determine whether the associations between CRF and the body composition variables were independent of PA, CRF and PA (light-intensity or steps/day) were entered into a regression model with each body composition variable. CRF, but not PA was significantly associated with %BF (β=-0.34, p=0.01), TFM (β=-0.31, p=0.03), VAT (β=-0.48, p=0.02) and VAT/SAT (β= -0.43, p=0.01). The associations between CRF and body composition measures were also independent of SES (housing density) and appear in Table 3.5.

Table 3.5 Independent associations of cardiorespiratory fitness and physical activity with body composition measurements.

%Body fat				
n= 46	**R = 0.401**	**R² = 0.161**	**s.e.e = 5.83**	**P < 0.057**
	β	**B**	**s.e.e**	***P* value**
Predicted VO_{2max} (ml/kg/min)	-0.337	-0.498	0.213	0.024
Steps per day	-0.201	-0.000	0.000	0.161
Housing density (person/room)	-0.019	-0.088	0.673	0.895
Trunk fat mass (kg)				
n= 46	**R = 0.401**	**R² = 0.101**	**s.e.e = 6.69**	**P < 0.057**
	β	**B**	**s.e.e**	***P* value**
Predicted VO_{2max} (ml/kg/min)	-0.323	-0.547	0.244	0.030
Steps per day	-0.235	-0.000	0.000	0.103
Housing density (person/room)	0.088	0.471	0.772	0.544

VO_{2max}, maximal oxygen consumption; ml/kg/min, millilitres per kilogram per minute.

3.3.6 Associations between PA, sedentary time and CRF and metabolic outcomes

Associations between PA, sedentary time and CRF and metabolic outcomes, unadjusted and adjusted for fat mass (FM), in kilograms (kg) presented in Table 3.6. Increasing sedentary time was positively associated with serum TG concentrations and TG/HDL-C ratio, before and after adjusting for FM (kg). MVPA (min/day) was inversely associated with 2-hour plasma glucose levels and steps/day was inversely associated with fasting serum insulin concentrations and HOMA-IR, however these associations were no longer significant when adjusting for FM (kg). Light-intensity PA was not associated with any metabolic outcomes, and none of the PA variables, sedentary time or CRF, were associated with resting blood pressure (data not shown). Greater CRF (predicted VO_{2max}) was associated with an improved lipid profile (lower TC and LDL-C concentrations, and reduced TC/HDL-C and TG/HDL-C ratios) and insulin sensitivity (lower fasting serum insulin concentrations and HOMA-IR, and higher Matsuda indices), before and after adjusting for FM (kg). However, when adjusting for VAT none of the serum lipid profile components as well as measures of insulin sensitivity remained significant.

Table 3.6 Associations between sedentary time, physical activity, cardiorespiratory fitness and metabolic outcomes, unadjusted and adjusted for fat mass (kg).

		TC (mmol/L)	LDL-C (mmol/L)	HDL-C (mmol/L)	TG (mmol/L)	TC/HDL-C	TG/HDL-C	GLU (mmol/L)	2-hr GLU (mmol/L)	INS (mU/L)	HOMA-IR	MATSUDA INDEX
Sedentary time (min/day)	*Unadjusted*	*r* = -0.01	*r* = -0.01	*r* = 0.19	***r* = 0.33***	*r* = 0.15	***r* = 0.34****	*r* = 0.01	*r* = 0.13	*r* = 0.05	*r* = 0.07	*r* = 0.05
	Adjusted for FM (kg)	*r* = 0.03	*r* = 0.05	*r* = 0.19	***r* = 0.36****	*r* = 0.16	***r* = 0.34***	*r* = 0.20	*r* = 0.14	*r* = 0.15	*r* = 0.14	*r* = 0.18
Light-intensity PA (min/day)	*Unadjusted*	*r* = -0.10	*r* = -0.03	*r* = -0.05	*r* = -0.24	*r* = -0.04	*r* = -0.16	*r* = -0.05	*r* = -0.12	*r* = -0.15	*r* = -0.16	*r* = 0.11
	Adjusted for FM (kg)	*r* = 0.11	*r* = 0.04	*r* = 0.05	*r* = 0.23	*r* = 0.05	*r* = 0.16	*r* = 0.21	*r* = 0.12	*r* = 0.28	*r* = 0.30	*r* = 0.19
MVPA (min/day)	*Unadjusted*	*r* = -0.20	*r* = 0.11	*r* = -0.00	*r* = 0.03	*r* = 0.06	*r* = 0.02	*r* = -0.06	***r* = -0.27***	*r* = -0.07	*r* = -0.12	*r* = 0.02
	Adjusted for FM (kg)	*r* = 0.09	*r* = 0.14	*r* = 0.04	*r* = 0.06	*r* = 0.08	*r* = 0.03	*r* = 0.21	*r* = 0.12	*r* = 0.28	*r* = 0.30	*r* = 0.19
Steps per day	*Unadjusted*	*r* = -0.09	*r* = -0.09	*r* = -0.11	*r* = -0.18	*r* = 0.06	*r* = -0.08	*r* = -0.13	*r* = -0.16	***r* = -0.25***	***r* = -0.27***	*r* = 0.13
	Adjusted for FM (kg)	*r* = 0.02	*r* = 0.11	*r* = 0.11	*r* = 0.19	*r* = 0.07	*r* = 0.09	*r* = 0.22	*r* = 0.16	*r* = 0.22	*r* = 0.26	*r* = 0.19
Predicted VO_{2max} (ml/kg/min)	*Unadjusted*	***r* = -0.42****	***r* = -0.45****	*r* = 0.13	*r* = -0.28	***r* = -0.42****	***r* = -0.30***	*r* = -0.21	*r* = -0.28	***r* = -0.37***	***r* = -0.41****	***r* = 0.39***
	Adjusted for FM (kg)	***r* = -0.32***	***r* = -0.37***	*r* = 0.14	*r* = 0.19	***r* = -0.36***	***r* = -0.31***	*r* = 0.28	*r* = 0.28	***r* = -0.40***	***r* = -0.40***	***r* = 0.36***

Values are Pearson product-moment correlation coefficients (top row, unadjusted values) & Partial correlation coefficients (bottom row, values adjusted for fat mass (FM) in kilograms (kg)). min/day, minutes per day; PA, physical activity; MVPA, moderate- to vigorous-intensity physical activity; VO_2max, maximal oxygen consumption; ml/kg/min, millilitres per kilogram per minute; TC, total cholesterol; mmol/L, millimoles per litre; LDL-C, low-density lipoprotein cholesterol, HDL-C, high-density lipoprotein cholesterol; TC/HDL-C, total cholesterol to high-density lipoprotein cholesterol ratio; TG/HDL-C, triglycerides to high-density lipoprotein cholesterol ratio; GLU, fasting plasma glucose;2-hr GLU, 2-hour plasma glucose; INS, fasting serum insulin; mU/L, milliunits per Litre; HOMA-IR, homeostasis assessment model of insulin resistance; MATSUDA INDEX, measure of insulin sensitivity [171]. p< 0.05; ** p<0.01*

To determine whether the associations between CRF and the metabolic outcomes were independent of PA, CRF and PA (MVPA and steps/day) were included in a regression model together with each metabolic outcome variable. Only the association between CRF and serum lipid concentrations ((TC (β= -0.42, p=0.01), LDL-C (β= -0.45, p=0.01), TC/HDL-C ratio (β= -0.42, p=0.01), TG/HDL-C ratio (β= -0.30, p=0.04)) and insulin sensitivity (fasting serum insulin (β= -0.37, p=0.04), HOMA-IR (β= -0.41, p=0.01) remained significant in the model, and not PA, even after adjusting for FM (kg) as well as SES (housing density) and appear in Table 3.7.

Table 3.7 Independent associations of cardiorespiratory fitness, physical activity, SES and body fat with measures of insulin resistance.

Fasting serum insulin (mU/L)				
n= 41	**R = 0.510**	**R² = 0.260**	**s.e.e = 0.20**	**P < 0.024**
	β	**B**	**s.e.e**	***P* value**
Predicted VO_{2max} (ml/kg/min)	-0.434	-0.022	0.008	0.008
Steps per day	-0.191	-0.000	0.000	0.205
Housing density	0.293	0.046	0.023	0.053
Body fat (kg)	-0.001	-0.000	0.002	0.994
HOMA-IR				
n= 41	**R = 0.589**	**R² = 0.347**	**s.e.e = 1.48**	**P < 0.003**
	β	**B**	**s.e.e**	***P* value**
Predicted VO_{2max} (ml/kg/min)	-0.459	-0.188	0.059	0.003
Steps per day	-0.260	-0.000	0.000	0.069
Housing density	0.323	0.404	0.172	0.024
Body fat (kg)	0.049	0.006	0.019	0.735

VO_{2max}, maximal oxygen consumption; ml/kg/min, millilitres per kilogram per minute.

3.4 Discussion

Although 96.1% of the apparently healthy black SA women involved in this study were overweight or obese, more than half of them met the global recommendations on PA for health [72] and the recommended goal of ≥10 000 steps/day. The study showed that the more time spent in light-intensity PA, as well as steps/day and not MVPA, were associated with lower body fat (trunk fat mass (TFM)). Steps/day were also found to be associated with improved measures of insulin sensitivity (fasting serum insulin concentrations and HOMA-IR), whereas reduced sedentary time was associated with higher serum lipid profiles (TG and TG/HDL-C ratio), independent of FM (kg). Higher CRF was associated with reduced body fat (%BF and TFM), as well as improved measures of insulin sensitivity (fasting insulin serum and HOMA-IR) independent of fat mass (kg) and PA, but not VAT. Furthermore, although there were no associations between CRF and any of the PA variables, CRF was inversely associated with sedentary time.

In this sample of black SA women, the majority of PA time was spent in light-intensity activity (~5.3 hrs/day), which together with steps/day were associated with reduced body weight and total adiposity (%BF). Similarly, Cook et al. (2008) [79] reported a dose-dependent relationship between ambulatory activity (number of steps/day) and reduction in obesity risk amongst a rural sample of SA women using pedometry. After adjusting for age, motor vehicle access, education, tobacco use and co-morbidities, BMI was shown to be 1.4 kg/m^2 lower per 5 000 steps/day. Together these results show favourable associations between daily activity (steps/day) and reduced body composition measures. To date, most research has focused only on the effects of MVPA, with little attention on light-intensity activities. Higher levels of MVPA are associated with lower BMI [158] and favourable patterns of body fat distribution [158,198]. In contrast and irrespective of the majority of women meeting the recommended MVPA guidelines, results from the present study showed that greater light-intensity PA, and not MVPA, was associated with lower measures of body fat or its distribution. This may be due to the relatively low level of MVPA performed by the women involved in the present study compared to higher levels performed by women in larger prospective studies [40,199]. However, a more recent meta-analysis comparing objectively measured PA energy expenditure (PAEE) amongst adult women from HICs and LMICs have questioned the impact which PAEE has on body composition [189]. Despite group differences in body size reported by Dugas et al. (2011) [189], total PAEE was the same for both groups. Thus, the

disparity in the prevalence of obesity that exists between HICs and LMICs may be the result of other lifestyle factors. Future large-scale international studies should examine the independent effects of light-intensity PA on body composition.

I also showed that increased PA was associated with improved insulin sensitivity. Specifically, steps/day was associated with fasting serum insulin concentrations and HOMA-IR, while MVPA was associated with 2-hour plasma glucose levels. However, all of these associations were not independent of total body fat. This contrasts to other studies that have shown an association between total PA and reduced metabolic risk for T2D, independent of differences and changes in adiposity [47,48,49,190]. The low intensity of the activity performed by the participants in this study could possibly explain this difference. High intensity PA is associated with metabolic changes, including an increase in glucose transporter type 4 (GLUT4) for example, that increase target tissue sensitivity (liver, skeletal muscle and adipose tissue), and leads to an overall improvement in plasma glucose regulation, which is independent of the effects on body fatness [200,201].

The results from the present study showed that with increasing fitness, measures of total adiposity (%BF) were significantly reduced. Comparably, Cook et al. (2009) [80] used a similar measure to predict CRF amongst a group of rural SA women (~36.3 years) and showed that those with the highest CRF had significantly less body fat. In contrast to the study of Cook et al. (2009) [80], I did not show an association between CRF and PA (light-intensity, MVPA and steps/day). This may be due to the women in our subsample accumulating less steps/day (~10 459 vs. ~13 600/day) and completing less MVPA than the rural women, who performed almost 8 times the amount of MVPA per day (~253 vs. ~31 min/day). Furthermore, evidence from exercise training-based studies show CRF level to be influenced by genetic factors [202] as well as high intensity PA [203]. Intervention studies are therefore required, especially amongst population groups from low-middle income countries to determine whether an increase in MVPA translates into an increase in CRF level and its associated health benefits.

In contrast to PA, the associations between CRF and improved serum lipid concentrations and measures of insulin sensitivity, were independent of fat mass. Notably, these associations were also independent of PA. These results support those from a prospective study in which individuals who increased their CRF over a period of 1-year had reduced levels of fasting plasma glucose and fasting serum

insulin, and increased concentrations of HDL-C at follow-up (*ProActive* trial) [127]. Further, low CRF level has been shown to be a strong and independent predictor of incident metabolic syndrome, independent of BMI [128]. Such findings and those from the present study highlight the potential benefits of increasing CRF, especially amongst population groups at risk for developing T2D.

Unique to my study was my ability to measure body fat distribution using DXA- and CT-scanning techniques. The negative association between increasing CRF and VAT is of significance as results from the Framingham Heart Study showed that VAT was more closely associated with insulin resistance than SAT [204]. In this study of black SA women, I showed that the association between CRF and insulin sensitivity is mediated via VAT. This was a surprising result given that research from our laboratory [21] and others such as Lovejoy et al. (1996) [213] have shown that black women have less VAT than BMI-matched white women, and that insulin sensitivity was more closely associated with SAT than VAT. Nonetheless, this study emphasises the importance of having a high CRF level to derive metabolic health-benefits. Public health strategies should aim to educate and encourage women to increase CRF level and future intervention studies should aim to measure CRF level as well as its association with metabolic risk factors for CVD and T2D.

In contrast to other studies [132,205,206], we did not find an association between sedentary time and body composition measurements, however we did show an inverse association between sedentary time and CRF. This finding is supported by cross-sectional studies in young adolescent girls [36,207,208,209], as well as in an intervention study that showed a reduction in sedentary behaviour increased CRF level [210]. Despite no associations with body composition, I showed an association between sedentary time and serum lipid concentrations (TG and TG/HDL-C ratio). This finding is supported by other studies that have shown an association between sedentary behaviour and increased risk for CVD and metabolic related diseases [134,136,151,152]. It has been proposed that these effects may be mediated by a reduction in lipoprotein lipase (LPL) activity when exposed to acute and chronic periods of sedentary behaviour [191,211,212]. Notably, black SA (and USA) women have a more favourable serum lipid profile than their white counterparts, characterised by lower serum TG concentrations [22,184], as well as higher LPL activity [183]. Based on the results of this small study, I hypothesise that increasing sedentary behaviour with urbanisation in black SA women will be associated with increased serum lipid

concentrations, and a consequent increase risk for CVD. However, large-scale prospective studies are required to test this hypothesis.

The strengths of the present study include the use of robust and high precision measurements including accelerometry to measure free-living PA time, DXA- and CT-scanning techniques to quantify body composition and body fat distribution, as well as an OGTT to estimate insulin sensitivity. Although the number of women who completed the submaximal CRF step-test was low, the study still showed independent associations between body composition measures, metabolic risk factors for CVD and T2D and CRF level.

In conclusion, the present study highlights the importance of light-intensity PA and CRF level which were associated with reduced adiposity and metabolic risk for CVD and T2D, amongst a sample of apparently healthy black SA women. Although, the majority of women met the global recommendation of PA for health [72], it was light-intensity PA and CRF, rather than MVPA, which were more closely related to reduced total and trunk fat mass, and improvement in insulin sensitivity. These findings should be confirmed in larger independent cohorts. Based on these preliminary findings, public health messages should aim to encourage and increase daily PA, including light-intensity PA, whilst reducing sedentary behaviours to reduce obesity levels and risk factors for CVD and T2D, but at the same time develop strategies to increase CRF.

CHAPTER FOUR

SUMMARY AND CONCLUSIONS

Summary and conclusions

SA is currently undergoing rapid epidemiological transition [11,156], and increased urbanisation associated with decreases in PAEE [15]. The prevalence of obesity is highest in black SA women, who also have a disproportionately high prevalence of IR and T2D compared to their white counterparts [21]. It is, however, not known whether PA, inactivity, sedentary behaviour (time) and/or CRF are associated with obesity and associated risk factors for CVD and T2D.

The main objective of this thesis was to measure and describe PA patterns in a sample of apparently healthy black SA women. Furthermore, to compare body composition and metabolic risk factors for CVD and T2D, between active and inactive groups classified according to international PA recommendations for health [66] (study 1, part 1, cross-sectional analysis), and to determine whether PA level predicts changes in body composition and metabolic risk factors for CVD and T2D, over a 5.5-year follow-up period (study 1, part 2, longitudinal analysis). In addition, study 2 aimed to examine the independent effects of PA, CRF and sedentary time on body composition and metabolic risk factors for CVD and T2D (cross-sectional analysis).

The main findings of this thesis are summarised in Table 4.1:

Table 4.1 Summary of the main findings**.**

Study 1 - **part 1, cross-sectional study**	- The majority of black women in this cohort were sufficiently active according to current GPAQ criteria (61%) and recent WHO PA criteria (71.4%). - Active women had lower body weight and body fat, as well as higher serum HDL-C concentrations, and were more insulin sensitive (lower fasting serum insulin concentrations and HOMA-IR), compared to inactive women. The differences in metabolic outcomes were mediated by body weight.
Study 1 - **part 2, longitudinal study**	- Although active women at baseline had significantly less body fat at follow-up compared to inactive women, body weight and fat mass increased similarly in both groups over the 5.5-year follow-up period. - Independent of age and body weight, DBP decreased significantly in women who were active at baseline, but did not change in women who were inactive at baseline. - Fasting serum lipid and plasma glucose concentrations did not change significantly and remained relatively low in both groups. Mean fasting serum insulin levels were lower in the active group compared to the inactive group at baseline and follow-up, and did not change significantly in either group.
Study 2	- Although 96.1% of this cohort of black SA women were overweight or obese, more than half of them met the global recommendations for PA for health [72] and the recommended goal of ≥10 000 steps/day. - Greater time spent in light-intensity PA, as well as steps/day, but not MVPA, were associated with lower body fat (TFM). - Steps/day were associated with improved measures of insulin sensitivity (fasting serum insulin concentrations and HOMA-IR), and increased sedentary time was associated with higher serum lipid profiles (TG and TG/HDL-C ratio), independent of FM (kg). - Higher CRF was associated with reduced body fat (%BF and TFM), and improved serum lipid concentrations and measures of insulin sensitivity (fasting insulin serum and HOMA-IR), independent of TFM and PA, but not VAT. - CRF did not correlate with any of the PA variables, but was inversely associated with sedentary time.

Previous studies have shown that lower PA is associated with an increased risk for obesity [90,91], CVD and T2D [106,107]. To my knowledge, this is the first study to categorise physical activity levels in urban black SA women, who have a high prevalence of obesity, to determine if these criteria distinguish overall metabolic risk in this population. Part 1 (cross-sectional analysis) of the first study of this thesis compared body composition and metabolic risk factors for CVD and T2D, between active and inactive groups. Using subjective PA measures, the majority (61%) of women were sufficiently active, and had lower CVD-risk compared to those who failed to meet PA recommendations of 150 min/week of moderate-intensity PA, or 75 min/week of vigorous-intensity PA, or a combined equivalent. These findings therefore highlight the importance of encouraging PA (MVPA) among black urban SA women, which is associated with decreased body weight and body fat, and an improved metabolic profile. To my knowledge, this is the first study in South Africa that has shown significant differences in body composition and metabolic risk factors for CVD and T2D, in active vs. inactive black urban women.

Part 2 of the first study of this thesis then went on to determine whether PA level predicted changes in body composition and metabolic risk factors for CVD and T2D, over a 5.5-year follow-up period (longitudinal analysis). At follow-up, body weight had increased significantly in both activity groups, but this increase in body weight was not associated with an increase in metabolic risk in either group. Possible explanations these findings may relate, in part to the short follow-up period (5.5 years), and the relatively young age and small size of the cohort. DBP did decrease significantly in the active group (78±7 vs. 74±14 mmHg, p=0.039), but not in the inactive group. Future studies may assist in determining whether a change in PA level with increasing age is associated with a change in CVD-risk.

Although the GPAQ has been shown to be a useful tool to capture PA data in large epidemiological studies [15,43], it is reliant on subjective recall and is only able to characterise MVPA, and therefore unable to quantify 'light' or 'incidental' activity. These components can be captured by using an objective measure of PA, namely accelerometry. Thus, the aim of the second study of this thesis was to examine the independent effects of PA (light-intensity, MVPA and steps/day), CRF (estimated VO_{2max}) and sedentary time, on body composition and metabolic risk factors for CVD and T2D (cross-sectional analysis) in a sample of black urban adult women. Similar to the results found when using subjectively measured PA, the majority (51.3%) of the women were categorised as sufficiently active. In this study, I showed that light-

intensity PA and steps/day were both associated with lower adiposity, and that increased steps/day and MVPA were associated with improved measures of insulin sensitivity, via the effect of PA on body fat. These findings highlight the importance of increasing daily PA, irrespective of intensity. Intervention studies using different physical activity intensities should be designed in this population to determine whether light intensity exercise leads to similar health outcomes as higher intensity physical activity.

To my knowledge, this is the first study that has objectively measured sedentary time, and its association with body composition and metabolic health outcomes, in this population. Similar to HIC studies, I showed that time spent in sedentary behaviour was associated with dyslipidaemia, independent of body fat. This has major implications not only for SA's public health policy, but also internationally, as this field of research is still in its infancy compared to PA research. To date, the majority of public health policies focus mainly on increasing daily MVPA, with little or no focus on decreasing sedentary behaviour. Thus, it seems crucial for public health policies world-wide to now devise sedentary guidelines to discourage time spent involved in sedentary activities like sitting, while also raising awareness of the detrimental health effects associated with sedentary behaviour.

Another unique feature of this thesis includes the measurement of CRF and its association with body composition and metabolic outcomes. Notably, high CRF was associated with a lower total and central fat mass, as well as an improved lipid profile and higher insulin sensitivity, independent of adiposity level. Interestingly, I found that CRF was inversely associated with sedentary time, but not with any of the PA variables, possibly due to variability in the PA measures used. Based on these results, physical activity recommendations to increase CRF in order to improve metabolic health should be encouraged. Future studies should focus on investigating ways of increasing CRF in this population.

The studies in this thesis have some limitations that need to be noted. Both studies included participants which were not randomly sampled, but rather recruited through local newspapers, church groups and universities (conveniently sampled). Thus, the results may not be representative of the black SA population. We only focused on black SA women as they present with the highest level of obesity in South Africa [155] and may therefore be at the highest risk of future metabolic disease. Future studies should focus on men, as well as other ethnic groups. Furthermore, in Study 1

(Chapter 2), there was a difference in age between the women who were categorised as active and inactive. Although the analyses were adjusted for differences in age, this does not take into account the physiological changes associated with ageing. However, the decrease in PA with age may reflect a social/behavioural effect in this relatively young sample, and this should be investigated further. Due to the relatively small number of participants followed-up for part 2 of Study 1, the longitudinal results presented in this thesis offer preliminary findings, and highlight the need for a larger and longer follow-up study, in order to track changes in overall risk for CVD and T2D in black urban women. We were also unable to measure PA change over the 5.5-year follow-up period, and its relationship with obesity, and metabolic risk outcomes for CVD and T2D.

Highlights of this thesis include the use of objectively measured PA level, sedentary time and CRF level in Study 2. In addition, I also used sophisticated radiological scanning techniques, DXA and CT, to measure body composition. These techniques provide more information on body fat distribution which is particularly relevant in this population of predominantly obese women, who have previously been shown to have less visceral fat and more peripheral fat than their white counterparts. Furthermore, the longitudinal nature of Study 1 (part 2), to my knowledge, is the first follow-up design reported in SA. Lastly, I examined PA in relation to insulin sensitivity measured using an OGTT, as opposed to recently reported fasting samples [80,83].

In summary, this thesis has important implications for public health practices and messaging. Public health messages should aim to encourage an increase in daily PA (light-intensity, MVPA and steps/day) whilst reducing sedentary behaviours, and at the same time develop strategies to increase CRF. In the SA context, this thesis highlights the importance of each of these behaviours, in decreasing overall risk for obesity and metabolic diseases (CVD and T2D) in black urban SA women.

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APPENDICES

SUBJECT QUESTIONNAIRE-ENGLISH VERSION

Subject Number: _____ Date: _____

SOCIO-DEMOGRAPHIC QUESTIONNAIRE
Longitudinal follow-up study
Genotype and Phenotype Interactions in Black South African Women

Contact Information:
Miss Kasha Dickie
Cell: 082 881 4436
kasha.dickie@uct.ac.za

SUBJECT CODE:

ANCESTRY

Ancestry: Tribal or national background (e.g. Xhosa, Zulu, Dutch, English):

Grandfather _____

Father _____

Grandmother _____

Grandfather _____

Mother _____

Grandmother _____

Self: _____

CONTRACEPTION

Contraception:
None: ☐
Pills ☐
Name: _____Duration: _____

☐
Injection
Name: _____Duration:_____

IUD ☐
Date inserted: _____

Sterilization (tubes tied) ☐
Date: _____

Other ☐
Details: _____

Menstrual cycle: Regular Yes ☐ No ☐
Start date of last menstrual cycle: _____

HIV STATUS

1	Do you know your HIV status?	YES..... NO.....
2	If yes, are you:	Positive..... Negative..... Unwilling to disclose ……
3	When was your last test?	.....
4	Are you receiving treatment for HIV/AIDS	YES..... NO.....

MEDICATION		
1a	Do you use any medicine regularly or daily that a doctor or nurse has prescribed?	YES..... NO.....
1b	How many different medicines do you use regularly (more than once a month)?	NUMBER: .....
1 c	Name of medication and dosage	
1 d	Do you use nutritional or other supplements?	YES NO
1 e	Name the supplement and dosage:	

DEMOGRAPHIC AND SOCIOECONOMIC DETAILS:
SUBJECT CODE: _____

How many people living in your household, including you?
..... people
How many rooms do you have in your house (including kitchen, lounge, dining room, bedrooms)?
.....rooms
In your home, how many rooms are there just for sleeping?
.....rooms
How would you describe your home (tick the one that best describes it)?

Room/garage attached /not attached to house		House		Shared house	
Flat		Hostel		Other:	

How would you describe the ownership of your home (tick the one that best describes it)?

Own with no bond/mortgage		Own with bond/mortgage		Rent the house	
Rent a room		Pay board and lodging (e.g. residence)		Free accommodation	
Subsidised housing		Other			

What type of household water do you have access to?

Indoor water		Only outside tap water		Other water source	

What type of toilet do you have?

Flush inside		Only flush outside	
Outside toilet		Other:	

Which of the following do you have in your household at the present time?

	YES	NO		YES	NO
Electricity			Telephone		
Television			Video machine		
Radio			Microwave		
Motor vehicle			Computer		
Fridge			Cellular telephone		
Stove and oven			Mnet		
Washing machine			DSTV		

Marital status:

Single		Divorced/separated	
Married		Widowed	
Living with partner, not married			

How many children do you have? ..... children
How many pregnancies have you had? .....pregnancies

What are the ages of the children? .....

Education (last standard passed):

No formal education		Std 8 (Grade 10)	
Sub A/B (Grade 1-2)		Std 9 (Grade 11)	
Std 1-3 (Grade 3-5)		Matric (Grade 12)	
Std 4-5 (Grade 6-7)		College or Technicon	
Std 6-7 (Grade 8-9)		University	

Are you currently doing work for which you get payment?
Yes ..... No .....

14. For how long have you being doing this? .....

15. How many days a week do you work? .....

16. How do you receive payment?

Monthly salary		Daily wage	
Weekly wage		Informal trading or	

		vendor	
Casual hourly rate			

Describe your occupation .....

Period of current employment: .....

19. Household income from all sources (tick the appropriate boxes)

Salary (monthly)		Wage (weekly)	
Casual work		No of days working/week	
Income from informal work		No of days working/week	
Grants		Specify:	
Support from partner		Support from family	

Monthly Household Income:

R 0 to R 2 500 ☐

R 2 500 to R5 000 ☐

R 5 000 to R 7500 ☐

R 7 500 to R 10 000 ☐

R 10 000 to R 15 000 ☐

R 15 000 to R 20 000 ☐

R 20 000 to R 30 000 ☐

Other give range .....- .....

Not willing to disclose: .....

How many people do you support with this income?

Adults: .....

Children:.....

Are you covered by a Medical Aid or a Medical Benefit Scheme, or any scheme that helps you pay for health care or drug services?

Yes ☐ No ☐

Name of medical insurance? .....

Full medical cover ☐
Savings plan ☐
Hospital plan ☐
Other: .....

We would like to know more about the community in which you live. Which of the facilities listed below are within about 2km from your house that you can walk to within 20 min? Do you use these facilities?

	Tick if facility present	Tick if you use facility	Do you walk there on most occasions		Tick if facility present	Tick if you use facility	Do you walk there on most occasions
Primary school				Internet café			
Secondary school				Bar/tavern			
Hospital				Nightclub			
Primary healthcare clinic (day hospital)				Cinema			
Private doctor				Restaurant (sit-down)			
Pharmacy/chemist				Community/recreational centre			
Police station				Place of worship (church)			
Shopping mall/centre				Library			
Fast food outlet				Sports fields/courts			
Convenience store				Gym			
Park (green area)				Petrol station			
Car dealership				Bus stop			
Train station				Taxi rank			
Street vendor				Hair salon			
Cell phone vendor				Bank			

Which of the following are in your neighborhood? (tick if yes)

	Yes		Yes
Postal service		Gravel roads	
Street lighting in working condition		Tar roads	
Piped water supply		Garbage removal	

Which language do you speak at home? .....

27. How would you self identify your ethnicity? .....

FAMILY MEDICAL HISTORY

SUBJECT CODE: _____

NO.	QUESTIONS AND FILTERS	CODING CATEGORIES	SKIP
1	Now I would like to ask you about your family. Do you have a close blood relative (grandparents, father, mother, brother, sister or child) who has ever had any of the following conditions:		
1a	High Blood Pressure?	YES.....1 NO.....2 DON'T KNOW.....8 If yes, who? …… …… …… …… ……	
1b	Heart attack or angina or chest pain when exerting himself/herself?	YES.....[1] NO.....[2] DON'T KNOW.....[8] If yes, who…… …… …. …… …… …… …… …… …… ……	

NO.	QUESTIONS AND FILTERS	CODING CATEGORIES	SKIP
1c	Was this relative younger or older than 50 years old when they first had a heart attack, angina or chest pain?	YOUNGER THAN 50 YEARS …… …… …… OLDER THAN 50 YEARS …… …… …… DON'T KNOW …… …… ……...	
1d	Stroke?	YES.....[1] NO.....[2] DON'T KNOW.....[8] If yes, who? …… …… …….. …… …… …… …… …… …… …… ……	
1e	Diabetes?	YES.....[1] NO.....[2] DON'T KNOW.....[8] If yes, who? …… …… ……	

NO.	QUESTIONS AND FILTERS	CODING CATEGORIES	SKIP
		…… Adult/ child onset? …… …… ……	
1f	Obesity? (Were they abnormally large? Or have difficulty moving?)	YES.....[1] NO.....[2] DON'T KNOW.....[8] If yes, who? …… …… …… …… …… …… ……	

QUALITY OF LIFE AND CLINICAL CONDITIONS

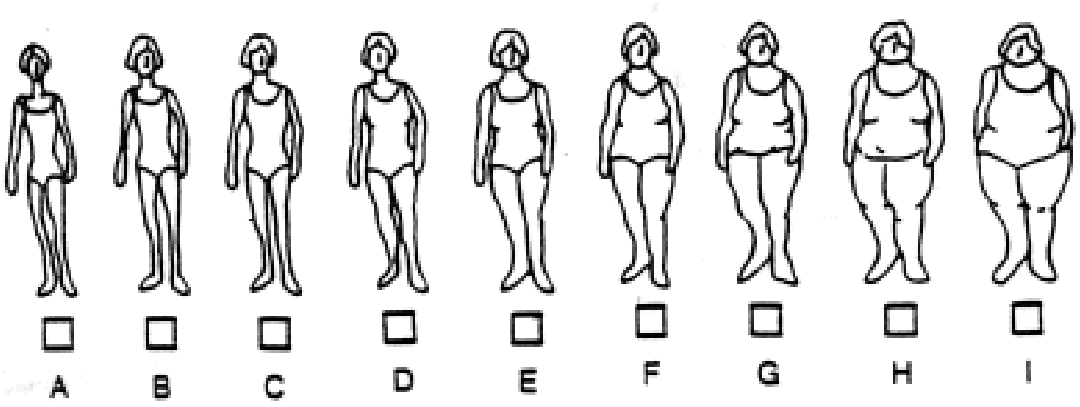
SUBJECT CODE: _____

NO.	QUESTIONS AND FILTERS	CODING CATEGORIES	SKIP
1a	Would you say your health is : 'poor, average, good, or very good/excellent'?	POOR.....[1] AVERAGE.....[2] GOOD.....[3] VERY OOD/EXCELLENT.....[4]	
1b	Do you personally think that you are underweight, normal weight or overweight?	UNDERWEIGHT.....[1] NORMAL WEIGHT.....[2] OVERWEIGHT.....[3] DON'T KNOW.....[8]	
2	Has a doctor or nurse or health worker at a clinic or at hospital told you that you had or have any of the following conditions:		
2a	High Blood Pressure?	YES.....[1] NO.....[2] DON'T KNOW.....[8]	
2b	Heart attack or angina (chest pains)?	YES.....[1] NO.....[2] DON'T KNOW.....[8]	
2c	Stroke?	YES.....[1] NO.....[2] DON'T KNOW.....[8]	
2d	High blood cholesterol or fats in the blood?	YES.....[1] NO.....[2] DON'T KNOW.....[8]	
2e	Diabetes or Blood Sugar?	YES.....[1] NO.....[2] DON'T KNOW.....[8]	
2f	Emphysema/Bronchitis?	YES.....[1] NO.....[2] DON'T KNOW.....[8]	

NO.	QUESTIONS AND FILTERS	CODING CATEGORIES	SKIP
2g	Asthma?	YES.....[1] NO.....[2] DON'T KNOW.....[8]	
2h	Sore joints, e.g. Arthritis, gout?	YES.....[1] NO.....[2] DON'T KNOW.....[8]	
2i	Osteoporosis?	YES.....[1] NO.....[2] DON'T KNOW.....[8]	
2j	Epilepsy / fits?	YES.....[1] NO.....[2] DON'T KNOW.....[8]	
2k	TB?	YES.....[1] NO.....[2] DON'T KNOW.....[8]	
2l	How many episodes of TB have you ever been treated for?	NUMBER OF TB EPISODES …….. Are you currently on TB medications? ……. When was your last TB episode: ……	
2m	Cancer?	YES.....[1] NO.....[2] DON'T KNOW.....[8] If yes, what? …… ……..	

BODY IMAGE ASSESSMENT

SUBJECT CODE: _____



Choose the picture of a woman that you think is

Thin		Normal weight		Fat	

Choose the picture of the woman you think will:

Look best		Be the strongest	
Be clumsy		Be the weakest	
Have more respect than the others		Be the happiest	
Have less respect than the others		Be the most unhappy	

Choose the woman that:

You would want to look like		Your friend will want you to look like	
Your husband / partner will want you to look like		Your children will want you to look like	

Which of the pictures do you think you look the most like?

.....

How happy are you with your present weight?

Happy		Somewhat happy		Unhappy	

Do you think you are:

Underweight		Normal weight		Overweight	

No.	Question:	YES	NO	Amount
7	Have you ever thought that you are thin?			N/A
8	Have you ever thought that you are fat?			N/A
9	Has your husband or partner ever told you that you are thin?			N/A
10	Have your friends ever told you that you are thin?			N/A

11	Have your children ever told you that you are thin?			N/A
12	Has your husband or partner ever told you that you are fat?			N/A
13	Have your friends ever told you that you are fat?			N/A
14	Have your children ever told you that you are fat?			N/A
15	Do you worry about being thin?			N/A
16	Do you worry about being fat?			N/A
17	Have you lost weight in the last 3-6 months without trying?			N/A
18	Have you gained weight in the last 3-6 months without trying?			N/A
19	Have you ever tried to lose / are currently trying to lose weight?			N/A
20	Have you ever tried to gain / are currently trying to gain weight?			N/A

Choose the method that you used / are using to lose weight:

Reduced the amount of food I eat		Starve myself	
Exercise more		Use weight-reducing medications	
Skip more meals		Other	
Use a specific diet:		N/A	

Choose the method that you think caused you to gain weight

Increase the amount of food I eat		Eat more meals than I usually eat each day	
Exercise more		Take supplements to increase energy intake:	
Use a specific diet:		Other or N/A	

23. If a woman your age is thin, she would:

Have more friends	yes	no	Be beautiful	yes	no
Feel better about herself	yes	no	Feel more like a woman	yes	no
Be healthier	yes	no			

24. If a woman your age is fat, she would:

Have more friends	yes	no	Be beautiful	yes	no
Feel better about herself	yes	no	Feel more like a woman	yes	no
Be healthier	yes	no			

HABITS AND LIFESTYLE

	PHYSICAL ACTIVITY (Modified STEPs Core data set) The next questions are about the time you spend doing different types of physical activities. This includes activities you do at home, at work, travelling from place to place and during your spare time. You are requested to answer the questions even if you don't consider yourself to be an active person.		
	Occupation-related Physical Activity (paid or unpaid work): When answering the following questions, think back over the past 12 months and consider (think of) a usual week:		Go to:
1	Does your work involve mostly sitting or standing still, OR walking for very short periods (less than 10 minutes)?	YES.....[1] NO.....[2]	Q.4
2a	Does your work involve vigorous activities, (like heavy lifting, digging, or heavy construction) for at least 10 minutes at a time?	YES.....[1] NO.....[2]	Q.3a
2b	In a usual week, how many days do you do vigorous activities as part of your work?	.....DAYS	
2c	On a usual day on which you do vigorous activities, how much time do you spend doing such work?	.....HOURS .....MINUTES	
3a	Does your work involve moderate-intensity activities (like brisk walking or carrying light loads) for at least 10 minutes at a time?	YES.....[1] NO.....[2]	Q.4
3b	In a usual week, how many days do you do moderate-intensity activities as part of your work?	.....DAYS	
3c	On a usual day on which you do moderate-intensity activities, how much time do you spend doing such work?	.....HOURS .....MINUTES	
4	How long is your usual workday?	.....HOURS .....MINUTES	
	Travel-related Physical Activity: Other than activities that you've already mentioned; I would like to ask you about the way you travel to and from places (to work, to shopping, to market, to church, etc).		
5a	Do you walk or use a bicycle (pedal cycle) for at least 10 minutes at a time to get to and from places?	YES.....[1] NO.....[2]	Q.6
5b	In a usual week, how many days do you walk or cycle for at least 10 minutes to get to and from places?	.....DAYS	
5c	On a usual day, how much time do you spend walking and cycling for travel	.....HOURS .....MINUTES	

	Non-work related and leisure time Physical Activity: The next questions ask about activities you do in your leisure or spare time, for recreation or fitness. Do not include the physical activities you do at work or for travel already mentioned		
6	In your leisure or spare time do you do any vigorous or moderate-intensity physical activity lasting more than 10 minutes at a time?	YES.....[1] NO.....[2]	Q.9
7a	In your leisure or spare time, do you do any vigorous activities (like running or strenuous sports, weightlifting) for at least 10 minutes at a time?	YES.....[1] NO.....[2]	Q.8a
7b	IF YES, in a usual week, how many days do you do vigorous activities as part of your leisure or spare time?	.....DAYS	
7c	How much time do you spend doing this on a usual day?	.....HOURS .....MINUTES	
8a	In your leisure or spare time, do you do any moderate-intensity activities (like brisk walking, cycling or swimming) for at least 10 minutes at a time?	YES.....1 NO.....2	Q.9
8b	IF YES, in a usual week, how many days do you do moderate-intensity activities as part of your leisure or spare time?	.....DAYS.	
8c	How much time do you spend doing this on a usual day?	.....HOURS .....MINUTES	
	Sitting / Resting Activity: Now I would like to ask you about the time spent sitting or resting, not including sleeping, in the past 7 days. This may include time sitting at a desk, visiting friends, reading, or sitting down to watch television during working hours and leisure or spare time.		
9.	Over the past 7 days, how much time did you spend sitting or reclining (lying) on a usual day (exclude sleeping)?	.....HOURS .....MINUTES	

SEDENTARY BEHAVIOUR QUESTIONNAIRE

SUBJECT CODE: _____Date: _____

Interviewer: Please ask the respondent the following questions which relates to the time they spend sitting during various activities.

Ask them to think about a usual day or a normal day for each of the questions.
All answers are per day.

We are very interested in the amount of time people spend sitting. I am going to ask you a few questions about your sitting behavior. These questions all refer to a usual day, and please answer in hours and minutes per day.

	Question	Week day (hours: minutes)	Week end day (hours: minutes)
1a	How much time do you spend sitting while you are at work? (per day)	Hrs: Min:	Hrs: Min:
1b	How many days per week do you work?		..... days
1c	Do you work on the week-end?		Yes ☐ No ☐
2	How much time do you spend sitting while watching TV per day?	Hrs: Min:	Hrs: Min:
3	How much time do you spend sitting while using the computer per day, excluding your normal working hours	Hrs: Min:	Hrs: Min:
	Question	Week day (hours: minutes)	Week end day (hours: minutes)
4	How much time do you spend sitting while travelling from place to place (e.g. in car, bus, train)	Hrs: Min:	Hrs: Min:

5	How much time do you spend sitting while eating and socialising and relaxing on a week day (Monday – Friday)?	Hrs: Min:	Hrs: Min:
Sleep The following question relates to the amount of time you spend sleeping.			
6	How many hours per day do you sleep?	Hrs: Min:	Hrs: Min:

TOBACCO USE (WHO STEPwise Questionnaire)

			Go to:
1a	Do you currently smoke any tobacco products, such as cigarettes, cigars, or pipes?	YES.....1 NO.....2	 Q.4a
1b	Do you currently smoke tobacco products daily?	YES.....1 NO.....2	 Q.4a
2a	How old were you when you first started smoking daily?	.....YEARS OLD IF "YOU DON'T REMEMBER", 98	 Q.3
2b	If you do not remember how old you were, do you remember how long ago it was?	.....WEEKS AGO [1]	
		.....MONTHS AGO [2]	
		.....YEARS AGO [3]	
3	On average, how many of the following items do you smoke each day? (CHECK EACH ITEM, IF NOT SMOKING AN ITEM, CODE 00)	.....MANUFACTURED CIGARETTES	
		.....HAND-ROLLED CIGARETTES	

		..... PIPES FULL OF TOBACCO	
		.....CIGARS/CHEROOTS/CIGARILLOS	
		.....OTHER [96] (SPECIFY)	
4a	In the past, did you ever smoke daily?	YES[1] NO[2]	
4b	How old were you when you stopped smoking daily?	.....YEARS OLD. .....IF "YOU DON'T REMEMBER", [98]	
4c	If you do not remember how old you were, do you remember how long ago it was?	..... WEEKS AGO [1]	
		.....MONTHS AGO [2]	
		.....YEARS AGO [3]	

ALCOHOL INTAKE

1 standard drink is equal to 10 g of pure alcohol:
200 ml of beer
1 glass of wine
1 tot (25 ml) spirits
1 small glass (50ml) of sherry/port

How often do you have a drink containing alcohol?

Never		2-3 times per week	
Monthly or less		4 or more times per week	
2-4 times per month			

On a typical WEEK day, how many drinks containing alcohol do you drink? (how many standard drinks)

1 or 2		7, 8 or 9	
3 or 4		10 or more	
5 or 6		0	

On a typical WEEKEND day, how many drinks containing alcohol do you drink? (how many standard drinks)

1 or 2		7, 8 or 9	
3 or 4		10 or more	
5 or 6		0	

PSYCHOLOGICAL QUESTIONNAIRE (Kessler 10)

The next ten questions are about how you have been feeling in the past 4 weeks: (Tick the appropriate box)					
	None of the time 1	A little of the time 2	Some of the time 3	Most of the time 4	All of the time 5
In the past four weeks, about how often did you feel worn out for no good reasons?	☐	☐	☐	☐	☐
In the past four weeks, about how often did you feel nervous?	☐	☐	☐	☐	☐
In the past four weeks, about how often did you feel so nervous that nothing could calm you down?	☐	☐	☐	☐	☐
In the past four weeks, about how often did you feel hopeless?	☐	☐	☐	☐	☐
In the past four weeks, about how often did you feel restless or fidgety?	☐	☐	☐	☐	☐
In the past four weeks, about how often did you feel so restless you could not sit still?	☐	☐	☐	☐	☐
In the past four weeks, about how often did you feel depressed?	☐	☐	☐	☐	☐
In the past four weeks, about how often did you feel that everything was an effort?	☐	☐	☐	☐	☐
In the past four weeks, about how often did you feel so sad that nothing could cheer you up?	☐	☐	☐	☐	☐
In the past four weeks, about how often did you feel worthless?	☐	☐	☐	☐	☐

END OF QUESTIONNAIRE

FOR OFFICE USE

SUBJECT CODE: _____

TESTING SESSIONS

TESTING SESSION 1 – Fasting bloods, OGTT, Questionnaires, Anthropometry

Date of testing: ..... Time of testing:.....
Time of last meal/drink: ..... Hours fasted:.....
How would you describe your health TODAY? (How are you feeling?):

☐ Good ☐ Fair ☐ Poor

If POOR, explain why: .....

OGTT:
Fasting blood sample: Tubes: purple ☐, grey ☐, 3 x 9.5 ml yellow ☐
Drink: ☐ Time: .....Comments: .....

30 min: ☐ Time: .....Comments: .....

60 min ☐Time: ..... Comments:.....

90 min: ☐Time: .....Comments:.....

120 min:☐ Time: .....Comments:.....

ACTIGRAPH:
Date issued: .....
Number/ Code of actigraph issued:.....

TESTING SESSION 2 – Fitness test, DEXA, CT Scan

8-minute Step-Test:
Seated Resting Heart rate: .....bpm.
Standing Resting Heart rate: .....bpm

3- min Heart rate response: _____
Comments: _____

6- min Heart rate response:_____
Comments: _____

9- min Heart rate response:_____
Comments: _____

12- min Heart rate response:_____
Comments: _____

1-min post test Heart rate response: _____
Comments: _____

DEXA: Full Body ☐ Half Body ☐
Comments: _____

ANTHROPOMETRIC DATA SHEET

SUBJECT CODE: _____

DATE					2	0	_	_
	d	d	m	m	y	y	y	y

WEIGHT					kg
HEIGHT (CM)					cm
MID-UPPER-ARM CIRCUMFERENCE					cm
WAIST CIRCUMFERENCE					cm
HIP CIRCUMFERENCE					cm
SYSTOLIC BLOOD PRESSURE					mm Hg
DIASTOLIC BLOOD PRESSURE					mmHg
HEART RATE					bpm

Measurement:	1			2			3		
BICEP SKINFOLD									
TRICEP SKINFOLD									
SUBSCAPULAR SKINFOLD									
SUPRAILIAC SKINFOLD									
ABDOMINAL SKINFOLD									
FRONT THIGH SKINFOLD									
MEDIAL CALF SKINFOLD									

CHECKLIST

	Tick box if done	Comments
Date screened		
Informed consent:		
Blood pressure:		
Fasting bloods:		
Glucose:		
Basic Anthropometry:		
Socio-Dem Questionnaire:		
OGTT:		
FITNESS TEST:		
DEXA:		
CT:		
Food Frequency Questionnaire		
Dietary attitudes & Beliefs Questionnaire:		
Feedback		

USE OF THE ACTIGRAPH ACCELEROMETER

Instruction Sheet for hip monitor:

Please wear this hip monitor for 7 days from when you leave the UCT lab. During this time, please carry on with all your normal activities.

Description:

The hip monitor is a movement sensor and should be removed when you go to bed and put back on when you get up. The hip monitor is not waterproof; please remove it when showering, bathing and swimming. Whenever you need to remove the sensor, please reattach it as soon as you can.

Placement:

Place the belt around your waist. Please, make sure that it is placed approximately on the centre of your right hip (see picture below).

Please, take care that the monitor sits snugly around your hip and that it is not too loose.

Return:

When you have completed your measurement, please return the monitor to Ms Nandipha Sinyana [Field Worker].

Thank you!

USE OF THE MACHUFFE ANALYSER

VERSION 1.9.0.3, TO CALCULATE ACTIGRAPH ACCELROMETER COUNTS/ MIN ACCORDING TO FREEDSON CUT-POINTS