THE EFFECT OF A SINGLE BOUT OF HIGH-INTENSITY SPRINT EXERCISE PROGRAMME COMPARED TO TRADITIONAL HIGH-INTENSITY SPRINT INTERVAL EXERCISE AND ENDURANCE EXERCISE ON INFLAMMATORY MARKERS, LIPID PROFILE AND HEALTH-RELATED PHYSICAL FITNESS MEASUREMENTS IN PARTICIPANTS WITH ELEVATED CARDIOVASCULAR DISEASE RISK

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A Thesis submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in fulfilment of the requirements for the degree of Doctor of Philosophy in the field of Therapeutic Sciences.

Johannesburg, 2021

Declaration

I, Nivash Rugbeer, declare that this Thesis is my own, unaided work. It is being submitted for the degree of Doctor of Philosophy in the field of Therapeutic Sciences at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other university.

Nivash Rugbeer

Name of candidate Signature of candidate

31 day of March 2021 in Pretoria

Dedication

To my mother (Sharitha Rugbeer) and grandmother (Dhanwanthi Mathabhik Ramdhani), my living goddesses, I dedicate this work to both of you. To my late father (Rajendra Rugbeer), your dedicated work ethic was a shining example for me to complete this work. Thank you, Dad, for teaching me that work is worship. The wonderful memories I have of you will continue to inspire me. I surrender this work and fruits of this work to Bhagavan and Bhagavati—Jai Sai Ram!

Presentations arising from this study

1. Rugbeer, N. Effect of the 90-second ‘Gear’ exercise programme on cardiometabolic risk factors in persons with an elevated risk of cardiovascular disease, oral presentation at the Wits Faculty of Health Sciences Virtual Research Day, University of the Witwatersrand, South Africa, 15 October 2020.

Publications arising from this study

1. Rugbeer N, Constantinou D, Torres G. Effect of the 90-second ‘Gear’ exercise programme on cardiometabolic risk factors in persons with an elevated risk of cardiovascular disease. South African Journal of Sports Medicine 2021;33:1-8. DOI: 10.17159/2078-516X/2021/v33i1a8894
2. Rugbeer N, Constantinou D, Torres G. Comparison of high-intensity training versus moderate-intensity continuous training on cardiorespiratory fitness and body fat percentage in persons with overweight or obesity: A systematic review and meta-analysis of randomized controlled trials. Journal of Physical Activity and Health 2021. DOI: 10.1123/jpah.2020-0335.

Abstract

Background: A sedentary lifestyle increases the risk of cardiovascular disease (CVD). Inactivity is a global burden, and escalating work and family commitments directly impact exercise adherence. The study aimed to compare the effect of the novel time-efficient 'Gear' exercise programme (90-second 'Gear' exercise programme) repeated at different times in the day (GEP-DT) and the effect of the 18-minute 'Gear' exercise programme repeated at one point in time (GEP-OT) with traditional exercise on cardiometabolic risk factors, inflammatory markers and cardiorespiratory fitness (CRF) measurements in sedentary persons with an elevated risk of CVD. The study addressed the aims and objectives in two published studies (study 1 and study 3) and two studies that are under review for publication in international journals (study 2 and study 4). Study 1 is a meta-analysis and systematic review comparing the effect of high-intensity interval training (HIIT) versus moderate-intensity continuous training (MICT) and sprint interval training (SIT) versus MICT on CRF and body fat percentage in overweight or obese persons. Study 2 investigated the association between CRF measurements, cardiometabolic risk factors and inflammatory markers in overweight or obese persons. Study 3 investigated the effect of the GEP-DT and GEP-OT on cardiometabolic risk factors in persons with an elevated risk of CVD. Study 4 investigated the effect of the GEP-DT and GEP-OT on markers of inflammation and CRF in persons at risk of CVD.

Methods: Study 1 entailed a systematic search of randomised controlled trials (RCTs) using the health science databases that occurred up to April 2020. Twenty-six studies were included for complete analysis. A total of 784 participations were analysed. The unstandardised mean difference for each outcome measurement was extracted from the studies and pooled with the random-effects model.

Study 2 adopted a cross-sectional design. Eighty-two participants from the university participated in the study. The outcome measurements were inflammatory markers, CRF measurements, cardiometabolic risk factors and the Framingham risk score.

Study 3 implemented a six-week, RCT. The outcome variables were low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglycerides (TG), total cholesterol, glycated haemoglobin (HbA1c), blood pressure and body composition. Forty-eight participants completed the study. Participants were randomly assigned to

either the GEP-DT: cycled for 90 seconds, repeated three times per day, for three days per week (n = 12); GEP-OT: cycled for 90 seconds followed by four minutes and 30 seconds rest, repeated three times at one point in time, for three days per week (n = 14); 30 minutes of moderate-intensity continuous cycling repeated three days per week at 55-69% HR_{max} (n = 11); and the controls (CTRL), who were encouraged not to exercise (n = 11).

Study 4 adopted a RCT. Forty-eight participants completed the study. The outcome variables were high-sensitivity C-reactive protein, erythrocyte sedimentation rate (ESR), interleukin-6 (IL-6), peak oxygen consumption ($VO2_{peak}$) and ventilatory threshold measurements (health-related CRF measurements). Participants were randomly assigned to either the GEP-DT: cycled for 90 seconds, repeated three times/day, for three days per week (n = 12); the GEP-OT: cycled for 90 seconds followed by four minutes and 30 seconds rest, repeated three times at one point in time, for three days per week (n = 14); 30 minutes of moderate-intensity continuous cycling repeated three days per week at 55-69% HR_{max} (n = 11); and the controls, who were encouraged not to exercise (n = 11).

Results: Study 1: MICT was significantly better at improving CRF compared with sprint interval training (SIT) (MD = −0.92; 95% CI = -1.63 to −0.21; p = 0.01; I^2 = 10%). There was no significant difference between MICT versus HIIT on CRF (MD = −0.52; 95% CI = −1.18 to 0.13; p = 0.12; I^2 = 23%). There was no significant difference in body fat percentage between MICT versus HIIT and MICT versus SIT.

Study 2: A moderate, negative correlation was found between HbA1c and load at ventilatory threshold (VT-L) (R_s = −0.441; p<0.001). Moreover, there was a positive correlation between ESR and body fat percentage (R_s = 0.438; p<0.001). Multiple linear regression showed that $VO2_{peak}$ was inversely related to age (β = −0.007; p = 0.048). VT-L was significantly inversely related to HbA1c (β = −0.089; p = 0.001). For every one-unit increase in the VT-L, HbA1c decreased by 9.31%.

Study 3: The 90-second GEP-DT intervention reduced HbA1c, post six- weeks of training, with a moderate effect size (MD = −0.1±0.4; % Δ = −1.3%; d = −0.70; d (95% CI): −1.55, 0.14). The GEP-OT group demonstrated a decrease in TG post-training with a large effect size (MD = −0.6±1.3; % Δ = −31.9%; d = −0.83; d (95% CI): −1.68,

0.01). The GEP-OT group decreased blood TG with a large effect size (MD = −0.6±1.3; % Δ = −31.9%; d = −0.83). The MICE group demonstrated a large effect size for diastolic blood pressure (DBP), which showed a significant reduction in DBP post-training (MD = −5.4±3.8; % Δ = -6.8%; d = −0.81; d (95% CI): −1.68, 0.06). This group also demonstrated a large effect size for body fat percentage, which showed a significant reduction in body fat percentage post-training (MD = −0.7±2.1; % Δ = −2.5; d = −0.83; d (95% CI): −1.70, 0.04).

Study 4: The 90-second GEP-DT demonstrated a moderate increase in VT-L (MD = 8.18±12.30; % Δ = 14.53; d = 0.77; d (95% CI): −0.17, 1.64), $VO2_{peak}$ at ventilatory threshold (MD = 2.93±6.08; % Δ = 53.76; d = 0.66; d (95% CI): −0.18, 1.50) and metabolic equivalent at ventilatory threshold (MD = 0.83±1.76; % Δ = 52.23; d =0.65; d (95% CI): −0.19, 1.49). The GEP-OT group demonstrated a large effect size for VT-L (MD = 11.79±18.77; % Δ = 18.86; d = 0.81; d (95% CI): −0.02, 1.63). Furthermore, this group demonstrated a moderate effect size for $VO2_{peak}$ at ventilatory threshold (MD = 3.59±6.73; % Δ = 50.21; d = 0.72; d (95% CI): −0.10, 1.53), ventilatory equivalent at ventilatory threshold (MD = 8.05±14.66; % Δ = 44.65; d = 0.63; d (95% CI): −0.18, 1.44) and metabolic equivalent at ventilatory threshold (MD = 1.03±1.91; % Δ = 50.49; d = 0.72; d (95% CI): −0.09, 1.54). The 18-minute GEP-OT group demonstrated a substantial decrease in IL-6 post six-weeks of training (% Δ = −77.27); however, the probability value was insignificant.

Conclusions: MICT was significantly better at improving CRF when compared to SIT in overweight or obese persons.). For every one-unit increase in the VT-L, HbA1c decreased by 9.31%. The novel 90-second ‘Gear’ exercise programme moderately reduced HbA1c, and the 18-minute GEP-OT lowered blood TG. MICE decreased DBP and body fat percentage. ‘Gear’ exercise programmes raised the ventilatory threshold point, which prevented premature fatigue and improved the efficiency of the cardiorespiratory system. Gear’ exercise programmes will encourage future research in persons with NCD, and it should be considered as a public health initiative to promote exercise in clinical, home and work environments because it is a time-efficient exercise intervention.

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List of Abbreviations

ANOVA: analysis of variance

BF (%): body fat percentage

BMI: body mass index

cm: centimetres

CRF: cardiorespiratory fitness

CS: citrate synthase

CTRL: control group

CVD: Cardiovascular disease

DBP: diastolic blood pressure

ESR: erythrocyte sedimentation rate

FRS: Framingham risk score

GEP-DT: ‘Gear’ exercise programme repeated at different times during the day

GEP-OT: ‘Gear’ exercise programme repeated at one point in time

GLUT4: glucose transporter four protein

HbA1c: glycated haemoglobin

HDL-C: high-density lipoprotein cholesterol

HIIT: high-intensity interval training

HR_{max}: maximal heart rate

HR: heart rate

HRR: HR reserve

hs-CRP: high-sensitivity C-reactive protein

IL-6: interleukin-6

ISAK: International Standards for Anthropometric Assessment

Kg: kilogram

Kg/m^2: kilogram per meter squared

LDL-C: low-density lipoprotein cholesterol

m: metre

MICE: moderate-intensity continuous exercise

MICT: moderate-intensity continuous training

mm: millimetres

n: number

NCD: non-communicable diseases

PEDro: Physiotherapy Evidence Database

PGC-1α: peroxisome proliferator-activated receptor-γ coactivator 1 alpha

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

RCT: randomised controlled trial

SBP: systolic blood pressure

SD: standard deviation

SIT: sprint interval training

TC: total cholesterol

TG: triglycerides

TNF: tumour necrosis factor

$VO2_{max}$: maximal oxygen consumption

$VO2_{peak}$: peak oxygen consumption

$VO2_{peak}$-L: load at peak oxygen consumption

$VO2_{peak}$-Mets: metabolic equivalent at peak oxygen consumption

VO2R: VO2 reserve

$VO2_{peak}$-Rf: respiratory frequency at peak oxygen consumption

$VO2_{peak}$-VE: ventilatory equivalent at peak oxygen consumption

VT-L: load at ventilatory threshold

VT-Mets: metabolic equivalent at ventilatory threshold

VT-Rf: respiratory frequency at ventilatory threshold

VT-VE: ventilatory equivalent at ventilatory threshold

VT-$VO2_{peak}$: peak oxygen consumption at ventilatory threshold

WC: waist circumference

Outline of this Thesis

This thesis is presented in 7 chapters (Figure 1), with the structure of each being as follows:

Chapter 1 provides the background and introduction of the thesis. Furthermore, the problem statement, aims and objectives and significance of the study will be discussed in this section.

Chapter 2 reviews the literature regarding exercise terminology; metabolic and physiological adaptation to high-intensity training; and the effect of high-intensity training on metabolic and cardiovascular markers, inflammatory markers and peak oxygen consumption.

Chapter 3 presents a study published in the Journal of Physical Activity and Health Rugbeer N, Constantinou D, Torres G. Comparison of high-intensity training versus moderate-intensity continuous training on cardiorespiratory fitness and body fat percentage in persons with overweight or obesity: A systematic review and meta-analysis of randomized controlled trials. Journal of Physical Activity and Health 2021. DOI: https://doi.org/10.1123/jpah.2020-0335.

Chapter 4 presents a study that is under review by the European Journal of Sports Science titled: “The association between cardiorespiratory fitness measurements, cardiometabolic risk factors and inflammatory markers in overweight or obese persons.”

Chapter 5 presents a study published in the South African Journal of Sports Medicine. Rugbeer N, Constantinou D, Torres G. Effect of the 90-second ‘Gear’ exercise programme on cardiometabolic risk factors in persons with an elevated risk of cardiovascular disease. South African Journal of Sports Medicine 2021;33:1-8. DOI: 10.17159/2078-516X/2021/v33i1a8894

Chapter 6 presents a study that is under review by Research in Sports Medicine titled: “Effect of the 90-second ‘Gear’ exercise programme on markers of inflammation and cardiorespiratory fitness in overweight or obese sedentary persons.”

Chapter 7 answers the research question, presents the study limitations, outlines the significance of the findings and makes recommendations for further research.

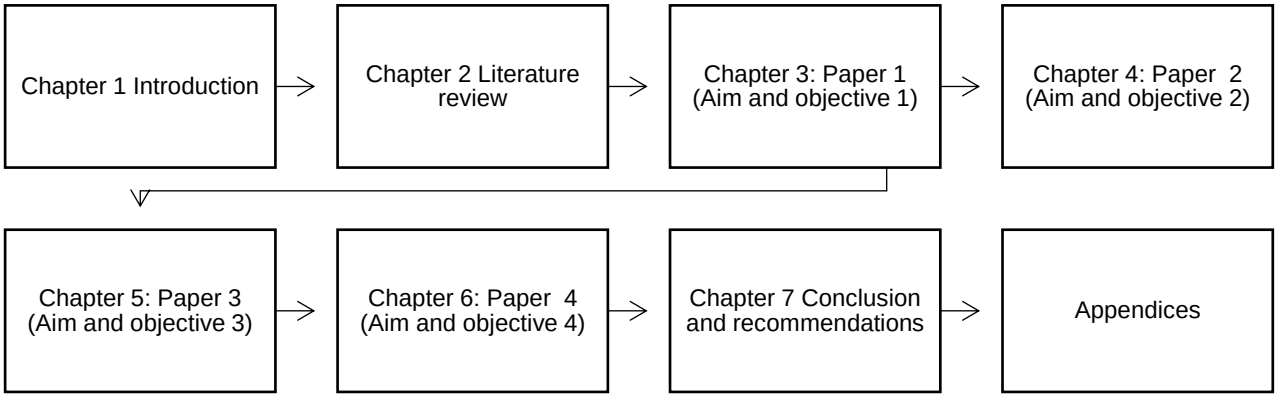

Figure 1 Outline of the thesis

Chapter 1 Introduction

1.1 Background

Cardiovascular disease (CVD) refers to coronary artery disease, hypertension, pulmonary embolism, peripheral artery disease and deep vein thrombosis that affect the heart and blood vessels (1, 2). CVD reduces the quality of life of people (3) and is the leading cause of mortality worldwide (4, 5). In 2017, CVD accounted for 17.8 million deaths globally, and 35.6 million years lived with functional debility (3, 6). Furthermore, 80% of CVD mortality worldwide occurs in low to middle-income countries (7). South Africans have a high prevalence of diabetes (15%), dyslipidaemia (18%) and hypertension (25%), especially in populations with low socioeconomic status (8). Stroke, ischaemic heart disease, hypertension and dyslipidaemia are major CVDs that affect South Africans (9).

The CVD risk profile of South Africans from different districts is used to provide a clustered analysis aimed at developing target public health guidelines and policies to address modifiable lifestyle risk factors such as physical inactivity, excessive salt intake and harmful use of alcohol (9). Moreover, a prospective cohort study of participants aged 35-70 years from 302 rural and 367 urban communities in 20 countries showed that people from low-middle income countries with low levels of education had a better CVD risk profile. However, they had higher incidents of CVD mortality attributed to poorer health care (10). Therefore, policies addressing health care services in South Africa are imperative to address the burden of CVD.

There is a direct relationship between elevated CVD risk factors and CVD, which leads to premature death (9, 11, 12). Modifiable risk factors, such as physical inactivity, smoking, excess alcohol consumption, elevated glucose and blood pressure, hypercholesterolaemia and obesity, should be addressed to reduce CVD risk (9, 13). Cardiorespiratory fitness (CRF) is regarded as the most crucial predictor of CVD and mortality, independent of other modifiable risk factors (14).

CRF is the efficiency of the heart, lungs and blood vessels to supply active tissues with oxygenated blood to sustain moderate-vigorous exercise (15). Low CRF is the leading cause of cardiovascular mortality (14, 16, 17). Moreover, a recent prospective population-based study showed that CRF was inversely associated with colorectal

cancer, the incidence of cardiovascular and respiratory disease and premature mortality (18). CRF is a vital physiological measurement associated with desirable health outcomes and wellbeing (19). Furthermore, CRF is independently associated with age, socioeconomic status, ethnicity, body composition, resting heart rate (HR), smoking, alcohol consumption and high-sensitivity C-reactive protein (hs-CRP) (15). CRF reduces premature mortality and enhances cardiometabolic protection through adaptations to vascular, biological, psychosocial, metabolic, cardiovascular, autonomic, anti-ischaemic, antithrombotic and anti-inflammatory pathways (5) (Figure 1.1).

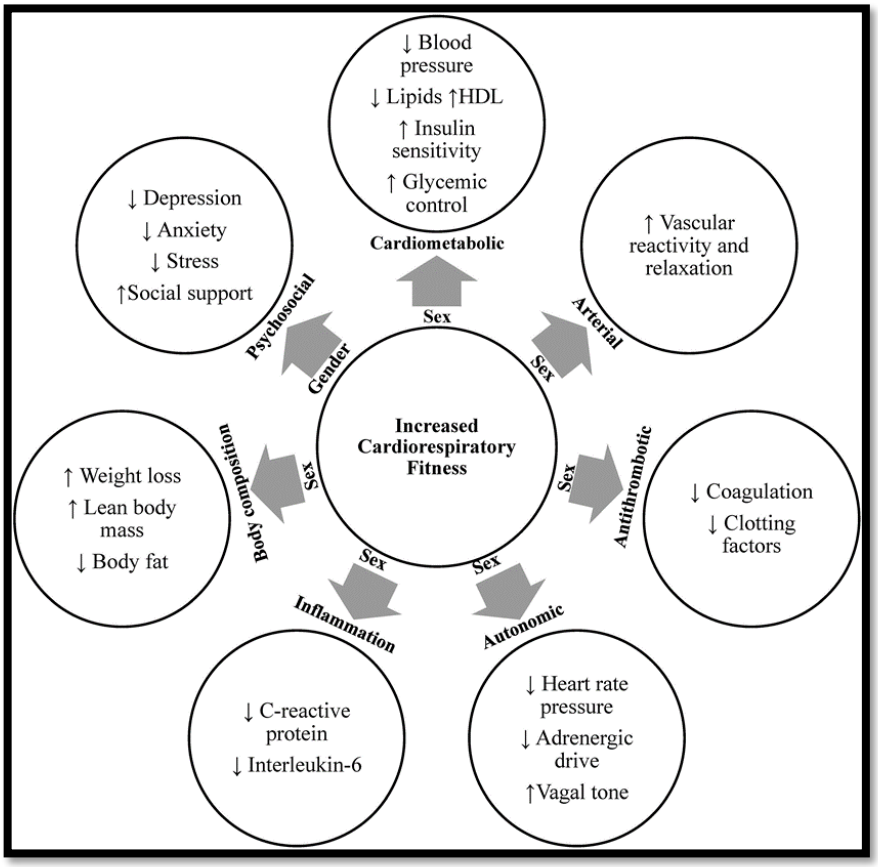

Figure 1.1 The physiological benefits and pathways preventing premature mortality due to increased cardiorespiratory fitness (5)

Exercise interventions increase CRF and are crucial in cardiac rehabilitation (20, 21). Participation in a cardiac rehabilitation programme increases physical activity levels (22). The objective of a cardiac rehabilitation programme is to perform a structured exercise programme aimed at promoting healthy behaviour by encouraging adherence to exercise, optimising holistic wellbeing and education and implementing psychological interventions and healthy lifestyle choices in daily life (23). Cardiac

rehabilitation is advocated for patients who sustain an acute myocardial injury and cardiac surgery but is underutilised (23, 24). However, a paradigm shift is required to prescribe a cardiac rehabilitation programme before a cardiac incident to prevent the decline of physical and cognitive physiological functions (25). Furthermore, the frequency, intensity, type, duration, volume and progression of exercise should be addressed to optimise $VO2_{peak}$ during cardiac rehabilitation.

Thirty minutes of continuous exercise on most days of the week is frequently recommended in cardiac rehabilitation (5, 26). A systematic review and meta-analysis showed that exercise training, as the fundamental principle in cardiac rehabilitation, improves the quality of life and peak oxygen consumption ($VO2_{peak}$) (27). An increase in one metabolic equivalent, maintained for more than a year, is directly related to a 25% reduction in all-cause mortality (28). However, another study concluded that traditional cardiac rehabilitation exercise programmes do not significantly increase $VO2_{peak}$, which prevents patients from achieving the health-related benefits of cardiac rehabilitation (29).

A recent study showed that adults who performed 10 to 59 minutes per week of either light-to-moderate or vigorous-intensity physical activity were associated with a reduced risk of all-cause mortality (30). Moreover, higher levels of light-to-moderate or vigorous-intensity physical activity (≥600 min/week) were found to be associated with a lower risk of all-cause and cancer-specific mortality (30). In addition, vigorous physical activity provided superior benefits in all-cause mortality and disease-specific mortality compared with moderate physical activity (30). The study did however report several shortcomings, such as physical activity was recalled and not objectively measured, participants' follow-up physical activity data were not available, and disabilities and dietary intake were not accounted for in this study (30). Therefore, the findings must be interpreted with these shortcomings in mind. A systematic review and meta-analysis of 174 articles showed that higher volume of physical activity is associated with a lower risk of metabolic, immune, cerebrovascular and CVDs; however, significant gains occurred at lower levels of activity (3000-4000 metabolic equivalent minutes/week), except for breast cancer (31) (Figure 1.2). The limitations reported in this review were that the results were based on cohort studies, which could have biased outcomes due to residual confounding variables. Publication bias was also evident in this review and

the review only focussed on volume ignoring the role of the intensity of physical activity on non-communicable diseases (NCD) (31).

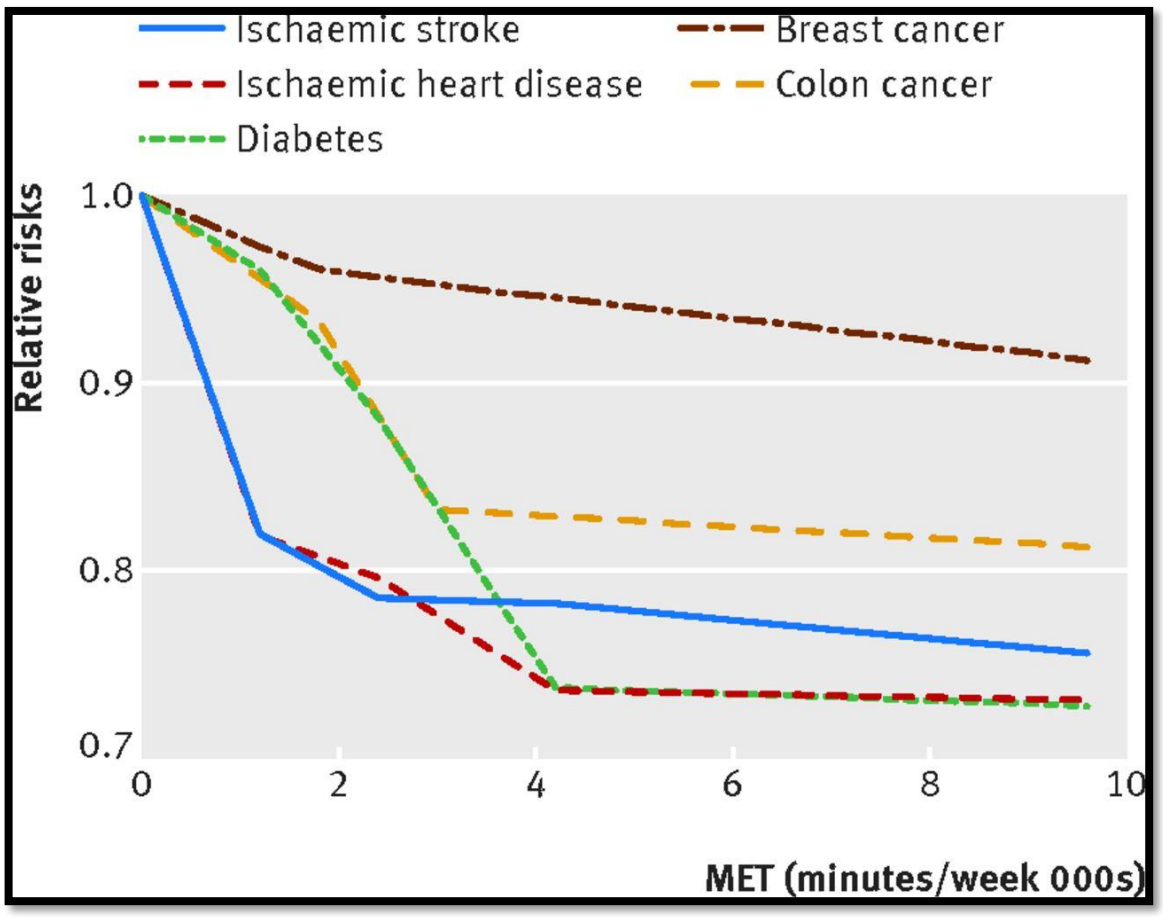

Figure 1.2 Dose-response relationship between the volume of physical activity and relative risk of colon cancer, breast cancer, ischaemic heart disease, diabetes and ischaemic stroke (31)

There is empirical evidence of mental and physical health benefits of exercise in cardiac rehabilitation; however, participation and adherence to cardiac rehabilitation are low (32). Participation in cardiac rehabilitation accounts for 15-30% of patients (33). Unfamiliar equipment, fatigue, fear of a cardiac incident, ignorance of the services available, perceptions of heart disease and financial constraints are common barriers in cardiac rehabilitation (5, 34). Most importantly, the prominent barrier to cardiac rehabilitation is the perceived lack of time to participate in the exercise programme (35). Therefore, a targeted, individualised exercise programme based on empirical evidence is required to address the barriers experienced by persons with or at risk of CVD (5). Moreover, there is a need in these times to incorporate a time-efficient exercise programme that addresses types of exercise, intensity, duration, frequency,

volume and progression, psychosocial and CVD risk profile to optimise the benefits of cardiac rehabilitation (5).

The current study investigated the effect of the novel single bout of a high-intensity exercise programme ('Gear' programme) compared to traditional endurance exercise on inflammatory markers, lipid profile and health-related physical fitness measurements in participants with elevated CVD risk. The aim was to identify the physiological and cardiometabolic effects and benefit derived from minimal exercise. Therefore, we hypothesised that the novel 90-second single bout of high-intensity exercise programme ('Gear' programme) performed three times a week would result in beneficial physiological adaptation and a protective response against CVD risk.

1.2 Problem statement

CVDs correlate directly with mortality risk globally and in African countries, and pose a considerable burden to the African countries (8, 9, 36, 37). Traditional health approaches are reactive and treatment-based rather than preventative. Furthermore, due to escalating family and work commitments, there is a lack of adherence to an exercise programme. Therefore, the current study investigated the effect of the novel single bout of high-intensity exercise programme ('Gear' programme) compared to traditional endurance exercise on inflammatory markers, lipid profile and health-related physical fitness measurements in participants with elevated CVD risk.

1.3 Aims and objectives

Table 1.1 Aims and objectives of the study

Aims	Objectives
1. To conduct a meta-analysis and systematic review comparing high-intensity training with MICT on CRF and body fat percentage in overweight or obese persons.	1.1 PRISMA guidelines were used to conduct a systematic review.

2. To determine the association between cardiometabolic risk factors, inflammatory markers and CRF in persons at risk of CVD.	2.1 CVD risk was measured at baseline. 2.2 Lipid profile was measured at baseline. 2.3 Inflammatory markers were measured at baseline. 2.4 Fasting blood glucose and glycated haemoglobin were measured at baseline. 2.5 Peak oxygen consumption and ventilatory threshold were measured at baseline by means of a submaximal stress test.
3. To determine the effect of a single bout of a high-intensity exercise programme ('Gear' programme) compared to moderate-intensity continuous exercise (MICE) on cardiometabolic blood parameters and body composition.	3.1 Lipid profile was measured at baseline and post-intervention. 3.2 Fasting blood glucose and glycated haemoglobin were measured at baseline and post-intervention. 3.3 Body composition was measured at baseline and post-intervention.
4. To determine the effect of a single bout of a high-intensity exercise programme ('Gear' programme) compared to MICE on inflammatory markers and CRF.	4.1 Inflammatory markers were measured before and after the interventions. 4.2 Peak oxygen consumption was measured before and after the interventions. 4.3 Load at ventilatory threshold was measured before and after the interventions. 4.4 Ventilatory equivalent was measured before and after the interventions.

1.4 Significance of the study

Escalating work and family commitments directly affect exercise adherence. A sedentary lifestyle increases the risk of CVDs. Cardiac rehabilitation exercise guidelines lean towards symptomatic treatment rather than preventative care for NCD. Therefore, an exercise intervention is required to be time-efficient, inclusive and easily implemented at home or the workplace. The exercise intervention should be safe and address preventative medicine and cardio-protective health in persons at risk of CVD. Therefore, the current study created the new proposed 'Gear' exercise programme (high-intensity programme) and compared the effect of the novel programme on cardiometabolic risk factors, CRF measurements and inflammatory markers to traditional exercise in persons at risk of CVD. Chapter 2 will review the literature regarding the metabolic and physiological adaptation to high-intensity training and the

effect of high-intensity training interventions on cardiometabolic markers, inflammatory markers and CRF measurements.

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Chapter 2 Literature review

2.1 Introduction

CVD is the leading cause of global mortality (1). However, the incidence of CVD can be reduced by regular physical activity (2) or half the recommended amount of physical activity guidelines (3.75–7.49 MET-hours per week) in persons who are sedentary (3). Physical activity improves overall health and reduces biological risk factors for CVD (3). Physical activity is defined as bodily movements that increase basal metabolic rate and result in energy expenditure (4). Although there are health-related physical activity benefits, participation in physical activity is low (5, 6). A study showed a 20% lower mortality risk in persons who perform less than 7.5 MET-hours per week compared to persons who reported no physical activity (7). Furthermore, a 31% and 37% lower risk of mortality was reported in persons who performed at 1 to 2 times more and 2 to 3 times more than the recommended 7.5 MET-hours per week, respectively, when compared to persons who reported no physical activity (7). In the South African context, 57.4% of South Africans self-reported that they were physically inactive (8). Therefore, interventions are required to address this concern from a public health perspective.

A randomised crossover trial showed three bouts of body weight stair climbing for 1-minute per bout produced a positive mood state after the brief exercise intervention (9). Apart from nutritional, social, psychological and educational interventions, time-efficient exercise interventions are required worldwide. This will promote participation in physical activity and adherence to exercise, especially in the current age of escalating work and family commitments. There is paucity in the literature about the physiological and metabolic effects of structured low-volume, time-efficient and single bout exercise programmes in persons at risk of CVD. Therefore, this chapter discusses exercise terminology, metabolic and physiological adaptation to high-intensity training, and the effect of high-intensity training interventions on cardiometabolic markers, inflammatory markers and CRF.

2.2 Exercise terminology

An exercise programme comprises vital components, such as frequency, intensity, time and type to achieve personal, health or fitness goals. Exercise as a modality of treatment for persons with CVDs is divided into endurance and strength components

(10, 11). Endurance exercise is rhythmical activities performed continuously for more than 20 minutes, which promotes aerobic conditioning and metabolism and prevents fatigue (11). Strength training is specialised exercise, which uses resistance to generate muscular force and promote muscular hypertrophy (11).

Interval training is defined as an intermittent period of exercise interspersed with a period of rest. High-intensity training is differentiated into high-intensity interval training (HIIT) and sprint interval training (SIT) (12). HIIT is defined as alternate bouts of near maximal effort (80%-95% of maximal HR), followed by periods of recovery. SIT, which includes alternate bouts of all-out or maximal effort and supramaximal effort followed by periods of recovery (12) (Figure 2.1). The various modifications of HIIT and SIT are confusing. Therefore, the novel 'Gear' exercise programme produces a step-wise increment in exercise intensity at brief periods during the exercise bout, which is self-paced and time-efficient compared with traditional high and moderate-intensity exercise programmes.

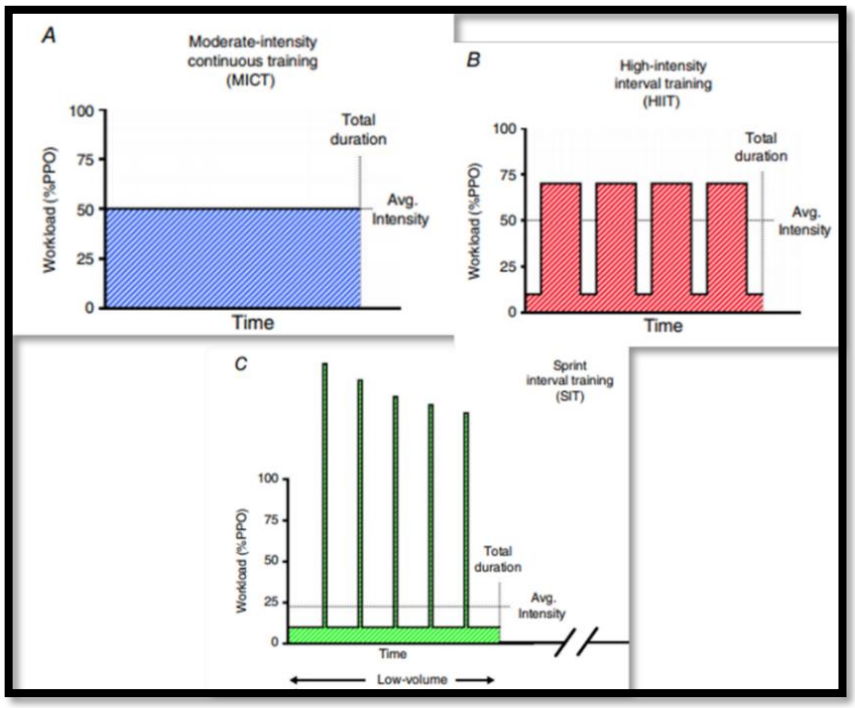

Figure 2.1 Different types of exercise interventions expressed as peak power output (13)

2.3 Metabolic and physiological adaptation to high-intensity training

The physiological adaptation to high-intensity training is attributed in animal studies to the activation of peroxisome proliferator-activated receptor-γ coactivator 1 alpha (PGC-1α), which regulates mitochondrial biogenesis in the muscle (14). It has also been postulated that exercise intensity influences PGC-1α activation in human skeletal muscle (15). HIIT increases calcium release and uses more glycogen as fuel compared with low-intensity exercise (13). This increases the availability of free radicals, ions and metabolites, which increase the activation of signalling proteins (5'-adenosine monophosphate-activated protein kinase) (13). The signalling proteins cause a greater gene expression rate of PGC-1α, which regulates mitochondrial biogenesis in the muscle (13). Therefore, HIIT increases mitochondrial protein synthesis, which increases mitochondrial content in the cell (Figure 2.2).

SIT increases the concertation of calcium in the cell by the disintegration of the ryanodine receptor of the sarcoplasmic reticulum, which promotes mitochondrial biogenesis (13). SIT for two to three minutes (excluding the recovery period) performed three times per week for six weeks resulted in increased skeletal mitochondrial enzymatic activity (16). Moreover, six sessions of this protocol increased skeletal muscle oxidative capacity, which increased citrate synthase and cytochrome oxidase (17, 18). Therefore, high-intensity training (HIIT and SIT) increases the efficiency of cellular metabolism.

A continuous bout of endurance exercise increased PGC-1α expression, which promotes mitochondrial biogenesis (15, 19). However, high-intensity training significantly increases stroke volume, mitochondrial respiratory rate and oxygen utilisation in peripheral blood at matched workloads of moderate-intensity continuous training (MICT) (13). This increases maximal oxygen consumption ($VO2_{max}$) (CRF) in comparison to MICT. Paradoxically, a study showed that short-term SIT and MICT produced similar increases in muscle oxidative capacity (17). HIIT superiorly increases $VO2_{max}$ compared to MICT when energy expenditure is matched in both the exercise interventions (20). Therefore, the exercise load and the duration of the training interval are crucial factors that improve $VO2_{max}$ (20).

Other potential benefits from increased PGC-1α uptake are rapid glucose uptake, resistance to sarcopenia and decreases inflammation (21, 22). Furthermore, the

benefits derived from HIIT was hypothesised based on glycogen depletion during 30-seconds of the acute bout of exercise (23), which directly improves insulin sensitivity (24). A total of six sessions of full out high-intensity training for 30-seconds performed for two weeks improved oxidative capacity in sedentary, overweight individuals (24). This adaptation was attributed to the improved glucose transport capacity due to the glucose transporter four (GLUT4) protein. GLUT4 is the insulin-regulated glucose transporter found primarily in adipose tissues and striated muscle (skeletal and cardiac). Skeletal muscle GLUT4 increased by approximately two-fold after HIIT compared with high-volume endurance training (25).

HIIT also induced higher expression and translocation of GLUT4 on skeletal muscle cell membrane when compared to MICT (26). The reason for this is that insulin sensitivity is directly related to the recruitment of muscle fibres and HIIT recruits more muscle fibres compared those recruited during MICT (27). The physiological benefits of fat loss with high-intensity training are due to augmented post-exercise oxygen consumption (28), changes in appetite (28), and increase in epinephrine (29), catecholamines (29), growth hormone (30) and norepinephrine (31), which promotes lipid decomposition. There are numerous physiological and cardiometabolic benefits of high-intensity training. However, the time commitment for high-intensity training is similar to traditional MICT, considering the rest intervals between high-intensity bouts (32). Therefore, a time-efficient exercise programme is required to provide insight into the physiological and cardiometabolic benefits derived from minimal high-intensity exercise.

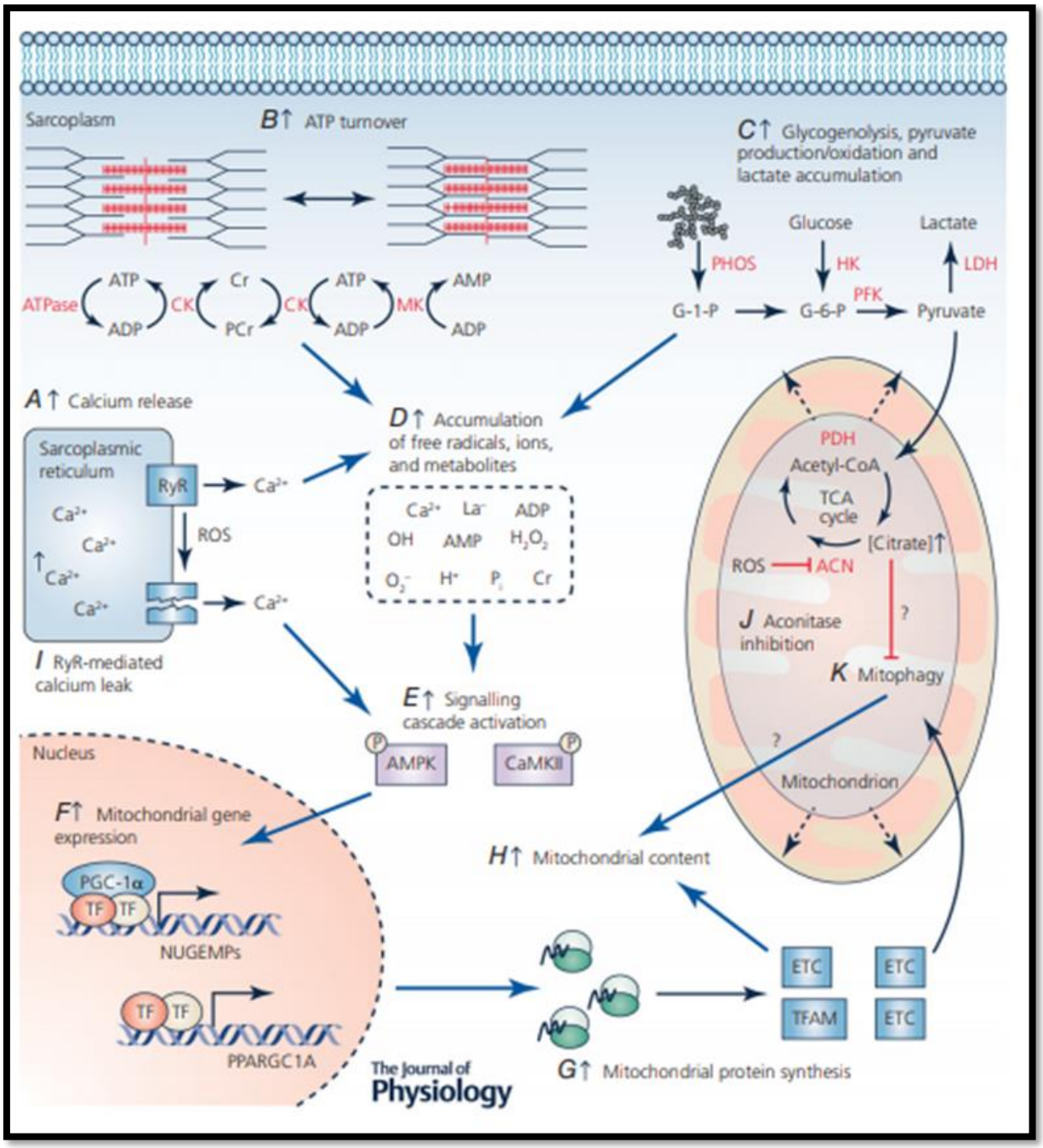

Figure 2.2 Physiological mechanisms of high-intensity training (13)

2.4 The effect of high-intensity training interventions on cardiometabolic risk factors

The prevalence of cardiometabolic risk factors is high (33). Cardiometabolic risk factors increase the risk of a cerebrovascular or cardiovascular acute incident, which harms overall health and wellbeing (33). High-intensity training has gained widespread popularity in the last decade, especially its role in reducing cardiometabolic risk factors (34). Empirical evidence suggests that HIIT and SIT elicit cardiometabolic health

benefits. SIT (six-second sprints with nine-second rest, repeated 80 times) and HIIT (four-minutes cycling at 90% of $VO2_{peak}$ with three-minutes rest between intervals, repeated approximately nine times) was more beneficial in improving insulin levels and insulin sensitivity compared with MICE (cycling for approximately 61 minutes at 60% of $VO2_{peak}$) in women who were overweight (35). HIIT (one-minute running at maximal aerobic speed with one-minute passive recovery for five km, three times per week for five weeks) and MICT (running at 70% of maximum aerobic speed for five km, three times per week for five weeks) resulted in acute changes in lipoprotein profile of active men. However, favourable long-term increase in high-density lipoprotein cholesterol (HDL-C) was evident in the HIIT group (36). HIIT (15-second effort at 80% of maximum aerobic speed with 15-seconds active recovery for four to eight minutes, three times per week for 12 weeks) and SIT (15-second effort at 100% of maximum aerobic speed with 15 seconds active recovery for four to eight minutes, three times per week for 12 weeks) decreased insulin levels, rate pressure product, blood pressure and leptin blood levels (37). However, only SIT decreased waist circumference (WC) in adolescent females who were obese (37).

HIIT (60-seconds cycling repeated ten times at approximately 83% of peak power, twice a week for eight weeks) improved WC, $VO2_{peak}$, high cross-sectional area and the physical health component of quality of life (38). Furthermore, 60-seconds cycling repeated ten times at approximately 83% of peak power, three times per week for eight weeks reduced body fat percentage, total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) and increased mental health-related quality of life (38). Therefore, higher frequencies of HIIT have a desirable effect on the lipid profile in apparently healthy persons who are sedentary (38). High-intensity training produced greater benefits in insulin sensitivity than continuous aerobic training in men who were overweight or obese (39). SIT (all-out cycling repeated four to six times, 1:1 work to rest ratio, three times per week for four weeks) significantly reduced low-density lipoproteins and uric acid levels in overweight persons diagnosed with type 1 diabetes mellitus compared to normal-weight individuals diagnosed with type 1 diabetes mellitus (40). HIIT (30-second sprint with four-to-five-minute passive recovery, three times per week for nine weeks) reduced waist-to-hip ratio and WC compared to the control group (CTRL) (41). HIIT significantly reduced body mass, fat mass, TC, triglycerides (TG), low-density lipoprotein in persons who were obesity compared with persons with normal weight (42). A South African based study found that HIIT (cycling for 60-

seconds at 90-100% $VO2_{peak}$ interspersed with 30-seconds of rest for a duration of 18-34 minutes repeated for ten days) and continuous moderate-intensity training (cycling for 18-24 minutes at 60-70% of peak oxygen for ten days) did not result in statistically significant improvements in insulin resistance. However, the HIIT group demonstrated a large effect on insulin resistance (43).

A systematic review and meta-analysis showed that HIIT significantly decreased diastolic blood pressure (DBP) at night compared with MICT ($d = -0.456$, $p<0.05$) (44). Another systematic review and meta-analysis showed that short-term moderate-intensity training and high-intensity training improved body composition without weight changes in overweight or obese persons (45). Moreover, a meta-analysis of 39 studies revealed that HIIT reduced visceral, abdominal and total fat in persons with normal weight and persons who were overweight or obese (46). HIIT at more than 90% of peak HR was more effective in reducing total adiposity. Therefore, HIIT is beneficial to reduce body composition and total adiposity.

A systematic review also revealed that HIIT is an attractive option to decrease cardiometabolic risk factors for overweight or obese persons (47). This review showed that 12 weeks of HIIT reduced body fat percentage, resting HR, WC, DBP and systolic blood in overweight or obese persons (47). However, a meta-analysis of 22 articles showed that HIIT provided similar benefits to MICT for TC and body composition in overweight or obese adults, which provides conflicting evidence about the superiority of high-intensity training vs MICT on cardiometabolic markers (20). The divergent HIIT programmes and SIT programmes limit the validity of any meta-analysis approach to address cardiometabolic health in overweight or obese persons (48). The reviews were limited to body composition and glycolipid risk factors; however, CVD risk encompasses many other variables (20).

The lowest time commitment of SIT required to improve cardiometabolic health is a total of ten minutes, which comprised maximal effort cycle sprints for 20-second repeated three times with active recovery of two minutes, three times per week for 12 weeks (49). The study only included men, and the authors indicated that this type of training cannot be generalised to everyone and requires a high level of motivation (49). A practical HIIT programme of less than 15 minutes improved cardiometabolic risk factors (48). Although these protocols are time-efficient, a single bout of exercise

during the working day may be a desirable option to reduce exercise time-commitment to a minimum. A recent study showed promising benefits in CRF by implementing SIT at different times in the day in sedentary healthy men (50). However, there is a lack of evidence on the effect of minimal bouts of high-intensity intervals during the working day on cardiometabolic risk factors in persons at risk of CVD. A meta-analysis revealed that exercise intensity was not significantly related to drop-out rates in HIIT. Drop-out rates were significantly related to the volume of HIIT (higher time effort/week and overall time effort/intervention and longer session time) (51). Therefore, a new high-intensity exercise programme is required to address the time and volume shortcomings of traditional high and moderate-intensity exercise in persons at risk of CVD.

2.5 The effect of high-intensity training interventions on inflammatory markers

Inflammation is strongly associated with a sedentary lifestyle contributing and CVD, cancer, pulmonary disease, metabolic disease, depression and dementia. An increase in interleukin-6 (IL-6), hs-CRP and tumour necrosis factor (TNF) further increases this risk of cardiometabolic disease (52). Inactivity results in an increase in visceral fat and adipokines release, which increases IL-6, TNF and CRP (53). Low-grade inflammation is a state of elevated IL-6, TNF and CRP (52). Low-grade inflammation is also associated with insulin resistance, atherosclerosis and tumour growth (54). Exercise promotes an anti-inflammatory effect and reduces the risk of chronic metabolic and cardiorespiratory diseases (52).

Three mechanisms of exercise result in an anti-inflammatory state. The first mechanism is a reduction in visceral fat mass (52). The decrease in visceral fat mass results in higher adiponectin levels and lower levels of pro-inflammatory adipokines and IL-6 (55-57). The second mechanism is an increased production of anti-inflammatory cytokines from contracting skeletal muscles (58, 59). The third mechanism involves a reduced expression of toll-like receptors on monocytes and macrophages (60). Toll-like receptors detect microbial pathogens in response to danger signals (61). Activation of the toll-like receptors results in antigen-specific adaptive immunity (62). Mechanism, physical activity and structured exercise can reduce systemic inflammation (63).

HIIT (i.e., exercising on the treadmill at 70-90% of maximal HR, three days per week for 12 weeks), reduced pro-inflammatory interleukins in women with metabolic syndrome (64). Paradoxically, other clinical trials showed that HIIT, prolonged sprint and HIIT, and MICE did not change plasma inflammatory cytokine levels in adults at elevated risk for type 2 diabetes mellitus (65) and sedentary persons (41). Furthermore, a systematic review showed that HIIT had no significant effect on IL-6 and hs-CRP in overweight or obese persons (47). A meta-analysis of 29 studies agrees with this finding and showed that there were no significant changes in hs-CRP and IL-6 in the HIIT group compared with the CTRL (66).

The effect of exercise on chronic inflammation may not be as straightforward as the literature suggests (67). A combination of HIIT and MICT may be required to maximise overall health (67). MICE and HIIT reduced adiponectin and IL-6; however, only HIIT increased TNF-α in adults who were overweight or obese (68). Conflictingly, MICT had a superior effect on lymphocytes, leukocytes, neutrophils and monocytes compared with HIIT in young, healthy men aged 18-20 years (69). Literature is equivocal pertaining to the type of exercise that promotes an anti-inflammatory effect.

A meta-review of 33 systematic reviews showed that HIIT reduced inflammatory markers versus non-active controls. However, HIIT reduced some inflammatory markers compared to active controls (70) across population groups. Another meta-analysis and systematic review in overweight or obese persons showed that the effect of HIIT is inconclusive (47). The duration of the individual bout of exercise is a crucial factor when considering the anti-inflammatory effect of IL-6 (47). Previous studies have prescribed modes of exercise, intensity, duration and frequency that are unappealing for the general population of persons with an elevated CVD risk profile (71, 72). There is a gap in the literature regarding the anti-inflammatory effect of a brief single bout of a high-intensity exercise programme repeated at different times in the day in persons at risk of CVD.

2.6 The effect of high-intensity training interventions on cardiorespiratory fitness

CRF is the efficiency of the heart to pump oxygenated blood to active muscles and the extraction of oxygen by active skeletal muscles to sustain exercise or physical activity

(73). CRF is the strongest predictor of mortality and CVD in persons with and without chronic diseases (74, 75). The gold standard to measure CRF is $VO2_{peak}$ or $VO2_{max}$ test, and it is a crucial indicator of exercise tolerance (76). Moreover, high levels of CRF (≥ 85% of age-predicted $VO2_{max}$) increased the quality of life and reduced the overall risk of cardiorespiratory and cardiometabolic diseases (77). More significant improvements in $VO2_{max}$ occurred after a high-intensity interval-based programme than endurance training, irrespective of matched training volume (78).

Despite the reduced training volume of HIIT and SIT, the literature suggested that two to sixteen weeks of this type of training improved $VO2_{max}$ compared to traditional endurance training (79, 80). Other studies supported this finding (17, 18, 49). However, the protocols used in these studies were SIT and not HIIT. This suggests that high-intensity training (HIIT and SIT) is beneficial in improving $VO2_{max}$ (81). Moreover, HIIT improved $VO2_{max}$ compared to MICT when energy expenditure was matched in both the exercise interventions (20).

HIIT has also been shown to increase CRF in persons with cardiometabolic disease or in those that have risk factors for CVD. High-intensity training improved $VO2_{max}$ in participants with lifestyle risk factors for cardiometabolic diseases compared to a matched volume of endurance training (12). Another study showed that training at 75% of $VO2_{max}$ resulted in greater improvements in CRF compared to training at 50% of $VO2_{max}$ in persons with obesity (82). HIIT (15-second effort at 80% of maximum aerobic speed with 15 seconds active recovery for four to eight minutes, three times per week for 12 weeks) and SIT (15-second effort at 100% of maximum aerobic speed with 15 seconds active recovery for four to eight minutes, three times per week for 12 weeks) increased $VO2_{max}$ in adolescent females who were obese (37). The HIIT group (60 seconds cycling repeated ten times at approximately 83% of peak power, twice a week for eight weeks) improved $VO2_{peak}$ compared to the CTRL in sedentary persons (38). HIIT significantly improved $VO2_{max}$ in obese persons (42). HIIT improved $VO2_{peak}$ and post-exercise HR recovery compared with MICT in persons with ischaemic heart disease (83).

A meta-analysis showed that SIT (six-second sprints with nine seconds rest, repeated 80 times), HIIT (four minutes cycling at 90% of $VO2_{peak}$ with three minutes rest between intervals, repeated approximately nine times) and MICT (cycling for approximately 61

minutes at 60% of $VO2_{peak}$) are equally effective in improving CRF in women who were overweight (35). However, a multi-centre comparison of oxygen consumption of 677 participants from five countries and eight universities showed that high-volume interval training (more than 15 minutes of high-intensity effort per session) had a significantly greater absolute $VO2_{peak}$ compared with low volume high-intensity training, SIT and MICT (84). Furthermore, a systematic review and meta-analysis showed that low-volume HIIT increased CRF more than the MICT and CTRL groups in persons who were normal weight, overweight or obese (85). A meta-review of 33 systematic reviews agrees with the studies that HIIT improved CRF compared with active and non-active CTRLs in various population groups (70).

Although empirical evidence suggests that HIIT improved CRF, the studies only used $VO2_{peak}$ or $VO2_{max}$ as the essential measurement of CRF. However, other crucial physiological measures of CRF, such as ventilatory equivalent, ventilatory threshold and the workload corresponding to these measurements, are essential for cardiovascular health and exercise prescription (86). Due to limitations in methods, heterogeneity of participants and training programmes, it is difficult to draw definite conclusions about the effect of intensity, frequency and duration on cardiovascular adaptation in apparently healthy participants and persons at risk of cardiometabolic diseases. A close investigation of high-intensity training reveals that it is not a time-efficient intervention, considering the rest intervals between the high-intensity bouts (32). Furthermore, a brief bout of high-intensity exercise at different times of the day will drastically minimise the time-commitment of exercise (32). Therefore, a new protocol is required to enable the flexibility of an individualised perceived high-intensity effort, which will allow the attainability of the health-related benefits of this type of training.

2.7 Conclusions

Research is equivocal on the effect of effect of HIT (HIIT and SIT) vs MICT on CVD risk factors, inflammatory markers and CRF.

Despite the reduced training volume of HIIT and SIT, the literature suggests that two to sixteen weeks of this type of training improves CRF compared with traditional endurance training (79, 80). However, due to limitations in methods, heterogeneity of participants and training programmes, it is difficult to draw definite conclusions about

the effect of intensity, frequency and duration on cardiovascular adaptation in persons at risk of cardiometabolic diseases.

There is a lack of adherence to long-duration high-intensity training programmes in persons at risk of CVD and who are overweight or obese (87). There are conflicting views about the anti-inflammatory effect of prolonged endurance training and an acute bout of high-intensity training. Furthermore, there is a gap in the literature regarding the anti-inflammatory effect of a brief single bout of a high-intensity exercise programme repeated at different times in a day in persons at risk of CVD.

A new time-efficient exercise programme is required for persons at risk of CVD to address inflammatory, cardiorespiratory and cardiometabolic health-related benefits associated with exercise. The new ‘Gear’ exercise programme is proposed to bridge the gaps in the literature.

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Chapter 3 Comparison of high-intensity training versus moderate-intensity continuous training on cardiorespiratory fitness and body fat percentage in overweight or obese persons: A systematic review and meta-analysis of randomised controlled trials

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3.1 Abstract

Background: High-intensity training comprises sprint interval training (SIT) and high-intensity interval training (HIIT). The study compared high-intensity training with moderate-intensity continuous training (MICT) on cardiorespiratory fitness (CRF) and body fat percentage in overweight or obese persons.

Methods: A systematic search of randomised controlled trials using the health science databases occurred up to April 2020. Twenty-six studies were included for complete analysis. A total of 784 participations were analysed. The unstandardised mean difference for each outcome measurement was extracted from the studies and pooled with the random-effects model.

Results: MICT was significantly better at improving CRF compared with SIT (MD = -0.92; 95% CI = -1.63 to -0.21; p = 0.01; I^2 = 10%). Furthermore, there was no significant difference between MICT versus HIIT on CRF (MD = -0.52; 95% CI = -1.18 to 0.13; p = 0.12; I^2 = 23%). There was no significant difference in body fat percentage between MICT versus HIIT and MICT versus SIT.

Conclusions: MICT was significantly better at improving CRF than SIT in overweight or obese persons.

Keywords: body composition, cardiovascular health, obesity, overweight, exercise prescription

A video abstract can be viewed on the following link:
https://twitter.com/JPAHjournal/status/1388159217043902467

3.2 Introduction

The global prevalence of obesity is alarming. The World Health Organisation reported that approximately 39% of the worldwide population of 18 years or older (40% of women and 39% of men) were overweight (1). Moreover, 13% of the global population (11% of men and 15% of women) were obese (1). Overweight and obesity are defined as increased body mass to height (2), which increases overall adiposity and contributes to NCD, such as cancer, type 2 diabetes mellitus, hypertension and CVD (3). Excessive weight gain is linked to depression (4), low levels of physical functioning (5), poor quality of life and premature death (6).

High-intensity training has become a popular exercise choice amongst overweight and obese persons (7). High-intensity training is categorised as either HIIT and SIT (8). HIIT incorporates high-intensity activity (85-95% of peak HR), lasting for a few seconds or minutes interspersed with rest periods or low-intensity exercise (≤ 40% of peak HR) (9, 10). This type of high-intensity training has a positive effect on CRF, body composition (11, 12), central adiposity (13) and cardiometabolic disease risk factors (14, 15). A recent meta-review of 33 systematic reviews reported that HIIT compared to non-active controls improved lean muscle mass, some inflammatory markers, cardiac and vascular function, glycaemic control, blood glucose, HR, CRF and anthropometric variables (16). Furthermore, HIIT improved muscle structure, CRF and some inflammatory markers when the intervention was compared to active controls (16).

The second category of high-intensity training is SIT. SIT encompasses maximal or supra-maximal effort that exceeds the workload required to elicit maximal oxygen uptake. The sprint intervals last for 20 to 30 seconds, followed by complete rest or active recovery for four to five minutes (8). SIT resulted in a 29% significantly greater reduction in absolute fat mass than MICT (17). Inconsistent with this finding, SIT resulted in similar body composition and CRF improvements compared with MICT in overweight or obese women (18). Furthermore, a systematic review and meta-analysis revealed similar benefits of fat reduction in HIIT, SIT and MICT, which were not clinically meaningful (19). Therefore, the plethora of literature is scanty on the superior effects of HIIT and SIT compared with MICT on body fat percentage and CRF in overweight and obese persons.

Regardless of the presence or absence of cardiometabolic risk factors, high CRF levels reduce the overall risk of mortality and cardiorespiratory disease (20). High-intensity training (HIIT and SIT) and MICT reduced body mass and improved CRF in women who were overweight (21). Systematic reviews and meta-analyses comparing the superior effect of high-intensity training (HIIT and SIT) with MICT revealed that high-intensity training superiorly increases CRF (8, 22-24) and decreases body composition (22) compared with MICT in overweight and obese persons. Conversely, other studies reported comparable and similar improvements in this comparison on body composition (11, 19, 25-27) and CRF (27) in this population group. However, one review indicated that low-volume HIIT had no significant effect on body composition in persons with normal weight, overweight and obesity (24).

The surfeit of literature provides conflicting evidence about the optimal prescription of high-intensity training (HIIT and SIT) to improve CRF and reduce body fat percentage in overweight or obese persons. The published systematic reviews concluded findings on the combined comparison of high-intensity training (HIIT and SIT) with MICT in overweight and obese persons. Thus, there is paucity in the literature regarding the independent comparison of HIIT versus MICT and SIT versus MICT on CRF and body fat percentage in this population group. Therefore, the systematic review and meta-analysis aimed to compare MICT versus HIIT and MICT versus SIT on CRF and body fat percentage in overweight or obese persons. Secondly, the systematic review will identify gaps in the literature and provide areas of focus for future research.

3.3 Methods

3.3.1 Search strategy

The current systematic review and meta-analysis used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for evaluating health care interventions in clinical practice (28). A systematic search of randomised controlled trials (RCTs) using the focal health science databases, such as PubMed, Web of Science, Cochrane Library, Science Direct and Physiotherapy Evidence Database (PEDro) was undertaken on the 2nd of December 2019, the 19th of February 2020 and the 18th of April 2020. The search items used to obtain relevant RCTs were as follows: high-intensity interval exercise, SIT, high-intensity training in overweight or obese persons, or persons with high body mass index (BMI) or body fat percentage or lean body mass or $VO2_{max}$ or CRF or cardiopulmonary fitness or $VO2_{max}$ or $VO2_{peak}$.

3.3.2 Inclusion and exclusion criteria

The current review accepted RCTs published in peer-reviewed journals from 1970 to 2020. The authors selected RCTs written in English. Studies were included in the review if the study population had a mean body-mass index equal to or greater than 25 kilograms per meter squared (kg/m^2) and were 18 to 60 years old. The MICT group was the intervention group, and the HIIT and SIT groups were the comparison groups. The RCTs included in the final analysis reported one of the following outcome measurements, viz. body fat percentage and CRF ($VO2_{max}$ or $VO2_{peak}$). The study employed HIIT intervention at ≥60% of VO2 reserve (VO2R) or HR reserve (HRR) or ≥ 77% maximal HR (HR_{max}) and MICT at 40-59% VO2R or HRR or 64-76% HR_{max} (29). The current study included HIIT sessions lasting four or less minutes per set interspersed with an interval of rest or active recovery (30) and SIT sessions of maximal effort with and without active recovery. Studies were excluded if the participants had a BMI of less than 25 kg/m^2; the details of the exercise (frequency, intensity, time and type) interventions were unknown (22), and if the participants had any known and significant cardiovascular, metabolic, respiratory and neurological comorbidity. Furthermore, studies were excluded if there was any significant co-intervention, such as fasting, psychological, pharmacological and nutritional interventions (22).

3.3.3 Outcome measurements

The primary outcome measurement in the current systematic review was CRF expressed as $VO2_{max}$ or $VO2_{peak}$. The secondary outcome measurement was body fat percentage in overweight or obese persons.

3.3.4 Selection of studies

Two authors (DT, PC) screened the articles independently for eligibility and inclusion in the current study. Thereafter, the authors excluded abstracts considering the study design, intensity of HIIT and MICT, comparison of exercise intervention protocols, BMI and age of the study population. Finally, DT and PC screened the full text of the selected articles for inclusion based on the comparison of HIIT versus MICT and SIT versus MICT.

3.3.5 Risk management

The PEDro scale was used to rate the included RCTs' quality (Table 3.1) (31). This rating tool is founded on the Delphi list, and it rates the internal validity of RCTs (31). The study did not consider blinding of subjects and blinding therapists when computing

the quality of the RCTs because these items are not feasible and hard to replicate in the design of HIIT and MICT interventions (32). Studies were classified as good quality (>61%), fair quality (45.4-61%) and poor quality (<45.4%) (33, 34).

Table 3.1 Quality analysis of randomised control trials using the PEDro scale

Study	RA	CA	BC	BA	AF	ITT	BGC	PEV	%	Q
Baekkerud FH (36)	√	X	√	X	√	X	√	√	63	Good
Barry JC (53)	√	X	√	X	X	X	√	√	50	Fair
Bartlett DB (54)	√	X	√	X	X	X	√	√	50	Fair
Cheema BS (37)	√	√	√	√	X	√	√	√	88	Good
Cocks M (50)	√	X	√	X	√	X	√	√	63	Good
Cooper HF (49)	√	X	√	X	√	X	√	√	63	Good
Eskelinen J (48)	√	X	√	X	√	X	√	√	63	Good
Fisher G (47)	√	√	√	√	X	√	√	√	88	Good
Gerosa-Neto J (55)	√	X	√	X	X	X	√	√	50	Fair
Higgins S (51)	√	X	√	X	√	X	√	√	63	Good
Hornbuckle LM (38)	√	X	√	X	X	√	√	√	63	Good
Keating S (39)	√	√	√	√	√	√	√	√	100	Good
Kong Z (56)	√	X	√	X	X	X	√	√	50	Fair
Kong Z (57)	√	X	√	X	X	X	√	√	50	Fair
Lunt H (40)	√	√	√	√	X	√	√	√	88	Good
Nie J (41)	√	X	√	X	√	X	√	√	63	Good
Rafiei H (58)	√	X	X	X	√	X	√	√	50	Fair
Ram A (7)	√	X	√	X	X	X	√	√	50	Fair
Robinson E (42)	√	X	√	X	√	X	√	√	63	Good
Sawyer BJ (52)	√	X	√	√	X	X	√	√	63	Good
Shepherd SO (43)	√	X	√	X	√	X	√	√	63	Good
Skleryk JR (60)	√	X	√	X	X	X	√	√	50	Fair
Sun S (44)	√	X	√	X	√	X	√	√	63	Good
Umamaheswari K (59)	√	X	√	X	X	X	√	√	50	Fair
Vella CA (45)	√	X	√	X	√	X	√	√	63	Good
Zhang H (46)	√	X	√	X	√	X	√	√	63	Good

RA, random allocation; CA, concealed allocation; BC, baseline comparability; BA, blind assessors; AF, adequate follow-up; ITT, intention-to-treat analysis; BGC, between-group comparisons; PEV, point estimates and variability; %, percentage; Q, quality.

3.3.6 Data extraction and management

The authors' surnames, publication year, study design, age range, participants' baseline characteristics, body-mass index, sample size, type of training, frequency and intensity of training were documented on an Excel spreadsheet (Table 3.2; Section 3.4.4). The authors were contacted through email if the relevant data of the included studies were not provided in the full text of the paper. Data management and forest plot comparisons of CRF and body fat percentage measurements between the HIIT, SIT and MICT groups were analysed using RevMan 5.3. The unstandardised mean difference and standard deviation for each outcome measurement were extracted from the articles and pooled with the random-effects model (35). The random effects model was used because it takes into account differences between individual study effects. According to the Cochrane handbook, the standard deviation was calculated using other statistical parameters, such as confidence intervals, standard error of the mean, p-values and t-values if studies did not report the change from baseline standard deviation (35). The level of significance was set at $p<0.05$ and 95% confidence intervals.

3.3.7 Heterogeneity

The sample size, type, duration, intensity of interventions, gender differences, nutritional and lifestyle factors, seasonal changes, energy expenditure and inherent differences result in heterogeneity observed in the current study. Heterogeneity was computed using I2 in the current study. The quantification of heterogeneity in the current systematic review categorises substantial heterogeneity as 50-90%. (35).

3.3.8 Sensitivity analysis

Studies were excluded if the exercise intensity was less than 60% of VO2R or HRR or less than 77% HR_{max} in the HIIT group. The MICT group had to accumulate a minimum of 20-minutes of continuous rhythmical exercise at 40-59% VO2R or HRR or 64-76% HR_{max} to be included in the current study. Furthermore, the review did not include studies with exercise interventions for less than two weeks, including resistance exercises or transitory or polarised or circuit exercise interventions and combined high-intensity (HIIT and SIT) and MICT interventions. Therefore, the review strictly compared the effect of HIIT versus MICT and SIT versus MICT on body fat percentage and CRF in overweight or obese persons.

3.4 Qualitative results

3.4.1 Results of the literature search

The primary search resulted in 9571 records from electronic databases. After screening and removing the duplicated titles and abstracts, 1427 studies were included for potential review. The analysis of the eligibility criteria resulted in 61 studies meeting the requirements of the current review. However, 26 studies were included in the final comprehensive analysis after narrowing the eligibility criteria to the inclusion and exclusion criteria of the studies (Figure 3.1).

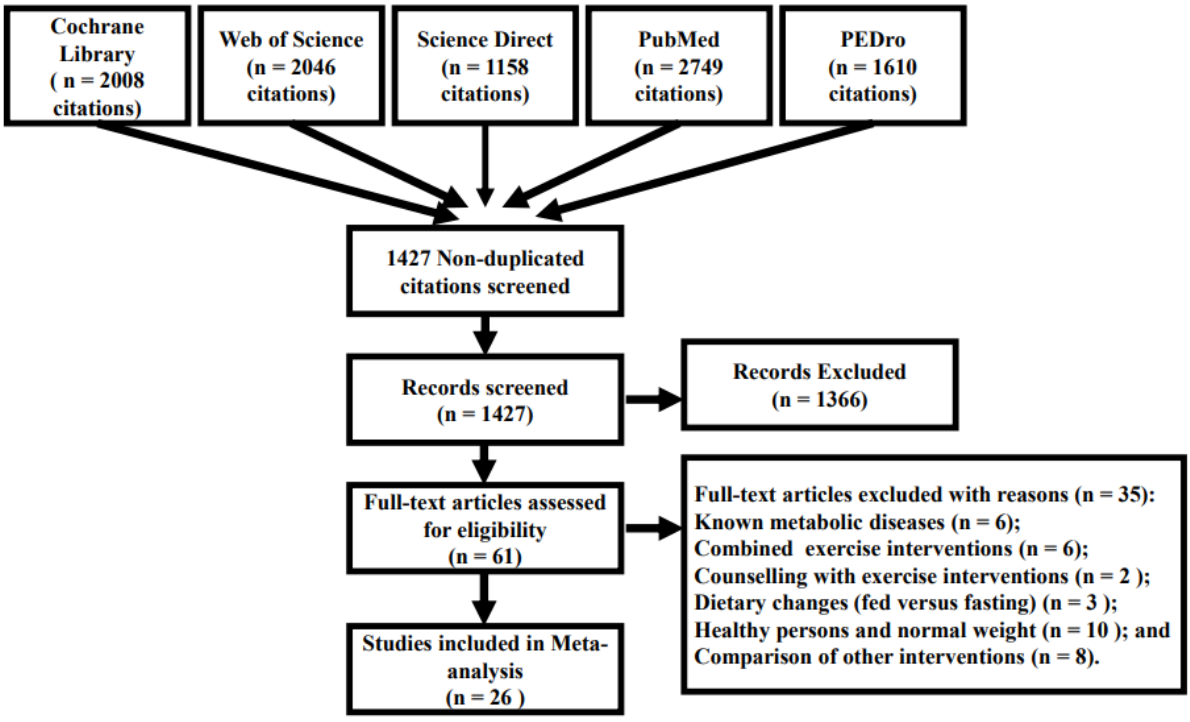

Figure 3.1 PRISMA diagram of the literature search strategy

PEDro, Physiotherapy Evidence Database; n, number.

3.4.2 Risk of bias in included studies

The quality of the eligible studies for complete review was good overall. Of the 26 studies, 17 were good quality studies (36-52), and nine were fair quality studies (7, 53-60). Only 12 studies justified sample size (7, 36, 40, 45, 49-53, 56, 57, 60), which underestimated the effect on the outcome measurements of the interventions and predisposed the studies to type I and type II errors. Seven studies reported the method of randomisation, such as computer-generated (37, 50, 58), lot method (59), stratified according to $VO2_{max}$ and visceral fat values (55), variable permuted block sizes using strata factoring in sex and age of the participants (53), and using matched $VO2_{peak}$,

age and BMI (50). Moreover, four studies provided details about allocation concealment (37, 39, 40, 47). Thus, the other articles were prone to selection bias.

3.4.3 Characteristics of the included studies

After extensive analysis of the relevant studies, 26 published RCTs were included for complete and narrative analysis. The age of participants ranged from 17 to 60 years, and the mean age for the HIIT, MICT and SIT groups was 30, 28 and 31 years, respectively. The total number of participants that successfully completed the exercise interventions was 784 (MICT = 362, HIIT = 292 and SIT = 130). The mean sample size for each group was as follows: MICT = 14; HIIT = 15; and SIT = 14. Not all studies reported sex; however, more women than men participated in the RCTs (38-46, 51, 53, 54, 57, 58).

3.4.4 Characterises of the interventions

Most studies compared the effect of MICT versus HIIT on CRF (17 studies) and body composition (15 studies) in overweight or obese persons. However, nine studies compared MICT with SIT on CRF and seven studies compared this group effect on body fat percentage in this population group. Most of the participants were encouraged to maintain normal dietary intake for the duration of the study period. The frequency of the intervention ranged from two to five times per week for six to twelve weeks. However, eight studies reported training for less than six weeks (42, 48, 50, 53, 56-58, 60), and three studies reported training for more than twelve weeks (37, 38, 59).

The duration of the exercise interventions varied from 20 to 30 minutes (HIIT), 20 to 40 minutes (MICT) and 17 to 30 minutes (SIT). Cycling was the preferred modality of exercise. However, two studies reported the use of walking, jogging or running on the treadmill or outdoor fields (36, 55), and a unique study included boxing as a means of HIIT (37). Four studies used a combination of training modalities, such as walking, cycle ergometers, elliptical trainers and treadmills (42, 45, 53, 58). Studies conducted HIIT at least 60% of VO2R or HRR or at least 77% HR_{max}, and SIT at the all-out perceived effort.

Table 3.2 Study characteristics

Study	Design	Participants	Age	BMI	Sample size	Frequency	Exercise intensity	Conclusion
Baekkerud et al., 2017 [36]	RCT	Overweight or obese persons.	Overall: 41 ±9 MICT: NR 4HIIT: NR 1HIIT: NR	Overall: 30±4 MICT: NR 4HIT: NR 1HIIT: NR	MICT: 9 4HIT: 8 1HIIT: 9	3x/week for 6-weeks.	MICT: running or walking for 45-min at ~70% of HRmax. 4HIIT: 4X4-min at ~85%–95% of HRmax with 3-min of active recovery. 1HIIT: 10X1-min intervals at ~90% of HRmax with 3-min active recovery.	4HIT was superior to 1HIIT and MICT with regard to improvements in cardiorespiratory fitness in overweight or obese persons.
Barry et al., 2018 [53]	RCT	Adults with obesity.	Overall: 48.9±10.7 MICT: 43.8±10.6 HIIT: 50.4±7.6	MICT: 31.1±5.3 HIIT: 33.3±8.9	MICT: 17 HIIT: 16	5x/week for 2-weeks.	MICT: 20-60 min of continuous exercise at ~65% HRpeak. HIIT: 1-min at ~90% HRpeak with 1-min recovery at a low intensity, progressed from 4×1-min intervals to 10×1-min intervals.	There were no significant differences observed for measures of body composition.
Bartlett et al., 2018 [54]	RCT	Persons who were sedentary.	Overall: 43±11 MICT: 45±10 HIIT: 42±12	MICT: 28.1±4.7 HIIT: 28.1±6.1	MICT: 13 HIIT: 14	MICT: 5x/week for 10-weeks. HIIT: 3x/week for 10-weeks.	MICT: cycling at ~70% of HRmax for 30–45 min. HIIT: cycle sprints of between 15-60 sec at >90% of HRmax, with 45-120 sec of active rest for 18-25 min.	HIIT is a time-efficient exercise option to improve neutrophil and monocyte function.
Cheema et al., 2015 [37]	RCT	Men and women with abdominal obesity	Overall: 39±17 Walking: 36±15 Boxing: 43±19	Walking: 30.8±2.6 Boxing: 32.0 ±5.9	Walking: 6 Boxing: 6	4x/week for 16-weeks.	Walking: 50-min at ~64-77% of HRmax. Boxing: 50-min of supervised boxing training at ~86-95 of HRmax. Intervals were prescribed at 2:1 (2 min of high intensity activity	Boxing training (HIIT) may elicit a better therapeutic effect on cardio-metabolic health and HRQoL outcomes than an equivalent dose of brisk walking (MICT).
Cocks et al., 2016 [50]	RCT	Young men with obesity.	Overall: 25±1 MICT: 26±2.0 SIT: 24±2.0	MICT: 33.7±1.5 SIT: 35.8±0.8	MICT: 8 SIT: 8	MICT: 5x/week SIT: 3x/week	MICT: cycling 40-60 min at ~65% ˙VO2peak. SIT: 4-7 constant workload cycle sprints of 200% Wmax followed by 120-sec of active recovery.	SIT and MICT increased cardiorespiratory fitness; however, MICT significantly reduced % body fat compared to SIT.
Cooper et al., 2016 [49]	RCT	Middle-aged men who were sedentary.	Overall: 40-60 ET: NR P-SIT: NR A-SIT: NR	ET: 30.6±3.4 P-SIT: 29.7±4.1 A-SIT: 29.7±4.0	ET: 15 P-SIT: 15 A-SIT: 15	3 days/week for 12-weeks.	ET: 50–60 min cycling and 80% HRmax. P-SIT: 4–10×30-sec sprint effort with passive recovery. A-SIT: 4–10×30-sec sprint effort with active recovery.	All interventions altered whole-body fat mass, abdominal visceral adipose tissue. P-SIT promoted comparable cardiorespiratory fitness improvements to that of endurance training.
Eskelinen et al., 2015 [48]	RCT	Men who were sedentary.	Overall: 40-55 MIT: 48 SIT: 47	MIT: 26.4 SIT: 25.9	MIT: 14 SIT: 14	Six sessions within 2-weeks	MIT: 40–60 min cycling at 60% of VO2 peak. SIT: 4–6x30-sec of all-out cycling with 4 min recovery.	The mean changes in body composition were similar in both training modes. High intensity training increased cardio-respiratory fitness.
Fisher et al., 2015 [47]	RCT	Overweight or obese men.	Overall: 17-22 MIT: 20.0±1.5 HIT: 20.0±1.5	MIT: 29.0±3.4 HIT: 30.0±3.1	MIT: 10 HIT: 13	MIT: 5x/week for 6-weeks HIT: 3x/week for 6-weeks	MIT: cycling at ~55-65% of VO2peak for 45-60 min. HIT: cycling at ~85% of peak power for 4x30-sec intervals with 4-min rest.	Both interventions reduced blood lipids, body fat (%) and improved cardiorespiratory fitness. MICT led to a greater improvement in overall cardiorespiratory fitness.

Study	Design	Participants	Age	BMI	Sample size	Frequency	Exercise intensity	Conclusion
Gerosa-Neto et al., 2019 [55]	RCT	Adult men with obesity.	Overall: 29.6±4.9 MICT: 20.9±1.6 HIIT: 21.0±1.1 CON: 20.8± 1.1	MICT: 35.9±4.3 HIIT: 34.3±2.3 CON: 35.4±3.3	MICT: 13 HIIT: 13 CON: 6	3x/week for 6-weeks.	MICT: 35-min at ~65% of VO2max. HIIT: 10 repetitions of 1:1 min work to passive recovery ratio at 100% VO2max.	HIIT and MICT improved cardiorespiratory fitness in men with obesity.
Higgins et al., 2016 [51]	RCT	Young women with overweight or obesity.	Overall: 20.4±1.5 MICT: NR SIT: NR	Overall: 30.3±4.5 MICT: NR SIT: NR	MICT: 29 SIT: 23	3x/week for 6-weeks.	MICT: cycling at ~60-70% HRR at matched energy expenditure of SIT. SIT: 30-sec 'all-out' sprints followed by 4-min of active recovery.	SIT reduces adiposity and increases aerobic capacity more than MICT of equal estimated energy expenditure.
Hornbuckle et al., 2017 [38]	RCT	Young African-American women with obesity.	Overall: 30.5±6.8 SS: 28.3±6.1 HIIT:32.1±7.0	SS: 32.7±5.3 HIIT: 36.8±4.3	SS: 3 HIIT: 11	3x/week for 16-weeks.	SS: treadmill walking at ~60–70% of HRmax. HIIT: 32-min of treadmill HIIT alternating 3-min at ~60–70% of HRmax with 1-min at ~80–90% of HRmax.	HIIT was more effective at reducing waist circumference and increasing daily steps/day than SS treadmill exercise.
Keating et al., 2013 [39]	RCT	Overweight adults.	Overall: 42.8±1.4 CON: 44.1±1.9 HIIT: 41.8±2.7 PLA: 42.9±2.8	CON: 28.5±0.6 HIIT: 28.2±0.5 PLA: 28.2±0.6	CON: 11 HIIT: 11 PLA: 11	3x/week for 12-weeks.	CON: cycling for 30-45-min at ~50-65% of VO2peak. HIIT: weeks 1-4: 4X30–45 sec at ~120% of VO2peak (20–180 sec rest) and weeks 5–12: 6X60-sec (120 sec rest). PLA: one fortnightly supervised exercises performed for two weeks and a 5-min cycle at ~30 W.	Continuous aerobic exercise training is effective for improving fat distribution independently of weight loss. However, HIIT elicited comparable fitness benefits to continuous exercise.
Kong et al., 2016 [56]	RCT	Overweight or obese young women.	Overall: 18-30 MICT: 19.9±2.1 HIIT: 19.8±0.8	MICT: 26.2±2.4 HIIT: 25.5±2.1	MICT: 8 HIIT: 10	4x/week for 5-weeks.	MICT: 40-min of cycling at ~65% of VO2 peak. HIIT: 60X8-sec at ~90% of VO2 peak with 12 sec recovery.	HIIT improved cardio-respiratory fitness and blood glucose. Neither interventions had an effect on body composition.
Kong et al., 2016 [57]	RCT	Overweight or obese young women.	Overall: 18-30 MVCT: 20.5±1.9 HIIT: 21.5±4.0	MVCT: 25.5±2.1 HIIT: 25.8±2.6	MVCT: 13 HIIT: 13	4 days/week for 5-weeks.	MVCT: cycling at 60% of VO2 peak for 40-min. HIIT: cycle sprints at ~90% VO2peak for 8-sec followed by 12-sec of passive rest repeated 60 times.	Both interventions were effective in improving cardiorespiratory fitness in young women with overweight or obesity.
Lunt et al., 2014 [40]	RCT	Adults with obesity.	Overall: 35 to 59 Walk: 45.7±5.7 AIT: 49.1±4.8 MVIT: 53.5±7.2	Walk: 32.9±3.7 AIT: 32.4±3.0 MVIT: 32.2±3.7	Walk: 14 AIT: 9 MVIT: 9	3x/week for 12-weeks.	Walk: 33-min at ~65–75% of HRmax. AIT: 4x4-min of walking or jogging at 85-95% HRmax with 3-min active recovery. MVIT: 3-6 repetitions of all-out jogging up a hill for 30-45 sec with 4-min active recovery.	Aerobic interval training resulted in modest improvements in cardiorespiratory fitness in persons with obesity.
Nie et al., 2018 [41]	RCT	Young women with obesity.	Overall: 18-22 MICT: 20.9±1.6 HIIT: 21.0±1.1 CON: 20.8± 1.1	MICT: 26.9±3.0 HIIT: 26.93±3.6 CON: 26.8±4.0	MICT: 14 HIIT: 16 CON: 13	3-4 days/week for 12-weeks.	MICT: cycling at ~60% of VO2max until 300KJ of work was achieved. HIIT: cycling at ~90% of VO2max with 3-min of complete recovery until 300KJ of work was achieved.	HIIT and MICT led to a similar decrease in body composition, and a similar increase in cardiorespiratory fitness.
Rafiei et al., 2019 [58]	RCT	Overweight or obese women at risk of type 2 diabetes	Overall: 48.9±10.7 MICT: 46.0±12.9 HIIT: 51.8±8.5	MICT: 34.1±6.1 HIIT: 33.9±9.5	MICT: 7 HIIT: 8	5x/week for 2-weeks.	MICT: 20–50 min of continuous activity at ~65% HRpeak. HIIT: 4–10X1-min at ~90% HRpeak with 1-min rest period.	HIIT or MICT led to significant reduction in body mass and similar improvements in cardiorespiratory fitness.

Study	Design	Participants	Age	BMI	Sample size	Frequency	Exercise intensity	Conclusion
Ram et al., 2020 [7]	RCT	Men with overweight or obesity.	Overall: 18-45 MICT: 26.0±8.0 HITT: 30.0±6.0	MICT: 27.4±4.0 HITT: 28.1±4.1	MICT: 12 HITT: 16	3x/week for 6-weeks.	MICT: ~65-75% of HRmax for 30 min. HIIT: ~90% of HRmax for 10x1 min intervals with 1 min recovery at 15% of Wpeak.	HIIT and MICT improved aerobic fitness. The interventions did not improve body composition.
Robinson et al., 2015 [42]	RCT	Overweight or obese adults at risk of type 2 diabetes	Overall: NR MICT: 52±10 HIIT: 52±10	MICT: 31.4±4.1 HIIT: 32.9 ±6.6	MICT: 18 HIIT: 20	10 sessions over 2-weeks.	MICT: 20-50 min of continuous activity at ~ 60–65% of HRpeak. HIIT: 10x1-min intervals at ~85–90% of HRpeak with a work-to-rest ratio of 1:1.	Both interventions significantly improved cardiorespiratory fitness and reduced inflammatory markers.
Sawyer et al., 2016 [52]	RCT	Adults with obesity.	Overall: 35.1±8.1 MICT: NR HIT: NR	MICT: 34.5±3.2 HIT: 37.4±6.2	MICT: 9 HIT: 9	3X/week for 8-weeks.	MICT: cycling for 30-min at ~70–75% of HRmax. HIT: 10x1-min intervals at ~ 90–95% of HRmax with 1-min of active recovery.	Both HIIT and MICT groups had similar increases in cardiorespiratory fitness in adults with obesity.
Shepherd et al., 2015 [43]	RCT	Persons who were sedentary.	Overall: 42±11 MICT: 43±11 HIT: 42±11	MICT: 27.7±4.6 HIT: 27.7±5.0	MICT: 36 HIT: 42	MICT: 5x/week for 10-weeks. HIT: 3x/week for 10-weeks.	MICT: cycling for 30-45 min at ~70% of HRmax. HIT: cycle sprints between 15-60 sec at >90% HRmax with 45-120 sec of active recovery.	HIT improved insulin sensitivity, VO2max, reduced abdominal fat mass and caused favourable changes blood lipids.
Skleryk et al., 2013 [60]	RCT	Men with obesity.	Overall: 26-45 TER: 37.1±1.4 SIT: 40.2±2.3	TER: 35.2±1.8 SIT: 32.2±2.1	TER: 8 SIT: 8	TER: 10 sessions for 2-weeks. SIT: 6 sessions for 2-weeks.	TER: cycling at ~65% VO2peak for 30 min. SIT: 8–12×10-sec cycle sprints.	TER or SIT did not elicit any measurable metabolic adaptations in this population group.
Sun et al., 2019 [44]	RCT	Overweight women.	Overall: Not reported MICT: 20.9±1.4 HIIT: 21.5±1.8 SIT: 21.4±1.1	MICT: 26.5±2.6 HIIT: 26.3±2.3 SIT: 26.0±2.5	MICT: 14 HIIT: 14 SIT: 14	3x/week for 12-weeks.	MICT: 61-min of cycling at ~60% VO2 peak. HIIT: 9X4-min at ~90% VO2peak with 3-min rest. SIT: 80×6-sec cycle sprints with 9-sec rest.	All training modes improved VO2peak and reduced body mass. High intensity training is beneficial than MICT in improving insulin sensitivity.
Umamahes wari et al., 2018 [59]	RCT	Overweight persons.	Overall: 19-35 50-74%: 24.3±6.2 75%-84%: 23.2±5.6	50-74%: 29.24±2.5 9 75%-84%: 29.69±3.2	50-74%: 37 75%-84%: 35	50-74%: 5 days/week for 15-weeks. 75%-84%: 3 days/week for 15-weeks.	50-74%: 40-min of steady cycling. 75-84%: 8-sec sprint cycling followed by 12-sec of low intensity cycling for 20-min	High intensity exercise is more effective in changing the body composition in overweight persons.
Vella et al., 2017 [45]	RCT	Overweight or obese adults.	Overall: 18-44 MICT: 28.9±8.1 HIIT: 23.1±6.6	MICT: 33.1±6.0 HIIT: 29.9±3.3	MICT: 9 HIIT: 8	4x/week for 8-weeks.	MICT: running, cycling or elliptical at ~55-59% HRR for 20-minutes. HIIT: 10x1-min intervals at ~75-80% HRR with 1-min active recovery.	HIIT increases VO2 peak and reduces low density lipoprotein cholesterol compared with MICT. However, HIIT may be associated with an increase in inflammation.
Zhang et al., 2017 [46]	RCT	Female university students with obesity.	Overall: 18-22 MICT: 20.9±1.4 HIT: 21.5±1.7 CON: 20.8±1.1	MICT: 25.7 HIT: 25.3 CON: 26.4	MICT: 15 HIT: 15 CON: 13	3-4x/week for 12-weeks.	MICT: cycling at ~60% VO2max until 200KJ and 300KJ of work was reached. HIT: 4-min at >90% HRmax with 3-min active recovery until 200KJ and 300KJ of work was reached.	MICT and HIIT resulted in similar quantitative reduction in abdominal visceral fat.

RCT, randomised control trial; MVCT, moderate-to-vigorous intensity continuous exercise training; HIIT, high-intensity interval training; HIT, high-intensity training; SIT, sprint interval training; AIT, aerobic interval training; MVIT; maximal volitional intensity training; HR_{max}, maximal heart rate; MCT, moderate continuous training; HRR, heart rate reserve; $VO2_{peak}$, peak oxygen consumption; $VO2_{max}$, maximal

oxygen consumption; NR, not reported; CON, control; PLA, placebo; TER, traditional exercise recommendations; P-SIT, sprint interval training with passive recovery; A-SIT, sprint interval training with active recovery; SS, steady-state exercise.

3.4.5 Quantitative results

Seventeen studies reported $VO2_{max}$ or $VO2_{peak}$ as an outcome parameter for CRF (7, 36-38, 40-47, 52, 54, 56-58). There was no significant difference in CRF between MICT versus HIIT in overweight or obese persons (MD = -0.52; 95% CI = -1.18 to 0.13; p = 0.12; I^2 = 23%) (Figure 3.2).

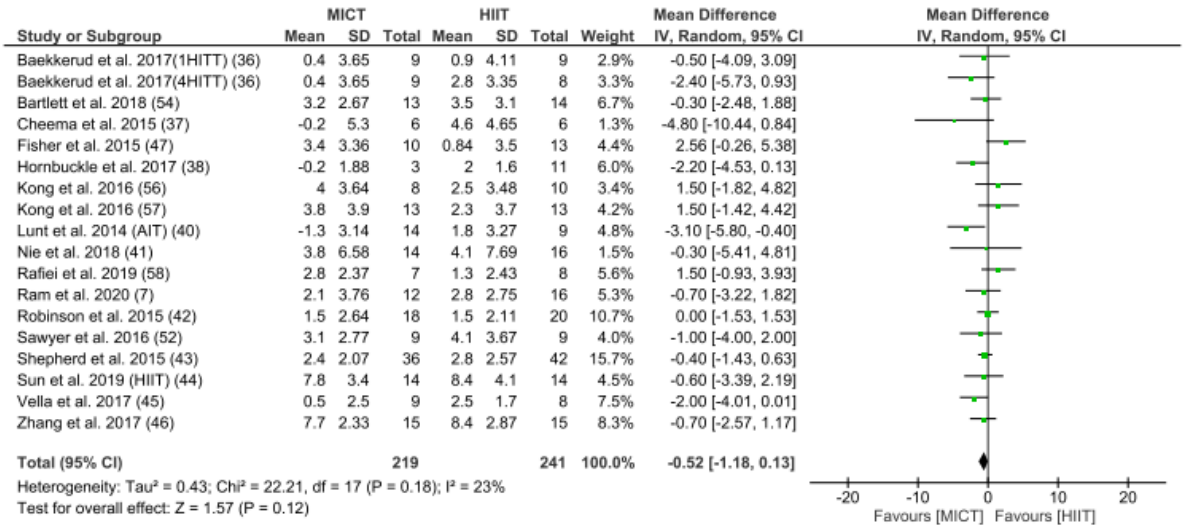

Figure 3.2 Forrest plot depicting changes in cardiorespiratory fitness [maximal oxygen consumption ($VO2_{max}$) and peak oxygen consumption ($VO2_{peak}$)] (MICT versus HIIT unstandardised mean difference in ml/kg/min)

Nine studies reported $VO2_{max}$ or $VO2_{peak}$ as an outcome parameter for CRF in this analysis (39, 40, 44, 48-51, 55, 60). MICT was significantly better at improving CRF compared with SIT in overweight or obesity persons (MD = -0.92; 95% CI = -1.63 to -0.21; p = 0.01; I^2 = 10%) (Figure 3.3).

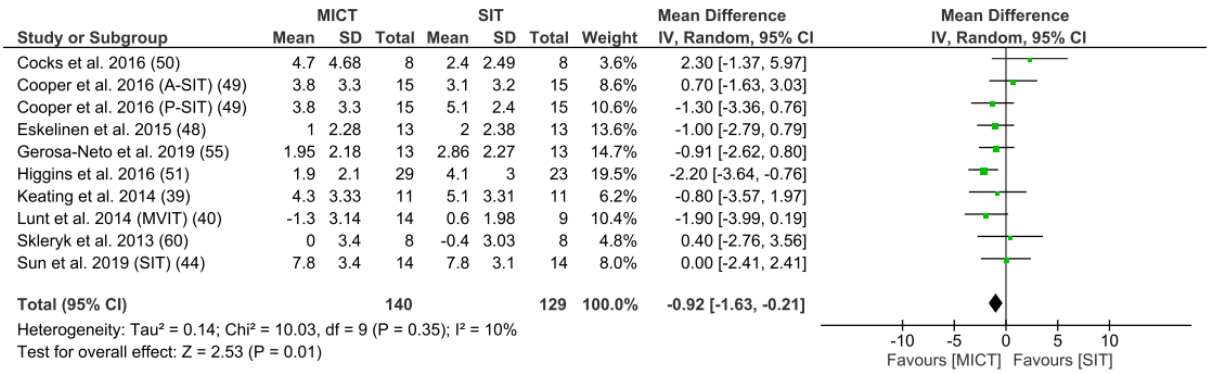

Figure 3.3 Forrest plot depicting changes in cardiorespiratory fitness [maximal oxygen consumption ($VO2_{max}$) and peak oxygen consumption ($VO2_{peak}$)] (MICT versus SIT unstandardised mean difference in ml/kg/min)

Fifteen studies reported body fat percentage as an outcome parameter (7, 37, 38, 40, 41, 43, 45-47, 52-54, 56, 57, 59). There was no significant difference in body fat percentage between MICT versus HIIT in overweight or obese persons (MD = 0.31; 95% CI = -0.13 to 0.75; p = 0.17; I^2 = 42%) (Figure 3.4).

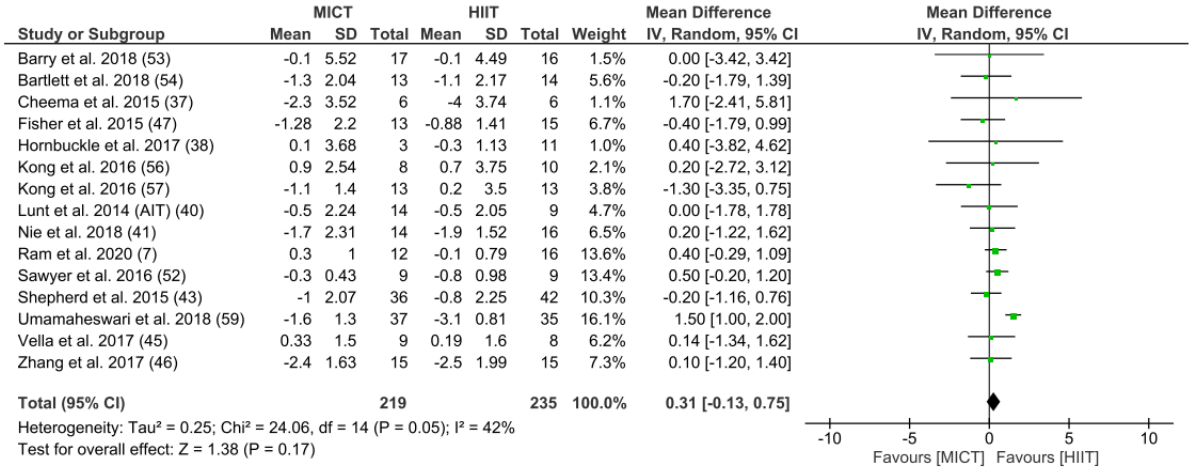

Figure 3.4 Forrest plot depicting changes in body fat percentage (MICT versus HIIT unstandardised mean difference in %)

Seven studies reported body fat percentage as an outcome parameter (39, 40, 48-51, 60). There was no significant difference in body fat percentage between MICT versus SIT in overweight or obese persons (MD = 0.26; 95% CI = -0.21 to 0.74; p = 0.28; I^2 = 33%) (Figure 3.5).

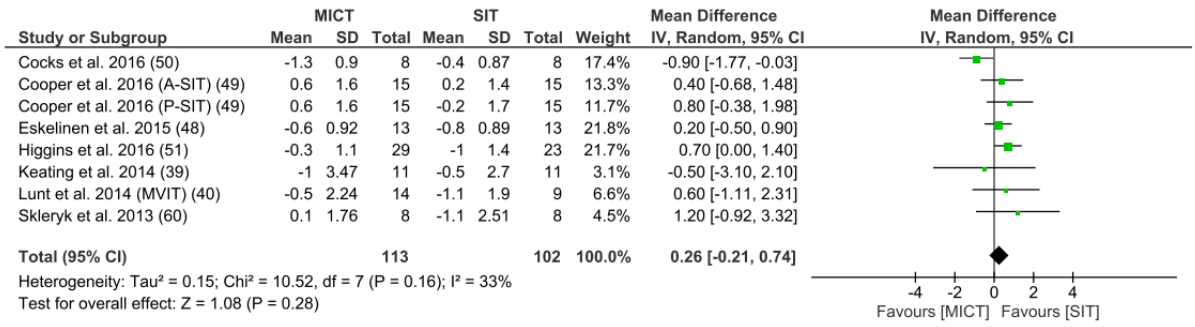

Figure 3.5 Forrest plot depicting changes in body fat percentage (MICT versus SIT unstandardised mean difference in %)

There was low heterogeneity across in changes in CRF (MICT versus HIIT and MICT versus SIT) and body fat percentage between (MICT versus SIT). However, there was moderate heterogeneity in body fat percentage changes between MICT and HIIT (Figure 3.6).

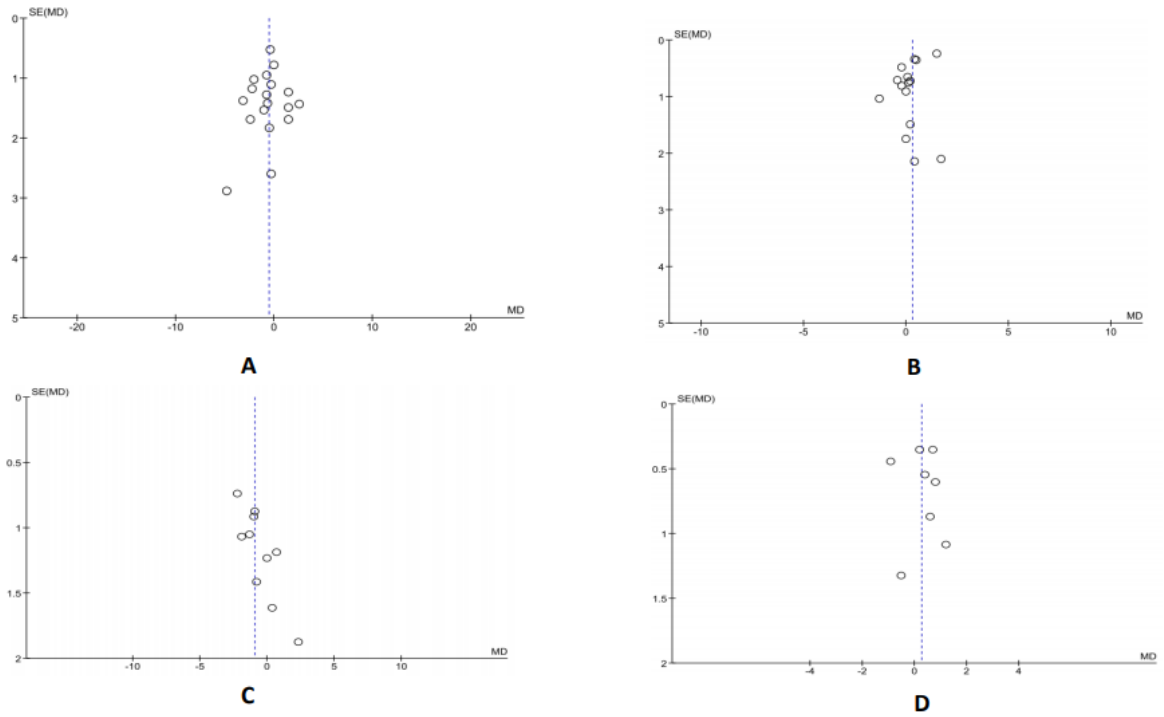

Figure 3.6 Funnel plots showing heterogeneity A: Cardiorespiratory fitness (MICT versus HIIT); B: Body fat percentage (MICT versus HIIT); C: Cardiorespiratory fitness (MICT versus SIT); D: Body fat percentage (MICT versus SIT)

3.5 Discussion

The primary finding of this meta-analysis suggests that MICT was significantly better at improving CRF ($VO2_{max}$) compared with SIT in overweight or obese persons. Low CRF is directly related to heart disease (61). Furthermore, 3.5 ml/kg/min improvement in maximal oxygen uptake was associated with a 15% reduction in the risk of CVDs (61). MICT increases the oxygen supply to active muscle tissues through mitochondrial biogenesis and oxidative enzymes, which improves preload and stroke volume (62). This improves CRF in overweight or obese persons. Moreover, MICT increases muscle metabolism and increased capillarisation and recruitment of slow-twitch muscle fibres, which are fatigue-resistant and increases the capacity of active muscles to efficiently uptake oxygen to sustain exercise (62). This favours the increase in CRF during MICT in overweight and obese persons.

The novel finding that MICT was superior to SIT at improving CRF differs from other studies (22, 24, 27, 63). A previous meta-analysis showed that high-intensity training (HIIT and SIT) and MICT resulted in a statistically significant improvement in $VO2_{max}$ (HIIT SMD: -0.966 and MICT SMD: -0.690) (27). However, the meta-analysis reported high heterogeneity and publication bias (27), which could have influenced the finding of the study. A meta-analysis of persons with obesity indicated that high-intensity training (HIIT and SIT) resulted in greater improvement of CRF compared with MICT (MD 1.83; 95% CI 0.70 to 2.96) (22). This finding must be interpreted with caution because the authors did not use the change from baseline, or the corresponding 95% CI or p-values of that change; the small sample sizes of the included studies could have resulted in bias and underpowered the studies to show a significant effect; the study reported variation heterogeneity in the assessment of outcomes, and; selection bias was evident (22).

Low-volume high-intensity training (HIIT and SIT) induced greater improvements in CRF than MICT in normal weight, overweight or obese persons (SMD: -0.175; 95% CI -0.318 to -0.031) (24). Paradoxically, a multicentred comparison study showed that high-volume HIIT had more responders to improved $VO2_{peak}$ compared to MICT and low-volume high-intensity training (HIIT and SIT) (63). However, this study reported several limitations, such as participants with and without NCD were included in the analysis, more men than women were analysed, the training status was not controlled, the age of participants varied considerably (18 to 81 years), and individual studies

included in the analysis did not control nutritional status, small sample size, medication use, adherence to the exercise interventions, sleep and smoking status (63). Furthermore, participants assigned to the MICT group exercised at higher intensities, and those assigned to the HIIT group did not meet the target exercise intensities (63). The rationale for the current systematic review's conflicting finding originates from the premise of high-intensity training. The aforementioned meta-analyses included studies with high-intensity training (SIT and HIIT) versus MICT and did not distinguish the true effect of HIIT versus MICT and SIT versus MICT in overweight and obese persons. Therefore, the authenticity of the result from the current review stems from the strict comparison of MICT versus SIT.

The risk of cardiometabolic diseases increases substantially due to excessive body fat in obesity, which causes insulin resistance, inflammation, endothelial dysfunction, coronary calcification and a sympathetic dominant state (64). The secondary finding was that there was no significant difference in reducing body fat percentage between MICT versus HIIT and MICT versus SIT. This finding is consistent with another systematic review and network meta-analysis, which reported no difference between the MICT and HIIT groups on body fat percentage, irrespective of the protocols being equalised or not (25). Furthermore, high-intensity training (MD = -1.26; 95% CI: -1.80 to -0.72) and MICT (MD = -1.48; 95% CI: -1.89 to -1.06) resulted in a comparable decrease in body fat percentage (19). Another meta-analysis revealed that inter-group HIIT and MICT resulted in statistically significant reductions in body fat percentage; however, no significant intra-group difference was observed in this meta-analysis (27). Low-volume HIIT had no significant effect on body fat percentage compared to MICT (SMD: -0.063, 95% CI -0.383 to 0.257) (24). Moreover, short-term HIIT and MICT show similar effectiveness across all body composition measures in overweight and obese persons (11). Contradictory to this finding, another meta-analysis reported that high-intensity training (HIIT and SIT) resulted in a greater significant reduction in body fat percentage compared with MICT in persons with obesity (65, 66) (MD -1.69; 95% CI -3.10 to -0.27) (22). However, this result should be interpreted with caution because the study used post-test scores and not change scores (22). Exercise intensity, frequency and volume are not independent factors reducing body fat percentage and the risk of obesity but are reliant on hormonal, psychological, diet, environmental, behavioural, energy expenditure and lifestyle factors (64). Due to the complexity of the factors contributing to obesity, the current study and other systematic reviews and meta-

analyses showed an insignificant superiority of MICT versus HIIT and MICT versus SIT in body fat percentage. It is plausible that there are limitations of the study that could have influenced the results obtained in this review. The first is the small sample size observed in the included studies, which could have overestimated or underestimated the outcome variables. The second is that there were not enough randomised SIT programmes compared to HIIT in overweight or obese persons. Third, English-only publications were included in the study. Lastly, CRF has a strong genetic influence (67); thus, future studies are encouraged to investigate responders and non-responders to exercise.

3.6 Future directions

Research in the future should address the following gaps in the literature:

1. The effect of a single bout of elevated exercise intensity, and at different times of the day, on cardiometabolic risk in overweight or obese persons;
2. The effect of this intervention on cardio-metabolic risk factors, physical fitness parameters (not only $VO2_{max}$) and inflammatory markers;
3. Comparison of this time-efficient protocol on repeated high-intensity training at a single point in time and continuous moderate-intensity exercise on cardio-metabolic risk factors, physical fitness parameters and inflammatory markers; and
4. Future studies are encouraged to investigate responders and non-responders to exercise in overweight or obese persons.

3.7 Conclusions

MICT was significantly better at improving CRF ($VO2_{max}$) than SIT in overweight or obese persons. The finding warrants clinicians, exercise physiologists and health care providers to prescribe MICT to improve CRF in overweight or obese persons. Furthermore, there was no significant difference between MICT versus HIIT on CRF. There was no significant difference in body fat percentage between MICT versus HIIT and MICT versus SIT in overweight or obese persons.

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Chapter 4 The association between cardiorespiratory fitness measurements, cardiometabolic risk factors and Inflammatory markers in overweight or obese persons

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4.1 Abstract

Objective: To investigate the association between cardiorespiratory fitness (CRF) measurements, cardiometabolic risk factors and inflammatory markers in overweight or obese persons.

Methods: The study adopted a cross-sectional design. Eighty-two participants from the university participated in the study. The outcome measurements were inflammatory markers, CRF measurements, cardiometabolic risk factors and the Framingham risk score.

Results: Multiple linear regression showed that peak oxygen consumption was inversely related to age (β = -0.007, p = 0.048). There was a moderate, negative correlation between glycated haemoglobin (HbA1c) and load at ventilatory threshold (VT-L) (Rs = -0.441, p<0.001). Moreover, there was a positive correlation between erythrocyte sedimentary rate and body fat percentage (Rs = 0.438, p<0.001). VT-L was significantly inversely related to HbA1c (β = -0.089, p = 0.001). For every one-unit increase in the VT-L, the HbA1c variable decreased by 9.31%.

Conclusion: Knowledge of correlates related to CRF will encourage targeted interventions to improve cardiorespiratory health of overweight or obese persons. An increase in VT-L reduces HbA1c, which decreases the risk of microvascular disease.

Keywords: obesity; cardiorespiratory fitness; inflammation; health; cardiometabolic disease

4.2 Introduction

Chronic low-grade inflammation, autophagy and oxidative stress initiate the vicious cycle of NCD (1). Chronic low-grade inflammation is a state of elevated IL-6, TNF and hs-CRP for a prolonged period (2). This state is positively correlated with disease severity (3). Visceral abdominal fat is a crucial contributor to chronic inflammation, which increases the risk of insulin resistance and type 2 diabetes (4). A significant increase in visceral and abdominal fat mass results in lower levels of adiponectin and increases levels of pro-inflammatory adipokines and IL-6 (5-8). Furthermore, the increase in free fatty acids in circulation alters insulin signalling pathways, known as lipotoxicity (9, 10). Lipotoxicity, physical inactivity and an unhealthy diet reduce CRF (11).

CRF is the efficiency of the respiratory system to oxygenate blood at the cellular level and the circulatory system to supply the oxygenated blood to active muscles aimed at sustaining exercise or physical activity (12, 13). CRF is the strongest predictor of reduced mortality and CVD in apparently healthy persons and persons with non-communicable conditions (14, 15). The gold standard to measure CRF is $VO2_{peak}$, and it is a crucial indicator of exercise tolerance (16). The determinates of $VO2_{peak}$ are oxygen availability, gas exchange of oxygen and carbon dioxide across the alveolar barrier, the strength of the respiratory muscles, the carrying capacity of oxygen to active skeletal muscles and the optimal extraction and utilisation of oxygen in skeletal muscles (17, 18). A recent meta-analysis showed that an increase in one metabolic equivalent (3.5 $mL.kg^{-1}.min^{-1}$) was associated with an 8% reduction in the risk of type 2 diabetes mellitus (19). Moreover, persons with a fitness level of more than five metabolic equivalents had a significantly decreased risk of mortality (35% - 55%), compared to persons with lower fitness levels (20).

Obesity has a strong association with NCD (21, 22). Low CRF and android obesity are associated with type 2 diabetes mellitus (11, 23), CVD (24), dementia (25), depression (26) and cancer (27). In recent years, global epidemiological research on risk factors associated with NCD has become popular (28-30). However, studies investigating CRF variables, cardiometabolic risk factors and inflammatory markers as essential variables related to CVD risk are scarce in the South African context, especially in overweight or obese persons. Therefore, the current study will investigate the

association between CRF measurements, cardiometabolic risk factors and inflammatory markers in overweight or obese persons.

4.3 Methods

4.3.1 Design of the study

A cross-sectional study was adopted to investigate the association between CRF measurements, cardiometabolic risk factors and inflammatory markers in overweight or obese persons.

4.3.2 Population/unit of analysis and sampling strategy

The prevalence of CVD peaks at early adulthood in Africa (40-49 years) (31). Therefore, the study included sedentary participants aged 30 to 49 years who did not undergo any cardiovascular and musculoskeletal surgery within the preceding six months and not taking chronic medication. Participants from the university were invited to participate in the study. Eighty-two participants qualified to participate after the implementation of the inclusion and exclusion criteria.

4.3.3 Procedure

The participants signed an informed consent document before the primary researcher conducted the initial screening to determine eligibility to be study participants based on the study's inclusion criteria. A physician medically cleared the eligible participants to participate in the study. After that, a phlebotomist drew venous blood to measure inflammatory markers, and the researcher measured lipid and glucose with a point-of-care device, body composition and CRF. The Framingham risk score (FRS) was calculated using the Medscape online calculator.

4.3.3.1 Metabolic markers

The participants underwent an eight-hour fast before the researcher measured fasting TG, TC, HDL, LDL and LDL/HDL using the CardioChek® PA meter (Polymer Technology Systems, Indianapolis, United States of America). The CardioChek®PA has 62.7% sensitivity, 76.1% specificity and a 76.4% positive predictive value for TC (32). Fasting random glucose and glycated haemoglobin (HbA1c) were measured using the Accutrend GCT machine (Roche Diagnostics, Mannheim, Germany) and the A1CNow®+ (Polymer Technology Systems, Indianapolis, United States of America), respectively. A reputable laboratory (AMPATH) measured IL-6, hs-CRP and erythrocyte sedimentation rate (ESR) following standard procedures.

4.3.3.2 Body composition

The International Standards for Anthropometric Assessment (ISAK) guidelines were used to measure body composition (33). Height, body mass, BMI, WC, hip circumference and body fat percentage were measured using the ISAK guidelines (33).

4.3.3.3 Framingham risk score

The FRS is a valid score used to predict the long-term risk of coronary arterial disease over ten years (34). The score is calculated based on coronary risk factors, such as gender, age, TC, high-density lipoproteins, smoking habits and systolic blood pressure (SBP) (35). The Medscape online calculator was used to calculate the ten-year CVD risk profile of the sample. The equation factored in the following outcome measurements: HDL-C, TC, gender, blood pressure, age, smoking history and history of chronic diseases. The classification of the FRS is as follows: low risk < 10%, intermediate risk = 10-20% and high risk > 20% (35).

4.3.3.4 Cardiorespiratory fitness

CRF was measured using a graded cardiorespiratory submaximal test. The Wattbike® (Wattbike Pro, Woodway, Germany) and the automated laboratory cardiopulmonary metabolic cart (Cosmed K4 b^2, Rome, Italy) were used to conduct the test and measure CRF, respectively. The test entailed participants cycling at 55W for one minute, after which the power was increased by 15W/min. The participants had to maintain the incremental target power increase per minute until the submaximal HR target was achieved. The test was terminated at 85% of age-predicated maximal heart rate (HR_{max}) or if participants voluntary stopped or signs and symptoms of CVD presented or abnormal haemodynamic responses were observed (36). Oxygen uptake was determined continuously on the automated laboratory cardiopulmonary metabolic cart (Cosmed K4 b^2, Rome, Italy). $VO2_{peak}$ was obtained from the Cosmed machine using the Fick equation, and ventilatory threshold was measured using the V-slope method.

4.3.4 Ethics

Ethical clearance was obtained from the University of the Witwatersrand Human Research Ethics Committee (Medical) (M170239) and the Tshwane University of Technology Faculty Committee for Research Ethics (REC/2016/10/005). The study was ethically designed and implemented in accordance with the Declaration of Helsinki (last update: October 2008), which adhered to principles of confidentiality, privacy and anonymity.

4.3.5 Data analysis

Data were analysed using the Statistical Package for Social Science Version 23.0 (SPSS) for Windows® software. The normality of data was analysed using histograms, Q-Q plots, and the Kolmogorov-Smirnov and Shapiro-Wilk tests. Non-normally distributed variables were reported as median (first quartile to third quartile), and normally distributed variables were reported as mean (± standard deviation). Frequency tables were used to indicate the demographic profile and medical history of the participants. Spearman's rank correlation was used to determine the correlation between the outcome variables. Linear univariate regression was conducted to determine the variables that will be included in the multivariate regression model. Variables included in these univariate regression analyses were chosen based on evidence from the literature. After conducting the univariate linear regression analyses, variables with a p-value < 0.25 were included in the multivariate model (37). The reason for the reference value of 0.25 is that traditional levels of 0.05 failed to identify significant variables that should have been included in the multivariate analyses (38, 39). Linear multivariate regression was conducted to determine the association of CRF, inflammatory and cardiometabolic variables. The dependant variable was CRF. The continuous dependent variable that had a skewed distribution was log-transformed to normality before being used in the multivariate regression analyses. The level of significance was set at $p<0.05$.

4.4 Results

There was a high representation of women (83%) compared to men (17%) in the study, and the majority of the participants had completed secondary schooling (82%). Participants reported experiencing symptoms of frequent cramps in the leg (23%) and migraines or recurrent headaches (25%). Participants indicated a family history of hypertension (45%), diabetes mellitus (31%) and leukaemia or cancer under the age of 60 years (13%). The participants reported undesirable lifestyle behaviours, such as cigarette smoking (12%), alcohol consumption (49%), the use of extra sugar (30%) and table salt (58%) (Table 4.1).

Table 4.1 Demographic profile and reported medical history (n = 83)

Variable	N	%
1.1 Gender		
Male	14	16.9
Female	69	83.1
1.2 Education		
Grade school	1	1.2
Junior high school	1	1.2
High school	68	81.9
College (1-3 years)	7	8.4
Post-graduate school (≥ 4 years)	6	7.2
1.3 Frequent cramps in your leg		
Yes	19	22.9
No	64	77.1
1.4 Migraines or recurrent headaches		
Yes	21	25.3
No	62	74.7
1.5 Family history of high blood pressure		
Yes	37	44.6
No	46	55.4
1.6 Family history of diabetes		
Yes	26	31.3
No	57	68.7
1.7 Family history of leukaemia or cancer under age 60 years		
Yes	11	13.3
No	72	86.7
1.8 Cigarette, pipe or cigar smoking		
Yes	10	12.0
No	73	88.0
1.9 Alcohol consumption		
Yes	41	49.4
No	42	50.6
1.10 Extra sugar use		
Yes	25	30.1
No	57	68.7
1.11 Extra salt use		
Yes	48	57.8
No	34	41.0
1.12 Eat differently on weekends as compared to weekdays		
Yes	63	75.9
No	19	22.9

Observed values are expressed as N, the number of participants; %, percentage.

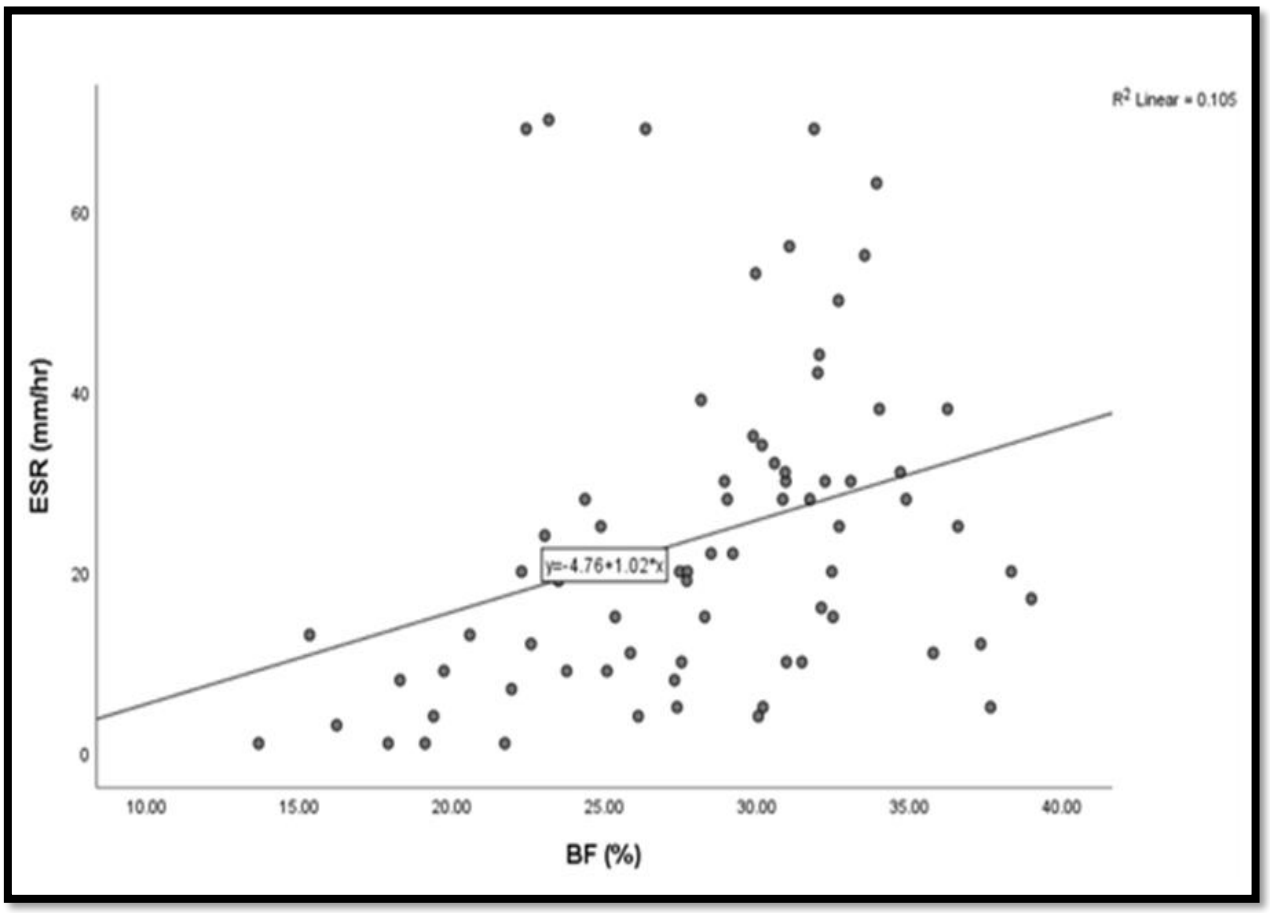
The median age of participants was 38 years (IQR 32-43 years). The average number of participants had elevated ESR (M = 23.69±18.70 mm/hr). Furthermore, the participants had low CRF and FRS (Table 4.2).

Table 4.2 Descriptive statistics for the outcome variables

Variable	N	Mean or median
Age (years)	77	37.00 (32.00-42.50)
SBP (mmHg)	74	113.85 (±14.32)
DBP (mmHg)	74	80.77 (±9.60)
HR (bpm)	74	77.92 (±10.10)
Height (m)	72	1.63 (±0,08)
We (kg)	72	81.40 (69.70-92.75)
BMI (kg/m^2)	72	30.94 (26.88-35.18)
WC (cm)	72	95.00 (82.25-100.00)
HC (cm)	72	110.00 (110.00-120.75)
WtHR	72	0.82 (0.78-0.88)
BF (%)	72	28.26 (±5.79)
TC (mmol/L)	77	3.95 (3.40-4.74)
HDL-C (mmol/L)	77	1.29 (±0.32)
LDL-C (mmol/L)	69	2.26 (±0.81)
TG (mmol/L)	77	1.14 (1.14-1.78)
TC/HDL	75	3.10 (2.70-3.90)
LDL-C/HDL-C	69	1.60 (1.30-2.30)
Non-HDL-C (mmol/L)	75	2.87 (±0.88)
FGB (mmol/L)	77	5.05 (±0.59)
HbA1c (%)	76	5.92 (±0.42)
ESR (mm/hr)	76	23.69 (±18.70)
HsCRP (mg/l)	75	3.30 (1.90-8.60)
IL-6 (pg/ml)	76	3.80 (1.80-7.63)
VT-L (W)	63	55.00 (55.00-70.00)
$VO2_{peak}$ (mL/min/kg)	65	10.70 (8.76-14.10)
FRS (%)	74	0.96 (0.62-1.58)

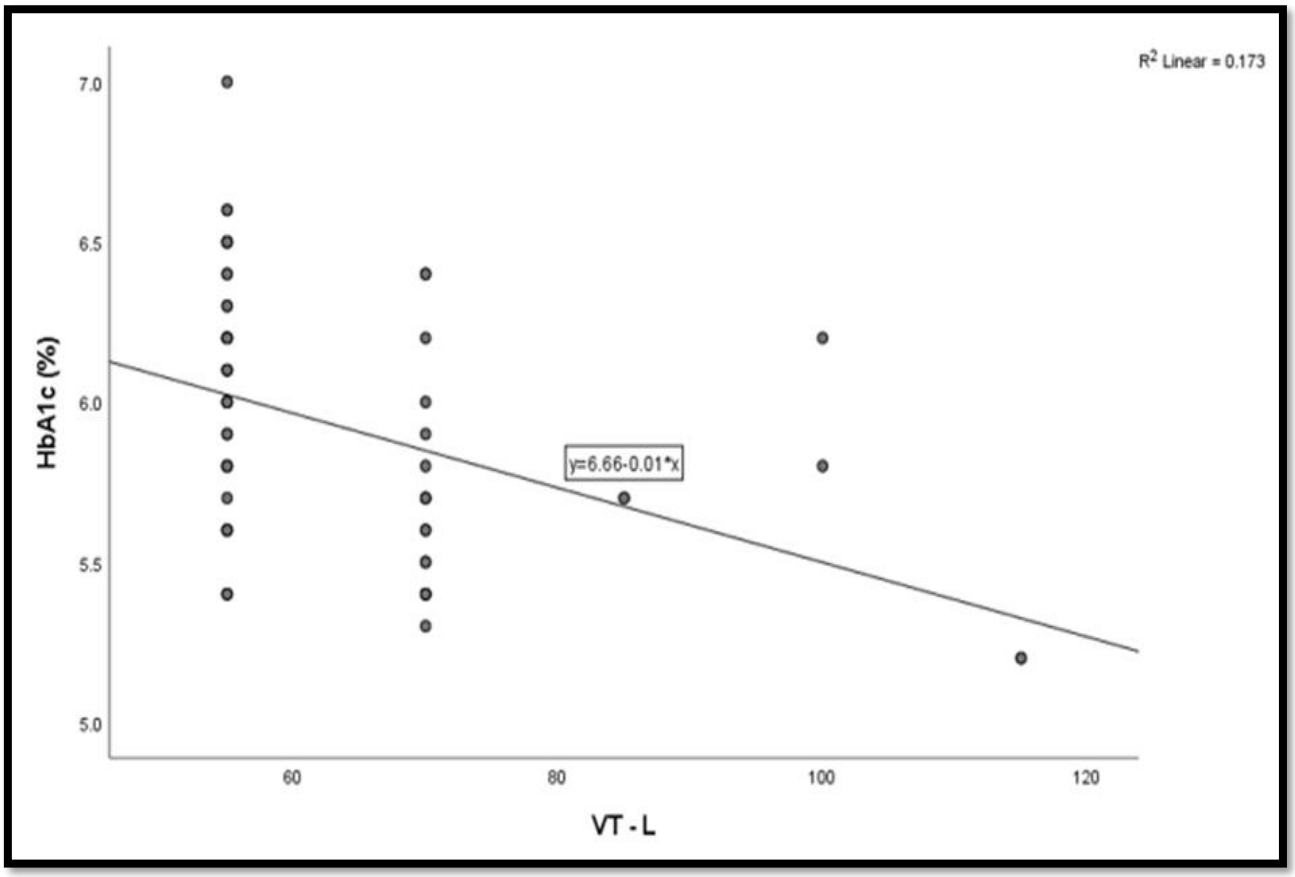
Observed values are expressed as N, number of participants; Mean (± standard deviation), Median (interquartile range); SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; We, body mass; BMI, body mass index; WC, waist circumference; HC, hip circumference; WtHR, waist-to-hip ratio; BF (%), body fat percentage; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglycerides; FG, fasting glucose; HbA1c, glycated haemoglobin; ESR, erythrocyte sedimentation rate; hs-CRP, high-sensitivity C-reactive protein; IL-6, interleukin-6; VT-L, load at ventilatory threshold; $VO2_{peak}$, peak oxygen consumption; FRS, Framingham risk score.

A Spearman's correlation was used to determine the association between all cardiorespiratory, cardiometabolic and inflammatory variables. A positive, significant moderate correlation was only observed for ESR and body fat percentage (R_s = 0.438, n = 72, p<0.001) (Figure 4.1), and a negative, significant moderate correlation was only observed for glycated haemoglobin and load corresponding to ventilatory threshold (R_s = -0.441, n = 63, p<0.001) (Figure 4.2).



ESR, erythrocyte sedimentation rate; BF (%), body fat percentage

Figure 4.1 Scatter plot depicting the relationship between erythrocyte sedimentation rate and body fat percentage



HbA1c, glycated haemoglobin; VT-L, load at ventilatory threshold

Figure 4.2 Scatter plot depicting the relationship between glycated haemoglobin and corresponding load at ventilatory threshold

The results of univariate linear regression analyses for each of the cardiometabolic variables and inflammatory markers against $VO2_{peak}$ and load corresponding to ventilatory threshold are shown in Table 4.3. After conducting the univariate linear regression, the following variables were included as independent variables in the multiple regression model ($p<0.25$): Age, SBP, BMI, WC, body fat percentage, HDL-C, HbA1c and ESR (Table 4.3) against $VO2_{peak}$; and SBP, BMI, body fat percentage, HbA1c, ESR and FRS against load at ventilatory threshold (VT-L).

Table 4.3 Univariate regression analyses of peak oxygen consumption and load at ventilatory threshold with study variables

Variable	VO_{2peak}		VT-L	
	standardised β	p-value	standardised β	p-value
Age (years)	-0.350	0.004	-0.009	0.945
SBP (mmHg)	0.170	0.175	0.309	0.014
We (Kg)	-0.150	0.234	-0.068	0.596
BMI (kg/m^2)	-0.289	0.020	-0.196	0.123
WC (cm)	-0.179	0.154	-0.082	0.534
BF (%)	-0.366	0.003	-0.245	0.053
TC (mmol/L)	0.023	0.855	0.100	0.436
HDL (mmol/L)	-0.215	0.086	-0.097	0.450
LDL (mmol/L)	0.056	0.676	0.103	0.449
HbA1c (%)	-0.287	0.020	-0.429	0.000
ESR (mm/hr)	-0.329	0.007	-0.173	0.175
HsCRP (mg/l)	0.021	0.867	0.021	0.868
IL-6 (pg/ml)	-0.028	0.824	-0.153	0.232
FRS (%)	0.130	0.301	0.236	0.063

Observed values are expressed as a standardised β, standardised beta coefficient; p-value, probability value; $VO2_{peak}$, peak oxygen consumption; VT-L, load at ventilatory threshold; SBP, systolic blood pressure; We, body mass; BMI, body mass index; WC, waist circumference; BF (%), body fat percentage; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; HbA1c, glycated haemoglobin; ESR, erythrocyte sedimentation rate; hs-CRP, high-sensitivity C-reactive protein; IL-6, interleukin-6; FRS, Framingham risk score.

Multiple linear regression showed that $VO2_{peak}$ was inversely related to age (β = -0.007, p = 0.048) (Table 4.4). Furthermore, BMI (β = -0.005, p = 0.343), body fat percentage (β = -0.003, p = 0.557), HDL-C (β = -0.066, p = 0.283), glycated haemoglobin (β = - 0.055, p = 0.268) and ESR (β = -0.001, p = 0.234) were negatively associated with $VO2_{peak}$; however, the probability value for the associations was insignificant (p>0.05) (Table 4.4). There was a positive insignificant association between CRF and SBP (β = 0.002, p = 0.128) and WC (β = 0.000, p = 0.876). The model explains 32.5% of variance (Table 4.4).

Multiple linear regression showed that VT-L is significantly related to SBP (β = 0.002, p<0.039) and glycated haemoglobin (β = -0.089, p = 0.001) (Table 4.5). For every one-unit increase in the VT-L, the SBP increases by 0.20%, and for every one-unit increase

in the VT-L, the glycated haemoglobin variable decreases by 9.31%. The model explains 32.3% of variance (Table 4.5).

Table 4.4 Multiple regression analysis for isolating principal determinants of peak oxygen consumption

Dependent variable	Independent variables	β-coefficient (se)	Lower 95% CI for β	Upper 95% CI for β	p-value	R squared
$VO2_{peak}$ (mL/kg/min)	Age (years)	-0.007 (0.003)	-0.014	0.000	0.048	0.325
	SBP (mmHg)	0.002 (0.001)	-0.001	0.005	0.128	
	BMI (kg/m^2)	-0.005 (0.005)	-0.016	0.006	0.343	
	WC (cm)	0.000 (0.002)	-0.004	0.005	0.876	
	BF (%)	-0.003 (0.004)	-0.011	0.006	0.557	
	HDL-C (mmol/L)	-0.066 (0.061)	-0.188	0.056	0.283	
	HbA1c (%)	-0.055 (0.049)	-0.153	0.043	0.268	
	ESR (mmhr)	-0.001 (0.001)	-0.003	0.001	0.234	

Observed values are expressed as β-coefficient (se), beta coefficient(standard error); lower 95% CI for β, lower confidence interval for beta; upper 95% CI for β, upper confidence interval for beta; p-value, probability value; R squared, R squared for the full model; $VO2_{peak}$, log-transformed peak oxygen consumption; SBP, systolic blood pressure; BMI, body mass index; WC, waist circumference; BF (%), body fat percentage; HDL-C, high-density lipoprotein cholesterol; HbA1c, glycated haemoglobin; ESR, erythrocyte sedimentation rate

Table 4.5 Multiple regression analysis for isolating principal determinants of load at ventilatory threshold

Dependent variable	Independent variables	β-coefficient (se)	Lower 95% CI for β	Upper 95% CI for β	p-value	R squared
VT-L (W)	SBP (mmHg)	0.002 (0.001)	0.000	0.004	0.039	0.323
	BMI (kg/m^2)	-0.001 (0.002)	-0.005	0.003	0.640	
	BF (%)	-0.001 (0.002)	-0.005	0.004	0.790	
	HbA1c (%)	-0.089 (0.025)	-0.139	-0.040	0.001	
	ESR (mmhr)	-0.000 (0.001)	-0.001	0.001	0.810	
	FRS	0.005 (0.012)	-0.019	0.029	0.678	

Observed values are expressed as β-Coefficient (se), beta coefficient(standard error); lower 95% CI for β, lower confidence interval for beta; upper 95% CI for β, upper confidence interval for beta; p-value, probability value; R squared, R squared for the full model; VT-L, load at ventilatory threshold; SBP, systolic blood pressure; BMI, body mass index; BF (%), body fat percentage; HbA1c, glycated haemoglobin; ESR, erythrocyte sedimentation rate; FRS, Framingham risk score

4.5 Discussion

The study highlights that there was a moderate, negative correlation between HbA1c and VT-L; moreover, there was a positive correlation between ESR and body fat percentage. The second finding was that CRF was significantly inversely related to age; furthermore, BMI, body fat percentage, HDL-C, HbA1c and ESR were negatively associated with CRF. However, the probability value for the associations was insignificant. Lastly, the excessive intake of alcohol, sucrose and salt reported by participants increases the risk of CVD. Therefore, one negative lifestyle behaviour induces several physiological processes, compounded by other negative lifestyle behaviours, which reduces the quality of life and requires professional multidisciplinary practices (40, 41).

Inflammation is required for the repair of tissues; however, tissue damage results if homeostasis is not maintained and chronic inflammation ensues (42). Chronic inflammation causes diabetic kidney disease (43), insulin resistance (44) and CVD (45). Furthermore, visceral abdominal fat is a crucial contributor to chronic inflammation, which increases the risk of insulin resistance and type 2 diabetes mellitus (4). ESR is a laboratory measurement of systemic inflammation, and an increase in this inflammatory marker is observed in patients with congestive heart failure, chronic kidney disease, malignancy, autoimmune disease, heart disease and communicable infections. A recent study indicated that several cytokines are correlated with BMI, HbA1c and lipids in African American women (4). The unique finding of the current study is that ESR directly correlates with body fat percentage. Therefore, ESR and body fat percentage measurements are vital physiological measurements in the screening of persons at risk of cardiometabolic diseases and infectious diseases.

Anaerobic threshold is a compensatory exercise point below which there is an increase in respiratory compensation (a disproportionate rise in expired carbon dioxide with oxygen uptake) and metabolic acidosis (46). This physiological measurement is an essential indicator of exercise prescription (47, 48). Anaerobic threshold is synonymous to ventilatory threshold (increase in ventilation equivalent and carbon dioxide in the blood), lactate threshold (increase in lactate, carbon dioxide and hydrogen ions) and glucose threshold (increase in glucose used due to the increase in glycogenolysis and the inhibition of insulin secretion) (49). The current study measured this point using the V-slope method (50); the normative value of oxygen consumption

at the anaerobic threshold is 40% of $VO2_{max}$ (50). HbA1c is a reliable measurement of blood glucose control (51). It is reported that a 1% reduction in HbA1c is directly related to a 37% reduction in microvascular complications (52). The current study showed that for every one-unit increase in the VT-L, the glycated haemoglobin variable decreases by 9.31%. Therefore, VT-L is an important measurement to be considered when prescribing exercise intensity in overweight or obese persons, especially persons with microvascular conditions. Moreover, VT-L is a measure of CRF.

CRF is a vital physiological measurement associated with desirable health outcomes and well-being (53). CRF is the efficiency of the heart, lungs and blood vessels to supply active tissues with oxygenated blood to sustain moderate-vigorous exercise (53). Low CRF has devastating consequences on health and overall wellbeing. Low CRF is a strong predictor of cancer and general mortality (54), metabolic syndrome (55) and depression (56). The study showed that CRF was significantly inversely related to age; furthermore, BMI, body fat percentage, HDL-C, HbA1c and ESR were negatively associated with CRF. However, the probability value for the associations did not reach statistical significance. The finding concurs with a recent systematic review, which indicated a negative association of CRF with weight, BMI, body fat, WC, DBP and hs-CRP (53). The current study adds HbA1c and ESR to the list of known negative correlates, which will encourage target interventions to improve cardiovascular health and screening in overweight and obese persons.

4.6 Conclusions

The primary findings of the study were that there was a moderate, negative correlation between HbA1c and VT-L. Moreover, there was a positive correlation between ESR and body fat percentage. The second finding was that CRF was significantly inversely related to age; furthermore, BMI, body fat percentage, HDL-C, HbA1c and ESR were negatively associated with CRF. However, the probability value for the associations was insignificant. Knowledge of correlates of CRF will encourage pro-active screening and targeted interventions to improve cardiorespiratory health of overweight or obese sedentary persons.

4.7 Acknowledgements

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4.8 Contributors

NR was the primary researcher. All authors were involved in the study design and review process.

4.9 Funding

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4.10 Competing interests

None declared.

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Chapter 5 Effect of the 90-second 'Gear' exercise programme on cardiometabolic risk factors in persons with an elevated risk of cardiovascular disease

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5.1 Abstract

Background: High-intensity interval training (HIIT) has recently gained popularity in improving cardiometabolic health. However, a close investigation of HIIT reveals that the exercise duration is similar to moderate-intensity continuous exercise.

Objective: To compare the effect of the time-efficient 'Gear' exercise programmes to traditional exercise on cardiometabolic risk factors in persons with an elevated risk of cardiovascular disease.

Methods: The study implemented a six-week, randomised controlled trial. The variables were low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglycerides (TG), total cholesterol, glycated haemoglobin (HbA1c), blood pressure and body composition. Forty-eight participants completed the study. Participants were randomly assigned to either the 'Gear' exercise programme repeated at different times during the day (GEP-DT): cycled for 90 seconds, repeated three times per day, for three days per week (n = 12); the 'Gear' exercise programme repeated at one point in time (GEP-OT): cycled for 90 seconds followed by four minutes and 30 seconds rest, repeated three times at one point in time, for three days per week (n = 14); 30 minutes of moderate-intensity continuous cycling repeated three days per week at 55-69% HR_{max} (n = 11); and the controls, who were encouraged not to exercise (n = 11).

Results: The 90-second GEP-DT intervention reduced HbA1c post six-weeks of training (MD = −0.1±0.4, % Δ = −1.3%, d = -−0.70). The GEP-OT group decreased blood TG with a large effect size (MD = −0.6±1.3, % Δ = −31.9%, d = −0.83).

Conclusions: The novel 90-second 'Gear' exercise programme moderately reduced HbA1c, and the 18-minute GEP-OT lowered blood TG. 'Gear' exercise programmes will encourage future research in persons with NCD. It should be considered as a public health initiative to promote exercise in clinical, home and work environments.

Keywords: lipids, glycaemia, health promotion, cardiovascular health, public health

5.2 Introduction

CVD is the leading cause of mortality worldwide. Sedentary behaviour alters metabolic and cardiovascular biomarkers and increases the risk of cardiometabolic diseases (1). Exercise is a critical factor to improve cardiometabolic health. Health benefits are associated with following at least 150 minutes of moderate physical activity or 75 minutes of vigorous physical activity per week (2). Furthermore, the prevention of weight gain is prominent when physical activity is performed at a minimum of three metabolic equivalents for more than 150 minutes per week (3). However, the optimal duration and intensity of exercise required to improve cardiometabolic health warrants further investigation in the current times of limited time and escalating work and family commitments.

HIIT has recently gained popularity as a time-efficient exercise intervention aimed at improving cardiometabolic health in different population groups. A randomised controlled trial reported that HIIT (nine by four-minute intervals at ~90% $VO2_{peak}$ with three minutes rest) was superior at improving insulin sensitivity compared with MICE in overweight women (4). A contemporary meta-analysis showed that HIIT provided similar benefits to those undertaking MICE for improving body composition and TC in overweight or obese adults (5). Thus, research seems inconsistent concerning the optimal duration, intensity and type of exercise aimed at improving cardiometabolic health in overweight or obese adults.

A meta-review of 33 systematic reviews reported that HIIT improved some inflammatory markers, cardiac and vascular functions, blood glucose, glycaemic control, CRF, HR, weight and body fat percentage variables (6). However, traditional HIIT with repeated sprints may result in undue stress on the cardiovascular system (7). A close investigation of HIIT reveals that it is not a time-efficient intervention considering the repeated high-intensity bouts followed by rest intervals during the exercise session (8). A brief bout of exercise during different periods of the day will drastically minimise the time commitment of training (8).

Mind-body exercise interventions improve general mental and physical health due to the direct influence of the nervous system on immune and endocrine functions (9). The ‘Gear’ exercise programme uses visualisation to enable participants to cognitively construct the increase and decrease of gears in a car to represent an increase and

decrease in speed and intensity before and during the exercise session. The ‘Gear’ exercise programme is new, and this is the first study to test the principles of this exercise programme. Therefore, the current study aimed to investigate the effect of the novel ‘Gear’ exercise programme on cardiometabolic risk factors in persons with an elevated risk of CVD.

5.3 Methods

5.3.1 Design of the study

The study implemented a randomised controlled pre-test and post-test exercise intervention study design.

5.3.2 Ethics approval

The study was conducted in accordance with the Declaration of Helsinki. Ethical clearance was obtained from the University of the Witwatersrand’s Human Research Ethics Committee (Medical) (M170239) and the Tshwane University of Technology’s Research Ethics Committee (REC/2016/10/005). The University of the Witwatersrand’s Human Research Ethics Committee (Medical) required a sperate informed consent form for the control group and exercise groups.

5.3.3 Population/unit of analysis and sampling strategy

Staff from the university were invited to participate in the study voluntarily. Participants were screened using a questionnaire to ensure that they met the inclusion criteria of the study. Participants were included in the study if they were between 30 and 49 years old and had two or more risk factors for CVD, such as physical inactivity, were overweight or obese, and had elevated blood pressure and elevated lipid profile. The participants should not have had any signs and symptoms of CVD, such as chest pain, dyspnoea, syncope, orthopnoea, tachycardia, known heart murmurs and unusual fatigue with activities of daily living. A physician medically cleared the participants for participation in the study. Participants were randomly assigned to the following groups using the Fishbowl Draw Method: ‘Gear’ exercise programme repeated at different times during the day (GEP-DT): cycled for 90 seconds, repeated three times per day, for three days per week (n = 12); ‘Gear’ exercise programme repeated at one point in time (GEP-OT): cycled for 90 seconds followed by four minutes and 30 seconds rest, repeated three times at one point in time, for three days per week (n = 14); 30 minutes of moderate-intensity continuous cycling repeated three days per week at 55-69%

HR_{max} (n = 11); and the controls, who were encouraged not to exercise (n = 11). Few participants were unable to participate in the follow-up assessments due to work commitments, family responsibilities and orthopaedic injuries not related to the exercise interventions (Figure 5.1). Forty-eight participants completed the study (GEP-DT = 12; GEP-OT = 14; MICE = 11; CTRL = 11). The exercise programmes did not result in adverse events (Figure 5.1).

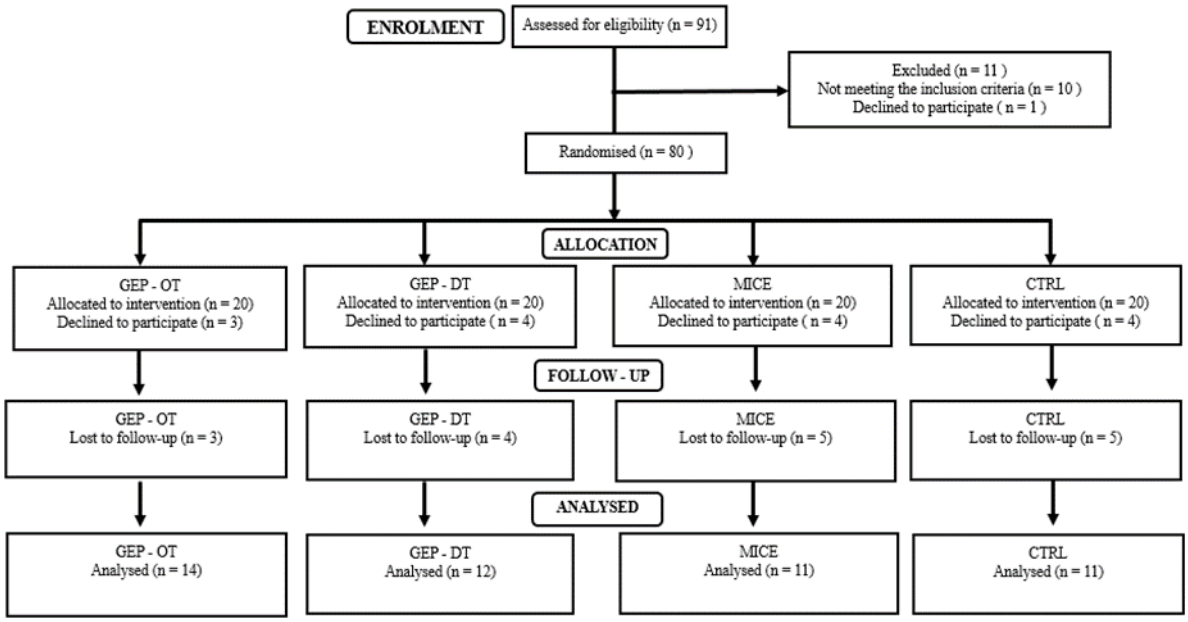

Figure 5.1 Consort diagram

GEP-OT: 'Gear' exercise programme repeated at one point in time; GEP-DT: 'Gear' exercise programme repeated at different times during the day; MICE, moderate-intensity continuous exercise; CTRL: control group

5.3.4 Procedure

5.3.4.1 Lipid profile

The fasting lipid profile was measured using the CardioChek® PA meter (Polymer Technology Systems, Indianapolis, United States of America). The test was conducted after the participants had adhered to an eight hour overnight fast and was performed according to standard manufacturer procedures. The A1CNow®+ (Polymer Technology Systems, Indianapolis, United States of America) was used to measure HbA1c using the standard manufacturer recommended procedure.

5.3.4.2 Blood pressure

An appropriately sized blood pressure cuff (Gold Series DS66 Trigger Aneroids, Welch Allyn, United States) was used on the non-dominant arm to measure blood pressure

using standardised techniques. Blood pressure was measured twice on the non-dominate arm, and the average measurement was documented.

5.3.4.3 Body composition

ISAK guidelines were used to measure height (Seca 213, Hamburg, Germany), body mass to the nearest 0.1 kg (Tanita digital scale, model HD-319, Tanita Corporation, Tokyo, Japan), BMI, skinfolds (Harpenden skinfold calliper, Baty International, West Sussex, United Kingdom), WC and HC.

5.3.4.4 Exercise programmes

Blood pressure and HR were documented before the commencement of the exercise session. The exercise session was conducted three times per week for six weeks on alternate days of the week. The mode of exercise was stationary cycling on a Wattbike® (Wattbike Pro, Woodway, Germany) with the air resistance set at one to facilitate cycling speed. Dietary and fluid intake was not controlled. The researcher (a biokineticist) supervised all exercise sessions. The new proposed GEP-DT and GEP-OT integrates and stimulates the function of the mind and body during the exercise session using visualisation. The GEP-DT commenced with a visualisation process. A car analogy was used to explain the exercise intervention. The participants were encouraged to visualise the increase and decrease of gears in a car to represent the increase and decrease of speed and intensity in the exercise intervention, respectively. The speed and intensity at the different gears were mentally constructed. The gears remained constant on the bike. The participants increased the gears mindfully, relevant to their perceived increase in speed and intensity, which was self-paced, enabling them to be in control of the exercise session.

Once the visualisation process was completed, the participants commenced the GEP-DT with a 30-second warmup (self-paced visualisation gear 2). Participants then increased the intensity gradually over 30 seconds using the visualisation technique (visualisation gear 3 for 10 seconds, visualisation gear 4 for 10 seconds and visualisation gear 5 for 10 seconds). After reaching a peak self-paced speed at visualisation gear 5, the participants reduced the speed by decreasing the intensity every 10 seconds for 30 seconds (visualisation gear 4 for 10 seconds, visualisation gear 3 for 10 seconds and visualisation gear 2 for 10 seconds). Hence, the participants geared up and geared down in a self-controlled manner, which acted as a stimulus for them to be mindful of the exercise session. The total duration of the GEP-DT per

session was 90 seconds. This exercise intervention was repeated three times a day, with a total time commitment of four minutes and 30 seconds per day (Figure 5.2). The GEP-OT was similar to the GEP-DT protocol; however, participants repeated three repetitions of the intervention at one point in time with a rest period of four minutes and 30 seconds per repetition. Therefore, the total duration of the GEP-OT was 18 minutes per session (Figure 5.2). Participants in the MICE group performed moderate-intensity continuous cycling for 30 minutes at 55–69% of HR_{max}. The participants in the CTRL did not exercise and continued with their daily administrative and household tasks, which were low-intensity activities (less than 3 metabolic equivalents) (Figure 5.2). A demonstration of the 'Gear' exercise programme can be viewed on the following link: https://www.youtube.com/watch?v=KAbkRg9ex94

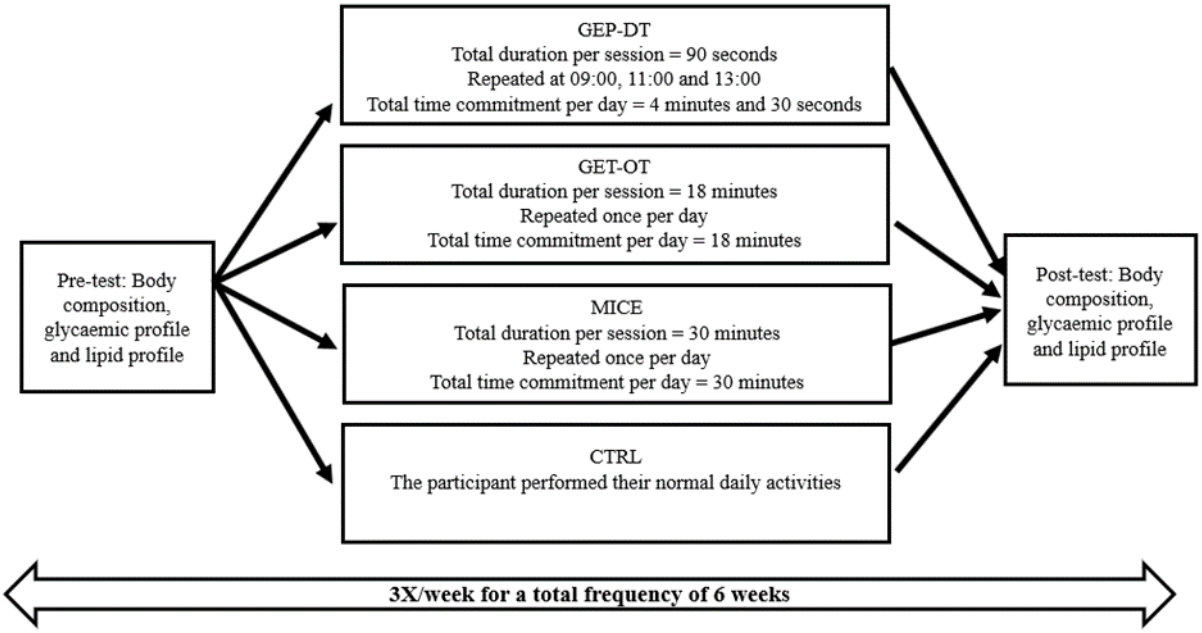

Figure 5.2 Exercise programmes

GEP-OT, 'Gear' exercise programme repeated at one point in time; GEP-DT, 'Gear' exercise programme repeated at different times during the day; MICE, moderate-intensity continuous exercise; CTRL, control group

5.3.5 Data analysis

Data were analysed using SPSS Statistics for Windows®, version 23.0 (SPSS Inc., Chicago, Ill., USA). The study was powered to detect between-group differences using G*Power version 3 (ten or more participants per group with an acquired physiological

effect size of 0.25 at α = 0.05). Normality of data was analysed using the Shapiro-Wilk test, histograms and Q-Q plots. Non-normal variables were log-transformed, and the variables were included in the analysis thereafter. Univariate analysis was conducted to determine baseline differences in age, fitness level and body weight between the subject groups. A paired-samples t-test was used to determine intra-group differences in the exercise interventions. The repeated measures analysis of variance (ANOVA) was used to compare intergroup differences. If interaction effects were observed, the Bonferroni post hoc test was used to compare treatment effects between the various groups. Effect size (d) was calculated to determine the clinical significance between the exercise groups and the CTRL. The effect size was classified according to small effect size (d ≥ 0.20), moderate effect size (d ≥ 0.5) and large effect size (d ≥ 0.8), respectively. The effect size was accepted as a true effect if the effect size confidence intervals did not cross both the positive and negative 0.20 thresholds. The effect size was considered to be unclear if this occurred. The level of significance was set at $p<0.05$.

5.4 Results

The mean age of participants in the training groups was GEP-OT = 37 years, GEP-DT = 39 years, MICE = 40 years and CTRL = 38 years. More women than men participated in the study. There was no significant difference in age, fitness level and body mass between the subject groups at baseline (Table 5.1). The GEP-DT group had the highest adherence rate (87%) and the shortest significant exercise time commitment of four minutes and 30 seconds compared with the GEP-OT (18 minutes) and MICE (30 minutes). There was a significant difference in kilocalories in all the exercise groups. The average kilocalorie expenditure in the MICE group was 16 times that of the GEP-DT. There was a significant difference in peak HR, average power, peak power, average power/body mass, peak power/body mass and cadence between the GEP-DT vs MICE and the GEP-OT vs MICE. The GEP-OT (129±13 bpm) had the highest peak exercise HR compared to MICE and GEP-DT. Moreover, the GEP-DT (110±9 bpm) had the highest average exercise HR compared to the other groups (Table 5.2).

Table 5.1 Demographic profile of the participants

Variable	GEP-OT (n=14)	GEP-DT (n=12)	MICE (n=11)	CTRL (n=11)	p-value
The ratio of women to men	11/3	12/0	8/3	9/2	N/A
Age (years)	37±5	39±7	40±6	38±5	0.68
Body mass (kg)	79.9±11.9	85.1±23.4	83.2±14.7	84.6±17.9	0.87
$VO2_{peak}$ ($mL \cdot min^{-1} \cdot kg^{-1}$)	11.7±3.8	11.7±3.5	12.3±4.1	10.1±3.3	0.56

Data are presented as mean±standard deviation; n, number; N/A, not applicable; GEP-OT, 'Gear' exercise programme at one point in time; GEP-DT, 'Gear' exercise programme repeated at different times during the day; MICE, moderate-intensity continuous exercise; CTRL, control group; $VO2_{peak}$, peak oxygen consumption; p-value, probability value

Table 5.2 Training data of participants in the exercise intervention groups

Training variables	GEP-OT	GEP-DT	MICE	p-value
Adherence (%)	82	87	77	N/A
Time commitment (minutes)	18	4.5	30	0.001*#&
Average heart rate (bpm)	108.7±9.62	110.2±8.67	109.4±5.00	0.24
Average heart rate (% of max heart rate)	60.1±5.37	60.7±4.39	60.6±3.09	0.35
Peak heart rate (bpm)	128.5±12.9	126.7±11.9	120.2±5.91	0.001*#
Peak heart rate (% of max heart rate)	71.0±7.39	69.8±6.31	66.6±3.12	0.001*#
Average power (W)	61.7±32.8	57.8±23.2	31.0±14.6	0.001*#
Peak power (W)	127.1±68.4	116.8±55.6	52.2±28.0	0.001*#
Average power/body mass (W/Kg)	0.76±0.37	0.76±0.55	0.38±0.20	0.001*#
Peak power/body mass (W/Kg)	1.58±0.80	1.54±0.88	0.62±0.29	0.001*#
Kilocalories (Kcal)	66.2±9.48	9.26±2.11	148.0±27.5	0.001*#&
Cadence (RPM)	56.5±13.1	53.7±7.99	43.5±9.76	0.001*#
Peak Cadence (RPM)	75.0±16.5	72.8±7.99	51.9±11.0	0.001*#

Data are presented as mean±standard deviation; %, percentage; bpm, beats per minute; W, watts; W/kg, watts/kilograms; Kcal, kilocalories; RPM, revolutions per minute; GEP-OT, 'Gear' exercise programme repeated at one point in time; GEP-DT, 'Gear' exercise programme repeated at different times during the day; MICE, moderate-intensity continuous exercise; NA, not applicable; p-value, probability value

* Significant difference between MICE vs GEP-DT ($p<0.01$)

Significant difference between MICE vs GEP-OT ($p<0.01$)

& Significant difference between GEP-OT vs GEP-DT ($p<0.01$)

There was a significant decrease in the mean DBP within the MICE group (p = 0.01). The SBP and body composition variables were insignificant with the subject groups (p>0.05) (Table 5.3). There was a significant increase in HbA1c within the MICE group (p = 0.01). The other metabolic variables showed insignificant differences within the subject groups (p>0.05) (Table 5.4).

The MICE group demonstrated a large effect size for DBP when compared to the CTRL group, which showed a true large meaningful reduction in DBP post-training (MD = -5.4±3.8, % Δ = -6.8%, d = -0.81, d (95% CI): -1.68, 0.06). This group demonstrated a large effect size for body fat percentage compared to the CTRL group, which showed a true large meaningful reduction in body fat percentage post-training (MD = -0.7±2.1, % Δ = -2.5, d = -0.83, d (95% CI): -1.70, 0.04) (Table 5.5). Although the MICE group showed a moderate effect size for body mass, BMI and TG the confidence intervals crossed the lower positive threshold (0.20); therefore, the effect is unclear for body mass, BMI and TG in the MICE group (Table 5.5 and 5.6)

The effect is unclear for body fat percentage and BMI in the GEP-DT group (Table 5.5). The 90-second GEP-DT intervention reduced HbA1c post six weeks of training with a moderate effect size compared to the CTRL group, which showed a true moderate meaningful reduction in HbA1c post-training (MD = -0.1±0.4, % Δ = -1.3%, d = -0.70, d (95% CI): -1.55, 0.14) (Table 5.6). This group demonstrated a large effect size for LDL-C/HDL-C, which showed a true large meaningful increase in LDL-C /HDL-C post-training (MD = 0.2±0.6, % Δ = 8.2, d = 0.89, d (95% CI): -0.05, 1.84) (Table 5.6).

The GEP-OT group demonstrated a decrease in TG post-training with a large effect size when compared to the CTRL group, which showed a true large, meaningful reduction in TG post-training (MD = -0.6±1.3, % Δ = -31.9%, d = -0.83, d (95% CI): -1.68, 0.01) (Table 5.6). Although the MICE group showed a moderate effect size for TG, the confidence intervals crossed the lower positive threshold (0.20); therefore, the effect is unclear for TG in the MICE group (Table 5.6).

Analysis of covariance showed no significant group x time interactions on blood pressure, body composition and metabolic markers post six weeks of exercise in persons with an elevated risk of CVD (p>0.05) (Tables 5.5 and 5.6).

Table 5.3 Intra-group comparisons of blood pressure and body composition measurements across the subject groups

Intra-group Analysis				
Variables	**GEP-OT**	**GEP-DT**	**MICE**	**CTRL**
SBP (mmHg)				
N	14	12	11	11
Pre-test (M±SD)	113.0±13.1	111.0±13.6	113.0±12.0	110.0±13.0
Post-test (M±SD)	110.9±11.5	108.0±8.30	108.7±12.3	105.2±10.5
p-value	0.38	0.37	0.16	0.07
DBP (mmHg)				
N	14	12	11	11
Pre-test (M±SD)	79.1±5.98	78.4±7.33	80.0±9.48	78.73±6.50
Post-test (M±SD)	77.3±7.91	78.0±6.38	74.6±9.59	77.36±6.86
p-value	0.34	0.84	**0.00$_a$**	0.46
BM (Kg)				
N	14	12	11	11
Pre-test (M±SD)	79.9±12.0	85.1±23.4	83.2±14.7	84.6±18.0
Post-test (M±SD)	80.2±11.6	85.6±23.8	83.2±14.2	85.5±18.4
p-value	0.68	0.31	1.00	0.20
BMI (Kg/m^2)				
N	14	12	11	11
Pre-test (M±SD)	29.5±4.71	32.2±9.80	31.0±5.44	31.3±5.09
Post-test (M±SD)	29.8±4.86	32.2±9.59	31.0±5.51	31.8±5.52
p-value	0.31	0.93	0.99	0.08
WC (cm)				
N	14	12	11	11
Pre-test (M±SD)	90.6±8.97	89.8±19.1	93.7±11.8	97.1±12.8
Post-test (M±SD)	88.4±9.39	91.3±14.4	91.5±10.4	95.3±10.9
p-value	0.12	0.57	0.28	0.23
BF (%)				
N	14	12	11	11
Pre-test (M±SD)	27.3±7.10	28.9±6.21	27.9±6.41	28.0±4.93
Post-test (M±SD)	27.7±6.37	28.7±5.48	27.2±5.57	29.3±6.65
p-value	0.65	0.78	0.28	0.14

Data are presented as mean±standard deviation; N, number of participants; p-value, the probability value within each subject group; a, Intra-group significance $p<0.05$; GEP-OT, 'Gear' exercise programme repeated at one point in time; GEP-DT, 'Gear' exercise programme repeated at different times during the day; MICE, moderate-intensity continuous exercise; CTRL, control group; SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; WC, waist circumference; BF (%): body fat percentage

Table 5.4 Intra-group comparisons of metabolic markers across the subject groups

Intra-group analysis				
Variables	**GEP-OT**	**GEP-DT**	**MICE**	**CTRL**
TC (mmol/L)				
N	14	12	11	11
Pre-test (M±SD)	3.91±0.91	4.17±0.89	4.46±1.08	4.23±1.00
Post-test (M±SD)	3.86±0.75	4.12±1.20	4.33±0.94	4.32±1.04
p-value	0.88	0.78	0.43	0.76
HDL-C (mmol/L)				
N	14	12	11	11
Pre-test (M±SD)	1.24±0.35	1.26±0.27	1.40±0.37	1.15±0.21
Post-test (M±SD)	1.38±0.36	1.27±0.31	1.48±0.49	1.23±0.24
p-value	0.08	0.74	0.24	0.15
LDL-C (mmol/L)				
N	11	9	9	10
Pre-test (M±SD)	2.03±0.84	2.15±0.0.55	2.31±0.82	2.58±0.82
Post-test (M±SD)	1.91±0.77	2.38±1.10	2.13±0.66	2.45±0.85
p-value	0.69	0.42	0.41	0.60
TG (mmol/L)				
N	14	12	9	10
Pre-test (M±SD)	1.85±1.38	1.84±0.89	1.24±0.59	1.37±0.48
Post-test (M±SD)	1.26±0.49	2.04±1.39	1.23±0.49	1.72±0.85
p-value	0.15	0.70	0.98	0.19
TC/HDL-C				
N	14	12	11	11
Pre-test (M±SD)	3.37±1.23	3.39±0.84	3.32±0.91	3.81±1.12
Post-test (M±SD)	2.94±0.79	3.32±0.96	3.13±0.94	3.58±1.05
p-value	0.10	0.46	0.20	0.10
LDL-C/HDL-C				
N	11	9	9	10
Pre-test (M±SD)	1.82±0.97	1.84±0.55	1.86±0.79	2.36±0.88
Post-test (M±SD)	1.57±0.74	1.99±0.83	1.68±0.86	2.02±0.81
p-value	0.43	0.49	0.36	0.06
Non-HDL-C (mmol/L)				
N	14	12	11	11
Pre-test (M±SD)	2.67±0.91	2.90±0.81	3.06±1.02	3.09±0.99
Post-test (M±SD)	2.48±0.73	2.85±1.10	2.85±0.87	3.02±1.06
p-value	0.47	0.75	0.15	0.82
FG (mmol/L)				
N	14	12	11	11
Pre-test (M±SD)	5.07±0.60	4.86±0.60	5.16±0.76	5.02±0.43
Post-test (M±SD)	4.92±0.48	4.89±0.54	5.28±0.46	5.05±0.34
p-value	0.27	0.84	0.55	0.76

HbA1c (%)				
N	14	12	11	11
Pre-test (M±SD)	5.90±0.40	6.02±0.34	5.78±0.28	5.93±0.31
Post-test (M±SD)	6.01±0.46	5.94±0.36	5.97±0.26	6.10±0.44
p-value	0.26	0.49	**0.00$_a$**	0.12

Data are presented as mean±standard deviation; N, number of participants; p-value, the probability value within each subject group; GEP-OT, 'Gear' exercise programme repeated at one point in time; GEP-DT, 'Gear' exercise programme repeated at different times during the day; MICE, moderate-intensity continuous exercise; CTRL, control group; a, Intra-group significance $p<0.05$; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglycerides; FG, fasting glucose; HbA1c, glycated haemoglobin

Table 5.5 Inter-group comparisons of blood pressure and body composition measurements across the subject groups

	Inter-group analysis				
Variables	**GEP-OT**	**GEP-DT**	**MICE**	**CTRL**	**p-value (GxT)**
SBP (mmHg)					
Δ Score	-2.10±8.90	-3.00±11.2	-4.30±9.37	-4.80±8.00	
% Δ	-1.90	-2.70	-3.81	-4.36	0.89
d (95% CI)	0.32 (-0.48, 1.11)	0.18 (-0.64, 1.00)	0.06 (-0.78, 0.89)	N/A	
DBP (mmHg)					
Δ Score	-1.80±6.70	-0.40±6.90	-5.40±3.80	-1.37±5.90	
% Δ	-2.28	-0.51	-6.75	-1.74	0.24
d (95% CI)	-0.07 (-0.86, 0.72)	0.15 (-0.67, 0.97)	**-0.81$_c$ (-1.68, 0.06)**	N/A	
BM (Kg)					
Δ Score	0.30±2.50	0.50±1.70	0.00±1.50	0.90±2.00	
% Δ	0.38	0.59	0.00	1.06	0.86
d (95% CI)	-0.26 (-1.05, 0.53)	-0.22 (-1.04, 0.60)	-0.51 (-1.36, 0.34)	N/A	
BMI (Kg/m^2)					
Δ Score	0.30±1.10	0.00±0.90	0.00±0.60	0.50±0.90	
% Δ	1.02	0.00	0.00	1.60	0.49
d (95% CI)	-0.20 (-0.99, 0.60)	0.56 (-1.39, 0.28)	-0.65 (-1.51, 0.20)	N/A	
WC (cm)					
Δ Score	-2.20±5.10	1.50±8.40	-2.20±6.60	-1.80±4.70	
% Δ	-2.43	1.67	-2.35	-1.85	0.42
d (95% CI)	-0.08 (-0.87, 0.71)	0.48 (-0.35, 1.31)	-0.07 (-0.91, 0.77)	N/A	
BF (%)					
Δ Score	0.40±2.70	-0.20±2.80	-0.70±2.06	1.30±2.70	
% Δ	1.47	-0.69	-2.51	4.64	0.31
d (95% CI)	-0.33 (-1.13, 0.46)	-0.55 (-1.38, 0.29)	**-0.83$_c$ (-1.70, 0.04)**	N/A	

Data are presented as Δ Score, mean difference±standard deviation of mean difference (absolute change score); % Δ, relative percent change from baseline (relative change score); p-value (GxT), the interaction probability value between the subject groups and time from the repeated measures analysis of variance; d (95% CI), effect size (95% confidence interval of effect size); b, moderate effect size (compared to the CTRL); c, large effect size (compared to the CTRL); N/A, not applicable; GEP-OT, 'Gear' exercise repeated programme at one point in time; GEP-DT, 'Gear' exercise programme repeated at different times during the day; MICE, moderate-intensity continuous exercise; CTRL, control group; SBP, systolic blood pressure; DBP, diastolic blood pressure; BM, body mass; BMI, body mass index; WC: waist circumference

Table 5.6 Inter-group comparisons of metabolic markers across the subject groups

	Inter-group analysis				
Variables	**GEP-OT**	**GEP-DT**	**MICE**	**CTRL**	**p-value (TxG)**
TC (mmol/L)					
Δ Score	-0.05±1.04	-0.05±0.62	-0.13±0.50	0.09±1.00	
% Δ	-1.28	-1.20	-2.91	2.13	0.94
d (95% CI)	-0.14 (-0.93, 0.65)	-0.17 (-0.99, 0.65)	-0.28 (-1.12, 0.56)	N/A	
HDL-C (mmol/L)					
Δ Score	0.14±0.30	0.01±0.12	0.08±0.22	0.08±0.20	
% Δ	11.3	0.79	5.71	6.96	0.28
d (95% CI)	0.23 (-0.56, 1.02)	-0.43 (-1.26, 0.40)	0.00 (-0.84, 0.84)	N/A	
LDL-C (mmol/L)					
Δ Score	-0.12±1.10	0.23±0.79	-0.18±0.60	-0.13±0.80	
% Δ	-5.91	10.7	-7.79	-5.04	0.69
d (95% CI)	0.01 (-0.85, 0.87)	0.45 (-0.46, 1.36)	-0.07 (-0.97, 0.83)	N/A	
TG (mmol/L)					
Δ Score	-0.59±1.31	0.20±1.64	-0.01±0.63	0.35±0.79	
% Δ	-31.9	10.9	-0.81	25.5	0.44
d (95% CI)	**-0.83$_c$ (-1.68, 0.01)**	-0.11 (-0.95, 0.73)	-0.50 (-1.42, 0.41)	N/A	
TC/HDL-C					
Δ Score	-0.43±0.89	-0.07±0.34	-0.19±0.50	-0.23±0.40	
% Δ	-12.8	-2.06	-5.72	-6.04	0.63
d (95% CI)	-0.28 (-1.07, 0.52)	0.43 (-0.40, 1.26)	0.09 (-0.75, 0.92)	N/A	
LDL-C/HDL-C					
Δ Score	-0.25±0.98	0.15±0.60	-0.18±0.50	-0.34±0.50	
% Δ	-13.7	8.15	-9.68	-14.4	0.73
d (95% CI)	0.11 (-0.74, 0.97)	**0.89$_c$ (-0.05, 1.84)**	0.32 (-0.59, 1.23)	N/A	
Non-HDL-C (mmol/L)					
Δ Score	-0.19±0.93	-0.05±0.56	-0.21±0.50	-0.07±0.90	
% Δ	-7.12	-1.72	-6.86	-2.27	0.99
d (95% CI)	-0.13 (-0.92, 0.66)	0.03 (-0.79, 0.85)	-0.19 (-1.03, 0.65)	N/A	
FG (mmol/L)					
Δ Score	-0.15±0.50	0.03±0.40	0.12±0.66	0.03±0.30	
% Δ	-2.96	0.62	2.33	0.60	0.55
d (95% CI)	-0.42 (-1.22, 0.37)	0.00 (-0.82, 0.82)	0.18 (-0.66, 1.01)	N/A	
HbA1c (%)					
Δ Score	0.11±0.40	-0.08±0.40	0.19±0.10	0.17±0.30	
% Δ	1.86	-1.33	3.29	2.87	0.18
d (95% CI)	-0.17 (-0.96, 0.62)	**-0.70$_b$ (-1.55, 0.14)**	0.09 (-0.75, 0.93)	N/A	

Data are presented as Δ Score, mean difference±standard deviation of mean difference (absolute change score); % Δ, relative percent change from baseline (relative change score); p-value (GxT), the interaction probability value between the subject groups and time from the repeated measures analysis of variance; d (95% CI), effect size (95% confidence interval of effect size); b, moderate effect size

(compared to the CTRL); c, large effect size (compared to the CTRL); N/A, not applicable; GEP-OT, 'Gear' exercise programme repeated at one point in time; GEP-DT, 'Gear' exercise programme at different times during the day; MICE, moderate-intensity continuous exercise; CTRL, control group; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglycerides; FG, fasting glucose; HbA1c, glycated haemoglobin

5.5 Discussion

The primary finding of the study was that the 90-second GEP-DT intervention moderately decreased HbA1c in comparison to the CTRL group. The participants in the GEP-DT group significantly expended fewer calories compared to the other exercise groups, which suggests that the benefits derived from the GEP-DT intervention are less reliant on calories expended during the exercise session. There was no significant difference in age, fitness level and body mass between the groups at baseline, which did not influence the effect of the exercise interventions. HbA1c is the gold standard to measure glycaemic control (10), and an absolute change of 1% reduction in HbA1c is associated with 37% reduction in microvascular complications, 21% reduction in diabetes-related mortality and 14% of myocardial infarction (11). Furthermore, an absolute decrease of at least 0.3% in HbA1c is considered a clinically meaningful value by the European medicine agencies (12). The study showed a clinically significant moderate effect at a comparatively lower absolute change of 0.1%. However, this was achieved at a lower exercise volume compared to traditional models of training.

A systematic review and meta-analysis investigating the effects of familiar MICE and HIIT protocols revealed no significant differences in lipid profiles between the groups (13). The current study concurs with the finding of this review. However, the novel finding is that the new GEP-OT lowered triglyceride levels in persons with an elevated risk of CVD with a large effect size irrespective of the insignificant probability value between the respective groups due to the small sample size. Non-HDL-C and elevated TG are crucial mediators for residual atherosclerotic CVD risk (14). Thus, the GEP-OT group demonstrated a large decrease in effect size for TG post six weeks of training, which provides an atheroprotective and cardioprotective effect in persons with an elevated risk of CVD. Although the 90-second GEP-DT raised the LDL-C/HDL-C, a study indicated that enhancing the function rather than increasing the levels of HDL-C is associated with a clinical effect in lowering the risk of CVD (15).

MICE significantly decreased DBP. An international Korean longitudinal study revealed a J-shaped relationship relevant to DBP in the general population (16). The Korean study suggested that the general population is at risk of all-cause mortality with a DBP of less than 60 mmHg (16). The reason for this finding is that coronary perfusion occurs during diastole. Coronary blood flow to the myocardium is hindered when DBP is less than 60 mmHg. MICE decreased DBP in the current study; however, the participants' mean DBP post-exercise was greater than 60 mmHg, which may have a cardioprotective effect in this group of participants. The MICE reduced body fat percentage with a large effect size. This finding concurs with a pilot randomised controlled trial showing a reduced body fat and body weight after engaging in light-intensity training (17). MICE releases non-esterified fatty acids and oxidises free fatty acids. This increases the capacity of the muscle to take up non-esterified fatty acids by enhancing the requirement and number of capillaries, which stimulates the mobilisation of abdominal adipose tissue non-esterified fatty acids and decreases the risk of CVD (18).

5.6 Conclusion

The novel 90-second 'Gear' exercise programme moderately reduced HbA1c, and the 18-minute GEP-OT lowered blood TG. MICE decreased DBP and body fat percentage. The 'Gear' exercise programmes will encourage future research in persons with NCD and should be considered as a public health initiative to promote exercise in clinical, home and work environments.

5.7 Study limitations

More women than men participated in this study, and the study did not account for the potential effect of the different phases of the menstrual cycle. The study also did not control the nutrition status. The CTRL's activities were self-reported and not objectively measured. Moreover, the study had a small sample size because it was powered by traditional high-intensity programmes.

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5.10 Conflict of interest

The authors have no conflict of interest.

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Chapter 6 Effect of a novel 90-second 'Gear' exercise programme on markers of inflammation and cardiorespiratory fitness measurements in persons at risk of cardiovascular disease

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6.1 Abstract

Aim: The study compared the effect of the novel 'Gear' exercise programmes on inflammatory markers and cardiorespiratory fitness (CRF) measurements in persons at risk of cardiovascular disease.

Methods: Forty-eight participants completed the study. Participants exercised three times per week on alternate days each week for six weeks. Participants were randomly assigned to either the 'Gear' exercise programme repeated at different times during the day (GEP-DT), the 'Gear' exercise programme repeated at one point in time (GEP-OT), moderate-intensity continuous exercise group (MICE) (30 minutes at 55 - 69% of HR_{max}) or the control group (CTRL).

Results: The 90-second GEP-DT demonstrated a moderate increase in VT-L (load at ventilation threshold) (MD = 8.18±12.30, % Δ = 14.53, d = 0.77, d (95% CI): (−0.17, 1.64)), VT-$VO2_{peak}$ (peak oxygen consumption at ventilatory threshold) (MD = 2.93±6.08, % Δ = 53.76, d = 0.66, d (95% CI): (−0.18, 1.50)) and VT-Mets (metabolic equivalent at ventilatory threshold) (MD = 0.83±1.76, % Δ = 52.23, d =0.65, d (95% CI): (−0.19, 1.49)). The GEP-OT group demonstrated a large effect size for VT-L (MD =11.79±18.77, % Δ = 18.86, d = 0.81, d (95% CI): (−0.02, 1.63)). Furthermore, this group demonstrated a moderate effect size for VT-$VO2_{peak}$ (MD =3.59±6.73, % Δ = 50.21, d = 0.72, d (95% CI): (−0.10, 1.53)), VT-VE (ventilatory equivalent at ventilatory threshold) (MD = 8.05±14.66, % Δ = 44.65, d = 0.63, d (95% CI): (−0.18, 1.44)) and VT-Mets (MD = 1.03±1.91, % Δ = 50.49, d = 0.72, d (95% CI): (−0.09, 1.54)). The 18-minute GEP-OT group demonstrated a substantial decrease in interleukin-6 post six weeks of training (% Δ = -77.27); however, the probability value was insignificant.

Conclusions: The GEP-DT and GEP-OT raised the VT-L, which prevented premature fatigue and improved the efficiency of the cardiorespiratory system.

Keywords: cardiorespiratory fitness, exercise prescription, ventilatory threshold, oxygen consumption

6.2 Introduction

A growing body of evidence suggests chronic low-grade inflammation is associated with cardiometabolic diseases (1, 2). Chronic low-grade inflammation is an increase in pro-inflammatory cytokines, which increases insulin resistance and triggers the immune response (3). Exercise has a systematic and direct effect on immune function. A recent meta-analysis showed that aerobic training has a positive effect on anti-inflammatory markers in heathy older and middle-aged persons (4). However, significant heterogeneity of inflammatory markers was observed in the study, and the included studies did not standardise the frequency, intensity, type and duration of aerobic exercise (4).

HIIT performed at 85% of $VO2_{peak}$ for two weeks improved resting inflammatory profile and circulating and adipose tissue in overweight or obese men (5). Conflictingly, another study reported that HIIT might be associated with an increase in inflammation in persons who are sedentary, overweight or obese (6). A recent meta-analysis reported that the effect of HIIT on inflammation remains unclear (7), and the duration of a single bout of HIIT is an essential factor that determines the magnitude of anti-inflammation (8).

CRF is the strongest predictor of reduced mortality and CVD in persons with and without chronic diseases (9). An international study indicated that HIIT was superior to MICE in improving CRF (10), while other studies reported no significant difference between the exercise interventions (11, 12). The results are inconsistent concerning the optimal prescription of exercise to improve CRF and anti-inflammation in persons at risk of CVD.

The most significant barrier to exercise is lack of time, especially with escalating work and family commitments in the current times. Furthermore, moderate-intensity exercise and high-intensity training, when factoring the rest intervals between high-intensity bouts, are not time-efficient. Factoring in the shortcomings from literature, it prompted the authors to design a novel patient-centred and time-efficient ‘Gear’ exercise programme for persons at risk of CVD. Thus, the current study compared the effects of the new ‘Gear’ exercise programmes with traditional exercise on inflammatory markers and CRF measurements in persons at risk of CVD.

6.3 Methods

6.3.1 Experimental design

The study adopted a randomised control pre-test and post-test six-week exercise intervention study.

6.3.2 Ethical approval

Ethical clearance was obtained from the University of the Witwatersrand, Human Research Ethics Committee (Medical) (M170239) and the Tshwane University of Technology, Faculty Committee for Research Ethics (REC/2016/10/005). The study was ethically designed, and it used ethical principles from the Declaration of Helsinki.

6.3.3 Population/unit of analysis and sampling strategy

The study included participants aged 30 to 49 years with no diagnosed cardiovascular, metabolic and/or respiratory communicable or NCD. Forty-eight participants completed the study (Figure 6.1). Thirty-two participants dropped out of the study due to personal and work commitments, fatigue, influenza infection and the presentation of cardiovascular symptoms and orthopaedic injuries not related to the exercise programmes (Figure 6.1). Six participants did not complete the follow-up assessments for inflammatory markers due to personal reasons. The exercise programmes did not result in adverse events (Figure 6.1). The participants who met the inclusion criteria of the study and were medically cleared by the physician to participate in the study were randomly assigned to either one of the following groups: GEP-DT, GEP-OT, MICE and CTRL.

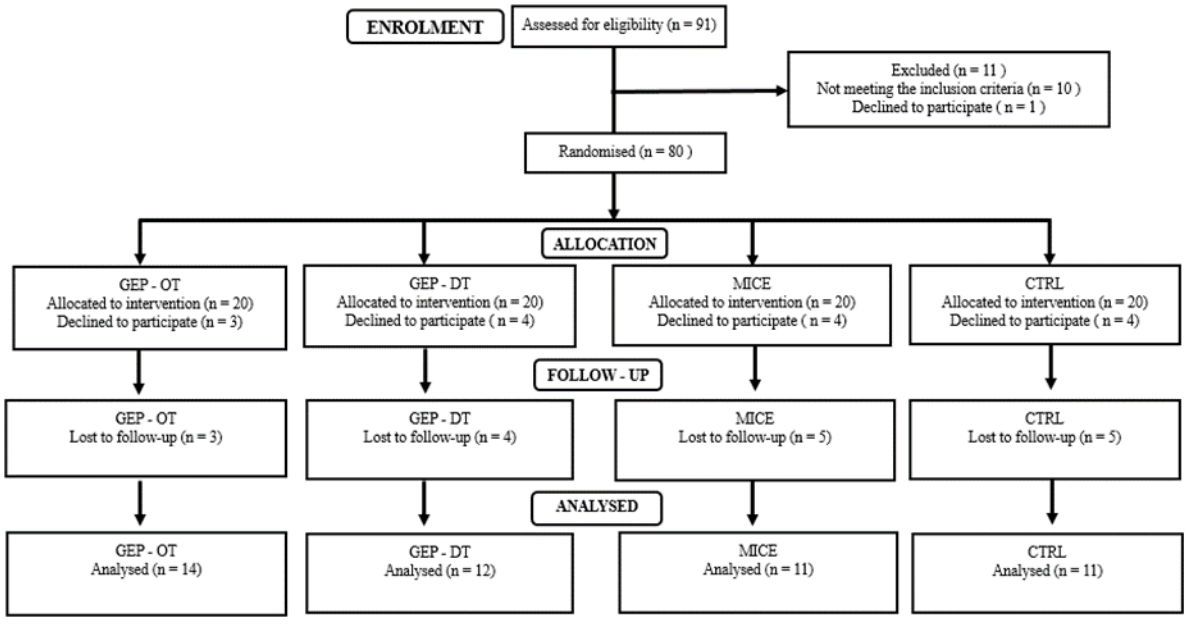

Figure 6.1 Consort diagram

GEP-OT, ‘Gear’ exercise programme repeated at one point in time; GEP-DT, ‘Gear’ exercise programme repeated at different times during the day; MICE, moderate-intensity continuous exercise; CTRL, control group

6.3.4 Procedure

6.3.4.1 Bloods

Blood samples were taken to measure inflammatory cytokines (IL-6, hs-CRP and ESR) before and after the six-week study period. The laboratory used universally accepted international guidelines for testing. The laboratory measured IL-6, hs-CRP and ESR inflammatory markers using the Beckman DXI800, Beckman AU5800 and Westergren ESR-Starsed Interrliner machines, respectively.

6.3.4.2 Cardiorespiratory graded sub-maximal exercise test

The participants performed a graded sub-maximal exercise test on the Wattbike® (Wattbike Pro, Woodway, Germany). The researcher adjusted the saddle height of the participants using the greater trochanter as a reference point. The participants cycled at 55 watts for one minute, after which the target increased by 15 watts per minute. The participants were educated to maintain the target displayed on the screen. No verbal encouragement was awarded throughout the test to ensure standardisation. Oxygen consumption was determined continuously on an automated laboratory cardiopulmonary metabolic cart (Cosmed K4 b^2, Rome, Italy). The gas analyser was calibrated before each test using a gas mixture of known concentration (15% O_2 and 5% CO_2) and ambient air. Participants breathed through a sterilised facemask attached to a one-way valve. The turbine was calibrated before each exercise test using a syringe. The test was terminated if participants reached 85% of their predicted maximal HR, or they experienced signs and symptoms of CVD. $VO2_{peak}$ was obtained from the Cosmed machine, using the Fick equation, and the ventilatory threshold was measured using the V-slope method. The participants rested for six minutes after the termination of the test. The researcher measured blood pressure and HR every minute during the six-minute recovery period.

6.3.4.3 Exercise programmes

Mind-body exercise interventions improve general mental and physical health due to the direct influence of the nervous system on immune and endocrine functions (13). Therefore, the GEP-DT commenced with a visualisation process administered by the primary researcher. The primary researcher used a car analogy to explain the ‘Gear’

exercise interventions. The participants had to visualise the increase and decrease of gears in a car to represent the increase and decrease of speed and intensity, respectively. This mindfulness trigger enabled the participants to become aware of the exercise during the session. The participants increased the gears, mindfully, relevant to their perceived increase in speed and intensity, which was self-paced and enabled the participants to be in control of the exercise session, which resulted in the efficient neural regulation of effort during the exercise session (14) (Figure 6.2). The GEP-OT was similar to the GEP-DT; however, participants repeated three repetitions of the intervention at one point in time with a rest period of four minutes and 30 seconds per repetition (Figure 6.2). The MICE group performed moderate-intensity continuous exercise for a total duration of 30 minutes at 55-69% of predicated HR_{max}, and participants in the CTRL continue with their usual daily activities (Figure 6.2). A demonstration of the 'Gear' exercise programme can be viewed on the following link: https://www.youtube.com/watch?v=KAbkRg9ex94

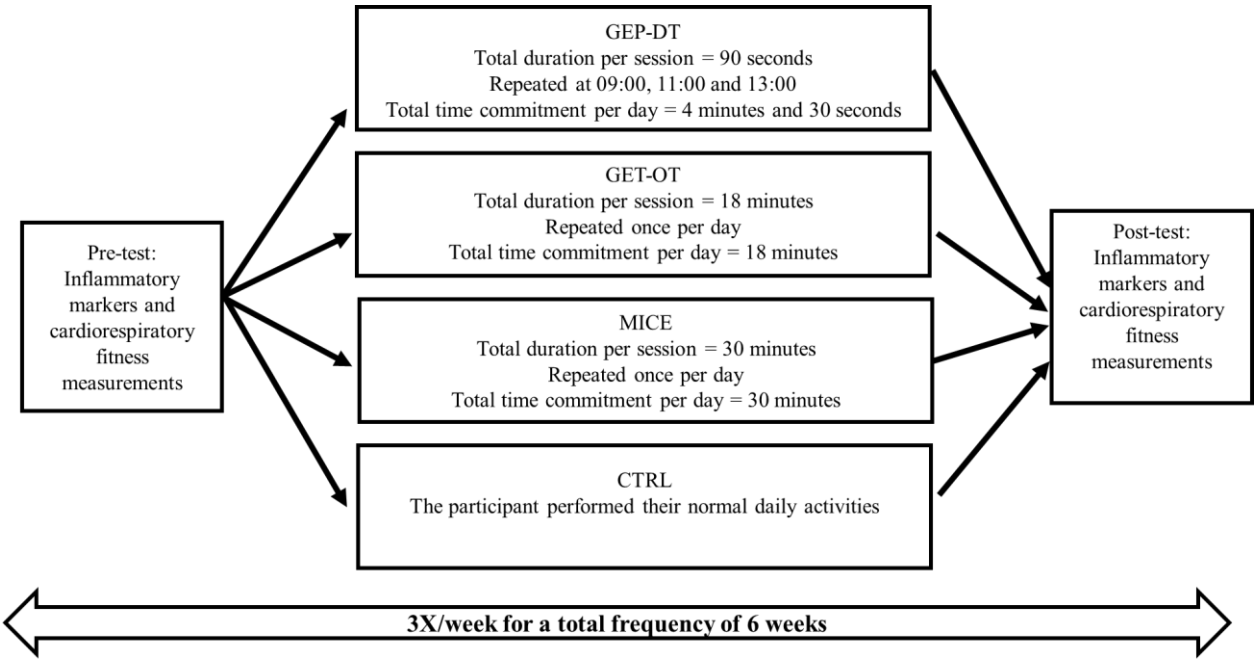

Figure 6.2 Exercise programmes

GEP-OT, 'Gear' exercise programme repeated at one point in time; GEP-DT, 'Gear' exercise programme repeated at different times during the day; MICE, moderate-intensity continuous exercise; CTRL, control group

6.3.4.4 Data analysis

Data were analysed using the IBM SPSS Statistics for Windows®, Version 26.0. Armonk, NY: IBM Corp. The study was powered using G*Power version 3 (15); the

study required at least ten participants per group, factoring the physiological effect size of 0.25 at α = 0.05, which concurred with a previous study of this nature (16). Normality of data was analysed using histograms, Q-Q plots, box plots, Shapiro-Wilk test and Kolmogorov-Smirnov (K-S) tests. Non-normal variables were log-transformed and included in the univariate analysis. Univariate analysis was conducted to determine baseline differences in age and body composition measurements. A paired-samples t-test was used to determine intra-group differences in the exercise interventions. The repeated-measures ANOVA was used to compare intergroup differences. If interaction effects were observed, the Bonferroni post-hoc comparison was used to determine treatment effects between the various groups. Effect size (d) was calculated to determine the clinical significance of the exercise interventions on the outcome variables. An ES of 0.2-0.49 represented a small effect, 0.5-0.79 a moderate effect and at least 0.8 a large effect (17). The level of significance was set at $p<0.05$.

6.4 Results

There was no significant difference in age and body composition measurements between the subject groups, thus these variables did not influence the effect of the exercise interventions (Table 6.1). The GEP-DT group had the highest exercise adherence rate (87%). Participants in the MICE group performed the longest duration of exercise (M = 30 minutes) (Table 6.2). The MICE group had the lowest peak power output (M = 52W), average power/body mass (M = 0.379 W/Kg), peak power/body mass (M = 0.616 W/kg) cadence (M = 44 rpm) and peak cadence (M = 52 rpm). However, participants in this group expended the greatest number of calories per exercise session compared with the other groups (M = 148 Kcal) (Table 6.2).

Table 6.1 Demographic profile of participants

Training Variables	GEP-OT	GEP-DT	MICE	CTRL	P value
Number (n)	14	12	11	11	N/A
Men (%)	21.4	0	27.3	18.2	N/A
Women (%)	78.6	100	72.7	81.8	N/A
Age (years)	36.79±5.37	38.50±6.60	39.64± 6.28	38.45±4.99	0.68
SBP (mmHg)	113±13.14	111±13.55	113.00±12.02	110±12.99	0.92
DBP (mmHg)	79.07±5.98	78.42±7.33	80.00±9.48	78.73±6.50	0.96
We (Kg)	79.87±11.97	85.05±23.37	83.22±14.67	84.64±17.96	0.87
BMI (kg/m^2)	29.47±4.71	32.19±9.80	30.98±5.44	31.25±5.09	0.76
WC (cm)	90.64±8.97	89.83±19.08	93.73±11.82	97.09±12.83	0.56
HC (cm)	109.93±10.67	117.17±20.00	110.45±9.81	112.09±11.25	0.54
BF (%)	27.33±7.10	28.88±6.21	27.89±6.41	28.01±4.93	0.94

Observed values are expressed as n: number of participants, baseline mean and ± mean and standard deviations and univariate analysis to determine between group differences expressed at P value, GEP-OT: gear exercise program repeated at one point in time , GEP-DT: gear exercise program at different times during the day, MICE: moderate-intensity continuous exercise, CTRL: control group, SBP: systolic blood pressure, DBP: diastolic blood pressure, We: body mass, BMI: body mass index, WC: waist circumference, HC: hip circumference, BF:% body fat.

Table 6.2 Training data of participants in the exercise intervention groups

Training variables	GEP-OT	GEP-DT	MICE	p-value
Adherence (%)	82.000	87.000	77.000	N/A
Time commitment per session (minutes)	18.000	4.300	30.000	0.00* â€‡
Average heart rate (bpm)	110.208	108.690	109.362	0.244
Average heart rate (%)	60.749	60.060	60.574	0.350
Peak heart rate (bpm)	126.655	128.477	120.216	0.00* â€
Peak heart rate (%)	69.826	71.022	66.562	0.00* â€
Average power (W)	57.840	61.724	30.974	0.00* â€
Peak power (W)	116.766	127.080	52.207	0.00* â€
Average power/body mass (W/Kg)	0.756	0.763	0.379	0.00* â€
Peak power/body mass (W/Kg)	1.544	1.583	0.616	0.00*#
Kilocalories (Kcal)	9.259	66.161	148.013	0.00* â€‡
Cadence (rpm)	53.748	56.466	43.526	0.00* â€
Peak Cadence (rpm)	72.848	74.983	51.879	0.00* â€

Observed values are expressed as means GEP-OT, 'Gear' exercise program repeated at one point in time; GEP-DT, 'Gear' exercise program repeated at different times during the day; MICE, moderate-intensity continuous exercise; NA, not applicable.

* Significant difference between MICE vs GEP-DT (p<0.01).

â€ Significant difference between MICE vs GEP-OT (p<0.01).

‡ Significant difference between GEP-OT vs GEP-DT (p<0.01).

There was a significant difference within the GEP-OT group for VT-L (p = 0.04), VT-Rf (respiratory frequency at ventilatory threshold) (p = 0.04) and $VO2_{peak}$-L (load at peak oxygen consumption) (p = 0.03). There was no significant difference in the inflammatory and CRF variables within the other groups (p>0.05) (Table 6.3).

The 90-second GEP-DT demonstrated a moderate increase in VT-L (MD = 8.18±12.30, % Δ = 14.53, d = 0.77, d (95% CI): −0.17, 1.64), VT-$VO2_{peak}$ (MD = 2.93±6.08, % Δ = 53.76, d = 0.66, d (95% CI): −0.18, 1.50) and VT-Mets (MD = 0.83±1.76, % Δ = 52.23, d =0.65, d (95% CI): −0.19, 1.49) (Table 6.4).

The GEP-OT group demonstrated a large effect size for VT-L (MD =11.79±18.77, % Δ = 18.86, d = 0.81, d (95% CI): −0.02, 1.63). Furthermore, this group demonstrated a moderate effect size for VT-$VO2_{peak}$ (MD = 3.59±6.73, % Δ = 50.21, d = 0.72, d (95%

CI): -0.10, 1.53), VT-VE (MD = 8.05±14.66, % Δ = 44.65, d = 0.63, d (95% CI): −0.18, 1.44) and VT-Mets (MD = 1.03±1.91, % Δ = 50.49, d = 0.72, d (95% CI): −0.09, 1.54) (Table 6.4).

Analysis of covariance showed no significant group x time interactions on inflammatory markers and CRF variables post six weeks of exercise in persons at risk of CVD ($p>0.05$) (Table 6.4).

Table 6.3 Intra-group comparison of inflammatory markers and cardiorespiratory fitness variables within the subject groups

	Intra-group analysis			
Variables	**GEP-OT**	**GEP-DT**	**MICE**	**CTRL**
ESR (mm/hr)				
N	13	12	7	10
Pre-test (M±SD)	13.92±10.48	25.50±18.47	21.29±19.02	22.30±10.23
Post-test (M±SD)	18.77±20.24	21.50±15.94	20.14±17.65	21.50±10.65
p-value	0.30	0.39	0.85	0.75
HsCRP (mg/l)				
N	13	12	7	10
Pre-test (M±SD)	6.85±4.98	3.64±3.71	3.24±3.21	5.60±5.30
Post-test (M±SD)	7.29±6.79	4.42±5.23	3.67±2.84	4.92±3.04
p-value	0.78	0.17	0.59	0.54
IL-6 (pg/ml)				
N	13	12	7	10
Pre-test (M±SD)	17.38±28.95	16.06±25.48	11.59±25.98	3.32±2.59
Post-test (M±SD)	3.95±2.36	12.91±24.02	3.44±2.90	3.58±1.55
p-value	0.12	0.52	0.43	0.71
VT-L (W)				
N	14	11	11	11
Pre-test (M±SD)	62.50±11.39	56.36±4.52	61.82±7.83	70.00±16.43
Post-test (M±SD)	74.29±16.04	64.55±12.14	70.00±23.24	68.64±18.32
p-value	**0.04***	0.05	0.24	0.72
VT-$VO2_{peak}$ (mL/min/kg)				
N	14	12	11	11
Pre-test (M±SD)	7.15±5.05	5.45±4.09	7.41±4.61	8.25±4.99
Post-test (M±SD)	10.74±6.02	8.38±6.88	6.23±5.22	7.63±4.96
p-value	0.07	0.12	0.48	0.66
VT-VE (mL/min)				
N	14	12	11	11
Pre-test (M±SD)	18.03±11.37	15.68±9.90	17.82±9.36	22.04±12.91
Post-test (M±SD)	26.08±13.79	21.44±17.89	16.35±13.10	21.55±15.77
p-value	0.06	0.26	0.70	0.89
LT-METS				
N	14	12	11	11
Pre-test (M±SD)	2.04±1.44	1.57±1.16	2.11±1.32	2.35±1.41
Post-test (M±SD)	3.07±1.71	2.39±1.98	1.77±1.49	2.17±1.41
p-value	0.07	0.13	0.47	0.66
$VO2_{peak}$-L (W)				
N	14	11	11	11
Pre-test (M±SD)	86.07±18.10	78.18±7.83	89.09±22.34	83.64±14.16
Post-test (M±SD)	93.57±22.57	85.00±13.42	94.55±21.50	86.36±22.70
p-value	**0.03***	0.10	0.22	0.44

$VO2_{peak}$ (mL/min/kg)				
N	14	12	11	11
Pre-test (M±SD)	11.72±3.80	11.66±3.48	12.31±4.12	10.14±3.27
Post-test (M±SD)	13.16±4.97	11.36±4.82	11.85±3.91	10.95±3.20
p-value	0.14	0.76	0.55	0.50
$VO2_{peak}$-VE (mL/min)				
N	14	12	11	11
Pre-test (M±SD)	27.57±11.57	27.78±9.00	27.95±9.01	25.36±11.23
Post-test (M±SD)	32.17±15.83	27.48±10.54	28.13±9.78	29.51±15.03
p-value	0.15	0.90	0.93	0.41
$VO2_{peak}$-METS				
N	14	12	11	11
Pre-test (M±SD)	3.26±1.16	3.26±1.02	3.43±1.01	2.78±0.97
Post-test (M±SD)	3.73±1.56	3.22±1.31	3.34±0.98	3.09±1.02
p-value	0.17	0.88	0.68	0.47

Observed values are expressed as N, number of participants; pre-test (M±SD), pre-test mean±standard deviation; pre-test (M±SD), post-test mean±standard deviation; p-values, probability values within the subject groups; GEP-OT, 'Gear' exercise program repeated at one point in time; GEP-DT, 'Gear' exercise programme repeated at different times during the day; MICE, moderate-intensity continuous exercise; CTRL, control group; ESR (mm/hr), erythrocyte sedimentation rate; hs-CRP (mg/l), high-sensitivity C-reactive protein; IL-6 (pg/ml), interleukin-6; VT-L, load at ventilatory threshold VT-$VO2_{peak}$, peak oxygen consumption at ventilatory threshold; VT-VE (mL/min), ventilatory equivalent at ventilatory threshold; VT-Mets, metabolic equivalent at ventilatory threshold; $VO2_{peak}$-L (W), load at peak oxygen consumption; $VO2_{peak}$ (mL/min/kg), peak oxygen consumption; $VO2_{peak}$-VE (mL/min), ventilatory equivalent at peak oxygen consumption; $VO2_{peak}$-Mets, metabolic equivalent at peak oxygen consumption

Table 6.4 Inter-group comparison of inflammatory markers and cardiorespiratory fitness variables between the subject groups

	Intergroup analysis				
Variables	**GEP-OT**	**GEP-DT**	**MICE**	**CTRL**	**TxG (P)**
ESR (mm/hr)					
Δ Score (MD±SD)	4.85±16.09	-4.00±15.62	-1.14±15.17	-0.80±7.79	
% Δ	34.84	-15.69	-5.40	-3.59	0.48
d	0.43 (-0.41, 1.26)	-0.25 (-1.09, 0.59)	-0.03 (-0.10, 0.94)	N/A	
HsCRP (mg/l)					
Δ Score (MD±SD)	0.45±5.71	0.77±1.83	0.43±2.01	-0.68±3.41	
% Δ	6.42	21.43	13.27	-12.14	0.58
d	0.23 (-0.59, 1.06)	0.55 (-0.31, 1.40)	0.38 (-0.60, 1.35)	N/A	
IL-6 (pg/ml)					
Δ Score (MD±SD)	-13.44±29.22	-3.15±16.40	-8.14±25.61	0.26±2.12	
% Δ	-77.27	-19.61	-70.32	7.83	0.13
d	-0.62 (-1.46, 0.22)	-0.28 (-1.12, 0.56)	-0.52 (-1.50, 0.47)	N/A	
VT-L (W)					
Δ Score (MD±SD)	11.79±18.77	8.18±12.30	8.18±21.60	-1.36±12.47	
% Δ	18.86	14.53	13.23	-1.94	0.22
d	**0.81$ (-0.02, 1.63)**	**0.77# (-0.10, 1.64)**	0.54 (-0.31, 1.39)	N/A	
VT-VO2 peak (mL/min/kg)					
Δ Score (MD±SD)	3.59±6.73	2.93±6.08	-1.18±5.31	-0.62±4.52	
% Δ	50.21	53.76	-15.92	-7.52	0.07
d	**0.72$ (-0.10, 1.53)**	**0.66# (-0.18, 1.50)**	-0.11 (-0.95, 0.72)	N/A	
VT-VE (mL/min)					
Δ Score (MD & SD)	8.05±14.66	5.77±16.97	-1.47±12.20	-0.48±11.75	
% Δ	44.65	36.73	-8.25	-2.22	0.18
d	**0.63# (-0.18, 1.44)**	0.42 (-0.40, 1.25)	-0.08 (-0.92, 0.75)	N/A	
VT-Mets					
Δ Score (MD±SD)	1.03±1.91	0.83±1.76	-0.34±1.50	-0.17±1.26	
% Δ	50.49	52.23	-16.11	-7.66	0.07
d	**0.72# (-0.09, 1.54)**	**0.65# (-0.19, 1.49)**	-0.12 (-0.96, 0.71)	N/A	
VO2 peak-L (W)					
Δ Score (MD±SD)	7.50±11.39	6.82±12.30	5.45±13.87	2.73±11.26	
% Δ	8.71	8.72	6.13	3.25	0.71
d	0.42 (-0.38, 1.22)	0.35 (-0.50, 1.19)	0.22 (-0.62, 1.05)	N/A	
VO2 peak (mL/min/kg)					
Δ Score (MD±SD)	1.43±3.45	-0.29±3.26	-0.45±2.41	0.82±3.83	
% Δ	12.29	-2.57	-3.74	7.99	0.43
d	0.17 (-0.62, 0.96)	-0.31 (-1.14, 0.51)	-0.40 (-1.24, 0.45)	N/A	
VO2 peak-VE (mL/min)					
Δ Score (MD±SD)	4.60±11.22	-0.31±8.28	0.18±6.89	4.15±16.15	0.59

% Δ	16.68	-1.08	0.64	16.36	
d	0.03 (-0.76, 0.82)	-0.35 (-1.18, 0.47)	-0.32 (-1.16, 0.52)	N/A	
VO2 $_{peak}$-METS					
Δ Score (MD±SD)	0.47±1.20	-0.04±0.92	-0.09±0.71	0.31±1.38	
% Δ	14.42	-1.23	-2.62	11.15	0.51
d	0.12 (-0.67, 0.92)	-0.30 (-1.12, 0.52)	-0.36 (-1.21, 0.48)	N/A	

Observed values are expressed as Δ Score (MD±SD), change score±standard deviation; % Δ, percent change from baseline; p-values; d, effect size; TxG (P), probability value between the subject groups; #, moderate effect size; $, large effect size; GEP-OT, 'Gear' exercise programme repeated at one point in time; GEP-DT, 'Gear' exercise programme repeated at different times during the day; MICE, moderate-intensity continuous exercise; CTRL, control group; ESR (mm/hr), erythrocyte sedimentation rate; hs-CRP (mg/l), high-sensitivity C-reactive protein; IL-6 (pg/ml), interleukin-6; VT-L, load at ventilatory threshold; VT-$VO2_{peak,}$ peak oxygen consumption at ventilatory threshold; VT-VE (mL/min), ventilatory equivalent at ventilatory threshold; VT-Mets, metabolic equivalent at ventilatory threshold; $VO2_{peak}$-L (W), load at peak oxygen consumption; $VO2_{peak}$ (mL/min/kg), peak oxygen consumption; $VO2_{peak}$-VE (mL/min), ventilatory equivalent at peak oxygen consumption; $VO2_{peak}$-Mets, metabolic equivalent at peak oxygen consumption

6.5 Discussion

The primary finding of the study is that the GEP-DT and GEP-OT increased power output (load) corresponding to the ventilatory threshold. Participants in these exercise groups performed more work at higher intensities before the onset of the ventilatory threshold. An international study has stressed the importance of considering the individualised ventilatory threshold to prevent overestimating exercise intensity during exercise programme prescription (18). The first ventilatory threshold point indicates an increase in carbon dioxide proportionally with oxygen consumption due to the buffering capacity of bicarbonate ions in the blood (19). However, as exercise intensity increases, there is a disproportionate increase of exhaled carbon dioxide (VCO_2) and oxygen uptake (VO_2) with a concomitant increase in ventilatory equivalent (VE) (20). This is known as ventilatory threshold 2, and it indicates the inability of the intracellular bicarbonates to counteract metabolic acidosis (19). Physical activity or exercise above the second ventilatory threshold point decreases exercise capacity and effort. The GEP-OT and GEP-DT groups raised the ventilatory threshold point, which delayed metabolic acidosis by reducing the accumulation of hydrogen ions and preserving the linear increase in VE with VO_2 and VCO_2 (21), which increased exercise capacity post-training. An international study accentuated the importance of $VO2_{peak}$ and HR, corresponding to the ventilatory threshold in overweight or obese persons (22). Thus,

the current study concurs with this finding and highlights the beneficial effect of the 'Gear' exercise programmes at improving exercise capacity in persons at risk of CVD

The 'Gear' exercise programmes resulted in favourable exercise physiological adaptations in overweight or obese persons. The physiological exercise benefits derived by the GEP-DT and GEP-OT are explained by the Fick equation [$VO2_{max}$ = HR X SV X (CaO_2 – CVO_2)], which is an essential determinant of myocardial ischemia (23). The GET-DP and GEP-OT groups performed more work to reach $VO2_{peak}$; $VO2_{peak}$ is an essential measurement of cardiovascular fitness. The availability of oxygen is dependent on arterial saturation of oxygen, amount of haemoglobin, carbon dioxide, blood pH, HR, stroke volume, mitochondrial density and capillary density (23). There is a linear relationship between work rate and oxygen consumption; however, it plateaus when approaching limitations in cardiac output, stroke volume of tissue extraction and the manifestation of signs and symptoms of CVD. An increase in oxygen uptake (3.5 ml/kg/min) was significantly associated with a 15% reduced risk of CVDs (24). Therefore, the GEP-DT group achieved a higher load corresponding to $VO2_{peak}$, which may provide a cardio-protective benefit in persons at risk of CVD.

The 18-minute GEP-OT group demonstrated a substantial decrease in IL-6 post six weeks of training (% Δ = -77.27); however, the probability value was insignificant. Inflammation is strongly associated with NCD and poor mental health-related quality of life (25). The GEP-OT demonstrated an anti-inflammatory effect post six weeks of training, which promotes mental and health-related quality of life. However, the exercise programmes did not significantly reduce markers of inflammation. This finding is in alignment with other studies (7, 26). The reason for this finding is that inflammatory markers are influenced by visceral and abdominal fat mass (27) and duration of exercise (28). Since there was no significant reduction in visceral fat in the study, and the duration of exercise was minimal, the exercise programmes had no significant effect on ESR, hs-CRP and IL-6 inflammatory markers in persons at risk of CVD. Therefore, future studies should investigate the effect of the new GEP-OT intervention on interleukin levels in overweight or obese persons and other population groups at risk of NCD due to the promising and novel finding in this study.

6.6 Conclusions

The exercise interventions did not significantly reduce inflammatory markers. The GEP-OT and GEP-DT groups raised the ventilatory threshold point, which resulted in increased exercise capacity following the interventions. The GEP-DT group achieved a higher load at the corresponding $VO2_{peak}$, which can increase exercise tolerance and may provide a cardio-protective benefit in persons at risk of CVD. The GEP-OT increased load and ventilatory equivalent corresponding with respiratory quotient, which delayed the onset of the respiratory compensation point. This physiological benefit prevented premature fatigue and improved cardiorespiratory efficiency in persons at risk of CVD. Based on the promising findings presented in this paper, future research is required to investigate the effects of the 'Gear' exercise programmes on high-performance variables in the different codes of sport. Furthermore, healthcare practitioners can adopt the principles of the 'Gear' exercise programmes and test them on different modes of exercise in persons with NCD.

6.7 Study limitations

More women than men participated in the study, and the study did not account for the potential effect of the different phases of the menstrual cycle. The current study did not control nutrition status, responders and non-responders to exercise. Six participants did not complete the follow-up assessments for inflammatory markers due to personal commitments.

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6.10 Conflict of interest

The authors have no conflict of interest

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Chapter 7 Conclusion and recommendations

7.1 Conclusion

Exercise prescription involves the following variables: frequency, intensity, duration, type of activity, volume and progression. An individualised prescription of MICT and SIT is required to curtail the risk of CVD in overweight or obese persons. However, escalating work and family commitments impact exercise adherence. Therefore, the novel 'Gear' exercise programme was conceptualised as a time-efficient exercise programme. The novel 90-second 'Gear' exercise programme moderately reduced HbA1c, and the 18-minute GEP-OT lowered blood TG, which indicated that the programme may provide a cardio-protective effect. Furthermore, the 90-second and 18-minute 'Gear' exercise programmes raised the ventilation threshold point. This physiological response prevented premature fatigue and improved the efficiency of the cardiorespiratory system. Based on the promising findings of the new proposed 'Gear' exercise programme in persons with elevated CVD risk, future research is required to investigate the effects of the 'Gear' exercise programmes on persons with NCD and high-performance variables in the different codes of sport.

7.2 Clinical/practical recommendations

- MICT was significantly better at improving CRF (VO_{2max}) compared with SIT and HIIT in overweight or obese persons.
- An increase in body fat percentage results in an increase in ESR
- An increase in VT-L results in a decrease in HbA1c
- The 90-second GEP-DT intervention reduced HbA1c post six-weeks of training. This reduces the risk of microvascular conditions.
- The 18 minute- GEP-OT group demonstrated a decrease in TG with a large effect size, which reduces the risk of CVD.
- GEP-DT and GEP-OT raised the ventilation threshold point, which increased exercise capacity.
- The GEP-DT and GEP-OT groups achieved a greater load at the corresponding $VO2_{peak}$, which provided a cardio-protective benefit in overweight or obese persons.

- GEP-OT increased VT-L and VT-VE corresponding with respiratory quotient, which delayed the onset of premature fatigue.
- The physiological benefits derived from GEP-DT and GEP-OT prevented premature fatigue and improved cardiorespiratory efficiency in persons at risk of CVD.
- MICE decreased DBP within the norms and increased VT-L in the current study. Therefore, reduces the risk of cerebrovascular diseases and CVDs.
- All exercise programmes were useful in the current study. Therefore, exercise reduces the risk of CVD and improves cardiorespiratory efficiency; however, the 'Gear' exercise programme is a time-efficient protocol.

7.3 Recommendation for future research

Research in the future should address the gaps in the literature:

- Comparison of this time-efficient protocol on repeated high-intensity training at a single point in time and continuous moderate-intensity exercise on cardiometabolic risk factors, physical fitness parameters and inflammatory markers.
- Future studies are encouraged to investigate responders and non-responders to exercise in overweight or obese persons.
- The 'Gear' exercise programmes will encourage future research in persons with NCD, and it should be considered as a public health initiative to encourage exercise in clinical and work environments.
- Based on the promising findings presented in this study, future research is required to investigate the effects of the 'Gear' exercise programmes on health-related quality of life variables in persons with cardiometabolic diseases.
- Use the principles of the 'Gear' exercise programme on different modes of exercise in the clinical and sporting environment. Translating research from the laboratory into the working and home environments.
- Future large-scale studies between the 'Gear' exercise programme and MICT should be non-inferiority studies rather than trying to prove improved outcomes.

7.4 Strengths and limitations

- The first is the small sample size observed in the included studies, which could have overestimated or underestimated the outcome variables.
- The second is that CRF has a strong genetic influence; thus, future studies are encouraged to investigate responders and non-responders to exercise.
- More women than men participated in the study. It is crucial to note that there are few studies of this nature with a higher representation of women compared to men.
- The study did not account for the potential effect of the different phases of the menstrual cycle. However, there are
- The study did not control the nutrition status.
- The study used the Wattbike®; however, the principles of the ‘Gear’ exercise programmes can be implemented without the use of sophisticated equipment; and should be investigated using different equipment and modes of activity.
- The ‘Gear’ exercise programme is a new time-efficient exercise protocol that reduced the risk of CVD in persons with cardiometabolic risk factors.
- The novel exercise intervention can be easily implemented in different clinical, home and corporate settings, without the need for gym attire.
- The high drop-out rate due to work commitments, family responsibilities and orthopaedic injuries not related to the exercise interventions could have influenced the results. However, this is not unique to this study.

Appendix A Information sheet

DEMOGRAPHIC DETAILS

Study ID: _____

Circle Appropriate Response

Age	
Gender	1 = Male 2 = Female

Appendix B Medical questionnaire

Study ID: _____

Family Physician and/or Primary Health Care Provider:

Doctor/Other_____ Phone _____

Address _____ _____ City

May I send a copy of your consultation to your physician or primary health care provider and consult with them as necessary?

□ Yes □ No

Signature:_____

Sex:

□ Male □ Female

Education:

□ Grade School □ Jr. High School □ High School

□ College (2-4 years) Graduate School □ Degree _____

What is (are) your purpose (s) for participation in this fitness programme?

□ To determine my current level of physical fitness and to receive recommendations for an exercise programme.

□ Other (please explain) _____

_____

_____

_____

_____

Present Medical History

Check those questions to which you answer yes (leave the others blank).

□ Has a doctor ever said your blood pressure was too high?
□ Do you ever have pain in your chest or heart?
□ Are you often bothered by a thumping of the heart?
□ Does your heart often race?
□ Do you ever notice extra heartbeats or skipped beats?
□ Are your ankles often badly swollen?
□ Do cold hands or feet trouble you even in hot weather?
□ Has a doctor ever said that you have or have had heart trouble, an abnormal electrocardiogram (ECG or EKG), heart attack or coronary?
□ Do you suffer from frequent cramps in your legs?
□ Do you often have difficulty breathing?
□ Do you get out of breath long before anyone else?
□ Do you sometimes get out of breath when sitting still or sleeping?

- ☐ Has a doctor ever told you your cholesterol level was high?
- ☐ Has a doctor ever told you that you have an abdominal aortic aneurysm?
- ☐ Has a doctor ever told you that you have critical aortic stenosis?

Comments: _____
_____
_____
_____

Do you now have or have you recently experienced:

- ☐ Chronic, recurrent or morning cough?
- ☐ Episode of coughing up blood?
- ☐ Increased anxiety or depression?
- ☐ Problems with recurrent fatigue, trouble sleeping or increased irritability?
- ☐ Migraine or recurrent headaches?
- ☐ Swollen or painful knees or ankles?
- ☐ Swollen, stiff or painful joints?
- ☐ Pain in your legs after walking short distances?
- ☐ Foot problems?
- ☐ Back problems?
- ☐ Stomach or intestinal problems, such as recurrent heartburn, ulcers, constipation or diarrhea?
- ☐ Significant vision or hearing problems?
- ☐ Recent change in a wart or a mole?
- ☐ Glaucoma or increased pressure in the eyes?
- ☐ Exposure to loud noises for long periods?
- ☐ An infection such as pneumonia accompanied by a fever?
- ☐ Significant unexplained weight loss?
- ☐ A fever, which can cause dehydration and rapid heartbeat?
- ☐ A deep vein thrombosis (blood clot)?
- ☐ A hernia that is causing symptoms?
- ☐ Foot or ankle sores that will not heal?
- ☐ Persistent pain or problems walking after you have fallen?
- ☐ Eye conditions such as bleeding in the retina or detached retina?
- ☐ Cataract or lens transplant?
- ☐ Laser treatment or another eye surgery?

Comments: _____
_____
_____
_____

Women only answer the following. Do you have:

- ☐ Menstrual period problems?
- ☐ Significant childbirth - related problems?
- ☐ Urine loss when you cough, sneeze or laugh?

Date of the last pelvic exam and / or Pap smear _____

Comments: _____
_____
_____
_____

Are you on any type of hormone replacement therapy?_____

People answer the following:

List any prescription medications you are now taking: _____
_____
_____

List any self-prescribed medications, dietary supplements, or vitamins you are now taking:_____
_____
_____

Date of last complete physical examination: _____

□ Normal □ Abnormal □ Never □ Cannot remember

Date of last chest X-ray: _____

□ Normal □ Abnormal □ Never □ Cannot remember

Date of last electrocardiogram (EKG or ECG): _____

□ Normal □ Abnormal □ Never □ Cannot remember

Date of last dental checkup: _____

□ Normal □ Abnormal □ Never □ Cannot remember

List any other medical or diagnostic test you have had in the past two years: _____
_____
_____

List hospitalizations, including dates of and reasons for hospitalization: _____
_____
_____

List any drug allergies: _____
_____
_____

Past Medical History

Check those questions to which your answer is yes (leave others blank).

□ Heart attack if so, how many years ago? _____
□ Rheumatic Fever
□ Heart murmur
□ Diseases of the arteries
□ Varicose veins
□ Arthritis of legs or arms
□ Diabetes or abnormal blood-sugar tests
□ Phlebitis (inflammation of a vein)

- ☐ Dizziness or fainting spells
- ☐ Epilepsy or seizures
- ☐ Stroke
- ☐ Diphtheria
- ☐ Scarlet Fever
- ☐ Infectious mononucleosis
- ☐ Nervous or emotional problems
- ☐ Anemia
- ☐ Thyroid problems
- ☐ Pneumonia
- ☐ Bronchitis
- ☐ Asthma
- ☐ Abnormal chest X-ray
- ☐ Another lung disease
- ☐ Injuries to back, arms, legs or joint
- ☐ Broken bones
- ☐ Jaundice or gall bladder problems

Comments: _____
_____
_____
_____

Family Medical History

Father:

☐ Alive Current age _____

My father's general health is:

☐ Excellent ☐ Good ☐ Fair ☐ Poor

Reason for poor health: _____

☐ Deceased ☐ Age at death _____

Cause of death: _____

Mother:

☐ Alive Current age _____

My mother's general health is:

☐ Excellent ☐ Good ☐ Fair ☐ Poor

Reason for poor health:
_____

☐ Deceased ☐ Age at death _____

Cause of death: _____

Siblings:

Number of brothers _____ Number of sisters _____ Age range _____

Health problems _____

Familial Diseases

Have you or your blood relatives had any of the following (include grandparents, aunts and uncles, but exclude cousins, relatives by marriage and half-relatives)?

Check those to which the answer is yes (leave other blank).

- ☐ Heart attacks under age 50
- ☐ Strokes under age 50
- ☐ High blood pressure
- ☐ Elevated cholesterol
- ☐ Diabetes
- ☐ Asthma or hay fever
- ☐ Congenital heart disease (existing at birth but not hereditary)
- ☐ Heart operations
- ☐ Glaucoma
- ☐ Obesity (20 or more pounds overweight)
- ☐ Leukemia or cancer under age 60

Comments: _____
_____
_____
_____

Other Heart Disease Risk Factors

Smoking

Have you ever smoked cigarettes, cigars or a pipe?

☐ Yes ☐ No

(If no, skip to diet section)

If you did or now smoke cigarettes, how many per day? ___ _____ Age started

If you did or now smoke cigars, how many per day? _____ Age started _____

If you did or now smoke a pipe, how many pipefuls a day? Age started _____

If you have stopped smoking, when was it? _____

If you now smoke, how long ago did you start? _____

Diet

What do you consider a good weight for yourself? _____

What is the most you have ever weighed (including when pregnant)? _____

How old were you? _____

My current weight is: _____

One year ago, my weight was: ___

At age 21 my weight was:_____

Number of meals you usually eat per day:

_____

Number of times per week you usually eat the following:

Beef _____ Fish _____ Desserts_____

Pork _____ Fowl _____ Fried Foods _____

Number of servings (cups, glasses, or containers) per week you usually consume of:

Homogenized (whole) milk _____Buttermilk _____ Skim (nonfat) milk _

2% (low-fat) milk _____1% (low-fat) milk _____ Coffee _____

Tea (iced or not) _____Regular or diet sodas _____ Glasses of water___

Do you ever drink alcoholic beverages?

□ Yes □ No

If yes, what is your approximate intake of these beverages?

Beer:

□ None □ Occasional □ Often If often, _____ per week

Wine:

□ None □ Occasional □ Often If often, _____ per week

Hard Liquor:

□ None □ Occasional □ Often If often, _____ per week

At any time in the past, were you a heavy drinker (consumption of six ounces of hard liquor per day or more)?

□ Yes □ No

Comments: _____

_____

_____

_____

Do you usually use oil or margarine in place of high cholesterol shortening or butter?

□ Yes □ No

Do you usually abstain from extra sugar usage?

□ Yes □ No

Do you usually add salt at the table?

□ Yes □ No

Do you eat differently on weekends as compared to weekdays?

□ Yes □ No

Comments: _____

_____

Appendix C Outcome measurements

Study ID: _____

Resting Measurement	
Resting Blood Pressure (Right Hand)	
Resting Blood Pressure (Left Hand)	
Resting Heart Rate	
Height (m)	
Weight (Kg)	
BMI	
Waist Circumference	
Hip Circumference	
Waist to Hip Ratio	

Skinfold Measurements	
Triceps (mm)	
Biceps (mm)	
Subscapula (mm)	
Abdomen (mm)	
Suprailiac (mm)	
Quadriceps (mm)	
Calf (mm)	
% Body Fat	

Cholesterol and Glucose	
TChol	
HDL	
CAL. LDL	
TRIG	
TCHOL/HDL	
HDL/LDL	
Non-HDL	
Fasting Glucose	
HbA1c	

Inflammatory Markers	
Interleukin 6	
High sensitivity C- reactive protein	
Erythrocyte sedimentation rate	

EXERCISE STRESS TEST

Exercise Stress Test Power (watts)	Time	Heart Rate	Blood Pressure	RPE
55	1 min			
70	2 min			
85	3 min			
100	4 min			
115	5 min			
130	6 min			
145	7 min			
160	8 min			
175	9 min			

Recovery (Time)	Heart Rate	Blood Pressure	RPE
0 min			
1 min			
2 min			
3 min			
6 min			

Appendix D Measurements before and after the exercise interventions

Study ID: _____

Date: _____

Measurements Before and After Exercise Intervention	
Blood Pressure (Right Hand)	
Blood Pressure (Left Hand)	
Heart Rate	
Perceived signs and symptoms before and after the exercise session	

Appendix E Informed consent form for the exercise groups

Project Title: The Effect of a Single Bout of High-Intensity Sprint Exercise Programme Compared to Traditional High-Intensity Sprint Interval Exercise and Endurance Exercise on Inflammatory Markers, Lipid Profile and Health Related Physical Fitness Measurements in Participants with Elevated Cardiovascular Disease Risk

Study leader: Mr N Rugbeer, B (Hons) Biokinetics, PGCE, M. Sport Science (Research).

Good day, my name is Nivash Rugbeer, I am a PhD student at the University of the Witwatersrand. I would like to invite you to consider participating in a research study, entitled “The effect of temporal single bout of high intensity exercise in participants with elevated cardiovascular disease risk.”

Before agreeing to participate, it is important that you read and understand the following explanation of the purpose of the study, the study procedures, benefits, risks, discomforts, and precautions as well as the alternative procedures that are available to you, and your right to withdraw from the study at any time.
1. This information leaflet is to help you to decide if you would like to participate. You need to understand what is involved before you agree to take part in this study.
2. If you have any questions, do not hesitate to ask me.
3. You should not agree to take part unless you are satisfied about all the procedures involved.
4. You may not participate in another investigational medicine research study, nor take any other investigational medicine during your participation in this study.
5. You should not have participated in an investigational medicine research study within the past 60 days.
6. If you decide to take part in this study, you will be asked to sign this document to confirm that you understand the study. You will be given a copy to keep.
7. No costs will be incurred by you for any medical tests.

WHAT IS THE STUDY ALL ABOUT?
Cardiovascular diseases refer to illnesses that affect the heart and blood vessels. Cardiovascular diseases account for 48% of the deaths globally and was the leading contributor to death in both developed and developing countries. Globally the leading cause of death is lack of cardiorespiratory fitness. Lack of attention is awarded to persons who are at increased risk of cardiovascular disease, which may be a critical point of life requiring interventions to preserve function and ability. In South Africa many people do not participate in exercise due to the lack of time availability. Therefore, the purpose current study determines the effect of a single bout of high intensity exercise required to illicit benefits in cardiovascular health. This will minimise time and improve adherence to exercise.

LENGTH OF STUDY AND NUMBER OF PARTICIPANTS
- The study will be performed in South Africa at the Tshwane University of Technology
- Approximately 72 participants will participate in this study from Tshwane

University of Technology and the Pretoria West area. All participants, who meets the inclusion criteria of the study will participate in the study. The participants will be between the ages of 30 and 49 years

- The total length of time required for your participation in this study will be a maximum of two months
- You will be asked to visit me three times per week for six weeks during the study.

WHAT WILL YOU BE REQUIRED TO DO IN THE STUDY?

If you decide to take part in the study, you will be required to do the following:

- You will first be asked questions and examined to see if you qualify for this study
- To sign this informed consent form
- To complete a Medical History administered by the physician
- Obtain medical clearance prior participation from the physician. Screening for eligibility, complete medical clearance form and medical examination by a physician, will take approximately 60 minutes to complete
- Provide consent to the Phlebotomist to draw the following blood markers (Lipoproteins, total cholesterol/ triglycerides, blood glucose and inflammatory markers)
- Allow the biokineticist to measure resting blood pressure, height, weight, skinfolds, waist circumference, hip circumference and submaximal exercise stress test with gas analysis
- Engage in the intervention, which would be randomly assigned to you for six weeks
- You will be allocated to either the experimental and control groups
- Once medically cleared by the physician for participation you will be randomly assigned to the exercise or control group
- The time commitment for the endurance group will be 45 minutes. Thirty minutes will be the exercise intervention and 15 minutes will be allocated for the recovery period
- The time commitment for the high intensity exercise group will be 120 seconds. Thirty seconds will be the warm-up, followed by 30 seconds of the exercise intervention and 60 seconds recovery
- The requirement that participants must abstain from exercise, caffeine and alcohol consumption during the course of the intervention, i.e., for a period of 10 weeks
- The control group will continue with their daily activities in-keeping with the inclusion and exclusion criteria of the study. Thereafter, they will attend the pre-test and post-test days only

At each following visit you will undergo:

- Visit 1 – (week 1): Screening for eligibility, complete medical clearance form and medical examination by a physician. This will approximately take 60 minutes.
- Visit 2 – (week 1): Before the exercise intervention, blood markers, will be drawn by a qualified phlebotomist from AMPATH laboratories. A total of 3 teaspoons of blood will be drawn, this will take approximately 30 minutes.
- Visit 3 – (week 2): Before the exercise intervention resting blood pressure,

height, weight, skinfolds, waist circumference, hip circumference and submaximal exercise stress test with gas analysis will be measured by a qualified biokineticist (PhD student). The approximate duration of this evaluation will be 60 minutes.

- Visit 4-21 (Week 3 – Week 8): Engage in the exercise intervention 3X/week, which would be randomly assigned to you for six weeks. The time commitment for the endurance group will be 45 minutes. Thirty minutes will be the exercise intervention and 15 minutes will be allocated for the recovery period. The time commitment for the high intensity interval exercise group will be 120 seconds. Thirty seconds will be the warm-up, followed by 30 seconds of the exercise intervention and 30 seconds recovery.
- Visit 22 (Week 9): Post-test after the exercise intervention, which includes the blood markers, will be drawn by a qualified phlebotomist from AMPATH laboratories. A total of 3 teaspoons of blood will be drawn, this will take approximately 30 minutes.
- Visit 23 (Week 9): Post-test exercise submaximal test after the exercise intervention. A total of 60 minutes is required to complete this assessment.

ARE THERE ANY CONDITIONS THAT MAY EXCLUDE YOU FROM THE STUDY?

- Low and high-risk patients classified according to the American College of Sports Medicine guidelines,
- Underwent cardiovascular and respiratory surgery,
- Implantable pacemaker,
- Injuries making exercise on cycle difficult,
- Diagnosed cardiac, metabolic or respiratory pathology and associated symptoms,
- Participants <35 years and >49 years,
- Not medically cleared to participate in the study, and
- If you are pregnant or breastfeeding or planning to become pregnant during the study period, you may not take part in the study.

CAN ANY OF THE STUDY PROCEDURES RESULT IN PERSONAL RISK, DISCOMFORT OR INCONVENIENCE?

- Nausea and fast heart rate during high intensity interval exercise may occur. However, in a recent systematic review, which investigated the safety of high-intensity training revealed that only 13 participants from 156 had adverse acute cardiovascular responses. To minimise the risk, you will be medically screening and cleared by the physician to participate in the study,
- There is a negligible possibility of a heart attack. However, during supervised cardiac rehabilitation a retrospective study of approximately 5,000 participants over 7 years reported a low incidence of acute cardiovascular events with high intensity interval exercise (HIIE) in patients with established cardiac disease. They further postulated 1 nonfatal heart attack per 23,182 hours of HIIE, emphasising that HIIE is safe when implemented under supervision by exercise professionals. According to the American College of Sports Medicine (ACSM), staff trained with basic life support reduces the risk of a cardiac incidence up to six times. Therefore, to enhance safety of all participants in the current study, all individuals actively involved in the project will be trained in basic cardiac life support and will have a sport and exercise background,
- Venepuncture (i.e., drawing blood) is normally done as part of routine medical

care and present a slight risk of discomfort. Drawing blood may result in faintness, inflammation of the vein, pain, bruising or bleeding at the puncture site. There is also a slight possibility of infection. Your protection is that experienced personnel perform the procedures under sterile conditions. A total of 9ml of blood will be drawn before and after the exercise intervention. Therefore, a total of 18ml of blood (i.e., 4 teaspoons) will be collected over the course of the entire study, and

- If there is an unforeseen event, we will offer complementary biokinetic rehabilitation, within our scope of practice. Please note that the complementary services are limited only to biokinetic rehabilitation services.

WHAT ARE THE POTENTIAL BENEFITS THAT MAY COME FROM THE STUDY?

- Your participation in this study will contribute to medical knowledge in actively promoting time efficient exercise-based interventions aimed at reduce the risk of cardiovascular disease, disability and promote functional independence. This will ultimately improve quality of life of participants with elevated risk factors for cardiovascular disease.
- You will have access to your medical records and results. Personal feedback together with a written referral report to a medical practitioner will be provided to all participants for whom the research team detects suspected cardiovascular disease during the study.

WILL YOU RECEIVE ANY FINANCIAL COMPENSATION OR INCENTIVE FOR PARTICIPATING IN THE STUDY?

- Please note that you **will not** be paid to participate in the study.

WHAT ARE YOUR RIGHTS AS A PARTICIPANT IN THIS STUDY?

- Your participation in this study is voluntary. You have the right to withdraw at any stage without any penalty or future disadvantage whatsoever. You do not have to provide the reason/s for your decision. Your withdrawal will in no way influence your continued care and relationship with the health care team. Note that you are not waiving any legal claims, rights or remedies because of your participation in this research study.

HOW WILL CONFIDENTIALITY AND ANONYMITY BE ENSURED IN THE STUDY?

- All information obtained during the course of this study, including hospital records, personal data and research data will be kept strictly confidential. Data that may be reported in scientific journals will not include any information related to your name, surname and physical address.
- The study data will be coded so that it will not be linked to your name. Your identity will not be revealed while the study is being conducted or when the study is reported in scientific journals. All the data sheets that have been collected will be stored in a secure place. Any information that is obtained in connection with this study and that can be identified with you will remain confidential and will be disclosed only with your permission or as required by law. The information received during the project will only be used for research purposes and will not be released for any employment-related performance evaluation, promotion and/or disciplinary purposes. Data will be kept for 6 years if not published and 2 years if published. The data will be stored under lock and key and will be destroyed after 6 years.

IS THE RESEARCHER QUALIFIED TO CARRY OUT THE STUDY?

- The researcher is a qualified biokineticist and accredited exercise is medicine professional. The BTech biokinetic students will be trained by the primary researcher to administer the intervention safely and effectively.

HAS THE STUDY RECEIVED ETHICAL APPROVAL?

- This clinical study protocol has been submitted to the University of the Witwatersrand, Human Research Ethics Committee (HREC) and written approval has been granted by that committee.
- I do not have any financial or personal interests with this organisation that may bias my actions.

WHO CAN YOU CONTACT FOR ADDITIONAL INFORMATION REGARDING THE STUDY?

For the duration of the study, you will be under the care of Nivash Rugbeer, who can be contacted during office hours at Tel (012) 382-6623, E-mail rugbeern@tut.ac.za. If at any time between your visits, you feel that any of your symptoms are causing you any problems, or you have any questions during the study, please do not hesitate to contact me.

Supervisors from this department who are working on this study are:

- Dr Georgia Torres and Professor Demitri Constantinou.
- If you want any information regarding your rights as a research participant, or complaints regarding this research study, you may contact Prof. Cleaton-Jones, Chairperson of the University of the Witwatersrand, Human Research Ethics Committee (HREC), or Ms Z Ndlovu / Mr Rhulani Mkansi / Mr Lebo Moeng – administrative officers.

Telephone number; 011 717 2700/2656/1234/1252

Email address;Zanele.ndlovu@wits.ac.za

Rhulani.mkansi@wits.ac.za

Lebo.moeng@wits.ac.za.

The ethics committee is an independent committee established to help protect the rights of research participants at (011) 717 2301.

- For research information you can contact Nivash Rugbeer at Tel (012) 382-6623, E-mail rugbeern@tut.ac.za

EMERGENCY CARE

Standardised emergency procedures will be followed. The primary researcher is trained in First Aid level 2. All students who will be assisting in the exercise intervention will have a BTech qualification in sport and exercise technology. The students will be certified in basic life support. In an event of an emergency, Netcare 911 (082911) and Lifemed 911 (086 108 6911) will be called to offer emergency care and transport the participant to the nearest hospital. The response time will be 15 and 16 minutes, respectively.

DECLARATION: CONFLICT OF INTEREST

No publication prohibitions, conditions or limitations were placed on the researcher.

EMPLOYMENT VULNERABILITY

Vulnerability is an important ethical principle applicable to this project. In order to address all the potential participants' employment vulnerability, the following statement must be included in the "Anonymity and Confidentiality" section of the revised Information Leaflet: The information received during the project will only be used for research purposes and not be released for any employment-related performance evaluation, promotion and/or disciplinary purposes.

Appendix F Informed consent form for the control group

Project Title: The Effect of a Single Bout of High-Intensity Sprint Exercise Programme Compared to Traditional High-Intensity Sprint Interval Exercise and Endurance Exercise on Inflammatory Markers, Lipid Profile and Health Related Physical Fitness Measurements in Participants with Elevated Cardiovascular Disease Risk

Study leader: Mr N Rugbeer, B (Hons) Biokinetics, PGCE, M. Sport Science (Research).

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Before agreeing to participate, it is important that you read and understand the following explanation of the purpose of the study, the study procedures, benefits, risks, discomforts, and precautions as well as the alternative procedures that are available to you, and your right to withdraw from the study at any time.

1. This information leaflet is to help you to decide if you would like to participate. You need to understand what is involved before you agree to take part in this study.
2. If you have any questions, do not hesitate to ask me.
3. You should not agree to take part unless you are satisfied about all the procedures involved.
4. You may not participate in another investigational medicine research study, nor take any other investigational medicine during your participation in this study.
5. You should not have participated in an investigational medicine research study within the past 60 days.
6. If you decide to take part in this study, you will be asked to sign this document to confirm that you understand the study. You will be given a copy to keep.
7. No costs will be incurred by you for any medical tests.

WHAT IS THE STUDY ALL ABOUT?

Cardiovascular diseases refer to illnesses that affect the heart and blood vessels. Cardiovascular diseases account for 48% of the deaths globally and was the leading contributor to death in both developed and developing countries. Globally the leading cause of death is lack of cardiorespiratory fitness. Lack of attention is awarded to persons who are at increased risk of cardiovascular disease, which may be a critical point of life requiring interventions to preserve function and ability. In South Africa many people do not participate in exercise due to the lack of time availability. Therefore, the purpose current study determines the effect of a single bout of high intensity exercise required to illicit benefits in cardiovascular health. This will minimise time and improve adherence to exercise.

LENGTH OF STUDY AND NUMBER OF PARTICIPANTS

- The study will be performed in South Africa at the Tshwane University of Technology
- Approximately 72 participants will participate in this study from Tshwane

University of Technology and the Pretoria West area. All participants, who meets the inclusion criteria of the study will participate in the study. The participants will be between the ages of 30 and 49 years

- The total length of time required for your participation in this study will be a maximum of two months
- You will be asked to visit me three times per week for six weeks during the study.

WHAT WILL YOU BE REQUIRED TO DO IN THE STUDY?

If you decide to take part in the study, you will be required to do the following:

- You will first be asked questions and examined to see if you qualify for this study
- To sign this informed consent form
- To complete a Medical History administered by the physician
- Obtain medical clearance prior participation from the physician. Screening for eligibility, complete medical clearance form and medical examination by a physician, will take approximately 60 minutes to complete
- Provide consent to the Phlebotomist to draw the following blood markers (Lipoproteins, total cholesterol/ triglycerides, blood glucose and inflammatory markers)
- Allow the biokineticist to measure resting blood pressure, height, weight, skinfolds, waist circumference, hip circumference and submaximal exercise stress test with gas analysis
- Continue with your daily activities for 6 weeks, in-keeping with the inclusion and exclusion criteria of the study. Thereafter, attend the post-test days only
- The requirement that participants must abstain from exercise, caffeine and alcohol consumption during the course of the intervention, i.e., for a period of 10 weeks

At each following visit you will undergo:

- Visit 1 – (week 1): Screening for eligibility, complete medical clearance form and medical examination by a physician. This will approximately take 60 minutes.
- Visit 2 – (week 1): Before the exercise intervention, blood markers, will be drawn by a qualified phlebotomist from AMPATH laboratories. A total of 3 teaspoons of blood will be drawn, this will take approximately 30 minutes.
- Visit 3 – (week 2): Before the exercise intervention resting blood pressure, height, weight, skinfolds, waist circumference, hip circumference and submaximal exercise stress test with gas analysis will be measured by a qualified biokineticist (PhD student). The approximate duration of this evaluation will be 60 minutes.
- Visit 4-21 (Week 3 – Week 8): Engage in your normal daily activities for 6 weeks, in-keeping with the inclusion and exclusion criteria of the study.
- Visit 22 (Week 9): Post-test after the exercise intervention, which includes the blood markers, will be drawn by a qualified phlebotomist from AMPATH laboratories. A total of 3 teaspoons of blood will be drawn, this will take approximately 30 minutes.

- Visit 23 (Week 9): Post-test exercise submaximal test after the exercise intervention. A total of 60 minutes is required to complete this assessment.

ARE THERE ANY CONDITIONS THAT MAY EXCLUDE YOU FROM THE STUDY?

- Low and high-risk patients classified according to the American College of Sports Medicine guidelines,
- Underwent cardiovascular and respiratory surgery,
- Implantable pacemaker,
- Injuries making exercise on cycle difficult,
- Diagnosed cardiac, metabolic or respiratory pathology and associated symptoms,
- Participants <35 years and >49 years,
- Not medically cleared to participate in the study, and
- If you are pregnant or breastfeeding or planning to become pregnant during the study period, you may not take part in the study.

CAN ANY OF THE STUDY PROCEDURES RESULT IN PERSONAL RISK, DISCOMFORT OR INCONVENIENCE?

- Nausea and fast heart rate may occur, during the exercise stress test. To minimise the risk, you will be medically screening and cleared by the physician to participate in the study. Blood pressure, heart rate and perceived exertion will be measure at rest, at the end of every stage of the test and during recovery to further minimise the risk. Active recovery will be conducted to reduce venous pooling
- There is a negligible possibility of an angina, shortness of breath and syncope. According to the American College of Sports Medicine (ACSM), staff trained with basic life support reduces the risk of a cardiac incidence up to six times. Therefore, to enhance safety of all participants in the current study, all individuals actively involved in the project will be trained in basic cardiac life support and will have a sport and exercise background. Vital signs (blood pressure, heart rate and rating of perceived exertion) will be measured before during and after the test and an active recovery will be conducted, to minimise the listed symptoms
- Venepuncture (i.e., drawing blood) is normally done as part of routine medical care and present a slight risk of discomfort. Drawing blood may result in faintness, inflammation of the vein, pain, bruising or bleeding at the puncture site. There is also a slight possibility of infection. Your protection is that experienced personnel perform the procedures under sterile conditions. A total of 9ml of blood will be drawn before and after the exercise intervention. Therefore, a total of 18ml of blood (i.e., 4 teaspoons) will be collected over the course of the entire study
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WHAT ARE THE POTENTIAL BENEFITS THAT MAY COME FROM THE STUDY?

- Your participation in this study will contribute to medical knowledge in actively promoting time efficient exercise-based interventions aimed at reduce the risk of cardiovascular disease, disability and promote functional independence. This will ultimately improve quality of life of participants with elevated risk factors for cardiovascular disease.

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IS THE RESEARCHER QUALIFIED TO CARRY OUT THE STUDY?

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HAS THE STUDY RECEIVED ETHICAL APPROVAL?

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- I do not have any financial or personal interests with this organisation that may bias my actions.

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contact me.
Supervisors from this department who are working on this study are:

- Dr Georgia Torres and Professor Demitri Constantinou.
- If you want any information regarding your rights as a research participant, or complaints regarding this research study, you may contact Prof. Cleaton-Jones, Chairperson of the University of the Witwatersrand, Human Research Ethics Committee (HREC), or Ms Z Ndlovu / Mr Rhulani Mkansi / Mr Lebo Moeng – administrative officers.

Telephone number; 011 717 2700/2656/1234/1252

Email address;Zanele.ndlovu@wits.ac.za

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The ethics committee is an independent committee established to help protect the rights of research participants at (011) 717 2301.

- For research information you can contact Nivash Rugbeer at Tel (012) 382-6623, E-mail rugbeern@tut.ac.za

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Standardised emergency procedures will be followed. The primary researcher is trained in First Aid level 2. All students who will be assisting in the exercise intervention will have a BTech qualification in sport and exercise technology. The students will be certified in basic life support. In an event of an emergency, Netcare 911 (082911) and Lifemed 911 (086 108 6911) will be called to offer emergency care and transport the participant to the nearest hospital. The response time will be 15 and 16 minutes, respectively.

DECLARATION: CONFLICT OF INTEREST
No publication prohibitions, conditions or limitations were placed on the researcher.

EMPLOYMENT VULNERABILITY
Vulnerability is an important ethical principle applicable to this project. In order to address all the potential participants' employment vulnerability, the following statement must be included in the "Anonymity and Confidentiality" section of the revised Information Leaflet: The information received during the project will only be used for research purposes and not be released for any employment-related performance evaluation, promotion and/or disciplinary purposes.

Appendix G Ethical clearance certificate

R14/49 Mr Nivash Rugbeer

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M170239

NAME: (Principal Investigator)	Mr Nivash Rugbeer
DEPARTMENT:	Centre for Exercise Science and Sports Medicine School of Therapeutic Sciences Department of Sport, Rehabilitation and Dental Sciences Tshwane University of Technology
PROJECT TITLE:	The Effect of a Single Bout to High Intensity Sprint Exercise Programme Compared to Traditional High Intensity Sprint Interval Exercise and Endurance Exercise on Inflammatory Markers, Lipid Profile and Health Related Physical Fitness Measurements in....
DATE CONSIDERED:	24/02/2017
DECISION:	Approved unconditionally
CONDITIONS:	Title Change (27/09/2017)
SUPERVISOR:	Prof Demitri Constantinou
APPROVED BY:	Professor CB. Penny Co-Chairperson, HREC (Medical)
DATE OF APPROVAL:	03/07/2017

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary in Room 10004,10th floor, Senate House/3rd floor, Phillip Tobias Building, Parktown, University of the Witwatersrand. I/We fully understand the conditions under which I am/we are authorised to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit to the Committee. **I agree to submit a yearly progress report**. The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. in this case, the study was initially review February and will therefore be due in the month of February each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature Date

Appendix H Turnitin report