The effect of continuous moderate intensity exercise training combined with high intensity interval training on cardiovascular disease risk factors

Brendon Hugh Roxburgh

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Abstract

Cardiovascular diseases (CVD) and type 2 diabetes are a major health and economic burden on society and without intervention, incidence will continue to increase. High intensity interval training (HIIT) is emerging as a time efficient strategy for improving risk factors of CVD and type 2 diabetes; however, there is a lack of research on HIIT in sedentary, at-risk individuals. Whilst HIIT has shown superior improvement in CVD risk factors, when compared with continuous moderate intensity exercise training (CMIET), it may be unrealistic to exclusively adopt this form of training as a lifestyle change. **PURPOSE:** The purpose of this study was to compare how 12 weeks of HIIT and CMIET affected cardiorespiratory fitness (VO_{2max}), insulin sensitivity and other risk factors for CVD, in sedentary individuals at moderate risk of CVD. **METHODS:** Twenty nine sedentary subjects at moderate risk of CVD were recruited for 12 weeks of exercise training. Subjects were randomised into three groups: HIIT (n=9; 8-12 x 60 sec at 100% VO_{2max}, 150 sec active recovery), CMIET (n=10; 30 min at 45-60% oxygen consumption reserve (VO_2R)) and a sedentary control group (n=10). Participants in the HIIT group performed a single weekly bout of HIIT and four weekly sessions of CMIET, whilst the CMIET group performed five weekly CMIET sessions. Cardiorespiratory fitness, insulin sensitivity (HOMA model), blood lipids, body composition and quality of life were measured pre and post intervention. Probabilistic magnitude-based inferences were determined to assess the likelihood that the true value of the effect represented substantial change. **RESULTS:** Relative VO_{2max} increased by 10.1% in in the HIIT group (32.7 ± 9.2 to 36.0 ± 11.5 $mL \cdot kg^{-1} \cdot min^{-1}$) and 3.9% in the CMIET group (33.2 ± 4.0 to 34.5 ± 6.1 $mL \cdot kg^{-1} \cdot min^{-1}$), whilst there was a 5.7% decrease in the control group (30.0 ± 4.6 to 28.3 ± 6.5 $mL \cdot kg^{-1} \cdot min^{-1}$). It was 'unclear' if a clinically significant difference existed between the HIIT and CMIET groups. There was a decrease in insulin sensitivity for both exercising groups (HIIT: 101 ± 27.3 to 90.3 ± 29.0%; CMIET: 95.6 ± 42.6 to 84.1 ± 25.6%), with a 'possibly trivial' clinical inference between groups. **CONCLUSION:** Both exercising groups showed clinically meaningful improvements in $VO_{2max,}$ body composition (hip and waist circumference), systolic and diastolic blood pressure and total and LDL cholesterol. However, it remains 'unclear' whether one type of exercise training regimen elicits a superior CVD risk factor reduction relative to its counterpart.

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List of Abbreviations

ACLS – Aerobic Center Longitudinal Study
ACSM – American College of Sports Medicine
AMPK – Adenosine monophosphate-activated kinase
ATP – Adenosine triphosphate
ATPS – Ambient temperate and pressure saturated
BMI – Body mass index
BP – Blood pressure
CAD – Coronary artery disease
CMIET – Continuous moderate intensity exercise training
CVD – Cardiovascular disease
CO_2 – Carbon dioxide
DBP – Diastolic blood pressure
ECG – Electrocardiogram
EE – Energy expenditure
FATP-1 – Fatty acid transporter protein 1
FFA – Free fatty acid
FFM – Fat free mass
GLUT4 – Glucose transporter 4
HDL – High density lipoprotein
HIIT – High intensity interval training
HOMA – Homeostasis model assessment
HOMA2 – Homeostasis model assessment 2
HOMA2S – Insulin sensitivity
HR – Heart rate
HF_{max} – Maximum heart frequency
HR_{max} – Maximum heart rate
HR_{peak} – Peak heart rate
HRR – Heart rate reserve
IMTG – Intramuscular triglyceride
ITT – Insulin tolerance test
LDIT – Long duration interval training
LDL – Low density lipoprotein
LIIT – Low intensity interval training
METs – Metabolic equivalents
min – Minute
n/c – No change
NO – Nitric oxide
O_2 – Oxygen
OGTT – Oral glucose tolerance test
RCT – Randomised control trial
RER – Respiratory exchange ratio
RM – Repetition maximum
RPE – Rating of perceived exertion
SB – Single bout
SBP – Systolic blood pressure
sec – Second
SIT – Sprint interval training
SST – Serum-separating tube
STPD – Standard temperature and pressure dry
TC – Total cholesterol
TG – triglyceride
VE – Minute ventilation
VLDL – Very low density lipoprotein
VO_2 – Oxygen consumption
VO_{2max} – Maximal oxygen consumption
VO_2R – Oxygen consumption reserve
WHO – World Health Organisation
wk - Week

Chapter 1. The Problem

1.1. Introduction

Cardiovascular disease (CVD) is the leading cause of death in New Zealand, accounting for approximately 39% of all deaths (123). It is predicted that by 2013, 150,000 adults will suffer from type 2 diabetes (52). In the Counties Manukau region alone, CVD and type 2 diabetes contributed to 46% of the total inpatient hospitalisation costs ($101 million) in 2008 and the Auckland District Health Board estimates that CVD is responsible for $100 million in direct costs annually (1, 35). Of concern, is the fact that CVD and type 2 diabetes are largely preventable, with the 'epidemic' of type 2 diabetes and CVD, driven by the increasing prevalence of overweight and obesity (1, 122). If the problem is not addressed, by 2021, type 2 diabetes alone is predicted to cost New Zealand $1.78 billion annually, 15% of the nation's total health budget (52). Therefore, a safe and effective intervention is necessary to prevent such diseases and improve metabolic and cardiovascular health in New Zealand (1, 122). Regular exercise and physical activity has been shown to favourably improve risk factors for CVD and other diseases associated with inactivity and obesity, such as type 2 diabetes (61, 138, 147). Despite recent advances in our understanding of the beneficial effects of exercise on cardiovascular and metabolic health, the optimum exercise prescription required to elicit favourable responses remains unclear. High intensity interval training (HIIT) is emerging as a potential time efficient strategy for health promotion (64). High intensity interval training, when compared to continuous moderate intensity exercise training (CMIET), has resulted in superior improvements in cardiorespiratory fitness (VO_{2max}), insulin action and sensitivity, endothelial function, systolic blood pressure, hip and waist circumference and lipid oxidation (109, 135, 150, 164). Given 'lack of time' is one of the most common reasons for individuals not meeting minimum physical activity requirements (28), it seems logical to develop a time efficient and practical intervention.

1.2. Cardiorespiratory fitness as a risk factor for CVD

Cardiovascular diseases, such as coronary artery disease (CAD), account for approximately 5800 deaths in New Zealand each year (80). By positively modifying various CVD risk factors that contribute to the progression of the disease, the risk of mortality from heart disease can be significantly reduced (72, 73, 104). Historically, prevention and rehabilitation exercise programs have been designed with the intent to reduce excess levels of blood pressure, cholesterol, and fat mass. While hypertension, high cholesterol, and obesity undoubtedly contribute to heart disease risk, more recent research has shown that cardiorespiratory fitness may be a more powerful predictor of CVD (15, 17). One of the very first studies to explore the connection between cardiorespiratory fitness and heart health was published in 1989 in a hallmark paper; it was reported that an inverse relationship existed between cardiorespiratory fitness and risk for CVD (17), with similar findings were reported in 1996 (15). In both studies it was shown this relationship held true for individuals with no other risk factors for CVD, one risk factor for CVD, and two or more CVD risk factors.

Research published from the Aerobics Center Longitudinal Study (ACLS) has consistently shown an inverse relationship between cardiorespiratory fitness and mortality rates (14). Figure 1.1 shows data from the ACLS demonstrating that low cardiorespiratory fitness, as determined by a maximal treadmill exercise test, accounts for approximately 16% of all deaths in men and women. This number is significantly greater than all other risk factors measured, with hypertension in males being the only risk factor with a similar attributable fraction.

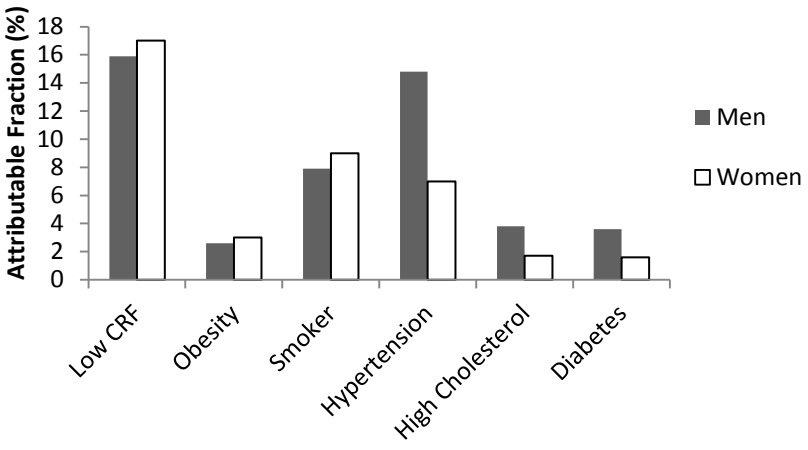


Figure 1-1: Attributable fractions (%) for all-cause deaths in 40 842 (3333 deaths) men and 12 943 (491 deaths) women in the Aerobics Center Longitudinal Study. Figure adapted from Blair (2009) (14).

In a separate study, using the same data from the ACLS, Wei and associates (159) highlighted that low cardiorespiratory fitness was as important as type 2 diabetes and other CVD risk factors, in predicting CVD mortality and all-cause mortality in overweight and obese men. When comparing relative risk for all-cause mortality, both low cardiorespiratory fitness and type 2 diabetes were equal (3.1; 95% CI, 2.5 - 3.8 vs. 3.1; 2.3 - 4.2); this was slightly higher than the relative risks for both smoking (3.0; 2.2 - 4.2), high cholesterol (2.7; 2.1 – 3.5) and hypertension (2.3; 1.7 – 2.9) (159).

Church and colleagues (39) have also illustrated the importance of cardiorespiratory fitness as a risk factor for CVD. In this cohort, 2316 men with type 2 diabetes were followed for a mean period of 15.9 years. During this time, there were 179 deaths attributable to CVD. The researchers plotted the risk of CVD against levels of cardiorespiratory fitness for three different body mass index (BMI) groups (see Figure 1-2). The figure highlights that despite being overweight and having a high BMI, if you have a moderate or high cardiorespiratory

fitness, you are at a considerably lower risk of CVD mortality, than those with the same BMI, but low cardiorespiratory fitness. Given the alarming increases in BMI observed globally over the last couple of decades, it is encouraging to know that by increasing cardiorespiratory fitness, CVD mortality can still be reduced (39). Also of significance is that the most obese men in this study, who had a moderate/high cardiorespiratory fitness level, had less than half the risk of CVD mortality, than normal weight men, with low cardiorespiratory fitness levels.

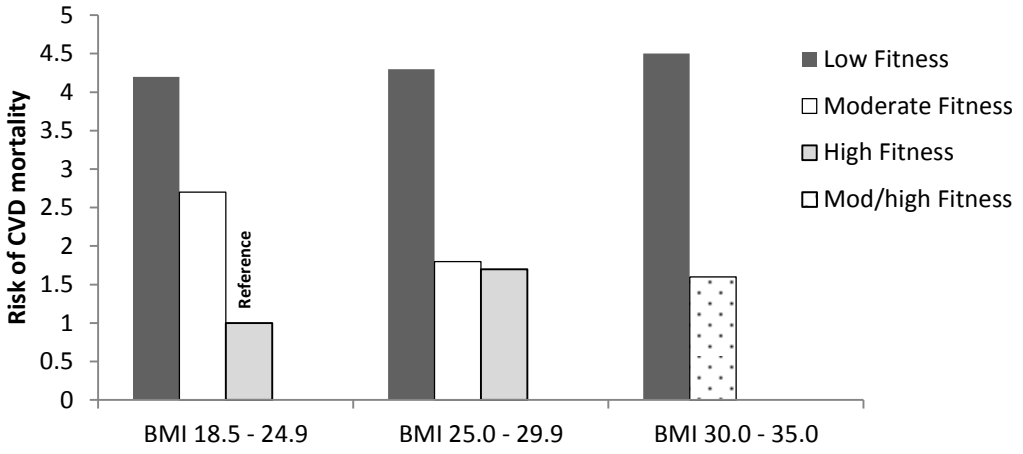


Figure 1-2: Risk of cardiovascular disease mortality by cardiorespiratory fitness and BMI ($kg \cdot m^2$) categories. Figure adapted from Church et al. (2005) (39).

An earlier study done by Blair et al. (15) ranked over 25,000 men and 7000 women by levels of cardiorespiratory fitness and their number of risk factors for CVD, and compared their risk of mortality. As shown in Figure 1-3 and Figure 1-4, those with the lowest cardiorespiratory fitness and most risk factors, have the highest risk of mortality. Interestingly, those with the highest cardiorespiratory fitness and most risk factors for CVD, have a smaller risk of mortality, compared to individuals with the lowest level of cardiorespiratory fitness and no risk factors for CVD. The authors stated that physicians should encourage sedentary patients to become physically active and improve their cardiorespiratory fitness, as it appears to protect against other CVD risk factors and other predictors of mortality (15).

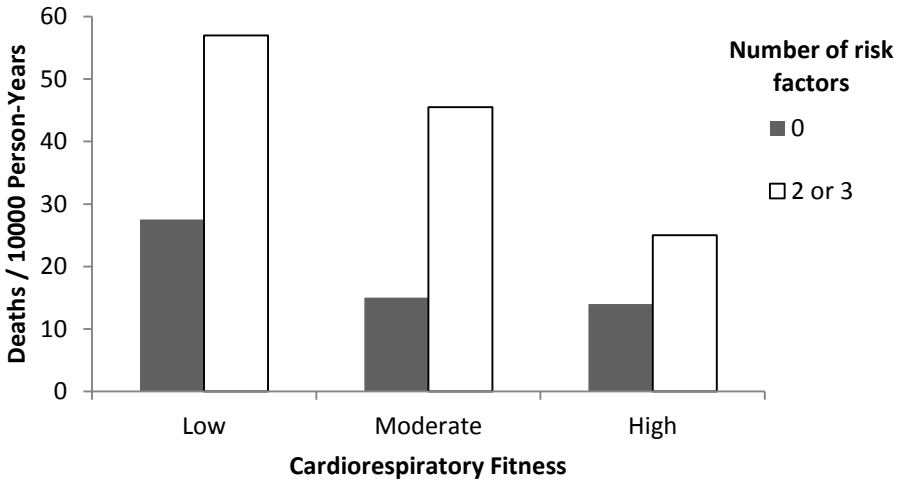


Figure 1-3: Cardiorespiratory fitness and all-cause mortality by the number of risk factors in men. Figures adapted from Blair (1996) (15).

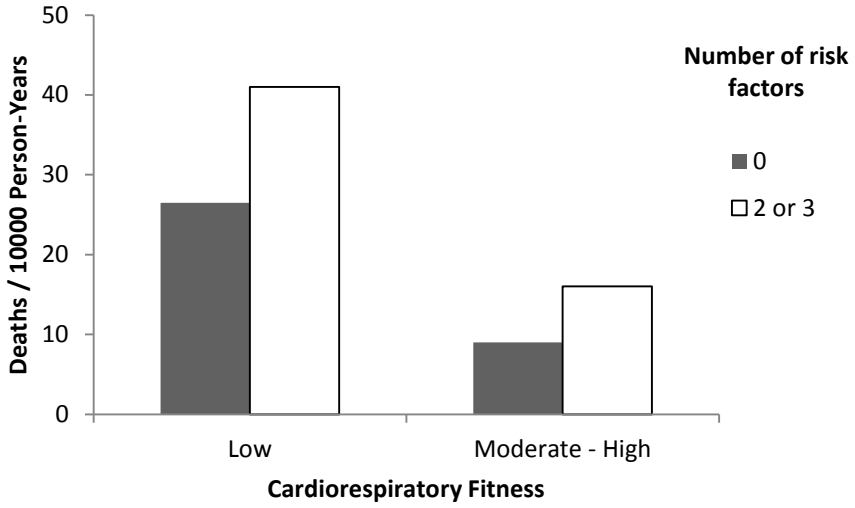


Figure 1-4: Cardiorespiratory fitness and all-cause mortality by the number of risk factors in women. Figures adapted from Blair (1996) (15).

1.3. Pathophysiology of insulin resistance

Insulin is produced in the beta cells of the pancreas and is released in response to rising blood sugar levels (95). When levels of blood sugar rise, insulin is released from the Islets of Langerhans within the beta cells of the pancreas, to stimulate the uptake of glucose from the blood into muscle and fat tissue cells, as well as initiating storage via glycogenesis (95). Glucose is transported from the blood to these cells, by the glucose transporter 4 (GLUT4). Insulin then binds to the receptors of the cell causing the GLUT4 transporters fuse together with the plasma membrane, resulting in glucose diffusing into the cell (134).

Individuals who have impaired insulin sensitivity or are insulin resistant, tend to have higher blood glucose concentrations, despite the presence of high levels of insulin (95). In this state, insulin is unable to promote the translocation of glucose from the blood, into muscle and fat cells; similarly, it is unable to suppress liver glucose production (95). Ten & Maclaren (146) define insulin resistance as an impaired ability of plasma insulin, at normal concentrations to adequately promote peripheral glucose disposal, suppress hepatic glucose, and inhibit very low density lipoprotein cholesterol (VLDL) output (146). Insulin resistance is indicated by either a blood test (fasting levels of insulin greater than 15 $\mu U/mL^{-1}$) or by an oral glucose tolerance (OGTT). The OGTT is a medical test where glucose is consumed orally and blood samples are taken at specified time intervals, to determine how quickly it is disposed from the blood. The World Health Organisation (WHO) state that blood glucose levels greater than 7.8 mmol/L (>140 mg·dL) at 120 min post-test are deemed to be hyperinsulinemic, and indicate insulin resistance (162).

A powerful risk factor for insulin resistance and cardiovascular disease is central adiposity (2, 169). Central adiposity is defined in adults as having a waist-to-hip ratio >0.9 for males or >0.85 for females (171). Abdominal adipose tissue differs to adipose tissue found in the lower body, in that it has a higher metabolic activity (75). The increased intra-abdominal fat stores lead to an increased release of free fatty acids (FFAs) into the portal circulation (13). An increase in FFAs is problematic as it leads to intramyocellular lipid accumulation in muscle cells and hepatocytes of humans. This causes hepatic insulin extraction to decrease, leading to hyperinsulinemia and eventually insulin resistance (13). This has been proposed to play a critical role in the development of insulin resistance (77). Muscle glycogen synthase activity and glycogenesis are inhibited due to the increased intracellular FFAs and their metabolites which are present in central adiposity (58, 77, 107). Insulin receptor phosphorylation is impaired by the FFAs, resulting in the impaired translocation of glucose transporter type 4 (GLUT4) to the plasma membrane in response to insulin stimulation (77).

1.4. Overview of exercise intensity on cardiorespiratory fitness

The benefits of regular exercise training largely depend on the intensity of the exercise or the amount of work performed during training (25, 76, 94). One of the first studies linking exercise intensity to changes in cardiorespiratory fitness was by Shephard (137) whom showed the most effective exercise regimes were ones with higher intensities. Numerous reviews and meta-analyses have since reaffirmed these pioneer findings (25, 142, 160). These reviews highlight training intensity as one of the fundamental training principles in exercise prescription for increasing cardiorespiratory fitness (25, 142, 160).

Interval training became a popular method for improving cardiorespiratory fitness because of its ability to perform greater volumes of high intensity exercise, consequently eliciting greater improvements (160). A study conducted in the 1970's showed that high intensity intervals (4 sessions/week; 4-5 x 2 min at 90-100% VO_{2max} ; 1 min rest) enhanced cardiac output, to a greater extent than lower intensity, continuous loads (4 sessions/week; 20 min at 70-80% VO_{2max}), contributing to an increase in cardiorespiratory fitness (44).

1.5. Overview of exercise intensity on insulin sensitivity

One of the first studies examining the effects of different exercise intensities on metabolic health demonstrated that six months at low to moderate exercise intensities (3-4 days/week, 30 min at 40% of heart rate reserve (HRR)) was insufficient at stimulating improved whole body insulin sensitivity (as determined by OGTT) (136). However, the higher intensity group (3-4 days/week, 30-45 min at 75% HRR) improved glucose clearance, as shown by a 23% reduction in insulin area under the curve during OGTT (136). Houmard et al. (86) compared the effect of vigorous (group 1: ~20 km/week at 65-80% of VO_{2max}; group 2: ~35 km/week at 65-80% of VO_{2max}) and moderate intensity exercise (group 3: ~20 km/week at 40-45% of VO_{2max}) on insulin action in 154 sedentary, overweight and pre-diabetic individuals. Training volume was measured by total exercise time with group 1 performing ~115 minutes per week and groups 2 and 3 exercising for ~170 minutes per week. Following the six month intervention, insulin sensitivity was improved significantly more in the higher volume groups (group 2: 82.7 ± 15.3%; group 3: 88 ± 18.7%), compared with the low volume group (37.6 ± 8.9%; $P < 0.05$) (86). These findings are strengthened by the fact that insulin sensitivity deteriorated in the control group (-4.0 ± 7.0%; $P < 0.05$). This is an interesting finding as it suggests that there is both an intensity and volume threshold required for eliciting favourable

metabolic adaptations. The authors stated that exercise duration is an important consideration when designing exercise interventions for improving insulin sensitivity (86). A potential limitation of this study is that the post-intervention glucose tolerance test was done only 24 hours following the last exercise bout. This makes it difficult to conclude whether it is indeed a chronic training effect, or an acute effect resulting from the last exercise training session (86).

1.6. Research Aims

The primary research aim of this study was:

1) To compare changes in VO_{2max} following 12 weeks of CMIET and CMIET combined with HIIT, in sedentary individuals at moderate risk of CVD.

The secondary research aims of this study were:

1) To compare changes in insulin sensitivity following 12 weeks of CMIET and CMIET combined with HIIT, in sedentary individuals at moderate risk of CVD.
2) To compare changes in blood pressure, blood lipids, anthropometric measures and quality of life following 12 weeks of CMIET and CMIET combined with HIIT, in sedentary individuals at moderate risk of CVD.

1.7. Experimental Hypotheses

The following experimental hypotheses were proposed:

H_0: Twelve weeks of CMIET combined with HIIT will be as effective as CMIET at improving $VO_{2max,}$ in sedentary individuals at moderate risk of CVD.

H_1: Twelve weeks of CMIET combined with HIIT will be more effective than CMIET at improving $VO_{2max,}$ in sedentary individuals at moderate risk of CVD.

H_0: Twelve weeks of CMIET combined with HIIT will be as effective as CMIET at improving insulin sensitivity, in sedentary individuals at moderate risk of CVD.

H_1: Twelve weeks of CMIET combined with HIIT will be more effective than CMIET at improving insulin sensitivity, in sedentary individuals at moderate risk of CVD.

H_0: Twelve weeks of CMIET combined with HIIT will be as effective as CMIET at improving blood pressure, blood lipids, anthropometric measures and quality of life, in sedentary individuals at moderate risk of CVD.

H_1: Twelve weeks of CMIET combined with HIIT will be more effective than CMIET at improving blood pressure, blood lipids, anthropometric measures and quality of life, in sedentary individuals at moderate risk of CVD.

1.8. Significance of this study

This study will determine the effects of a single weekly bout of HIIT, combined with CMIET in a group of sedentary individuals at risk of developing CVD. Research has shown that HIIT may be superior at improving cardiorespiratory fitness, insulin sensitivity and some cardiovascular risk factors compared to CMIET (50, 62, 82, 84, 112, 150); however, due to the high levels of motivation required to regularly perform HIIT (42, 109), it seems more realistic to combine the two types of training to promote adherence and achieve the greatest positive changes in cardiovascular and metabolic health. The authors of this study are not aware of any studies which have investigated the impact of performing HIIT one day a week, combined with CMIET on cardiorespiratory fitness or health related outcomes, such as insulin sensitivity and blood lipids. Similarly, this form of interval training is novel and is yet to be studied in an overweight and sedentary population. Recent reviews on HIIT have highlighted the need to control training volume in training studies; this protocol is unique in that keeps the exercise volume (relative caloric expenditure), frequency and duration constant in both exercise groups, with the only difference between the groups being the one HIIT session per week. With the increasing trend of medical and health bodies advocating the 'Exercise is Medicine' message, health and exercise professionals need accurate information on optimal exercise volume and intensity to prescribe HIIT safely and effectively as medicine. With research into differing training volumes of HIIT lacking, there is a need to fill this gap, which this study will help address.

Chapter 2. Literature Review

2.1. Introduction

High intensity interval training has been used for decades by athletes as a superior and rapid way of improving cardiorespiratory fitness (84, 103). High intensity interval training involves alternating between short bouts (10 sec – 5 min) of high-intensity (above anaerobic threshold) interspersed with recovery bouts (10 sec – 4 min) of low-intensity exercise or rest (103). As cardiorespiratory fitness has been shown to be a strong predictor of cardiovascular mortality, HIIT has become an attractive intervention due to its superior effects on VO_{2max}, relative to conventional endurance training (17, 84, 101, 118). Furthermore, studies suggest that the effects of HIIT appear to be superior to moderate intensity-continuous training for improving cardiac structure and function, endothelial function, quality of life and components of metabolic health such as lipid profile, glucose tolerance and insulin sensitivity (5, 120, 131, 135, 158, 164, 165). Not only is the magnitude of the improvements greater, but the time required to achieve them is less than continuous training (42, 64, 121). Given 'lack of time to exercise' is one of the most common barriers to performing regular physical activity and exercise in many populations, it seems appropriate to develop a training regimen that not only improves metabolic health and reduces the risk of chronic disease, but is also time efficient (28, 71, 127, 154).

2.2. Overview – High Intensity Interval Training

Whilst there is no universal definition for HIIT, it generally refers to repeated bouts of exercise at a supra-maximal intensity (>100% VO_{2max}) or at an intensity above anaerobic threshold (85-100% VO_{2max}) (67). High intensity interval training is traditionally associated with activities such as cycling, running or walking and differs from strength training, in that the brief, intense physical efforts don't induce or promote hypertrophy of muscle fibres (133). Depending on the exercise intensity, a single bout may last from a few seconds, up to several minutes; each exercise bout is separated by very low intensity exercise or rest, lasting from 10 seconds up to three-to-four minutes (67). The type of recovery in between intervals is an important parameter with regards to exercise prescription. Active recovery involves a recovery where the subject is still exercising at a low-to-moderate intensity (35-65% VO_{2max}), while passive recovery involves total rest and no exercise at all.

The two most prevalent forms of HIIT found in research are sprint interval training (SIT) and long duration interval training (LDIT). Sprint interval training involves a supra-maximal, all-out effort and generally lasts up to 30 seconds. A common form of this is repeated 30 second Wingate tests (31, 32, 112, 114, 130); Tabata (144) has had favourable results with 20 second maximal efforts, separated by only 10 seconds recovery. The other common form of interval training involves bouts of 3-5 minutes at an intensity just below maximum (85-95% VO_{2max}). These longer durations are separated by a recovery period of 2-5 minutes at a very low intensity or passive recovery.

In the 1930's the Swedish developed a form of interval training called 'Fartlek training' (74, 111). Fartlek is a less structured form of interval training and involves variations in intensity throughout the workout, but not necessarily at set intervals. Fartlek training sessions can last anywhere between 30 minutes to 2 hours. Athletes are instructed to follow their intuition and do what they were capable of at the moment. The approach became very popular following the setting of several new world records by Swedish athletes who had adopted the regimen. During the 1940's athletics took 'a back seat' to World War 2, but running great, Emil Zatopek rekindled people's interest after winning 3 long distance running gold medals at the 1952 Helsinki Olympic Games (74). His training regimen involved performing a high volume of intervals (40-60 repetitions of 400 m), running at a moderate-to-high intensity, with a short recovery interval in between (74, 111).

Whilst interval training was being practiced earlier, the first research investigating its effectiveness was not performed until the early 1950's. Christenson (38) took two well-trained subjects and compared the effects of continuous running on a treadmill at 12.4 miles/hour and intermittent running (30 sec run: 30 sec rest) at the same speed. When running continuously, both subjects fatigued after approximately four minutes; each achieved VO_{2max}, high blood lactate levels and high heart rates. When the subjects ran intermittently, blood lactate increased only slightly, oxygen consumption was lower and heart rate was constant (140-150 beats·min^{-1}). From his findings, he concluded that interval training was a more economical way of work, more demanding on the circulatory and respiratory system and more likely to promote efficient chemical reactions (38).

During the 1960's, a number of studies were done investigating interval training; in 1968, Ekblom, Astrand & Saltin et al. (55) conducted a 16 week training study where all subjects alternated between SIT, LDIT and cross country running, resulting in a 16% increase in VO_{2max}. Roskamm (132) showed that two forms of interval training elicited a greater increase in 'maximum work performance', compared to CMIET and standard military training. Cunningham & Faulkner (43) also conducted a six week training study, with participants alternating between SIT and CMIET, five times a week. Following the training, net oxygen uptake had increased 48% and run time increased 23%. Interval training was also examined in high risk groups during this time. Whilst there were limited details published regarding the specific interval protocol, Kasch & Boyer's (92) intervals stressed the myocardium to a 'slight hypoxic state', in individuals with ischemic heart disease. Following the six months training, the average increase in relative VO_{2max} was 54% (19.9 vs. 30.6 $mL \cdot kg^{-1} \cdot min^{-1}$). The subjects also decreased resting heart rate (79 $beats \cdot min^{-1}$ vs. 67 $beats \cdot min^{-1}$) and blood pressure (134/86 vs. 125/80 mmHg), with seven subjects lowering their diastolic blood pressure by an average of 11mmHg.

Despite the benefits of HIIT being identified 60 years ago, there has been a lack of randomised control trials (RCTs) to further strengthen the evidence for HIIT being a safe and effective form of exercise (43, 92, 132). Health organisations advocate for moderate intensity exercise as they believe adherence would be greater, compared with higher intensity exercise, resulting in greater health outcomes overall (125). Similarly, HIIT was considered only safe for athletes with high levels of aerobic and anaerobic fitness, strengthening the rationale for health and exercise professionals to encourage CMIET to the general and diseased populations (8, 161). Research on HIIT is now more popular, with a number RCTs

confirming that HIIT is a safe and effective form of exercise, including people with CVD (120, 131, 158, 165).

2.3. Changes in cardiorespiratory fitness following HIIT in sedentary & recreationally trained individuals

2.3.1. Long duration intervals – Sub-maximal intensity

One of the earlier and more comprehensive HIIT studies was conducted by Hickson et al. (84). At this time, it was largely believed that several years of endurance training was required for a sedentary individual to achieve an aerobic capacity of a highly trained athlete (VO_{2max} = >60 mL·kg^{-1}·min^{-1}). The eight healthy subjects ranged from very sedentary (VO_{2max} = 22.7-26.4 mL·kg^{-1}·min^{-1}) to recreationally active (VO_{2max} = 45-53 mL·kg^{-1}·min^{-1}). The ten week training program involved alternating each day between biking and running, six days a week. The bike protocols involved six bouts of cycling (five minutes duration), at 100% of their VO_{2max}, followed by a 2 minute recovery at 50-60% VO_{2max}. The running protocol involved running for 30-40 minutes as fast as they could (84). Within the first week, VO_{2max} had increased on average by 5% ($P < 0.05$). The total average increase over the 10 week period was 44% or 16.8 mL·kg^{-1}·min^{-1} ($P < 0.05$). As expected, the two sedentary individuals increased their aerobic capacity the most with an increase of 52% & 53% respectively; one of the subjects continued with the protocol for an additional three weeks and increased his aerobic capacity further to a total increase of 77% (22.7 to 42.8 mL·kg^{-1}·min^{-1}). One of the recreationally trained athletes increased his VO_{2max} from 45 mL·kg^{-1}·min^{-1} to 67.2 mL·kg^{-1}·min^{-1}; the later value being similar to highly trained endurance athletes (84).

Due to the research design including both HIIT and high intensity continuous exercise, it is difficult to conclude whether these changes in VO_{2max} are solely the result of HIIT.

Franch et al. (62) compared how two different types of HIIT and continuous training influenced aerobic capacity in recreational runners (n =36; VO_{2max} = 54.8 ± 3.0 $mL \cdot kg^{-1} \cdot min^{-1}$). The participants were divided equally into three groups; a SIT group (30-40 x 15 sec at 20.4 km/h, 15 sec rest), a LDIT group (4-6 x 4 min at 16.6 km/h, 2 minutes inactive rest), or continuous running (15 km/h, ~26 min) (62). After the six week training period, aerobic capacity increased the most in the LDIT (6%; $P < 0.0001$) and continuous training (5.9%; $P < 0.0001$) groups, compared with the short interval group (3.6%; $P < 0.01$). Time to exhaustion at 85% VO_{2max} also increased significantly more in the LDIT group compared to the SIT group (67%; $P < 0.0001$ & 65%; $P < 0.001$) (62). Unfortunately, training volume was not controlled in this study making it difficult to compare the relative effects of SIT and LDIT on cardiorespiratory fitness.

One of the more comprehensive training studies, outlining the benefits of LDIT was done by Helgerud et al (82). The authors of the study compared the effects of two differing traditional aerobic protocols and two differing HIIT protocols and how they influenced VO_{2max}. Forty healthy men (VO_{2max} = 57.4 ± 6.5 $mL \cdot kg^{-1} \cdot min^{-1}$) were randomly assigned to one of four groups; a continuous moderate intensity group (45 min at 70% HR_{max}), continuous training at lactate threshold (24.25 min at ~85% HR_{max}), short intervals (47 x 15 sec at 90-95% HR_{max}, 15 sec recovery at 70% HR_{max}) or long intervals (4 x 4 min 90-95% HR_{max}, 3 min recovery at 75% HR_{max}). The training regimens lasted a total of 8 weeks, consisting of 3 sessions per week. Relative VO_{2max} increased in both the short interval (5.5%) and long interval groups

(7.2%), but no change was observed in either continuous training groups. These improvements in VO_{2max} are largely due to improvements in stroke volume, with the greatest changes observed in the longer intervals (144.2 ± 21.9 vs. 159.2 ± 21.9 $mL \cdot beat^{-1}$; $P < 0.01$), compared to the shorter (148.7 ± 18.3 vs. 162.7 ± 20.7 $mL \cdot beat^{-1}$; $P < 0.05$) (82). Blood volume, red blood cell mass and haemoglobin did not increase in any of the groups, suggesting blood volume and oxygen-carrying capacity are not responsible for the changes in VO_{2max}. The authors concluded, that due to the shorter intervals being difficult to administer and the superior results observed with longer intervals, longer intervals are recommended for improving VO_{2max} (82). It should be noted that the participants in this study had a high level of fitness before the study.

A meta-analysis has shown that individuals with high a VO_{2max} (>55-60 $mL \cdot kg^{-1} \cdot min^{-1}$) are less likely to improve endurance performance with an increase in sub-maximal training volume (110). It is hypothesized that highly trained athletes reach a plateau in the metabolic adaptations that result from sub-maximal endurance training. The author did note that highly trained individuals tended to respond better to HIIT, compared to continuous training (110).

2.3.2. Sprint interval training

MacDougall et al. (112) examined the effects of supra-maximal (absolute intensity not specified) HIIT on aerobic capacity. Twelve recreationally trained individuals (VO_{2max} = 51 ± 1.8 mL·kg^{-1}·min^{-1}) performed three HIIT sessions a week (4-10 x 30 sec all-out cycle sprints, 2.5-4 min active recovery at 25 watts) over seven weeks. Maximal oxygen consumption increased from 51 ± 1.8 to 54.5 ± 1.1 mL·kg^{-1}·min^{-1}. Tabata et al. (144) took recreationally trained subjects (n=14; VO_{2max} = ~50 mL·kg^{-1}·min^{-1}) and exercised them at levels well above their VO_{2max}. The HIIT group performed 8 x 20 second intervals at 170% VO_{2max} (10 sec rest, 5 days/week) and the continuous training group exercised for 60 minutes at 70% VO_{2max} (5 days/week) for a period of six weeks (144). The greatest gains in aerobic capacity were seen in the HIIT group (15% vs. 9.4%; $P < 0.05$) (144).

Burgomaster and associates (31) compared the effects of six weeks SIT and CMIET on metabolic training adaptations. The 'untrained' men and women (n=20; VO_{2max} = 41 mL·kg^{-1}·min^{-1}) were split into two groups; the SIT group performed 4-6, 30 second Wingate tests (mean power ~500 watts) with 4.5 minutes active recovery (30 watts) between bouts, three times per week. The CMIET group cycled continuously for 40-60 minutes at ~65% VO_{2max} (mean power ~150 watts), five times per week (31). The time commitment each week was approximately 1.5 hours in the SIT group compared with 4.5 hours per week in the CMIET group. Similarly, the total training volume was ~225 kJ compared with ~2250 kJ per week in the CMIET group. After three weeks of training, the SIT group had increased their VO_{2max} significantly more than the CMIET group (44 ± 2 vs. 42 ± 2 mL·kg^{-1}·min^{-1}; $P < 0.05$).

Interestingly, in the following three weeks, VO_{2max} remained unchanged in the SIT group, but increased an average 3 $mL \cdot kg^{-1} \cdot min^{-1}$ in the CMIET group (31).

Similar to the previous study, McKenna et al. (114) utilized the '30 second Wingate' model and produced successful results. Eight healthy males (VO_{2max} = 47.1 ± 2.6 $mL \cdot kg^{-1} \cdot min^{-1}$) performed three sessions per week of 4-10, 30 second 'all-out' sprints (absolute intensity not specified) on a cycle ergometer, with a recovery time which progressively decreased to 3 minutes by week 5. Maximal oxygen consumption was significantly increased following the seven weeks of SIT training (47.1 ± 2.6 vs. 53 ± 2.6 $mL \cdot kg^{-1} \cdot min^{-1}$; $P < 0.05$) (114). Similarly, Harmer and colleagues (79) reported that SIT (4-10 all out cycle sprints, 3-4 minutes rest, three days/week, seven weeks) increased VO_{2max} by 7% (3.79 ± 0.16 vs. 4.05 ± 0.15 $L \cdot min^{-1}$; $P = 0.07$) (79).

Whilst there is considerable evidence that short intervals at a supra-maximal intensity have very favourable effects on VO_{2max} (31, 79, 112, 114, 130, 144), Little et al. (109) point out that it might not be suitable for general and clinical populations (e.g obese and older individuals). These types of intervals require a high level of subject motivation to maintain the 'all out' intensity and due to the nature of the protocol, it can often leave subjects feeling nauseas and in discomfort (42, 109). Unfortunately, there is a lack of data on adherence rates to interval training. However, King et al. (97) did show that less frequent (3 sessions/week, 40 min), high intensity exercise (73-88% of HR_{peak}) was associated with greater long-term adherence, compared with a high frequency (5 sessions/week, 30 min), low intensity (60-73% HR_{peak}) program. Coyle (42) suggests that before this type of training is adopted in a diseased population, a clinical application of SIT needs to be developed. Furthermore, the incidence of

injury with such a protocol needs to be assessed and whether swimming and/or cycling are the ideal modalities, compared with running (42).

2.3.3. Optimal training volume for changes in cardiorespiratory fitness

One of the unanswered questions surrounding interval training is what the optimal volume and the minimum training volume are, to improve cardiorespiratory fitness. Many HIIT studies have involved study durations of two-to-six weeks, examining whether this is sufficient stimulus for metabolic training adaptations. Similarly, a number of these studies have short training durations, with training protocols requiring as little as 300kJ of very intense exercise per week (29-32, 66). It remains unclear, whether cardiorespiratory fitness can be increased with very low volumes of HIIT or what the optimal prescription is, to get the largest increases

Rodas et al. (130) had five moderately active individuals performing sprint intervals on a cycle ergometer (8-12 x 15 sec at >100% VO_{2max}, 45 sec rest) each day, for two weeks. The mean increase in VO_{2max} was 11.3% ($P < 0.05$) (130). An earlier study conducted by Burgomaster et al. (32), also examined SIT's effect on VO_{2max}. The duration in this study was two weeks and involved three exercise sessions each week, where subjects (n=7; VO_{2max} = 45 ± 3.7 $mL \cdot kg^{-1} \cdot min^{-1}$) were asked to perform 4-7 'all out' 30 second Wingate cycle tests, separated by 4 minutes of active recovery (<30W). As well as re-examining VO_{2max} after the training study, functional endurance capacity was measured by measuring time to volitional fatigue cycling at 80% of their HR_{max}. Following the six training sessions, cycle endurance time had increased by 100% (51 ± 11 vs. 26 ± 5 min; $P < 0.05$); The validity of these findings

is enhanced due to the fact that the control group showed no change following no training intervention (32).

The issue with many of the SIT studies is that the exercise interventions are not practical and are unlikely to be adapted in to an individual's lifestyle. Coyle et al. (42) raised concerns that the 'all-out', supra-maximal type intervals may not be safe, practical and/or tolerated by certain individuals, especially sedentary and overweight individuals. With this in mind, Little et al. (109) studied the effects of a more practical two week SIT intervention in men (n=7; VO_{2max} = 46 ± 2 $mL \cdot kg^{-1} \cdot min^{-1}$). In an effort at matching the stimulus of the supra-maximal interval protocols, the intensity was reduced approximately 50%, but the duration of each interval was increased to compensate (109). Earlier work done by Dudley et al. (53) showed that simply matching work using a lower intensity, but increasing duration may not elicit the same training effect. To counter this, Little et al. (109) doubled the number of intervals compared to those of Burgomaster et al. (32), which the protocol is modified from. The protocol for this study involved six training sessions over two weeks, but adopted a more conservative training protocol (109). Each training session involved 8-12, 60 second intervals at 100% of peak power output achieved in testing (mean peak power = 355 ± 10 W), separated by 75 seconds of active recovery at 30 W (109). Rather than retesting cardiorespiratory fitness after the trial, they measured the training effects on functional exercise performance. The subjects completed a 50 kJ & 750 kJ cycling protocol, where the subject cycled as fast as possible until they achieved 50 kJ and 48 hours later, 750 kJ. Results showed there was an 11% ($P < 0.05$) improvement in time to complete 50 kJ & 9% ($P < 0.05$) improvement in time to complete 750 kJ. A possible limitation with this study is the high cardiorespiratory fitness (VO_{2max} = 46 ± 2 $mL \cdot kg^{-1} \cdot min^{-1}$) in the subjects before the

intervention. In light of the positive results observed in healthy individuals in this study, future research should focus on practical HIIT interventions which can be applied to diseased individuals or individuals at-risk of disease.

Talanian et al. (145) has provided further evidence that very intense SIT is not required to elicit improvements in $VO_{2max,}$ in a short period of time. The researchers took eight healthy women (VO_{2max} = 36.3 ± 3.7 $mL \cdot kg^{-1} \cdot min^{-1}$) who performed seven HIIT sessions, over two weeks. Each session involved ten, four minute cycling bouts at approximately 90% VO_{2max}, separated by two minutes rest. After the seven sessions, VO_{2max} increased an average 13% (36.3 ± 3.7 vs. 40.9 ± 3.2 $mL \cdot kg^{-1} \cdot min^{-1}$) (145).

Whilst a number of these SIT studies lasting two weeks showed an improvement in endurance performance, very few showed an improvement in VO_{2max} (29, 30, 66). This suggests that peripheral adaptations were responsible for the improved exercise capacity. Rodas et al. (130) reported an increase in VO_{2max} with two weeks of SIT; however the subjects performed the training each day, making the training volume considerably greater. Little et al. (109) & Talanian et al. (145) also showed the improvement in VO_{2max}, but they performed longer duration intervals, thus increasing the training volume. These findings suggest that a minimum volume of HIIT may be necessary to increase VO_{2max}.

2.4. Changes in cardiorespiratory fitness following HIIT in overweight/high-risk individuals

Due to the favourable results of HIIT in a large number of studies using healthy individuals, more recent attention has been on using HIIT in higher-risk populations. Despite concerns surrounding the appropriateness of SIT for overweight/obese and higher risk populations, Whyte et al. (164) investigated whether similar results would be observed as those seen in healthy individuals (31, 79, 112, 114, 130, 144). Ten sedentary men with a BMI greater than 30 $kg \cdot m^2$ (VO_{2max} = 32.8 ± 1.0 $mL \cdot kg^{-1} \cdot min^{-1}$) performed six SIT sessions over two weeks. Each session consisted of 4-6 'all-out', 30 second sprints against a constant force set at 0.065 kg/kg^{FFM}, separated by a 4.5 minutes cycling at 30W. Maximal oxygen consumption was increased by 9.5% (32.8 ± 1.4 vs. 35.9 ± 1.6 $mL \cdot kg^{-1} \cdot min^{-1}$; P = 0.015). Despite these results, the authors suggested SIT may only be appropriate for younger individuals without cardiovascular disease, and should be commenced after an initial period of moderate intensity activity to reduce the risk of injury. As mentioned earlier, SIT requires high levels of motivation, and it remains unclear whether individuals can attain the observed benefits from this study if performing SIT unsupervised (164).

The effect of LDIT on cardiovascular health in sedentary and obese men was studied by Schjerve et al. (135). Forty subjects (VO_{2max} = 24.7 ± 1.53 $mL \cdot kg^{-1} \cdot min^{-1}$) were randomized to either LDIT (4 x 4 min at 85-95% HR_{max}, 3 min active recovery at 50-60% HR_{max}), CMIET (47 min at 60-70% HR_{max}) or strength training (4 sets, 5 reps at 90% of 1 repetition maximum (1RM) leg press & 30 reps of abdominal and back exercises). Maximal oxygen consumption in the LDIT group increased twice as much as continuous and strength training (33% vs. 16% & 10%; $P < 0.01$) (135).

Long duration interval training has been studied in individuals with metabolic syndrome to examine its effect on CVD risk factors and cardiorespiratory fitness. Metabolic syndrome is a cluster of cardiovascular risk factors, which affects 32% of Maori and 39% of Pacific Islanders in New Zealand and increases the risk of death from coronary heart disease (63, 78, 89, 102). Tjonna and associates (150) took 32 patients with metabolic syndrome (VO_{2max} = 34 $mL \cdot kg^{-1} \cdot min^{-1}$) and randomized them into either HIIT, CMIET or a control group. The HIIT training protocol involved four intervals of either walking or running at gradient on the treadmill at an intensity equivalent to 90% of maximum heart frequency (Hf_{max}) for 4 minutes, with 3 minutes active recovery at 70% of Hf_{max}. To equalise caloric expenditure between the two groups, the CMIET group exercised for 47 minutes at 70% of Hf_{max}. Both groups exercised three times per week, but the point of difference with this study was its prolonged, 16 week duration. The largest increase in cardiorespiratory fitness was seen in the HIIT group, which increased 35%, compared to 16% in the continuous training group ($P < 0.01$) (150).

2.4.1. Physiological and metabolic adaptations to HIIT

Several physiological changes are thought to be responsible for the superior improvements in cardiorespiratory fitness following HIIT in sedentary and recreationally trained individuals. Following HIIT, the ability to regenerate Adenosine Triphosphate (ATP) through aerobic and anaerobic pathways is enhanced, which is achieved by an increased expression of type I muscle fibres, capillarisation and greater oxidative enzyme activity (37, 83, 112, 130, 139, 144). Although somewhat paradoxical, there is a significant increase in the percentage of type 1, slow twitch muscle fibres following SIT and LDIT; this increase in slow twitch fibres, is matched with a decrease in fast twitch, type 2b fibres (108, 140). HIIT is performed intermittently and still requires a significant oxidative requirement, consequently, the slow twitch fibres are utilised more than the fast twitch fibres, whilst replenishing depleted phosphocreatine stores and removing accumulated lactate, during recovery periods (108). Whilst there are possible limitations when using muscle biopsies to represent global changes in muscle, the authors stated that they were vigilant to standardize the muscle biopsy technique to reduce the risk of bias (108). This meant all biopsies were done by the same person, biopsies were performed on the same leg and repeat biopsies taken as close to the original as possible (within 2-3 cm).

An increased oxidative enzyme activity appears to be the most common adaptation to HIIT in sedentary and moderately trained individuals. Changes in the maximal activities of 'marker' enzymes such as citrate synthase indicate an increase in muscle oxidative potential (88, 112, 124, 130); Burgomaster et al. (32) have shown that six sessions of 4-7, 30 seconds, 'all-out' cycle sprints, increase citrate synthase as much as 6-7 days of traditional endurance exercise training (2 hours/day, ~65% VO_{2max}) (36, 141). In a separate study, MacDougall (112)

mentions that training at an intensity greater than VO_{2max}, may be a more important component, than the volume of training to stimulate an increase in muscle oxidative potential. As detailed earlier, Gibala et al. (66) utilised a SIT protocol which had a total exercise volume approximately 90% lower than the endurance group; of significance was the relatively similar adaptations in skeletal muscle oxidative capacity between both exercise groups. This suggests that SIT may be a time-efficient way to elicit changes in skeletal muscle oxidative capacity that are normally associated with endurance training (66).

High intensity interval training has been shown to improve VO_{2max} by eliciting favourable changes in central and peripheral factors (46). Daussin et al. (46) investigated how CMIET & HIIT alter components of VO_{2max} in sedentary males and females (n=10; VO_{2max} = 26.3 ± 1.6 $mL \cdot kg^{-1} \cdot min^{-1}$). This study was unique because it utilised a cross-over study design and both training protocols were designed so they expended the same amount of calories in each session. Subjects were split in to either HIIT (3 days/week, 8 weeks, 4-5 x 4 min at lactate threshold – 1 min 90% VO_{2max}) or 20-35 minutes of CMIET (~61% VO_{2max}), then deconditioned for three months and then did the other protocol. A greater increase in VO_{2max} was observed following interval training (26.3 ± 1.6 vs. 35.2 ± 3.8 $mL \cdot kg^{-1} \cdot min^{-1}$; $P < 0.01$), compared to the continuous training (27.9 ± 2.2 vs. 30.3 ± 2.4 $mL \cdot kg^{-1} \cdot min^{-1}$; $P = 0.07$). Interestingly, cardiac output was only altered following HIIT (17.5 ± 1.3 to 19.5 ± 1.8 $L \cdot min^{-1}$; $P < 0.01$) due to changes in maximal heart rate (165 ± 5 vs. 172 ± 4 $beats \cdot min^{-1}$; $P < 0.05$) and maximal stroke volume (107 ± 7 vs. 113 ± 8 $mL \cdot beat^{-1}$; $P < 0.05$); no change was observed following CMIET. Aterio-venous oxygen difference was calculated indirectly via the Fick equation and had improved following both training regimens (46); the changes were

slightly greater in the CMIET group (11 ± 0.8 vs. 12.7 ± 1.0 mL·100mL^{-1}; $P < 0.01$), compared with HIIT (11 ± 0.9 vs. 12.1 ± 1.0mL·100mL^{-1}; $P < 0.05$).

The findings Daussin et al. (46) in healthy individuals are similar to those reported by Trilk and colleagues (153) in overweight/obese women. Twenty eight sedentary women were randomly assigned to a control group or a SIT group whom performed a modified protocol from Burgomaster et al. (32). The four week training regimen involved 4-7 bouts per session of cycling 'all-out' (no absolute intensity given) against a fixed resistance of 0.05 kg/kg of body weight for 30 seconds, separated by 4 minutes of active recovery, three times a week. Following the four weeks training, heart rate was significantly lower (-11 beats·min^{-1} or -8.1%; $P < 0.001$) and stroke volume significantly higher (9.7 mL·beat^{-1} or 11%; $P < 0.001$) whilst cycling at 50% VO_{2max}. These adaptations corresponded with a 12% improvement in cardiorespiratory fitness (2.53 mL·kg^{-1}·min^{-1}; $P < 0.05$) (153). In a separate study, it was shown that following 12 weeks of interval training, several mechanisms were responsible for the larger stroke volume; end diastolic volume and blood volume were both increased, but no change in myocardial contractility was observed during maximal exercise (157). The increased stroke volume, as well as increased para-sympathetic and decreased sympathetic stimulation of the sino-atrial node and altered intrinsic firing rate of the sino-atrial node are all mechanisms responsible for reducing the exercising heart rate (149).

Of interest is the similar changes in carbohydrate metabolism following endurance training and SIT (29, 30). The changes reported in both training groups included: increased glycogen content, a reduced rate of glycogen utilisation and increased total muscle GLUT4 content (29, 30). The two week long SIT protocols were insufficient stimuli to alter selected markers of

lipid metabolism. However, when Burgomaster and associates (31) examined mitochondrial markers for skeletal content following six weeks of SIT and endurance training, pyruvate dehydrogenase E1α protein content and β-hydroxyacyl-CoA dehydrogenanse, markers of carbohydrate and lipid oxidation, had similar increases in both training groups at the end of the study (31). Whilst two weeks of SIT was insufficient to influence lipid metabolism, Talanian et al.'s (145) long duration interval study, of equal duration was able to increase β-hydroxyacyl-CoA dehydrogenanse and other markers of lipid metabolism. Similarly, whole-body fat oxidation was increased by 36% during a 60 minute cycling test at 65% of pre-training VO_{2max} (145)

2.5. Changes in insulin sensitivity following HIIT

2.5.1. Long duration intervals – Sub-maximal intensity

In Tjonna et al's (150) study, as described earlier, longer duration intervals at a sub-maximal intensity were superior for improving VO_{2max}, compared to CMIET. The authors of this study also compared the training effect on insulin action by examining phosphorylation of the anti-insulin receptor antibody in the presence of insulin (150). In this study, the LDIT improved insulin action more than CMIET with a 2.5-15 fold increase ($P < 0.001$) in insulin stimulated receptor phosphorylation. The homeostasis assessment model (HOMA), which is used to estimate insulin sensitivity and beta cell function in the pancreas, showed a significant increase in insulin sensitivity (62.2 ± 8.0 vs. 77.2 ± 4.9%; $P < 0.05$) and beta-cell function (76.8 ± 12.6 vs. 97.0 ± 9.2%; $P < 0.05$) following HIIT, whilst insulin sensitivity decreased in the continuous (64.4 ± 5.7 vs. 50.2 ± 4.9%; $P < 0.05$) and control groups (60.0 ± 7.9 vs. 59.3 ± 8.2%; $P < 0.05$). An improvement in insulin action in the muscle is likely to be

responsible for these changes, as exercise decreases intracellular accumulation of triglycerides and promotes fatty acid oxidation (21). Horowitz (85) believes that following exercise, instead of fatty acid intermediates accumulating in the skeletal muscle, which can induce insulin resistance, the long-chain fatty acyl-CoA are taken up by the skeletal muscle and oxidised or stored as intramyocellular triglycerides (IMTG) (81). The fatty acid intermediates activate pro-inflammatory pathways that are known to impair insulin action within skeletal muscle (167). However, regular exercise may help protect against insulin resistance by serving as a more 'favourable metabolic fate' for fatty acids entering the muscle cell, rather than the formation of fatty acid intermediates. This theory, leads to the possibility that the benefits of exercise on insulin sensitivity are not the result of adaptations gained from months of training, rather the effect of the last exercise session (85).

To explore skeletal muscle lipid metabolism further, Tjonna and associates (150) also researched how HIIT altered fatty acid transporter protein 1 (FATP-1) activity. The transporter protein FATP-1 is responsible for the uptake of fatty acids to the muscle and may be linked with lipid storage; if FATP-1 activity can be reduced, there is less risk of intramuscular lipid accumulation and consequently, reduced risk of insulin resistance (69). There was a three-to-four fold ($P < 0.05$) decrease in FATP-1 activity, which was only observed in the HIIT group; in previous research this has been linked with the prevention of fat-induced insulin resistance (96, 150).

Borghouts et al. (23) has also examined the effects of four weeks of LDIT on insulin sensitivity in 18 young and healthy, but 'untrained' subjects (VO_{2max} = 43.1 ± 5 $mL \cdot kg^{-1} \cdot min^{-1}$). One group performed 12, three minute intervals at 80% of pre-training W_{max} (mean power

output: 209 ± 32 watts), separated by two minutes recovery at 40% of pre-training W_{max}. The comparison group also performed the same protocol, but their intensities were at 40% or pre-training W_{max} (mean power output 92 ± 16 watts), whilst recovery was at 20% of pre-training W_{max}. The researchers performed an insulin tolerance test (ITT) and the data from this allowed them to examine the decline in blood glucose, relative to time and calculate an insulin sensitivity index (IS_{index}) via the slope of a linear regression line. Not surprisingly, given the lack of training stimulus in the low intensity group, improvements in VO_{2max} and insulin sensitivity were greater in the high intensity group ($P < 0.05$) (23). The mean IS_{index} was similar in the high intensity and low intensity groups before training (-0.1898 ± 0.058 vs. -0.1892 ± 0.045), however after training the only significant increase was seen in the HIIT group (-0.2358 ± 0.051; $P < 0.005$). Similarly, blood glucose values during the ITT were significantly lower after HIIT, compared to low intensity. Although the specific mechanism for the improved glucose uptake in this study is unknown, it is likely that there is a beneficial effect on insulin expression and/or GLUT4 activity within the skeletal muscle (23, 48). The protocols were designed so duration and frequency were matched, but given the exercise intensities were so varied, the total volume of the high intensity group was nearly three-fold greater than that of the low intensity group (9216 vs 3643 kJ); this makes it difficult to determine whether these findings are the consequence of an altered exercise intensity, total energy expenditure or a combination of both (23).

2.5.2. Sprint interval training

There has been greater attention placed on SIT and its effect on insulin sensitivity, compared to LDIT. Many of these studies have adopted training protocols from Burgomaster et al. (32), where exercise sessions involve 4-6, 30 second, 'all-out' Wingate sprints against a resistance of 0.5-0.75 kg/kg of body weight. As detailed previously, Whyte et al. (164) examined whether two weeks of SIT is sufficient to elicit improvements in cardiorespiratory fitness and health related outcomes in sedentary overweight/obese men. In this training study, insulin sensitivity index (as defined by Matsuda et al. (113)) increased by 23.3 % ($P < 0.05$) and fasting insulin decreased by 24.6% (10.42 ± 1.91 vs. 7.86 ± 1.38 $mU \cdot L^{-1}$; $P < 0.05$), 24 hours post-intervention, compared with baseline. However, when these values were measured 72 hours post-intervention, these values did not differ significantly from baseline (164). The magnitude of the changes in this study are similar to those observed following 6-8 weeks of continuous moderately intensity training in untrained and moderately trained individuals (9, 126, 144). Whilst there was a modest improvement in insulin sensitivity following the training protocol, this was lost at the 72 hour post-intervention follow up; this is similar to other exercise interventions which have reported similar transient changes in insulin sensitivity (26, 33). However, it is inconclusive whether these findings are an acute effect of exercise. Given that activation of adenosine monophosphate-activated kinase (AMPK) increases glucose uptake in to skeletal muscle via the translocation of GLUT4 following four, 30-second cycle sprints, this is likely to be an acute effect, rather than a training adaptation (68, 152).

An interesting physiological response to SIT is the degree of glycogen depletion. It has been shown that 2-4, 30-second sprints (~40-80 kcal) can deplete muscle glycogen concentrations

by 30-45%, which is equivalent to approximately 45-90 minutes of continuous moderate intensity exercise (20, 68, 100). This is relevant as the reduced glycogen concentration activates glycogen synthase, stimulating the translocation of GLUT4 and consequently increasing glucose uptake in to the muscle (90). The metabolic changes observed with relatively low total energy expenditure may be in part due to the rapid glycogen-depleting effect of SIT. These changes have previously only been reported following traditional endurance training (68). It is encouraging from a clinical standpoint that these changes may be possible with reduced volumes of exercise.

A more recent study by Richards et al. (129) took 31 sedentary males (VO_{2max} = 35.3 mL·kg^{-1}·min^{-1}) whom participated in a two week SIT study. The subjects were divided into three groups; 1) a training group where subjects performed six sessions of 4-7, 30 sec 'all-out' cycle sprints, separated by four minutes recovery, 2) sedentary control group, and 3) single bout of sprint interval cycling (4 x 30 sec all-out sprints; 4 min recovery). The research design permitted the authors to determine whether changes in insulin sensitivity are an acute response or a short-lived training effect. Insulin sensitivity was measured via the "gold standard" measurement for insulin sensitivity, the hyperinsulinaemic euglycaemic clamp technique (19, 47). This technique measures the amount of glucose required to compensate for an increased insulin level, whilst maintaining a blood glucose level of 5-5.5 mmol/L (47). This study showed that short-term SIT significantly (P = 0.04) increases insulin sensitivity (1.66 ± 0.61 mL·kg^{-1}·min^{-1}), and to a greater extent when compared to a single bout of sprint interval cycling (0.82 ± 0.93 mg·kg^{-1}·min^{-1}) and sedentary controls (0.34 ± 0.40 mg·kg^{-1}·min^{-1}) (129). This suggests that the increased insulin sensitivity following SIT is indeed a training effect as insulin sensitivity was not significantly altered after a single bout (129).

A further study of low volume SIT assessed its effects on insulin action in 16 young and healthy men (48 ± 9 $mL \cdot kg^{-1} \cdot min^{-1}$) (5). The protocol was similar to that of Burgomaster et al. (32) and had subjects performing six sessions of 4-6, 30 second cycle 'all-out' sprints, separated by four minutes recovery, over a period of two weeks. Insulin sensitivity was estimated using the Cederholm index (34); this index is calculated via a formula which considers body weight, plasma glucose and insulin concentrations from an oral glucose tolerance test (34). Fasting glucose and insulin concentrations were unaltered following two weeks of SIT. Despite this, insulin sensitivity via the Cederholm index was enhanced following training (80 ± 6 vs. 98 ± 5 $mg \cdot l^{2} \cdot mmol \cdot^{-1} \cdot mU^{-1} \cdot min^{-1}$; $P < 0.01$) (5). Because no muscle biopsies were taken during the study, it is impossible to know the mechanisms surrounding this change; however, given the findings of previous research, the authors believe an increased expression of GLUT4 and increased glycogen synthesis was responsible for the enhanced insulin sensitivity (5, 29).

As noted earlier, Little et al., (109) formulated a more practical form of HIIT, which would be more appropriate for those at a higher risk of cardiovascular and/or metabolic disease. They based it on the Burgomaster (32) protocol, but modified it by reducing the exercise intensity, but increasing the duration and number of repetitions. Interestingly, despite the reduced intensity, the subjects still exhibited favourable improvements in GLUT4. In this two week study, GLUT4 protein content increased by 119% ($P = 0.04$) following training.

Future research

Further research is required to investigate the effects of more practical forms of HIIT, especially in at-risk and clinical populations. Many training interventions have utilized protocols requiring high levels of subject motivation and it remains unknown whether they could sustain these protocols as part of their lifestyle, in an everyday setting. Research is still required to determine the optimal volume and dosage of HIIT for improvements in insulin sensitivity and to a lesser extent maximal oxygen consumption. In addition to this, specific details are required on minimal dosages required to get improvements. Most of the research on HIIT has only followed subjects for up to 12 weeks, so it is unclear what the magnitude of changes are following this. Another omission from the research is information on injury rates from HIIT interventions; given the higher intensity nature of the exercise, there may also be an increased risk of injury, which could differ across various forms of exercise. Once these areas of research are completed, health and exercise professionals will have a better understanding and knowledge to prescribe HIIT safely and effectively in various populations.

Conclusion

The evidence on HIIT to date implies that it is an effective and time efficient method for improving cardiorespiratory fitness through changes in muscle oxidative capacity and central and peripheral cardiovascular function. Both SIT and LDIT have consistently shown greater improvements in cardiorespiratory fitness, when compared to CMIET. However, with SIT, especially studies with short intervention periods, it appears that some of the changes in performance are the result of peripheral adaptations, rather than improvements in cardiorespiratory fitness per-se. It seems that HIIT is very effective in improving insulin sensitivity in various populations via decreased intracellular accumulation of triglycerides and increased fatty acid oxidation. Less conclusive though, is whether this improvement in insulin sensitivity is an acute change or if it is a short-term training adaptation. Despite overwhelming scientific evidence that regular physical activity is effective in the prevention of chronic diseases, most adults fail to meet the physical activity guidelines due to 'lack of time'. Given HIIT may make better use of one's time, and its superior effects on cardiorespiratory fitness, it seems logical to prescribe it to those who can tolerate it. However, it is not understood whether this form of training provides all of the benefits associated with traditional endurance training. For this reason, it seems ideal to combine both forms of training into a 'weekly plan' to try overcome barriers to physical activity and exercise, yet achieve the optimal training adaptations and positive health changes. Therefore, the objective of the present study is to deliver a 12 week exercise intervention combining a single weekly bout of HIIT with CMIET, in individuals at moderate risk of CVD and compare it against CMIET on how it influences cardiorespiratory fitness, insulin sensitivity and other cardiovascular risk factors.

Table 2-1: Effect of HIIT on cardiorespiratory fitness (VO_{2max}), glucose regulation, blood pressure (BP), lipids and other physiological measures

Study	Participant characteristics	Details of intervention	Sample size (n)	Intensity/duration of exercise	ΔVO_{2max}	Glucose regulation	BP	Lipids	Other
Babraj et al. (5)	16 young, trained men; normal BMI	2 weeks 3 sessions/wk Cycle ergometer	SIT (16)	4-6 x 30 sec 'all-out' sprints, 4 min recovery		Insulin sensitivity (Cederholm index) ↑23%			
Borghouts et al. (23)	18 young untrained adults	4 weeks 5 sessions/wk Cycle ergometer	HIIT (9) LIIT (9)	HIIT: 12 x 3 min @ 80%W_{max} LIIT: 12 x 3 min @40%W_{max}	HIIT ↑7% LIIT ↑4.9%	Insulin sensitivity: HIIT ↑24% LIIT ↑8.4%			
Burgomaster et al. (32)	20 young, normal weight adults	6 weeks SIT: 3 session/wk CMIET: 5 session/wk Cycle ergometer	SIT (10) CMIET (10)	SIT: 4-6 x 30 sec 'all-out' sprints, 4.5 min recovery CMIET: 40-60 min @ 65%VO_{2max}	SIT ↑7.3% CMIET ↑9.8%				
Burgomaster et al. (30)	8 young, trained, normal weight adults	2 weeks 3 sessions/wk Cycle ergometer	SIT (8)	4-7 x 30 sec 'all out' sprints, 4 min recovery	n/c				

BMI = Body mass index; wk = week; SIT = Sprint interval training; HIIT = High intensity interval training; LIIT = Low intensity interval training; CMIET = Continuous moderate intensity interval training; n/c = no change

Study	Participant characteristics	Details of intervention	Sample size (n)	Intensity/duration of exercise	ΔVO_{2max}	Glucose regulation	BP	Lipids	Other
Burgomaster et al. (29)	8 young, trained, normal weight adults	6 weeks 3 sessions/wk Cycle ergometer	SIT (8)	4-6 x 30 sec 'all-out' sprints, 4.5 min recovery		GLUT4 ↑25%			
Daussin et al. (46)	10 untrained, middle aged adults	8 weeks 3 sessions/wk Cycle ergometer	LDIT (10) CMIET (10) Cross-over design	LDIT: 4-7 x 4 min @LT, 1 min @90% P_{max} CMIET: 20-35 min @61% P_{max}	LDIT ↑34% CMIET ↑11%				
Franch et al. (62)	36 trained male adults	6 weeks 3 sessions/wk Treadmill	LDIT (12) SIT (21) CMIET (12)	LDIT: 4-6 x 4 min @94% HR_{max}, 2 min recovery SIT: 30-40 x 15 sec @92% HR_{max}, 15 sec recovery CMIET: 20-30 min @93% HR_{max}	LDIT ↑6% SIT ↑3.6% CMIET ↑5.9%				
Gibala et al. (66)	16 young, trained male adults	2 weeks 3 sessions/wk Cycle ergometer	SIT (8) CMIET (8)	SIT: 4-6 x 30 sec 'all out' sprints (~700W), 4min recovery CMIET: 90-120 min @ 65% VO_{2peak}	SIT^ ↓10.1% CMIET ↓7.5%				

^ = time to complete 750 kJ time trial cycle test; LDIT = Long duration interval training

Study	Participant characteristics	Details of intervention	Sample size (n)	Intensity/duration of exercise	ΔVO_{2max}	Glucose regulation	BP	Lipids	Other
Harmer et al. (79)	7 untrained male adults	7 weeks 3 sessions/wk Cycle ergometer	SIT (7)	4-10 x 30 sec 'all-out' sprints, 3-4 min recovery	↑7%				
Helgerud et al. (82)	40 trained male subjects	8 weeks 3 sessions/wk Treadmill	SIT (10) LDIT (10) LT (10) CMIET (10)	SIT:47 x 15 sec @90-95% HR_{max}; 15 sec recovery LDIT: 4 x 4min @90-95% HR_{max}, 3 min active recovery LT: 24.25 min @85% HR_{max} CMIET: 45 min @70% HR_{max}	SIT:↑5.5% LDIT:↑7.2% LT: ↑2% CMIET: ↓0.6%				**Stroke Volume** SIT:↑9% LDIT:↑10% LT: ↑1% CMIET: ↓1% **Cardiac Output** SIT:↑13% LDIT:↑10% LT: ↑1% CMIET: ↓1%
Hickson et al. (84)	8 trained adults	10 weeks 6 sessions/wk (3 LDIT cycle; 3 CMIET treadmill)	LDIT/CMIET (8)	LDIT: 6 x 5min @100% VO_{2max}; 2 min recovery CMIET: 30-40 min as fast as possible	↑44%				

Study	Participant characteristics	Details of intervention	Sample size (n)	Intensity/duration of exercise	ΔVO_{2max}	Glucose regulation	BP	Lipids	Other
Little et al. (109)	7 young recreationally trained males	2 weeks 3 sessions/wk Cycle ergometer	LDIT (7)	8-12 x 60 sec @100% VO_{2max}; 75 sec recovery	^↑9%				
MacDougall et al. (112)	12 young, trained males	7 weeks 3 sessions/wk Cycle ergometer	SIT (7)	4-10 x 30 sec 'all out' sprints; 2-4 min recovery	↑7.5%				
McKenna et al. (114)	8 young trained males	7 weeks 3 sessions/wk Cycle ergometer	SIT (8)	4-10 x 30 sec 'all out' sprints; 3-4 min recovery	↑14%				
Richards et al. (129)	31 young, overweight adults	2 weeks 3 sessions/wk Cycle ergometer	SIT (12) SB (9) CON (10)	SIT: 4-7 x 30 sec 'all out' sprints, 4 min recovery SB: as above for a 1 off session	N/A	Insulin sensitivity (clamp technique): SIT ↑27%; SB & CON n/c			

^ = time to complete 750 kJ time trial cycle test; SB = single bout

Study	Participant characteristics	Details of intervention	Sample size (n)	Intensity/duration of exercise	ΔVO_{2max}	Glucose regulation	BP	Lipids	Othr
Rodas et al. (130)	5 young, recreationally active males	2 weeks 7 sessions/wk Cycle ergometer	SIT (5)	2-7 x 15 sec 'all out'; 45 sec rest and 2-7 x 30 sec 'all out'; 12 min rest	↑11%				
Schjerve et al. (135)	27 middle-aged, obese adults	12 weeks 3 sessions/wk Treadmill	LDIT (14) CMIET (13)	LDIT: 4 x 4 min @ 85-95% HR_{max}, 3 min recovery CMIET: 47 min @ 60-70% HR_{max}	LDIT ↑33% CMIET ↑16%	n/c in fasting glucose or insulin	DBP: LDIT ↓7% CMIET ↓9% SBP: n/c	TC, TG or HDL n/c	
Tabata et al. (144)	14 young, recreationally active males	6 weeks 5 sessions/wk Cycle ergometer	SIT (7) CMIET (7)	SIT: 7-8 x 20 sec @170% VO_{2max}; 10 sec recovery CMIET: 60 min @ 70%VO_{2max}	SIT: ↑15% CMIET: ↑9%				
Talanian et al. (145)	8 young, recreationally active women	2 weeks 3-4 sessions/wk Cycle ergometer	LDIT (8)	10 x 4 min @~90%VO_{2max}; 2 min rest	↑13%				

DBP = diastolic blood pressure; SBP = systolic blood pressure; TC = total cholesterol; HDL = high density lipoprotein; TG = triglyceride

Study	Participant characteristics	Details of intervention	Sample size (n)	Intensity/duration of exercise	ΔVO_{2max}	Glucose regulation	BP	Lipids	Other
Tjonna et al. (150)	28 middle aged adults with metabolic syndrome	16 weeks 3 sessions/wk Treadmill	LDIT (11) CMIET (8) CON (9)	LDIT: 4 x 4 min @95%HR_{max}, 3 min recovery CMIET: 47 min @ 70% HR_{max}	LDIT: ↑35% CMIET: ↑16%	Insulin Sensitivity (HOMA): LDIT ↑15% CMIET n/c Fasting glucose: LDIT ↓4.3% CMIET n/c	SBP: LDIT ↓6.2% CMIET ↓7.6% DBP: LDIT ↓6.3% CMIET n/c	HDL: LDIT ↑22% CMIET n/c	
Trilk et al. (153)	28 sedentary & overweight /obese women	4 weeks 3 sessions/wk Cycle ergometer	SIT (14) CON (14)	SIT: 4-7 x 30 sec 'all out' sprints; 4 min recovery CON: maintain baseline PA	SIT: ↑12% CON: ↓1%				**Stroke Volume** SIT: ↑11% CON: ↓4% **Plasma Volume** SIT: ↑4% CON: n/c
Warburton et al. (157)	20 untrained males	12 weeks 3 sessions/wk Cycle ergometer	LDIT (6) CMIET (6) CON (8)	LDIT: 8-12 x 2 min @90% VO_{2max}; 2 min recovery CMIET: 30-48 min @~64% VO_{2max}	LDIT: ↑21% CMIET: ↑23% CON: n/c				**Blood Volume** LDIT: ↑10% CMIET: ↑12% CON: n/c
Whyte et al. (164)	10 young, overweight/obese men	2 weeks 3 sessions/wk Cycle ergometer	SIT (10)	4-6 x 30 sec 'all-out' sprints, 4.5 min recovery	↑9.5%	24h post-ex, fasting insulin ↓25%	SBP ↓5% DBP n/c	TC, TG or HDL n/c	

Chapter 3. Methods

3.1. Experimental Design: Overview

The study design for this intervention was a randomised control trial. The objective of this study was to determine whether 12 weeks of CMIET combined with one session per week of HIIT (HIIT group), was more beneficial than CMIET alone (CMIET group) for increasing cardiorespiratory fitness and insulin sensitivity in sedentary adults at moderate risk of CVD. This study also compared changes in blood pressure, blood lipids, body composition, resting heart rate and changes in perceived quality of life. The study design is summarized in Figure 3-1.

3.2. Sample Size Estimation

The primary outcome variable of this study was change in cardiorespiratory fitness between baseline and post-programme. The means and standard deviations of a previous study were examined and the effect size of this study was calculated (3). Assuming that a power of 0.80 was needed and the calculated effect size for change in cardiorespiratory fitness was 0.8, it was determined that 12 subjects were needed for each of the three groups. It is generally acknowledged that there is a 20-25% dropout in exercise training studies, therefore we aimed to recruit 15 participants to each group, to account for potential attrition (41).

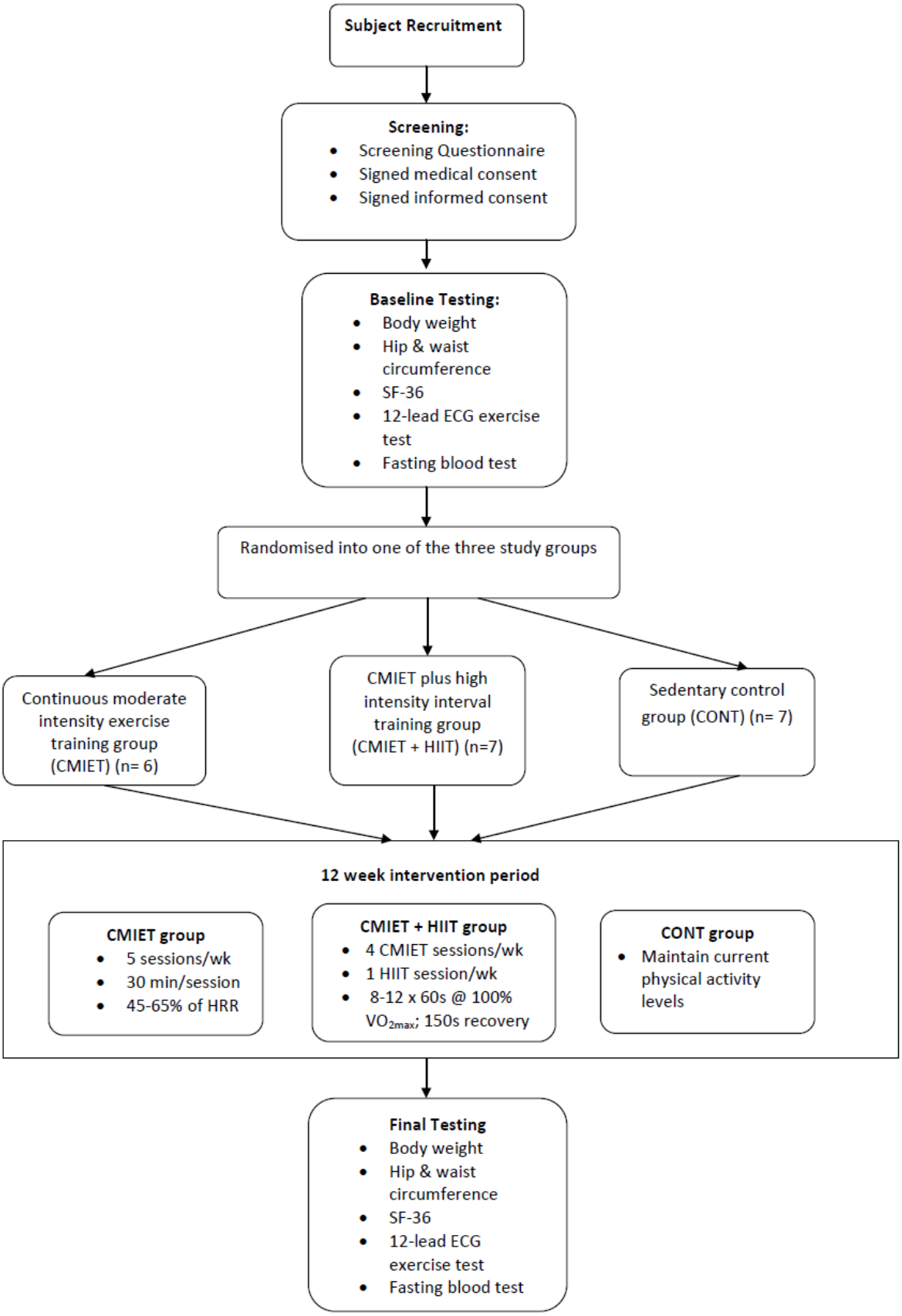


Figure 3-1: Overview of study design

3.3. Participant Recruitment

For this study, 29 individuals (10 male and 19 female) were recruited from the community in Central and Eastern Auckland, New Zealand. Prospective subjects were identified by either local general practitioners and/or nurses. The general practitioner and nurse provided all potential volunteers with details of the study and information on how to contact the student researcher, if they wished to participate in the study. Advertisements (Appendix A) were also placed around the Tamaki Campus at The University of Auckland, Glen Innes, Auckland, in a community newspaper (Howick and Pakuranga Times – see Appendix B) and various online websites (GetParticipants.com) and forums (TradeMe.co.nz and Gumtree.co.nz).

3.4. Participant Requirements

Individuals, whom were sedentary, classified as moderate risk for CVD (must have ≥ two negative risk factors from Appendix C) and aged between 18 and 55 years were recruited for this study. Participants from all ethnic backgrounds were considered for this study. In order to participate, participants must have met all of the inclusion criteria below.

3.4.1. Inclusion Criteria:

- No known cardiovascular, pulmonary or metabolic disease
- Have a sedentary lifestyle as per the American College of Sports Medicine's definition of "not participating in at least 30 min of moderate intensity (40-60% oxygen consumption reserve (VO_2R)) physical activity on at least three days of the week for the past three months" (148)

- Be at ‘moderate risk’ of atherosclerotic cardiovascular disease as defined by the American College of Sports Medicine (148)
- Male or female
- Be able to speak fluent English
- Aged 18-55 years
- No history of diabetic ketoacidosis [blood bicarbonate <15 mmol/L or pH <7.25 (venous) / <7.30 (arterial)] (128)
- Not receiving insulin therapy or taking hypoglycaemic medication
- No history of orthopaedic problems which would limit exercise
- Be able to perform vigorous exercise
- Be able to provide informed consent
- Clearance to exercise granted by general practitioner or other relevant health professional
- Non-cigarette smoker
- Be able to attend all supervised exercise sessions

If upon interview, any candidate met any of the following exclusion criteria in 3.4.2, they were not permitted to participate in the study.

3.4.2. Exclusion Criteria:

- Known cardiovascular, pulmonary or metabolic disease
- Resting blood pressure of >200 mmHg systolic and/or >110 mmHg diastolic (148)
- Body mass index >40 $kg \cdot m^2$ (148)
- Orthopaedic problems which limit the participants’ ability to perform exercise
- Under 18 years of age/over 55 years of age

- Unable to perform vigorous exercise
- Informed consent not provided
- Medical clearance to exercise not granted
- Current cigarette smoker or participants whom have quit within the previous six months or been exposed to environmental tobacco smoke
- Currently receiving insulin therapy or taking hypoglycaemic medication
- Unable to attend all supervised sessions

3.4.3. Provision of Information and Consents

This study was approved by the University of Auckland Human Participants Ethics Committee, on the 26th of January 2012 for a period ending on the 26th of January 2015 (reference 7764). Individuals who expressed an interest in participating in the study, were given a copy of the participant information sheet (Appendix D) outlining the rationale for the study, project procedures, associated risk and confidentiality. All participants were then followed up by the student researcher and given the opportunity to ask any questions regarding the study. All subjects who agreed to participate signed an informed consent (Appendix E) during the initial assessment. Participation in this study was completely voluntary and participants were able to withdraw from the study at any time, without having to provide the researchers with a reason. If subjects withdrew from the study or refused to participate, this in no way had an influence on future healthcare or treatment.

3.5. Testing Procedures

Before commencing the initial assessment, all participants underwent a screening questionnaire (Appendix F) to determine their eligibility for the study. If all inclusion and exclusion criteria were satisfied, medical clearance for exercise was sought from a qualified general practitioner for each participant. Once the student investigator had received the signed medical clearance, an initial assessment was scheduled. Prior to commencing the study, all procedures, requirements and expectations were outlined to all participants and the student researcher was available to answer any questions. All testing sessions were supervised by the student researcher and conducted at the University of Auckland's, Department of Sport and Exercise Science, Exercise Physiology Laboratory, located at 71 Merton Road, St Johns, Auckland. The student researcher was trained in pre-hospital emergency care and qualified medical practitioners and full resuscitation equipment were available on site in the event of an emergency.

3.5.1. Anthropometric Measures

3.5.1.1. Height

Height was measured in metres using a stadiometer (Invicta, IP1465, UK). Participants were asked to remove footwear before the measurement of height was obtained. The participants were instructed to stand with their feet together and against the back of the stadiometer, spine against the vertical pole of the stadiometer, whilst looking straight ahead and keeping the chin parallel with the floor. The headboard was then lowered down to rest against the vertex of the skull. The measurement was recorded to the nearest 0.1 cm and then the participant stepped off. This process was completed twice and if consecutive values differed by more

than 1 cm, a third measurement was taken and the values were averaged, to give the height for that participant.

3.5.1.2. Weight and body mass index

Participants were asked to remove items from their pockets, remove their footwear and remove any heavy clothing (e.g jackets, coats) before measuring their body mass. Weight in kilograms was measured on calibrated electronic scales (SECA 770, Germany; Calibrated 13/2/12 – 13/2/13). The same set of scales was used for the duration of the study. The scales were placed on a hard floor and participants were instructed to step on to the middle of the scales and look straight ahead. Weight was measured to the nearest 0.1 kg and then the participant stepped off. This process was completed twice and if consecutive values differed by more than 0.2 kg, a third measurement was taken and the values were averaged, to give the weight for that participant.

Body mass index was calculated using the formula below.

BMI ($kg{\cdot}m^{2}$) = weight / $height^{2}$

Weight = kg

Height = m

3.5.1.3. Hip & waist circumference

Waist and hip circumference were measured to assess body fat distribution. A cloth tape measure, placed on the skin surface was used for measuring waist circumference. Waist

circumference was measured horizontally, around the narrowest part of the torso, at the end of expiration (148). When measuring hip circumference, the cloth tape measure was placed against the participant's shorts or pants. Hip circumference was measured horizontally around the widest part of the buttocks at the end of expiration (148). The point where the '0' on the tape crossed the opposite end of the tape was deemed to be the measurement. All measurements were taken on the left hand side of the participant and participants were instructed to keep feet close together and arms at the side. Each measurement was taken three times and the average calculated (163). All measurements were performed in a private area to ensure the participants privacy.

3.5.2. Quality of life questionnaire

The Short Form (36) Health Survey (Appendix G) was employed to assess perceived physical and mental health. Participants were seated and instructed to complete the questionnaire as accurately as possible, with minimal input from the student researcher. The answers from the questionnaires were entered into a Microsoft Excel spreadsheet, which provided a score for Physical, Mental and Total Health.

3.5.3. Blood pressure

All resting blood pressure measurements were manually recorded via auscultation using a mercury sphygmomanometer (ALPK2, Japan) and stethoscope (3M™ Littmann™, Classic II SE, USA). The participant was instructed to sit on a chair with their spine resting against the back of the chair for at least four minutes. The cuff was placed around the left arm of the participant and inflated by the student researcher, whilst holding the participants arm at heart

level. The bell of the stethoscope was placed over the artery in the ante-cubital fossa and participants were instructed to relax and stay as still as possible to ensure accuracy. A deflation rate of approximately 2-3 mmHg per second was used to increase the accuracy of the single measure. Systolic blood pressure was defined as the first Korotkoff sound (clear appearance of tapping sound) and diastolic blood pressure as the complete disappearance of Korotkoff sound.

Blood pressure was also measured and recorded every three minutes during the exercise test to assess whether it was rising appropriately and within accepted limits. Measurements were stopped in the last few minutes of the exercise test to ensure there was no effect on the final expiratory and inspiratory gas analysis values.

3.5.4. Heart Rate

Heart rate was determined by the R-R interval on the 12-lead electrocardiogram (ECG) (Schiller, Cardiovit AT-10, Switzerland). The participant was instructed to sit on a chair with their spine resting against the back of the chair and resting heart rate was deemed to be the lowest value during the fourth and fifth minute of rest. Participants were instructed to relax and stay as still as possible to ensure accuracy.

Heart rate was also recorded at the end of each one minute stage throughout the exercise test. A participant's maximal heart rate was deemed to be the highest observed heart rate when the exercise test was stopped.

3.5.5. 12-lead Electrocardiogram and Cardiorespiratory Fitness Test

Equipment:

Expired oxygen (O_2) and carbon dioxide (CO_2) volumes were measured using an Ametek S-3A/I O_2 gas analyser and a CD-3A CO_2 gas analyser (AEI Technologies, USA). Values were recorded breath by breath and analysed by MAX II software program (AEI Technologies, USA). The exercise tests were conducted on a treadmill (Powerjog GX200, Maine).

Calibration:

Prior to each test the O_2 and CO_2 gas analysers were two-point calibrated using atmospheric gas (20.93% for O_2 and 0.04% for CO_2 respectively) and from known concentrations within a gas cylinder (BOC Ltd., alpha standard; 13.98 ± 0.07% of O_2 and 5.97 ± 0.03% of CO_2). Ventilatory flow volume (V_E) was measured by a turbine flow meter attached to the mouthpiece. This was calibrated every test using a 3L pump syringe (Series 5530 by Hans Rudolph, USA). Calibration was conducted twice, and considered correct if the calibration factor (average of 5 pumps) was between -50mL and +50mL inclusive. Environmental conditions in the laboratory were entered into the MAX II software programme before each test. Temperature (°C) and relative humidity (%) were collected from a weather station and barometric pressure (mmHg) was measured using a barometer (SATO Keriyoki, Japan). This allowed gas volumes to be converted from ambient temperature and pressure saturated (ATPS) to standard temperature and pressure dry (STPD). Patient details such as subject ID

and age were entered to identify results and body mass in kilograms was entered to allow for measurement of a relative cardiorespiratory fitness.

Pre-test procedures:

Each participant was instructed to avoid vigorous physical activity 24 hours before the exercise test and to avoid alcohol and caffeine 12 hours prior and food for two hours prior to the test. Subjects were instructed to consume 250 mL of water, one to two hours prior to the test, to standardise hydration.

All participants undertook a graded treadmill test to measure cardiorespiratory fitness and were required to be monitored by ECG for the duration of the test. Participants were made aware that they may experience some slight discomfort, caused by an abrasive used to clean the skin where electrodes were placed. The ECG was prepared using the guidelines in Appendix H, by the student researcher and/or a postgraduate student (PGDipSci-Cardiac Rehabilitation) from the Department of Sport and Exercise Science, University of Auckland. Female participants were given the option of having a female student prepare their ECG. A standard 12-lead ECG was attached to the subject's chest and a resting ECG print-out was obtained and checked by the student researcher for abnormalities that would contraindicate the performance of an exercise test (Appendix I). During this time, the procedure for the treadmill test, BORG rating of perceived exertion scale (22) (Appendix J) and ACSM symptom scale (148) (Appendix K) were explained in detail to the participants and they were given the opportunity to ask any questions.

Test protocol:

Before the participant was fitted with the head set and mouth-piece, they were familiarised with the treadmill and shown how to stop the treadmill safely. This included determining a walking speed for the exercise test which was a slightly faster speed than what the participant would normally walk on a level surface. Participants were then required to sit on a chair for at least five minutes whilst breathing through the mouthpiece. Resting oxygen consumption (VO_2) was measured as an average of all breaths during the fourth minute; resting heart rate was also taken as the lowest value on the ECG during this time and resting blood pressure was measured in the final minute of rest.

The protocol used for the graded treadmill test, was the Modified Balke protocol (Figure 3-2). Following five minutes of seated rest, the participants walked for one minute at a speed one km/h slower than their pre-determined testing speed. At the end of the first minute, the speed was increased to the pre-determined pace, where it remained constant for the remainder of the test. The first minute of the protocol was at a gradient of 0% and thereafter the gradient was increased each minute by 1%, until volitional fatigue. The protocol was designed with the intent of participants reaching VO_{2max} within 8-12 minutes. The test was considered a true maximum when two out of the following three parameters was achieved:

- A plateau in oxygen consumption, with increased workload: a 15 second average increase of less than 50 $mL \cdot min^{-1}$, despite an increase in workload
- Respiratory exchange ratio (RER) > 1.1
- Heart rate within 10 $beats \cdot min^{-1}$ of age-predicted maximum heart rate (220-age)

The test was terminated by the primary investigator if any of the termination criteria outlined in Appendix L were present.

Post-test

At the cessation of the test, the treadmill was stopped, the gas mask was removed and participants were given a chair to sit on and a glass of water. The ECG was monitored throughout recovery and blood pressure was taken within the first minute, and every two minutes thereafter. A final seated blood pressure and heart rate were recorded prior to the subject leaving.

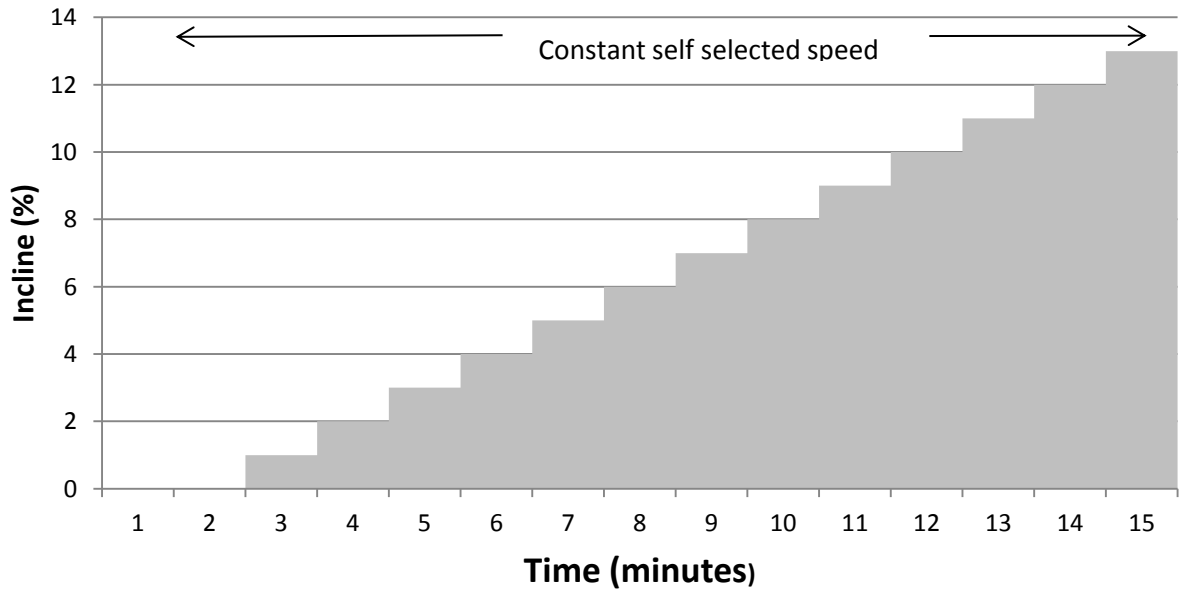


Figure 3-2: Modified Balke protocol for graded treadmill exercise testing. (Adapted from Dalleck et al., 2004 (45))

3.5.6. Fasting blood sample

Following the initial assessment, participants were instructed to report to a Diagnostic MedLab branch, no sooner than 48 hours after the exercise test and following an 8-12 hour fast. Participants were advised to abstain from consuming food or drink during this time, with plain water the only exception. A venous blood sample was obtained using standard phlebotomy techniques. Bloods were collected into 1 x fluoride tube for analysis of blood glucose and 1 x 3.5 mL serum-separating tube (SST) tube for lipid and insulin tests. Blood samples were analysed by a Roche Modular P system (Indianapolis, IN) for total cholesterol (TC), low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, triglycerides and blood glucose levels. Insulin was analysed by an Abbott Architect I4000 system (Illinois, USA). Insulin sensitivity (HOMA2S) was estimated by entering fasting glucose and insulin results into Levy et al.'s (105) published homeostasis model assessment 2 (HOMA2).

3.5.7. Post intervention re-testing

At the completion of the 12 week intervention participants were scheduled for a final assessment. To ensure the acute effects of the last exercise session on insulin sensitivity had vanished, the tests were conducted 2-3 days following the final exercise session (26). Waist and hip circumference, body weight, height, body mass index, resting heart rate, resting blood pressure, SF-36, cardiorespiratory fitness test and a blood sample were all repeated as per the guidelines stated previous.

3.6. Training Procedures

Following the initial assessment, participants were randomised to one of three intervention groups using a random number generator on Microsoft Excel. Participants in the exercising groups were required to complete five exercise sessions per week, for a period of 12 weeks. Exercise sessions were supervised by the student researcher at the Health & Performance Training Centre, Tamaki Campus, The University of Auckland, 71 Merton Road, St Johns, Auckland. The three intervention groups were:

1) Continuous moderate intensity exercise training (CMIET) – n = 10

   The CMIET protocol is based on widespread recommendations for physical activity (148). The ACSM guidelines state individuals should participate in moderate intensity (40-60% of VO_2R) physical activity five times per week, for at least 30 minutes a day. The specific protocol for this study involved walking on a treadmill for 15 minutes and cycling on a stationary bicycle for 15 minutes, at an intensity of 45-60% HRR. Participants exercised each week day, totalling 150 minutes of exercise per week. Assuming HRR correlates with VO_2R, this was used to prescribe and monitor the intensity of exercise (54). For weeks 1-4, subjects exercised at 45-55% of HRR and from week four onwards, subjects exercised at approximately 60% HRR. Assuming resting heart rate decreases, with an increase in fitness, HRR was re-assessed every four weeks.

2) CMIET combined with high intensity interval training (HIIT) – n = 9

   This protocol involved performing four CMIET sessions and one HIIT exercise session each week. The HIIT sessions were based on Little et al.'s (109) practical model which involves eight, 60 second intervals at 100% VO_{2max}, separated by 75

seconds active recovery. Little et al.'s (109) model was performed in men who had a high relative VO_{2max} (46 ± 2 $mL \cdot kg^{-1} \cdot min^{-1}$) so it was decided for this study to double the recovery time, to cater for the sedentary and higher risk participants. After four HIIT sessions, the number of repetitions increased to 10 and recovery time was kept constant. For the last four weeks, the number of repetitions increased to 12 and recovery time was kept constant. All interval sessions were conducted on the Wednesday of each week.

3) Control group – n = 10

   The control group were instructed to maintain their sedentary lifestyle and not increase physical activity levels, throughout the 12 weeks.

At the completion of the study, the control group was provided a voucher entitling them to a free 12 week exercise programme at the University of Auckland Cardiac Rehabilitation Clinic.

During the first exercise session, participants were given full instructions on how to safely operate the equipment. Each session included a warm-up and cool down; this included five minutes light cycling and a set of stretches. During all sessions exercise duration, workload, average heart rate, and ratings of perceived exertion (RPE) were recorded on the exercise prescription sheet (Appendix M) at the midpoint of each activity. Heart rate was recorded using a Polar FS3 heart rate monitor.

Participants were instructed not to change their diet throughout the study.

3.7. Measures

Anthropometric

- Body mass (kg)
- Height (m)
- Body mass index ($kg \cdot m^2$)
- Waist circumference (cm)
- Hip circumference (cm)

Cardiorespiratory fitness (VO_{2max}) test

- Resting VO_2 ($mL \cdot kg^{-1} \cdot min^{-1}$)
- Relative VO_{2max} ($mL \cdot kg^{-1} \cdot min^{-1}$)
- Absolute VO_{2max} ($L \cdot min^{-1}$)
- Peak exercise workload (METs)

Quality of life

- Short form 36 health survey (SF-36)

Fasting blood sample

- Total cholesterol (mmol/L)
- Low density lipoprotein cholesterol – LDL (mmol/L)
- High density lipoprotein cholesterol – HDL (mmol/L)
- Triglyceride (mmol/L)
- Blood glucose (mmol/L)
- Insulin (mmol/L)

Physiological measures

- Resting heart rate (beats·min^{-1})
- Resting blood pressure (mmHg)

3.8. Statistical Data Analysis

All data (VO_{2max}, anthropometric measures, quality of life, blood analysis and physiological measures) was entered into SPSS (version 18.0 for Windows). Mean values and standard deviations were calculated for each intervention group by using the 'compare means' function; pre and post outcome measures were entered as dependent variables, whilst the intervention groups were independent groups. Using group mean and standard deviation data, a between group effect size was calculated; this was done by calculating the difference between the means and dividing by the standard deviation (41). An 'independent samples T-test' was conducted, with uncertainty in estimates calculated as 90% confidence intervals. We made probabilistic magnitude-based inferences (as described by Batterham & Hopkins, 2006 (10)) using a published spreadsheet, to assess the likelihood that the true value of the effect represents substantial change (benefit or harm) (Figure 3-3).

P value	Value of effect statistic	Degrees of freedom	Level (%) for conf. limits	Threshold values for... benefit or +ive	harm or -ive			Chances that the true value of the effect statistic is... beneficial or substantially +ive	negligible or trivial	harmful or substantially -ive
			90	0.5	-0.5			#DIV/0! % #DIV/0!	#DIV/0! % #DIV/0!	#DIV/0! % #DIV/0!

1. Batterhorn & Hopkins (10) spreadsheet used for calculating clinical significance. P-value, effect size and degrees of freedom need to be determined and entered.

	group	N	Mean	Std. Deviation	t-test for Equality of Means: t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference
mean.change.vo2max	interval	7	3.2086	4.71467	2.243	12	.045	4.92714	2.19667
	control	7	-1.7186	3.39842					

2. Group data is entered into SPSS and an independent samples T-test calculation is done. This provides mean and standard deviation values to calculate the effect size and a p-value for the spreadsheet.

Input data provided:
Mean 1: 3.21
SD 1: 4.71
Mean 2: -1.71
SD 2: 3.40

Effect size

Output:
Cohen's *d*: 1.213

3. Effect size is then calculated using mean and standard deviation data from SPSS.

P value	Value of effect statistic	Degrees of freedom	Level (%) for conf. limits	Threshold values for... benefit or +ive	harm or -ive			Chances that the true value of the effect statistic is... beneficial or substantially +ive	negligible or trivial	harmful or substantially -ive
0.045	1.213	12	90	0.5	-0.5			89.3 % likely	10.2 % unlikely	0.4 % most unlikely
Clinical inference: likely benefical, most unlikely harmful; use. Mechanistic inference: likely +ive										

4. P-value, effect size and degrees of freedom data obtained in steps 2 & 3 is entered into the spreadsheet. Percentage values are then provided stating the chance that the true value of the effect statistic is beneficial, trivial and harmful and a clinical inference is made based on these values.

Figure 3-3: Example calculation of probabilistic magnitude based inferences, comparing relative VO_{2max} between HIIT and control groups

Chapter 4. Results

4.1. Participant Characteristics

There were 29 participants (10 male and 19 female) recruited for this study. Ten participants were randomised to the CMIET and control groups and nine randomised to the HIIT group. Nine individuals withdrew from the study before completion due to either a change in work or study commitments (5 participants), prolonged illness of a family member (2 participants), personal reasons (1 participant) and injury obtained outside of the study (1 participant). Mean values and standard deviations for participant characteristics before (pre) and after (post) the 12 week intervention are detailed in Table 4-1.

All subjects satisfied the inclusion criteria for this study. Two participants in the HIIT group were on anti-hypertensive medications (beta-blocker, ACE inhibitor and a calcium channel blocker) and one of these participants was also taking a lipid modifying medication (Simvastatin). Both participants had been taking these medications without a change in dosage for more than six months, and their prescription did not change during the study period.

Table 4-1: Participant characteristics for the HIIT, CMIET and Control groups before and after (pre and post) the 12 week intervention period

	HIIT Group (n=7)		CMIET Group (n=6)		Control Group (n=7)	
	Pre	**Post**	**Pre**	**Post**	**Pre**	**Post**
Age (years)	37.9 ± 7.1	-	36.5 ± 9.2	-	34.4 ± 4.7	-
Anthropometric						
Height (m)	1.68 ± 0.1	-	1.73 ± 0.1	-	1.67 ± 0.1	-
Body mass (kg)	85.9 ± 17.3	85.7 ± 16.7	90.2 ± 25.0	89.1 ± 25.4	81.7 ± 12.5	82.5 ± 12.7
BMI ($kg \cdot m^2$)	30.7 ± 6.3	30.6 ± 6.1	29.6 ± 4.7	29.4 ± 4.7	29.2 ± 4.2	29.5 ± 4.4
Hip circumference (cm)	111.4 ± 10.5	109.9 ± 10.6	112.5 ± 12.7	111.9 ± 11.7	110.9 ± 10.0	112.2 ± 9.6
Waist circumference (cm)	101 ± 16.6	99.7 ± 15.2	98 ± 15.2	97.1 ± 15.3	94.6 ± 13.1	96.9 ± 11
Quality of Life						
SF-36 Mental	60.6 ± 22.9	78.6 ± 20.4	62.2 ± 14.9	74 ± 16.8	62.9 ± 14.9	59.4 ± 23.3
SF-36 Physical	67 ± 20.1	78.7 ± 20.5	73.8 ± 15.4	78.7 ± 11.2	65.4 ± 13.1	68.6 ± 16.0
SF-36 Total	65 ± 20.7	79.3 ± 21.7	69.8 ± 14.5	79 ± 15.4	66.9 ± 10.7	65.9 ± 18.9
Blood Test						
Total Cholesterol (mmol/L)	6.2 ± 1.4	5.9 ± 1.3	5.8 ± 1.0	5.2 ± 1.1	5.5 ± 1.0	5.6 ± 1.1
LDL Cholesterol (mmol/L)	4.0 ± 1.2	3.5 ± 1.2	3.7 ± 0.8	3.1 ± 1.0	3.4 ± 1.0	3.5 ± 0.8
HDL Cholesterol (mmol/L)	1.5 ± 0.4	1.6 ± 0.5	1.3 ± 0.4	1.2 ± 0.3	1.6 ± 0.4	1.5 ± 0.3
Triglycerides (mmol/L)	1.4 ± 0.8	1.8 ± 1.2	1.9 ± 0.7	1.9 ± 0.8	1.1 ± 0.4	1.3 ± 0.7
Fasting blood glucose (mmol/L)	6.4 ± 2.9	6.7 ± 3.5	4.9 ± 0.6	4.9 ± 0.4	4.9 ± 0.5	4.9 ± 0.6
Fasting insulin(uU/mL)	8 ± 2.6	8.9 ± 2.3	9.9 ± 4.8	10.5 ± 4.9	9.4 ± 5.0	8.6 ± 5.2
HOMA2S (%)	101 ± 27.3	90.3 ± 29.0	95.6 ± 42.6	84.1 ± 25.6	110.8 ± 65.1	127.1 ± 77.0
Physiological Measures						
Resting VO_2 ($mL \cdot kg^{-1} \cdot min^{-1}$)	3.9 ± 0.51	4.0± 0.8	4.1 ± 0.7	4.0 ± 0.7	3.9 ± 0.7	3.9 ± 0.9
Relative VO_{2max} ($mL \cdot kg^{-1} \cdot min^{-1}$)	32.7 ± 9.2	36.0 ± 11.5	33.2 ± 4.0	34.5 ± 6.1	30.0 ± 4.6	28.3 ± 6.5
Absolute VO_{2max} ($L \cdot min^{-1}$)	2.7 ± 0.7	3.0 ± 0.7	3.0 ± 0.9	3.1 ± 1.2	2.4 ± 0.4	2.3 ± 0.5
Resting heart rate ($beat \cdot min^{-1}$)	74.7 ± 6.8	66.6 ± 8	73.5 ± 8.2	76.7 ± 4.6	76.9 ± 11.9	75.1 ± 10.2
Resting systolic blood pressure (mmHg)	130.9 ± 17.3	123.4 ± 15.0	128.7 ± 4.5	124 ± 5.1	120.9 ± 12.8	122.3 ± 12.1
Resting diastolic blood pressure (mmHg)	82 ± 8.5	78.6 ± 6.7	84.3 ± 3.4	77 ± 5.8	76.3 ± 6.2	76.3 ± 5.8

Data shown as mean ± standard deviation.

4.2. Exercise Training

Exercise training data was collected every session over the 12 week period, for each participant and mean and standard deviation values are summarised in Table 4-2. The exercise intervention groups were designed so both groups had similar exercise caloric expenditure, frequency, type and duration; the only major difference between the groups, was the single weekly interval training session in the HIIT group. Table 4-2 shows that despite the HIIT group performing a single weekly interval training bout, relative energy expenditure for each exercise session was similar between the HIIT and CMIET groups. Similarly, both the HIIT and CMIET groups had similar treadmill and cycle exercise intensities for their respective CMIET sessions. Adherence was high in both exercise groups for those participants whom completed the entire 12 week intervention. The highest adherence was for the HIIT sessions. Adherence was similar for the CMIET group and the HIIT group's CMIET sessions.

Table 4-2: Energy expenditure, exercise intensity and adherence for HIIT & CMIET groups

	HIIT		CMIET
	HIIT sessions	**CMIET sessions**	
Treadmill EE (Kcal)	146.1 ± 35.1	140.7 ± 31.9	146.8 ± 66.4
Treadmill intensity (METs)	9.5 ± 2.1	6.1 ± 1.5	6.2 ± 1.1
Cycle EE (Kcal)	-	122.3 ± 27.1	126.4 ± 37.8
Cycle intensity (METs)	-	5.3 ± 1.1	5.3 ± 0.6
HIIT Active recovery EE (Kcal)	102.7 ± 26.6	-	-
Total EE (Kcal)	248.8 ± 57.6	263 ± 59.3	273.2 ± 63.8
Relative Total EE ($Kcal \cdot kg^{-1}$)	2.9 ± 0.5	3.1 ± 0.6	3.0 ± 0.6
Adherence (%)	100 ± 0	87.5 ± 8.7	86.7 ± 5.9

Values expressed as mean ± standard deviation; EE = Energy Expenditure; METs = metabolic equivalents ($3.5\ mL \cdot kg^{-1} \cdot min^{-1}$). Assumes participants walked at 3.0 km/h on a flat surface (2.7 METs) during HIIT active recovery periods.

4.3. Maximal Oxygen Consumption

All participants completed the VO_{2max} test until voluntary exhaustion pre and post intervention, with all participants satisfying at least two criteria outlined in section 3.5.5, for a true maximum.

Figure 4-1 and Figure 4-2 highlight the changes in relative and absolute VO_{2max} following the 12 week intervention. Table 4-1 shows absolute VO_{2max} increased by 11.1% and 3.7% in the HIIT and CMIET groups and decreased by 4.2% in the control group. When adjusting VO_{2max} for any changes in body mass during the 12 week intervention, the magnitude of the changes were still similar (Table 4-1). Relative VO_{2max} increased 10.1% in the HIIT group and 3.9% in the CMIET group, but decreased by 5.7% in the sedentary control group.

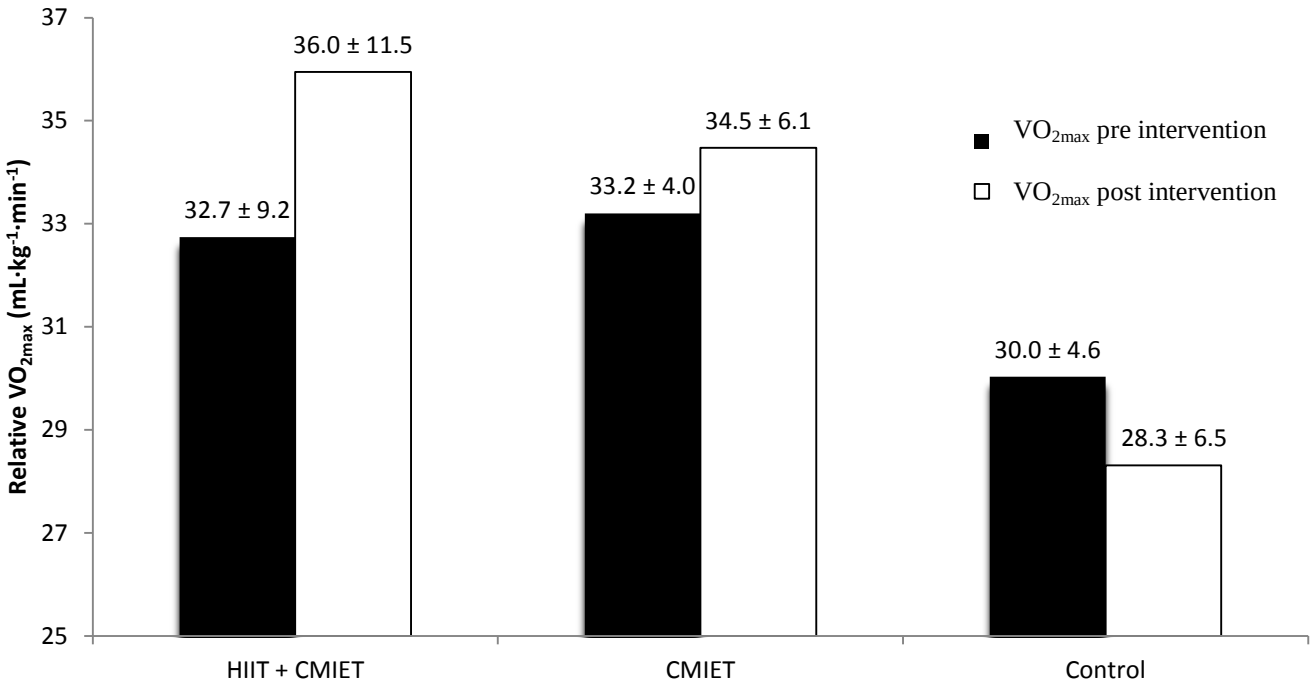


Figure 4-1: Changes in relative VO_{2max} before (pre) and after (post) 12 week intervention period.

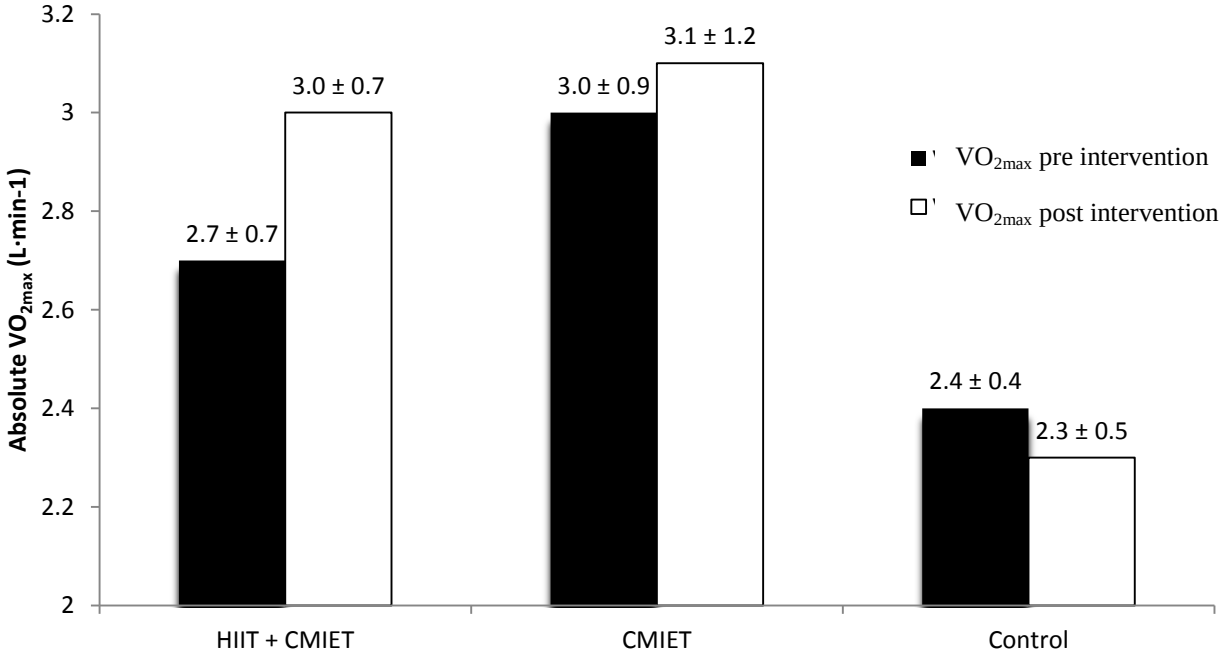


Figure 4-2: Changes in absolute VO_{2max} before (pre) and after (post) 12 week intervention period.

In order to make inferences about the effect of the interventions, the uncertainty in the effect, as expressed by 90% confidence intervals were calculated and the likelihood that the true value of the effect presents substantial change was determined; these are detailed in Table 4-3, Table 4-4 and Table 4-5.

When comparing pre and post relative VO_{2max} in the HIIT group, relative to the control group, there was a mean difference of 4.9 $mL \cdot kg^{-1} \cdot min^{-1}$ and it was deemed to be 'likely beneficial' (Table 4-4). When comparing pre and post relative VO_{2max} in the CMIET group, relative to the control group, there was a mean difference of 3.0 $mL \cdot kg^{-1} \cdot min^{-1}$ and CMIET was deemed 'possibly beneficial' (Table 4-5).

The primary research aim of the study was to assess changes in VO_{2max} following 12 weeks of CMIET combined with HIIT, compared to CMIET only. When comparing pre and post relative VO_{2max} values in the HIIT group, relative to the CMIET group, there was a mean difference of 1.9 $mL \cdot kg^{-1} \cdot min^{-1}$ and it remains 'unclear' whether one group was more beneficial compared to the other (Table 4-3). Similarly, when comparing the change in absolute VO_{2max} from pre to post between the same groups, it was still statistically 'unclear' whether or not one exercise training group elicited superior changes relative to its counterpart (Table 4-3).

Table 4-3: Effect of HIIT (relative to CMIET) on mean changes and chances that the true differences are substantial

			Chances that the true effect has substantial…		
	Mean Difference	**90% Confidence Interval**	**Benefit (%)**	**Harm (%)**	**Practical Assessment**
Anthropometric					
Body mass (kg)	0.8	-2.0, 3.7	10	39	Unclear
BMI ($kg \cdot m^2$)	0.1	-.0.5, 0.8	13	31	Unclear
Hip circumference (cm)	-0.9	-2.5, 0.7	58	4	Possibly beneficial
Waist circumference (cm)	-0.4	-2.6, 1.8	34	16	Possibly trivial
Quality of Life					
SF-36 Mental	6.2	-12.8, 25.2	39	9	Unclear
SF-36 Physical	6.9	-7.4, 21.2	49	5	Unclear
SF-36 Total	5.1	-9.9, 20.1	40	8	Unclear
Blood Test					
Total Cholesterol (mmol/L)	0.3	-0.5, 1.1	8	48	Unclear
LDL Cholesterol (mmol/L)	0.1	-0.6, 0.8	16	29	Unclear
HDL Cholesterol (mmol/L)	0.1	0 , 0.2	58	4	Possibly beneficial
Triglycerides (mmol/L)	0.4	-0.3, 1.1	4	60	Unclear
Fasting blood glucose (mmol/L)	0.3	-0.4, 1.0	7	43	Unclear
Fasting insulin(uU/mL)	0.2	-1.8, 2.2	16	24	Possibly trivial
HOMA2S (%)	0.8	-27.5; 29	19	21	Possibly trivial
Physiological Measures					
Resting VO^2 ($mL \cdot kg^{-1} \cdot min^{-1}$)	0.2	-0.4, 0.7	36	10	Unclear
Relative VO^{2max} ($mL \cdot kg^{-1} \cdot min^{-1}$)	1.9	-2.3, 6.2	48	5	Unclear
Absolute VO^{2max} ($L \cdot min^{-1}$)	0.1	-0.2, 0.5	42	7	Unclear
Resting heart rate ($beat \cdot min^{-1}$)	-11.3	-18.9, -3.8	95	0.2	Very likely beneficial
Resting systolic blood pressure (mmHg)	-2.8	-10.7, 5.2	42	9	Possibly trivial
Resting diastolic blood pressure (mmHg)	3.9	-2.8, 10.6	57	4	Unclear

BMI = Body mass index; SF-36 = Short form 36 health survey; LDL = low density lipoprotein; HDL = High density lipoprotein; HOMA2 = Homeostatic model assessment 2 – Insulin Sensitivity

Table 4-4: Effect of HIIT (relative to Control) on mean changes and chances that the true differences are substantial

	Mean Difference	90% Confidence Interval	Chances that the true effect has substantial… Benefit	Harm	Practical Assessment
Anthropometric					
Body mass (kg)	-1.1	-2.4, 0.2	72	2	Possibly beneficial
BMI ($kg \cdot m^2$)	-0.4	-0.9, 0.1	69	2	Possibly beneficial
Hip circumference (cm)	-2.9	-4.8, -1	95	0.2	Likely beneficial
Waist circumference (cm)	-3.6	-7.3, 0.0	80	1	Likely beneficial
Quality of Life					
SF-36 Mental	21.4	6.4, 36.5	93	0.2	Likely beneficial
SF-36 Physical	8.6	-1.2, 18.3	60	16	Unclear
SF-36 Total	15.3	4.0, 26.5	92	0.2	Likely beneficial
Blood Test					
Total Cholesterol (mmol/L)	-0.5	-1.2, 0.2	61	3	Possibly beneficial
LDL Cholesterol (mmol/L)	-0.6	-1.3, 0.1	73	2	Possibly beneficial
HDL Cholesterol (mmol/L)	0.1	-0.1, 0.1	24	14	Possibly trivial
Triglycerides (mmol/L)	0.1	-0.5, 0.8	11	31	Unclear
Fasting blood glucose (mmol/L)	0.3	-0.2, 0.8	4	56	Unclear
Fasting insulin(uU/mL)	1.7	-1.2, 4.6	4	56	Unclear
HOMA2S (%)	-27.1	-68.2; 14.0	3	61	Possibly harmful
Physiological Measures					
Resting VO^2 ($mL \cdot kg^{-1} \cdot min^{-1}$)	0.1	-0.5, 0.6	26	13	Unclear
Relative VO^{2max} ($mL \cdot kg^{-1} \cdot min^{-1}$)	4.9	1.0, 8.8	89	0.4	Likely beneficial
Absolute VO^{2max} ($L \cdot min^{-1}$)	0.4	0.1, 0.6	91	0.3	Likely beneficial
Resting heart rate ($beat \cdot min^{-1}$)	-6.4	-16.4, 3.6	59	3	Possibly beneficial
Resting systolic blood pressure (mmHg)	-8.9	-16.2, -1.5	89	0.5	Likely beneficial
Resting diastolic blood pressure (mmHg)	-2.3	-11.5, 7.0	35	8	Possibly trivial

Table 4-5: Effect of CMIET (relative to Control) on mean changes and chances that the true differences are substantial

	Mean Difference	90% Confidence Interval	Chances that the true effect has substantial… Benefit (%)	Harm (%)	Practical Assessment
Anthropometric					
Body mass (kg)	-1.9	-4.9, 1.0	62	3	Unclear
BMI ($kg \cdot m^2$)	-0.5	-1.3, 0.2	63	3	Possibly beneficial
Hip circumference (cm)	-1.9	-3.8, -0.2	86	1	Likely beneficial
Waist circumference (cm)	-3.2	-6.7, 0.2	83	2	Likely beneficial
Quality of Life					
SF-36 Mental	15.3	-6.2, 36.8	64	3	Possibly beneficial
SF-36 Physical	1.7	-11.4, 14.8	27	15	Unclear
SF-36 Total	10.2	-6.0, 26.4	59	3	Unclear
Blood Test					
Total Cholesterol (mmol/L)	-0.8	-1.5, 1.5	98	0.1	Very likely beneficial
LDL Cholesterol (mmol/L)	-0.7	-1.1, -0.3	80	0	Likely beneficial
HDL Cholesterol (mmol/L)	-0.1	-0.2, 0.1	7	43	Possibly harmful
Triglycerides (mmol/L)	-0.3	-0.7, 0.5	54	4	Possibly beneficial
Fasting blood glucose (mmol/L)	0	-0.7, 2.0	0	0	Most likely trivial
Fasting insulin(uU/mL)	1.5	-1.5, 4.6	6	53	Unclear
HOMA2S (%)	-27.9	-72.7; 16.9	4	61	Unclear
Physiological Measures					
Resting VO^2 ($mL \cdot kg^{-1} \cdot min^{-1}$)	-0.1	-0.5, 0.4	14	27	Unlikely beneficial
Relative VO^{2max} ($mL \cdot kg^{-1} \cdot min^{-1}$)	3.0	-0.5, 6.5	74	2	Possibly beneficial
Absolute VO^{2max} ($L \cdot min^{-1}$)	0.2	0, 0.5	72	2	Possibly beneficial
Resting heart rate ($beat \cdot min^{-1}$)	4.9	-4.6, 14.4	54	6	Unclear
Resting systolic blood pressure (mmHg)	-6.1	-10.7, -1.5	92	0.4	Likely beneficial
Resting diastolic blood pressure (mmHg)	-7.3	-15.2, 0.6	77	2	Likely beneficial

4.4. Blood analysis

Mean values and standard deviations for fasting cholesterol, blood glucose, insulin concentrations and estimated insulin sensitivity are presented in Table 4-1. Total cholesterol decreased by 4.8% and 10.3% respectively in the HIIT and CMIET groups, whilst it increased by 1.8% in the control group. The CMIET group had the largest decrease in LDL cholesterol, with a similar decrease observed in the HIIT group and a slight increase in the control group. The CMIET and control groups experienced decreases in HDL cholesterol, whilst there was a slight increase in the HIIT group. Triglycerides increased in the HIIT and control groups, with no change observed in the CMIET group. The only group to alter their fasting blood glucose values after the intervention was the HIIT group, where it increased slightly (Table 4-1). Both the HIIT and CMIET groups experienced increases in their fasting insulin concentrations, whilst this decreased by 8% in the control group. Consequently, estimated insulin sensitivity, as estimated by HOMA2S, decreased in both the HIIT and CMIET groups and the only increase was observed in the control group.

When analysing the mean differences for the fasting blood tests in the HIIT group, relative to the control group, there were mean differences of -0.5 and -0.6 mmol/L for total and LDL cholesterol respectively, and it was deemed to be ‘possibly beneficial’ for both (Table 4-4). With respect to fasting blood glucose and insulin, the true effect was deemed ‘unclear’. However, with a mean difference of -27.1% in insulin sensitivity, the HIIT group (relative to the control group) was deemed to be ‘possibly harmful’.

When examining CMIET, relative to the control group, there were observed mean differences of -0.8 and -0.7 mmol/L for total and LDL cholesterols, with each deemed to be 'very likely beneficial' and 'likely beneficial' (Table 4-5). The effect of CMIET on insulin sensitivity still remains 'unclear'. With respect to HDL cholesterol, CMIET was deemed to be 'possibly harmful'.

When analysing the mean differences for the fasting blood variables in the HIIT group, relative to the CMIET group, the only clinically significant difference was seen for HDL, where the HIIT group was deemed to be 'possibly beneficial' (Table 4-3). The true effect was said to be 'unclear' for total cholesterol, triglycerides and blood glucose, whilst LDL cholesterol, fasting insulin and insulin sensitivity had a 'possibly trivial' effect.

4.5. Anthropometric measures

The largest reduction in body mass was observed in the CMIET group, followed by the HIIT group; weight increased in the control group (Table 4-1). Despite the larger decrement of body mass in the CMIET group, the largest decreases in hip and waist circumference were in the HIIT group. Whilst there were still modest decreases in hip and waist circumference for the CMIET group, both variables increased in the control group.

When comparing the effect of the HIIT group, relative to the control group, on body mass and BMI change it was deemed to be 'possibly beneficial' and hip and waist circumference changes 'likely beneficial' (Table 4-4). The greatest mean differences were seen for waist circumference followed by hip circumference and body mass.

When comparing the effect of CMIET, relative to the control group, hip and waist circumferences had practical inferences of 'likely beneficial', whilst BMI was deemed to be 'possibly beneficial' (Table 4-5). Despite a mean difference of -1.9 kg for body weight, the true effect sill remained 'unclear'.

When comparing the effect of the HIIT group, relative to CMIET, on hip circumference, it was deemed 'possibly beneficial' with a mean difference of -0.9 cm (Table 4-3). There were mean differences of 0.8 kg and 0.1 $kg \cdot m^2$ for body mass and BMI, with both variables having 'unclear' practical inferences. The true effect on waist circumference was deemed 'possibly trivial', with a -0.4 cm mean difference.

4.6. Other physiological variables

Resting heart rate decreased by 10.8% and 2.3% in the HIIT and control groups, whilst it increased by 4.4% in the CMIET group (Table 4-1). Both exercising groups had decreases in systolic and diastolic blood pressures following the 12 week intervention. Systolic blood pressure increased in the control group and diastolic blood pressure remained unchanged.

When comparing the mean difference in resting heart rate in the HIIT group, relative to the control group, it was deemed 'possibly beneficial' (Table 4-4). Following a large mean difference of -8.9 mmHg in systolic blood pressure, it was deemed that the true effect was 'likely beneficial'.

The effect of CMIET, relative to the control group, on systolic and diastolic blood pressure were mean differences of -6.1 mmHg and -7.3 mmHg and this was deemed to be 'likely beneficial' for both (Table 4-5). Resting heart rate had a mean difference of 4.9 beat·min^{-1}, however, the inference for this effect is 'unclear'

When comparing the mean difference in resting heart rate in the HIIT group, relative to the CMIET group, it was deemed 'very likely beneficial' (Table 4-3). Although there were mean difference of -2.8 mmHg and 3.9 mmHg for systolic and diastolic blood pressures, these were said to be 'possibly trivial' and 'unclear' respectively.

4.7. Quality of life

All participants completed a SF-36 health survey to assess changes in perceived mental and physical health and mean scores and standard deviations are listed in Table 4-1. Perceived physical health increased across all the intervention groups, with the largest improvement seen in the HIIT group, followed by the CMIET and control groups. Perceived mental health increased by 29.7% and 19% in the HIIT and CMIET groups and decreased by 5.6% in the control group. Similar trends were observed for perceived total health, with a 22% and 13.2% increase in the HIIT and CMIET groups, whilst there was a slight 1.5% decrease in the control group.

When comparing the true effect in the HIIT group, relative to the control group for perceived mental and total health, it is deemed to be 'likely beneficial', whilst the practical inference for perceived physical health remains 'unclear' (Table 4-4).

The true effect of CMIET, relative to the control group on perceived mental health is deemed to be ‘possibly beneficial’. However, the true effect remains ‘unclear’ for perceived physical and total health (Table 4-5).

The true effect of the HIIT group, relative to CMIET alone on perceived mental, physical and overall health remains ‘unclear’, despite mean differences of 6.2, 6.9 and 5.1 respectively (Table 4-3).

Chapter 5. Discussion

5.1. Overview of Hypotheses

The primary research aim for this study was to compare the effects of 12 weeks CMIET combined with a single weekly bout of HIIT, and CMIET alone, on cardiorespiratory fitness in a group of sedentary adults at moderate risk of CVD. The results showed a 10.1% increase in relative VO_{2max} in the HIIT group and a 3.9% increase in the CMIET group. However, the clinical significance for this difference between the two groups still remains 'unclear'. Current data on the optimal prescription for HIIT is lacking, especially regarding minimum thresholds, and there is a need to develop a sustainable and time efficient HIIT intervention to slow the increasing rates of chronic disease. This study tells us that more than one session per week of HIIT, combined with CMIET may be necessary to get a clinically significant improvement in cardiorespiratory fitness, compared to CMIET alone.

5.2. Effects of the intervention on VO_{2max}

It is important to emphasize that due to the novelty of this intervention (combining CMIET and a single weekly bout of HIIT) and the sedentary 'at-risk' population involved, it is difficult to make comparisons to results of similar studies. Twelve weeks of CMIET combined with a single weekly bout of HIIT resulted in a mean increase in absolute VO_{2max} of 11.1%. In contrast, five sessions per week of CMIET over 12 weeks, only increased absolute VO_{2max} by 3.7%; despite these differences, according to statistical analysis, it is 'unclear' whether a clinically significant benefit or harm exists between both groups.

Although it was ‘unclear’ whether there was a clinically significant difference in the mean changes in VO_{2max} between both exercise training groups, previous research has exposed the benefits of improving VO_{2max} on all-cause mortality (104). Lee and associates (104) analysed data from the ACLS to quantify the effect of improving cardiorespiratory fitness, on all-cause and CVD mortality. The authors found that after adjusting for confounders, such as BMI change, for every 1 MET increase in cardiorespiratory fitness, there was an associated 15% (95% CI: 11-20%) and 19% (95% CI: 11-26%) lower risk of all-cause and CVD mortality. In the context of the current study this may be of clinical importance due to the 0.94 and 0.37 MET increase in cardiorespiratory fitness, in the HIIT and CMIET groups. One of the few prospective studies that examined how changes in cardiorespiratory fitness impacted all-cause mortality was a 1995 study by Blair et al. (16); the researchers in this study reported that in males, for every 2 MET increase in cardiorespiratory fitness, there was a decrease of 7.9% ($p = 0.001$) for all-cause mortality and 8.6% ($p = 0.027$) for CVD mortality (16). One of the possible mechanisms for this reduced risk is an improved risk factor profile (56). In the current study, there were numerous favourable improvements in the risk factor profile for the HIIT group including a 1.3% decrease in hip and waist circumferences, a 5.3% and 12.5% decrease in total and LDL cholesterol, a 6% and 4% decrease in systolic and diastolic blood pressure and the eradication of the sedentary lifestyle risk factor. Similar changes were observed for the CMIET group. However, in the control group, there was deterioration in the participant’s risk factor profile. For instance, over the 12 week period, there was a 0.5 MET decrease in cardiorespiratory fitness and correspondingly, there was a 1%, 1.2% and 2.4% increase in body mass, hip and waist circumferences, 1.8% and 3.8% increase in total and LDL cholesterol and the loss of HDL cholesterol as a positive risk factor (1.6 ± 0.4 to 1.5 ± 0.3 mmol/L).

The data in this study implies that the observed increases in cardiorespiratory fitness are not due to changes in body composition, as evidenced by similar increases in both absolute and relative VO_{2max} in both the HIIT (11.1% vs. 10.1%) and CMIET (3.7% vs. 3.9%) groups. Additionally, the 10.8% decrement in resting heart rate in the HIIT group, suggests that improvements in stroke volume maybe responsible for the observed increase in cardiorespiratory fitness (18, 149). Although this study did not measure changes in stroke volume, previous work has investigated how HIIT affects cardiovascular function (46, 157). As described in section 2.4.1, Daussin et al. (46) observed a 33.8% and 11.4% increase in VO_{2max} following HIIT and CMIET. The main finding from this study was that the mechanisms allowing improvement of VO_{2max} were different between the HIIT and CMIET groups (46). HIIT had both central and peripheral adaptations, with increases in cardiac output (17.5 ± 1.3 to 19.5 ± 1.8 $L \cdot min^{-1}$), stroke volume (107 ± 7 to 113 ± 8 mL) and arterio-venous difference (11.0 ± 0.9 to 12.1 ± 1.0 $mLO_2 \cdot 100mL^{-1}$), whilst only arterio-venous difference (11.0 ± 0.8 to 12.7 ± 1.0 $mLO_2 \cdot 100mL^{-1}$) improved following eight weeks of CMIET. Whilst Daussin et al.'s (46) study did not report resting heart values pre and post intervention, it is well established that resting heart rate decreases, when there is an increase in stroke volume (18, 149). Therefore, it is plausible, that with a clinically significant (very likely beneficial; benefit 95%, harm 0.2%) lowering of resting heart rate, following 12 weeks of CMIET combined with HIIT (74.7 vs. 66.6 $beat \cdot min^{-1}$), relative to CMIET only (73.5 vs. 76.7 $beat \cdot min^{-1}$), an increased stroke volume maybe responsible for the increased cardiorespiratory fitness.

A potential mechanism for the possible increase in stroke volume is an increase in blood volume (hypervolemia) (157). Warburton et al. (157) had 20 untrained males perform three

sessions a week of HIIT (8-12 x 2 min at 90% VO_{2max}; 2 min at 40% VO_{2max}), for a period 12 weeks. During this time, cardiorespiratory fitness increased 21%, with an 11% increase in stroke volume. The authors concluded that hypervolemia and the subsequent increased use of the Frank-Starling mechanism, was mainly responsible for an increase in left ventricular diastolic function; changes in plasma volume and red cell volume drove this change (157). The authors also reported little change in myocardial contractility. It is difficult to postulate why the authors failed to increase myocardial contractility, but research in mice suggests a very large volume of HIIT (6 weeks, 5 days/week, 1.5 hours/day, 85-90% VO_{2max}; number of repetitions not given) may be necessary to improve sarcoplasmic reticulum calcium uptake and myocardial contractility in healthy individuals (93).

It should be noted that lower resting heart rates may also be the result of an altered intrinsic firing rate of the sino-atrial node and/or an increase in para-sympathetic nervous system activity and a decreased sympathetic stimulation (149). However, in order for the body to maintain cardiac output, an increase in stroke volume is necessary, to compensate for the reduced heart rate (18). Furthermore, this strengthens the case for an increased stroke volume, as a result of the clinically significant difference in resting heart rate for the HIIT group, relative to the CMIET group.

5.3. Effects of the intervention on insulin sensitivity

Twelve weeks of CMIET combined with a single weekly bout of HIIT resulted in a 10.6% decrease in insulin sensitivity as estimated by the HOMA2 model. Likewise, a decrease of 12% was also recorded following 12 weeks of CMIET only. The effect of CMIET combined with HIIT (relative to CMIET only) had a 'possibly trivial' (possibly no benefit or harm) clinical significance.

It is difficult to hypothesize why insulin sensitivity did not improve in the current study, given that the majority of exercise training studies have shown that it is beneficial (24). Skeletal muscle is a primary target tissue for the clearance of glucose, so it is reasonable to assume changes in body composition, such as a decrease in muscle mass could reduce the clearance of glucose from the circulation by decreasing available glucose storage area (115). Although muscle mass was not measured in this study, in the CMIET group there was a 1.1 kg decrease in body weight, but only a 0.4 cm and 0.9 cm decrease in hip and waist circumference. It is possible that a decrease in muscle mass may account for the remainder of the weight loss. However, this does not explain the decrease in insulin sensitivity in the HIIT group, as there was a trivial 0.2 kg decrease in body mass, but a 1.5 cm and 1.3 cm decrease in hip and waist circumference, implying, body composition may have improved.

It is plausible that alterations in the extraction of insulin in the liver may have resulted in an increase in fasting insulin concentrations seen in both exercising groups. Hepatic insulin extraction is influenced by FFA levels, with increased FFA levels associated with impaired insulin uptake in the liver (11). It is possible that there was an increase in lipolysis caused by

the exercise induced reduction in fat mass, as predicted by reductions in hip and waist circumferences. The breakdown of triglycerides in adipose tissue may have transiently increased portal FFA levels, consequently increasing insulin concentrations via a reduced hepatic insulin uptake. Although this seems unlikely, especially given blood tests were done at least 48 hours post exercise, there was an observed increase in blood triglycerides for the HIIT group (1.4 ± 0.8 to 1.8 ± 1.2 mmol/L). However, it does not explain the increase in insulin for the CMIET group as there was no change in triglycerides (1.9 ± 0.7 to 1.9 ± 0.8 mmol/L).

Another potential reason for a decrease in insulin sensitivity is a change in diet, which was not controlled in this study. It is possible that despite being instructed to maintain the same diet, participants changed their diet after starting the exercise training programme. There are few prospective studies looking at how individuals eating habits change when they start an exercise program. Despite Evero et al. (57) showing that healthy young (22.2 ± 0.7 years), and trained (VO_{2peak} 44.2 ± 1.5 $mL \cdot kg^{-1} \cdot min^{-1}$) individuals have a reduced neural response for food, post-exercise, a recent study by Finlayson et al. (59) found conflicting results in older (39.6 ± 10.5 years) sedentary and obese/overweight (BMI – 31.3 ± 3.8 $kg \cdot m^2$) individuals, similar to the cohort in this study. The authors assessed how acute bouts of exercise and 12 weeks of exercise training affected the reward value of food. After an acute exercise bout, liking for all foods increased in 14 of the 34 participants. Similarly, these same people showed an increase in wanting high-fat sweet foods. Once followed up over the 12 weeks, these same 'non-responders' showed a smaller reduction in fat mass (1.7 ± 1.4 vs. 5.2 ± 2.4 kg). The authors concluded that for some individuals, exercise increases the reward value of food. This is important, as an increase in saturated fat and fructose, commonly found in high-

fat sweet foods, have been shown to increase diacylglycerol, which is an activator of novel protein kinase C (PKC) (142, 168); increases in both diacylglycerol and novel PKC are associated with impaired insulin sensitivity (117, 142). This is another potential explanation for the unexpected decrease in insulin sensitivity follow exercise training.

5.4. **Effects of the intervention on HDL and LDL**

High density lipoprotein is a strong predictor of major adverse coronary events and research suggests it's a more powerful predictor than LDL cholesterol (72). In the present study there was a clinically significant benefit (71% benefit; 4% harm) for HDL cholesterol for those in the HIIT group, relative to the CMIET group. Few studies exist that have investigated the effects on HDL in a comparable population, for a period longer than eight weeks. A 16 week LDIT study in middle aged adults with metabolic syndrome and very low baseline HDL levels, showed an increase in HDL (0.7 ± 0.1 to 0.8 ± 0.1 mmol/L; $p < 0.05$) following the intervention, whilst there was no significant increase in the CMIET group (150). Schjerve et al. (135) found in obese, middle aged adults, there was no increase in HDL following 12 weeks of LDIT or CMIET, although baseline values were greater in this study, compared to the previous.

In an analysis of four American studies, Gordon et al. found that for every 0.25 mmol/L increase in HDL, there was a corresponding 3% decrease in CHD risk (72). Other estimates found that for every for every 10% reduction in HDL, risk for CAD is increased by 13% (49). In the context of the current study this is of clinical relevance; the increase in HDL for the HIIT group (1.5 ± 0.4 to 1.6 ± 0.5 mmol/L) potentially lowers their risk of developing CAD,

which is of importance given that all participants are currently classified as ‘moderate risk’ for developing atherosclerotic CVD. Additionally, the decrease in HDL for both the CMIET (1.3 ± 0.4 to 1.2 ± 0.3 mmol/L) and control groups (1.6 ± 0.4 to 1.5 ± 0.3 mmol/L), potentially places participants at an increased risk of a coronary event.

High density lipoproteins play an important role in anti-atherogenic function with their ability to drive reverse cholesterol transport (151). Reverse cholesterol transport is a process that occurs in the systemic vasculature, where HDL interacts with cells to deliver excess cholesterol back to the liver for disposal as bile salts (151). Benefits have also been observed for its role in improving endothelial function by stimulating the production of endogenous nitric oxide synthase, nitric oxide (NO) release and the consequential vasorelaxatory effects in the vasculature (106, 170). Evidence is also growing around the role HDL plays in counteracting LDL oxidation, which is hypothesised to play a significant role in the pathogenesis of CAD (166). Additionally, some epidemiological studies suggest HDL has antioxidant effects via a cascade of cellular processes which prevent the oxidation of LDL (4).

As stated in the previous paragraph, LDL plays a detrimental role in the development of atherosclerotic CVD (98). Although it still remains ‘unclear’ if a clinically significant benefit exists for LDL in the HIIT group (relative to the CMIET group), it is encouraging that both exercise groups decreased LDL concentrations by 13% (HIIT) and 16% (CMIET) respectively. To the best of the researcher’s knowledge, only four studies have examined the effect of HIIT on LDL (LDIT: n = 4) and none of these studies have reported changes throughout the intervention (40, 116, 121, 156). On closer examination of each of these

studies, none of them had participants with elevated baseline levels of LDL. This may explain why there was a decrease in the current study, with both exercising groups above the ACSM risk stratification recommendation of <3.4 mmol/L (148).

A 2007 study attempted to quantify the effect of lowering LDL on all-cause mortality and risk of CHD event and death, by means of meta-analysis (73). The authors included 62 studies and found that on average, for every 1 mmol/L decrement in LDL, there was a 26%, 46% and 25% reduction in all-cause mortality, CHD mortality and CHD event (73). Elevated levels of LDL have been shown to be a key contributor for the initiation and progression of atherosclerotic plaque development (7). Exposure to high levels of LDL has been shown to decrease NO bioavailability which is a potent vasodilator and plays an important role in repairing damage to blood vessels (155). Reduced NO bioavailability is a characteristic of endothelial dysfunction and promotes LDL entry into the arterial intima. The LDL particle then becomes trapped and if there is no intervention from HDL particles, oxidation occurs, which is the beginning of atherogenesis (6). In the context of the current study, the reduction of LDL in both exercising groups potentially reduces the risk of developing atherosclerotic CVD in individuals already at moderate risk of developing CVD. Similarly, the study also shows, that those whom maintain a sedentary lifestyle like those in the control group, place themselves at greater risk of atherogenesis due to the cumulative increase in LDL and decrease in HDL.

5.5. Effects of the intervention on body composition

Central adiposity has a strong correlation with both CVD and type 2 diabetes (171). In the present study, both the HIIT (101 ± 16.6 to 99.7 ± 15.2 cm) and CMIET (98 ± 15.2 to 97.1 ± 15.3 cm) groups had clinically significant improvements in waist circumference, compared to the control group whose increased (94.6 ± 13.1 to 96.9 ± 11 cm). When comparing between both exercising groups, the clinical significance was deemed to be 'possible trivial', suggesting no difference. The results in this study were similar to those of Stensvold et al. (143) who performed a 12 week LDIT study in adults with metabolic syndrome. The authors of that study observed a modest decrease in waist circumference following LDIT (109.6 ± 10 to 108.3 ± 10.7 cm), and a small increase in the control group (108.7 ± 9.3 to 110.4 ± 9.0 cm). Tjonna and associates (150) were able to show slightly larger decreases in waist circumference for both LDIT (105.5 ± 4.1 to 100.5 ± 3.6 cm) and CMIET (105.1 ± 5.3 to 99.1 ± 5.0 cm) groups, in adults with metabolic syndrome over a 16 week period.

Of concern is the 2.3cm increase in waist circumference for participants in the control group. Kramer et al. (99) showed that for every 1cm increase in waist circumference, there was a 2% increases all-cause mortality risk. Other estimates show a 10cm increase, has an associated 16% and 25% increased risk in men and women (87). To the best of the author's knowledge, there is currently no existing research quantifying reductions in waist circumference on all-cause and CVD mortality rates. However, we do know that any reduction in central adiposity is of clinical importance as it may reduce FFA levels and lead to an improvement in whole body glucose uptake and insulin sensitivity (12).

5.6. Practical implications

Current exercise recommendations for healthy adults are for at least 150 minutes per week of moderate physical activity or at least 60 minutes per week of vigorous intensity exercise (148). The results of this study suggest that one session a week of a novel and practical form of HIIT combined with CMIET may not be more beneficial than CMIET alone for increasing cardiorespiratory fitness. However, what this study has confirmed is that HIIT combined with CMIET (compared to control group) elicits clinically significant improvements in cardiorespiratory fitness, body mass, BMI, waist and hip circumference, perceived mental health, total and LDL cholesterol, resting heart rate and systolic blood pressure.

When prescribing exercise by caloric expenditure, for general health, it is suggested individuals aim for 1000 kcal per week (119). This study has shown that substituting a session of CMIET for HIIT has minimal effect on relative caloric expenditure (3.0 vs. 2.9 $Kcal.kg^{-1}$) for that session. To ensure an individual adopts an exercise program as part of their lifestyle, it needs to be effective, time efficient and there needs to be variety to ensure they remain motivated (70, 91). It is encouraging to note, that should individuals adopt this practical form of HIIT to add variety to their exercise program, they are still meeting energy expenditure targets and promoting health related benefits. Exercise and health professionals will appreciate this as it allows individuals to add variety to their program, consequently promoting adherence (70, 91).

In response to suggestions that vigorous intensity exercise may be the reason for decreasing physical activity levels, recommendations for health benefits were changed to more regular,

moderate intensity exercise (3-6 METs) (125). In this study, individuals whom had previously been sedentary were motivated and able to train at vigorous intensities (9.5 METs). In fact, this form of exercise training was so popular that there was a 100% attendance for all HIIT sessions. It is the desire of the author that exercise and health professionals encourage individuals to participate in occasional higher intensity exercise of this nature as adherence appears to be good and previous research has highlighted the extra benefits of performing higher intensity exercise (25, 160). Whilst these findings are encouraging, they need to be taken in context. Like the majority of HIIT sessions, participants have higher motivation levels from having a regular social support base to encourage them, making the application of these training regimens limited to everyday situations. Additionally, access to facilities and cost are common perceived barriers to exercise and these were not a factor in this study.

5.7. Limitations

Sample Size

The main limitation in this study was an inability to recruit sufficient numbers of suitable participants to satisfy the pre-determined sample size requirements. Due to the strict inclusion/exclusion criteria, length and commitment necessary, it was difficult finding enough people, who were prepared to exercise five times per week, for a period of 12 weeks. The criteria for participants were very specific and this also had an effect on subject recruitment. For example, participants were required to be sedentary and have at least two risk factors for CVD, whilst safety constraints limited eligible participants to the ages of 18-55 years. Similarly, all participants were required to have started the study before the 19th of September 2012, to ensure the intervention and all testing could be completed before participants were unavailable during the Christmas holiday period. The location for the study also posed a barrier for some potential participants; geographically, Auckland is a very sparse city and the exercise location was not centrally located, and this made it unrealistic for many to attend regularly for 12 weeks. As a result of these difficulties, the HIIT group consisted of three males and four female, the CMIET group had two males and four females, whilst the control group had one male and six females complete the study.

A smaller sample size reduces the statistical power of a study and increases the probability of a type II error (failure to detect an existing effect or difference). However, the risk of a type I error (detecting an effect or difference does not actually exist) is not affected by a reduction in sample size. Because of the low sample size, it is possible that a clinically significant difference in cardiorespiratory fitness may exist between both exercise groups, however due to insufficient data, this was 'unclear'.

Participant attrition

In exercise training studies, there is an approximate 20-25% participant dropout (41). In the present study, there was an overall drop out of 31% (HIIT = 22%; CMIET = 40%; CON = 30%). It is generally considered that attrition under 5% is of minimal concern, but anything above this increases the risk of selection bias (54). Attrition has the potential to negate the effects of randomisation by disrupting the balance of the baseline characteristics, between groups.

Experimenter bias

Due to resources allocated to this study, the student researcher was not able to be blinded. Similarly, the student researcher was required to conduct all the testing for the study. All testing was done in a standardised manner, to ensure it was the same for every participant, before and after the study. Randomisation was done following the initial testing sessions to remove any bias from the initial testing session. Although for each participant during the final testing session, all guidelines were strictly and consistently adhered to, experimenter bias cannot be fully eliminated due to the lack of blinding.

Effect of diet

Whilst participants were instructed to not change their diet in any way during the intervention, the researchers have no way of ensuring this occurred. Surprisingly, there was no change in blood glucose or insulin values following both exercise interventions, suggesting alterations in dietary composition during the study may have negated the effects of exercise. As mentioned in section 5.3, isolated research has shown some overweight/obese

individuals increase their reward value of food, specifically high-fat sweet foods. It is possible that some participants changed dietary habits as a result of commencing the 12 week exercise training program, although a reduction in hip and waist circumferences in both exercising groups may refute this.

Control of habitual energy expenditure

Participants were instructed by the student researcher not to perform any additional training sessions outside of those prescribed as part of the exercise intervention. Whilst it is unlikely that any of the participants significantly increased their physical activity levels outside of the intervention, there is a possibility that as a result of participating in the training programme, participants were motivated to increase their general activity level (e.g. gardening). It is assumed that if this is a general response to exercise, that due to the randomisation, it will occur equally across both exercising groups and have little effect on the outcome measures. Similarly, due to the decrease in cardiorespiratory fitness in the control group, the authors are confident these participants maintained their sedentary lifestyle.

5.8. Future Research

Throughout the course of this study, a number of relevant avenues for future research have arisen. Firstly, a continuation of the current study to meet initial sample size targets and potentially detect clinically meaningful differences between the two exercising groups, where currently a number of variables are still unclear. A greater sample size may also confirm or clarify the unexpected findings around insulin sensitivity.

With the growing voice for the 'Exercise is Medicine' message, accurate information is needed on the optimal and minimal prescription for this exercise (27, 65). Whilst the research surrounding the effectiveness of HIIT is growing rapidly, the minimal thresholds for significant changes are lacking (65). With the current results of this study, it appears that one session a week of HIIT combined with CMIET, is not sufficient to provide a clinically significant increase in cardiorespiratory fitness, compared to CMIET only. The specific HIIT protocol adopted for this study was based on Little et al.'s (109) which was used in trained, healthy subjects. For the present study, this was modified to allow greater recovery time between intervals for the sedentary and higher risk participants. Many of the participants who completed the HIIT protocol commented that the recovery period could be shortened, as the 150 seconds was more than necessary. A shortened recovery time would not only make the protocol more time efficient, but the shorter recovery time may be the stimulus required to get clinically significant changes. With the goal of broadening knowledge around minimal thresholds for change, it would also be interesting to compare if two sessions a week combined with CMIET was more beneficial than the one session per week in the present study.

A big question surrounding the results of many of these HIIT studies and the motivation for the design of this exercise intervention is their ecological validity, or the ability to apply the results to everyday situations. Many of the studies, especially SIT interventions, require high levels of subject motivation and it is likely unrealistic to expect the general public to adopt this as part of their lifestyle. Whilst it is pleasing to see their effectiveness in athletic populations for improving cardiorespiratory fitness (5, 29-31), further research needs to explore how effective different HIIT interventions are in unsupervised settings (27, 68). Given that 50% of participants who start an exercise program, drop out within the first 3-6 months, it is possible that the extra motivation required to perform HIIT on a regular basis is not sustainable in non-athletic populations (51).

Due to the relatively novel nature of HIIT, compared to traditional CMIET, much of the research to date has been done in athletic populations. When compiling the literature review, there was a lack of research in at risk, clinical populations. When comparing CMIET, which has had its physiological and psychological effects in many clinical populations rigorously assessed, it is still unclear what effect HIIT may have on markers of health due to only isolated studies investigating them (27). Additionally, the mechanisms underpinning any changes need further investigation also (27).

5.9. Conclusion

Following the 12 week intervention, both exercising groups showed favourable improvements in $VO_{2max,}$ body composition (hip and waist circumference), systolic and diastolic blood pressure and total and LDL cholesterol, whilst there was no difference in insulin sensitivity. However, it still remains 'unclear' whether a clinically significant difference exists between the two exercise training groups. High intensity interval training is a relatively new and popular type of exercise training, but more research is needed to investigate the minimal requirements for improvements in health and fitness. This form of training was novel in that it utilised one session per week of HIIT, combined with CMIET. Whilst it proved effective, it was no more effective than CMIET alone. Further research is necessary to identify the specific threshold required to elicit more 'likely beneficial' clinical improvements in cardiorespiratory fitness and CVD risk factors.

Appendices

Appendix A – Advertisement

DEPARTMENT OF SPORT AND EXERCISE SCIENCE
Faculty of Science

THE UNIVERSITY OF AUCKLAND
NEW ZEALAND
Te Whare Wānanga o Tāmaki Makaurau

The effect of continuous moderate intensity exercise training combined with high intensity interval training on cardiovascular disease risk factors

If you have risk factors for cardiovascular disease (high blood pressure, cholesterol etc.), you are invited to participate in a research study, entitling you to a free 12 week supervised exercise program

The research involves attending 5 exercise sessions a week for 30-60 minutes and may involve some high intensity interval exercise. Blood pressure and heart rate will be monitored whilst exercising and you will get your fitness level and blood markers accurately tested.

For more information contact:
Researcher: Brendon Roxburgh
Email: b.roxburgh@auckland.ac.nz
Phone: (09) 9232540
Address: The University of Auckland, 71 Merton Road, Glen Innes, Auckland 1072

Research funded by start-up funds available to Dr Lance Dalleck

APPROVED BY THE UNIVERSITY OF AUCKLAND HUMAN PARTICIPANTS ETHICS COMMITTEE ON 26/1/12 for (3) years, Reference Number 7764.

Brendon Roxburgh b.roxburgh@auckland.ac.nz 09 9232540	Brendon Roxburgh b.roxburgh@auckland.ac.nz 09 9232540	Brendon Roxburgh b.roxburgh@auckland.ac.nz 09 9232540	Brendon Roxburgh b.roxburgh@auckland.ac.nz 09 9232540	Brendon Roxburgh b.roxburgh@auckland.ac.nz 09 9232540	Brendon Roxburgh b.roxburgh@auckland.ac.nz 09 9232540	Brendon Roxburgh b.roxburgh@auckland.ac.nz 09 9232540	Brendon Roxburgh b.roxburgh@auckland.ac.nz 09 9232540	Brendon Roxburgh b.roxburgh@auckland.ac.nz 09 9232540

Appendix B – Newspaper article

when it costs $5 for two.

Study needs hearty participants

PARTICIPANTS are needed for a study looking into how exercise can help prevent heart disease.

Cardiovascular disease is the leading cause of death in New Zealand and accounts for 40 per cent of all deaths each year.

Brendon Roxburgh, a University of Auckland researcher and supervisor of the Auckland Cardiac Rehabilitation Clinic, is calling for volunteers for a 12-week exercise-based study.

Mr Roxburgh says interval training, which is moderate exercise with intermittent short bouts of high-intensity exercise, may be more beneficial for reducing heart risk factors than traditional exercise.

However, he warns it can be "difficult and potentially unsafe for individuals with risk factors to perform interval training frequently enough to achieve benefits", and recommends supervised exercise for those who may have several risk factors.

People aged 18-45 who may be at risk of heart disease are needed for the study, which consists of a free, supervised exercise programme. "By participating in this research you'll be helping improve your own health, while helping us to learn how to best help others," he says.

For more details, see www.getparticipants.com/exercise.

Appendix C – ACSM risk stratification criteria

Atherosclerotic CVD risk factor thresholds for use with ACSM risk stratification. (Adapted from Thompson et al. (148))

POSITIVE RISK FACTORS	DEFINING CRITERIA
Age	Men ≥45 yr; Women ≥55 yr
Family history	Myocardial infarction, coronary revascularization,or sudden death before 55 yr of age in father or other male first-degree relative, or before 65 yr of age in mother or other female first-degree relative
Cigarette smoking	Current cigarette smoker or those who quit within the previous 6 months or exposure to environmental tobacco smoke
Sedentary lifestyle	Not participating in at least 30 minutes of moderate intensity (40%–60% VO_2R) physical activity on at least three days of the week for at least three months
Obesity	Body mass index ≥30 $kg \cdot m^2$ *or* waist girth ≥102 cm for men and ≥88 cm for women
Hypertension	Systolic blood pressure ≥140 mmHg and/or diastolic ≥90 mmHg, confirmed by measurements on at least two separate occasions, *or* on antihypertensive medication
Dyslipidaemia	LDL cholesterol ≥3.37 mmol/L *or* HDL cholesterol ≤ 1.04 mmol/L *or* on lipid-lowering medication. If total serum cholesterol is all that is available use ≥5.18 mmol/L
Pre-diabetes	Impaired fasting glucose ≥5.50 mmol/L, but ≤6.93 mmol/L *or* 2-hour values in OGTT ≥7.70 mmol/L, but ≤11.00 mmol/L confirmed by measurements on at least two separate occasions
NEGATIVE RISK FACTOR DEFINING CRITERIA	
High-serum HDL cholesterol	≥1.55 mmol/L

Appendix D – Participant information sheet

DEPARTMENT OF SPORT AND EXERCISE SCIENCE
Faculty of Science

THE UNIVERSITY OF AUCKLAND
NEW ZEALAND
Te Whare Wānanga o Tāmaki Makaurau

Department of Sport and Exercise Science
Building 734.321 261 Morrin Road,
Glen Innes, Auckland, New Zealand
Telephone 64 9 373 7599 ext.86887
Facsimile 64 9 373 7043
Email: sports-science@auckland.ac.nz
www.ses.auckland.ac.nz

The University of Auckland
Private Bag 92019
Auckland, New Zealand

Participant Information Sheet
For research participant

Project title: **The effect of continuous moderate intensity exercise training combined with high intensity interval training on cardiovascular disease risk factors**

Name of Researcher: **Brendon Roxburgh**

Researcher Introduction

My name is Brendon Roxburgh and I am a Masters of Science (MSc) student in the Department of Sport and Exercise Science at The University of Auckland.

Project description and invitation

I am inviting you to participate in a 12 week training study investigating the effects of traditional exercise training and interval training in individuals at risk of cardiovascular disease. I am seeking forty-five participants aged 18-55 years, male or female, non-smoking, not currently participating in regular physical activity and at moderate risk of developing cardiovascular disease (at least two risk factors). All information obtained in this study will be treated with complete confidentiality and may be used as part of my MSc thesis.

Rationale

Recent research suggests high intensity interval training may be more beneficial at improving cardio-respiratory fitness and insulin sensitivity, compared to traditional exercise training. With the number of people diagnosed with CVD out of control in New Zealand, a sustainable exercise intervention is necessary to help reduce this rate. It is believed interval training may produce greater health benefits, despite requiring similar/less time to do than traditional exercise training, making it an attractive form of exercise. However, to perform it daily is not realistic, hence why we are combining it with traditional exercise training to assess how it affects health.

Project procedures

In order to be accepted into the study you must be granted medical clearance to exercise from a general practitioner to ensure your safety whilst exercising.

Once referred, you will be given the participant information sheet and a consent form to complete, should you wish to join the study. Following this, you will undergo a screening test over the phone to determine your eligibility for the study. If all eligibility criteria are satisfied, a time for an initial assessment will be scheduled.

Initial assessment

– To be conducted at: The University of Auckland, 71 Merton Road, Glen Innes, Auckland. The initial assessment is expected to take **1 hour** of your time

You will be required to avoid alcohol and physical activity on the day prior to the assessment. We ask that you wear clothing and footwear that is suitable and comfortable for exercise. When you attend the initial assessment you will have the opportunity to ask any questions, before completing the informed consent form. From this, your body weight and hip and waist circumference will be measured. You will be asked to complete a short questionnaire which will assess how you perceive your physical and mental health and then your blood pressure will be measured. An electrocardiogram (ECG) is also required to assess your heart. This may involve shaving small amounts of body hair, and lightly sandpapering the skin to allow the electrodes to stick on to your skin. Please note, the abrading of the skin may cause mild discomfort.

Exercise test

You will be required to complete an exercise test on the treadmill. The objective of the test is to assess your level of fitness, so you will be required to exercise to fatigue. The test is designed to last for approximately 8-12 minutes. You have the right to stop the exercise test at any time. We require data on the air you breathe in and out, so throughout the test you will be required to breathe through a mouthpiece. You will also be required to have a blood pressure cuff on your arm throughout the test, so we can monitor your blood pressure. You will also have a number of wires connected to electrodes on your skin, which will monitor the electrical activity of your heart throughout the test. The exercise test may cause light headedness, shortness of breath and/or muscular fatigue.

Please be aware we may need to contact your general practitioner to clarify any information obtained during this assessment.

You will then be randomized into one of three exercise training groups:

- Group one – 30 minutes moderate intensity exercise, five times a week (Mon, Tue, Wed, Thur & Fri) on the cycle and treadmill
- Group two - 30 minutes moderate intensity exercise, four times a week (Mon, Tues, Thur & Fri) on the cycle and treadmill & one session a week of

high intensity interval training (Wed) that will involve 8-12 x 60s efforts on the cycle at an intensity equal to what you achieved in your exercise test, separated by 150s recovery at a very light intensity

- Group three – A control group where you are required to remain inactive

Following the initial assessment you will need to get a fasting blood sample taken from Diagnostic Medlabs. It is very important that you have not consumed any food or drink (water is ok) overnight, and have fasted for at least 12 hours before getting the blood sample.

The **duration of the study is twelve weeks** and all exercise will be performed at the UniSports Training Centre, 71 Merton Road, St Johns. The exercise sessions will involve stretching, a warm-up/down and a period of exercise as detailed above, with sessions lasting no longer than one hour. Sessions will be monitored by the student researcher and University of Auckland Sport and Exercise post-graduate students may also assist in delivering the exercise programmes. At the end of the study, you will be required to repeat the initial assessment, in order to assess any changes that may have occurred during the twelve weeks. **This final assessment will take 1 hour of your time**.

If you would like a copy of your results, please indicate on the informed consent form.

Note: Those subject whom are randomized into group three, will be given a free voucher at the end of the study for a 12 week monitored exercise programme at the University of Auckland Cardiac Rehabilitation Clinic.

Start-up funds available to Dr Lance Dalleck will be used to fund this study.

Storage of data

All data obtained from this study will be stored for the duration of the research may be used as part of my Masters of Science thesis. Data obtained from the study will be anonymously processed by computer software and analysed to be presented as part of my thesis. All data and participant information will be stored securely in a locked filing cabinet at the University of Auckland at 71 Merton Road, Glen Innes, Auckland and only the student investigator and primary investigator will have access to this. All data and participant information collected for the purpose of the study will be shredded and destroyed at the completion of the study; any electronic data will be destroyed using formatting software.

Right to withdraw from participation

Your participation in this study is voluntary and if you decide not to take part in the study, this will not affect any future care or treatment by any medical or health professional. If you are a student or staff member of the University of Auckland, your grades and/or job will in no way be impacted by your participation/non-participation in this study. You have the right to withdraw from participating in this study at any time

without explanation. Participants also have the right to withdraw their data from the study up to December 2012.

Anonymity and confidentiality

Due to the nature of this study, you may be exercising in an environment with other members from the study; therefore we cannot guarantee that your identity will be kept anonymous throughout the study. Please note that no research participant will be able to see or access any personal information. To ensure your safety when exercising, post-graduate students delivering your exercise will be informed of relevant information that may influence how you respond to exercise. Any data collected and displayed in results would be displayed in a way which does not disclose their identity. Each subject will be given an alphabetical and numerical code. The format of the code will be the first initial of the participant's first name and the first 3 letters of their last name, along with a 3 number code. i.e Brendon Roxburgh BROX013. Only the student researcher and primary investigator will have access to the codes and the identity of the subjects. The sheet with names and code-numbers will be kept in a separate and secure filing cabinet at the University of Auckland, 71 Merton Road, Glen Innes, Auckland and only the student researcher will have access to this.

Compensation

There is no cost to you for taking part in this study – all exercise training, testing and procedures are free of charge.

In the unlikely event of injury as a direct result of your involvement in this study, you may be covered by ACC under the Injury prevention, Rehabilitation and Compensation Act. ACC cover is not guaranteed and will be evaluated by ACC. If your claim by ACC is accepted, you still may not receive compensation. ACC generally only provides partial reimbursement of costs and expenses and there may be no lump sum compensation available. There is no cover for mental injury unless it is a result of physical injury. If you have ACC cover, generally this will affect your right to sue the investigators. More information is available from http://www.acc.co.nz or speak with the researchers if you have any questions.

Risks

Every measure is taken to minimise the risk of injury during the exercise tests and exercise training. There is a 1 in 10,000 risk of death during a graded exercise test. Staff are trained in first aid, a defibrillator and direct phone line is in the room and doctors are in the same complex as the testing and exercise training. During the blood sample and testing you may experience some discomfort. Also, the exercise training and exercise test may cause dizziness, muscular fatigue and/or shortness of breath. There is also a risk of muscular fatigue, light-headedness or shortness of breath during exercise. By following the exercise recommendations of the researcher and having a thorough warm up and cool down, you minimise this risk.

Contact details

Should you have any questions about this form or the study, please contact one of the people below and we will happily answer them for you.

Researcher: Brendon Roxburgh
Email: b.roxburgh@auckland.ac.nz
Phone: (09) 9232540
Address: The University of Auckland, 71 Merton Road, Glen Innes, Auckland 1072
Supervisor: Dr Lance Dalleck
Email: l.dalleck@auckland.ac.nz
Phone: (09) 9233766
Address: The University of Auckland, 261 Morrin Road, Glen Innes, Auckland
Head of Department: Assoc Prof Greg Anson
Email: g.anson@auckland.ac.nz
Phone: (09) 9232975
Address: The University of Auckland, 261 Morrin Road, Glen Innes, Auckland

For any queries regarding ethical concerns you may contact the Chair, The University of Auckland Human Participants Ethics Committee, The University of Auckland, Office of the Vice Chancellor, Private Bag 92019, Auckland 1142.
Telephone: (09) 373-7599 extn. 83771

APPROVED BY THE UNIVERSITY OF AUCKLAND HUMAN PARTICIPANTS ETHICS COMMITTEE ON 26/1/2012 for (3) years, Reference Number 7764.

Appendix E – Consent form

DEPARTMENT OF SPORT AND EXERCISE SCIENCE
Faculty of Science

THE UNIVERSITY OF AUCKLAND
NEW ZEALAND
Te Whare Wānanga o Tāmaki Makaurau

Department of Sport and Exercise Science
Building 734.321 261 Morrin Road,
Glen Innes, Auckland, New Zealand
Telephone 64 9 373 7599 ext.86887
Facsimile 64 9 373 7043
Email: sports-science@auckland.ac.nz
www.ses.auckland.ac.nz

The University of Auckland
Private Bag 92019
Auckland, New Zealand

CONSENT FORM
Research participant

THIS FORM WILL BE HELD FOR A PERIOD OF 6 YEARS

Project title: **The effect of continuous moderate intensity exercise training combined with high intensity interval training on cardiovascular disease risk factors**
Name of Researcher: **Brendon Roxburgh**

I have read and understood the Participant Information Sheet, have understood the nature of the research and why I have been selected. I have had the opportunity to ask questions and have them answered to my satisfaction.

- I agree to take part in this research.
- I understand my participation in this study is voluntary and that I am free to withdraw my participation at any time, and to withdraw any data traceable to me up to December 2012.
- I understand that blood samples will be taken and maybe frozen for up to two weeks before analysis
- I understand that I may be required to commit to an exercise programme requiring me to exercise for 30-60 minutes, five times per week, for a period no longer than **twelve weeks.** I understand that some of this exercise may be high intensity.
- I agree to attend two, initial and final testing sessions which may take up to **one hour each**
- I understand all risks involved in this study

- I understand that I may be exercising in the same room and at the same time as other people in the study, so I may be able to be identified as participating in this study. I am aware that all personal information will be kept confidential and secret.
- I understand that the student researcher may need to contact my general practitioner to seek further information to ensure my safety and eligibility for the study
- I wish / do not wish to receive the summary of findings.
- I understand that data will be kept until the completion of the study, after which it will be destroyed.

By signing this form, I agree to the above statements and I agree to take part in this research study.

Name _____

Signature _____ Date _____

APPROVED BY THE UNIVERSITY OF AUCKLAND HUMAN PARTICIPANTS ETHICS COMMITTEE ON 26/1/2012 for (3) years, Reference Number 7764.

Appendix F – Participant questionnaire

DEPARTMENT OF SPORT AND EXERCISE SCIENCE
Faculty of Science

THE UNIVERSITY OF AUCKLAND
NEW ZEALAND
Te Whare Wānanga o Tāmaki Makaurau

Department of Sport and Exercise Science
Building 734.321 261 Morrin Road,
Glen Innes, Auckland, New Zealand
Telephone 64 9 373 7599 ext.86887
Facsimile 64 9 373 7043
Email: sports-science@auckland.ac.nz
www.ses.auckland.ac.nz

The University of Auckland
Private Bag 92019
Auckland, New Zealand

Participant Questionnaire
For research participant

Project title: **The effect of continuous moderate intensity exercise training combined with high intensity interval training on cardiovascular disease risk factors**
Name of Researcher: **Brendon Roxburgh**

All information provided in this questionnaire is strictly confidential and only the principal investigator will have access to it. To ensure your eligibility and safety for the study, please answer all questions with honesty and accuracy.

Please select the appropriate box for your answer and complete additional information if required.

1) How old are you?

_____

2) Are you a smoker, or have you quit smoking in last six months?

☐ Yes ☐ No

3) Has your doctor ever told you that you have a heart condition and that you should only do physical activity recommended by a doctor?

☐ Yes ☐ No

If you answered yes, please state the condition (if known)

_____

4) Have you ever felt pain in your chest whilst doing any physical activity?

☐ Yes ☐ No

If you answered yes, when was the last time you felt the pain

Appendix G – Short form 36 health survey

SF36 Health Survey

INSTRUCTIONS: This set of questions asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities. Answer every question by marking the answer as indicated. If you are unsure about how to answer a question please give the best answer you can.

1. In general, would you say your health is: (Please tick **one** box.)
   - Excellent ☐
   - Very Good ☐
   - Good ☐
   - Fair ☐
   - Poor ☐

2. Compared to one year ago, how would you rate your health in general now? (Please tick **one** box.)
   - Much better than one year ago ☐
   - Somewhat better now than one year ago ☐
   - About the same as one year ago ☐
   - Somewhat worse now than one year ago ☐
   - Much worse now than one year ago ☐

3. The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much? **(Please circle one number on each line.)**

	Activities	Yes, Limited A Lot	Yes, Limited A Little	Not Limited At All
3(a)	**Vigorous activities**, such as running, lifting heavy objects, participating in strenuous sports	1	2	3
3(b)	**Moderate activities**, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	1	2	3
3(c)	Lifting or carrying groceries	1	2	3
3(d)	Climbing **several** flights of stairs	1	2	3
3(e)	Climbing **one** flight of stairs	1	2	3
3(f)	Bending, kneeling, or stooping	1	2	3
3(g)	Waling **more than a mile**	1	2	3
3(h)	Walking **several blocks**	1	2	3
3(i)	Walking **one block**	1	2	3
3(j)	Bathing or dressing yourself	1	2	3

4. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

	(Please circle one number on each line.)	Yes	No
4(a)	Cut down on the **amount of time** you spent on work or other activities	1	2
4(b)	Accomplished less than you would like	1	2
4(c)	Were **limited** in the **kind** of work or other activities	1	2
4(d)	Had **difficulty** performing the work or other activities (for example, it took extra effort)	1	2

5. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (e.g. feeling depressed or anxious)?

	(Please circle one number on each line.)	Yes	No
5(a)	Cut down on the **amount of time** you spent on work or other activities	1	2
5(b)	Accomplished less than you would like	1	2
5(c)	Didn't do work or other activities as **carefully** as usual	1	2

6. During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbours, or groups? (Please tick **one** box.)

- Not at all ☐
- Slightly ☐
- Moderately ☐
- Quite a bit ☐
- Extremely ☐

7. How much physical pain have you had during the past 4 weeks? (Please tick **one** box.)

- None ☐
- Very mild ☐
- Mild ☐
- Moderate ☐
- Severe ☐
- Very Severe ☐

8. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)? (Please tick **one** box.)

- Not at all ☐
- A little bit ☐
- Moderately ☐
- Quite a bit ☐
- Extremely ☐

9. These questions are about how you feel and how things have been with you during the past 4 weeks. Please give the one answer that is closest to the way you have been feeling for each item.

	(Please circle one number on each line.)	**All of the Time**	**Most of the Time**	**A Good Bit of the Time**	**Some of the Time**	**A Little of the Time**	**None of the Time**
9(a)	Did you feel full of life?	1	2	3	4	5	6
9(b)	Have you been a very nervous person?	1	2	3	4	5	6
9(c)	Have you felt so down in the dumps that nothing could cheer you up?	1	2	3	4	5	6
9(d)	Have you felt calm and peaceful?	1	2	3	4	5	6
9(e)	Did you have a lot of energy?	1	2	3	4	5	6
9(f)	Have you felt downhearted and blue?	1	2	3	4	5	6
9(g)	Did you feel worn out?	1	2	3	4	5	6
9(h)	Have you been a happy person?	1	2	3	4	5	6
9(i)	Did you feel tired?	1	2	3	4	5	6

10. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives etc.) (Please tick **one** box.)

- All of the time ☐
- Most of the time ☐
- Some of the time ☐
- A little of the time ☐
- None of the time ☐

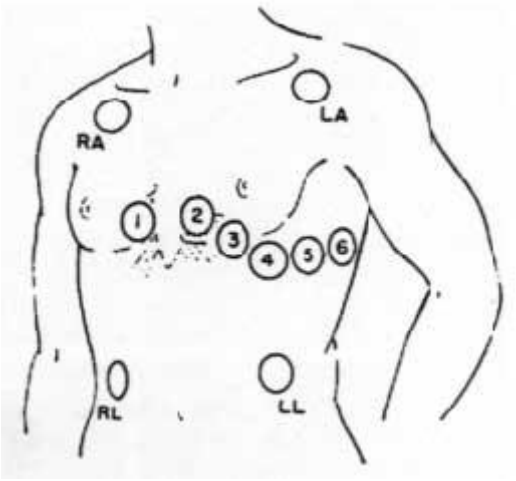
11. How TRUE or FALSE is each of the following statements for you?

	(Please circle one number on each line.)	**Definitely True**	**Mostly True**	**Don't Know**	**Mostly False**	**Definitely False**
11(a)	I seem to get sick a little easier than other people	1	2	3	4	5
11(b)	I am as healthy as anybody I know	1	2	3	4	5
11(c)	I expect my health to get worse	1	2	3	4	5
11(d)	My health is excellent	1	2	3	4	5

Thank You!

Appendix H – ECG Guidelines

1) Get subject to lie supine on the bed with shirt off
2) Each electrode site (as shown in the picture below) needs to be palpated individually, before the skin is prepped
3) Remove dead skin at the site by wiping with gauze. For males, hair may need to be shaven before wiping with gauze.
4) Wipe the excess dead skin with alcohol wipe
5) Place electrode on cleaned site
6) Repeat this for all 10 sites
7) Connect ECG leads to the corresponding electrode attached to the participant
8) Have the participant lay completely still for at least 15 seconds, before printing ECG trace



Appendix I – Contraindications to exercise testing

Contraindications to commencing exercise testing (Adapted from Fletcher et al. (60))

ABSOLUTE	RELATIVE
- Unstable angina	- Any arrhythmia
- Recent MI (with 2 days)	- 2^{nd}-3^{rd} degree AV node block
- No informed consent provided	- Arrhythmias
- Symptomatic aortic stenosis	- Hypertrophic cardiomyopathy
- Subject's safety at risk	- Mental impairment
- Uncontrolled cardiac arrhythmia	- Left main coronary stenosis
- Non-cardiac condition worsened by exercise	- Valvular disease
- Acute pulmonary embolism	
- Symptomatic heart failure	

Appendix J – Rating of perceived exertion scale (Adapted from Borg (22))

Perceived Exertion Scale (RPE)

"How hard do you feel you are exercising?"	
6	
7	Very, very light
8	
9	Very light
10	
11	Fairly light
12	
13	Somewhat hard
14	
15	Hard
16	
17	Very hard
18	
19	Very, very hard
20	

Appendix K – ACSM symptom scale (Adapted from Thompson et al. (148))

ACSM Symptom Scale

1	**Light, Barely noticeable**
2	**Moderate, Bothersome**
3	**Severe, Very uncomfortable**
4	**Most severe pain ever experienced**

Appendix L – Indications for terminating exercise testing

Indications for terminating exercise testing (Adapted from Fletcher et al. (60))

ABSOLUTE	RELATIVE
- Drop in systolic blood pressure (SBP) of ≥10mmHg from baseline SBP despite an increase in workload, when accompanied by other evidence of ischemia	- Drop in systolic SBP of ≥10mmHg from baseline SBP despite an increase in workload, in the absence of other evidence of ischemia
- Moderate-severe angina	- ST or QRS changes such as excessive ST depression
- Increasing nervous system symptoms	- Arrhythmias
- Signs of poor perfusion	- Fatigue, SOB, wheezing, leg cramps, or claudication
- Technical difficulties	- Development of bundle branch block (BBB) or intraventricular conduction delay
- Subject's desire to stop	- Increasing chest pain
- Sustained ventricular tachycardia	- Hypertensive response >250mmHg and/or a diastolic blood pressure of > 115mmHg
- ST elevation (≥ 1.0mm)	

Appendix M – Exercise prescription data sheet

ID: _____ Considerations: _____

MAXHR:_____ HRR 45%_____ 50%_____ 55%_____ 60%_____ 65%_____

Week one __/__/__	MON	TUE	WED	THUR	FRI
Pre HR&BP					
TM time/PRx					
Target HR					
TM HR&BP&RPE					
CYC time/PRX					
CYC HR&RPE					
CYC BP&WATTS					
Post HR&BP					
Notes					

Week two __/__/__	MON	TUE	WED	THUR	FRI
Pre HR&BP					
TM time/PRx					
Target HR					
TM HR&BP&RPE					
CYC time/PRX					
CYC HR&RPE					
CYC BP&WATTS					
Post HR&BP					
Notes					

Week three __/__/__	MON	TUE	WED	THUR	FRI
Pre HR&BP					
TM time/PRx					
Target HR					
TM HR&BP&RPE					
CYC time/PRX					
CYC HR&RPE					
CYC BP&WATTS					
Post HR&BP					
Notes					

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