Strength training and cardiovascular risk post-menses, with particular emphasis on the plasma lipoproteins: a controlled trial

By

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DISSERTATION

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ABSTRACT

Introduction: Cardiovascular disease affects a greater proportion of females than it does males, and is responsible for an estimated 52% of female deaths *per annum*, globally. Due to the loss of oestrogen associated with the menopause, post-menopausal females are at elevated risk for hypercholesterolaemia which is a primary risk factor for cardiovascular disease. It has not yet been conclusively established whether resistance training can be used to ameliorate hypercholesterolaemia.

Aim: This randomized controlled trial investigated what effect 12 weeks of progressive resistance training would have on plasma lipoproteins in a sample of post-menopausal females.

Methods: Caucasian women (n=30 intervention and n=18 control) between the ages of 55 and 65 years who were not taking hormone replacement therapy were recruited. Participants did not smoke, were sedentary, were not taking any form of cholesterol-lowering medication, had at least one cholesterol abnormality at baseline but were otherwise healthy and able to participate in a strength training programme. Following extensive medical pre-screening, information dissemination and voluntary consent, the sample was divided into two groups. The exercise sample undertook 12 weeks of resistance training on five days of the week. The control group received no intervention. Measurements were obtained at baseline and every four weeks thereafter and included measures of strength, biochemistry (oestradiol, testosterone, full blood lipid profile, glycated haemoglobin and sex hormone binding globulin), anthropometry, morphology and self-reports (dietary intake, energy expenditure and the profile of mood states questionnaire).

Results: There was no change to low density lipoprotein cholesterol, high density lipoprotein cholesterol, triglyceride content or total cholesterol as a result of the intervention. Back, chest and leg strength increased significantly ($p<0.01$) (increases of 51%, 35% and 43% respectively from baseline); waist circumference dropped ($p<0.01$) by 5% overall and diastolic blood pressure decreased significantly (-9%, $p<0.01$) in the exercise cohort but no change was noted in the matched control.

Dietary intake, energy expenditure and body mass remained unchanged in both samples. Morphology (sum of skinfolds, estimated body fat content and girth measures) did not change and nor did other biochemical measures (HbA_{1c} and sex hormone binding globulin) or hormone levels (oestradiol and testosterone). Despite the lack of overall change, an important finding was noted in individual results where a clear indication of 'responders' and 'non-responders' emerged.

Conclusion: Overall mean results suggest that 12 weeks resistance training undertaken five days of the week was ineffective in reducing hypercholesterolaemia in this sample. Despite there being no identifying characteristics determined in this sample, evidence of responders and non-responders to the intervention indicates that reliance on mean data may not be sufficient when analysing data from exercise interventions. Therefore, while progressive resistance training had a positive effect on strength, waist circumference and diastolic blood pressure, it did not positively influence the plasma lipoproteins in this cohort of post-menopausal women.

This dissertation is dedicated to

Leonard Eric Kelly and Jean Patricia Kelly

Who have quietly provided a safety net for me, in all ways, throughout this journey. My gratitude is infinite: thank you both for encouraging me to appreciate the importance of reading and of education from a young age, and now more recently, for supporting me as I undertook this challenge.

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LIST OF ABBREVIATIONS

1RM	1-Repetition Maximum (test of strength)
ACSM	American College of Sports Medicine
AHA	American Heart Association
BIA	Bio-electrical Impedance Analysis
BMI	Body Mass Index
BP	Blood Pressure
CDL	Chronic Disease of Lifestyle
CHAMPS	Community Health Activities Model Programme for Seniors
COPD	Chronic Obstructive Pulmonary Disease
CRP	C-Reactive Protein
DBP	Diastolic Blood Pressure
E2	Oestradiol
ECG	Electrocardiogram
EIM®	Exercise is Medicine®
HbA_{1c}	Glycated Haemoglobin
HDL-C	High Density Lipoprotein Cholesterol
HIV	Human Immuno-deficiency Virus
HRT	Hormone Replacement Therapy
IMT	Intima-Media Thickening
LDL-C	Low Density Lipoprotein Cholesterol
MRC	Medical Research Council (of South Africa)
NCD	Non-Communicable Disease
NCEP	National Cholesterol Education Programme
NHANES III	National Health and Nutrition Examination Survey
PAR-Q	Physical Activity Readiness Questionnaire
POMS	Profile of Mood States Questionnaire
QBoD	Quadruple Burden of Disease
RCT	Randomised Controlled Trial
SA	South Africa
SADHS	South African Demographic and Health Survey (2003)
SANHANES-1	South African National Health and Nutrition Examination Survey
SBP	Systolic Blood Pressure
SHBG	Sex Hormone Binding Globulin
T2D	Type II Diabetes
Tot-C	Total Cholesterol
TriG	Triglyceride
USA	United States of America
VO_2max	Maximal oxygen uptake
WHO	World Health Organisation
WHR	Waist-to-Hip Ratio
WSR	Waist-to-Stature Ratio

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Janet Viljoen

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1 INTRODUCTION TO THE STUDY

1.1 INTRODUCTION

Exercise intervention research has been defined by a number of senior researchers in the field. Each 'pioneer' has developed the rigorous methodological considerations the new generation of exercise intervention researchers engage with and employ in new research. Since the mid-1980s Haskell, Nicklas, Paffenbarger and colleagues were asking how much physical activity would be required to ameliorate certain conditions, and assessing the relationship between physical activity and longevity. Paffenbarger lived until 2007, and would have seen the emergence of the formalised field of Exercise Is Medicine® driven by Sallis, who saw his vision come to life in the creation of this field. Haskell, as Professor Emeritus at Stanford continues to research in the field, and more recently has highlighted the importance of a health care system that supports individuals in lifestyle change for the management of chronic disease (Haskell, 2003). Blair, also a past-chairperson of the American College of Sports Medicine, is equally well-published in the field of physical activity and health and recently posited that lack of physical activity is the single largest health problem of the 21st century. Kelley and Kelley (and colleagues with whom papers are published) continue to be the leading publishers of meta-analyses of exercise intervention efficacy, providing valuable insights and tools for other researchers in the discipline. Nicklas began investigating the effects of strength training exercise on overweight and obesity in older adults and specifically post-menopausal women from 1989. Nicklas has continued to focus on older populations with emphasis on post-menopausal samples, and more recently has investigated the efficacy of interventions in decreasing obesity as well as a investigating the effects of a 12 month activity intervention on the metabolic syndrome (Nicklas *et al.*, 2009; Wang *et al.*, 2012; Wang & Nicklas, 2011). This list of 'pioneers' is not finite yet provides an insight into the depth of knowledge in existence in the discipline in 2013. It is to this knowledge base that emerging researchers in the field contribute. An exercise-specific dose-response must be determined for effective implementation of physical activity as the fifth vital sign.

In its broadest sense this study contributes to the body of knowledge pertaining to chronic diseases of lifestyle, and the efficacy of physical activity in ameliorating the risks for these conditions, and the development of these diseases. Adding to the already substantial

understanding that has been developed on this topic over the course of many decades requires that the focus be narrow, specific, and that it fill an identifiable gap in this field.

Physical activity offers holistic health benefit to the individual and as such is recommended for health by the World Health Organisation, American Heart Association, American College of Sports Medicine, and South African Heart and Stroke Foundation. There is strong evidence to suggest that engaging in regular physical activity is fundamental to maintenance of good health. Many studies have evaluated the efficacy of regular aerobic endurance training and found it to have positive outcomes for risk conditions such as obesity (Shaw *et al.*, 2006), adult onset diabetes (Thomas *et al.*, 2006), hypertension (Pescatello *et al.*, 2004) and dyslipidaemia (Kelley & Kelley, 2013). Fewer studies have examined strength training in this regard and evidence for resistance training is less conclusive for most of the risk factors for CVD (Braith & Stewart, 2006; Gordon *et al.*, 2009; Pescatello *et al.*, 2004; Yoshizawa *et al.*, 2009). Those studies that have focussed on resistance training and the lipoproteins have employed three day per week designs, requiring low to moderate effort intensity and have yielded controversial results (Banz *et al.*, 2003; Dunstan *et al.*, 2002; Fahlmann *et al.*, 2002; Manning *et al.*, 1991; Prabhakaran *et al.*, 1999; Viljoen & Christie, 2011; Wooten *et al.*, 2011). For strength training to be adequately assessed greater frequency of training, in line with the American College of Sports Medicine's recommendation that adults must achieve thirty minutes of exercise daily for health benefit, must be assessed. In addition, higher intensity of effort must be assessed, to evaluate the effect of a higher exercise threshold on risk factors that have previously appeared not to respond to resistance training. The minimum time period required to elicit changes via physical activity should be linked to the understanding of the time required to elicit changes at the level of the muscle fibre, as this is what is most affected by, particularly, strength training (Hagerman *et al.*, 2000; Lexell *et al.*, 1995; Romero-Arenas *et al.*, 2013; Sale, 1988). Neural pathway changes may occur within eight weeks of training, and muscle fibre adaptations within 12 weeks of training. It follows, thus, that a programme of strength training shorter than twelve weeks (as has been employed) may not reveal responses, while programmes of longer than 12 weeks duration may not answer the question "what effect might this intervention have?" but instead, answer the question "does the effect last?" which would constitute a very different investigation.

Most information available to date in the literature is applicable to male samples. As pertains to CVD risk, once the menopause has occurred females are at equal if not greater

risk than male counterparts (Rollini *et al.*, 2009). Post-menopausal females cannot be compared to pre-menopausal females, and nor are the responses of this cohort similar to males of any age (Souza & Tezini, 2013). Post-menopausal females are economically active, and with today's life expectancy in many parts of the world can expect to live for upwards of 25 years beyond the menopause (Souza & Tezini, 2013). Optimising health and wellbeing in this population should be prioritised.

The global occurrence of cardiovascular disease in females is high (Rollini *et al.*, 2009). The American Heart Association estimated in 2012 that one in three women has some form of cardiovascular disease (Roger *et al.*, 2012). Females in the United States represent 52% of all deaths from CVD. Amongst adult females of Caucasian descent, an estimated 60% are overweight or obese and only 19% meet the recommended activity guidelines (Roger *et al.*, 2012). The recent South African National Health and Nutritional Examination Survey of 2013 reports similar statistics, and emphasises that dyslipidaemia is present in an estimated 50% of South African females aged 55-64 years. Abnormal low density lipoprotein cholesterol (52%), high density lipoprotein cholesterol (37%) and triglyceride content (35%) in this age group are indicative of insulin resistance linked to high carbohydrate diets. This in turn represents risk for cardiovascular events, particularly atherosclerosis-related such as venous thrombo-embolism and stroke, prevalent in the older female (Schenck-Gustafsson, 2009a). As Goedecke and colleagues have reported, dyslipidaemia is affected by ethnicity, and in South Africa it affects more white females than black counterparts (Evans & Goedecke, 2011; Goedecke, 2010).

The risk associated with dyslipidaemia is controversial (Noakes & Vlismas, 2012; Taubes, 2007). Elevated cholesterol, or abnormal levels of the lipoproteins, has been linked directly to risk of atherosclerosis, damage and occlusion of the arteries, and eventual cardiovascular event. Coupled with the effects of the loss of endogenous oestrogen in females at the time of the menopause, cholesterol is understood to be the mainstay of arterial plaque which leads directly to blood clots and the occurrence of thrombo-embolism and stroke (Khera *et al.*, 2011) . Termed the 'silent killer' it is linked to the sobering statistic that many females who succumb to a cardiovascular event did not present with symptoms beforehand (Roger *et al.*, 2012). An alternative viewpoint holds that cholesterol is not deleterious and should not be 'blamed' for cardiovascular events. Not a mainstream position, this argument holds that cholesterol is a primary 'building block' of cell membranes and neural function, and as such is a necessary part of the plasma

biochemistry (Maxfield & van Meer, 2010). This argument suggests that dietary restriction of cholesterol-containing foods is futile, as the cholesterol in the plasma is in fact produced by the liver and as such is of different chemistry to dietary cholesterol. Additionally, proponents of this viewpoint maintain that it is over-consumption of carbohydrate foods and the subsequent elevation of blood glucose and pro-inflammatory state encouraged by elevated plasma glucose concentrations that elevates risk for cardiovascular events (Ridker, 2012; Ridker, 2013). It is possible that both viewpoints hold merit. Cholesterol does indeed form the basis of atherosclerotic plaque, and plaque deposits do cause arterial blockage and subsequently fatal outcomes. The loss of oestradiol at the menopause does ultimately result in deteriorating health of the arterial walls, and an environment that encourages the deposition of plaque. Oestradiol is a powerful anti-inflammatory and its loss may infer a pro-inflammatory state – and together, CVD risk is elevated in the female (Souza & Tezini, 2013).

Risk post-menopause is not equal. As posited by some researchers, there is a 'window of opportunity' during which is it supposed that the oestrogen receptors remain active and should oestrogen replacement be administered, the receptors can theoretically respond to the synthetic derivative (Stevenson, 2009). Beyond five years post-menopause however, it is hypothesised that the receptors can no longer respond to any form of oestrogen (Stevenson, 2009). It is not clear whether non-drug interventions are also subject to this 'window' or whether the effects of advancing time *sans* oestrogen, combined with inevitably advancing age preclude positive outcomes. What is certain is that age does advance, and that this in itself presents as a risk for deteriorating health.

Stratification in risk factors for cardiovascular disease based on sex is a relatively new ideal, and highlights the need for the sexes to be treated very differently in examining risk for, and expression of CVD. The menopause and the adjunct hormonal changes render post-menopausal females a unique sample for analysis, and it is evident that insufficient attention has been paid to this population to date in comparison to the research engaging male samples of all ages.

1.2 STATEMENT OF THE PROBLEM

Due to the relative scarcity of research focused on females, post-menses, combined with the knowledge of the risk for cardiovascular disease associated with menopause, the current investigation aims to examine the effect of progressive resistance training on risk

factors for cardiovascular disease particularly dyslipidaemia (including evalution of total cholesterol, low density lipoprotein cholesterol, high density lipoprotein cholesterol and triglycerides). Additional risk factors under investigation will include anthropometry (body mass and body mass index), morphology (body fat content, circumferences, waist-to-hip ratio and waist-to-stature ratio), blood pressure (systolic and diastolic), biochemical (glycated haemoglobin and sex hormone binding globulin) and hormonal measures (oestradiol and testosterone).

1.3 HYPOTHESES

1.3.1 RESEARCH

It is hypothesised that a 12 week programme of progressive resistance training will positively affect cardiovascular risk factors, particularly dyslipidaemia, in post-menopausal females.

1.3.2 STATISTICAL

(i) There will be no change to blood lipid profile parameters over the course of 12 weeks, in that:

(a) There will be no change to total cholesterol over 12 weeks

H_o: $\mu TC_{ExE0} = \mu TC_{CoN0} = \mu TC_{ExE4} = \mu TC_{CoN4} = \mu TC_{ExE8} = \mu TC_{CoN8} = \mu TC_{ExE12} = \mu TC_{CoN12}$

H_a: $\mu TC_{ExE0} \neq \mu TC_{CoN0} \neq \mu TC_{ExE4} \neq \mu TC_{CoN4} \neq \mu TC_{ExE8} \neq \mu TC_{CoN8} \neq \mu TC_{ExE12} \neq \mu TC_{CoN12}$

(b) There will be no change to low density lipoprotein (LDL-C) over 12 weeks

H_o: $\mu LDL_{ExE0} = \mu LDL_{CoN0} = \mu LDL_{ExE4} = \mu LDL_{CoN4} = \mu LDL_{ExE8} = \mu LDL_{CoN8} = \mu LDL_{ExE12} = \mu LDL_{CoN12}$

H_a: $\mu LDL_{ExE0} \neq \mu LDL_{CoN0} \neq \mu LDL_{ExE4} \neq \mu LDL_{CoN4} \neq \mu LDL_{ExE8} \neq \mu LDL_{CoN8} \neq \mu LDL_{ExE12} \neq \mu LDL_{CoN12}$

(c) There will be no change to high density lipoprotein (HDL-C) over 12 weeks

H_o: $\mu HDL_{ExE0} = \mu HDL_{CoN0} = \mu HDL_{ExE4} = \mu HDL_{CoN4} = \mu HDL_{ExE8} = \mu HDL_{CoN8} = \mu HDL_{ExE12} = \mu HDL_{CoN12}$

H_a: $\mu HDL_{ExE0} \neq \mu HDL_{CoN0} \neq \mu HDL_{ExE4} \neq \mu HDL_{CoN4} \neq \mu HDL_{ExE8} \neq \mu HDL_{CoN8} \neq \mu HDL_{ExE12} \neq \mu HDL_{CoN12}$

(d) There will be no change to triglyceride content over the course of 12 weeks

H_o: $\mu TG_{ExE0} = \mu TG_{CoN0} = \mu TG_{ExE4} = \mu TG_{CoN4} = \mu TG_{ExE8} = \mu TG_{CoN8} = \mu TG_{ExE12} = \mu TG_{CoN12}$

H_a: $\mu TG_{ExE0} \neq \mu TG_{CoN0} \neq \mu TG_{ExE4} \neq \mu TG_{CoN4} \neq \mu TG_{ExE8} \neq \mu TG_{CoN8} \neq \mu TG_{ExE12} \neq \mu TG_{CoN12}$

(ii) There will be no change to biochemical risk factors over the course of 12 weeks

(a) There will be no change to glycated haemoglobin over the course of 12 weeks

H_o: $\mu HbA_{1cExE0} = \mu HbA_{1cCoN0} = \mu HbA_{1cExE4} = \mu HbA_{1cCoN4} = \mu HbA_{1cExE8} = \mu HbA_{1cCoN8} = \mu HbA_{1cExE12} = \mu HbA_{1cCoN12}$

H_a: $\mu HbA_{1cExE0} \neq \mu HbA_{1cCoN0} \neq \mu HbA_{1cExE4} \neq \mu HbA_{1cCoN4} \neq \mu HbA_{1cExE8} \neq \mu HbA_{1cCoN8} \neq \mu HbA_{1cExE12} \neq \mu HbA_{1cCoN12}$

(b) There will be no change to sex hormone binding globulin over the course of 12 weeks

H_o: $\mu SHBG_{ExE0} = \mu SHBG_{CoN0} = \mu SHBG_{ExE4} = \mu SHBG_{CoN4} = \mu SHBG_{ExE8} = \mu SHBG_{CoN8} = \mu SHBG_{ExE12} = \mu SHBG_{CoN12}$

H_a: $\mu SHBG_{ExE0} \neq \mu SHBG_{CoN0} \neq \mu SHBG_{ExE4} \neq \mu SHBG_{CoN4} \neq \mu SHBG_{ExE8} \neq \mu SHBG_{CoN8} \neq \mu SHBG_{ExE12} \neq \mu SHBG_{CoN12}$

(iii) There will be no change to hormone levels over the course of 12 weeks

(a) There will be no change to oestradiol levels over the course of 12 weeks

H_o: $\mu E2_{ExE0} = \mu E2_{CoN0} = \mu E2_{ExE4} = \mu E2_{CoN4} = \mu E2_{ExE8} = \mu\ E2_{CoN8} = \mu E2_{ExE12} = \mu E2_{CoN12}$

H_a: $\mu E2_{ExE0} \neq \mu E2_{CoN0} \neq \mu E2_{ExE4} \neq \mu E2_{CoN4} \neq \mu E2_{ExE8} \neq \mu E2_{CoN8} \neq \mu E2_{ExE12} \neq \mu E2_{CoN12}$

(b) There will be no change to testosterone levels over the course of 12 weeks

H_o: $\mu T_{ExE0} = \mu T_{CoN0} = \mu T_{ExE4} = \mu T_{CoN4} = \mu T_{ExE8} = \mu T_{CoN8} = \mu T_{ExE12} = \mu T_{CoN12}$

H_a: $\mu T_{ExE0} \neq \mu T_{CoN0} \neq \mu T_{ExE4} \neq \mu T_{CoN4} \neq \mu T_{ExE8} \neq \mu T_{CoN8} \neq \mu T_{ExE12} \neq \mu T_{CoN12}$

(iv) There will be no change to body composition (body mass, body mass index, waist circumference, all additional circumference measures, waist-to-hip ratio, waist-to-stature ratio, estimated body fat content, sum of skinfolds) over the course of 12 weeks

H_o: $\mu BC_{ExE0} = \mu BC_{CoN0} = \mu BC_{ExE4} = \mu BC_{CoN4} = \mu BC_{ExE8} = \mu BC_{CoN8} = \mu BC_{ExE12} = \mu BC_{CoN12}$

H_a: $\mu BC_{ExE0} \neq \mu BC_{CoN0} \neq \mu BC_{ExE4} \neq \mu BC_{CoN4} \neq \mu BC_{ExE8} \neq \mu BC_{CoN8} \neq \mu BC_{ExE12} \neq \mu BC_{CoN12}$

(v) There will be no change to blood pressure (systolic blood pressure and diastolic blood pressure) over the course of 12 weeks

H_0: $\mu BP_{ExE0} = \mu BP_{CoN0} = \mu BP_{ExE4} = \mu BP_{CoN4} = \mu BP_{ExE8} = \mu BP_{CoN8} = \mu BP_{ExE12} = \mu BP_{CoN12}$

H_a: $\mu BP_{ExE0} \neq \mu BP_{CoN0} \neq \mu BP_{ExE4} \neq \mu BP_{CoN4} \neq \mu BP_{ExE8} \neq \mu BP_{CoN8} \neq \mu BP_{ExE12} \neq \mu BP_{CoN12}$

(vi) There will be no change to strength over the course of 12 weeks, as determined by the following:

(a) There will be no change to latissimus dorsi "pulldown" strength

H_o: $\mu LAT_{ExE0} = \mu LAT_{CoN0} = \mu LAT_{ExE4} = \mu LAT_{CoN4} = \mu LAT_{ExE8} = \mu LAT_{CoN8} = \mu LAT_{ExE12} = \mu LAT_{CoN12}$
H_a: $\mu LAT_{ExE0} \neq \mu LAT_{CoN0} \neq \mu LAT_{ExE4} \neq \mu LAT_{CoN4} \neq \mu LAT_{ExE8} \neq \mu LAT_{CoN8} \neq \mu LAT_{ExE12} \neq \mu LAT_{CoN12}$

(b) There will be no change to "chest press" strength

H_o: $\mu CP_{ExE0} = \mu CP_{CoN0} = \mu CP_{ExE4} = \mu CP_{CoN4} =- \mu CP_{ExE8} = \mu CP_{CoN8} = \mu CP_{ExE12} = \mu CP_{CoN12}$
H_a: $\mu CP_{ExE0} \neq \mu CP_{CoN0} \neq \mu CP_{ExE4} \neq \mu CP_{CoN4} \neq \mu CP_{ExE8} \neq \mu CP_{CoN8} \neq \mu CP_{CoN8} \neq \mu CP_{ExE12} \neq \mu CP_{CoN12}$

(c) There will be no change to "leg press" strength

H_o: $\mu LEG_{ExE0} = \mu LEG_{CoN0} = \mu LEG_{ExE4} = \mu LEG_{CoN4} = \mu LEG_{ExE8} = \mu LEG_{CoN8} = \mu LEG_{ExE12} = \mu LEG_{CoN12}$
H_a: $\mu LEG_{ExE0} \neq \mu LEG_{CoN0} \neq \mu LEG_{ExE4} \neq \mu LEG_{CoN4} \neq \mu LEG_{ExE8} \neq \mu LEG_{CoN8} \neq \mu LEG_{ExE12} \neq \mu LEG_{CoN12}$

Where:

ExE:	Exercise group (progressive resistance training)
CoN:	Control group
0,4,8,12:	Weeks (measurements at four weekly intervals)
TC:	Total cholesterol ($mmol.L^{-1}$)
LDL:	Low density lipoprotein cholesterol ($mmol.L^{-1}$)
HDL:	High density lipoprotein cholesterol ($mmol.L^{-1}$)
TG:	Triglyceride content ($mmol.L^{-1}$)
HbA_{1c}	Glycated haemoglobin (%)
SHBG	Sex hormone binding globulin ($nmol.L^{-1}$)
E2	Oestradiol ($pmol.L^{-1}$)
T	Testosterone ($nmol.L^{-1}$)
BC:	Body composition

BP:	Blood pressure (mmHg)
LAT:	Latissimus dorsi strength (“lat pulldown”)
CP:	Chest strength (“chest press”)
LEG:	Lower limb strength (“leg press”)

1.4 STRUCTURE OF THE THESIS

Chapter 1 presents the research question and details the statistical hypotheses governing this intervention. Chapter 2 provides a review and critique of the available body of literature, with specific focus on dyslipidaemia as a risk factor for cardiovascular disease. Intervention options are reviewed, with particular focus on exercise. Chapter 3 provides detail of the recruitment strategy, administration of the project, the evidence-base for the methodological design, and sufficient methodological detail to facilitate replication of this study. Chapter 4 presents the findings, and these are discussed in the integrated discussion (Chapter 5). A brief synopsis is presented in Chapter 6, along with clarification of the decisions related to the initially stated statistical hypotheses. A list of peer-reviewed journal articles and conference proceedings which have been submitted and delivered during the course of this research has been included, as has a bibliography of works deemed influential during the development of this thesis and the academic maturation of the author. The reference list mentions all works referred to within this text. Please note the inclusion of a list of abbreviations, tables and figures for ease of reference, placed at the very beginning of the thesis. Accompanying documentation and information which bears relevance to the findings and the interpretation thereof is catalogued in the Appendices. The epilogue details the author’s experience of undertaking this PhD research between 2009 and 2013.

2 REVIEW OF RELATED LITERATURE

2.1 INTRODUCTION

Literature was sourced using available resources including, but not limited to, those presented in Figure 2.1. Relevant material was reviewed using the '*CONSORT*' guidelines for reliability and relevance of the study for inclusion into the literature review.

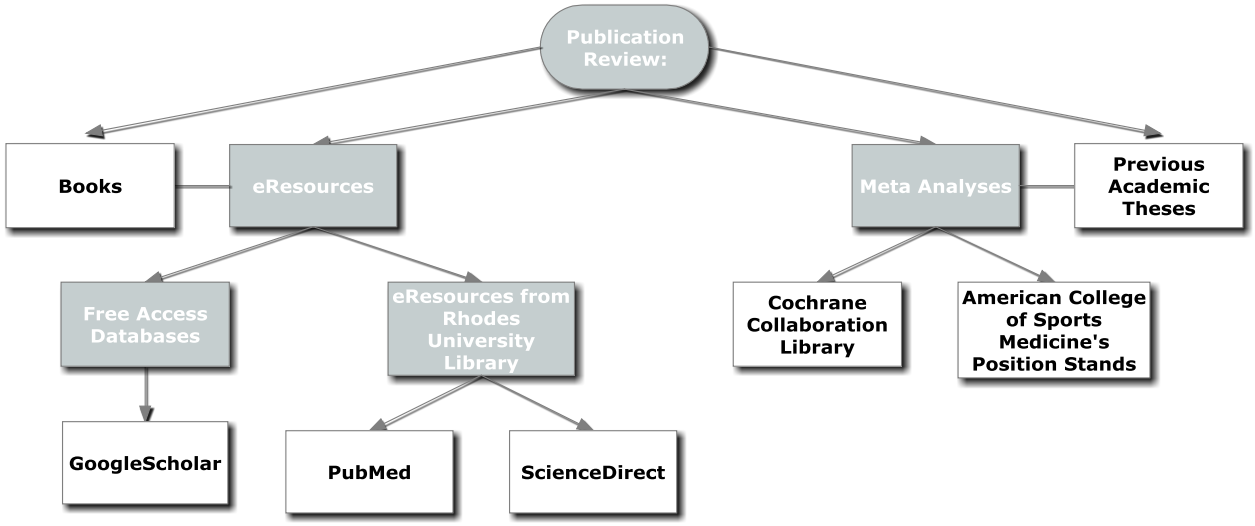


Figure 2.1: Publication review process and tools

The terminology used in searching for relevant literature is outlined in Figure 2.2. This is a representative but not complete list and other terms used included 'glycated haemoglobin', 'systolic/diastolic blood pressure', 'hypertension', 'sex-hormone binding globulin' to name but a few. Literature searches took place throughout the study duration, commencing in March 2009 and continuing until December 2013 and completion of the thesis.

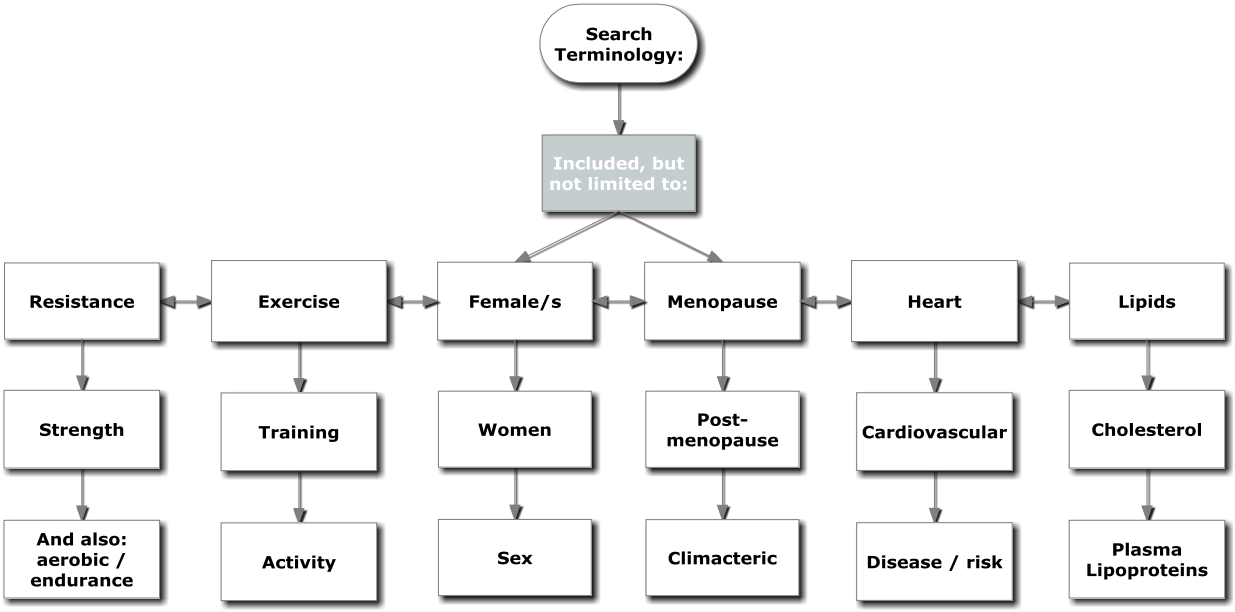


Figure 2.2: Search terminology employed

2.2 CARDIOVASCULAR DISEASE: FACTS AND FIGURES

According to the World Health Organisation in 2013, 63% of all deaths worldwide are attributable to "non-communicable diseases" (NCDs). Of the NCDs, the most predominant are cardiovascular disease, diabetes, cancers, and chronic pulmonary obstructive disease. In the United States the American Heart Association's 2012 update statistics revealed that 52% of female deaths are due to cardiovascular disease and that since 1984 female deaths due to CVD have exceeded male deaths from the same cause (American Heart Association, 2012). Despite an apparent decline in the number of deaths related to CVD between 1998 – 2008 by 31% in the US, the cost attributable to CVD rose by over $11 billion between 2007 – 2008 alone (American Heart Association, 2012). This indicates that morbidity associated with CVD is a more pressing concern than mortality from the disease: probably as medical care advances are made and drug regimes improve.

In South Africa, the 2003 Demographic and Health Survey attributed 29% of all deaths to NCDs with cardiovascular disease responsible for 11% of those deaths (SADHS, 2003). Risk factors for NCDs in females are rampant in South Africa: 56% of females are inactive, 72% of females are overweight of these 41% are obese, an estimated 41% of female South Africans have elevated blood pressure, and 37% present with dyslipidemia (SADHS, 2003). Considering the context of South Africa's "Quadruple Burden of Disease" (infectious diseases, HIV/AIDS, violence and non-communicable diseases) which has been exacerbated by the health and socio-economic transition since political change in

1994, the country faces an epidemic that is gaining traction, rather than being corralled. It is not all bad news: it is estimated that 80% of premature deaths due to NCDs could be prevented: and this is the arena in which lifestyle change and behaviour modification becomes fundamental (World Health Organisation, 2013).

Elevated blood cholesterol (>5.20 mmol.L^{-1}) affects an estimated 98.8 million Americans, with females encompassing 54% of this group (compared to 46% males) and white females 47% of that sample (compared to 41.2% black females affected) (Roger *et al.*, 2012). Hypercholesterolemia is prolific in the female population in South Africa: 2012 data revealed that ~50% of adult females (aged 55 – 64 years) have abnormally elevated total cholesterol levels (South African National Health and Nutrition Examination Survey, 2013). Elevated low-density lipoprotein (LDL-C) was identified in ~50% of this age group, and HDL-C and triglycerides were classified as abnormally high in 35% of females in this age range (although in the case of HDL-C "high" levels would be considered beneficent) (SANHANES-1, 2013). To place these figures in context, similarly elevated cholesterol levels were only noted in 20-30% of females aged 25-35 years (pre-menopausal) (SANHANES-1, 2013). The proportion of undiagnosed hyperlipidaemia is unknown.

2.3 FOCUS ON CHOLESTEROL

Chole- (bile) and *stereos* (solid) are taken from ancient Greek, to which the chemical suffix –ol (alcohol) is added. Cholesterol falls within the lipid class as a modified steroid responsible for many functions in the body, most importantly cell membrane permeability and fluidity (Hanukoglu, 1992). Apart from its role in the cell membrane cholesterol is also a precursor to synthesis of the steroid-based hormones (of which class oestradiol and testosterone are part), bile acids and the fat-soluble Vitamin D (Hanukoglu, 1992).

Distinct from cholesterol, the lipoproteins are transport molecules for cholesterol and triglycerides, neither of which are water-soluble (Brunzell *et al.*, 2008). Lipoproteins are comprised of apolipoproteins (the protein element), phospholipids, triglycerides and cholesterol. Very low density lipoprotein (VLDL) is produced in the liver and its primary role is to supply the tissues with free fatty acids (FFA) (Brunzell *et al.*, 2008). Low density lipoprotein (LDL) is a byproduct of VLDL and is the primary carrier of cholesterol in the body. High density lipoprotein (HDL) is produced by the liver and intestines, and may later be transformed into an LDL (Brunzell *et al.*, 2008; Hanukoglu, 1992).

Cholesterol is closely implicated in the genesis of atherosclerosis. A chronic inflammatory condition, as opposed to overt or acute inflammation, atherosclerosis represents a complex interaction between modified lipoproteins, macrophages, the immune system and cellular elements of the arterial wall (Brunzell *et al.*, 2008). Responsible for lesions and plaques that protrude into the lumen of the affected artery, atherosclerosis causes symptoms such as angina and claudication – early warning signs of declining arterial health. Fundamental to this process is cholesterol, as in the human, atherogenesis does not take place unless there are chronically elevated cholesterol levels (Brunzell *et al.*, 2008).

Biochemically, cholesterol transported by LDL (to form low density lipoprotein cholesterol, LDL-C) has a clear central role to play in atherosclerotic disease. It was posited as early as 1985 that clinically significant disease state related to cholesterol occurs when influx into the cell and efflux from the cell, a process continually occurring, becomes imbalanced (Mahley, 1985). That elevated levels of cholesterol are affected by both genetic and environmental factors raises the complexity of the issue of cholesterol, atherosclerosis and cardiovascular disease. Familial or genetic reasons for elevated cholesterol are often viewed as very different to elevated cholesterol that results from poor dietary choices or inactive living (Durrington, 2003). Latterly, scholarly thought has transcended the idea of these being so very independent, and credence is given to the concept that underlying genetic predispositions may be ‘activated’ by environmental triggers. Theoretical as this position may be, what remains clear is that elevated levels of cholesterol and of the lipoproteins require attention, and that lifestyle factors do indeed influence these levels (Bhatnagar *et al.*, 2008; Durrington, 2003).

Recommended levels of cholesterol and lipoprotein parameters are proposed in order to reduce risk exposure to atherosclerotic conditions as a result of elevated cholesterol levels (Table 2.1). Desirable levels are proposed for ‘healthy’ individuals, as presented in Table 2.1, but the guidelines are more conservative for those with diagnosed coronary artery disease or prior cardiac events.

Table 2.1: Recommended cholesterol levels for adult females

	LDL-C ($mmol.L^{-1}$)	HDL-C ($mmol.L^{-1}$)	TriG ($mmol.L^{-1}$)	TotC ($mmol.L^{-1}$)
US (American Heart Association)	<5.2	<1.8	>1.3	<3.8
Canada and Europe	<5.2	<2.6	>1.5	<1.7
South Africa (SA Heart&Stroke Foundation)	<5.2	<2.0	>1.5	(<1.7)

Note: SA does not specifically recommend TriG levels, most conservative recommendation inserted in brackets

2.4 FOCUS ON ATHEROSCLEROSIS

Initial views on the development of atherosclerosis were, perhaps, simplistic (Libby *et al.*, 2009). These views held that it was a passive process of deposition of lipid debris on the artery wall. Latterly prominent theories have developed which may better explain atherogenesis of which two stand out as having enjoyed the most attention: firstly, the concept of endothelial denudation and secondly, that of lipid oxidation (Williams & Tabas, 1995).

Endothelial denudation infers that injury to the endothelial wall of the arteries is central to atherogenesis, a theory sometimes referred to as the 'response to injury' hypothesis. While it is true that endothelial injury does disrupt the arterial wall resulting in increased permeability, this appears to be physiologically insufficient to explain the entire genesis of plaque adherence and artery narrowing (Williams & Tabas, 1995). The additional idea of 'turbulent blood flow' particularly at key points in the arterial system such as arterial branches, raised the additional idea that the shear stress this causes to the arterial walls creates weak points at which endothelial damage can occur, resulting in atherogenesis. Shear stress alone is also insufficient to result in widespread atherosclerosis which would ultimately result in cardiovascular risk and event (Williams & Tabas, 1995).

Lipid oxidation, a natural process, requires the liver to remove the oxidised product from the plasma. Any increase in oxidised products would simply result in rapid removal from the plasma in the context of a healthy, functioning liver (Williams & Tabas, 1995). It is unlikely, therefore, that this process is entirely responsible for atherogenesis.

Given the unlikelihood that either of the aforementioned hypotheses can be solely responsible for the problem of atherosclerosis, alternate biochemical and physiological processes must be considered. Williams and Tabas (1995) suggest that a likely genesis relates to retention of lipoproteins in the arterial wall: the "response to retention"

hypothesis. In short, it is proposed that in a situation of disruption, low density lipoprotein (LDL) is retained within the endothelium to an unnatural degree, causing the development of atheroma. This theory is based on the following facts: first, that all the molecules required for this hypothesis to 'work' are naturally present within a normal arterial wall and it is natural to conclude that disruption of this homeostasis in any way might result in derangement of an otherwise normal physiology. Second, that retained apolipoprotein B (apoB) is closely associated with the presence of arterial proteoglycans. Third, that lipoprotein lipase enhances the adherence of LDL to normal endothelial matrices and normal cell-surface proteoglycans. Fourth, the linkage between peritoneal macrophage production of lipoprotein lipase (LpL) and concomitant susceptibility to atherogenesis has been shown, albeit in mice models. Finally, sphingomyelinase (SMase) causes the formation of LDL aggregates typically seen after induced hypercholesterolaemia (in a rabbit model). SMase and LpL work together to cause massive retention and aggregation (Williams & Tabas, 1995).

The retention model has been developed over the course of recent decades to include inflammation which is now considered the key regulatory process in the genesis of atheroma in conjunction with altered cell biology (the retention theory refers) (Libby *et al.*, 2009). The characteristics of immunity must be understood in order to formulate the logic of inflammation in this process. Immunity in humans is 'innate' and 'adaptive'. Innate immunity is primitive: it mounts quickly in response to perceived foreign invaders, and is evident in all living organisms (Libby *et al*., 2009). Adaptive immunity is the response to more recent evolutionary change, and it requires an 'education' of the immune system to changes and is very specific to the situation it responds to (Libby *et al.*, 2009).

The inflammatory response linked to atherosclerosis utilises facets of both innate and adaptive immunity. The innate element of the response involves macrophages (monocytes) which are "profoundly enriched" in the presence of hyperlipidaemia (this noted in mice models) (Libby *et al.*, 2009). These monocytes tend to 'home' toward lesions on the arterial wall. In addition to the monocyte activity, exaggerated mast cell activity is further evidence for the participation of this immune response in atherogenesis, as is the link that has been identified between lipoproteins and scavenger receptors. The adaptive immune system involvement relates to the cellular response of T-lymphocytes which combine with dendritic cells (mononuclear phagocytes) to create antigens (Libby *et al.*, 2009).

If, as outlined by Libby and colleagues, inflammation is the key to the atherosclerotic process, the therapeutic target is thus inflammation. Current drugs to combat inflammation (non-steroidal anti-inflammatory drugs, gluco-corticosteroids, and anti-cytokine agents) are not viable options as none have been clinically validated for this purpose. Further research into this inflammatory process is required before specific drug therapy becomes available. Having said this, it is touted that the success of statin drugs in reducing atherosclerotic related CVD events is due in most part to their putative anti-inflammatory properties and not, in fact, to their LDL reducing capabilities (Libby *et al*., 2009).

2.5 FOCUS ON FEMALE HORMONES AND REPRODUCTIVE LIFESPAN

Understanding the effects of the cessation of menses (menopause) in females requires an understanding of the hormones that regulate the reproductive cycle throughout life. The anterior pituitary secretes follicular stimulating hormone (FSH) and luteinising hormone (LH) which are the principle regulators in the process of homeostatic regulation of female-specific sex hormones. FSH stimulates ovarian follicle growth and LH stimulates ovulation itself. Estrogen is the female sex-specific hormone, of which there are three variants: Estrone (E1) produced primarily in adipose tissue; Estradiol (E2) emanating from the ovaries (the strongest of the estrogens); and Estriol (E3) which is produced by the placenta during pregnancy (Coelingh Bennink, 2004). Other hormones involved in the process, in a secondary role, are the androgens which are produced by the adrenal glands, and inhibin, (which inhibits the release of FSH from the anterior pituitary), secreted by the follicular cells of the ovary (Coelingh Bennink, 2004).

The reproductive lifespan in which this array of hormones features begins at around the age of seven years, with “adrenarche” which is the onset of secretion of the adrenal hormones (the androgens, particularly testosterone). At this stage levels of FSH, LH and estrogen are low in girl children, until the age of 12 years when girls begin to experience elevated levels of FSH and LH during sleep which is termed ‘menarche’. FSH and LH stimulate the production of E2 in the ovaries and consequently the onset of ovulation. This process heralds the beginning of a reproductive lifespan that will last until the age of approximately 50 years (an average of 35 years of viable reproduction).

A woman’s reproductive lifespan is characterised by hormonally controlled 28-day cycles. Day 1 of this cycle is the onset of menstruation which might last four to eight days duration. Days 1 to 14 are termed the ‘follicular phase’, and days 14 to 28 the ‘luteal

phase'. Ovulation, or the release of an egg into the uterus for potential reproduction, takes place on day 14. Fewer than 400 eggs are released in total over the course of a female reproductive lifespan.

'Pre-menopause' signals the beginning of a decrease in ovarian sensitivity to FSH and LH, and may first be evident from the age of 37 years. This leads to reduced production of E2 from the ovaries, and in due course, failure to ovulate. Once menstruation becomes erratic 'peri-menopause' is experienced during which some post-menopausal symptoms may be experienced, but menstruation does still occur – albeit irregularly. Once menstruation has ceased for 12 consecutive months a woman is defined as being 'post-menopause'. Menopause refers to the final monthly menstruation, and is thus a specific period in time. Following the menopause, a phase referred to as the 'climacteric' is entered – usually wrongly referred to as 'menopause'. 'Menopausal age' is the length of time since menopause occurred.

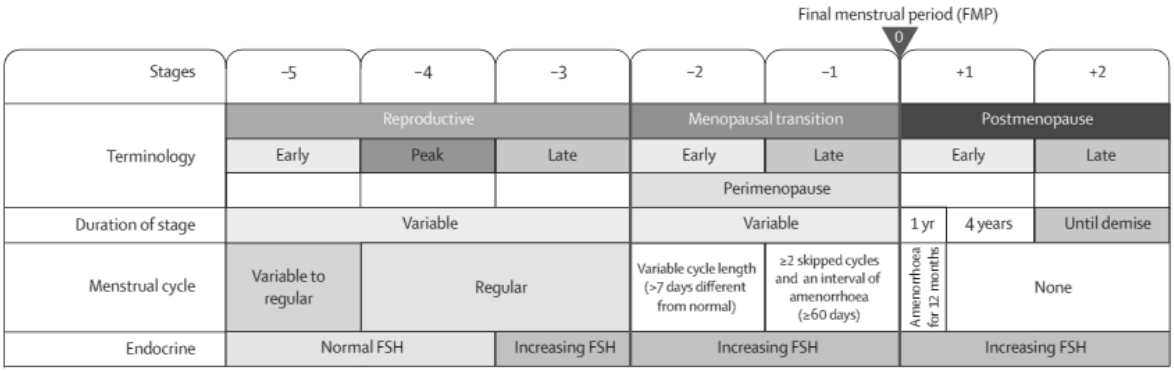


Figure 2.3: Stages of normal reproductive ageing (Nelson, 2008)

Menopause heralds not only the decline in endogenous estrogen levels and failure to ovulate, but also the rapid rise in risk for cardiovascular disease. This risk relates to the role of estrogen in the vascular system: repression of athero-promoting genes, and induction of athero-protective genes (Kim & Bender, 2009). It rapidly activates endothelial nitric oxide (eNOS) which regulates endothelial homeostasis (Kim & Bender, 2009). Estrogen is also a rapid vasodilator. Without E nitric oxide (eNOS) cannot be activated and clots by way of scar tissues may for on the endothelium as a result of inflammatory responses. Arterial narrowing coupled with endothelial dysfunction linked to reduced levels of E lead to reduced vasodilation and elevated risk of CV events (Kim & Bender, 2009).

Estradiol also controls body fluid balance. As E2 is a steroid based hormone it is by nature lipophilic and thus can access receptors inside the central nervous system (CNS). From this it is surmised that E2 itself may alter neural responses to neurotransmitters – for instance for body fluid balance, from baroreceptors in the vasculature. Ultimately, the presence of E2 results in lower blood pressure (Kim & Bender, 2009). Of note is that the two CVD for which females post-menses are most at risk are stroke and hypertension. In summation, in the absence of E2 the vascular environment in the body becomes pathology prone (Kim & Bender, 2009).

2.6 FOCUS ON POST-MENOPAUSAL FEMALES

To date women have been under-represented or excluded from large-scale trials investigating amelioration of chronic diseases (Schenck-Gustafsson, 2009b). There is thus a pressing general need to redress the imbalance of sex-specific information, as it is equally well established that females are at higher risk for chronic diseases particularly post-menopause (Lanz *et al.*, 2006; Ouyang *et al.*, 2009). Menopause and the related changes to the sex hormones in females results in dyslipidaemia, with increased low density lipoprotein combined with increased triglyceride content, and a suggestion that high density lipoprotein levels are also compromised (Collins, 2008; Schenck-Gustafsson, 2009b). Management of health post-menopause has been complicated in the new millennium, with release of data that detracted from the popularity of hormone replacement therapy (Farrell, 2003). Many women and medical practitioners prefer not to choose hormone replacement therapy as a means of managing the symptoms and known health parameter changes at the time of ovarian failure, but apart from drug interventions of other types (such as medication for blood pressure anomalies, and drugs for dyslipidaemia) the question remains: how best to manage menopause and its associated health changes? There is consistency in the message from researchers indicating that lifestyle management must be paramount in any strategy, and that exercise should form a primary part of any treatment regime (Collins, 2008; Farrell, 2003; Schenck-Gustafsson, 2009b). While the message is clear, the evidence-base is weak: reviews on the topic (such as these referenced) lead the reader to understand that exercise “may” be beneficial, or utilise single references to uphold the principle that exercise is positive (Collins, 2008; Schenck-Gustafsson, 2009b). In addition, female participants in the referenced trials appear to be between the ages of 40 and 65 years – which by definition must include some pre- or peri-menopausal individuals, thus contaminating the data (Van Gaal *et al.*,

1997). While the message is agreed with unequivocally (exercise is indeed beneficial), this population group (post-menopausal females) is continually juxtaposed with younger females, or matched male samples, providing a thin evidence base for the management of the cardiovascular health of a population at known risk.

In South Africa, females over the age of 50 years have consistently been at risk of dying from cardiovascular disease, as it has consistently been one of the top three causes of mortality for females in this age category since 1992 (Bradshaw *et al.*, 2003; Mayosi *et al.*, 2009). Most South African data has been derived from observational studies or nation-wide surveys to date, with no controlled trials dedicated to post-menopausal females and cardiovascular risk, to the best knowledge of this researcher. Post-menopausal females represent a major proportion of the economically active population, globally, and certainly in South Africa: understanding the best means of managing their health is pivotal to societal success.

2.7 SUMMARY OF LIFESTYLE INTERVENTIONS

The focus of this review is physical activity, particularly strength training. However, it is acknowledged that other intervention modalities do exist, in particular dietary change. A brief synopsis of the efficacy of dietary manipulation is presented prior to an in depth focus on aerobic endurance training in comparison to progressive resistance training.

A holistic alternative to medication is lifestyle intervention. Prudent dietary changes such as caloric restriction or specific macronutrient content manipulation have been positively associated with cholesterol reduction, and concomitant CVD risk amelioration (Brehm *et al.*, 2009; DeCaterina *et al.*, 2009; Noakes *et al.*, 2005). It is noted that dietary changes affect the body at the cellular level, affecting factors that promote atherogenesis – the forerunner to atherosclerosis which is the most important underlying cause of heart disease (DeCaterina *et al.*, 2006).

Recent assertions have challenged the prevailing understanding of cholesterol, its components, their role in health and risk for cardiovascular complications, and in fact, the need to focus on the lipoproteins in this context (Noakes & Vlismas, 2012; Taubes, 2007). Taubes challenges that the understanding of cholesterol to date has been the result of an oversimplification of a hypothesis which does not and has not reflected the underlying biology. While it has been understood and accepted for decades that the measure of ‘total

cholesterol' is meaningless in the prediction of risk, the relationship between plasma lipoprotein levels and dietary intake of cholesterol-containing foods has not been clearly ratified (Taubes, 2007). Two schools of thought have been and remain in existence: those who follow a fat-cholesterol hypothesis and those who believe that the axis of import is the carbohydrate-cholesterol theory (Taubes, 2007). These hypotheses bear relation to development of atherosclerosis and concomitantly, heart disease, yet it has also been affirmed that in managing risk of coronary artery disease that cholesterol levels, particularly in females, are of no consequence and that in fact older females with higher cholesterol values are at lower risk (Noakes & Vlismas, 2012).

Considered a controversial viewpoint today, it is possible that this approach to the plasma lipoproteins remains an over-simplification. Recent research has proposed that there are two means of approaching the problem of atherosclerosis: first, it can be viewed as lipid-driven, or secondly, it could be considered as the result of inflammation (Ridker, 2012). Current research into the lipoproteins with particular emphasis on the role of the pharmacotherapy for lipid reduction had noted that statin treatment reduces C-reactive protein (an inflammatory marker) just as effectively as the drug reduces low density lipoprotein cholesterol (Ridker, 2012).

Far from being 'out of date', an exploration into the effects of lipoproteins and the various lipid-lowering treatments, perhaps even novel considerations thereof, are still very necessary (Ridker, 2013). As the carbohydrate-cholesterol theory gains credence and the work of Ancel Keys is possibly refuted, the link between dietary intake and lipid levels will remain as pertinent as it ever was in the days of the fat-cholesterol hypothesis (Noakes & Vlismas, 2012; Taubes, 2007). Thus, research into the plasma content of lipoproteins and the ratios thereof becomes invaluable once again – this time in conjunction with novel markers for heart disease such as, for example, glycated haemoglobin and sex-hormone binding globulin (Brand & Van der Schouw, 2010; Kang & Kim, 2012; Livesey *et al.*, 2008; Rexrode *et al.*, 2003; Weinberg *et al.*, 2007; Xu *et al.*, 2007). Cardiovascular disease remains the foremost killer of post-menopausal females globally, responsible for an estimated 56% of female deaths in Europe compared to 43% of male deaths for the same age range (Rollini *et al.*, 2009; Schenck-Gustafsson, 2009). Until this fact is reversed or significantly altered, there is a responsibility for research scientists to continue to explore the mechanism for this risk post-menopause, exploring each avenue from multiple angles. While it may be as Noakes states on page 140: "(that) the theory that proposes that blood

cholesterol causes heart disease is as best tenuous, and at worst wrong…" this is no reason to cast the assumed danger associated with lipoproteins and atherosclerosis aside (Noakes & Vlismas, 2012)

An additional lifestyle intervention is physical activity. Generally accepted to be beneficial to health, movement has the additional potential to ameliorate many symptoms and risks simultaneously. While a drug intervention may focus specifically on one risk factor, and dietary interventions may also be target-focussed, movement is truly holistic and may offer concurrent physiological, musculo-skeletal and psycho-emotional benefits to the individual. Exercise has shown beneficence in treating obesity (Shaw *et al.*, 2006), hypertension (Pescatello *et al.*, 2004), blood glucose irregularities (Thomas *et al.*, 2006) and some cancers (Anzuini *et al.*, 2011). Regular and chronic activity (aerobic and resistance training) has shown some effectiveness in managing hypercholesterolaemia in specific populations (Fahlmann *et al.*, 2002; Prabhakaran *et al.*, 1999; Rainville & Vaccaro, 1984; Ready *et al.*, 1995; Slentz *et al.*, 2007; Wooten *et al.*, 2011). This efficacy is not conclusive, however, as meta-analyses of aerobic endurance interventions and progressive resistance training by Kelley *et al.*, 2006, Kelley & Kelley, 2006, and Kelley & Kelley, 2009 indicate. Kraus *et al*. (2002) indicate that it is the amount of exercise rather than intensity at which the traning is undertaken that is most likely to affect the lipoproteins.

2.7.1 DIETARY INTERVENTIONS

The evidence for dietary manipulation appears clear and consistent. Interventions that have focussed on dietary manipulation have demonstrated significant loss (-13%) of pre-intervention body mass with concomitantly positive effects on overall health (Al-sarraj *et al.*, 2009). With similar health benefit, caloric restriction (specifically the restriction of carbohydrate intake to 20-25% of daily caloric intake) and manipulation has been shown to reduce body fat percentage by ~11% (Al-sarraj *et al.*, 2009). Waist circumference, and by extension abdominal visceral fat (AVF) deposits, responds positively to hypo-caloric dietary restriction in overweight or obese adults, and reduction of AVF has been linked directly to reduced risk of cardiovascular disease (Eshghinia & Mohammadzadeh, 2013; Lowndes *et al.*, 2012; Odegaard *et al.*, 2011; Papadaki *et al.*, 2013; Tate *et al.*, 2012). Eshghinia and Mohammadzadeh (2013) employed an alternate fasting diet wherein participants ingested 25-30% of caloric requirements on Saturdays, Mondays and

Wednesdays, while reverting to habitual dietary intake on the other days. Lowndes and colleagues investigated the effect of replacing sucrose with 'high fructose corn syrup' (HFCS) in conjunction with a hypocaloric diet, and concluded that improvements to body composition occurred whether sucrose or HFCS were utilised in hypocaloric circumstances. Papadaki and colleagues tested the MODIFAST® "low calorie diet" which provided 800kcal.d^{-1} to each individual and reported positive weight and body composition related outcomes. Odegaard *et al*. found that a diet high in vegetables and fruit rather than a meat-reliant diet was inversely related to incidence of type II diabetes, while Tate *et al.* saw positive body composition change when sweetened soda beverages were replaced with plain water. In addition, specific food groups and items have been correlated to waist circumference in 28 937 female participants, indicating a strong dietary composition effect on abdominal visceral adiposity (Romaguera *et al.*, 2011).

Eight weeks to twelve months duration of dietary manipulation reduced waist circumference by 6% (Eshghinia & Mohammadzadeh, 2013) and 9% (Papadaki *et al.*, 2013) respectively when utilising meal replacement products and extreme caloric restriction in overweight individuals. While the reduction in abdominal fat content and thus waist circumference is a positive outcome, the probability of individuals maintaining a strict hypo-caloric diet in the long term is doubtful unless the individual is exceptionally motivated to adhere to the diet (Moreira *et al.*, 2011), thus introducing a limitation in the efficacy of dietary interventions. Other studies of at least eight weeks duration have evaluated the effect of removing or reducing single elements of the diet, including intake of sugar sweetened beverages, and sugar versus sweetener use (Odegaard *et al.*, 2011; Tate *et al.*, 2012). Arguably easier to promote, and an alternative to strict diet regimes, reducing the number of sweetened soda beverages reduced body weight in overweight adults by 2 kg, but it is not clear whether or not this loss of body mass is clinically significant for health outcomes. It does appear however, that whatever food items are consumed, the total caloric content must be reduced to create a situation of slight caloric debt in order to encourage weight loss, waist girth reduction and concomitantly improvements to health (Lowndes *et al.*, 2012).

Large-scale randomised controlled trials evaluating the effect of dietary changes on blood pressure have reported no effect as a result of dietary manipulation (Abedi *et al.*, 2010; Pan *et al.*, 2011; Whitt-Glover *et al.*, 2013). Reduced sodium intake does however appear to have a positive effect on blood pressure, particularly in 'salt-sensitive' individuals

(usually older adults) but a meta-analysis of 167 randomised controlled trials appears to disagree with this finding (Ben-Dov & Bursztyn, 2011; Graudal *et al.*, 2011). Weight loss itself is purported to have a positive effect on blood pressure (Siebenhofer *et al.*, 2011) and it is more likely that pronounced weight loss would be brought about by dietary caloric restriction rather than physical activity alone. Further indication that adherence to low-fat diets high in fibre and low in red meat content reduces incident hypertension is shown in results from the 'ARIC' (Atherosclerosis Risk in Communities) study (Weng *et al.*, 2013). Reduction of systolic and diastolic blood pressure infers a significant decrease in inherent risk for cardiovascular complications and events.

It has been noted that positive association exists between a diet of foods high in fats and the onset of Type II Diabetes, itself a condition but also cited as a risk factor for CVD (Odegaard *et al.*, 2011). It is suggested that diets high in red meat, refined foods and foods high in fat can increase risk of T2D by 18%, while in contrast, dietary selection of fruits and vegetables with fibre-rich content can reduce the risk of T2D by 15% (Li *et al.*, 2009; Nettleton *et al.,* 2008). A meta-analysis of 11 randomised controlled trials of one to 12 months duration (n=402) found a clinically significant drop in glycated haemoglobin measure (HbA_{1c}) of -0.5% following adherence to a 'low glycaemic index (GI)' dietary protocol (Thomas & Elliott, 2009). Glycaemic control in Type II diabetics was significantly increased, with concomitantly fewer hypoglycaemic events, suggesting that a low GI diet does improve the presence or severity of diabetes (Thomas & Elliott, 2009).

2.7.1.1 Plasma Lipoproteins

As the plasma lipoproteins are a primary focus of this dissertation, greater attention will be paid specifically to this risk factor in relation to dietary interventions. In assessing the role of diet in managing dyslipidaemia, the distinction between 'familial' and 'acquired' high cholesterol levels must be made. Familial, or genetically high cholesterol is considered apart from, and managed differently to, lifestyle-acquired dyslipidaemia which infers no genetic predisposition to this risk factor (Shafiq *et al.*, 2010).

It has generally been accepted that "healthy eating" contributes to reduced total cholesterol content in the bloodstream (Esmaillzadeh & Azadbakht, 2008). Weak evidence was found in a Cochrane Review relating 'low glycaemic index (GI)' dietary selections with improved serum cholesterol concentrations (Kelly *et al.*, 2008). In attempting to analyse the effects of a low fat dietary programme on acquired

hypercholesterolaemia, Smart *et al.* (2011) prescribed that well designed studies lasting longer than six months including healthy adults with evident hyperlipidaemia following a low fat diet (fat <20% of total daily energy intake) would be included for analysis. No studies meeting such criteria were found, and so it was concluded that no research of sufficient quality has evaluated this relationship to date (Smart *et al.*, 2011). A well-designed intervention that examined the effect of reduced dietary fat in the diet for eight weeks showed a 7% decrease to total cholesterol levels in post-menopausal females (Nicklas *et al.*, 1997). Contrary to expectations, low sodium intake has been noted to increase total cholesterol by 2.5% compared to high sodium intake in normo- and hypertensive populations (Graudal *et al.*, 2011). There is some limited support for consumption of oats and oatmeal on a regular basis for reducing total plasma cholesterol concentrations (p= 0.001), however these studies were short and of insufficient strength (Kelly *et al.*, 2009).

Puglisi *et al.*, (2008) demonstrably lowered LDL-C following an intervention combining dietary inclusion of raisins on a daily basis. A confounding factor of this study was that at the same time as raisins were added to the diet participants were also encouraged to take daily walks, so it cannot be established whether or not the raisins themselves are responsible for this positive outcome. Nicklas *et al.* (1997) reduced LDL-C in a post-menopausal sample by 6% following eight weeks of reduced dietary fat intake. Li *et al.* (2009) purported to lower LDL-C following regular consumption of nuts, and peanut butter products, while oats and oatmeal reduced LDL-C significantly (p<0.0001) following four to eight weeks of regular consumption (Kelly *et al.*, 2009). The studies engaging oatmeal consumption need cautious interpretation, however, as many were commercially sponsored by companies with vested interests. Noakes *et al.*, (2005) saw a significant drop in LDL-C but attribute this not specifically to dietary changes, but to overall loss of body mass amongst participants.

HDL-C decreased following dietary manipulation and restriction in three studies (Maruther *et al.*, 2009; Nicklas *et al.*, 1997; Noakes *et al.*, 2005), but remained unchanged following a low-fat versus high-fat dietary manipulation of an effective eight weeks duration (Klempel *et al.*, 2013). The ‘no change’ scenario was also found following adherence to a diet high in fruits and vegetables in a sample of post-menopausal females (Abedi *et al.*, 2010).

Restriction of carbohydrate intake is directly linked to decreased plasma triglyceride content and increased HDL-C concentrations (Al-sarraj *et al.*, 2009). A similar theme is reflected in the finding that reduction of dietary fat *per se* does not improve the plasma lipid profile but that changing the type of fat included in the diet has the more profound effect on triglycerides and the plasma lipoproteins (Summerbell et al., 2012). Thus, the 'fat-cholesterol' hypothesis is brought into question, however, the findings of Hooper *et al.* (2012) were primarily from male-centric studies and thus may not apply to females.

2.7.2 EXERCISE INTERVENTIONS

2.7.2.1 Introduction

A relatively new concept, exercise is medicine, was first introduced by the American College of Sports Medicine in 2007. Aimed at increasing the use of physical activity in therapeutic programmes to combat non-communicable disease of lifestyle, the EIM® movement is predicated on the knowledge that exercise is beneficial for health (Exercise is Medicine, 2012). For this movement to succeed, exercise must be considered a quantifiable therapy, along the lines of a drug, which can be prescribed. As such, the exact dose of the exercise, including the nature of activity, its duration, frequency and intensity, must be determined for any desired outcome.

In a letter to the United States President in September 2012, Pivarnik (President of the American College of Sports Medicine (ACSM), the world's largest Exercise Science association and leaders in the Exercise is Medicine® movement) stated that five of the world's costliest illnesses (cancers, cardiovascular disease, chronic obstructive pulmonary disease, diabetes and strokes) could be managed and perhaps even effectively prevented via lifestyle changes (ACSM, http://tinyurl.com/clwwj6y). Pivarnik reiterated that the EIM® movement is predicated on the belief that exercise should form a pivotal part of primary treatment for all individuals, and all chronic diseases of lifestyle origin. High quality studies have shown that exercise can ameliorate the dangers of most, if not all, chronic diseases, and the latest recommendations from the ACSM are that each adult should attain at least 150 minutes of moderate activity each week (preferably as 30 minutes per day) (ACSM, 2009).

Specific effects of exercise related to specific conditions are necessary, and a general activity guideline may not suffice. The following section outlines trials that have focussed

on specific aspects of health and disease state and summarises the dose of exercise and concomitant effects in each instance. As the focus of this investigation is an exercise intervention in post-menopausal females, the review presented is specific to “older” adults throughout.

2.7.2.2 Aerobic endurance training

2.7.2.2.1 Introduction

The needs of the older adult must be considered as different to those of the ‘younger’ adult, who may present with fewer risk factors (Chodzko-Zajko *et al.*, 2009). In 2007 the American College of Sports Medicine took the stand that 30 to 60 minutes of endurance-type activity per day, of a moderate intensity, was recommended for older adult populations. Walking, aquatic exercise and stationery cycling were suggested as ideal modes of exercise for this population (Chodzko-Zajko *et al.*, 2009). It was noted that aerobic training had a number of positive benefits for this population: improved aerobic capacity (an oxygen uptake increase of 3-4 $ml.kg^{-1}.min^{-1}$ following 16 weeks of training on three days of the week at 60% of calculated maximal oxygen uptake); cardiovascular function improvements (lower resting heart rate, as well as smaller increases in blood pressure during exercise, following activity of at least 60% maximal oxygen uptake (VO_2max) intensity); reduced total fat mass and abdominal visceral fat; and improved glucose transporter content and insulin function as metabolic alterations following moderate and high intensity training (Chodzko-Zajko *et al.*, 2009). Predominantly, these findings are specific to older male populations, with female populations receiving mention specifically for the effect of this type of training on bone health, and mineral density. The authors of this position stand concluded that it was not yet possible to define an exercise prescription that would suit all population groups, for all conditions. It appears true that the efficacy of any prescribed exercise programme or intervention is directly related to the individual, particularly the age and health status at the time of undertaking the intervention, and possibly, the levels of habitual physical activity to which the individual was accustomed throughout their lifespan (Chodzko-Zajko *et al.*, 2009).

2.7.2.2.2 Body Mass

Significant reductions to body mass have been noted following at least 12 weeks of endurance training in previously untrained participants (Cox *et al.*, 2010; Fox *et al.*, 1996; Lindahl *et al.*, 1998; Nieman *et al.*, 2002). Participants in these studies were female, post-

menopause, non-smokers and were overweight or obese prior to the interventions. Cox and colleagues found that swimming was superior to walking over a six month programme, with body mass and waist circumference responding better (although insignificantly) to swimming than to walking. Fox et al. and Nieman et al. combined dietary restriction and exercise, thus clouding the reliability of their results pertaining to exercise. Lindahl and colleagues reported that body mass and waist-to-hip ratio were positively altered following four weeks of “intense intervention” and remained lower than at baseline after 12 months of follow up in a cohort that refers to male and to female participants. In a trial of better quality, a cohort of females (average age 57.3±6.6 years) were required to exercise on three to four days of the week at an equivalent of 50% of heart rate maximum for six months (Arsenault et al., 2009). Body mass decreased by an average of 1.4 kg ($p<0.001$) coupled with a significant waist girth decline (2.4 cm) ($p<0.001$). Aerobic training undertaken on five days of the week (three days supervised and two days unsupervised) meeting a total of 45 minutes.day-1 for 12 months resulted in significant body mass reductions in post-menopausal females (aged 50 to 75 years) (Campbell *et al*., 2012). Caucasian post-menopausal females, in a separate trial, recorded modest body mass loss (-2.4%, $p<0.03$) following 12 months of moderate intensity aerobic training on five days of the week for a total of 225 min.week-1 (Mason *et al*., 2011). In contrast a sample that displayed strong links between intensity of training and aerobic fitness (50% - 150% of recommended physical activity per day) achieved no substantial changes to body mass (Church *et al*., 2007).

2.7.2.2.3 Body composition

Post-menopausal females (n=189, aged 56.7±5.8 years) demonstrated a significant decrease to body fat following 12 weeks of endurance training at an intensity of 65% of maximum heart rate on three or four days of the week (Yanagibori *et al.*, 1993). Similarly, female participants (age 62 years) who undertook no dietary changes and exercised at 54% of maximum heart rate reserve on five days of the week saw significant reductions to adipose tissue (Ready *et al.*, 1995). Overweight adults (predominantly female sample, but inclusion of two male participants per group) showed no change to body composition variables following 12 weeks of aerobic training on five days of the week for 30 minutes per session (Ho *et al.*, 2012). This finding may have been influenced by the fact that only three sessions per week were supervised while two were unsupervised. In addition, attendance at sessions by participants reached only 74%. Including both pre- and post-

menopausal females as well as males in the same sample introduces limitations. However, a study of overweight and sedentary adults (21 females and 17 males, n=38, age 18 – 70 years and average age 52.0 years) found that aerobic training at 65-85% of maximal oxygen uptake levels on five days of the week significantly reduced fat mass (1 %) and overall body mass (2 kg) (p<0.05) (Willis *et al.*, 2012).

Obese pre-menopausal females undertook 'light' (45 – 50% of maximum heart rate by Karvonen formula) or 'moderate' aerobic exercise (70-75% maximum heart rate) for a period of ten weeks and exhibited significant decreases to body fat percentage, fat mass and concomitant improvements to lean mass content (Morandi *et al.*, 2013). The researchers noted that the changes to body composition in this study were greater with moderate training than with 'light' aerobic training (Morandi *et al.*, 2013). In contrast pre-menopausal females (n=27) participating in a study over the course of 40 weeks showed no change to pre-intervention body composition, despite a routine 4.8 km "brisk" walk on four days of the week, and a demonstrable increase to VO_2max of 22% (Santiago *et al.*, 1995). Seals *et al.* (2001) also employed walking in an aerobic exercise intervention (40±4 minutes per day on 5.8±1.1 days of the week at an intensity of 70±2 % of maximal heart rate) to no effect in healthy, obese post-menopausal females.

2.7.2.2.4 Waist circumference

Most of the literature indicates that aerobic type exercise is effective in reducing abdominal fat in adult females, and by extension, waist circumference (Boutcher, 2011; Fisher *et al.*, 2011; Joseph *et al.*, 2011; Kwon *et al.*, 2010; Nicklas *et al.*, 2009). Boutcher (2011) evaluated studies which utlised 'high intensity interval training' (HIIT) to which end participants engaged in sprints at 90% of maximal oxygen uptake for between 6s and 4min followed by periods of low intensity or complete rest. HIIT was undertaken on three days of the week for two to six weeks. Nicklas *et al*. (2009) also utilised a high intensity exercise bout, defining "vigorous" as 70-75% of heart rate reserve in their candidates, and comparing this to a moderate bout of exercise, determined as 45-50% of the heart rate reserve. In contrast Fisher *et al*. (2011) and Joseph *et al*. (2011) utilised low to moderate intensity exercise, defined as 50-60% of heart rate reserve in the cohort managed by Joseph and colleagues, and as 65% increasing to 80% of maximum heart rate in the case of the cohort examined by Fisher and colleagues. Kwon *et al*. (2010) used the anaerobic threshold as the intensity guide for sessions lasting 60 minutes each, five times a week, for

12 weeks. Notably those studies employing moderate intensity activity noted consistently better results than those employing vigorous or “high” intensity designs.

A minority of well designed, randomised controlled studies indicate that aerobic exercise is not responsible for losses of abdominal fat or centimetres at waist girth (Ryan *et al.*, 2006; Sjögren *et al.*, 2012). Ryan and colleagues required participants to walk at 50-60% ofheart rate reserve on three days of the week for six months, for 45 minutes per session. These authors acknowledge a 78% compliance rate to the exercise sessions, which may be an influencing factor in the lack of change results. Sjögren *et al.* did not supervise the cohort and monitored activity via pedometry and activity diary only, which is arguably an unreliable means of assessing adherence to a specified programme. These authors stipulated that participants should amass 30 minutes of “moderate” activity daily.

Specific to post-menopausal females, studies are equivocal in recommending aerobic activity for waist circumference reduction, as opposed to dietary interventions by way of caloric restriction (Joseph *et al.*, 2011; Nicklas *et al.*, 2009; Ryan *et al.*, 2006). A limitation of many studies investigating the effect of aerobic training on abdominal girth is that dietary interventions are utilised as the ‘control’, thereby creating a ‘comparison’ rather than a true ‘controlled trial’ scenario. In further studies, dietary manipulation was combined with aerobic training, making it difficult to isolate the effect of the training itself. It does not appear that aerobic training is the best means of reducing abdominal visceral fat in any population, but particularly older females, and that caloric restriction alone is the most effective means of reaching this goal (Brinkley *et al.*, 2011).

2.7.2.2.5 Blood pressure

Engagement in sustained aerobic activity has been proven beneficial for reduction of high blood pressure (Chomiuk *et al.*, 2013; Ciolac, 2012; Cornelissen & Smart, 2013). This beneficence is supported by a meta-analysis of 54 randomised controlled trials investigating the effectiveness of aerobic training on hypertension (Whelton *et al.*, 2002). The positive outcomes of these studies appears to come with a caveat, however, as the ‘positive’ effects are limited to less than 5% change in either systolic or diastolic blood pressure, despite statistical significance. In addition, it appears that more activity (>150 min.week^{-1}) has greater effect than fewer minutes training (<120 min.week^{-1}), and that ‘moderate’ intensity is preferable to either ‘low’ or ‘high’ intensity (by ~0.5 mmHg in both instances) (Whelton *et al.*, 2002). Indeed, when compared to sustained aerobic training,

high intensity intermittent training (known as 'HIIT') was more effective in lowering blood pressure (Ciolac, 2012).

The efficacy of aerobic training was found to be inconclusive in well-designed trials of sufficient participant enrolment (Arsenault *et al.*, 2009; Church *et al.*, 2007; Maruf *et al.*, 2013). Thus it appears that to date no conclusive evidence exists indicating that aerobic training may effectively reduce hypertension in adults. This is ratified by the American College of Sports Medicine who state in a position stand that risk of hypertension is unlikely to be mitigated by endurance training in females (Pescatello *et al.*, 2004). The optimal programme design ("FIND" design) for treating or managing hypertension has yet to be found (Pescatello *et al.*, 2004).

2.7.2.2.6 Type II Diabetes

Exercise has been shown to be an effective treatment for individuals diagnosed with type II diabetes (T2D) as the blood-glucose uptake channels alter during the course of activity from insulin-mediated to muscle contraction-mediated (ACSM, 2010). Importantly, exercise training for T2D may combat not only the blood glucose irregularities, but may concomitantly ameliorate a number of the co-morbidities commonly associated with T2D, including blood pressure abnormalities, plasma lipoprotein abnormalities and weight gain (Bacchi *et al.*, 2012; Balducci *et al.*, 2012; Hansen *et al.*, 2009; Li *et al.*, 2012; Manders *et al.*, 2010; Van Dijk *et al.*, 2013). Endurance training is the traditional prescription for this condition, as it has the effect of improving whole-body sensitivity to glucose while enhancing the responsiveness of skeletal muscle to insulin (ACSM, 2010). Aerobic training may create an environment wherein metabolism switches to favour fat oxidation, an important metabolic shift in T2D patients, as the condition is associated with a greater reliance on carbohydrate metabolism (ACSM, 2010).

It appears however, that the intensity at which the endurance activity is undertaken is closely related to the efficacy of the insulin response to activity (Balducci *et al.*, 2012; Manders *et al.*, 2010; McAuley *et al.*, 2002). Moreover, the acute effects of an exercise bout must be considered separately from the chronic effects of consistent and habitual exercise routines, as the efficacy on insulin function, blood glucose content and the presence of glycated haemoglobin differ (Bacchi *et al.*, 2012; Balducci *et al.*, 2012; Hansen *et al.*, 2009; Manders *et al.*, 2010; Snel *et al.*, 2012; Van Dijk *et al.*, 2013). Additionally, inter-individual differences in response to aerobic type activity in persons with diagnosed

T2D must be borne in mind – as noted in a study reporting the positive reductions in blood glucose following a single bout of exercise (n=60) wherein nine participants showed elevated, not reduced, blood glucose 24 hours post-training (Van Dijk *et al.*, 2013).

Duration of the exercise bout appears to affect the insulin response, as well as blood glucose concentrations 24 hours post-training (Li *et al.*, 2012; Manders *et al.*, 2010). In addition, low intensity aerobic training seems to be superior in effect to moderate-high intensity exercise, but this effect may be due to the additional time spent engaging in low intensity training in order to match caloric expenditure of higher intensity training (Hansen *et al.*, 2009; Manders *et al.*, 2010). Furthermore, the frequency of training sessions is vital in acute management of insulin and blood glucose, and daily exercise sessions have proved more beneficial to T2D patients than alternate day exercise sessions of longer duration (Li *et al.*, 2012). It appears that adherence to chronic exercise does not necessarily improve daily control of hyperglycaemia, but does reduce the presence of glycated haemoglobin (Bacchi *et al.*, 2012; Balducci *et al.*, 2012; Hansen *et al.*, 2009).

While it is clear that exercise, specifically endurance type training, must be recommended to diabetic patients, the inter-individual variability in responses, the risk of hypoglycaemia during training, and the difference in acute and chronic benefits requires careful individual monitoring by medical practitioners. It must also be acknowledged that hyperglycaemia is not entirely eradicated via the training modality and that concomitant use of blood glucose-lowering medication may be a necessity (Bacchi *et al.*, 2012; Snel *et al.*, 2012)

2.7.2.2.7 Plasma Lipoproteins

A search in December 2013 on the large-scale “PubMed” database using the search terms “plasma lipids OR lipoproteins AND aerobic AND exercise AND post-menopausal” revealed five results of which only two were specific to the search terms (Brinkley *et al.*, 2011; Stevenson *et al.*, 1995). This search result indicates the scarcity of trial data relating exercise interventions (in this case aerobic endurance training) specific to post-menopausal females. For completeness, and in order to include those trials that had older men as well as post-menopausal women as participants, this review includes trials relating to “adults” (participants older than 18 years) as well as males. The focus remains, however, on the responses of females, post-menopause.

2.7.2.2.7.1 Total cholesterol

Sustained endurance activity has been shown to reduce total cholesterol concentrations effectively in previous studies (Behall *et al.*, 2003; Hashimoto *et al.*, 2011; Martins *et al.*, 2010; Rainville & Vaccaro, 1984; Yanagibori *et al.*, 1993; Yoshida *et al.*, 2010). The findings of these independent studies were ratified in a meta-analysis conducted in 2012, which concluded that aerobic training reduced total cholesterol effectively (Kelley *et al.*, 2012). On the other hand, studies of similar design revealed no positive effect on total cholesterol following at least 12 weeks of chronic aerobic training (Arsenault *et al.*, 2009; Ho *et al.*, 2012; Huffman *et al.*, 2013; Mediano *et al.*, 2010; Sales do Valle *et al.*, 2010; Shaw *et al.*, 2009; Stevenson *et al.*, 1995). Meta-analyses and reviews of randomised and controlled trials support the 'no response' findings (Kelley & Kelley, 2013; Leon & Sanchez, 2001; Tambalis *et al.*, 2009).

The results, while inconclusive, must be considered in context. A number of studies utilised a mixed group of participants (males and females) which may have led to contamination of results as it is known that there is a sex-based difference in response to exercise by the plasma lipoproteins (Behall *et al.*, 2003; Huffman *et al.*, 2013; Martins *et al.*, 2010). Other studies did not recruit a large enough sample size (fewer than ten individuals per arm) to draw definitive conclusions (Fett *et al.*, 2009; Hashimoto *et al.*, 2011; Malin *et al.*, 2012; Yoshida *et al.*, 2010) while other studies report on a combination of aerobic exercise and caloric restriction, again creating contamination of results (Kelley *et al.*, 2012; Mediano *et al.*, 2010; Sales do Valle *et al.*, 2010). The only study reporting directly on post-menopausal females recruited a large sample size and focussed on aerobic training alone, however this was not an intervention study but an analysis of the plasma lipoproteins in highly trained runners (Stevenson *et al.*, 1995). This study was well controlled, however, and provides insight into the positive effect of habitual and chronic adherence to moderately high aerobic activity in women, post-menopause. The authors note that the positive lipid profiles in the exercisers (compared to sedentary controls) may be more closely related to the body fat distribution and dietary choices of the runners, rather than to the exercise itself. This must be considered when studies report loss of body weight and body fat alongside improvements to the lipid profile, as was the case for Malin *et al.* (2012), Martins *et al.* (2010), Mediano *et al.* (2010), Sales *et al.* (2010), and Shaw *et al.* (2009). Overall, compliance to the exercise interventions reported here was between 70 – 80%, indicating that less exercise was actually completed by participants than the

methodologies initially required. However, this is a 'realistic' view of individuals' ability to adhere to a lifestyle intervention, and provides insight into applicability of exercise interventions for managing disease states.

2.7.2.2.7.2 Low density lipoprotein

Ideally lifestyle interventions aim to reduce LDL-C to <2 mmol.L^{-1}. Significantly reduced LDL-C was reported following at least 12 weeks of endurance activity, generally on three days of the week and for 45 minutes duration per session (Huffman *et al.*, 2013; Martins *et al.*, 2010; Mediano *et al.*, 2010; Sales do Valle *et al.*, 2010; Shaw *et al.*, 2009; Stefanick *et al.*, 1998; Yoshida *et al.*, 2010). Of importance is that the only study focussing on post-menopausal women was the research undertaken by Stefanick *et al.* (1998), however, this group utilised a "diet and exercise" model rather than isolating the exercise intervention.

Most studies report no change to LDL-C among post-menopausal females (Mohanka *et al.*, 2006; Murtagh *et al.*, 2005; Seals *et al.*, 2001; Weise *et al.*, 2005) and among adults in general (Fett *et al.*, 2009; Malin *et al.*, 2012; Stevenson *et al.*, 1995). Meta-analyses and reviews on the topic support the "no effect" conclusion (Kelley and Kelley, 2013; Kelley *et al.*, 2012; Leon and Sanchez, 2011; Tambalis *et al.*, 2009).

2.7.2.2.7.3 High density lipoprotein

Following 12 weeks of aerobic exercise at an intensity equivalent to 70% of heart rate reserve on three days of the week, Blumenthal *et al.* (1991) reported that HDL-C increased in a cohort of post-menopausal females (n=25). These authors did not analyse body composition in conjunction with an exploration of the plasma lipoproteins, and did not change or monitor dietary habits. While this positive movement of HDL-C was merely reported as a "trend" and was not statistically significant, it was noted in conjunction with decreasing total cholesterol suggesting that the plasma lipoproteins were somehow affected by the intervention. In the absence of body composition information the effect of any reduction to overall body mass or body fat content on the plasma lipoproteins cannot be assessed, and thus the validity of the finding must be questioned. Body composition changes were cited by two sets of authors who noted significantly improved lipid ratios following aerobic endurance interventions. Ready *et al.* (1995) and Yanagibori *et al.* (1993) both noted improved HDL-C in participants following at least 12 weeks of exercise, but in the context of significantly reduced body fat were forced to attribute these findings to composition status rather than the exercise itself.

Results for adults (male and female participants) in general are equally inconclusive with some studies revealing positive improvements to HDL-C (Huffman *et al.*, 2013; Martins *et al.*, 2010; Mediano *et al.*, 2010; Sales do Valle *et al.*, 2010) while others report no effect resulting from aerobic exercise intervention studies (Shaw *et al.*, 2009; Stevenson *et al.*, 1995; Yoshida *et al.*, 2010). Review papers and meta-analyses are divided in conclusions, with Kelley and Kelley (2013) and Kelley *et al.* (2012) concluding that aerobic endurance has no positive overall effect on HDL-C while Tambalis *et al.* (2009) indicate a positive effect overall.

2.7.2.2.7.4 Triglycerides

Plasma triglyceride (TriG) content may be affected by exercise in one of two ways: an acute effect may be noted directly after one exercise bout; or a chronic effect may be monitored over time. Most studies have evaluated the chronic effect of activity on the plasma lipoproteins, including triglycerides. Separating the positive effect of improved body composition including reduced fat content and the direct effect of exercise has been demonstrably difficult for a number of authors who report decreased TriG content following endurance training interventions (Behall *et al.*, 2003; Nieman *et al.*, 2002; Ready *et al.*, 1995; Yanagibori *et al.*, 1993). Other studies report a no-change scenario in various populations: neither healthy post-menopausal females nor young pre-menopausal females showed reduced TriG content following aerobic exercise interventions (daily walking for at least 12 weeks and a 24-week diet and exercise combination study) (Fox *et al.*, 1996; Seals *et al.*, 2001).

Results for the general adult population are inconclusive. Some studies report reductions in triglyceride concentrations following chronic aerobic training in both young and older populations of males and females (Hashimoto *et al.*, 2011; Huffman *et al.*, 2013; Martins *et al.*, 2010; Sales do Valle *et al.*, 2010), while others report no change (Shaw *et al.*, 2009; Yoshida *et al.*, 2010). Meta-analyses and review papers are once again divided on the topic: Kelley and Kelley (2013) ascertain that triglycerides are positively influenced by endurance training while Leon and Sanchez (2001) and Tambalis *et al.* (2009) maintain that there is no effect on this parameter.

The fact that triglycerides appear to be acutely affected by exercise should be noted – 90 minutes of continuous exercise significantly reduced triglycerides in a small sample of lean and active young adults (Sondergaard *et al.*, 2011). This mechanism whereby

triglycerides are utilised during exercise and show a marked decrease during and after exercise sessions may be of greater value in ameliorating diseases related to lifestyle than initially thought.

2.7.2.3 Progressive resistance training

2.7.2.3.1 Introduction

Adults who do not engage in strength training lose an average of 0.46 kg of lean body mass per year from the age of 40 years (Braith & Stewart, 2006). Maintenance of lean body mass is essential in preventing, and in assisting in the reversal of the condition known as “dynapenic obesity” which is the onset of overweight/obesity combined with the natural decline in muscle strength which accompanies aging (Braith & Stewart, 2006). Strength training is beneficent in maintaining musculo-skeletal health, which translates into functional wellbeing as an individual ages, and reduces the risk of falls, fractures and subsequent limitations to independence (Braith & Stewart, 2006; Sale, 1988). The evidence indicating that resistance training may be beneficial in targeting risk factors for cardiovascular diseases is less clear, with contradictions throughout the literature. There is a distinct need for well-controlled studies among diverse population groups in order to improve the evidence-base, and to answer the question as to the efficacy of resistance training in this regard (Braith & Stewart, 2006).

Progressive resistance training has previously been reported to reduce hypercholesterolaemia effectively in males and pre-menopausal females (Cauza *et al.*, 2005; Misra *et al.*, 2008). Literature is equivocal, however, on the effects of strength training on the plasma lipoproteins in older female cohorts. Of literature sourced during the preparation of this research project and thesis, 57% of articles specific to post-menopausal females indicated that resistance training had no effect on total cholesterol (TotC) levels, similarly 51%, 63% and 83% for low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C) and triglycerides (TriG) respectively. In contrast, 43% of the literature suggested that total cholesterol could be improved by engaging in regular strength training, the same percentage indicated LDL-C might be effectively managed, and 17% reported that triglyceride content could be adequately reduced. Only in the case of HDL-C did reports suggest an increase in the plasma lipoprotein content as a result of regular strength training, in 38% of studies canvassed. These studies relied on 3 day per week frequency designs, and often prescribed low to

moderate exersice intensity. Arguably the frequency and intensity must be re-visited as daily exercise is the current recommendation for health outcomes. Additionally, there are few samples comprising post-menopausal females, and those cohorts that do include this population often include age-matched male counterparts. Attention to females post-menses in this regard is required.

General physical activity guidelines from the ACSM pertaining to older populations and resistance training for general health improvement include two sessions of weight bearing exercise weekly, at an intensity matching “5-6” or “7-8” on a scale of “0-10” (this matches the 10-point ‘Rating of Perceived Exertion’ (RPE) Scale by Borg (Borg, 1982), although this was not specifically referred to in the position stand) (Chodzko-Zajko *et al.*, 2009). The recommendation is for the use of “major” muscle groups (by which the interpretation is to include primarily compound exercises rather than those of a simple, uni-joint nature) and to include eight to ten different exercises which are to be repeated eight to 12 times each (Chodzko-Zajko *et al.*, 2009). Specific mention is made of stair climbing and callisthenics as useful modes of resistance training for this population group.

The ACSM notes that resistance training may have the following benefits for the older adult: improved muscular strength, power, quality but not muscle endurance; body composition (by way of increased fat free mass and hypertrophy (10–62%) of the muscles); and bone health by way of preservation of bone mineral density, which is particularly important to the older female as bone mineral density declines by 3-4% per annum post-menopause (resistance training may mitigate this by 2% per annum) (Chodzko-Zajko *et al.*, 2009). It is further noted that there is robust evidence to support the fact that resistance training may effectively reduce the symptoms of clinical depression (by 25-88%) in diagnosed individuals (Chodzko-Zajko *et al.*, 2009).

The American College of Sports Medicine publishes position stands collating scientific evidence regarding safe and effective exercise programme design. Figure 2.4 represents the evidence published by the ACSM in 2009 pertaining to exercise prescription for older adults following ‘category A’ evidence (only well designed randomized controlled trials of significant number and with sufficient participants). Notably it is recommended that older adults participate in resistance training on at least two days of the week, and while not specifically aimed at the older adult, the finding that up to five days per week is considered safe.

The intensity of training for novice participants is set at 60% of the 1-repetition maximum determination of individual strength capacity, with progression encouraged up to and including 80% of the 1 RM. A range of exercises are recommended, incorporating not only uni- and bi-lateral joint inclusion but also multi-joint, whole body exercises to be repeated 8-12 times (repetitions) for 1-3 sets, with a maximum break of three minutes in between sets. Progression may occur quickly in those who are previously untrained, and while improvements may be noted as early as a few weeks into the training regime, noticeable strength improvements should not be expected prior to 12 weeks of consistent training (Sale, 1988).

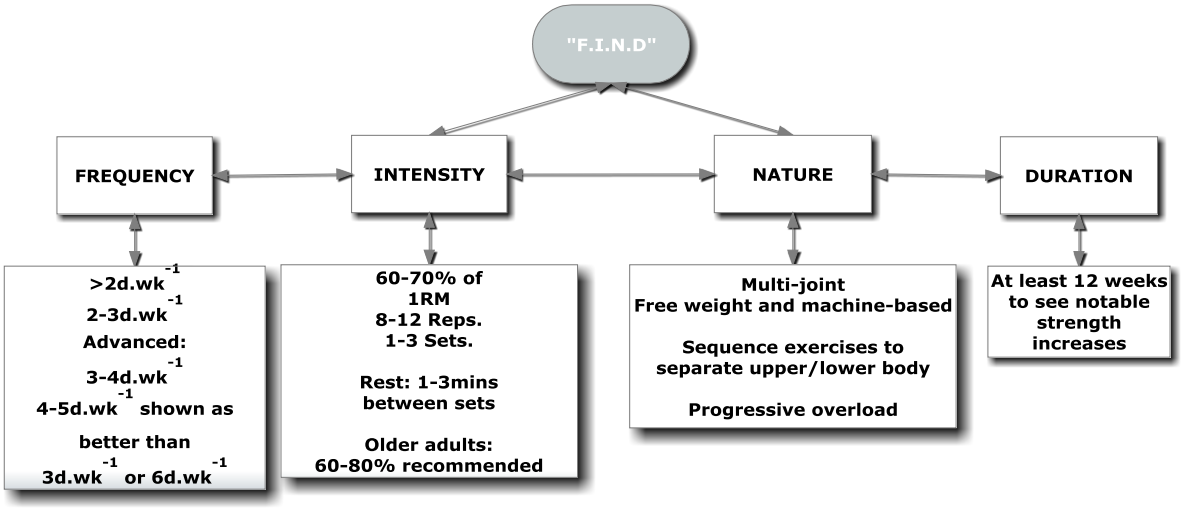


Figure 2.4: 'FIND' principles for resistance exercise prescription (ACSM, 2009)

2.7.2.3.2 Frequency of training

It appears that most designs have been conservative, preferring to err on the side of caution perhaps for the safety of participants or to satisfy ethics committees. A few studies prescribed resistance training on only two days of the week, with no additional training on the remaining five days (Blumenthal *et al.*, 1991; Yoshizawa *et al.*, 2009). Protocols defining a three day per week schedule were employed by the majority of studies investigating the effect of resistance training on a sample of post-menopausal females (some included males and others also included pre-menopausal females) (Bonganha *et al.*, 2012; Castenada *et al.*, 2002; Dunstan *et al.*, 2002; Fahlmann *et al.*, 2002; Manning *et al.*, 1991; Prabhakaran *et al.*, 1999; Viljoen & Christie, 2011; Wooten *et al.*, 2011; Yoshizawa *et al.*, 2009). No studies were located pertaining to older adults or older females in particular that employed a five day per week design, however, one study did so with reference to pre-menopausal females (Nindl *et al.*, 2011). Time spent on resistance

training per session was largely set at 45 minutes (including at least five minutes of warm up and/or cool down, usually an aerobic-type activity and stretches) (Castenada *et al.*, 2002; Dunstan *et al.*, 2002; Nelson *et al.*, 1994; Prabhakaran *et al.*, 1999b; Singh *et al.*, 1997). Replication of similar study designs to those employed in the cited literature making changes to the frequency of training sessions may reveal stronger associations between exercise, the intervention modality, and changes to risk factors, particularly plasma lipoprotein levels. To date, inconclusive findings yield no clear recommendation which in the opinion of this author may be due to infrequency of training.

2.7.2.3.3 Intensity of exercise

A number of studies reported engaging participants at an intensity at or below the recommended 60% of the 1 RM, arguably thus an insufficient intensity to elicit desired changes (Dunstan *et al.*, 2002; Herriott *et al.*, 2004; Vincent *et al.*, 2003). At the other end of the spectrum three studies were found employing an intensity greater than or equal to 75% of the pre-determined 1 RM (Bonganha *et al.*, 2012; Prabhakaran *et al.*, 1999b; Vincent *et al.*, 2003). Some reports refer to the intensity as a function of the 8 RM or the 12 RM intensity (Blumenthal *et al.*, 1991; Wooten *et al.*, 2011). The intensity of training must distinguish strength training as such, and bear no relation to aerobic training for the effects of strength training on risk factors to be clearly highlighted. The studies conducted to date may have been well designed and controlled yet the programme of resistance training may not have been at a high enough intensity to yield conclusive changes.

2.7.2.3.4 Duration of exercise

Studies utilising exercise interventions have typically lasted from a minimum of six or eight weeks duration (Elliott *et al.*, 2002; Fenicchia *et al.*, 2004; Herriott *et al.*, 2004), to a maximum of 24 weeks total study length (Bocalini *et al.*, 2009; Dunstan *et al.*, 2002; Nindl *et al.*, 2011; Viljoen & Christie, 2011; Vincent *et al.*, 2003). Most commonly selected durations in previously undertaken studies were 12 weeks (Blumenthal *et al.*, 1991; Campbell *et al.*, 1994; Joseph *et al.*, 1999; Manning *et al.*, 1991; Misra *et al.*, 2008; Wooten *et al.*, 2011; Yoshizawa *et al.*, 2009) or 16 weeks in some instances (Bonganha *et al.*, 2012; Castenada *et al.*, 2002; Cauza *et al.*, 2005; Maesta *et al.*, 2007; Ryan *et al.*, 1996). If the question asked by the research hypothesis is whether the strength training does or does not have an effect, rather than what the chronic effects of habitual activity might be, then 12 weeks is probably a suitable duration. This duration must be combined

with different frequencies of training and intensities of exercise in order to elicit associations.

2.7.2.3.5 Nature of exercise

Resistance training programmes can differ in the content of the exercises prescribed for participants. The predominant design noted in prior interventions engaging post-menopausal females is for exercises to be repeated for eight to ten repetitions per set, and repeated for three sets (Castenada *et al.*, 2002; Dunstan *et al.*, 2002; Yoshizawa *et al.*, 2009). The exercises included in the battery indicate researchers' preferences for major muscle groups and compound-type exercises engaging more than one joint simultaneously, for example the inclusion of bench press, lat pulldown, leg press and lunges (Castenada *et al.*, 2002; Dunstan *et al.*, 2002; Nelson *et al.*, 1994; Singh *et al.*, 1997; Yoshizawa *et al.*, 2009). The use of compound rather than simple exercises is important as this may also elicit the greatest change to energy expenditure, hastening morphological change in the individual. However, if the compound exercises are not at a high enough intensity then the greatest effect will not be the results of strength training but of aerobic endurance. This must be controlled for by ensuring that the intensity (as % of the 1RM) is progressed throughout the intervention.

2.7.2.3.6 Body Mass

Reduced body mass is not an expected outcome of a resistance training programme unless there is a concomitant restriction to dietary intake (Braith & Stewart, 2006). An additional means of encouraging body mass loss during strength training is the inclusion of endurance activity alongside the strength programme, a strategy employed in a study of female participants (n=31; age 28 years) over the course of 24 weeks (Nindl *et al.*, 2011). A significant decrease in overall body mass was noted, however the study design incorporated 1.5 hours of combination training on five days of the week. It must be concluded thus that the influence of the aerobic component to this training regime contributed toward the loss of mass more so than the strength component.

One further investigation was found concluding that 12 weeks of resistance training demonstrated a "trend" toward decreasing body mass in a cohort of post-menopausal females (n=25; age 45 – 55 years) (Blumenthal *et al.*, 1991). Whether this was indeed the case must be queried, as not only was the protocol designed to incorporate two days of training per seven day cycle, the intensity at which the exercises was completed was a

percentage of the 12-repetition maximum (12 RM) – arguably an intensity too low to produce any effect in terms of strength, or body composition (Blumenthal *et al.*, 1991). The American College of Sports Medicine has issued guidelines that suggest that programmes of regular training for health benefit, which includes the development of muscular strength and associated parameters, must take place on at least three days per seven day cycle for optimal improvements. A two-day regime is insufficient in this context.

A greater number of studies report no change to body mass following strength training interventions (Elliott *et al.*, 2002; Fahlmann *et al.*, 2002; Manning *et al.*, 1991; Viljoen & Christie, 2011; Vincent *et al.*, 2003). Apart from two of these studies all were at least 12 weeks in duration, which is theoretically sufficient to elicit body mass and composition changes (Manning *et al.*, 1991; Viljoen & Christie, 2011; Vincent *et al.*, 2003). The remaining two investigations were eight and ten weeks duration respectively – neither would be sufficient to suggest to this author that physical and physiological changes could necessarily be expected as it is hypothesised that changes noted in the first eight weeks of training in previously sedentary individuals is primarily due to neurological changes and pathway familiarisation (Sale, 1988).

2.7.2.3.7 Body composition

Most commonly expressed as the ratio of lean to fat mass (in percentage values) body composition is usually measured indirectly. Significant and positive changes to body composition have been reported following resistance training interventions, most probably as a result of an increased metabolic demand following muscular changes and also the training adaptations at the level of the muscle fibre following regular strength training (Sale, 1988). Significant reductions to body fat content and concomitant increases in lean mass content have been noted in females, both pre- and post-menopause (Banz *et al.*, 2003; Campbell *et al.*, 2009; Prabhakaran *et al.*, 1999b). In these studies diet was monitored and a dietary recall was provided in order to ensure that no dietary manipulation was taking place.

2.7.2.3.8 Waist circumference

Literature is in agreement that regular, chronic resistance training improves loss of fat mass in females, both pre- and post-menopause (Bea *et al.*, 2011; Brochu *et al.*, 2009; Ciolac & Greve, 2011). Direct effect of resistance training on reducing the waist circumference in post-menopausal females was noted in one study which admittedly

included caloric restriction in the research methodology (Brochu *et al.*, 2009). Reports were also clear that adherence to the training programme (attendance at sessions) was directly related to the body composition benefits derived from the exercise programme, with higher compliance leading to better effects (Bea *et al.*, 2011; Brochu *et al.*, 2009).

2.7.2.3.9 Blood pressure

General observations indicate that chronic resistance training may reduce systolic blood pressure by 3 mmHg and diastolic blood pressure by 2-4 mmHg in adult populations (Pescatello *et al.*, 2004). While seemingly small changes, these are influential as a reduction of 3 mmHg to systolic blood pressure is the equivalent of 5-9% reduction in risk of coronary heart disease, 8-14% reduction in risk of stroke, and an 8-14% reduction in risk of all-cause mortality (Pescatello *et al.*, 2004). Older adults respond similarly, but it has been noted that the response is slightly lower than that of younger adults: older populations have recorded systolic blood pressure decreases of 2% and diastolic blood pressure reductions of 1%, with no difference noted between males and females (Pescatello *et al.*, 2004). When prescribing exercise to combat hypertension, the ACSM position stand noted that resistance training may not produce sufficient benefit and thus the preference is for aerobic endurance training programmes (Pescatello *et al.*, 2004).

An important measure of incipient risk of cardiovascular event such as myocardial or cerebral infarction, blood pressure is transient and responds dynamically to physical demands (Yoshizawa et al., 2009). Expectedly, it will fluctuate during exercise training but it is important to assess blood pressure pre- and post-exercise during rest to ascertain arterial strain for risk assessment. Resistance training reportedly elicited no effect on blood pressure in a cohort of pre- and post-menopausal females (n=11) compared to a matched control (Yoshizawa *et al.*, 2009). The reliability of these results must be considered in light of the small sample size, and of the exercise programme design which indicated twice weekly training, arguably insufficient to elicit positive health responses including positive effects on blood pressure (Yoshizawa *et al.*, 2009). Systolic blood pressure was found to respond positively to a protocol of resistance training on three days of the week lasting 16 weeks (Castenada *et al.*, 2002). This finding was applicable to males and females over the age of 55 years (n=62).

2.7.2.3.10 Type II Diabetes

Resistance training, if progressive, will have the effect of increasing muscle mass, and this in turn may improve the uptake of blood glucose in diabetic patients (ACSM, 2010). The ACSM reports that progressive resistance training may have the following effects: a positive metabolic effect (only evaluated in male participants); and a potentially positive effect in the case of hypertension as a co-morbidity (ACSM, 2010). There is no recommendation for resistance training in the cases of the lipoproteins, cardiovascular capacity, or body mass control as targets in improving type II diabetic (T2D) patients' health (ACSM, 2010). This is due to the fact that there is insufficient evidence from previously published intervention trials for conclusions to be drawn, and highlights the need for further research into the efficacy of resistance training as a modality to reduce morbidity and mortality.

A test of glycated haemoglobin indicated that resistance training positively affected insulin sensitivity, function and glucose control in T2D and pre-diabetic participants (Dunstan *et al.*, 2002; Fenicchia *et al.*, 2004; Misra *et al.*, 2008). These findings were echoed in a review of the efficacy of strength training for glycaemic control in diabetics which concluded that in fact resistance protocols may elicit a greater metabolic effect thus influencing glycaemic control to a greater degree than aerobic protocols (Gordon *et al.*, 2009).

2.7.2.3.11 Plasma lipoproteins

2.7.2.3.11.1Total cholesterol

An interesting dichotomy exists in the literature in that studies of apparently similar design and participant characteristics elicit very different responses to the lipoproteins. Conclusive total cholesterol decreases have been noted in studies lasting 12 and 14 weeks duration, with three-day per week exercise session frequency (Fahlmann *et al.*, 2002; Prabhakaran *et al.*, 1999a; Wooten *et al.*, 2012).

No change to total cholesterol was observed repeatedly in unrelated studies (Dunstan *et al.*, 2002; Manning *et al.*, 1991; Viljoen & Christie, 2011; Vincent *et al.*, 2003). All these investigations recruited female participants, with one study including males in addition to the female cohort (Vincent *et al.*, 2003). The duration of the interventions ranged from 12 to 24 weeks, which is theoretically sufficient time to elicit changes to plasma lipoproteins,

in conjunction with other metabolic, physiological and musculo-skeletal adaptations to training (Dunstan *et al.*, 2002; Manning *et al.*, 1991; Viljoen & Christie, 2011; Vincent *et al.*, 2003). Intensity of effort was set at 50% - 80% of the one-repetition maximum (1 RM) in all studies, with progression according to strength accrual, and session frequency was set at three days per seven day cycle which has been shown to be adequate for health benefits, although suggestions more recently recommend that exercise be undertaken on at least five days of the week (ACSM guidelines).

2.7.2.3.11.2 Low density lipoprotein cholesterol

Authors who reported positive changes to total cholesterol values (in response to resistance training) also presented significant reductions to overall low density lipoprotein cholesterol content (Fahlmann *et al.*, 2002; Prabhakaran *et al.*, 1999a; Wooten *et al.*, 2012). Critical analysis of these results is essential as it is LDL-C which is credited, theoretically, with responsibility for the majority of lipoprotein-related cardiovascular risk in females (Schenck-Gustafsson, 2009b). Compared to the studies that reported no alteration to LDL-C level post-exercise intervention there appear to be no fundamental study design differences (Dunstan *et al.*, 2002; Manning *et al.*, 1991; Viljoen & Christie, 2011; Vincent *et al.*, 2003). Wooten *et al.* (2012) conducted a randomised controlled trial but each sub-group had a total of nine participants allocated to it. Conclusions from this study must be considered in this context, and thus the finding of positively affected LDL-C may be due to the sample size rather than the intervention itself. Inclusion of male participants may have reduced the reliability of the results in another study – but the results were stratified according to sex and the “no change” conclusion remains relevant for females, post-menopause (Vincent *et al.*, 2003). What cannot be directly assessed from the reports is the ultimate control executed over the participants, and of the study design. It is not known whether the dietary recalls were sufficient to monitor dietary changes, or whether the intensity of effort at each exercise session was maintained as reported. Further to these reservations, studies that continued for 24 weeks extend across different seasons by definition, and it is known that seasonal variation can influence lipoprotein levels particularly in females (Gordon *et al.*, 1988; Ockene *et al.*, 2004; Woodhouse *et al.*, 1993). Two studies with very similar designs yet conflicting results reflect this: Wooten *et al.* (2011) conducted pre- and post-intervention biochemical analyses and found that cholesterol levels were positively influenced. In contrast, Viljoen and Christie (2011) conducted biochemical tests every four weeks for 24-weeks and the

within-intervention perturbations indicated an initial decrease in cholesterol followed by an increase as the winter months approached. Knowledge of the annual timing of the interventions, as well as what transpired during the 24 weeks, is invaluable to the interpretation of the results.

2.7.2.3.11.3High density lipoprotein cholesterol

Most studies have not found any change to HDL-C levels following resistance training interventions in older adults, and specifically older females (Banz *et al.*, 2003; Dunstan *et al.*, 2002; Manning *et al.*, 1991; Viljoen & Christie, 2011; Vincent *et al.*, 2003). In contrast, a minority of research indicates improvement to HDL-C profiles following resistance training, but in at least one instance the resistance training was coupled with regular aerobic training and in other instances the female participants may have been taking hormone replacement medication which may have affected response to exercise (Blumenthal *et al.*, 1991; Fahlmann *et al.*, 2002; Nuri *et al.*, 2012).

2.7.2.3.11.4 Triglycerides

Plasma content of triglycerides did not change in studies employing resistance training as an intervention (Banz *et al.*, 2003; Dunstan *et al.*, 2002; Manning *et al.*, 1991; Viljoen & Christie, 2011; Vincent *et al.*, 2003). One study suggested that TriG concentration decreased significantly following strength training, however this study engaged only 15 participants per arm, and the individuals were >70 years of age (Fahlmann *et al.*, 2002). In addition, the duration of the intervention was 10 weeks and training took place on only three days of the week. These facts may detract from the veracity of this study.

2.8 ADDITIONAL RISK FACTORS FOR CARDIOVASCULAR DISEASE

2.8.1 GLYCATED HAEMOGLOBIN

Non-enzymatic glycosylation is the covalent bonding of a protein or a lipid with a glucose molecule in the absence of a controlling enzyme. More commonly referred to as “glycation”, the measure of glycated haemoglobin indicates a two to three month average for endogenous exposure to glucose (Silbernagel *et al.*, 2011).

The HbA_{1c} measure was introduced as a reliable diagnostic tool for identification of non-insulin dependent diabetes mellitus, Type II, by the American Diabetes Association in 2010 (Eskesen *et al.*, 2012). The reliability of this measure in predicting cardiovascular events in non-diabetic populations has since become evident, with studies suggesting that a 1%

increase in HbA_{1c} correlates to a 15-18% increase in relative risk of developing cardiovascular disease and associated complications (Thanopoulou *et al.*, 2010). The large scale prospective Copenhagen Heart Study (n = 5127) found that HbA_{1c} was significantly associated with adverse cardiovascular events, concluding that there was a trend toward an association between HbA_{1c} and all-cause mortality (Eskesen *et al.*, 2012). This conclusion was supported by the authors of the LURIC study ("Ludwigshafen Risk and Cardiovascular Study") and the ARIC ("Atherosclerosis Risk in Communities") study who noted that baseline HbA_{1c} was predictive of all-cause, cancer and cardiovascular mortality in 2686 participants with no history of diabetes (Selvin *et al.*, 2010; Sibernagel *et al.*, 2011).

The predictive value of HbA_{1c} is independent of fasting plasma glucose levels (FPG) measured via the post-challenge hyperglycaemia test (the oral glucose tolerance test - OGTT) (Silbernagel *et al.*, 2012). Measures of glycated haemoglobin display higher repeatability than the OGTT, and can be assessed in the non-fasting state (Selvin *et al.,* 2010). HbA_{1c} levels >6% have been associated with risk for developing NIDDM independent of FPG baseline levels – thus it has been concluded that glycated haemoglobin levels and mortality risk are associated independent of fasting plasma glucose but the reverse does not hold true (Selvin *et al.*, 2010). These findings suggest that the long-term exposure to glucose is a more reliable predictor of risk than post-challenge hyperglycaemia. HbA_{1c} has been defined as the most potent predictor of cardiovascular disease risk (Schulze *et al.*, 2004).

Systemic arterial compliance (SAC), which is a function of aortic flow and compliance, has been negatively correlated to HbA_{1c}, as has the presence of micro- and macro-vascular disease (Ikeda *et al.*, 2012; Nestel, 2006). Higher HbA_{1c} categories have been positively linked to a high Syntax Score (SX Score), which is an anatomical-based risk score developed to predict clinical outcomes in individuals with single or multi-vessel coronary artery disease from a lesion complexity aspect (Ikeda *et al.*, 2012). A higher SX score implies that the lesion complexity is higher, and a significant relationship (p=0.004) has been shown between the higher three quartiles of HbA_{1c} measures (>5.5%) and SX scores in non-diabetic individuals (Ikeda *et al.*, 2012). Notably, an HbA_{1c} level of >6.5% is the diagnostic criteria for the diagnosis of diabetes (as proposed by the ADA), but the risk associated with SX scores is identifiable from an HbA_{1c} level of 5.6% in non-diabetics

(Ikeda *et al.*, 2012). Similarly, an HbA_{1c} of 5.3±1.7% is required to predict negative SAC (arterial compliance) in non-diabetics (Nestel, 2006).

Table 2.2 provides an indication of hazard ratios related to HbA_{1c} levels for diabetes and CVD in non-diabetic populations.

Table 2.2: Multivariate adjusted hazard ratios (Selvin *et al.*, 2010)

	GLYCATED HAEMOGLOBIN CATEGORIES ***(After Selvin et al., 2010)***			
(HbA_{1c})	<5.0%	5.0 – 5.5%	5.5 – 6.0%	6.0 – 6.5%
Diabetes Hazard Ratio	0.52	1.00	1.86	4.48
CVD / Stroke Hazard Ratio	0.96	1.00	1.23	1.73
				INCREASING HEALTH RISK →

The role of physical activity in moderating glycaemic responses in diabetics, and non-diabetic individuals has been acknowledged, and the importance of exercise remains pivotal to glucose control (Reddigan *et al.*, 2012). Of particular note in the context of the current study is the finding that those individuals who are habitually active are protected against the risks of elevated HbA_{1c} – no matter what the level (Reddigan *et al.*, 2012). This protection is thought to emanate from the ability of aerobic endurance exercise to reduce risk associated with mitochondrial aging, while simultaneously increasing muscle mass and thus the sensitivity of the body to insulin (Reddigan *et al.*, 2012). Arguably resistance training, which is known to have a greater effect than aerobic training on the body composition (lean to fat mass ratio), may be more effective in this regard. Thus, it might be suggested that resistance training may offer an even greater protection against dysglycaemia than aerobic training, and concomitantly far greater protection to at-risk individuals with elevated HbA_{1c}. Contrary to this position, however, is research conducted on a diabetic population (HbA_{1c} 7.7±1.0%) (Church *et al.*, 2010). This controlled trial engaged a sample that comprised 63% females in either resistance training, aerobic endurance training, or a combination of both modalities (Church *et al.*, 2010). It was noted that only the combination of both training types resulted in a significant decrease to HbA_{1c} (-0.34%, p=0.03) (Church *et al.*, 2010).

Co-morbid conditions and risk factors have been identified in individuals expressing with adverse HbA_{1c} levels. It has been noted that those with high HbA_{1c} also have low high density lipoprotein cholesterol, elevated low density lipoprotein cholesterol and elevated levels of plasma triglycerides (Selvin *et al.*, 2010). These individuals have also been shown to be older and to present with higher body mass index ratios than individuals with low or normal HbA_{1c} levels (Selvin *et al.*, 2010). Behavioural correlations exist between physical activity and HbA_{1c} levels (negative correlation) and between use of drugs (such as statins and diuretics) and HbA_{1c} level (positive correlation) (Selvin *et al.*, 2010).

2.8.1.1 HbA_{1c} and macronutrient intake

Glycaemic control (indicated by the glycated haemoglobin measure) is important for delaying chronic microvascular conditions (Xu *et al.*, 2007). These authors reported that higher total fat intake (>25% of daily energy intake), with emphasis on saturated and monounsaturated fatty acids (>13% and >10% respectively) coupled with a low carbohydrate intake were all associated with poor glycaemic control (Xu *et al.*, 2007). In contrast a study engaging diabetic participants noted that macronutrient intake (carbohydrate, protein and fats) was not associated with glycaemic control but that high total energy intake irrespective of macronutrient content was responsible for poor control (Kang & Kim, 2012). It was acknowledged that carbohydrate intake does have the greatest effect on post-prandial glucose levels which is an acute measurement as opposed to the long-term, 'average' reflected by HbA_{1c}. Rather than fasting plasma glucose levels it is suggested that post-prandial hyperglycaemia is an isolated risk factor associated with the development of atherosclerosis, and consequently, cardiovascular disease (Gerich, 2002; Yoon, 2012). As such, tight glycaemic control has been suggested as a means of reducing risk for CVD. Postprandial glucose 'spiking' may contribute to atherosclerosis by means of one of a number of physiological processes: oxidative stress, endothelial dysfunction, or the formation of advanced glycation end-products (Yoon, 2012).

Further analysis of macronutrient intake and its relationship to HbA_{1c} considered the effect of the glycaemic index (GI) and glycaemic load (GL) of carbohydrates on the HbA_{1c} (Livesey *et al.*, 2008). A review of clinical trials revealed that the glycaemic impact of foods certainly did relate to risk of type 2 diabetes and also cardiovascular disease, as well as to bodyweight (Livesey *et al.*, 2008). Of particular note was the level of 'unavailable'

carbohydrate in foods (fibre, most particularly) as increased presence of this type of CHO was associated with increased insulin sensitivity (Livesey *et al.*, 2008).

2.8.2 SEX HORMONE BINDING GLOBULIN

It has been posited that low levels of sex hormone binding globulin in post-menopausal females is an indicator of the metabolic syndrome and increased risk of cardiovascular events (Rexrode *et al.*, 2003; Weinberg *et al.*, 2007). Four proposed quartiles of risk level associated with SHBG are presented in Table 2.3 (Ding *et al.*, 2009) A study of 200 post-menopausal females who were not using hormone replacement therapy noted strong associations between low SHBG and elevated cardiovascular risk – including adverse lipid profiles (Weinberg *et al.*, 2007). Similar findings were reported for a matched cohort, but the association with elevated risk profiles was found not to be independent of body mass index and other cardiovascular risk indices (Rexrode *et al.*, 2003). Observational studies have noted that higher levels of physical activity combined with a lower body mass and overall fat content are associated with higher SHBG levels (Campbell *et al.*, 2012).

Table 2.3: Sex hormone binding globulin risk categories (from Ding *et al.*, 2009)

	SEX HORMONE BINDING GLOBULIN (*n*mol.L^{-1}) PLASMA LEVEL RISK CATEGORIES			
	1	2	3	4
MEDIAN	**17.1**	**29.3**	**39.0**	**55.8**
RANGE	5.8 - 24.7	24.8 - 34.6	34.7 - 44.3	44.4 - 122.4

Hepatic SHBG production is mediated positively by oestradiol and negatively by testosterone (Brand & van der Schouw, 2010). Reduced levels of endogenous oestradiol, characteristic of the menopause, cannot fulfil this mediation role and concomitantly increased levels of testosterone, therefore, result in low levels of SHBG. Approximately 66% of testosterone found in females (which is approximately 5% that of the quantity in males) is bound to SHBG (Brand & van der Schouw, 2010).

Literature is clear that there is a link between greater androgenicity in post-menopausal females, who do not medicate with exogenous oestrogen, and greater risk for cardiovascular disease (Brand & van der Schouw, 2010; Lambrinoudaki *et al.*, 2006). Further details remain controversial not least because there have been very few studies of this relationship in post-menopausal females (Brand & van der Schouw, 2010; Pugeat *et*

al., 1995). Before conclusive statements can be made further evidence is required and more longitudinal studies relating SHBG to CVD risk must be undertaken (Brand & van der Schouw, 2010).

While cognisant of the limited number of studies and the need for further investigation into the relationship, it does appear that low levels of SHBG have been consistently associated with an atherogenic lipid profile (increased triglyceride concentration and decreased high density lipoprotein cholesterol respectively) (Brand & van der Schouw, 2010; Haffner *et al.*, 1990; Tchernof *et al.*, 1999). It has been postulated that the mechanism for this relationship may be the direct effect exerted on hepatic lipase and lipoprotein lipase (key enzymes in the regulation of triglyceride and HDL-C levels) by SHBG (Brand & van der Schouw, 2010). While SHBG has also been related to obesity *per se*, it has been specifically associated with abdominal obesity, which in turn has been connected to reduced levels of HDL-C and concomitantly, increased risk for CVD (Pugeat *et al.*, 1995). Further connections have been made between reduced SHBG and insulin resistance and hyperinsulinaemia and thus researchers have noted that lowered SHBG is an indicator of increased risk for non-insulin dependent diabetes (Pugeat *et al.*, 1995). Of particular note given the focus of this review on the efficacy of physical activity on risk reduction is the causal relationship proposed by researchers between SHBG and degree of physical 'fitness' of the individual (Pugeat *et al.*, 1995).

Limited research has been undertaken on the effect of exercise on SHBG levels. In one study, post-menopausal females aged between 50 and 75 years undertook an aerobic exercise intervention as part of a randomised controlled trial for 12 months. Exercise took place on five days of the week for 45 minutes per session. The participants in the exercise group presented with unchanged SHBG levels following the year's training (-0.7%, p=0.41) (Campbell *et al.*, 2012).

2.8.3 AGING

The selection of an 'older' female sample requires that attention be paid to the natural course of aging. The inevitable physiological and muscular changes that accompany advancing years significantly impact independence and activities of daily living (Chodzko-Zajko *et al.*, 2009). Aging infers a negative change in body composition, as body mass increases and fat free mass declines from the fourth decade and speeds up beyond 70 years of age. Fat free mass is lost at an average of 2-3% per decade beyond the age of

30 years (Chodzko-Zajko *et al.*, 2009). A particular characteristic of advancing age in females is the propensity toward an “apple” shaped figure: abdominal visceral fat deposits increase with age and also with hormonal changes (discussed below) (Chodzko-Zajko *et al.*, 2009). The cardiovascular disease risk that accompanies increasing levels of AVF is compounded by other age-related cardiovascular changes including elevated blood pressure during exercise (particularly in females), slowed heart rate responses to the onset of exercise, and the failure of the thirst sensation to adequately indicate changes in body fluid regulation (Chodzko-Zajko *et al.*, 2009). Stiffening of the chest wall infers difficulty breathing for many adults and maximal oxygen uptake is reduced by 9% per decade (approximately 0.40 -0.50 $ml^{-1}.min^{-1}.kg^{-1}.year^{-1}$).

2.8.4 THE MENOPAUSE

Prior to the menopause females are at lower risk of adverse cardiovascular related events than male counterparts. There is copious evidence to suggest that the mechanism responsible for this protection is the hormone oestradiol (the strongest of the oestrogen family) (Avis *et al.*, 2001; Avis *et al.*, 2004; Bruce & Rymer, 2009; Curtis, 2009; Franco *et al.*, 2009; Hellgren *et al.*, 2009; Kim & Bender, 2009; Ouyang *et al.*, 2009; Stevenson, 2009). Beyond the control of sexual reproduction, oestrogen (as oestradiol) is fundamental in the maintenance of body fluid balance. Dynamic homeostasis of body fluids involves the regulation of osmosis, volume and pressure (Curtis, 2009). In order to maintain perfusion rates and cellular function the cardiovascular system reacts (via blood pressure, heart rate and sympathetic nervous system activity), hormone levels fluctuate (to elicit direct effects on the periphery), and behaviour changes (such as ingestion of water or salt) occur (Curtis, 2009).

Peripherally, oestrogen is critical in the maintenance of endothelial homeostasis, which is in turn fundamental for vascular health. Oestrogen represses athero-promoting genes, increases vascular levels of nitric oxide synthase (eNOS), and encourages vasodilation via oestrogen receptors (Kim & Bender, 2009; Tezini *et al.*, 2008). Centrally, oestrogen receptors (primarily ERα and ER*β* have been found in large concentrations within the central nervous system (CNS). This finding, together with the knowledge that oestrogen is a steroidal, lipophilic hormone with the ability to access the CNS directly indicate clearly that oestrogen has a direct influence on central control of body fluid homeostasis (Curtis, 2009). Oestrogen is attributed with the ability to reverse hypertension, reduce resting blood

pressure and resting heart rate, and is also active in affecting the catecholamine responses as well as vascular reactivity in the periphery (Curtis, 2009).

The menopause infers the loss of endogenous oestrogen via the cessation of ovarian function (Curtis, 2009; Nelson, 2008). Associated directly with this event is a substantial rise in circulating total cholesterol and low density lipoprotein cholesterol (Matthews *et al.*, 2009). Research indicates that the natural chronological rise in lipoprotein content does not match the increase noted during the first year beyond the 'final menstrual period' (FMP) and that there is no ethnic disparity in this rapid rise toward elevated cardiovascular risk (Matthews *et al.*, 2009).

The urgent need for attention to the cardiovascular health status of post-menopausal females is further highlighted by the fact that it is estimated that over half of all females over the age of 65 years in the US meet the criteria for dyslipidaemia (Bhardwaj *et al.*, 2013). Approximately one woman dies of cardiovascular complications every six minutes in Europe, and an appreciably greater percentage of women than men succumb to heart disease on the continent (56% versus 43%) (Rollini *et al.*, 2009; Schenck-Gustafsson, 2009).

Statin-induced myopathy is experienced to a far greater extent in females than in males (1.5 to 1.7 times more) (Bhardwaj *et al.*, 2013). This knowledge of the effects, or indeed, lack of efficacy, of pharmacotherapy renders alternative treatments of primary importance. The accepted sex-related differences in cardiovascular risk and risk-expression must also be acknowledged and sex and hormone-specific cohorts studied.

2.8.4.1 Hormone Replacement Therapy

Management of health post-menopause has been confused in recent years by contradictory results emanating from observational and clinical trial studies (Coulter, 2011). In a review of more than 40 observational studies it was noted that females who were prescribed hormone replacement therapy post-menopause experienced a 30-50% reduction in cardiovascular events, whereas a review of large-scale randomised controlled trials reported unequivocally that HRT provided no support (primary prevention), or in fact increased risk (secondary prevention) (Coulter, 2011). The "timing" hypothesis has been widely accepted, and that infers that HRT may be most effective if it is prescribed from the instance of menopause (Coulter, 2011; Stevenson, 2009; Stevenson, 2009b). Despite the

'timing hypothesis' assertion, there remains doubt as to the cardio-protective nature of this treatment, and alternative health management therapy needs consideration.

2.8.5 PRESENCE OF HEART, LUNG, LIVER, KIDNEY OR OTHER DISEASE

There exists a close relationship between risk factors for cardiovascular disease: hyperinsulinaemia and hyperglycaemia, for example, present in pre-diabetics, have been associated with atherogenic risk (Haffner *et al.*, 1990). Hypertension occurs more frequently in individuals with elevated lipid concentrations than in normolipid individuals (Lye *et al.*, 2009). Chronic kidney disease has been implicated in cardiovascular disease risk and complications, and CVD has been found to occur ten to 30 times more frequently in dialysis patients than in healthy adults (Weiner, 2004). Chronic obstructive pulmonary disease has been linked to inflammation, particularly elevated levels of C-reactive protein, and via this mechanism, to elevated risk of cardiovascular diseases (Sin & Man, 2003). Using population based data from the NHANES III in the United States, it was revealed that 'forced expiratory volume in one second' (FEV_1) levels of 50-80% could be directly linked to sufficient inflammation to cause a two- to three-fold increase in cardiovascular disease risk status (Sin & Man, 2003). The link in this instance relates to the presence of 'chronic obstructive pulmonary disease' (COPD), symptomatic of which is a compromised FEV_1. Sin and Man (2003) found that in COPD patients, C-reactive protein (CRP) was concomitantly elevated, pointing to the association between COPD, elevated chronic inflammation, and imcreased risk of CVD. The authors suggest that an additive risk may exist where COPD and CRP elevation exist together.

Not only do chronic conditions often occur with co-morbidities, but medication prescribed to control chronic illness, such as those medications prescribed for Diabetes Mellitus, can affect cardiovascular risk. A number of accepted and frequently used medications to control T2D, for example, have been directly linked to improving cardiovascular risk parameters in at risk individuals (Chu *et al.*, 2002; Klonoff *et al*., 2008). Chu and colleagues examined the additional prescription of either Metformin or Troglitazone in patients (n=22) with T2D already medicated with 10 mg of Glyburide, daily. After 16 weeks it was evident that there was an accelerated decrease in fasting plasma glucose and in the HbA_{1c} in both groups, however Troglitazone proved more efficacious in reducing insulin resistance in those already receiving the maximal dose of sulfonylurea therapy. Klonoff *et al.* (2008) examined the long term (≥ three year adherence) effects of Exenatide, an

incretin mimetic. Better glycaemic control, reduced body weight and an overall reduction in CVD risk factors was noted in the sample (n=217, 64% male).

Chronic use (longer than 60 days) of anti-depressant medications (Paroxetine and Sertraline) was demonstrated to result in significant increases to low density lipoprotein cholesterol, and thus to have a measurably adverse effect on cardiovascular risk profiles in adults (Wei *et al.*, 2009). Similarly, other treatments may reduce the presence of risk factors during the use of the product, as was shown in the use of probiotics, which reduce inflammation and via this means, positively affect cholesterol profiles (Lye *et al.*, 2009). Corticosteroids, commonly used to treat chronic asthma and COPD, are designed to combat inflammation in the bronchii (Barnes & Pedersen, 1993). Use of these medications may have an impact on cardiovascular risk markers related to inflammatory status by decreasing the presence of inflammatory markers and thus the presence of risk in the individual (Barnes & Pedersen, 1993).

2.8.6 HABITS: SMOKING

Literature is clear and consistent in concluding that smoking increases risk of coronary artery disease and cardiovascular mortality (Beauchamp *et al.*, 2010; Cullen *et al.*, 1998; Gepner *et al.*, 2011; Imamura *et al.*, 2001; Mieczkowska *et al.*, 2012). Cardiovascular changes that contribute to risk in post-menopausal female smokers include elevated heart rate at rest, elevated systolic and diastolic daytime blood pressure and increase Intima-media thickening of the carotid arteries (Mieczkowska *et al.*, 2012). IMT is an established indicator of generalised atherosclerosis, and thickening of the right carotid artery correlated to duration and intensity of the smoking habit (Mieczkowska *et al.*, 2012). The mechanism by which intima-media thickening (IMT) occurs is possibly the result of increased adrenergic activity caused by smoking cigarettes, and may also be the result of frequent and greater increases in arterial blood pressure in smokers (Mieczkowska *et al.*, 2012).

Quite apart from the general cardiovascular and atherogenic effect, smoking cigarettes has a profound effect on the plasma lipoproteins, particularly in female samples (Beauchamp *et al.*, 2010; Cullen *et al.*, 1998; Gepner *et al.*, 2011; Imamura *et al.*, 2001). Female smokers have demonstrably higher levels of triglycerides and low density lipoproteins than non-smokers, as discussed by the authors of the “PROCAM” Munster Heart Study: smoking increased total cholesterol by 2%, triglycerides by 12% and

decreased high density lipoprotein cholesterol by 7% compared to matched non-smokers (Cullen *et al.*, 1998). This data may appear to be dated, as the study commenced in 1978, and critics would argue that modern techniques of analysis are superior: in addition, this study was a prospective epidemiological study rather than randomised and controlled. In defence, the sample size included 10 212 females and 20 699 males, of whom 32% of females smoked and 36% of the males smoked.

A more recent study engaged 3934 self-referred females between the ages of 40 and 59 years (Imamura *et al.*, 2001). Once again, the sample size may mitigate for the fact that this was not a randomised controlled study. The authors also indicate that the study findings were limited by data that was not at their disposal, such as knowledge of coffee consumption, family histories, habitual diet and menopausal status (Imamura *et al.*, 2001). The findings of this study indicated that current female smokers had the following differences when compared to matched non-smokers: HDL-C 15.5% lower; TotC/HDL-C ratio 23.7% higher; Trigycerides 27.4% higher; and LDL-C 6.5% higher (Imamura *et al.*, 2001). Paradoxically, the current and ex-smokers of the sample presented with lower systolic and diastolic blood pressure, in a non-dose dependent manner. Usually a reduced blood pressure is of cardio-protective benefit, but it appears that this reduction due to smoking is 'cancelled out' by the risk attributable to smoking alone (Imamura *et al.*, 2001).

That females are at greater risk for cardiovascular complications due to the habit of smoking is repeated with every reported study (Beauchamp *et al.*, 2010). Independent of confounding lifestyle factors, and age, female smokers presented with a significantly more atherogenic lipid profile than males in a recent research study (Beauchamp *et al.*, 2010). This association was confirmed in a randomised and controlled study in 2011, engaging 1504 adult (average age 45.4 years) smokers who were evaluated over the course of 12 months (Gepner *et al.*, 2011). Despite this sample being of mixed heritage (Caucasian and African American), mixed sex (males and females were included, 58% of the sample was female), and the knowledge that 5% of the sample were taking lipid-lowering medication, the results confirm what earlier studies had already indicated. Those who ceased smoking during the 12 month study had a significantly elevated high density lipoprotein cholesterol ($p<0.001$) compared to current smokers (Gepner *et al.*, 2011). This translated into a 4-6% reduction in risk for cardiovascular disease over the course of a decade. What was of interest to the authors was that smokers had a significantly lower body mass index than non-smokers or those who abstained from smoking during the study

(Gepner *et al.*, 2011). High density lipoprotein cholesterol should show decreases of 0.5 – 1.0% per kilogram of body weight lost: however, in smokers, the act of smoking counteracts this potentially positive effect (Gepner *et al.*, 2011).

2.8.7 HABITS: ALCOHOL INTAKE

Habitual smoking has been positively correlated to increased intake of alcohol (p<0.001) (Imamura *et al.*, 2001). Intake of alcoholic beverages by post-menopausal women has been found to be associated with cardio-protection in some studies, and in others an associative protection against breast cancer has been noted (Hartman *et al.*, 2012; Hvidtfeldt *et al.*, 2012; Rajpathak *et al.*, 2010; Tognon *et al.*, 2012). These results from clinical trials and prospective cohort studies indicate that alcoholic beverage intake does have a biochemical and physiological effect.

2.8.8 RACE: CAUCASIAN

Comparisons of African American and Caucasian American post-menopausal females have previously revealed racial differences related to metabolic risk factors for cardiovascular disease (Nicklas *et al.*, 1999; Nicklas *et al.*, 1997). It was noted that black females appear to gain more body mass post-menopause than white counterparts, and that the mechanisms for this may be linked to a racial difference in resting metabolic rate (5% higher in white females) and fat oxidation (17% higher in white females) (Nicklas *et al.*, 1999). Plasma leptin concentrations also appear to differ along racial lines, with resting energy expenditure related to leptin concentrations in African Americans but not in white post-menopausal American females (Nicklas *et al.*, 1997). As higher leptin levels are associated with lower abdominal obesity, lower levels of leptin, as noted in African American females (20% lower than white females) could be linked directly to higher levels of obesity and thus greater risk for cardiovascular disease.

South African female populations have also exhibited physiological and metabolic differences according to race. Differences in the presence and determinants of plasma lipoproteins have been recorded in black and white South African females (Goedecke *et al.*, 2010). Lower triglyceride concentrations, high density lipoprotein cholesterol, and greater concentrations of the smallest, densest low density lipoprotein cholesterol characterise the black South African female lipid profile, whereas the opposite is true of white South African females (Goedecke, 2010). The lipid profile in black females was correlated to socio-economic status, and particularly dietary protein intake, whereas in

white females the correlates were to lower insulin sensitivity and to lower visceral adipose tissue (Goedecke, 2010). The differences between the risk profiles of white and black females in South African extend to include disparate levels and types of inflammatory markers in each race, as well as adiponectin, and as previously mentioned with regard to an African American population, leptin (Evans & Goedecke, 2011).

2.9 PHARMACOLOGICAL TREATMENTS FOR DYSLIPIDAEMIA

The hydroxyl-methyl-glutaryl co-enzyme A (HMG coA) reductase inhibitors (statin drugs) do achieve their purported end goal: that is, plasma lipoproteins are effectively reduced by 20 to 30% with regular dosage (Eisenberg & Wells, 2009). As the pharmacotherapy of choice in primary and secondary prevention of dyslipidaemia, this efficacy is generally not challenged. There are other drug therapies available (bile-acid sequestrants, cholesterol absorption inhibitors, niacin and fibrates) but most medical practitioners select the HMG coA reductive inhibitors as first line of defence (Mosca, 2005).

Relative risk reduction associated with the effective lowering of the plasma lipoprotein content does not appear to be as clear (Gutierrez *et al.*, 2012). Controversy is evident particularly in relation to female samples, and especially post-menopausal female users (Bandyopadhyay *et al.*, 2001; Hague *et al.*, 2003; Mora *et al.*, 2010). Careful analysis of the literature reveals that not only is the experience of side effects from the medication a factor (myalgia, hepatotoxicity, dipstick-positive proteinuria, and rhabdomyolysis) but that there is evidence to suggest that females taking statin drugs present with greater relative risk for cardiovascular events post-treatment than pre-treatment (Bandyopadhyay *et al.*, 2001; Eisenberg & Wells, 2009; Hague *et al.*, 2003). With most (if not all) major clinical trials of statin drug treatments conducted with funding from major pharmaceutical companies and different brands of statins associated with different trials, it is understandable that adverse effects are not easy to determine in the trial reports (Gutierrez *et al.*, 2012). At face-value each trial reflects positive outcomes, and indeed, end-goal treatment success. Eisenberg and Wells (2009) draw the reader's attention to facts such as the unpublished CASHMERE study of atorvastatin which mirrored the results of the ASCOT trial (also atorvastatin) that indicates no protective effect for females, and indeed no improvement in carotid intima media thickening (IMT) – touted as an end goal aim of statins in effectively reducing risk. The NCEP trial extrapolated results pertaining to males to females – a statistically inappropriate assumption, given the significant

heterogeneity of the sex-stratified samples (Eisenberg and Wells, 2009). The ASCOT, MEGA and JUPITER trials of atorvastatin, pravastatin and rosuvastatin respectively suggested a ~10% increase in cardiovascular event risk in females taking the product; an increase in cerebral infarction in female users over the age of 60 years; and highlighted the anti-inflammatory effect on C-reactive protein (CRP) as primary end goal for all users. The CARE and the PROSPER trials (both of pravastatin) revealed a potentially increased risk of breast cancer incidence in female participants, and results suggesting that the medication may not be as effective for older women, compared to older men (Gutierrez *et al.*, 2012).

Even a suggestion of inefficacy, of an adverse side-effect (fatal cases of rhabdomyolysis, for example), or of increased risk raises alarms regarding the safe use of these products. In the US statins have long since been approved for use by males and females, despite insufficient evidence to suggest the safety or success in female samples – and this because clinical trials have collectively only included 20% female participants (Eisenberg & Wells, 2009; Krummel *et al.*, 2001). The American Heart Association recommends statins for treatment of dyslipidaemia in females despite inconclusive evidence (Gutierrez *et al.*, 2012). In this context it is the opinion of this author that it is necessary to offer an alternative treatment for at-risk populations presenting with dyslipidaemia. The aim of lipid-lowering therapy, of whatever nature, is optimal cardiovascular health (Mosca, 2005). The emphasis placed on lipid-lowering as a means of managing CVD risk must be considered in comparison to the alternative view which holds that cholesterol levels are not associated with risk for cardiovascular events (Noakes & Vlismas, 2012; Taubes, 2007) If reduction of CVD risk is accepted as the primary end-point, one of the initial steps should be to address lifestyle behaviours: most importantly smoking cessation, healthy dietary choices and regular physical activity (Mosca, 2005).

2.10 ADHERENCE AND RETENTION

There is an implicit understanding that should a desirable effect be found as a result of an intervention (in the case of this research, an exercise intervention) that adherence to the treatment in the long-term is critical for beneficence. Despite this, participant attrition remains a pivotal hurdle for researchers embarking on studies of this nature: not only is the veracity of the study called into question, but the individuals who stood to benefit willingly forego health improvements (Peterson *et al.*, 2012; Wilcox *et al.*, 2001). An

understanding of the factors that serve to motivate individuals is therefore critical not only to improving retention rates during the course of longitudinal trials but also for permanent lifestyle change behaviour (Scianni *et al.*, 2012). Previous studies have identified the role of the 'setting' of the intervention as critical to adherence and retention rates (Cox *et al.*, 2003; Greenberg *et al.*, 2009). Supervised group settings appear to produce higher retention than individual or home-based programmes. The "Sedentary Women Exercise Adherence Trial" (SWEAT) study found that 'type' of activity did not affect retention in a comparison of two different modes of aerobic activity and concurred that supervised settings were more effective in retaining participants (Cox *et al.*, 2010). Other investigators report that the 'rapport' between the research team and the participants is critical in preventing attrition, and that high turnover of research team staff is a negative influence on the cohort (M. Jackson et al., 2003). Practical barriers to participation include time, transport, costs involved and procedures (Scianni *et al.*, 2012).

Drop-outs from longitudinal studies are characterised as older, female individuals with a higher degree of medical burden and consequently the health status of these individuals is typically worse than those who remain in the study cohort (Peterson *et al.*, 2012). Long-term trial reports that exclude data from the individuals who did not complete the intervention, or who failed to provide follow-up information become biased and may result in unreliable treatment recommendations (Peterson *et al.*, 2012). Attrition of <5% of the total study population does not infer bias, while drop-outs totalling ≥20% of the sample introduces invalidity (Peterson *et al.*, 2012).

2.11 CONCLUSION OF LITERATURE REVIEW

Cardiovascular disease affects many individuals, particularly females post-menopause. Modifiable risk factors for CVD include habits such as inactivity, poor dietary intake, smoking or excessive use of alcohol, as well as conditions such as obesity, hypertension, dyslipidaemia and type II diabetes (adult onset). Known as the 'silent killer' dyslipidaemia affects an estimated 50% of South African women over the age of 55 years, and may contribute directly to the development of atherosclerotic conditions which in turn may lead to fatal events such as venous thrombo-embolisms or strokes. Existing drug therapy is effective in combatting dyslipidaemia but with females comprising only ~25% of trial participants to date, and associated side effects reported in female patients, drug therapies for dyslipidaemia appear limited until further research has been undertaken. An alternative

to drug prescription is the holistic and potentially more economically viable alternative of lifestyle modifications. Various options exist, including dietary modification, but the focus of this study is physical activity, particularly strength training, as a means of ameliorating and managing dyslipidaemia. Literature to date on the efficacy of strength training is controversial and does not offer clear recommendations for females. In addition, the design of exercise programmes has been very limited in that the majority of research has employed a three day per week exercise frequency, and an intensity ranging between 40% and 80% of the 1 RM. It is argued that a different exercise programme design, specifically higher frequency and greater intensity, would augment the efficacy of strength training and as a means of reducing risk associated with dyslipidaemia.

3 METHODS

3.1 RESEARCH DESIGN

This study evaluated the effect of progressive resistance training on the plasma lipoproteins in post-menopausal women. Designed as a randomised controlled trial it took place in an academic setting, and could not by its nature be blinded. Participants were, however, blinded to progress during the intervention and were not provided with measurement results until completion.

Table 3.1: Design matrix

	Week 0	Week 4	Week 8	Week 12
Exercise Group (ExE)	Measures	Measures	Measures	Measures
Control Group (CoN)	Measures	Measures	Measures	Measures

Where: "Measures" include measures of biochemistry, anthropometry, body composition, blood pressure, habitual activity via the CHAMPS questionnaire, food intake via dietary recall, strength via the 1-repetition maximum test, mood changes via the Profile of Mood States questionnaire, and self-reports.

The research design included two conditions representing the exercise intervention group and the matched control cohort (Table 3.1). Measures were taken every four weeks from baseline as it is known that neural, strength, metabolic and hormonal shifts due to exercise interventions can be observed from as early as four weeks.

3.2 ETHICAL APPROVAL

Ethical approval for this protocol was obtained in May 2011 from the Rhodes University Ethical Standards Committee (for research involving human participants) in Grahamstown, South Africa. All participants submitted written informed consent (Appendix B).

3.3 RESEARCH AIM

This research was conducted in order to evaluate the effect of a 12 week progressive resistance training programme on hypercholesterolaemia in post-menopausal women.

3.4 PARTICIPANTS

3.4.1 RECRUITMENT

Passive recruitment was undertaken in that information was disseminated via local print media, by means of a published "invitation letter", and a four-week series of informative articles, to which was attached an invitation to participate. Email information was widely

spread amongst the community, and “word of mouth” communication proved effective amongst the first groups of participants and their colleagues and acquaintances. Printed flyers were placed in local medical consulting rooms, pharmacies, religious centres as well as hair and beauty salons.

At the information briefing verbal and written information pertaining to the pre-screening phase, exercise programme, measurements to be taken and the requirements regarding maintaining habitual diet and daily levels of activity were clearly explained. Consent forms were discussed, and potential risks and benefits were honestly cited. Following this session, those who felt ready to commit were invited to select a random “participant code” and to select preferred times for pre-screening procedures (Figure 3.1).

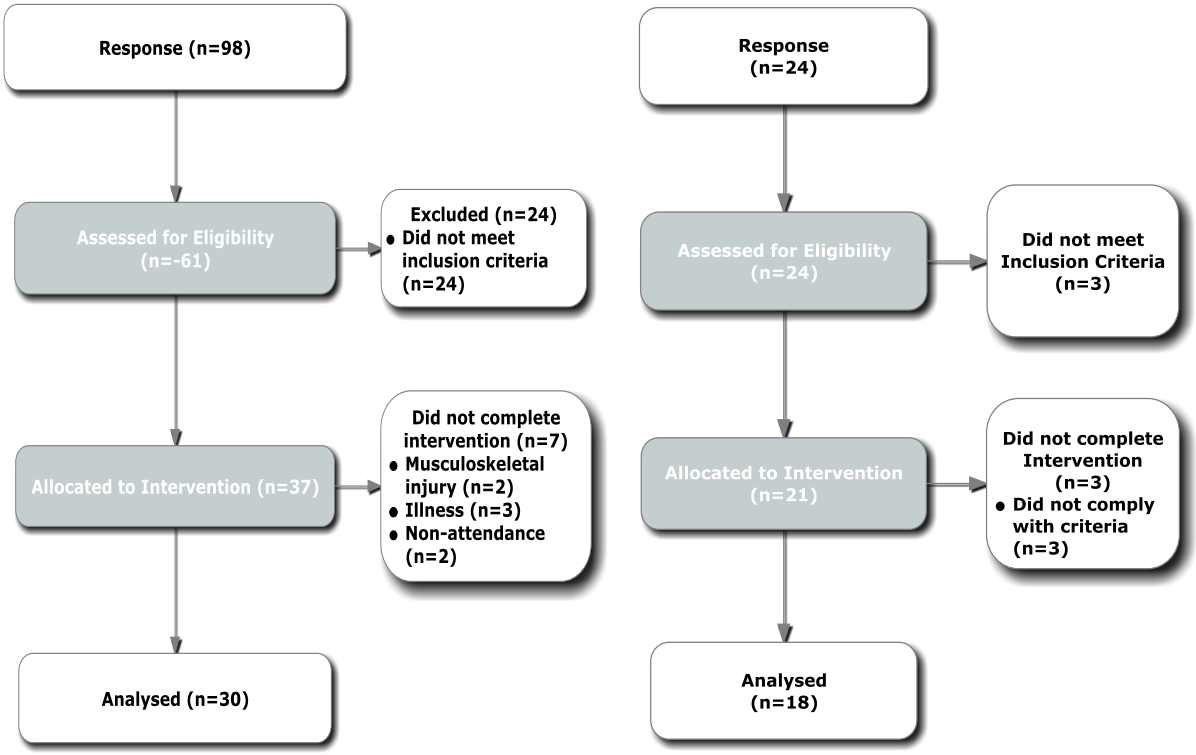


Figure 3.1: CONSORT Flow Diagram

3.4.2 INCLUSION CRITERIA

The following criteria were considered when recruiting individuals for participation:

Female: it is now accepted that cardiovascular disease is a primary cause of mortality amongst females, particular those post-menopause. In addition, attention to female samples is required, as only approximately 30% of trial participants to date have been female.

Age 55 to 65 years: age is an independent risk factor for cardiovascular disease, with exponential increase in occurrence beyond the age of 65 years. Restricting the age of the cohort increased the reliability of any results obtained. Age is related to the requirement that all participants be post-menopausal: the average (global) age at which the menopause occurs is 52 years.

Post-menopausal: Prior to the menopause it is known that females are at lower risk for CVD than male counterparts. Once ovarian function has ceased this landscape changes dramatically. As CVD is the primary killer of females post-menses, attention to this sample is required. Post-menopause was defined as at least 12 months since cessation of menstruation.

No hormone replacement therapy: no participants were taking HRT, or any bio-identical derivates of HRT during the course of the intervention. If individuals had previously taken HRT they had to have stopped the dose at least six months before initial pre-screening took place.

Healthy: self-reports of no heart, lung, liver or kidney disease, as medication for certain conditions would mask the effects of the exercise intervention. Health status was ratified by a physical examination by a medical practitioner in order to ratify self-reports.

No diabetes: glucose control and insulin function was assessed via a test for glycated haemoglobin, any recruit with a value >6.4% (as 6.5% is the level at which diabetes is indicated) was not accepted for the study.

Cholesterol-lowering medication: no participant was taking cholesterol-lowering medication (statins, fibrates or nicotinic acid), or natural derivatives (phyto-oestrogens).

Able to undertake exercise: all participants were of sound musculo-skeletal health. As is recommended for women over the age of 55 years, all candidates were examined by a medical practitioner prior to undertaking the exercise intervention.

Sedentary: defined as less than 20 minutes of structured or continuous activity on fewer than three days of the week. Self-reports were corroborated by assessing the baseline ‘Community health activities model program for seniors’ (CHAMPS) questionnaire, and was monitored throughout via repeat submissions thereof.

Non-smokers: participants were all non-smokers. If they had previously smoked, they had to have given up the habit at least 12 months prior to recruitment.

Caucasian: all participants were Caucasian. Prior investigations have revealed racial differences in expression of cardiovascular risk in both American and South African populations.

3.5 MEASUREMENTS

3.5.1 PHYSICAL EXAMINATION

Each potential exercise recruit was examined by a medical practitioner prior to selection for the programme. As this screening level was only for physical readiness to undertake exercise the control group did not have to submit to a physical examination as none were to undertake exercise. A standard physical examination assessed supine, seated and standing blood pressure; apical pulse rates; assessed the lungs via auscultation; checked reflexes at the patella-femoral joint and at the tibio-tarsal joint; and assessed balance both with eyes open and closed, standing on the right and then the left legs. The checklist used by the physician is included in Appendix C.

3.5.2 ELECTROCARDIOGRAM

To ensure that the recruited individuals were able to undertake physical activity safely a submaximal electrocardiogram (ECG) was administered in the presence of a medical practitioner.

The candidate was asked to sit on a stationery cycle (Cateye Ergociser EC1600, Japan), and the saddle height was adjusted accordingly. The nature of the equipment was explained and the principal researcher requested that the individual remove clothing on the torso.

A twelve lead ECG analysis was undertaken using a Bosch® (EKG 606, Germany) ECG unit, and the print-outs were recorded. The electrodes were held in place securely using Micropore® tape by Elastoplast® (Beiersdorf, Hamburg, Germany) as the unit pre-dated self-adhesive electrodes. Conduction of the electrical impulse was augmented using aqueous-based ECG Conduction Gel purchased at a pharmacy. Kendall Webcol™ (Tycohealthcare, Midrand, South Africa) alcohol pads saturated with 70% isopropyl alcohol were used to clean the skin to improve conduction, and also to clean the electrodes

following each application to a participant. Disposable Hi-Care® (distributed by Healthcare Technologies, Cape Town, South Africa) latex examination gloves (ISO 9001: 2008; conforms to ASTM D3578 (01) and EN455 (00) standards) dusted with absorbable corn-starch powder (powder level below 120 mg per glove) were worn by the researcher at all times.

When the ECG leads were satisfactorily attached, the participant was asked to remain seated and relaxed, while a reference trace was recorded. After one minute the physician indicated that the sub-maximal cycle protocol could commence (Table 3.2).

Table 3.2: Submaximal cycle ergometry protocol

Stage	Description	Time (min)	Duration (min)	Pedal Speed (rpm)	Power Output (Watts)
1	Reference	0-1	1	0	0
2	Activity 1	1-2	1	75	50
3	Activity 2	2-3	1	75	75
4	Activity 3	3-4	1	75	100
5	Recovery 1	4-5	1	0	0
6	Recovery 2	5-6	1	0	0
7	Recovery 3	6-7	1	0	0

Once the physician had approved the traces the principal researcher removed the Micropore™ tape and electrodes from the torso of the individual, and cleaned the areas with a fresh alcohol pad. Each of the electrodes was cleaned thoroughly with an alcohol swab in preparation for the next candidate. The surgical gloves were disposed of after each test.

While the pre-screening and readiness for exercise assessment as well as the sub-maximal ECG were only required for those recruits entering the exercise intervention, all other measurements (as reflect below) were conducted on both sample groups: exercise and control.

3.5.3 STRENGTH

The exercise protocol was progressive in nature, and as such needed to be related to the strength of the participants. A “1-repetition maximum” test was completed at baseline, and repeated at four week intervals.

The baseline 1 RM standardised the initial intensity of the strength-based exercises and ensured that the intensity remained challenging to the individual throughout the course of the programme. Three basic exercises were selected for this test, colloquially known as:

‘lat pulldown’, ‘chest press’ and ‘leg press’ (equipment used: Challenger series by Zest Fitness®, Cape Town, South Africa). These three muscular exertions reflect compound muscle recruitment, and were considered the best reflection of upper and lower extremity strength. Candidates were familiarised with the exercises to be used and were given a chance to execute the movements in practice prior to taking the 1 RM measurement on each occasion. Measurements of strength were undertaken in random orders on the day of testing, and sufficient rest between the upper and lower body measurements on each occasion was afforded to all participants.

3.5.3.1 Back (“Lat Pulldown”)

Using the pulley and adjustable weight-stack machine (Challenger series by Zest Fitness®, Cape Town, South Africa) of the same name this exercise requires strength and activation of not only the latissimus dorsi muscle but also the muscles of the shoulder (deltoid group), torso (rectus abdominis as well as the oblique groups), arms (triceps brachii and biceps brachii) and chest (pectoralis major).

The participant was guided to sit on the adjustable seat facing the weight stack. The participant was instructed to engage a symmetrical hand-grip slightly wider than shoulder-width apart. The researcher selected the weight-plates on the stack, and each time the individual completed one correct repetition the weight was increased by one plate (5 kg). As soon as the participant could not bend the elbows to a 90º angle on the downward effort, or control the bar and cable on the upward exertion, it was determined that the 1 RM had been reached. Verbal encouragement was given to the individual throughout this test. Instructions to the participant were derived from those suggested by previous authors (Phillips *et al.*, 2004).

3.5.3.2 Chest (“Chest Press”)

Using the similarly-named pulley and adjustable weight-stack machine (Challenger series by Zest Fitness®, Cape Town, South Africa), this exercise utilises the pectoralis major muscle of the chest, as well as anterior deltoid, posterior deltoid, triceps brachii and biceps brachii as well as muscles recruited for stabilisation during dynamic exercise. Recruits were asked to lie supine on the padded bench, with head supported, and were guided to grasp the handle-bar symmetrically, slightly wider than shoulder-width apart. While offering verbal encouragement as well as monitoring the correctness of the execution of each repetition, the researcher adjusted the weight-plates accordingly.

As suggested by previous investigators, two to three weight plates were added initially when it was observed that the individual found the resistance easy to manage. Once it became clear that strength was challenged, smaller increases were used (Phillips *et al.,* 2004). Once the participant could no longer lift the bar vertically without the help of the researcher the 1 RM was recorded.

3.5.3.3 Lower Body ("Leg Press")

This exercise utilises the commercially available leg press unit (Challenger series by Zest Fitness®, Cape Town, South Africa). In order to ensure safety during the execution of this exercise, two researchers assisted at this station. Initially the principal researcher demonstrated the exercise, as recommended previously (Phillips *et al.,* 2004). The participant was asked to lie back at a 45º angle on the back-support and directed to place their feet on the foot-plate hip-distance apart with toes facing forward. The safety bar and handles were demonstrated. Initially a low load of 40 kg was placed on the weight-rack. As soon as the individual had become accustomed to the foreign movement and the load, more plate weights were added.

A complete repetition was described for the purposes of this test as one movement commencing from a knee bend of 90º, pushing the weight on a 45º plane until the knees were almost entirely extended (but not over-extended), and then returning the legs to a knee-bend of 90º, before once again extending until the safety catch was inserted and the weight safely suspended. One researcher stood on either side of the machine and was able to assist if the weight became too onerous. Once the candidate could not complete one full repetition, or appeared under undue strain, the 1 RM was recorded.

3.5.4 BIOCHEMICAL ANALYSES

Fasting venous blood tests were conducted at baseline and repeated every four weeks throughout the 12 week protocol. Participants were instructed to fast from 22h00 on the previous evening, and the blood withdrawal occurred between 08h00 and 08h30. The initial tests also functioned as a 'screening' tool, and individuals presenting with diabetic conditions (as indicated by the HbA_{1c} test of glycated haemoglobin) or pre/peri-menopausal levels of oestradiol (>73 *p*mol.L^{-1}) were excluded from the cohort.

3.5.4.1 Glycated Haemoglobin

A Dimension® clinical chemistry system assay (Flex® reagent cartridge) was used to quantify the HbA_{1c} in the sampled blood by measuring both total haemoglobin content as well as haemoglobin A_{1c} presence. The HbA_{1c} measurement is based on a turbidimetric inhibition immunoassay (TINIA) principle and the measurement of total haemoglobin is based on the modification of the alkaline haematin reaction. Using these values, the proportion of glycated haemoglobin was calculated and reported. All haemoglobin variants that are glycated at the β-chain N-terminus and have epitopes identical to that of HbA_{1c} were measured by this assay test.

A sample of whole blood was added to the first cuvette containing lysing reagent in order to measure total haemoglobin. This reagent lysed the red blood cells while simultaneously converting the released haemoglobin to a derivative that has a characteristic absorbence spectrum. An aliquot of the lysed whole blood was transferred to a second cuvette where total haemoglobin concentration is measured at 405 nm and at 700 nm.

The same aliquot of whole blood transferred to the second cuvette was utilised to measure HbA_{1c}. The second cuvette contained an anti-HbA_{1c} buffering agent with which HbA_{1c} in the blood sample reacted to form a soluble antigen-antibody complex. The rate of this reaction was measured turbidimetrically at 340 nm and at 700 nm and was inversely proportional to the concentration of HbA_{1c} contained in the sample.

3.5.4.2 Total Cholesterol

A Dimension® clinical chemistry system Flex® reagent cartridge was used in conjunction with the ‘CHOL’ method to determine total cholesterol in samples of serum and plasma obtained from the participants via venipuncture of the forearm.

Cholesterol esterase (CE) catalysed the hydrolysis of cholesterol esters to produce free cholesterol. Along with pre-existing free cholesterol, these were oxidised in a reaction catalysed by cholesterol oxidase to form cholest-4-ene-3-one and hydrogen peroxide.

In the presence of horseradish peroxidise (HPO) the resultant hydrogen peroxide was used to oxidise N,N diethylaniline-HCl/4-aminoantipyrine (DEA-HCl/AAP) which produced a chormophore that absorbed at 540 nm. This absorbance was directly proportional to the total cholesterol concentration and was measured using a polychromatic (452, 540, 700 nm) endpoint technique.

It is important to note that complete clot formation had occurred before centrifugation. Storage adhered to recommendations that the specimens were stable for eight hours at room temperature, two days at 2-8 ºC, or frozen at -20 ºC for longer storage. The specimens were not repeatedly thawed and re-frozen.

3.5.4.3 Triglycerides

Measurement of the triglyceride content in the sampled plasma required application of the TGL method used on the Dimension® clinical chemistry system. This is an in vitro diagnostic test intended for the quantitative determination of triglyceride content. The samples obtained via venipuncture of the forearm were incubated with lipoprotein lipase (LPL_ enzyme reagent that converted triglycerides into free glycerol and fatty acids. Glycerol kinase (GK) catalysed the phosphorylation of glycerol by adenosine-5-triphosphate (ATP) to glycerol-3-phosphate. Glycerol-3-phosphate-oxidase oxidised glycerol-3-phosphate to dihydroxyacetone phosphate and hydrogen peroxide (H_2O_2). The catalytic action of peroxidise formed quinoneimine from H_2O_2 aminoantipyrine and 4-chlorophenol. The change in the absorbence due to the formation of quinoneimine was directly proportional to the total amount of glycerol in the sample and was measured using a bichromatic (510, 700 nm) endpoint technique.

Blood collection tubes did not have glycerol lubricated stoppers to prevent an erroneous result, and samples were stored between 2 – 8 ºC for optimal results.

3.5.4.4 Oestradiol

A Siemens® ADVIA Centaur® Oestradiol-6 III (E2-6 III) assay kit (Ref 01492657 or 01488773) was used to quantitatively determine the content of oestradiol in serum samples. By utilising chemiluminescent technology this assay allows for the production of a specific antibody (the 17β-oestradiol-6-antibody) which facilitates a wide range of applications of this assay kit. Oestradiol present in the individual's serum sample competes with acridinium ester-labeled oestradiol in the assay for a limited amount of rabbit anti-oestradiol antibody.

Blood samples were collected following universal guidelines for venipuncture in an accredited laboratory. Tubes containing serum were stoppered and stored upright at all times, and samples were allowed to clot before centrifugation took place. Samples were utilised within eight hours if stored at room temperature and where storage for longer than

eight hours was required, samples were refrigerated at 2-8 ºC or frozen (-20 ºC) if storage exceeded 48 hours duration. Thorough mixing following thawing and only one occurrence of defrosting was accepted protocol for frozen samples. Samples were checked to ensure that they were free of fibrin, particulate matter, and bubbles. It must be noted that heterophilic antibodies in the serum can interfere with the immunoassays, thus individuals who are routinely exposed to animals or animal serum may produce anomalous results.

The ADVIA Centaur® E2-6 III assay measures oestradiol concentrations up to 1000 *p*mol.L^{-1}. The minimum content detectable is 25.7 *p*mol.L^{-1}. Standardisation of the ADVIA Centaur E2-6 III assay is done internally.

3.5.4.5 Testosterone and sex hormone binding globulin

An Access chemiluminescent immunoassay (Beckman Coulter, California, United States) was used to evaluate the presence of testosterone in serum samples (Ref: 33560). Testosterone is produced by the Leydig cells in males, and by the ovaries, adrenal gland and peripheral fatty tissue in females. Females possess ten times less testosterone than male counterparts, and it is found bound to sex-hormone binding globulin (SHBG) and to albumin, with only a small volume in the free state.

All blood samples were collected following universal recommendations for venipuncture at an accredited laboratory. Before centrifugation samples were allowed to clot, and tubes were kept stoppered at all times. Following centrifugation, 500 µL of cell-free sample (fibrin and cellular matter was removed) was transferred to a storage tube and stoppered immediately. Samples were stored at room temperature (15º - 30 ºC) for no longer than eight hours. For occasions where assays could not be completed within eight hours, samples were refrigerated (2º - 8 ºC), or if the assay could not be completed within 48 hours, refrigerated (-20 ºC or colder). If frozen, samples were not defrosted and re-frozen more than twice.

The procedure is limited by the analytic range of detection (0.35 – 55.5 *n*mol.L^{-1}). The possibility exists of interference in the sample by heterophile antibodies, as may occur in individuals who have been regularly exposed to animals or who have received immunotherapy. Erroneous results may reflect, and further examination may be necessary. The investigator is also cautioned to consider the individual's total clinical presentation when examining the results.

3.5.5 ANTHROPOMETRY

With the exception of stature, all the descriptive measurements were obtained at baseline and then every four weeks thereafter for the duration of the twelve week protocol. The principal researcher was the tester in all instances, thereby increasing test reliability. Disposable latex surgical gloves were worn at all times as per clinical guidelines. The measurements were obtained at the same time of day in each instance.

3.5.5.1 Stature

The participant was asked to remove any footwear and stand against the Harpenden stadiometer (Harpenden Holtain® by Seritex Inc., United States of America), with medial malleoli in close proximity and spine erect, facing forward with chin raised parallel to the floor. Three anatomical sites touched the vertical: the heels, gluteus maximus and occipitus. The principal researcher took the measurement at the apex of the cranium. Stature (m) was recorded to the nearest millimetre.

3.5.5.2 Body mass

Body mass was measured with footwear removed, wearing minimal clothing, and with all items from pockets as well as belts and heavy items of jewelry removed. Participants were requested to stand in the centre of the Toledo® (Cleveland, Ohio) electronic scale bed and body mass was recorded to the nearest 0.01 kg.

3.5.5.3 Calculation of Body Mass Index

Stature and mass were used to calculate the body mass index (BMI), following the formula:

$$\text{Body Mass Index} = \text{body mass (kg)}.\ \text{stature (m)}^{-2}$$

3.5.5.4 Girths

Girth measures (cm) at selected sites on the body were obtained using a standard dressmaker's tape measure. Reliability of the circumference measures was maintained by keeping the tape measure at 90º to the long length of the anatomical part being measured, and by ensuring that all sites were anatomically marked. All measures were taken to the nearest 0.1 cm directly against the skin with no compression. The selected anatomical sites were: (i) mid-way between the acromion and the head of the ulnar; (ii) under-bust chest measure; (iii) waist at the level of the umbilicus; (iv) hip at the widest part across the

gluteal muscle group; (v) mid-way between the femoral head and the femoro-tibial joint; and (vi) mid-way between the femoro-tibial joint and the distal head of the fibula.

3.5.5.5 Calculation of waist to hip ratio

Waist circumference (cm) and hip girth (cm) were used to calculate the waist to hip ratio, as follows:

$$\text{WHR (ratio, unit)} = \text{waist (cm)} \div \text{hip (cm)}$$

3.5.5.6 Calculation of waist to stature ratio

Waist circumference (cm) was utilised together with Stature (m) to calculate the waist to stature ratio, as follows:

$$\text{WSR} = \text{waist (cm)} \div \text{stature (cm)}$$

3.5.5.7 Body composition

3.5.5.7.1 Skinfolds

Holtain Ltd® (Crymych, United Kingdom) skinfold callipers were used. Participants were asked to stand in a relaxed position while the principal researcher obtained the skinfold measures. Where applicable, the individual was asked to remove items of clothing so that the skinfold could be measured appropriately. It is important to note that these measures took place in a screened section of the laboratory. The callipers were held at 90º to the site being measured, and the subcutaneous tissue was grasped firmly in the thumb and forefinger of the left hand while the measure was taken with the calliper in the right hand to reduce calliper "sliding". The measures were taken at the same time of day in each instance, reducing the effect related to levels of tissue hydration, which can in turn affect the reliability of the skinfold measure. Careful anatomical marking of each site ensured that the measurements were taken at the same point on each individual at each test session.

Skinfolds were obtained at the following sites: tricep, sub-scapular, chest, mid-axillary, supra-iliac, abdomen and thigh. The sum of skinfolds was determined using this data, and entered into the Jackson-Pollock "seven-site" equation (females) for estimating body density and ultimately total lean body mass.

The Jackson-Pollock “seven-site” equation for females:

Body Density = 1.097 - (0.00046971 x sum of skinfolds) + (0.00000056 x square of the sum of skinfold sites) - (0.00012828 x age)

(Jackson, 1978).

3.5.5.7.2 Bio-electrical impedance Analysis

Body density and concomitantly body fat percentage was also measured using the Lipotrak® (Marulatech, Cape Town, South Africa) bio-electrical impedance analysis (BIA) equipment. Prior to the measurement the individual was asked to lie supine on a gymnastic mat on the floor. The right shoe and sock were removed. All jewelry and wristwatches on the right hand arm were removed, and any jewelry on the right foot was also taken off. The areas required were cleaned with a sterile Kendall Webcol™ (TycoHealthcare, Midrand, South Africa) alcohol pad. Self-adhesive electrode pads (Skintact® Easitabs by Leonhard Lang GmbH, Innsbruck, Austria) were attached at the proximal and distal ends of the third and fourth metacarpals on the right hand. On the lower limb the electrodes were placed proximally and distally between the third and fourth metatarsals on the right foot. The “crocodile” clips from the Lipotrak® unit were attached to the Skintact® electrode pads. Once the measure had been recorded, the clips and electrodes were removed from the skin and the area cleaned with a fresh alcohol pad.

The unit calculates ‘total body water’ (TBW) via the Lukaski & Bolonchuk (1988) formula:

$$0.372(S2 \div R) + 3.05(Sex) + 0.142(W) – 0.069(Age) = TBW$$

Where:

S = height (cm)
R = Resistance
W = weight (kg)
Sex = Male – “1”; Female – “0”
Age = (years)

The hydration constant of ‘fat free mass’ (FFM) is 0.73, so the calculation for FFM:

$$TBW \div 0.73 = FFM$$

Fat mass is calculated as:

$$W(kg) – FFM(kg) = (fat\ mass)\ (kg)$$

(Lukaski & Bolonchuk, 1988)

3.5.5.8 Blood pressure

Measured using a manual mercury sphygmomanometer (Baumanometer, New York, United States of America) and stethoscope, blood pressure (mmHg) was recorded while the individual was seated. Participants were asked to sit quietly for five to ten minutes on arrival for their measurements. The arm cuff was placed around the right arm, just above the level of the elbow joint, while the lower arm was supported on a firm surface.

The acoustic stethoscope (similar to an 'American Diagnostic Corporation' ADC 603 general diagnostic acoustic scope, www.stethoscope.com) was placed underneath the cuff, and the individual was asked to relax the arm, keeping it slightly bent. The blood pressure cuff was inflated to a maximum of 180 mmHg before deflation commenced and the mercury column on the sphygmomanometer was monitored in conjunction with auscultation via the stethoscope. The reading was repeated twice to ensure that experimenter-error had not occurred, and also to allow the effects of anxiety to dissipate.

Acknowledging that this measure is a 'reference' only, and not indicative of a true resting blood pressure, it was taken by the principal researcher at the same time of day at each re-test, and using the same equipment.

3.5.6 SELF REPORTED INFORMATION

3.5.6.1 Profile of Mood States

The 'Profile of Mood States" (POMS™) standard form questionnaire was completed at the commencement of the protocol and every four weeks until completion of the intervention (a copy of the questionnaire and scoring sheet can be found in Appendix D). The questionnaire was explained by the principal investigator prior to the first completion. Respondents were asked to report on the previous seven days when considering the questions. Once the questionnaires had been returned the principal researcher analysed each response according to the template provided by the POMS™ authors (McNair *et al.*, 1971).

3.5.6.2 Self Report Feedback

Participants were asked to provide subjective feedback at the completion of the exercise protocol about the experience of taking part in the study. Responses were guided by a set

of generic questions, but self-expression was encouraged. A copy of the set of questions may be found in Appendix E.

3.5.7 DIET

Diet required regular monitoring to ensure that significant changes did not occur. A three day (Tuesday, Thursday and Saturday), 24-hour dietary recall was required at baseline and every four weeks thereafter from each participant. Instruction on how to complete a dietary recall form was given at the commencement of the study by the principal researcher. To analyse the 3-day 24-hour dietary recall diaries used to monitor individuals' dietary intake the FoodFinder 3™ software programme for Windows® developed by the 'Nutritional Intervention Research Unit' (NIRU) and 'Biomedical Informatics Research Division' (BIRD) of the South African 'Medical Research Council' (MRC) in collaboration with 'WAMTechnology CC' was used. Permission to use this product was obtained and a licence for the software purchased from the MRC (http://foodfinder.mrc.ac.za/). A sample of the diet recall template may be found in Appendix F.

3.5.8 ENERGY EXPENDITURE

Energy expenditure required regular monitoring to ensure that significant changes did not occur. The 'Community Healthy Activities Model Program For Seniors' (CHAMPS) activity questionnaire for older adults was used to obtain quantitative information related to habitual activity levels of the participants both before selection and during participation. A copy of the questionnaire was given to each participant every four weeks (Appendix G). Pre-participation information ensured that self-reports of sedentary living were corroborated by conversion of reported activity to the metabolic equivalent ($MET.mins^{-1}$). Individuals who reported weekly activity exceeding 600 $MET.mins^{-1}$ were not considered "sedentary" and were not included in the study cohort. During the course of the exercise protocol, the CHAMPS analyses ensured that the participants were not undertaking additional activity in conjunction with the prescribed protocol as this would have had an effect on measured results. With permission from the author (Professor A. Stewart - personal communication with the principal researcher) the 'Community Healthy Activities Model Program For Seniors' (CHAMPS) activities questionnaire was used to evaluate the levels of additional physical activity undertaken by each participant.

3.6 EXERCISE INTERVENTION

The exercise sessions took place in the laboratory in the Department of Human Kinetics and Ergonomics at Rhodes University in Grahamstown, South Africa. All sessions were supervised by the principal researcher assisted by female postgraduate students. It has been noted previously that supervised, centrally located exercise sessions have 16% better compliance rates (an average of 90% attendance at sessions) than home-based, unsupervised programmes (where attendance rates of 75% can be expected) (Cox *et al.*, 2003).

Floor space of approximately 4 m x 6 m was dedicated to the research group's exercise intervention training sessions. Poster boards were used to define the boundary and offer additional privacy (five boards, each 2 m x 1.5 m). A non-slip plywood walkway in the same laboratory was used for travelling lunges, when required. Two Cosmed® stationery cycle ergometers were available for the five-minute warm-up.

The resistance training exercises required the following items of commercially available gym equipment: one adjustable bench; three burst proof Swiss exercise balls (diameter 65 cm); four 1 m x 1.5 m interlinking compressed foam floor exercise mats, 2 cm in thickness; six 0.6 m x 0.6 m x 0.3 m carpeted stackable square steps; one set each of 2 kg, 4 kg and 5 kg hand-held dumbbell weights with non-slip grip; one adjustable dumbbell set with rubberised non-slip grip facilitating weight variations from 2 kg to 15 kg per unit; one barbell with plate weights; one hip abduction/adduction weight-stack machine; one lat pulldown weight stack machine; and one shoulder flexion/extension weight stack machine.

During progression of the exercises 'free weight' variations of machine exercises were introduced. Abdominal crunches were executed on the Swiss ball for sagittal plane movement, and on the floor for oblique twists.

3.6.1 NATURE AND INTENSITY

Resistance training was the focus of this exercise programme. As such, the aerobic component (warm up) was limited to less than five minutes. Using the "1-repetition maximum" (1 RM) test results for upper and lower extremities, the exercises were initially set at 80% of the 1 RM, and adjusted every four weeks according to strength increases noted in re-tests of the 1 RM. Progression of the intensity is required in order to elicit morphological changes in the individual. At all stages of the programme, three sets of

each of eight prescribed exercises were completed, each set consisting of twelve repetitions.

At the session during which baseline body composition measures were obtained, participants were introduced to the first stage exercises, and given a short habituation trial. All the exercises were depicted pictorially on poster-boards in the exercise area, and were verbally explained by the researcher and assistants. All exercise sessions were supervised which allowed for constant correction and refinement of participants' execution of the various exercises.

The exercises selected for the programme were compound in nature, focusing on large muscle groups, functional exercises and whole-body effect.

Table 3.3 presents the exercises for each stage of the programme, and which muscles are primarily at work in the execution thereof. Rest allowance between sets was standardized at 30 seconds duration maximum and to 60 seconds between different exercises.

Table 3.3: Training programme

Stage	Weeks	Sets / Reps	Exercises	Primary Muscles Engaged (per selected exercise)
1	**1-4**	**3 x 12**	Hip Abduction	Gluteus Minimus, Medius and Maximus
			Lat pulldown	Latissimus Dorsi, Trapezius
			Step ups (30cm)	Rectus femoris, Vastus Medialis, Vastus Lateralis, Vastus Intermedius; as well as Semi-tendinosus, Semi-membranosus, and Biceps Femoris
			Chest press (bench with dumbbells)	Pectoralis Major, Latissimus Dorsi, Trapezius, Biceps Brachii and Triceps Brachii
			Shoulder pulldown	Pectoralis Major, Anterior Deltoid Deltoid group (posterior, medial and anterior)
			Wall-slide squats	Rectus femoris, Vastus Medialis, Vastus Lateralis, Vastus Intermedius; as well as Semi-tendinosus, Semi-membranosus, and Biceps Femoris
			Standing push-ups	Pectoralis Major, Latissimus Dorsi, Trapezius, Biceps Brachii and Triceps Brachii

			Abdominal crunches (on ball)	Rectus Abdominis
2	**5-8**	**3 x 12**	Hip abduction	Gluteus Minimus, Medius and Maximus
			Lat pulldown	Latissimus Dorsi, Trapezius
			Step (30cm) (with weight – dumbbells)	Rectus femoris, Vastus Medialis, Vastus Lateralis, Vastus Intermedius; as well as Semi-tendinosus, Semi-membranosus, and Biceps Femoris
			Chest press (on ball with dumbbell weights)	Pectoralis Major, Latissimus Dorsi, Trapezius, Biceps Brachii and Triceps Brachii (including stabilisers while on ball: transverse abdominis, external and internal obliques)
			Shoulder pulldown	Pectoralis Major, Anterior Deltoid Deltoid group (posterior, medial and anterior)
			Travelling lunges	Rectus femoris, Vastus Medialis, Vastus Lateralis, Vastus Intermedius; Semi-tendinosus, Semi-membranosus, and Biceps Femoris; gastrocnemius, tibialis anterior and soleus
			Bent over row	Pectoralis Major, Latissimus Dorsi, Trapezius, Biceps Brachii and Triceps Brachii
			Abdominal crunches (on ball)	Rectus Abdominis

3	**9-12**	**3 x 12**	Hip abduction	Gluteus Minimus, Medius and Maximus
			Lat pulldown	Latissimus Dorsi, Trapezius
			Step (50cm) with dumbbell weight	Rectus femoris, Vastus Medialis, Vastus Lateralis, Vastus Intermedius; as well as Semi-tendinosus, Semi-membranosus, and Biceps Femoris
			Chest press with barbell (on ball)	Pectoralis Major, Latissimus Dorsi, Trapezius, Biceps Brachii and Triceps Brachii (including stabilisers while on ball: transverse abdominis, external and internal obliques)
			Shoulder pulldown	Pectoralis Major, Anterior Deltoid
				Deltoid group (posterior, medial and anterior)
			'Goblet' squat with dumbbell weight	Rectus femoris, Vastus Medialis, Vastus Lateralis, Vastus Intermedius; Semi-tendinosus, Semi-membranosus, and Biceps Femoris; gastrocnemius, tibialis anterior and soleus
			Lunge with overhead shoulder press (dumbbell)	Pectoralis Major, Latissimus Dorsi, Trapezius, Biceps Brachii and Triceps Brachii; Rectus femoris, Vastus Medialis, Vastus Lateralis, Vastus Intermedius; Semi-tendinosus, Semi-membranosus, and Biceps Femoris; gastrocnemius, tibialis anterior and soleus
			Abdominal Crunches (on ball)	Rectus Abdominis
			Oblique twist crunches (on floor) holding 5kg dumbbell weight	Rectus abdominis, internal and external obliques, transverse abdominis

3.6.2 FREQUENCY AND DURATION

The exercise intervention was designed to progress over a period of twelve weeks in total. Each participant attended five sessions per week on weekdays. Each session lasted 30 minutes duration. Participants were offered a range of times at which to attend sessions, most self-selecting to diarise the same time daily. Attendance was logged on a register maintained by the researcher and assistants and results from individuals who did not meet the minimum criterion of 80% attendance were not included in the data set.

3.7 ADDITIONAL INFORMATION

3.7.1 EMERGENCY PROTOCOL - “IN CASE OF EMERGENCY” (ICE)

The risk of an adverse event occurring during exercise sessions of any nature could not be excluded. While every precaution was taken to prevent such eventualities (a pre-screening physical examination, readiness for exercise clearance, as well as a sub-maximal ECG evaluation), even completely healthy individuals could succumb to feeling faint, experiencing chest pains, executing a movement incorrectly and injuring a muscle or joint-tendon complex, or simply tripping and falling in the exercise area. All supervisors to the sessions were trained postgraduate Human Kinetics and Ergonomics students, and were instructed on the correct management of any adverse situation. Supervisors to the sessions were required to have mobile telephones with them in case of such emergencies. A “first aid kit” was made available in the facility for management of simple cuts, bruises and muscle injury. A medical practitioner agreed to availability for more serious injury, and telephonic details were clearly posted in the laboratory.

3.7.2 COMMUNICATION AND INFORMATION

Continual communication with each participant throughout the intervention was fundamental to ensuring good attendance and maintaining morale. Apart from daily face-to-face contact with participants at sessions, the principal researcher engaged in email and text message communication weekly, with information about sessions, feedback regarding progress of the study, reminders pertaining to measurements, and logistics surrounding measurement sessions. Following completion of the 12 week intervention period all sub-groups were invited to attend a social gathering where available results were shared and personal thoughts about participation were

voluntarily aired. Social cohesion among the participants was a strong motivator and loyalty to the principal researcher a fundamental relationship for adherence and retention to the study.

3.7.3 DEBRIEFING

Following completion of the study, all participants were given written copies of personal results from the three month period. In addition, the principal researcher ensured that these results were explained in consultation, and held informative meetings related to the results of the group as a whole. Specific queries were addressed, and further communication with the principal researcher was encouraged.

3.7.4 CONTROL GROUP

Requiring participants to remain sedentary must be viewed as ethically questionable. As such, in order to remediate the 12 week period of inactivity, control participants were offered the opportunity to participate in activity once the intervention period was complete.

3.8 RESEARCH TIMELINE

The research project commenced following ethical approval in June 2011 (refer to Figure 3.2). Recruitment of study participants was done in phases, for both ExE and CoN. The limitations of recruiting individuals in phases, not least of all the seasonal variation in lipid profiles, are acknowledged. Insofar as was possible the control and exercise groups commenced in the same months of the year, albeit in different years. Recruitment proved difficult and slow, and dropout was also a concern when completing the sample (n=30 for ExE and n=18 in CoN). Despite the relatively large pool from which to draw recruits, the inclusion criteria were necessarily restrictive and many interested individuals could not participate.

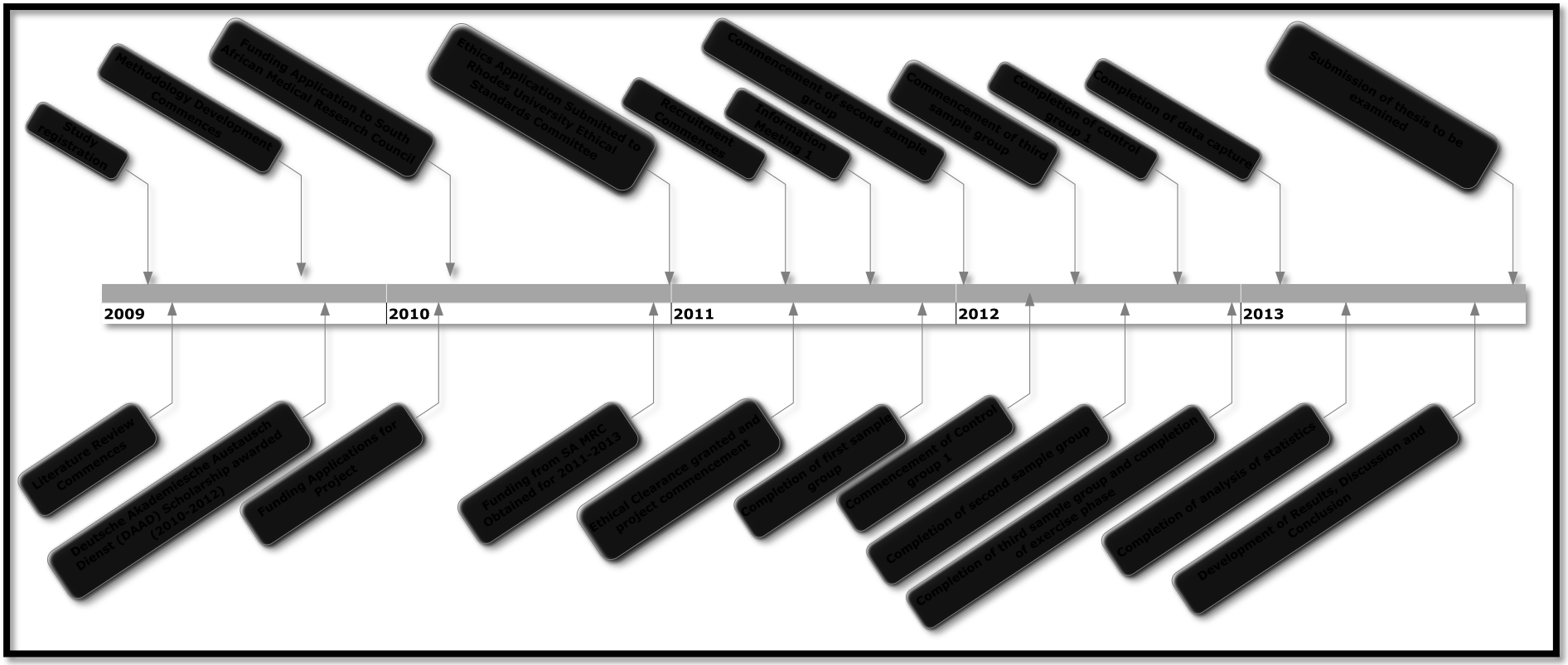


Figure 3.2: Timeline of the research project

3.9 STATISTICAL ANALYSIS

Significance level was set at 5% (p=0.05). Raw data was entered into Microsoft Excel® spreadsheets and the 'data filter' tool was used to obtain basic descriptive results (mean, standard deviation, coefficient of variation, minimum/maximum values and correlations as r^2) for ExE and CoN. Effect size was calculated using Cohen's effect size index formula: $d = (Mean_1 – Mean_2)/(s_w)$ (Cohen 1988, pp 19-74). Using the software programme SPSS version 21, a repeated measures analysis of variance was used with variables (strength (back, chest and leg), dietary intake (total caloric intake as well as carbohydrate, protein and fat intake per day), energy expenditure, plasma lipoproteins (TotC, LDL-C, HDL-C and TriG), HbA_{1c}, SHBG, E2, T, girth measures, skinfold site measures, sum of skinfolds, body mass index, waist to hip ratio, waist to stature ratio, systolic blood pressure, diastolic blood pressure, and each sub-variable for the profile of mood states questionnaire) at time points (weeks 0, 4, 8, 12) as the dependent variables and Group (ExE and CoN) as the factor. Tukey post-hoc tests identified the time points at which significant differences were noted. Thereafter, Wilks and Pillai's multivariate tests for repeated measures analyses, Mauchly's sphericity test and Levene's test for homogeneity of variances were utilized for complete analysis of the data. Images of the spreadsheet and database can be found in Appendix F. The statistical data is appended in Appendix G.

4 RESULTS

4.1 DEMOGRAPHICS

With respect to participant characteristics here was no significant difference between the exercise group (ExE) and the control sample (CoN) at baseline. Demographic data are presented in Table 4.1.

Table 4.1: Baseline demographic data

	EXERCISE	CONTROL
	(Group ExE)	(Group CoN)
Sample size (n)	30	18
Age (years)	59.8 ± 3.1	58.8 ± 3.3
Stature (m)	1.6 ± 0.1	1.7 ± 0.1
Body mass (kg)	79.2 ± 12.8	75.3 ± 11.1
Attendance at sessions (%)	≥ 75.0	N/A
Full time employment (%)	76.7	89.5

4.2 ADHERENCE

Thirty individuals met the attendance criteria in group ExE. CoN (n=18) did not undertake any form of exercise, and were only required to attend measurement sessions every four weeks. Four individuals recorded 100% attendance (ExE), 16 reached an attendance of more than 90% and five attended more than 80% of the stipulated sessions (60 sessions in total). Four individuals were retained in the sample having attended more than 78% of the sessions as it was deemed unnecessary to discount this data on the basis of one additional missed session.

Twenty three (7%) individuals in ExE were healthy throughout the intervention period, while five experienced repeated bouts of illness that resulted in absenteeism (common cold, influenza, bronchitis and sinusitis). Six (20%) reported joint complaints in the initial health screening, but no condition that would preclude resistance training. One individual had bilateral hip replacements which restricted strength expression. Knee and lumbar spine discomfort were cited by the other respondents. There were no health complaints which may have compromised attendance at measurement sessions within CoN.

4.3 DIETARY INTAKE

At baseline total caloric intake was not significantly different between ExE and CoN. There was no change to caloric intake over time in either group (Table 4.2). Daily caloric intake is categorised as “average to high” for older females. At baseline carbohydrate intake was the same in both groups. There was no significant change over time in either ExE or CoN. Baseline protein intake was not significantly different at week 0 (ExE and CoN) and there was no significant change over time. At week 0, fat intake was the same in ExE and CoN. There was no change over time in either group.

Table 4.2: Dietary intake

		CALORIC INTAKE		CHO		PROTEIN		FAT	
		(kJ.day^{-1})	CV (%)	(g.day^{-1})	CV (%)	(g.day^{-1})	CV (%)	(g.day^{-1})	CV (%)
ExE (n=30)	**WEEK 0**	7149 ± 1981	(28%)	184 ± 61	(33%)	66 ± 27	(40%)	56 ± 22	(39%)
	WEEK 4	7520 ± 2590	(34%)	196 ± 65	(33%)	72 ± 31	(43%)	67 ± 33	(49%)
	WEEK 8	7529 ± 2641	(35%)	187 ± 63	(34%)	71 ± 35	(49%)	67 ± 41	(61%)
	WEEK 12	7149 ± 1981	(28%)	196 ± 83	(42%)	69 ± 27	(39%)	71 ± 31	(44%)
CON (n=18)	**WEEK 0**	6533 ± 1924	(30%)	157 ± 53	(34%)	63 ± 29	(45%)	57 ± 24	(42%)
	WEEK 4	7136 ± 2619	(37%)	179 ± 63	(36%)	70 ± 34	(49%)	59 ± 36	(55%)
	WEEK 8	6984 ± 1612	(23%)	168 ± 54	(32%)	77 ± 22	(29%)	67 ± 29	(44%)
	WEEK 12	7006 ± 1798	(26%)	159 ± 48	(30%)	75 ± 27	(37%)	66 ± 25	(37%)

Data is expressed as “mean ± standard deviation”; CV = Coefficient of Variation presented in brackets

4.4 ENERGY EXPENDITURE

At baseline energy expenditure for ExE and CoN was not significantly different. Without including the energy expended at the intervention exercise sessions (ExE) energy expenditure was monitored at four week intervals. Energy expenditure increased significantly (F=3.210, df=(3,78), p=0.03) at week 4 (ExE) but decreased thereafter and was not significantly different to baseline at weeks 8 and 12 (Table 4.3). In CoN a significant increase was noted at week 8, which differed significantly to baseline (F=3.664, df=(3,36), p=0.02) and to week 4 (F=3.664, df=(3,36), p=0.02). By week 12 activity was the same as at baseline in CoN.

Table 4.3: Energy expenditure

	WEEK 0		WEEK 4		WEEK 8		WEEK 12	
	Energy Expenditure ($kJ.day^{-1}$)	CV (%)	Energy Expenditure ($kJ.day^{-1}$)	CV (%)	Energy Expenditure ($kJ.day^{-1}$)	CV (%)	Energy Expenditure ($kJ.day^{-1}$)	CV (%)
ExE (n=30)	1602 ± 1491	(93%)	**2790 ± 2768***	(99%)	2199 ± 3056	(139%)	1860 ± 2126	(114%)
CON (n=18)	1041 ± 1219	(117%)	1054 ± 1316	(125%)	**2558 ± 3356*** #	(131%)	1526 ± 2547	(167%)

*Energy expenditure is expressed as "mean ± standard deviation"; CV = Coefficient of Variation presented in brackets; * denotes significant difference to week 0 (baseline); # indicates significant difference to week 4; **[bold]** font highlights significant differences.*

4.5 STRENGTH

An overview of strength results is presented in Table 4.4. At baseline there was no difference between ExE and CoN for back and leg strength. Chest strength exhibited a significant (F=6.68, df=(1,31), p=0.01) group effect at baseline, with ExE significantly (p=0.01) stronger than CoN. There was no change to chest strength in CoN over the course of the intervention (Figure 4.1). ExE chest strength increased significantly (F=8.48, df=(3,81), p<0.01) from baseline to weeks 8 and 12, with week 4 measure significantly (p<0.01) weaker than week 12.

Table 4.4: Strength measures (ExE, n=30; CoN, n=18)

		CHEST STRENGTH		BACKSTRENGTH		LEG STRENGTH	
		(kg)	CV (%)	(kg)	CV (%)	(kg)	CV (%)
ExE (n=30)	**WEEK 0**	23.4 ± 6.4	(27%)	26.3 ± 7.5	(29%)	94.7 ± 27.2	(29%)
	WEEK 4	**26.3 ± 9.5***	(36%)	**37.0 ± 2.7***	(7%)	**110.3 ± 28.0***	(25%)
	WEEK 8	**28.4 ± 9.0***	(32%)	**38.8 ± 11.0***	(28%)	**126.3 ± 30.8*** #**	(24%)
	WEEK 12	**31.5 ± 11.5*** #**	(37%)	**39.7 ± 11.6***	(29%)	**135.0 ± 29.4*** #**	(22%)
CON (n=18)	**WEEK 0**	18.0 ± 2.7	(15%)	42.5 ± 5.8	(14%)	110.0±26.5	(24%)
	WEEK 4	17.0 ± 5.7	(31%)	**21.0 ± 2.2***	(10%)	114.0±34.4	(30%)
	WEEK 8	19.0 ± 6.5	(34%)	**34.0 ± 7.4#**	(22%)	100.0±23.5	(24%)
	WEEK 12	19.0 ± 6.5	(34%)	**34.0 ± 7.4#**	(22%)	100.0±23.5	(24%)

*Strength is expressed as "mean ± standard deviation"; CV = Coefficient of Variation presented in brackets; * denotes significant difference to week 0 (baseline); # indicates significant difference to week 4; **[bold]** font highlights significant differences.*

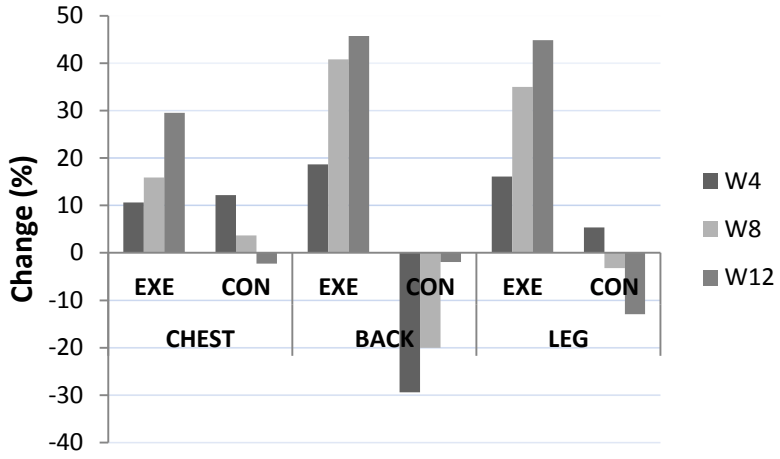


Figure 4.1: Strength change as % of baseline (ExE, n=30; CoN, n=18) over time

Back strength exhibited a time effect between ExE and CoN (F=9.44, df=(3,93), P<0.01) with ExE increasing and CoN decreasing over time. CoN strength decreased significantly (F=13.02, df=(3,12), p<0.01) from baseline to week 4, but increased to weeks 8 and 12. Week 4 was significantly weaker (F=13.02, df=(3,12), p<0.01) than weeks 8 and 12 in this group. ExE increased back strength significantly (F=25.53, df=(3,81), p<0.01) over time, with baseline significantly weaker than weeks 4, 8 and 12. Weeks 8 and 12 were in turn significantly (p<0.01) stronger than week 4.

There was a significant interaction (F=8.34, df=(8,34), p<0.01) between ExE and CoN over time for leg strength. As CoN strength declined, so ExE strength improved. There was no change in strength over time in CoN. ExE strength increased significantly (F=29.43, df=(3,87), p<0.01) over time. Leg strength at weeks 4, 8 and 12 was significantly (p<0.01) stronger than baseline. Weeks 8 and 12 were in turn significantly (p<0.01) stronger than week 4. Individual data indicate that increased strength was noted in 93%, 5% and 8% of individuals (ExE, back, chest and leg), comparing favourably to CoN, with increases for 5%, 42% and 21% of individual candidates respectively.

4.6 PLASMA LIPOPROTEINS

Each plasma lipoprotein component is discussed individually in this section. A comparison of the plasma lipoprotein measures at four week intervals for ExE and CON is presented for ease of reference in Table 4.5. At baseline ExE and CoN were

not significantly different. There were no significant changes over time for any lipoprotein measure in both ExE and CoN.

Table 4.5: Plasma lipoproteins

		LDL-C		HDL-C		LDL:HDL		TriG		Tot-C	
		(mmol.L^{-1})	CV (%)	(mmol.L^{-1})	CV (%)	(ratio)	CV (%)	(mmol.L^{-1})	CV (%)	(mmol.L^{-1})	CV (%)
ExE (n=30)	**WEEK 0**	4.2 ± 0.9	(21%)	1.6 ± 0.4	(25%)	2.7 ± 0.9	(35%)	1.3 ± 0.8	(62%)	5.8 ± 1.1	(19%)
	WEEK 4	3.9 ± 0.9	(23%)	1.6 ± 0.4	(25%)	2.7 ± 0.9	(35%)	1.3 ± 0.8	(62%)	5.6 ± 1.0	(18%)
	WEEK 8	4.0 ± 0.8	(20%)	1.6 ± 0.4	(25%)	2.6 ± 0.9	(35%)	1.4 ± 0.9	(64%)	5.7 ± 1.0	(18%)
	WEEK 12	3.9 ± 0.9	(23%)	1.6 ± 0.4	(25%)	2.6 ± 1.0	(37%)	1.4 ± 1.1	(79%)	5.7 ± 1.0	(18%)
CON (n=18)	**WEEK 0**	4.3 ± 1.0	(23%)	1.7 ± 0.4	(24%)	2.7 ± 1.2	(43%)	1.3 ± 0.7	(54%)	6.3 ± 0.3	(5%)
	WEEK 4	4.2 ± 1.1	(26%)	1.7 ± 0.5	(29%)	2.8 ± 1.4	(50%)	1.3 ± 0.7	(54%)	6.1 ± 0.2	(3%)
	WEEK 8	4.0 ± 0.6	(15%)	1.7 ± 0.4	(24%)	2.8 ± 1.1	(39%)	1.2 ± 0.5	(42%)	6.1 ± 0.3	(5%)
	WEEK 12	4.0 ± 1.1	(28%)	1.6 ± 0.5	(31%)	2.7 ± 1.2	(45%)	1.1 ± 0.5	(45%)	5.9 ± 0.3	(5%)

Where data is expressed as "mean ± standard deviation"; ***CV*** *= Coefficient of Variation presented in brackets*

4.6.1 LOW DENSITY LIPOPROTEIN CHOLESTEROL

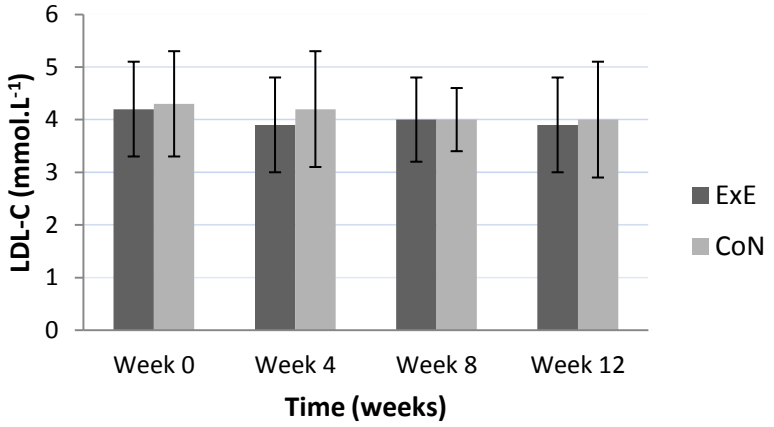


Figure 4.2: Low density lipoprotein cholesterol (ExE, n=30); CoN, n=18) over time

There was no change over time in ExE or CoN (Figure 4.2). Mean low density lipoprotein (LDL-C) (n=30) at baseline was 4.2±0.9 mmol.L^{-1} (ExE) and 4.3±1.0 mmol.L^{-1} (CoN) (Table 4.6). According to the National Cholesterol Education Programme's 2013 guidelines for healthy cholesterol levels in adult females, 4.1-4.9 mmol.L^{-1} is described as "high LDL-C" (NCEP, 2013). Despite no significant change ExE and CoN dropped to the "borderline high" category (3.4-4.1 mmol.L^{-1}) by week 4 and week 8 respectively, however Cohen's effect size was calculated to be "small" (d=0.17). Individual data revealed that 40% (ExE) and 63% (CoN) group reduced LDL-C over the 12 week intervention, with 1% and 1% respectively exhibiting no change and 43% and 21% (ExE and CoN) showing increased LDL-C (Figure 4.3).

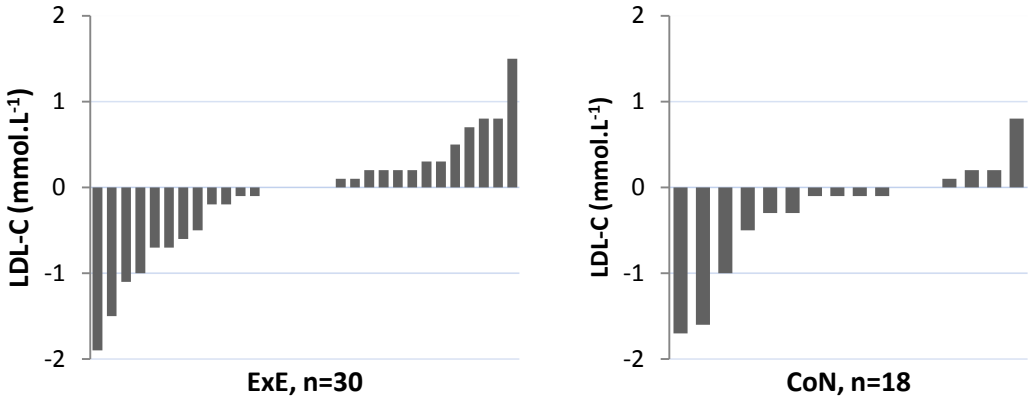


Figure 4.3: Change in LDL-C from baseline to week 12

4.6.2 HIGH DENSITY LIPOPROTEIN CHOLESTEROL

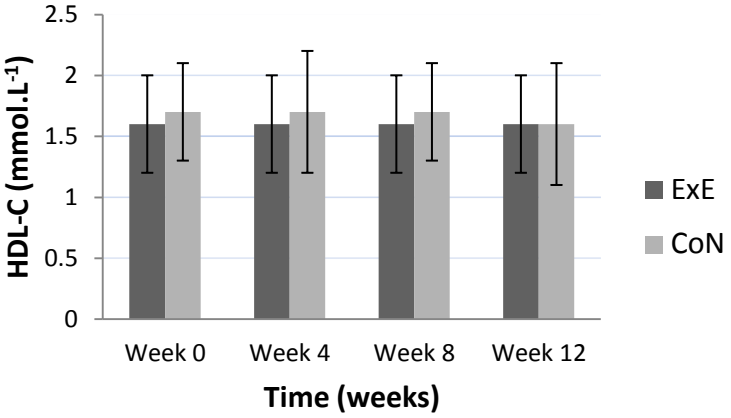


Figure 4.4: High density lipoprotein cholesterol (ExE, n=30); CoN, n=18)

For HDL-C, ExE and CoN were not significantly different at baseline. HDL-C did not change significantly over time in ExE or CoN (Cohen's effect size: d=0.00). The average HDL-C at baseline was 1.6±0.4 mmol.L^{-1} (ExE) and 1.7±0.41mmol.L^{-1} (CoN) which places both groups in the "high HDL-C" category for adult females (NCEP, 2013) (Table 4.5, Figure 4.4). Individual analyses reveal that 37% (ExE) and 53% (CoN) had reduced HDL-C over the course of the 12 week engagement (Figure 4.5). Of ExE, 20% exhibited no change, while 21% of CoN had unaltered HDL-C by week 12. Increased HDL-C was noted in 43% of ExE, and in 26% of CoN.

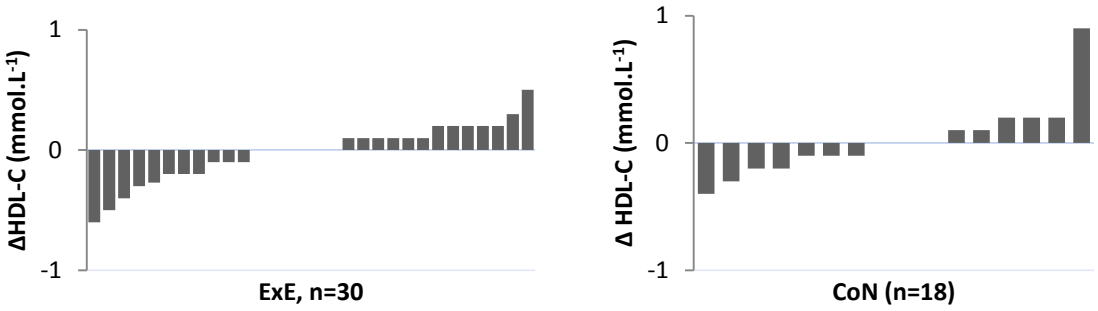


Figure 4.5: Change in HDL-C from baseline to week 12

4.6.3 TRIGLYCERIDE CONTENT

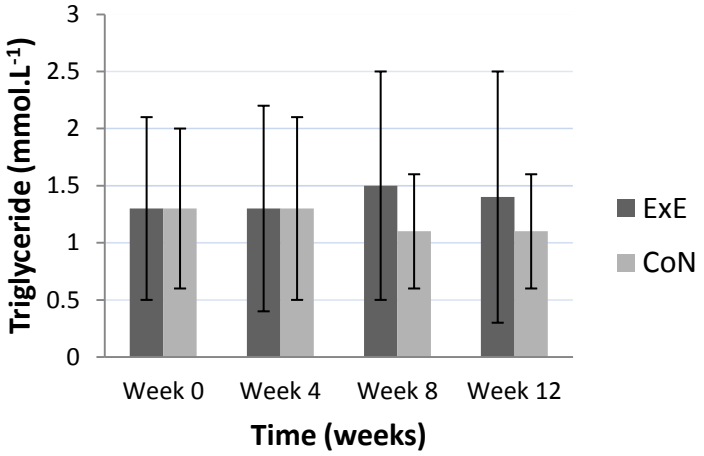


Figure 4.6: Triglyceride content (ExE, n=30; CoN, n=18)

Baseline TriG was not significantly different between ExE and CoN (Figure 4.6). There was no significant change to TriG content in either ExE or CoN (Figure 4.7). ExE and CoN mean was consistently <1.7 mmol.L^{-1}, described as “desirable” by cholesterol guidelines for adult females (NCEP, 2013). The effect size for the changes to this variable were “small” when Cohen’s effect size was calculated (d=0.05). Despite no significant exercise effect the individual responses are noteworthy. A decrease was noted in 50% (ExE) and 47% (CoN) (Figure 4.8). No change to values was experienced in 17% and 21% respectively, while an increase was recorded in 33% and 16% of participants (ExE and CoN).

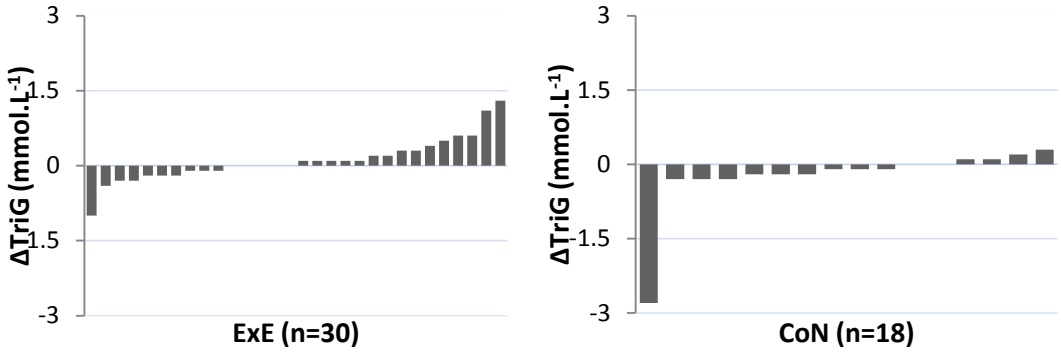


Figure 4.7: Change to TriG from baseline to week 12

4.6.4 LDL: HDL RATIO

No change was noted in ExE or CoN over time (Table 4.5). LDL:HDL ratio was 2.7±0.9, 2.7±0.9, 2.6±0.9 and 2.6±1.0 at weeks 0, 4, 8 and 12 respectively in ExE, and 2.7±1.2, 2.8±1.4, 2.8±1.1 and 2.7±1.2 at the same time points in CoN.

4.6.5 TOTAL CHOLESTEROL CONTENT

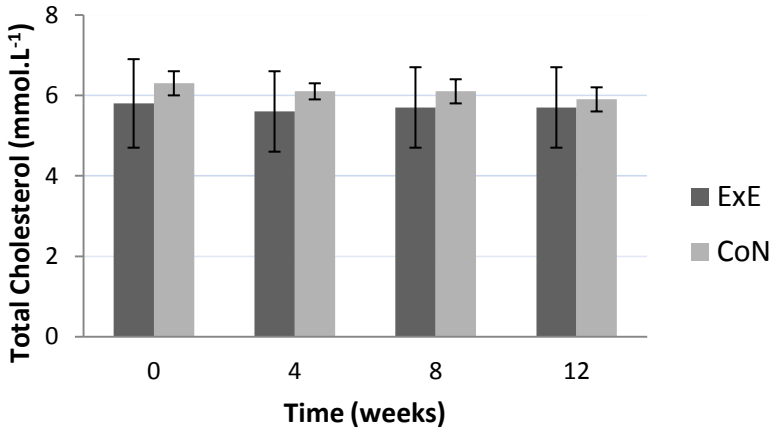


Figure 4.8: Total cholesterol (ExE, n=30; CoN, n=18)

Total cholesterol was not significantly different at baseline (ExE and CoN) (Figure 4.9). At baseline ExE and CoN mean data exceeded the maximum target level for TotC (<5.2 mmol.L^{-1}) and fell within the "high" category throughout the intervention (NCEP, 2013) (Table 4.6). No significant change was noted over time in ExE or in CoN (Table 4.5) and the calculated effect size was "small" (d=0.05). Individual data indicated that 57% (ExE) showed reduced total cholesterol as did 47% of CoN (Figure 4.10). No change was recorded for 3% (ExE) and 16% (CoN), while 40% of ExE had increased levels by the end of the study compared to 26% of CoN.

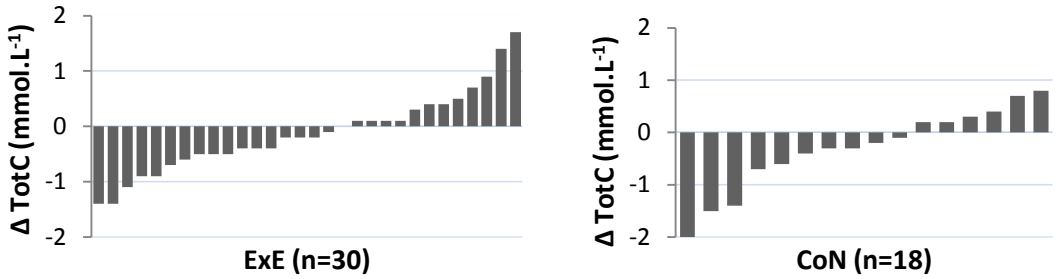


Figure 4.9: Change in total cholesterol from baseline to week 12

Table 4.6: Baseline plasma lipoprotein values compared to recommended levels

	LDL-C	HDL-C	TriG	Tot-C
	(mmol.L^{-1})	(mmol.L^{-1})	(mmol.L^{-1})	(mmol.L^{-1})
Baseline (ExE, n=30)	**4.2**	**1.6**	**1.3**	**6.0**
Baseline (CoN, n=30)	**4.3**	**1.7**	**1.3**	**6.4**
Classification (USA data)	High	Best	Desirable	Borderline High
Recommended (SA Heart Foundation)	<2.0	>1.2	(<1.7)	<5.0

Where data is expressed as "mean ± standard deviation"; ***CV*** *= Coefficient of Variation presented in brackets*

4.7 GLYCATED HAEMOGLOBIN

At baseline glycated haemoglobin (HbA_{1c}) was the same in ExE and CoN. Baseline HbA_{1c} was within "normal" levels in ExE and CoN (>6.5% indicates diabetic conditions) however, both ExE and CoN mean values fell within the first 'risk ratio' category for heart disease and stroke according to the stratification by Selvin *et al.* (2010). There was a significant (F=3.96, df=(3,138), p=0.01) group interaction over time as CoN increased at weeks 4 and 8 and decreased at week 12, while ExE decreased at weeks 4 and 8 and increased at week 12. There was however no significant change over time within CoN (Table 4.7). ExE HbA_{1c} levels increased significantly (F=3.46, df=(3,87), p=0.02) between week 4 and week 12, but as the group mean had dropped from week 0 to week 4, baseline was not different to week 8 or week 12. The effect size within the samples was "small" by Cohen's effect size calculation (d=0.09).

Table 4.7: Mean Glycated Haemoglobin

	WEEK 0		WEEK 4		WEEK 8		WEEK 12	
	HbA_{1c} (%)	CV (%)	HbA_{1c} (%)	CV (%)	HbA_{1c} (%)	CV (%)	HbA_{1c} (%)	CV (%)
ExE (n=30)	5.7 ± 0.6%	(11%)	5.6 ± 0.4%	(7%)	5.6 ± 0.4%	(7%)	**5.8 ± 0.5%**[#]	(9%)
CON (n=18)	5.4 ± 0.3%	(6%)	5.6 ± 0.3%	(5%)	5.6 ± 0.2%	(4%)	5.5 ± 0.4%	(7%)

Mean Glycated Haemoglobin (HbA_{1c}) is expressed as "mean ± standard deviation"; CV = Coefficient of Variation presented in brackets; [#] indicates significant difference to week 4; ***[bold]*** *font highlights significant differences.*

Table 4.8: Multi-variate adjusted hazard ratios for HbA_{1c}

HbA_{1c} (%)			Hazard Ratio	
Category	**Baseline***		**Diabetes**	**CVD / Stroke**
	ExE (n=30)	**CoN (n=18)**		
<5.0			0.52	0.96
5.0 – 5.5		**5.4±0.3**	1	1
5.5 – 6.0	**5.7 ± 0.5**		1.86	1.23
6.0 – 6.5			4.48	1.73
>6.5			16.47	1.95

* No change over time (p>0.05) (From: Selvin *et al*., 2010)

Table 4.8 highlights that ExE fell within the first risk category at baseline (hazard ratio of 1.23 for CVD and/or stroke) and this risk level did not change over time. CoN, on the other hand had a 'risk ratio' of 1.00 at baseline, rose into the next risk category (HR=1.86 for diabetes and 1.23 for CVD/stroke) when measured at weeks 4 and 8, but dropped back to between 5.0-5.5% at week 12. As there was no significant change over time in CoN, the effect size of the change which inferred an increased risk category is noteworthy. Secondly, it is worth noting that diagnosis of Diabetes Mellitus (Type II), for which HbA_{1c} is considered the most reliable diagnostic tool, occurs for an HbA_{1c} of 6.5% or above. Note that no individuals were diabetic in this sample, and levels >6.5% were excluded.

Despite no positive exercise effect positive individual changes were noted (Figure 4.10). However, these changes did not translate into risk category shifts (no increased or decreased risk related to this parameter) and are thus simply mentioned for interest. A decrease was noted over 12 weeks in 26.7% (ExE) and 26.3% (CoN), while an increase was recorded for 60.0% (ExE) and 47.4% (CoN), with 13.3% recording no change (ExE) compared to 26.3% (CoN).

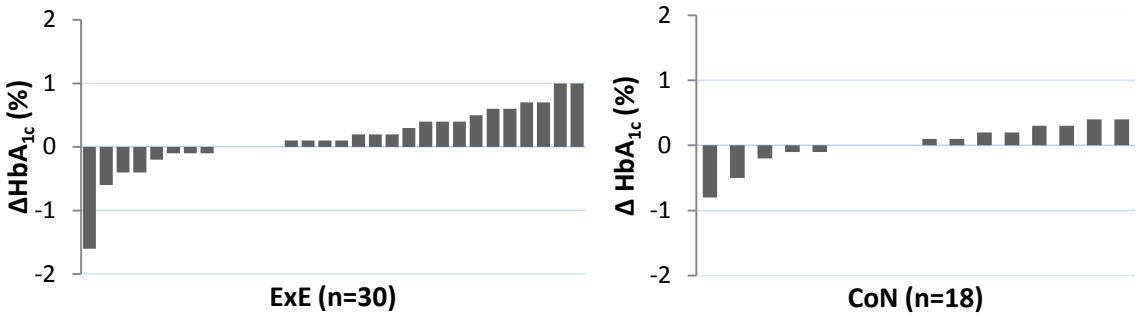


Figure 4.10: Glycated haemoglobin change from baseline to week 12

4.8 SEX HORMONE BINDING GLOBULIN

Baseline sex hormone binding globulin (SHBG) was not significantly different (ExE and CoN). There was no significant change to SHBG over time in either ExE or CoN (effect size d= 0.00) (Table 4.9). Despite no exercise effect, the individual responses are noteworthy. A decrease was recorded in 47% (ExE) and 47% (CoN). No change was recorded for 3% and 11% respectively, while 50% increased levels in ExE compared to 42% in CoN (Figure 4.11).

Table 4.9: Sex hormone binding globulin

	WEEK 0		WEEK 4		WEEK 8		WEEK 12	
	SHBG (*n*mol.L^{-1})	CV (%)	SHBG (*n*mol.L^{-1})	CV (%)	SHBG (*n*mol.L^{-1})	CV (%)	SHBG (*n*mol.L^{-1})	CV (%)
ExE (n=30)	52.9 ± 34.2	(65%)	50.8 ± 31.6	(62%)	50.4 ± 30.1	(60%)	52.7 ± 39.0	(74%)
CON (n=18)	56.8 ± 44.6	(79%)	56.0 ± 37.8	(68%)	59.9 ± 37.8	(63%)	59.5 ± 36.6	(62%)

Sex Hormone Binding Globulin (SHBG) is expressed as "mean ± standard deviation"; CV = Coefficient of Variation presented in brackets.

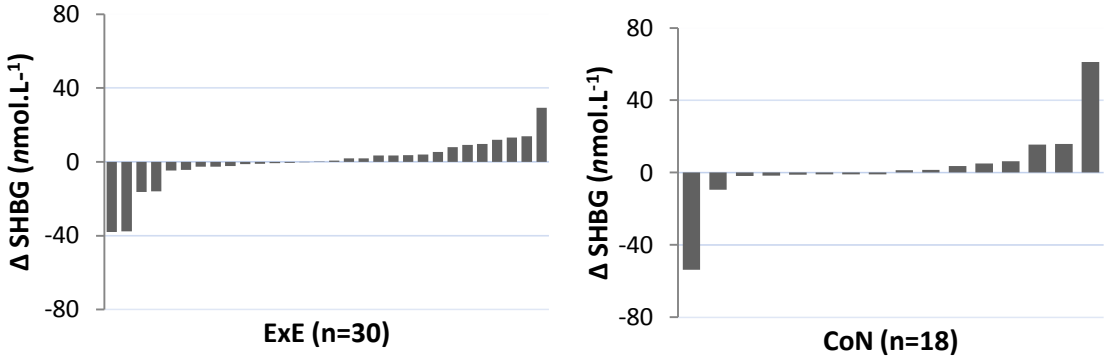


Figure 4.11: Sex hormone binding globulin change from baseline to week 12

SHBG levels in adult females should be between 18-144 *n*mol.L^{-1} (www.mayomedicallaboratories.com). Average SHBG at baseline for the ExE and CoN cohorts was 53.8±35.7 *n*mol.L^{-1} and 57.0±46.1 *n*mol.L^{-1}, and these did not change over time during the course of the intervention, placing the cohort in category 4 for cardiovascular risk associated with sex hormone binding globulin (least risk) (Table 4.10).

Table 4.10: Sex hormone binding globulin risk categorisation (From Ding *et al.*, 2009)

SHBG (*n* mol.L^{-1}) plasma level risk categories				
	1	**2**	**3**	**4**
Median	17.1	29.3	39	55.8
Range	5.8-24.7	24.8-34.6	34.7-44.3	44.4-122.4

An atherogenic lipid profile may also be associated with low levels of SHBG. Significant directional correlations between these variables were noted for weeks 8 ($p<0.01$) and 12 ($p=0.01$) in ExE, and for all time periods in CoN ($p=0.05$ at weeks 0 and 8; $p<0.01$ at weeks 4 and 12) (Table 4.11).

Table 4.11: Correlation coefficients (r^2) for sex hormone binding globulin and HDL-C

	CORRELATION COEFFICIENT (r^2): SHBG & HDL-C			
	WEEK 0	WEEK 4	WEEK 8	WEEK 12
ExE (n=30)	0.2	0.2	**0.3***	**0.4$^{\#}$**
CON (n=18)	**0.4***	**0.6$^{\#}$**	**0.4***	**0.5$^{\$}$**

Significant correlations are indicated by [***bold*** *] font; * (p=0.05), $^{\#}$ (p<0.01), $^{\$}$ (p=0.02)*

4.9 OESTRADIOL

All participants were within the "post-menopausal" range (<73 *p*mol.L^{-1}) at baseline (Table 4.12**Error! Reference source not found.**). A significant ($F=7.32$, $df=(1,46)$, $p=0.01$) group effect was evident, with CoN levels measuring significantly ($p=0.01$) higher than ExE at all measurement points. No change was noted over time in ExE or in CoN, which indicates that post-menopause status was stable and not likely to have affected the results. Cohen's effect size calculation yielded a "small" effect size (d=0.03). Individual changes to oestradiol occurred in comparatively few participants.

In ExE 13% decreased and 20% increased, while in CoN 17% decreased and 33% increased oestradiol levels (Figure 4.12).

Table 4.12: Oestradiol levels

	WEEK 0		WEEK 4		WEEK 8		WEEK 12	
	Oestradiol ($p$mol.L^{-1})	CV (%)	Oestradiol ($p$mol.L^{-1})	CV (%)	Oestradiol ($p$mol.L^{-1})	CV (%)	Oestradiol ($p$mol.L^{-1})	CV (%)
ExE (n=30)	46.9 ± 11.4	(24%)	47.9 ± 12.8	(27%)	48.5 ± 14.4	(30%)	47.5 ± 12.3	(26%)
CON (n=18)*	50.4 ± 14.7	(29%)	58.2 ± 27.6	(47%)	58.7 ± 15.8	(27%)	57.8 ± 20.5	(35%)

*Where Oestradiol levels are expressed as "mean ± standard deviation"; **CV** = Coefficient of Variation presented in brackets; ***** indicates between group significant difference (CoN higher than ExE throughout (p=0.01)*

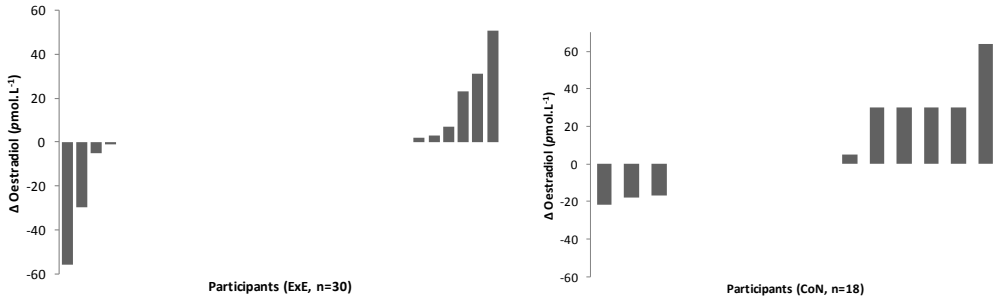


Figure 4.12: Individual oestradiol changes (ExE and CoN) over time

4.10 FREE TESTOSTERONE

At baseline there was no significant difference (p>0.05) between ExE and CoN (Table 4.13). At week 4 ExE levels were significantly higher than at baseline (F=4.84, df=(3,87), p<0.01). CoN measures did not change significantly over time. Individual data indicated that 23% (ExE) and 37% (CoN) experienced decreased levels over the course of 12 weeks (Figure 4.13). Only 23% of ExE experienced no change compared to 42% in CoN. An increase was noted for 53% (ExE) compared to 21% (CoN). There was a "small" effect size (d=0.13) according to Cohen's calculation.

Table 4.13: Total free testosterone

	WEEK 0		WEEK 4		WEEK 8		WEEK 12	
	Total Free Testosterone ($n$mol.L^{-1})	CV (%)	Total Free Testosterone ($n$mol.L^{-1})	CV (%)	Total Free Testosterone ($n$mol.L^{-1})	CV (%)	Total Free Testosterone ($n$mol.L^{-1})	CV (%)
ExE (n=30)	0.7 ± 0.4	(58%)	**0.7 ± 0.4***	(56%)	0.8 ± 0.3	(43%)	0.8 ± 0.4	(51%)
CON (n=18)	0.9 ± 0.4	(45%)	0.8 ± 0.4	(51%)	0.8 ± 0.5	(52%)	0.8 ± 0.5	(60%)

*Total free testosterone is expressed as "mean ± standard deviation"; CV = Coefficient of Variation presented in brackets; * denotes significant difference to week 0 (baseline); **[bold]** font highlights significant differences.*

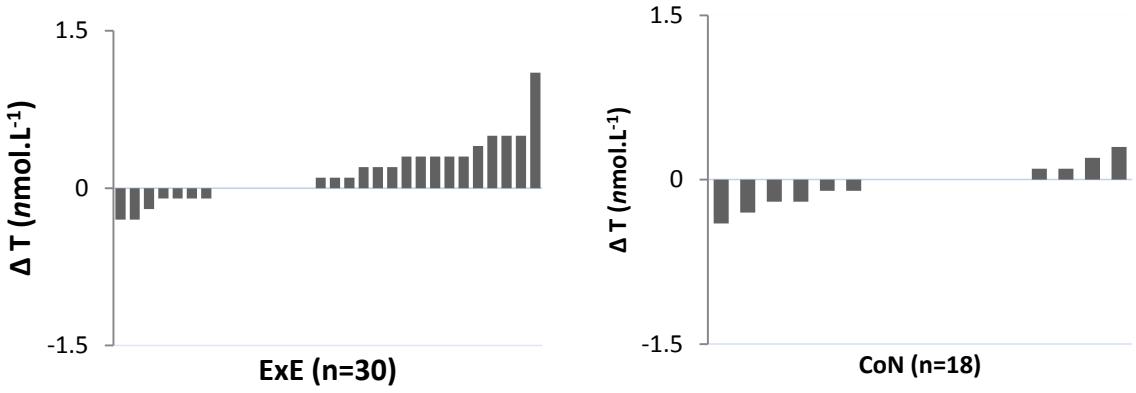


Figure 4.13: Change in free testosterone levels from baseline to week 12

4.11 ANTHROPOMETRY AND MORPHOLOGY

4.11.1 BODY MASS

At baseline there was no significant difference between ExE and CoN. A significant increase occurred over time in CoN (F=6.25, df=(3,54), p<0.01) and a significant decrease took place in ExE (F=7.10, df=(3,87), p<0.01) (Table 4.14). Despite the significant decrease in ExE, the overall total loss (1.2kg) was not clinically significant. This loss falls within 5% of baseline body mass, as was required of all participants to ensure that body mass loss did not compromise the results.

Table 4.14: Body mass

	WEEK 0		WEEK 4		WEEK 8		WEEK 12	
	Mass (kg)	CV (%)	Mass (kg)	CV (%)	Mass (kg)	CV (%)	Mass (kg)	CV (%)
ExE (n=30)	79.2 ±12.8	(16%)	78.5 ± 13.1	(17%)	**78.3 ± 12.7***	(16%)	**78.0 ± 12.9***	(17%)
CON (n=18)	75.3 ± 11.3	(15%)	75.6 ± 11.2	(15%)	**76.2 ± 11.0***	(14%)	**76.1 ± 10.7***	(14%)

*Body mass is expressed as "mean ± standard deviation"; CV = Coefficient of Variation presented in brackets; * denotes significantly different to Week 0 (baseline); **[bold]** font highlights significant differences.*

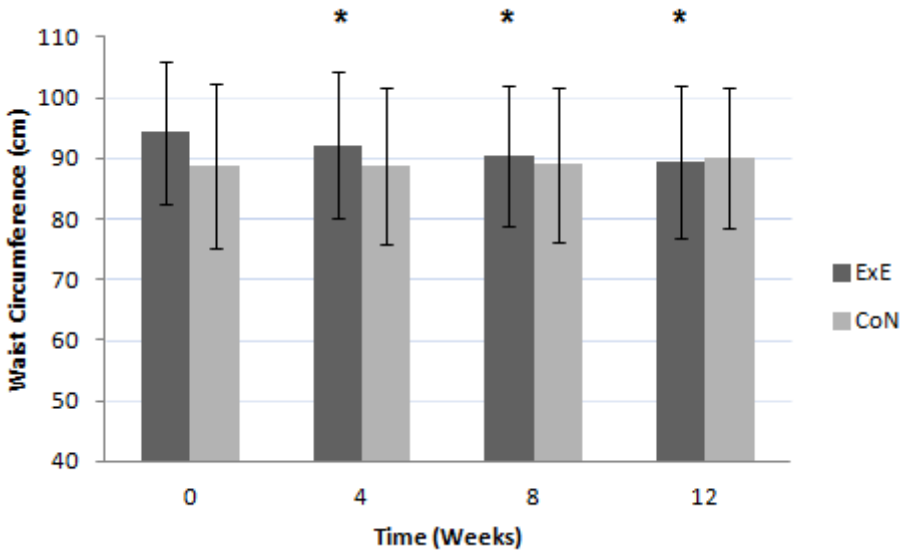
4.11.2 WAIST CIRCUMFERENCE

At baseline waist circumference was not significantly different between ExE and CoN. There was a significant decrease in ExE over time (F=12.37, df=(3,87), p<0.01) (Table 4.15, Figure 4.14). No significant change was noted in CoN (Figure 4.15). The decrease in ExE was steady at ~2.0 cm per four weeks for eight weeks, but did not change thereafter. ExE did not meet the guideline of less than 88.0 cm for reduced risk of cardiovascular complications, and while CoN met the criterion at baseline, an overall increase put this group out of the "ideal" range as well.

Table 4.15: Waist circumference

	WEEK 0		WEEK 4		WEEK 8		WEEK 12	
	Waist Circumf. (cm)	CV (%)	Waist Circumf. (cm)	CV (%)	Waist Circumf. (cm)	CV (%)	Waist Circumf. (cm)	CV (%)
ExE (n=30)	94.3 ± 11.8	(13%)	**92.2 ± 12.1***	(13%)	**90.4 ± 11.7***	(13%)	**89.4 ± 12.6***	(14%)
CON (n=18)	88.7 ± 13.5	(15%)	88.7 ± 12.9	(15%)	89.0 ± 12.8	(14%)	90.1 ± 11.5	(13%)

*Waist circumference is expressed as "mean ± standard deviation"; CV = Coefficient of Variation presented in brackets; * denotes significant difference to week 0 (baseline); **[bold]** font highlights significant differences.*



Where: * indicates significant difference to Week 0

Figure 4.14: Waist circumference (ExE, n=30, and CoN, n=18) over time

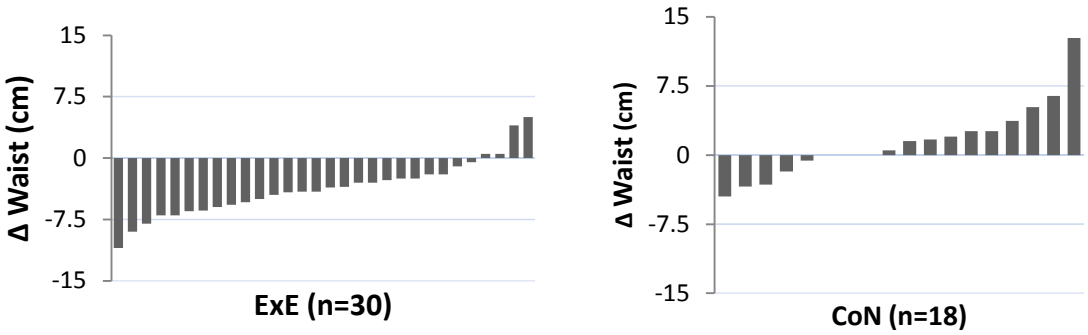


Figure 4.15: Waist circumference change from baseline to week 12

Individually, 87% (ExE) and 21% (CoN) saw successful reductions. An increase was recorded for 13% (ExE) and 53% (CoN) (Figure 4.16).

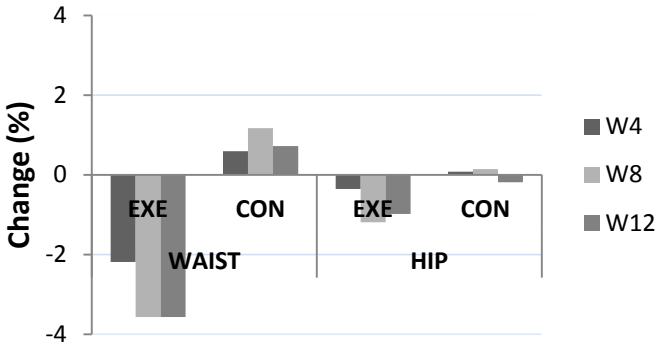


Figure 4.16: Change to waist and hip circumference presented as % of baseline (ExE, n=30); CoN, n=18)

Waist circumference displayed non-significant and weak correlation to HDL-C in group ExE (Table 4.16). In contrast, the association between waist circumference and HDL-C appeared strong in group CoN (r^2=0.4, 0.5, 0.6 and 0.5 at weeks 0, 4, 8 and 12).

Table 4.16: HDL-C and Waist Circumference (r^2) in ExE and CoN

Correlation coefficient (r^2): Waist Circumference and HDL-C				
	Week 0	Week 4	Week 8	Week 12
ExE	0.3	0.2	0.2	0.2
CoN	0.4	0.5	0.6	0.5

4.11.3 HIP CIRCUMFERENCE

At baseline ExE and CoN did not differ significantly. There was no significant change to hip circumference over the course of the 12 week intervention in ExE or CoN (Figure 4.16, Table 4.17). Despite no effect resulting from the exercise intervention (p>0.05) individual data reveal nuances of movement: 67% (ExE) compared to 21% (CoN) reduced circumference while an increase was noted in 27% (ExE) and 16% (CoN), with no change evident for 7% and 63% respectively.

Table 4.17: Hip circumference

	WEEK 0		WEEK 4		WEEK 8		WEEK 12	
	Hip Girth (cm)	CV (%)	Hip Girth (cm)	CV (%)	Hip Girth (cm)	CV (%)	Hip Girth (cm)	CV (%)
ExE (n=30)	108.0 ± 8.2	(8%)	107.6 ± 8.7	(8%)	106.7 ± 8.6	(8%)	106.9 ± 8.1	(8%)
CON (n=18)	106.2 ± 7.3	(7%)	106.3 ± 7.2	(7%)	106.4 ± 7.1	(7%)	106.0 ± 5.3	(5%)

Hip circumference is expressed as "mean ± standard deviation"; CV = Coefficient of Variation presented in brackets.

4.11.4 ADDITIONAL GIRTH MEASUREMENTS

These measurements provide an indication of changes at both the central and peripheral regions (Table 4.18). There were no significant differences between ExE and CoN at baseline.

Table 4.18: Additional girth measurements (ExE, n=30; CoN, n=18)

		UPPER ARM		CHEST		THIGH		CALF	
		(cm)	CV (%)	(cm)	CV (%)	(cm)	CV (%)	(cm)	CV (%)
ExE (n=30)	**WEEK 0**	30.7 ± 3.5	(11%)	90.2 ± 9.6	(11%)	52.3 ± 5.0	(10%)	36.4 ± 2.8	(8%)
	WEEK 4	30.7 ± 3.4	(11%)	90.2 ± 10.1	(11%)	52.2 ± 5.2	(10%)	36.4 ± 3.0	(8%)
	WEEK 8	30.4 ± 3.4	(11%)	90.4 ± 9.2	(10%)	51.7 ± 5.2	(10%)	36.9 ± 2.9	(8%)
	WEEK 12	30.6 ± 3.3	(11%)	90.5 ± 9.2	(10%)	52.0 ± 5.1	(10%)	36.3 ± 2.8	(8%)
CON (n=18)	**WEEK 0**	29.3 ± 3.0	(10%)	89.4 ± 11.1	(12%)	50.3 ± 5.0	(10%)	36.0 ± 2.5	(7%)
	WEEK 4	29.6 ± 3.1	(10%)	89.8 ± 11.0	(12%)	**50.8 ± 4.8***	(10%)	36.2 ± 2.8	(8%)
	WEEK 8	29.9 ± 3.1	(10%)	90.1 ± 10.9	(12%)	51.2 ± 4.7	(9%)	36.4 ± 3.0	(8%)
	WEEK 12	29.3 ± 3.2	(11%)	88.7 ± 10.7	(12%)	51.0 ± 4.9	(10%)	35.9 ± 2.6	(7%)

*Girth measures are expressed as "mean ± standard deviation"; CV = Coefficient of Variation presented in brackets; * denotes significant difference to week 0 (baseline); **[bold]** font highlights significant differences.*

4.11.4.1 Upper arm (Triceps brachii)

At baseline there was no difference between ExE and CoN. There was no significant change to tricep girth in ExE or in CoN over time. Despite the lack of exercise effect, individual data indicated decreases for 50% (ExE) and 33% (CoN) over time.

4.11.4.2 Chest (under-bust)

At baseline ExE and CoN were similar and no change occurred. Despite no overall exercise-related effect, a decrease was noted in 43% (ExE) and 33% (CoN), and an increase in 50% (ExE and CoN).

4.11.4.3 Thigh (Mid-quadriceps)

There was no significant difference between ExE and CoN at baseline. There was no significant change over time in ExE, while a significant increase (F=3.48, df=(3,51), p=0.02) was noted in CoN between baseline and week 4. While the exercise training did not elicit a significant change, a decrease was noted in 43% (ExE) and in 17% (CoN), with an increase recorded for 60% (ExE) and 67% (CoN).

4.11.4.4 Calf (Mid-gastrocnemius)

A baseline ExE and CoN were the same. There was no significant change over time in either cohort. Individual results, despite the absence of a significant exercise effect, remain important. A decrease occurred for 43% (ExE) and 28% (CoN) while an increase was noted in 53% and 56% (ExE and CoN).

4.11.5 BODY COMPOSITION

4.11.5.1 Sum of Skinfolds

There was no significant difference between groups (ExE and CoN) at baseline, and there was no change over time in either group (Table 4.19).

Table 4.19: Sum of skinfolds

	WEEK 0		WEEK 4		WEEK 8		WEEK 12	
	Skinfold Measures (mm)	CV (%)	Skinfold Measures (mm)	CV (%)	Skinfold Measures (mm)	CV (%)	Skinfold Measures (mm)	CV (%)
ExE (n=30)	198.1 ± 42.5	(21%)	201.1 ± 44.0	(22%)	191.6 ± 56.2	(29%)	197.9 ± 37.9	(19%)
CON (n=18)	190.7 ± 59.1	(31%)	193.4 ± 58.7	(30%)	196.1 ± 58.3	(30%)	192.9 ± 59.9	(31%)

Sum of skinfold measurements are expressed as "mean ± standard deviation"; CV = Coefficient of Variation presented in brackets.

4.11.5.2 Individual Skinfold Sites

There was no difference at baseline between ExE and CoN at all skinfold sites (tricep, mid-axillary, chest, sub-scapular, abdominal, supra-iliac and front thigh). There was no change over time to tricep, mid-axillary, chest, sub-scapular, supra-iliac or front thigh in either ExE or CoN (Table 4.20, overleaf). At the abdominal site there was no change over time in CoN, but a significant (F=3.40; df=(3,87), p=0.02) change over time was noted in ExE. Week 8 was significantly (p=0.02) higher than week 0, but week 12 was lower (p=0.02) than weeks 4 and 8. Despite no change at

all sites in CoN, and all but the abdominal site in ExE, individual data remain noteworthy. Data were elevated for 40% and 42% (ExE and CoN) of participants at week 12 compared to week 0, while 7% and 16% showed no change from baseline (Figure 4.17).

Table 4.20: Skinfold measures (ExE, n=30; CoN, n=18)

		TRICEP		CHEST		ABDOMEN		SUPRA-ILIAC		SUB-SCAPULAR		MID-AXILLARY		FRONT THIGH	
		(cm)	CV (%)	(cm)	CV (%)	(cm)	CV (%)	(cm)	CV (%)	(cm)	CV (%)	(cm)	CV (%)	(cm)	CV (%)
ExE (n=30)	WEEK 0	26.5 ± 6.5	(25%)	20.7 ± 5.9	(29%)	33.9 ± 8.5	(25%)	23.3 ± 8.0	(35%)	26.9 ± 8.0	(30%)	29.6 ± 7.6	(26%)	37.0 ± 7.5	(20%)
	WEEK 4	26.3 ± 7.2	(27%)	21.7 ± 5.2	(24%)	35.5 ± 8.7	(24%)	21.7 ± 8.0	(37%)	27.9 ± 8.5	(30%)	30.5 ± 8.3	(27%)	37.3 ± 7.2	(19%)
	WEEK 8	25.3 ± 6.8	(29%)	21.4 ± 5.7	(27%)	**35.5 ± 8.5***	(24%)	23.0 ± 6.6	(29%)	26.2 ± 8.6	(33%)	30.0 ± 6.4	(29%)	37.3 ± 6.4	(17%)
	WEEK 12	25.9 ± 6.4	(25%)	23.1 ± 6.9	(30%)	**33.5 ± 7.4**$^{\#\$}$	(22%)	21.7 ± 7.4	(34%)	26.4 ± 8.1	(31%)	31.1 ± 7.7	(25%)	36.2 ± 6.5	(18%)
CON (n=18)	WEEK 0	23.9 ± 7.0	(29%)	18.8 ± 6.9	(37%)	34.6 ± 13.3	(38%)	20.3 ± 10.6	(52%)	24.8 ± 10.3	(43%)	30.8 ± 11.2	(36%)	38.1 ± 10.2	(27%)
	WEEK 4	24.7 ± 7.2	(29%)	19.9 ± 7.5	(38%)	34.3 ± 12.7	(37%)	20.1 ± 10.6	(53%)	24.7 ± 10.3	(42%)	31.1 ± 11.1	(36%)	38.8 ± 10.0	(26%)
	WEEK 8	25.5 ± 7.5	(29%)	21.0 ±8.1	(39%)	34.0 ± 12.2	(36%)	19.9 ± 10.7	(54%)	24.7 ± 10.2	(41%)	31.5 ± 11.1	(35%)	39.5 ± 9.7	(25%)
	WEEK 12	25.1 ±6.8	(27%)	20.3 ± 9.8	(48%)	34.8 ±13.3	(38%)	18.1 ± 9.3	(52%)	23.7 ± 11.1	(47%)	33.0 ± 12.1	(37%)	38.0 ±8.6	(23%)

*Where Skinfold Site Measures measures are expressed as "mean ± standard deviation"; **CV** = Coefficient of Variation presented in brackets; * denotes significant difference to week 0; # denotes significant difference to week 4; $ denotes significant difference to week 8; **[bold]** font highlights significant differences.*

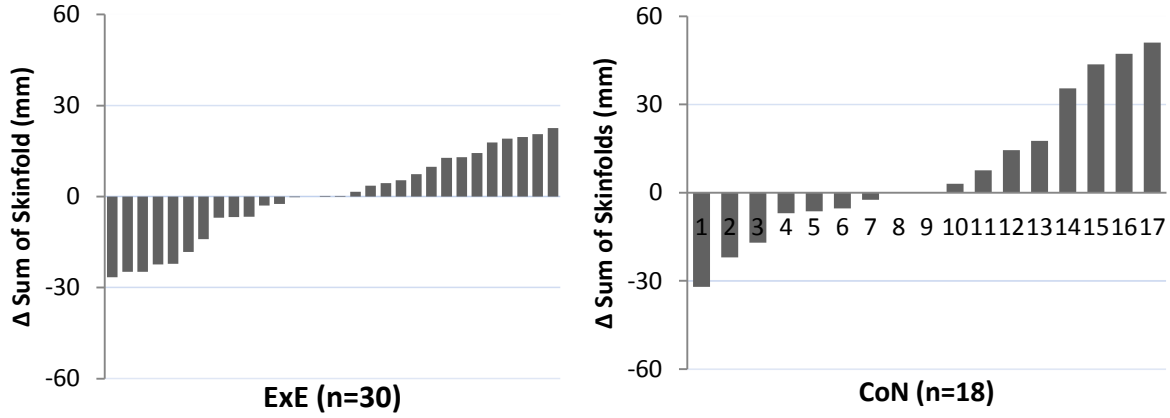


Figure 4.17: Change to sum of skinfolds from baseline to week 12

4.11.5.3 Estimated body fat content (%): calliper method

There was no difference between groups at baseline (Table 4.21) and no change occurred over time in either sample. Estimated fat greater than 35% is considered "obese" in risk categorisation placing both groups in this zone at baseline. Despite no overall change individual data reflect interesting changes that may be clinically relevant (Figure 4.18). Decreased body fat was estimated in 37% (ExE) and 42% (CoN). No change was recorded for 10% and 16% (ExE and CoN), while 53% and 42% showed an increase over time (ExE and CoN). Neither ExE nor CoN mean data changed significantly over time therefore no risk reduction related to "overweight/obese" categorisation occurred.

Table 4.21: Body fat content estimation

		CALLIPER ESTIMATION		BIA ESTIMATION	
		(%)	CV (%)	(%)	CV (%)
ExE (n=30)	WEEK 0	38.8 ± 6.1	(16%)	41.3 ± 5.6	(14%)
	WEEK 4	39.6 ± 6.3	(16%)	41.3 ± 5.6	(14%)
	WEEK 8	39.5 ± 6.2	(16%)	41.8 ± 6.0	(14%)
	WEEK 12	39.5 ± 5.7	(14%)	41.0 ± 6.0	(15%)
CON (n=18)	WEEK 0	38.9 ± 7.2	(19%)	38.5 ± 7.2	(19%)
	WEEK 4	39.6 ± 7.5	(19%)	38.3 ± 7.1	(19%)
	WEEK 8	39.4 ± 7.2	(18%)	38.7 ± 6.8	(18%)
	WEEK 12	39.6 ± 7.1	(18%)	36.9 ± 7.3	(20%)

Body fat estimations are expressed as "mean ± standard deviation"; CV = Coefficient of Variation presented in brackets.

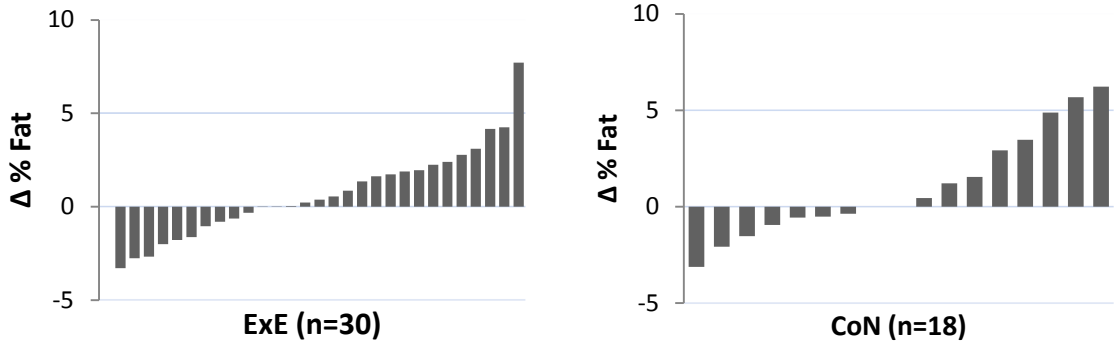


Figure 4.18: Change to % body fat from baseline to week 12 (calliper technique)

4.11.5.4 Estimated % fat: bio-electrical impedance analysis technique

There was no difference between groups ExE and CoN at baseline, and no change over time. Estimated fat content was higher than 30% in 90% (ExE) and 79% (CoN), and of these 83% and 100% respectively recorded values greater than 35%. Baseline estimated fat content greater than 40% was noted for 57% (ExE) and 67% (CoN). BIA estimations also place both samples in the "overweight" risk category, and this did not change over time. Despite no overall reduction to fat mass following the exercise intervention, individual data revealed that 37% (ExE) and 21% (CoN) of participants had lower fat percentage at week 12 compared to baseline (Figure 4.19). A further 17% and 32% experienced no shift to body composition. In the exercise group 47% showed an increase over time, compared to 58% in the matched control.

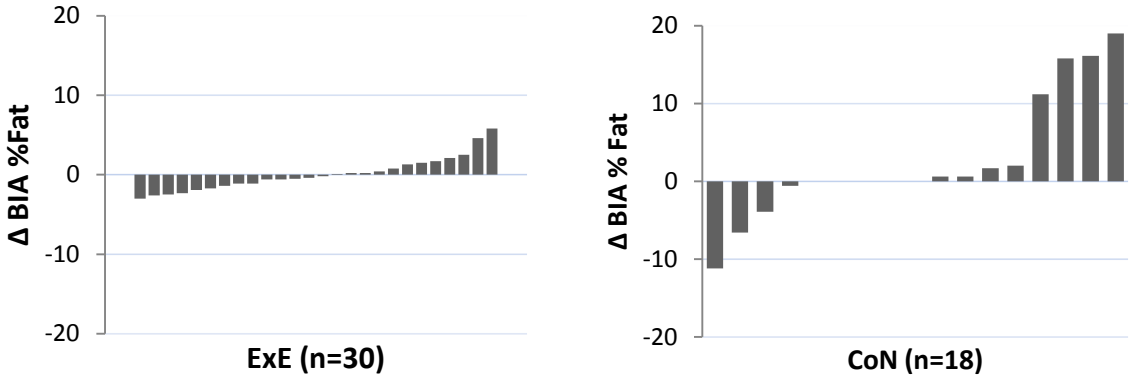


Figure 4.19: Change to BIA % fat estimation from baseline to week 12

A strong correlation existed between waist circumference and body fat percentage (skinfold calliper method) (r^2=0.44), sum of skinfolds (r^2=0.57), and bio-electrical impedance analysis (r^2=0.65).

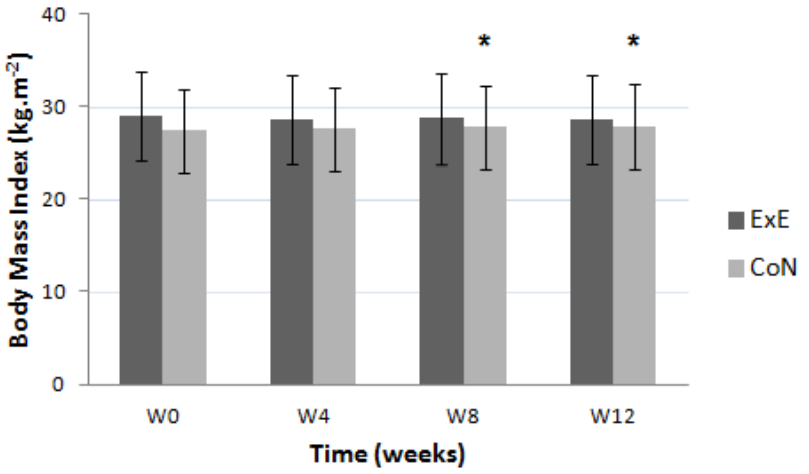
4.11.6 BODY MASS INDEX

There was no difference between ExE and CoN at baseline. ExE did not change over time, however CoN increased significantly at weeks 8 and 12 compared to week 0 (*F*=7.29, *df*=(3,51), *p*<0.01) (Table 4.22, Figure 4.20). At baseline both groups were classified "overweight" according to BMI normative data, and this did not change over time.

Table 4.22: Body mass index

	WEEK 0		WEEK 4		WEEK 8		WEEK 12	
	Body Mass Index ($kg.m^{-2}$)	CV (%)	Body Mass Index ($kg.m^{-2}$)	CV (%)	Body Mass Index ($kg.m^{-2}$)	CV (%)	Body Mass Index ($kg.m^{-2}$)	CV (%)
ExE (n=30)	29.1 ± 4.5	(15%)	27.6 ± 4.8	(17%)	28.8 ± 4.5	(16%)	28.7 ± 4.6	(16%)
CON (n=18)	27.4 ± 4.8	(18%)	27.6 ± 4.8	(17%)	**27.8 ± 4.9***	(18%)	**27.8 ± 4.8***	(17%)

*Body mass index are expressed as "mean ± standard deviation"; CV = Coefficient of Variation presented in brackets; * denotes significant difference from baseline; **[bold]** font highlights significant data.*



Where: * denotes significant difference to week 0

Figure 4.20: Body mass index (ExE, n=30; CoN, n=18)

There was no overall exercise effect, however reductions to BMI occurred in 77% (ExE) and 11% (CoN). An increase was evident in 20% and 74% (ExE and CoN) respectively. Compared to females aged 50 years and older in the NHANES III study the current sample (ExE and CoN) presents with a higher BMI on average (Table 4.23). The median BMI values (ExE and CoN) were also higher than that of the NHANES III adult American population (Kuczmarski *et al.*, 1997; Must *et al.*, 1991). According to the World Health Organisation's classifications based on BMI values, ExE and CoN were "overweight" on average, and this did not change during the course of the investigation.

Table 4.23: BMI comparison between current sample and previous literature

	BMI ($kg.m^{-2}$) Mean	BMI ($kg.m^{-2}$) Median
ExE (n=30)	29.1	28.6
CoN (n=18)	27.4	27.5
NHANES III*	26.9	26.1
WHO Classification	≥25.0	≥25.0
	"Overweight"	"Overweight"

* (Kuczmarski *et al*., 1997; Must *et al*., 1991)
Where: 'BMI'=body mass index; 'NHANES III'=Third National Health and Nutrition Examination Survey (United States); 'WHO'=World Health Organisation

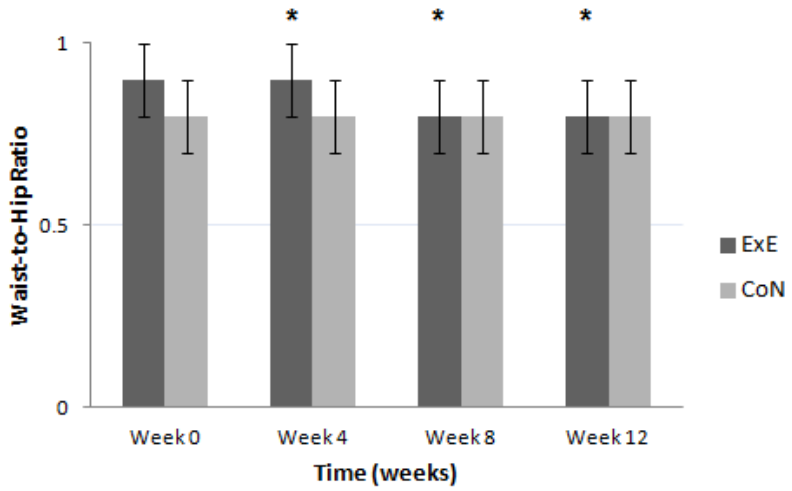
4.11.7 WAIST-TO-HIP RATIO

There was no difference between groups at baseline. ExE decreased significantly (*F*=8.31, *df*=(3,87), *p*<0.01) over time while there was no change in CoN (Table 4.24, Figure 4.21). Individual data showed that 77% and 27% (ExE and CoN) had reduced waist-to-hip ratios. No change was exhibited by 13% and 37% (ExE and CoN). An increase was noted for 10% and 37% (ExE and CoN).

Table 4.24: Waist-to-hip ratio

	WEEK 0		WEEK 4		WEEK 8		WEEK 12	
	Waist-to-Hip Ratio	CV (%)	Waist-to-Hip Ratio	CV (%)	Waist-to-Hip Ratio	CV (%)	Waist-to-Hip Ratio	CV (%)
ExE (n=30)	0.9 ± 0.1	(11%)	**0.9 ± 0.1***	(11%)	**0.8 ± 0.1***	(13%)	**0.8 ± 0.1***	(13%)
CON (n=18)	0.8 ± 0.1	(13%)	0.8 ± 0.1	(13%)	0.8 ± 0.1	(13%)	0.8 ± 0.1	(13%)

*Waist-to-hip ratio is expressed as "mean ± standard deviation"; CV = Coefficient of Variation presented in brackets; * denotes significant difference from baseline; **[bold]** font highlights significant data.*



Where: * denotes significant difference to week 0

Figure 4.21: Waist-to-hip ratio (ExE, n=30; CoN, n=18)

4.11.8 WAIST-TO-STATURE RATIO

At baseline ExE and CoN did not differ. There was a significant decrease (*F*=12.05, *df=(*3,87*)*, *p*=<0.01) from baseline to weeks 4, 8 and 12 in ExE, but no change in CoN (Table 4.25). Overall, 93% of ExE demonstrated a reduction compared to 22% in CoN (Figure 4.22). An increase was recorded in 13% (ExE) and in 50% (CoN).

Table 4.25: Waist-to-stature ratio

	WEEK 0		WEEK 4		WEEK 8		WEEK 12	
	Waist-to-Stature Ratio	CV (%)	Waist-to-Stature Ratio	CV (%)	Waist-to-Stature Ratio	CV (%)	Waist-to-Stature Ratio	CV (%)
ExE (n=30)	0.6 ± 0.1	(17%)	**0.6 ± 0.1***	(17%)	**0.6 ± 0.1***	(17%)	**0.6 ± 0.1***	(17%)
CON (n=18)	0.5 ± 0.1	(20%)	0.5 ± 0.1	(20%)	0.5 ± 0.1	(20%)	0.5 ± 0.1	(20%)

*Waist-to-stature ratio is expressed as "mean ± standard deviation"; CV = Coefficient of Variation presented in brackets; * denotes significant difference from baseline; **[bold]** font highlights significant data.*

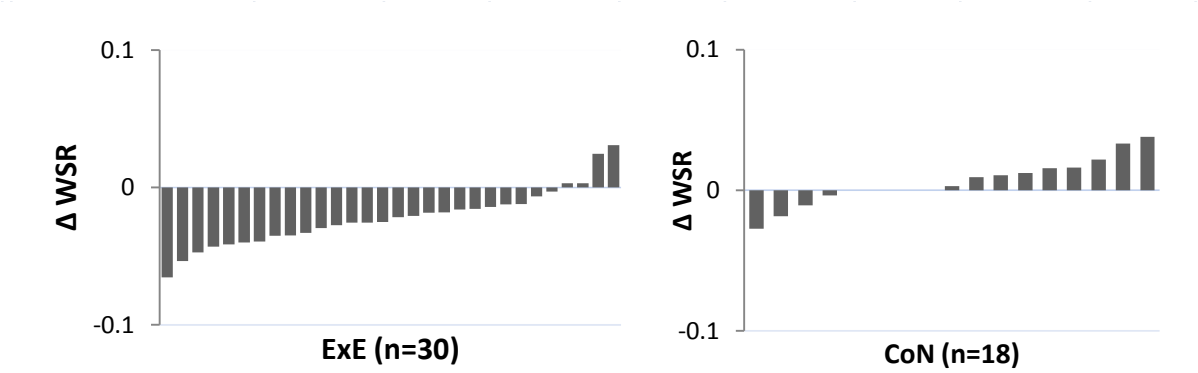


Figure 4.22: Change to waist-to-stature ratio from baseline to week 12

4.11.8.1 Correlations

Baseline waist-to-stature ratio correlated very strongly to body mass index and to waist circumference in both ExE and CoN, as well as waist-to-hip ratio in group CoN (r^2=0.8) but exhibited a weaker correlation (r^2=0.5) with waist-to-hip ratio in group ExE (Table 4.26). Waist circumference exhibited a very strong relationship with BMI in both groups, as well as with waist-to-hip ratio in the control sample, but displayed a weak relationship with waist-to-hip ratio in ExE (r^2=0.5).

Table 4.26: Correlation coefficients (r^2) for anthropometric variables at baseline

		CORRELATION COEFFICIENT (r^2) AT BASELINE			
		BMI	**WC**	**WHR**	**WSR**
ExE (n=30)	**BMI**	1.0	**0.8***	0.2	**0.8***
	WC	**0.8***	1.0	**0.5***	1.0
	WHR	0.2	**0.5***	1.0	**0.5***
CoN (n=18)	**BMI**	1.0	**0.7#**	**0.4***	**0.8#**
	WC	0.7#	1.0	**0.9#**	1.0
	WHR	0.4	**0.9#**	1.0	**0.8#**

*"**BMI**" = Body Mass Index; "**WC**" = Waist Circumference; "**WHR**" = Waist to Hip Ratio; "**WSR**" = Waist to Stature Ratio. Significant correlations are indicated by [**bold**] font; * (p=0.05) and # (p<0.01).*

In CoN all surrogate measures of obesity were significantly (p<0.05) correlated to each other. ExE revealed significant correlations for BMI and waist circumference (p=0.05), BMI and WSR (p=0.05), waist circumference and WSR (p<0.01), and WHR and WSR (p<0.01) (Table 4.27). LDL-C showed a consistent moderate association to all anthropometric variables in CoN, but was only significantly (p=0.05) correlated to waist circumference. HDL-C demonstrated a moderate positive and significant (p≤0.05) relationship to anthropometric variables, specifically BMI (r^2=0.3), waist circumference (r^2=0.3) and waist-to-stature ratio (r^2=0.3) in group ExE and to BMI (r^2=0.6), WC (r^2=0.4) and waist-to-stature ratio (r^2=0.4) in CoN.

Table 4.27: Correlation coefficients (r^2) for anthropometric variables and cardiovascular risk factors at baseline

	ExE (n=30)				CoN (n=19)			
	BMI	**WC**	**WHR**	**WSR**	**BMI**	**WC**	**WHR**	**WSR**
SBP	0.2	0.1	0.0	0.1	0.0	0.0	0.0	0.0
DBP	0.2	0.1	0.0	0.1	0.0	0.0	0.1	0.0
Tot-C	0.1	0.1	0.0	0.1	0.1	0.2	0.2	0.2
LDL-C	0.1	0.0	0.0	0.0	**0.3**	**0.4***	**0.3**	**0.3**
HDL-C	**0.3***	**0.3***	0.2	**0.3***	**0.6**$^{\#}$	**0.4***	0.2	**0.4***
TriG	0.1	0.1	0.1	0.1	**0.3**	0.1	0.1	0.2
HbA_{1c}	0.0	0.0	0.0	0.1	0.2	0.2	0.2	**0.3**

*Where '**BMI**' = Body Mass Index; '**WC**' = Waist Circumference; '**WHR**' = Waist to Hip Ratio; '**WSR**' = Waist to Stature Ratio; '**SBP**' = Systolic Blood Pressure; '**DBP**' = Diastolic Blood Pressure; '**Tot-C**' = Total Cholesterol; '**LDL-C**' = Low Density Lipoprotein Cholesterol; '**HDL-C**' = High Density Lipoprotein Cholesterol; '**TriG**' = Triglyceride Content; '**HbA_{1c}**' = glycated haemoglobin; shaded blocks with values in **[bold]** font indicate "moderate" to "strong" relationships. Significant correlations are indicated by * (p=0.05) and $^{\#}$ (p<0.01)*

4.12 CARDIOVASCULAR FUNCTION RESULTS

At baseline there was no difference between groups. Blood pressure results for groups ExE and CoN are presented in Table 4.28.

Table 4.28: Systolic and diastolic blood pressure (ExE, n=30; CoN, n=18)

		SYSTOLIC BP		DIASTOLIC BP	
		(mmHg)	CV (%)	(mmHg)	CV (%)
ExE (n=30)	**WEEK 0**	131.5 ± 12.9	(10%)	86.6 ± 12.5	(14%)
	WEEK 4	136.6 ± 18.0	(13%)	83.2 ± 9.4	(11%)
	WEEK 8	134.2 ± 15.5	(12%)	**77.3 ± 8.9*** $^{\#}$	(12%)
	WEEK 12	131.2 ± 16.5	(13%)	**78.9 ± 9.4***	(12%)
CON (n=18)	**WEEK 0**	137.7 ± 21.2	(15%)	85.6 ± 11.8	(14%)
	WEEK 4	135.6 ± 17.5	(13%)	82.1 ± 11.3	(14%)
	WEEK 8	136.2 ± 18.3	(13%)	80.6 ± 12.5	(16%)
	WEEK 12	132.3 ± 15.9	(12%)	80.2 ± 9.4	(12%)

*Blood pressure is expressed as "mean ± standard deviation"; CV = Coefficient of Variation presented in brackets; * denotes significant difference from baseline; $^{\#}$ denotes significant difference to week 4; **[bold]** font highlights significant data.*

4.12.1 SYSTOLIC BLOOD PRESSURE

There was no significant change to systolic blood pressure over time in either group (Table 4.28). Despite no exercise mediated change, it is worth noting that individual results indicated that 43% and 47% (ExE and CoN) recorded reductions at week 12 compared to baseline (Figure 4.23). A further 23% and 26% (ExE and CoN) experienced no change, while 33% and 21% (ExE and CoN) had elevated readings at week 12. Average readings for both ExE and CoN fell within the "pre-hypertensive" category (130-139 mmHg) at baseline and at each measurement point thereafter according to the *American Heart Association*'s risk categorisation.

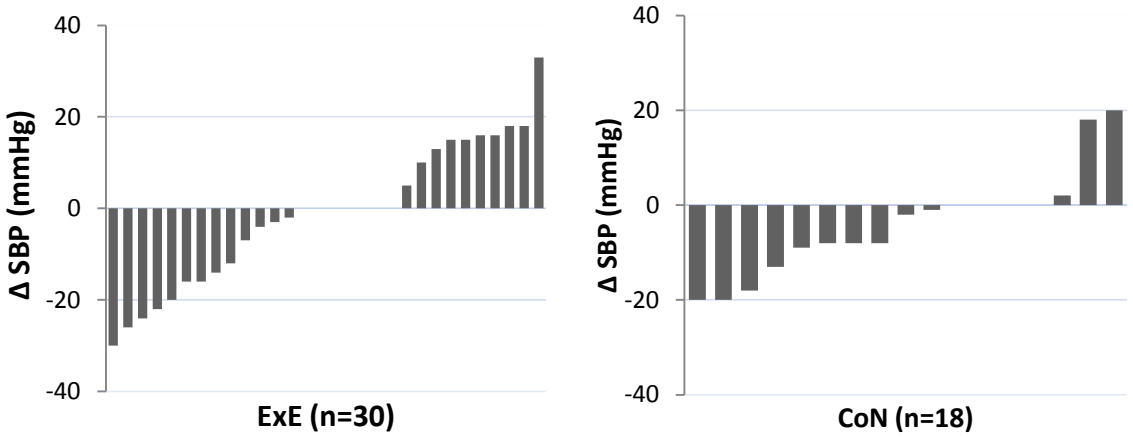


Figure 4.23: Change to systolic blood pressure from baseline to week 12

4.12.2 DIASTOLIC BLOOD PRESSURE

There was no change in CoN but there was a significant decrease over time in ExE (F=10.047, df=(3,87), p<0.01)) (Table 4.28). ExE decreased significantly (p<0.01) at weeks 8 and 12 compared to baseline, and the measure at week 8 was significantly (p<0.01) lower than at week 4. Sixty percent of ExE and 58% (CoN) recorded a drop in diastolic blood pressure (Figure 4.24). No change was noted for 33% and 16% (ExE and CoN), with 7% and 26% respectively experiencing an overall increase. Mean diastolic blood pressure in ExE and CoN was "pre-hypertensive" (80-89 mmHg) at baseline, but had reduced to within the "normal" range (<80 mmHg) by week 8 (ExE) and week 12 (CoN).

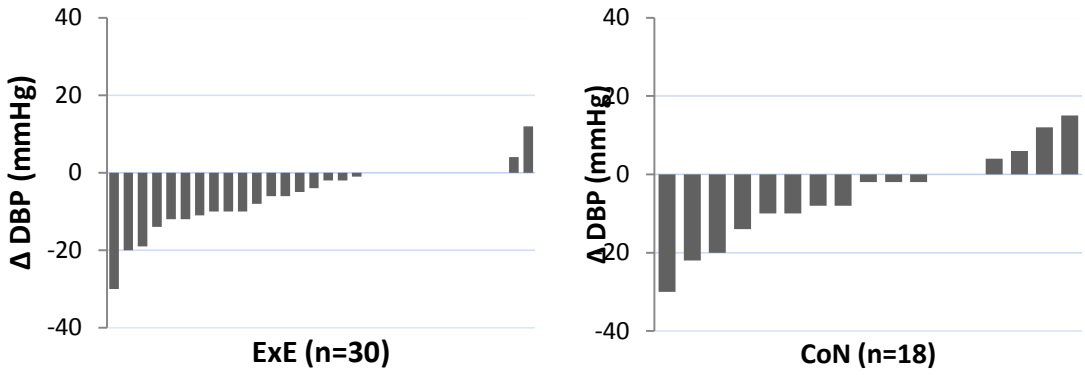


Figure 4.24: Change to DBP from baseline to week 12

4.13 SELF REPORTED BEHAVIOURAL VARIABLES

4.13.1 PROFILE OF MOOD STATES QUESTIONNAIRE

Questionnaire response rate was 100%. Table 4.29 reflects the scores for the seven measurable items on the profile of mood states questionnaire scoring tool. Tension score was not different between groups at baseline. No change occurred in either ExE or CoN over the course of the intervention (**Error! Reference source not found.**). ExE and CoN presented with similar depression scores at baseline. No change was evident for this factor in either cohort.

Table 4.29: Profile of Mood States (ExE, n=30; CoN, n=18)

		TENSION		DEPRESSION		ANGER		FATIGUE		CONTROL		VIGOUR		TOTAL MOOD DISORDER	
		(POMS Score)	CV (%)	(POMS Score)	CV (%)	(POMS Score)	CV (%)	(POMS Score)	CV (%)	(POMS Score)	CV (%)	(POMS Score)	CV (%)	(POMS Score)	CV (%)
ExE (n=30)	WEEK 0	7.0 ± 4.2	(60%)	5.9 ± 4.8	(81%)	6.1 ± 4.4	(72%)	6.2 ± 5.1	(82%)	5.6 ± 2.7	(48%)	16.5 ± 7.7	(47%)	13.0 ± 19.8	(152%)
	WEEK 4	6.6 ± 4.4	(67%)	5.8 ± 7.2	(124%)	4.9 ± 4.2	(86%)	6.8 ± 5.8	(85%)	5.2 ± 2.5	(48%)	16.6 ± 6.2	(37%)	12.6 ± 23.2	(184%)
	WEEK 8	5.8 ± 4.5	(78%)	4.5 ± 4.8	(107%)	4.4 ± 4.8	(109%)	4.6 ± 4.6	(100%)	5.2 ± 3.0	(58%)	18.7 ± 6.2	(33%)	7.8 ± 20.4	(262%)
	WEEK 12	5.8 ± 4.4	(76%)	6.5 ± 5.9	(91%)	5.1 ± 4.5	(88%)	5.6 ± 4.5	(80%)	5.5 ± 2.9	(53%)	17.0 ± 7.5	(44%)	9.7 ± 20.9	(215%)
CON (n=18)	WEEK 0	8.0 ± 5.5	(69%)	9.1 ± 9.6	(105%)	7.5 ± 7.8	(104%)	7.5 ± 5.6	(75%)	6.4 ± 3.2	(50%)	14.8 ± 5.3	(36%)	15.5 ± 32.1	(207%)
	WEEK 4	5.3 ± 2.9	(55%)	6.6 ± 5.2	(79%)	5.4 ± 4.3	(80%)	6.1 ± 4.6	(75%)	5.0 ± 2.4	(48%)	12.9 ± 5.7	(44%)	14.5 ± 23.5	(162%)
	WEEK 8	6.2 ± 4.0	(65%)	6.8 ± 6.2	(91%)	6.4 ± 6.8	(106%)	**3.7 ± 3.9***	(105%)	5.3 ± 2.1	(40%)	14.7 ± 6.1	(41%)	13.6 ± 21.1	(155%)
	WEEK 12	6.9 ± 4.9	(71%)	7.8 ± 9.5	(122%)	5.1 ± 5.8	(114%)	5.1 ± 5.4	(106%)	5.5 ± 2.5	(45%)	11.7 ± 5.5	(47%)	18.9 ± 25.3	(134%)

*POMS scores are expressed as "mean ± standard deviation"; **CV** = Coefficient of Variation presented in brackets; * denotes significant difference from baseline; **[bold]** font highlights significant data.*

Mean scores for 'anger' were not different at week 0, and did not change over time (ExE and CoN). Baseline fatigue scores for groups ExE and CoN were similar. There was a significant decrease in CoN (F=4.84; df=3,39, p=0.01) from week 0 to week 8, but no difference to baseline at weeks 4 and 12. There was no change over time in ExE.

There was no difference in Control scores at baseline (ExE and CoN). No change occurred over time in either group. Vigour scores were similar at baseline in ExE and CoN. No change took place in either cohort over time. At baseline Total Mood Disorder scores for ExE and CoN were not significantly different. No change occurred over time in ExE or in CoN.

4.13.2 SELF-REPORTS: EXERCISE INTERVENTION COHORT

ExE undertook exercise and were asked about this experience (questionnaire response rate 100%). CoN did not do any activity and were asked a separate set of questions, presented in the next section.

Table 4.30: Self-reported factors influencing motivation (ExE, n=30)

	REASONS PROVIDED			
	Supervised/ Group Setting	**Improve Health/ Strength**	**Aesthetic**	**Commitment to Researcher/ Study**
Pre-Study	**33%**	25%	25%	0%
During Intervention	14%	23%	0%	**46%**
Post-Study	11%	**33%**	11%	0%

*Shaded blocks with values in **[bold]** font represent highest percentage of responses per phase*

Prior to selection for the study participants were motivated by the knowledge that the study would take place in a small group setting, and that it would be supervised (33%) (Table 4.30). Knowledge of the benefits of exercise and a desire to improve body condition, at this stage for aesthetic reasons, were also strong motivators (25% for each category). Lower ranked motivators included the need to take positive action against the degeneration of known risk factors, and aging (13% and 4%).

The motivation to volunteer for the study and the subsequent motivation to continue to adhere to the exercise programme appeared to be driven by different factors (**Error! Reference source not found.**). Continued adherence was primarily due to loyalty to the research study and to the primary researcher (46%). The second strongest motivator was the social cohesion of the small group setting (14%) followed by notable improvements to musculo-skeletal strength (23%) and positive reinforcement from family, friends and colleagues (18%).

In terms of physical changes, positive responses were elicited from 89%, and 11% indicated that no change had been noted. Respondents who answered “yes” to

experiencing physical changes reported strength improvement (43%) followed by loss of notable fat mass (26%) and improved agility and flexibility (22%) (Table 4.31). A minority of respondents reported reduced chronic muscle and joint ache (9%).

Table 4.31: Changes self-reported by participants in ExE (n=30)

DOMAIN	FACTOR	RANKED IMPORTANCE OF FACTOR (as % of all factors listed)
Physical	↑ Strength	**18**
	↓ Fat Mass	11
	↑ Flexibility	9
Physiological	↑ Energy	**14**
	↑ Digestive Function	12
Emotional / Mood	↑ 'Control' [a]	**33**
	↓ Stress / Depression	4

[a] *'Control' refers to "improved control over physical changes"; [* ***bold*** *] text highlight the factors most frequently cited*

Of the respondents, 94% responded that physiological changes had been experience, while 6% noted that these had not occurred. Those who responded positively listed improved energy levels during the day (35%) and improved digestion and bowel function (30%) as the most obvious changes (Table 4.32). Improved cardiovascular function (slower heart rate, deeper and slower breathing) was listed by 20% of respondents while a "general improvement" was noted by 15%.

The majority of respondents (72%) had noted mood changes, and 28% had not experienced any change. Of those who responded "yes" the greatest positive change was "improved control over physical changes" (80%), followed in equal measures by reduced stress and decreased levels of depression (10%) (Table 4.32).

The respondents indicated that they would continue to exercise once the research study was completed (94%). Reasons for intention to continue exercise were to maintain fat mass loss (33%), the social element of exercise in small groups (11%), maintenance of psycho-emotional health (11%) and to continue to manage an existing health problem (11%).

For reasons such as the ease of developing a routine, 72% of respondents indicated that 5 $d.week^{-1}$ was preferred, and that the daily routine was easier to adhere to than a 3 $d.week^{-1}$ programme. Time management was cited as a problem, and 11%

responded that in future they would not prefer a 5 d.week^{-1} programme. Some respondents (17%) indicated that 5 d.week^{-1} was suitable for a limited time period (such as the twelve week research study) but that beyond this it would be preferable to maintain a routine of three or 4 d.week^{-1} instead.

4.13.3 SELF REPORTS: MATCHED CONTROL COHORT

Sedentary on recruitment, 100% of respondents indicated that no additional activity had been undertaken. The majority of respondents indicated that completing a diet recall diary did not lead to changed dietary behaviour, nor the intent to change dietary patterns (67%). On the other hand, 33% indicated that this task had influenced food choices and would influence food selection in the future. Four-weekly measurements of body mass, site circumferences and body composition may have consciously or subconsciously encouraged the control group to be more aware of their physical condition. Whether this engagement influenced an intent to change behaviour, or brought about an immediate subtle change in physical behaviour, was denied by 33% of respondents. However, 67% admitted that the intent to change was a result of the regular focus on body morphology.

4.14 SUMMARY OF INDIVIDUAL RESULTS

Individual responses to known risk factors for CVD were analysed, and are presented in Table 4.32. In ExE 16 individuals responded to more than 4 of the 11 identified risk factors while in CoN, eight individuals responded to ≥ 4 variables. Three participants were identified in ExE as 'best' responders to the intervention when the plasma lipoproteins were isolated (using a response of ≥0.5 mmol.L^{-1} as the minimum change for clinically relevant change). One individual was identified in CoN as a 'best' responder based on clinically relevant improvements to three of the four measured lipoproteins. Of note is the preponderance of morphological responses in ExE which is not seen in CoN. Positive and clinically relevant plasma lipoprotein responses were identified in 17% of ExE and 18% of CoN. Similar stratification was noted for diastolic blood pressure change, with clinically relevant improvements for 33% in ExE and 27% in CoN. The similarity in number of positive responses in both group indicates a very small margin which might be attributable to the strength training and emphasizes the importance of identifying characteristics of 'responders' and 'non-responders'.

Please view Table 4.32 overleaf.

Table 4.32: Summary of individual responses to identify cases of risk reduction

Δ = week 12 - week 0											
	Risk Factors										
Case	Mass	Waist	WSR	LDL-C	HDL-C	TriG	TotC	HbA_{1c}	SHBG	SBP	DBP
1	-0.58	-4.5	-0.03	0	-0.27	0	0.1	-0.2	-0.5	15	0
2	-2.56	-2	-0.01	0.2	-0.4	0.5	-0.2	-0.1	-15.9	-7	-2
3	2.44	-2.5	-0.02	-1	-0.1	0.1	-0.9	-1.6	0.7	0	-10
4	0.06	-2.5	-0.01	0.3	0.1	0.2	0.3	-0.4	-37.6	0	-5
5	-1.82	-6.5	-0.04	-1.5	-0.3	1.3	-0.6	0.1	-2.6	-2	0
6	-0.56	4	0.024	0.2	0.1	-0.2	-0.4	0.1	-38	-20	-20
7	-0.66	-4.2	-0.03	-0.2	0.5	-0.2	-0.2	-0.1	12	0	-10
8	-0.18	-11	-0.07	-0.5	-0.2	-0.1	-1.1	-0.4	-1.2	10	0
9	-3.04	-0.5	-0	0.8	0	1.1	1.4	0	-16.3	-26	-10
10	-1.42	-3.5	-0.02	-1.9	-0.2	0.6	-1.4	0.5	13.8	5	-30
11	-3.08	-7	-0.04	-0.1	0.3	0.1	-0.1	0	1.8	13	-19
12	-2.14	-2	-0.01	-0.7	0.2	0.3	-0.5	0.7	8	16	-12
13	-6.78	-5.7	-0.03	-1.1	0.1	-0.4	-1.4	0.7	-4.4	16	-10
14	-2.04	-3	-0.02	0	0	0	-0.9	0.1	-2.7	33	-4
15	-1.64	-7	-0.04	0	-0.6	0.1	-0.7	0	-4.7	-16	-6
16	-3.96	-3	-0.02	-0.2	0.1	0.1	-0.4	-0.6	1.8	-22	-6
17	-0.3	-8	-0.05	0.2	0.1	-0.1	0.4	0.4	4	0	4
18	-1.06	-5.4	-0.03	-0.7	-0.1	0.2	-0.2	0.2	3.4	23	-5
19	-1.06	-2.7	-0.02	0.2	0.2	0	0.1	-0.1	9.2	-3	-14
20	-2.32	-3.6	-0.02	0.5	-0.2	0.4	0.9	0.2	9.7	-4	-52
21	1.28	-5	-0.03	-0.6	0.2	-0.3	-0.4	0.6	-2.2	18	4
22	-2.44	-6	-0.04	0	0	0	-0.5	0.1	-1.1	0	0
23	-1.52	-4.1	-0.03	0.8	0.1	-1	0.4	0.2	5.3	18	0
24	0.96	-1	-0.01	0	0.2	0	0.7	0.4	3.5	15	-1
25	0.7	0.5	0.003	0.1	-0.5	-0.3	-0.5	0	-0.7	-12	-2
26	-2.74	-6.4	-0.04	0.3	-0.1	-0.2	0.1	0.6	13.1	-30	-12
27	-2.46	-4.1	-0.03	1.5	0.2	0.6	1.7	0.3	-0.1	-14	0
28	2	0.5	0.003	0.7	0	0.1	0.5	1	29.3	-16	12
29	-0.48	-9	-0.05	0.1	0	-0.1	0.1	1	3.7	-4	-8
30	1.86	5	0.031	-0.1	0	0.3	0	0.4	0.2	-24	0
31	3.84	3.7	0.022	0.2	0.2	0.1	0.2	-0.1	15.5	-20	-30
32	0.82	-0.6	0	0.2	-0.4	0.2	-2	0.4	-1	-18	-10
33	0.82	2.6	0.016	0	0	-0.2	-0.3	-0.2	-1.6	-9	-8
34	0.48	1.5	0.009	-0.1	0	-0.3	-0.2	0.2	-53.8	-20	-22
35	0.12	6.4	0.038	-0.1	-0.1	-0.1	-0.7	-0.8	-1.8	-8	-20
36	0	-3.4	-0.02	-0.3	0.1	-0.3	0.2	0	0	0	0
37	2.08	0	0	0.8	0.2	-0.2	0.4	0.1	5	18	12
38	3.7	2.6	0.016	0.1	0.2	-0.1	0.8	-0.5	-0.9	-8	15
39	1.36	-1.8	-0.01	-0.5	-0.2	-0.1	-0.1	-0.1	15.9	0	4
40	0.2	0.5	0.003	-1.6	-0.2	0.3	-0.3	0.4	6.3	-2	6
41	-0.4	-4.5	-0.03	-0.1	0	0	0.7	0	-0.9	2	-2
42	1.36	0	0	-1	-0.1	-0.2	-1.4	0.3	-1.1	-13	-14
43	-0.94	-3.2	-0.02	-0.1	-0.3	0	-0.4	0.1	-9.4	-8	-8
44	0.6	1.7	0.011	-1.7	-0.1	0.1	-0.6	0.2	3.7	20	-2
45	0.9	2	0.012	-0.3	0.1	-0.3	0.3	0.3	1.5	0	-2
46	0.66	5.2	0.033	0	0.9	-2.8	-1.5	0	1.3	-1	-10
47	0	12.7	0.077	0	0	0	0	0	61.2	0	0

Where: shading represents a positive change to the variable; [bordered block] represents clinically relevant change; [code] with border represents best responders.

5 DISCUSSION

Plasma lipoproteins were not positively influenced by 12 weeks of progressive resistance training (**Error! Reference source not found.**). The findings of this study thus do not support the initial hypothesis. This despite stable body mass and dietary intake, significant strength increases and a stable menopausal hormonal milieu. In contrast to the lack of effect on the blood lipid profile, waist circumference decreased significantly (p<0.01) over time as did diastolic blood pressure (p<0.01). As risk indices for cardiovascular disease these changes are important and represent extremely positive findings in this sample.

Table 5.1: Summary of significant changes from baseline

ExE (n=30)						CoN (n=18)					
Variable	**0**	**4**	**8**	**12**	***p***	**Variable**	**0**	**4**	**8**	**12**	***p***
Strength: Leg		↑	↑	↑	<0.01	Strength: Leg		-	-	-	
Chest		↑	↑	↑	<0.01	Chest		-	-	-	
Back		↑	↑	↑	<0.01	Back		↓	-	-	<0.01
HbA_{1c}		↓	-	-	0.02	HbA_{1c}		-	-	-	
Testosterone		↑	-	-	<0.01	Testosterone		-	-	-	
Blood Pressure: Diastolic		↓	↓	↓	<0.01	Blood Pressure: Diastolic		-	-	-	
Circumference: Waist		↓	↓	↓	<0.01	Circumference: Waist		-	-	-	
Thigh		-	-	-		Thigh		↑	-	-	0.02
Skinfolds: Abdominal		↑	↑	↑		Skinfolds: Abdominal		-	-	-	
Calculations: BMI		-	-	-		Calculations: BMI		-	↑	↑	<0.01
WHR		↓	↓	↓	<0.01	WHR		-	-	-	
WSR		↓	↓	↓	<0.01	WSR		-	-	-	
POMS: Fatigue		-	-	-		POMS: Fatigue			↓		0.01

Strength increased by 35% (chest), 51% (back) and 43% (leg). Waist circumference decreased by -4.9 cm (-5%), indicative of a reduction independent of CVD risk reduction. CoN displayed a gradual loss of strength over time, except for back strength which dropped significantly (-20%) within the first eight weeks of the intervention. This loss of strength has direct implications for musculo-skeletal injury and low back pain associated with reduced postural control (Heliovaara, 1989). Despite these changes, the plasma lipoproteins remained unchanged. Based on NCEP classifications 33% of participants had high TotC, 43% had high LDL-C, 13% had high triglyceride content and 10% had low HDL-C at baseline. The small fluctuations recorded do not represent any clinical benefit and occurred in both groups, entirely independent of the exercise intervention. Strength training increases muscle mass, power and endurance, and promotes metabolic acceleration as well as a change to substrate utilisation (Sale, 1988). Lipid oxidation is encouraged, and

yet morphology (estimated body fat content) remained unchanged in this sample. Fatty acid metabolism is closely related to the biological synthesis of cholesterol, as discovered by Bloch and Lynen in 1964 (Nobel prize winners for medicine or physiology). If, in the current sample, fatty acid metabolism was indeed increased due to additional lean mass and metabolic acceleration, it had no effect on the lipoprotein concentration in the blood plasma (Table 5.2). Perhaps the lack of oestrogen in the form of oestradiol, as is characteristic of the climacteric, was influential in this non-response (Pappa & Alevizaki, 2012). Of interest with respect to oestradiol is the significant difference between groups, as CoN had consistently higher levels of oestradiol than ExE throughout the intervention and despite undertaking no form of exercise, recorded similar patterns of change to ExE. The significant physiological role played by oestradiol in tissue-specific function may well be influential in the responses of females, post-menses, both systemically and biochemically. The increase of oestradiol in CoN at week 4, while not statistically significant may represent a functionally relevant change that has concomitantly influenced other indices, such as the plasma lipoprotein responses.

Produced in greatest concentration by the ovaries (pre-menopause), oestradiol is also manufactured by the liver, adrenal glands, breast tissue and fat cells (Cui *et al.*, 2013). Post-menses, extra-gonadal sites are the primary source of oestrogen, with localised synthesis more active in the mesenchymal cells of adipose than is noted prior to menopause (Cui *et al.*, 2013). If fat cells produce sufficient oestradiol to change the hormonal milieu sufficiently, then individuals with greater volumes of adipose tissue may present with higher levels of circulating, naturally produced oestrogen. This would suggest that overweight or obese candidates would possibly represent “responders” while lean participants would show a dampened response (“non-responders”). This is counter-argumentative to the position of Flock *et al.* who posit the opposite: that lean individuals will respond better than obese individuals (Flock *et al.*, 2011). In the current sample LDL-C decreased positively (a marginal effect size, but if consistent, clinically relevant) in 75% of obese candidates and in none of the “normal weight” individuals. The LDL-C decreases in the obese candidates translated into a risk category drop in 50% as opposed to no change in risk categorisation for the lean individuals. This finding seems intuitively correct as obesity is associated with hyperlipidaemia and dyslipidaemia, particularly in older

females (Garrison *et al.*, 1980). Hypothetically, the natural drive toward homeostasis might create a suitable physiological milieu for change to occur.

Table 5.2: Summary of strength change from baseline and associated effect on the plasma lipoproteins

ExE (n=30)						CoN (n=18)					
Variable	**0**	**4**	**8**	**12**	***p***	**Variable**	**0**	**4**	**8**	**12**	***p***
Strength: Leg		↑	↑	↑	<0.01	Strength: Leg		-	-	-	
Chest		↑	↑	↑	<0.01	Chest		-	-	-	
Back		↑	↑	↑	<0.01	Back		↓	-	-	<0.01
Lipoproteins: LDL-C		-	-	-		Lipoproteins: LDL-C		-	-	-	
HDL-C		-	-	-		HDL-C		-	-	-	
TriG		-	-	-		TriG		-	-	-	
TotC		-	-	-		TotC		-	-	-	

HDL-C is the transport lipoprotein, least dense, and desirable in quantity. HDL-C concentrations are increased by the presence of oestrogens, thus by inference, are naturally lower in post-menopausal females (Shai *et al.*, 2004). The primary role of this lipoprotein is to transport cholesterol to the liver for excretion. A primary characteristic of dyslipidaemia is high LDL-C coupled with low HDL-C. If the primary transport lipoprotein is present in sub-optimal quantities, the theoretical assumption would thus be a compromised excretion rate of LDL-C and other particles such as triglycerides. Compromised transport and excretion may intuitively lead to a build up of the water-insoluble cholesterols in the blood plasma resulting in an atherogenic milieu. Added to this is the deregulation of LDL-C receptors. Should a cell be deficient in cholesterol additional LDL-C receptors are created to accommodate additional cholesterol deposition. Once this system de-regulates, more LDL-C particles appear in the blood which should be oxidised and taken up by macrophages for removal. Oestrogen is a sex steroid and as noted by Bloch and Lynen, bile and the oestrogen family are made from cholesterol. If both cholesterol and oestradiol are so closely related, it may appear reasonable to wonder whether the cessation of function of the female sex hormone and its associated receptors on the cell membranes may in some way affect cholesterol uptake and transport, leading to higher volumes of LDL-C in the plasma with no means of excretion. Post-menopausal females represent a unique population in this regard, and warrant specific biochemical investigations given the importance of oestradiol to structural and functional homeostasis in the body.

Triglyceride content has been identified as the lipid marker most strongly associated with non-lipid CVD risk variables, particularly BMI and physical activity levels (Shai *et al.*, 2004). Interestingly, in the current sample TriG demonstrated no significant correlations with surrogate markers of obesity, but HDL-C correlated significantly to BMI, WC and WSR in ExE and CoN. In the present group 40% had TriG levels <1.7 $mmol.L^{-1}$ at baseline, while 13% presented with levels >1.7 $mmol.L^{-1}$. Furthermore, TriG has the highest variance in the sample as a whole (>50%) while the other lipid variables show consistent variance of ~20%. Lower levels are desirable, and the characteristics of those with lowest TriG indicate that the individuals were lower than average body mass and BMI, average waist circumference, and lower than average WHR. The suggestion that leanness is associated with lower TriG levels is incorrect however, as the body mass range in this subgroup was 56-88 kg, BMI range 22-32 $kg.m^{-2}$, waist circumference 70-106 cm and WHR 0.6-0.9. Intra-individual characteristics beyond the "obvious" may provide insight into the mechanisms of TriG presence or absence, such as macronutrient intake (with excess carbohydrate intake suggestive of elevated TriG levels) or liver function (inability of the liver to adequately process fatty acids may result in elevated levels of TriG in the plasma) (Table 5.3). Compared to the group mean both those individuals with exceptionally low TriG and those with exceptionally high TriG at baseline consumed fewer kilojoules per day overall, fewer carbohydrates per day overall, but did consume average volumes of protein and fats. This insight into the dietary intake of post-menopausal women in conjunction with biochemical indices is important in adding to the existing understanding about the supposed link between dietary intake and cholesterol levels.

Table 5.3: Triglyceride levels at baseline

	Dietary Intake	kJ ($kJ.day^{-1}$)	CHO ($g.day^{-1}$)	Protein ($g.day^{-1}$)	Fat ($g.day^{-1}$)
Baseline Levels	**Group Mean**	**7149**	**184**	**66**	**56**
Triglycerides < 1 $mmol.L^{-1}$	Case 1	7540	162	78	70
	Case 2	5793	147	93	53
	Case 3	7003	170	59	62
	Case 4	6819	163	59	59
	Case 5	5895	173	49	50
	MEAN	**6610**	**163**	**68**	**59**
Triglycerides >1.7 $mmol.L^{-1}$	Case 1	9397	167	109	82
	Case 2	6485	154	56	47
	Case 3	4791	175	26	27
	Case 4	6962	181	61	69
	MEAN	**6908**	**169**	**63**	**56**

A position that has gained traction in recent years has been the concept that cholesterol is not an indicator of cardiovascular risk at all (Noakes & Vlismas, 2012; Taubes, 2007). Two opposing theories have been proposed, one that atherosclerosis is lipid driven, the other than it is inflammation driven, thus it may be possible that reducing systemic inflammation would reduce vascular events rather than focussing on reducing cholesterol (Ridker, 2012; Ridker, 2013). Given that cholesterol is a fundamental 'building block' of cell membranes, steroid-based hormones, and central to neural pathway communication, it is naturally occurring and necessary. In fact cells use cholesterol as a central lipid for regulating cellular lipid homeostasis (Maxfield & van Meer, 2010). In this context the findings of the present study are positive, as cholesterol was not decreased, and in some individual instances the various lipoproteins increased in presence. Overall, LDL-C and HDL-C increased in 43% of participants, while TriG and TotC increased in 33% and 40% of candidates respectively. A novel approach would be to consider this effect of the exercise as markedly positive in this regard. The "diet (fat) – heart" hypothesis is firmly entrenched and the belief is widespread that excess dietary fat elevates cholesterol which in turn may lead to cardiovascular disease if left unchecked (Noakes & Vlismas, 2012; Taubes, 2007). It was the work of Ancel Keys that convinced the health and medical fraternity that dietary fat elevated cholesterol and that this predicted heart disease. It is interesting to pair the arguments against the dangers of cholesterol with the information relating to trials of statin drugs. Statins

unequivocally reduce cholesterol content, particularly LDL, by at least 30%. As such, they are effective medications. What has yet to be conclusively evidenced, however, is whether the 30% reduction in presence of LDL-C in fact translates into any meaningful reduction in risk of adverse cardiovascular event (Eisenberg & Wells, 2009; Hague *et al.*, 2003). Certainly in female candidates, this has yet to be observed (Hague *et al.*, 2003; Krummel *et al.*, 2001; Mora *et al.*, 2010; Mosca, 2005). It would be controversial and indeed ground-breaking if increasing cholesterol parameters could be linked to improved health, reduced risk of heart disease and reduced risk of age-related illness such as Alzheimer's or Parkinson's Disease which has been linked, tenuously, to low levels of cholesterol resulting in poor health of the brain cell membranes and subsequent failure of neuronal pathways.

Pro-inflammatory markers have been found to dampen the lipoprotein response to dietary interventions aimed at lowering plasma lipoprotein content (Flock *et al.*, 2011). In the absence of naturally occurring oestradiol, which is an anti-inflammatory, arterial health declines and it is natural that inflammatory responses should occur within the arterial walls. Should pro-inflammatory markers be present in the plasma it is thus possible that the lipoprotein response to any intervention, including physical activity, may be dampened. Inflammatory markers were not measured during this study, but it is recommended that future investigations incorporate measures to assess the validity of this posited relationship.

The significant waist circumference (-5%) decrease points directly to altered metabolism of visceral fat deposits, and the added burden on the liver as it creates bile and excretes fatty acids. As this is also the route of excretion for cholesterol (Zhao & Dahlman-Wright, 2010), it may be that this transport route is over-burdened and must re-establish a balance before notable decreases to plasma lipoproteins can be identified. Additional mobilisation of adipose deposits may contribute to additional triglyceride presence in the plasma. Trials involving dietary restriction have noted waist circumferences decreases of -9%, -6% and -5% previously (Eshghinia & Mohammadzadeh, 2013; Lowndes *et al.*, 2012; Papadaki *et al.*, 2013). These trials differed fundamentally to the current trial as they required weight loss of the participants, included male and female candidates and significantly restricted caloric intake. Restriction of caloric intake is not a successful long-term approach to managing weight and curbing obesity – not least of all because the body is

'programmed' to return to homeostasis and prefers "surfeit" to "deficit" states (King *et al.*, 2007).

Aerobic endurance training has resulted in modest (<5%) drops to waist circumference in trials of 24 weeks engaging adults (male and female) (Joseph *et al.*, 2011; Sjögren *et al.*, 2012). Previous resistance training trials report no change to waist circumference, or no difference in the change between sample groups (Brochu *et al.*, 2009; Ciolac & Greve, 2011; Willis *et al.*, 2012). The decision to design this intervention as a 5 $d.week^{-1}$ programme emanated from the evidence already present in the literature: most studies have employed a 3 $d.week^{-1}$ design and results to date pertaining to post-menopausal females are inconclusive. Given current recommendations by the *American College of Sports Medicine* (ACSM) that exercise be undertaken for thirty minutes daily in order to derive health benefit, it is recommended that research into more frequent exercise sessions be undertaken, and that 5-7 $d.week^{-1}$ designs be considered.

The 5 $d.week^{-1}$ design employed in this trial should be considered novel and controversial. The intensity is arguably higher than may be safe for older, previously sedentary females. The frequency of sessions may elicit musculo-skeletal injury due to reduced recovery time, and at the very least, should elicit muscle fatigue, delayed onset muscle soreness, and reduce proclivity to exercise in the candidates. That none of these outcomes were realised is in itself a finding, lending credence to the applicability of this challenging design. That adherence in this context was excellent, and compliance to the exercise programme ensured via supervision, infers that the intensity and volume of the sessions was adhered to – and thus the argument that the intended intensity and frequency was not manageable is nullified.

For the first time in the associated literature, post-menopausal females older than 55 years of age cannot be referred to as "older adults" with the inference that they must be treated more "carefully" than younger adults or pre-menopausal females. This has resulted in exercise trials proving fruitless, no doubt leading to frustrations in the participants and the research teams. Admittedly the current cohort were carefully screened for underlying medical conditions, but at the same time, this is a standard recommendation for any person commencing an exercise regime (ACSM, 2013).

All variables revealed the presence of “responders” and “non-responders” to the intervention. Mean values in this context may conceal inter-individual effects. Responders may also be termed “compensators” or “non-compensators” as it is posited that additional physical activity creates perturbations in the energy balance system which leads to the individual compensating, whether autonomically or volitionally (Blundell *et al.*, 2003; Ho *et al.*, 2012; King *et al.*, 2007; King *et al.*, 2008). The compensatory mechanisms thus represent a potential barrier to the efficacy of the exercise to improve factors such as body weight. The body comprises a complex network of interactions designed to maintain homeostasis and prevent catastrophic change. Governed by the brain (the “central governor”) part of the feedback system involves metabolites from the periphery, such as may signal changes as a result of physical activity and the concomitant energy imbalance (Noakes *et al.*, 2005). Identifying the characteristics of responders may provide useful insight into how exercise can be used most effectively in managing chronic conditions.

Responders to the exercise intervention for the plasma lipoprotein variables were evaluated. The responses greater than (or equal to) -0.5 $mmol.L^{-1}$ were selected to ensure a moderate ‘effect size’, and an interesting picture emerges (Table 5.4). LDL cholesterol responders were above the current cohort average for body mass, body mass index, waist circumference and had three out of four lipoprotein measure abnormalities. Conversely, HDL-C responders were thinner, leaner, possessed less abdominal visceral fat (via waist circumference measure) but presented with 100% abnormal lipoprotein measures. Tryglyceride responders were the smallest group and this small sub-cohort were similar to the LDL-C responders in that they were fatter, heavier and possessed more AVF than the group as a whole, but in this instance no dyslipidaemia was evident (25%). TotC responders were below the group average for body mass, body mass index and presented with two lipid abnormalities (50%).

Perhaps these trends are not as counter-intuitive as first appear. LDL-C, TriG and TotC responders had to reduce the variable to improve health status, while HDL-C responders had to record an increase over time to “respond”. Responders for LDL-C, TriG and TotC were initially “higher than average” for general body morphology, while HDL-C responders were “lower than average” morphology. It has been observed that the body is more easily able to cope with surfeits than deficits (King *et*

al., 2007) – and while that statement is related to energy imbalances, it is quite possible that it may apply to biochemical homeostasis too. Research has been undertaken on general adult populations but this is the first study to this author's knowledge that identifies the characteristics of responders in post-menopausal females (Table 5.4).

Table 5.4: Summary of characteristics of ExE plasma lipoprotein "responders"

Characteristics of Responders	Body Mass (kg)	BMI ($kg.m^{-2}$)	WC (cm)	WHR (ratio)	LDL-C ($mmol.L^{-1}$)	HDL-C ($mmol.L^{-1}$)	TriG ($mmol.L^{-1}$)	TotC ($mmol.L^{-1}$)
Group Mean	**79.2**	**29.1**	**94.3**	**0.9**	**4.2**	**1.6**	**1.3**	**5.8**
LDL-C Responders	85.1	31.6	101.6	0.9	4.5	1.6	1.5	6.3
HDL-C Responders	76.7	28.6	93.3	0.9	3.9	1.5	1.1	5.7
TriG Responders	87.7	31.3	100.5	0.9	4.1	1.4	1.4	5.7
TotC Responders	78.5	28.9	94.8	0.9	4.1	1.6	1.5	6

CoN responders showed no identifiable characteristics (Table 5.5). The LDL-C responders appear to be above group average for body mass, body mass index, and waist circumference, but the range within the group of identified responders renders mean data meaningless in this context. Body mass ranged from 64-92 kg, and waist circumference from 88-117 cm. One respondent was removed from the analysis, as that participant's reponses were considered anomalous given the size of the response (-1.5 $mmol.L^{-1}$ for LDL-C), and the investigator's knowledge that her dietary habits are not 'usual' due to a range of allergies. It is also the belief of the researcher that this participant may have begun undertaking exercise during the intervention, although this could not be ratified. Removal of this individual from the group results made no difference to mean data, but removal from the individual analysis ensured that no incorrect assumptions were drawn. Of further note pertaining to CoN is the fact that there were no individuals who responded when considering TriG and HDL-C. Those responses that did occur cannot be considered clinically relevant for risk reduction.

Table 5.5: Summary of characteristics of CoN plasma lipoprotein "responders"

Characteristics of Responders	Body Mass (kg)	BMI ($kg.m^{-2}$)	WC (cm)	WHR (ratio)	LDL-C ($mmol.L^{-1}$)	HDL-C ($mmol.L^{-1}$)	TriG ($mmol.L^{-1}$)	Tot-C ($mmol.L^{-1}$)
Group Mean	75.3	27.4	88	0.8	4.3	1.7	1.3	6.3
LDL-C Responders	80.7	29.3	101.2	0.9	4.3	1.7	1.2	6.3
Tot-C Responders	76.2	26.5	82.5	0.8	4.4	1.5	1.3	6.2

Clinical trials evaluating the efficacy of statin drugs as a therapy observe a 30-40% reduction in risk related specifically to LDL-C. Each -1 $mmol.L^{-1}$ reduction in LDL-C can be matched to a 4.4% reduction in risk of non-fatal cardiovascular events (Gutierrez *et al.*, 2012). However it has to be stated that females are under-represented in trials of statin therapies, generally (Gutierrez *et al.*, 2012; Mora *et al.*, 2010; Mosca, 2005; Ridker, 2013). In the current sample 12 weeks of progressive resistance training decreased LDL-C by 0.3 $mmol.L^{-1}$ inferring a 7% reduction in LDL-C and concomitantly, 1.3% CV event risk reduction if compared to statin therapy. HDL-C was normal or "desirable" in 90% of participants at baseline, and did not change over time in ExE, but recorded a 6% drop in CoN. It is possible that desirable levels attenuated any change. The individuals with lowest HDL-C at baseline did not, however, record particular increases to HDL-C so a negative HDL cholesterol balance did not encourage increases in this cohort. Triglyceride content increased by 8% in ExE and decreased by 15% in CoN. The cohort did not present with hypertriglyceridaemia at baseline (13% were above recommended levels at baseline) which may have attenuated any change to the TriG plasma concentration. Total cholesterol content decreased by a modest 2% in ExE and by 6% in CoN, however neither decrease represents a clinically significant overall change.

HbA_{1c} reflects a 2-3 month average glucose exposure and has low intra-individual variability in individuals who are not diabetic (Sibernagel *et al.*, 2012). The current cohort, comprising individuals who were not diabetic, showed elevated risk for CVD as 77% presented with an HbA_{1c} of >5.3% at baseline (80% at week 12), while 16% of these had an HbA_{1c} ≥6.0%. Arterial stiffness is closely related to values greater than 5.3% (Nestel, 2006). Additionally, glycated haemoglobin attenuates plaque regression in atherosclerotic conditions (Daida *et al.*, 2012). At week 12 the 'responders' had not decreased HbA_{1c} sufficiently to reduce associated risk of CVD or stroke (as per categorisation proposed by Selvin *et al.*). At baseline, participants with HbA_{1c} ≥6% were not homogeneous: body mass ranged from 62-91 kg, BMI from 21-35 $kg.m^{-2}$, waist circumference from 70-109 cm and the WHR from 0.7-1.0. Anthropomorphic variables could not be used to predict baseline HbA_{1c}, nor to identify responders. How glucose exposure is related to cardiovascular disease is not clear but it is possibly related to inflammation, which is associated with repetitively elevated blood glucose (Eskesen *et al.*, 2012; Selvin *et al.*, 2010). Of

note is that no association was identified between carbohydrate intake (responsible for elevating blood glucose and the glycaemic response) and HbA_{1c} in ExE, whereas a significant correlation was identified in CoN at week 8 (p=0.02) and week 12 ($p \leq 0.01$) (Table 5.6). Total caloric intake correlated significantly ($p \leq 0.01$) to HbA_{1c} in ExE indicating that there may be a stronger link to overall caloric consumption than to specific macronutrients. In general, ExE and CoN increased HbA_{1c} levels by 2% overall, with 27% and 26% (ExE and CoN) of participants recording decreases. As none of the participants with levels over 5.3% at baseline decreased to below this level after 12 weeks of training, no effective reduction in risk of CVD occurred.

Table 5.6: Correlation between HbA_{1c} and dietary intake in ExE and CoN

	Correlation (r^2)							
	Week 0		**Week 4**		**Week 8**		**Week 12**	
	ExE	**CoN**	**ExE**	**CoN**	**ExE**	**CoN**	**ExE**	**CoN**
HbA_{1c} & kJ Intake	**0.4**$^{\#}$	0	**0.4**$^{\#}$	0	**0.4**$^{\#}$	0.3	0.2	0
HbA_{1c} & CHO Intake	0	0.2	0.4	0	0.3	**0.5**$^{\$}$	0.1	**0.6**$^{\#}$

Significant correlations are indicated by [***bold*** *] font,* $^{\#}$ *(p ≤ 0.01),* $^{\$}$ *(p=0.02)*

Testosterone increased by 21% overall in ExE and by 11% in CoN. Testosterone is a steroid hormone, as is oestradiol, and is derived from cholesterol. Men possess up to 20 times the volume of Testosterone that is present in females, but of note is that females are exceptionally sensitive to perturbations in Testosterone content (Jones & Saad, 2009; Saad & Gooren, 2009). Strong associations between Testosterone and the characteristics of the Metabolic Syndrome have been identified in men, with lower levels of T related to increased AVF and to risk of T2D (Jones & Saad, 2009). Low T has also been implicated in the development of atherosclerosis – but whether this can be extrapolated to a females sample is not known (Jones & Saad, 2009; Saad & Gooren, 2009). Despite the sexes having differing volumes of the hormone, T has the same genesis in males and females, and functions similarly. Resistance training increases levels of T in men (Jones & Saad, 2009), and the assumption is, thus, that the same should happen in females. Over 12 weeks, T increased by 21% in the intervention group. Moreover, of all measures recorded in the current cohort, Testosterone (and the associated sex hormone binding globulin) shows the highest

variance (~60% throughout). The pattern of individual response is noteworthy too, in both ExE and CoN. If one considers only the responders, and ignores those individuals in whom no change was noted, 30% (ExE) and 60% (CoN) showed reduced T over time. Conversely, 70% (ExE) and 40% (CoN) demonstrate an increase over time. This marked difference in the response of the two groups suggests a potential link between testosterone and the intervention (strength training). In females, the oestradiol:testosterone ratio has been negatively associated with total and LDL-cholesterol, and positively linked to HDL-C (Dai *et al.*, 2012). In the present sample the E2/T ratio decreased by 35% (comparable to the 27% decline cited by Dai and colleagues as descriptive of females with CHD) after 12 weeks of resistance training, which according to Dai *et al.* and He *et al.* infers an increased risk of CHD in post-menopausal females as the balance between E2 and T has been compromised (Dai *et al.*, 2012; He *et al.*, 2007).

These links require more attention, as such, a dramatic increase in risk seems unlikely over the course of 12 weeks – unless it is indicative of a risk increase that hasn't been identified by the other variables measured in this trial. Sex hormone binding globulin is low in men with low T levels (Saad & Gooren, 2009). In addition, SHBG is cited as an amplifier of E2 (Dai *et al.*, 2012). SHBG is related to androgenicity, and thus it is expected that the movements of T and SHBG should be mirrored. This was not the case in the current sample as SHBG did not change overall. It appears that the strength training intervention elevated circulating T levels (or another mechanism was involved in this change) independent of any change to SHBG. In the current sample the extraordinary response of two individuals in CoN required further attention. Characteristics of each of the individuals are presented in Table 5.7. A fascinating picture emerges, presenting the individual whose SHBG level dropped by -57.8 *n*mol.L^{-1} as a much leaner individual than the participant who increased SHBG by 61.2 *n*mol.L^{-1}. It is however the hormone levels that offer the best insight into these changes: testosterone was particularly low in Case 2 (positive responder) as opposed to Case 1 (negative responder), while oestradiol was in fact in excess of post-menopausal levels in Case 2 (>73 *p*mol.L^{-1}) at baseline. Case 2 later recorded post-menopausal levels of oestradiol, and by rights inclusion in the sample was erroneous, but this insight is valuable. It points, once again, to the link between oestradiol and other biochemical CVD risk factors.

Table 5.7: Characteristics of 'extreme' SHBG responders (CoN)

Responder Characteristics	Δ SHBG	Body Mass	BMI	WC	WHR	E2	T
	(*n* mol.L^{-1})	(kg)	(kg.m^{-2})	(cm)	(ratio)	(*p* mol.L^{-1})	(*n* mol.L^{-1})
Case 1	-57.8	55.5	21.4	68.5	0.7	43	0.9
Case 2	61.2	88.2	32	84.3	0.8	100	0.4

Waist circumference dropped by 5% overall in ExE and increased by 2% in CoN. Waist showed a strong association with estimated fat content (calliper method r^2=0.4, BIA r^2=0.7) and to the sum of skinfolds (r^2=0.6). As has been posited previously, however, WC showed a stronger association to other anthropometric surrogates than to estimated fat content (r^2=0.8 with BMI, r^2=0.5 with WHR and r^2=1.0 with WSR). Notably, estimations of body fatness may not be the most relevant indicators of body composition and it may be worth investigating the association of BMI and WC with lean body mass or visceral adipose alone. Abdominal obesity (reflected by WC and WSR) is more directly related to CVD risk than whole-body fatness (as indicated by BMI). The current data do not reveal a particular superiority between these measures in relation to CVD risk variables.

The waist-to-stature ratio has in turn been cited as a superior measure of adiposity and a consistent predictor of CVD risk compared to WC alone (Ho *et al.*, 2003; Hsieh & Muto, 2005; Rastovic *et al.*, 2013; Rodrigues *et al.*, 2010; Song *et al.*, 2013). Conversely, there is evidence to support all the surrogate measures of obesity (BMI, WC, WSR and WHR) as effective risk markers (Flegal *et al.*, 2009; Njamdorj *et al.*, 2009). In the current cohort the surrogate markers were equally, and weakly, associated with other cardiovascular risk markers. A WSR cut-off of ~0.50 has been posited for most populations (Ho *et al.*, 2003; Hsieh & Muto, 2005; Rastovic *et al.*, 2013; Rodrigues *et al.*, 2010). ExE presented with a mean WSR of 0.6 throughout the intervention, and CoN with a mean ratio of 0.5. An easily assimilated message for public health would be that waist circumference should be less than half of stature for health purposes.

Diastolic blood pressure was positively affected by the exercise intervention, with an 8% reduction overall. Previous trials have also shown similar decreases in older, adult populations (Braith & Stewart, 2006; Fagard, 2006; Martel *et al.*, 1999). Prior

cohort DBP decreases have been, on average, -3.5 mmHg or -2-4%, certainly much lower than the present sample's drop of -7.7 mmHg (-9%). This may be due in part to the current investigation's exercise programme design, based on a 5 day per week frequency, high intensity, and use of compound rather than simple exercises. The positive DBP finding may also be indicative of a number of systemic changes including improved arterial compliance, or reduced intima-media thickening (Fagard, 2006; Umpierre & Stein, 2007). While speculation about the mechanism of change is not an exact science, a clear reduction to risk related to venous thrombo-embolism or stroke has occurred in this cohort. A few studies have suggested that resistance training decreases arterial compliance (in young, healthy men) (Kawano *et al.*, 2006; Miyachi *et al.*, 2004). The issue of arterial compliance is certainly controversial, as a well-designed trial engaging healthy young men lasting for 12 weeks with resistance training on 5 days of the week found no such deterioration in arterial compliance, as did a small scale investigation of older adults (incorporating both men and women) (Cortez-Cooper *et al.*, 2008; Rakobowchuk *et al.*, 2005). The Cortez-Cooper results for older adults must be replicated, however, as the intensity of the exercise was low (50% of 1 RM) and exercise was only undertaken on three days of the week. Conversely, improved endothelial function and improved arterial stiffness have been noted, as must have occurred in this sample to facilitate the improvement to DBP (Umpierre & Stein, 2007). A suggestion by Kawano *et al.* is to combine resistance training and aerobic endurance activity to attenuate the effects of strength training on compliance – a particularly positive suggestion as combined training often results in enhanced responses in other variables (Kawano *et al.*, 2006). Further research into endothelial health and arterial compliance, particularly in older, overweight or obese post-menopausal females, is warranted.

Unless the individual perceives value from participation in the training programme, there is little reason for long-term adherence to physical activity. Enhancement of quality of life has been found to be a potent motivator for adherence to exercise in women, as have enjoyment, and social interaction (Ferrand *et al.*, 2008; Jewson *et al.*, 2008; Segar *et al.*, 2008). POMS standard questionnaire submissions in the present cohort suggest no overall mood shifts due to strength training, but self-reported perceptions suggest otherwise. It is possible that POMS is not the right tool to use in this context, despite its reliability and validity in monitoring emotional

changes in post-menopausal women (Wyrwich & Yu, 2011). POMS sensitivity to changes over time has also been ratified, as has test-retest reliability (Gibson, 1997; Wyrwich & Yu, 2011). Self-reports indicate clearly that the individuals associated a range of positive perceptions with undertaking the resistance training intervention. That these changes could not be associated with equable POMS scores does not render them less important. A fundamental outcome for public health and exercise is medicine was that 100% of previously sedentary post-menopausal respondents indicated a desire to continue exercising beyond the confines of the study.

A criticism of this controlled trial is that the control sample was required to remain sedentary for 12 weeks, which is in direct opposition to the field in which this research took place – exercise as medicine. An initial design had considered low intensity exercise methods such as Yoga or Tai Chi for the control sample, but literature suggests that low intensity forms of exercise such as these have positive effects on aerobic capacity, balance and flexibility in older adults (Audette *et al.*, 2006). Other research has found that yoga practice may alter leptin and adiponectin levels, indicative of biochemical effect which may extend to the plasma lipoproteins (Kiecolt-Glaser *et al.*, 2012; Kiecolt-Glaser *et al.*, 2010). Positive psychological efficacy and stress reduction potential has also been identified (Cramer *et al.*, 2012). This evidence precluded the use of alternative forms of activity for the control. In order to be ethically compliant, the controls remained sedentary but were offered the chance to commence activity after the completion of the intervention period.

The findings of this controlled trial must be considered in the context of inevitable limitations. Dietary intake and energy expenditure were self-reported, and the reliability of these reports infers complete honesty by the participants. Diet was in turn not controlled but instead was maintained as ‘habitual’ and it is acknowledged that this may naturally have fluctuated intra-individually. Seasonal variation in lipid levels has been noted and may have been the cause of some of the variations in the lipid parameters noted in the study (Ockene *et al.*, 2004). The exercise and control samples were ultimately of different sizes as recruits dwindled. Recruitment also took place in stages in order to facilitate sufficient participants. Biochemical measurements were completed at an accredited laboratory, but the results obtained are as sensitive to change as the assays allow – which is to say that biochemical analyses may not be sensitive enough to identify changes related to the strength

training intervention. Anthropometric and morphological measurements were all obtained by the principal researcher to avoid inter-investigator bias and to strengthen reliability and validity. The reliability is, however, determinant on the consistency of the investigator, the anatomical marking of measures, and the skill with which the researcher obtained these measures. It is possible that investigator error could have affected some of the results. While certain medications were excluded, such as cholesterol lowering medication, oestrogen or general hormone replacement, and other medications were reported on there were individuals who took bio-identical supplements or other prescription medication (anti-depressants were commonly acknowledged) and the effect of these on the results is not known. As far as the exercise programme design is concerned, the prescription of intensity was monitored via the supervision of sessions, but not by a direct physiological measure, such as heart rate. Thus, it is acknowledged that some individuals may not have adhered to the intensity as prescribed.

Despite the limitations of this study it has a number of strengths. The inclusion criteria delineated to a homogeneous sample of post-menopausal females within a narrow age range of ten years who were Caucasian, not taking hormone replacement therapy, did not smoke, were sedentary on recruitment and who were not taking any cholesterol-lowering medication. As such this study adds valuable insight to the knowledge base on post-menopausal females, who are known to be at high risk for cardiovascular complications. Measures were repeated every four weeks providing four separate measurement sets for ExE and CoN, which is an added strength of this study as most prior literature has reflected “before and after” measures only. The range of biochemical measures obtained represents a distinguishing characteristic of this intervention too. Few studies, if any, to the author’s knowledge have measured sex hormone binding globulin, testosterone, oestradiol and HbA_{1c} repeatedly at four week intervals. With HbA_{1c} and sex hormone binding globulin accepted as ‘novel’ predictors of cardiovascular disease risk, this information provides valuable insight. The intervention was well controlled in the context of being a “real world” study. All the exercise sessions were supervised and adherence to the programme was excellent. Retention to studies is often problematic, and in this instance the small group design and the relationship between the researcher and participants positively affected compliance. The design

of the exercise intervention adds a novel aspect to the existing body of literature in that the findings indicate that higher intensity and greater frequency of exercise sessions was feasible within this population.

6 SUMMARY AND RECOMMENDATIONS

6.1 INTRODUCTION

The current investigation evaluated the effect of resistance training on plasma lipoproteins in post-menopausal females. Hypercholesterolaemia is diagnosed in approximately 37% of adult South African females, with an unknown number of undiagnosed cases in existence (Bradshaw *et al.*, 2003; Mayosi *et al.*, 2009). It is estimated that 63% of South African adult females are insufficiently active. There are alternative means of managing hypercholesterolaemia but drawbacks with regard to drug regimes include side effects, and the experience of female patients in this regard is well documented, ranging from severe muscle pain to amnesia recorded in users of statins. An alternative to drug treatment is lifestyle behaviour change, which may take the form of dietary or activity manipulation. Dietary change, by way of caloric restriction and also by means of macronutrient selection has positively affected cholesterol parameters in this population, as noted in previous research. There is less clarity as far as exercise interventions are concerned, and in this category, there appears to be a greater body of evidence for aerobic endurance training than for progressive strength training. Despite the greater volume of evidence utilising aerobic endurance interventions for the amelioration of hypercholesterolaemia, there remains little conclusive evidence for either exercise modality when post-menopausal females are considered. It is for this reason that exercise, particularly the under-studied strength training, must be evaluated for efficacy in managing elevated lipids and lipoproteins in females, particularly those without endogenous oestradiol.

The key finding of this trial was that resistance training, resulting in significant increases to upper and lower body strength, did not have a positive overall effect on the plasma lipoproteins in a sample of post-menopausal females. This may have been due to a number of mechanisms, the most obvious being the lack of endogenous oestrogen in this sample.

The novelty of this RCT lies first and foremost in the ‘FIND’ design. Compared to prior investigations, this design is the first to this author’s knowledge to engage post-menopausal females in high intensity resistance training on five days of the week, inferring consecutive training days. Additionally, this study represents a

comprehensive overview both of anthropomorphic measures as well as biochemical analyses. Most prior investigations have measured pre- and post-trial whereas in this investigation measures were repeated at four week intervals providing an important insight into the time progression of effects. The range of measures is also a marked characteristic as most previous trials have been primarily biochemically focussed with some inference to morphology, or have been focussed on the morphology without much insight into biochemical change. Certainly, there are few if any studies on post-menopausal females that combine anthropometry, morphology, strength, biochemical as well as self-reported insights. This study provides a holistic, in depth insight and it would be vital for this study design to be replicated by other investigators to ratify these findings in different populations. Compared to literature on the adherence and retention of participants to similar exercise interventions the current cohort exceeded all previous estimates of compliance. Perhaps the best comparison is the 'SWEAT' trial (sedentary women's exercise adherence trial) reported on by Cox *et al.* The current cohort was not incentivised, and yet the remarkably high levels of adherence to the programme, combined with better than expected retention are noteworthy. What did prove difficult was recruitment to the study, in the context of strict inclusion criteria, a narrow age range, and a relatively small population to draw from. It would be important to compare the current recruitment difficulty with the experiences of other investigators, in order to better understand this element of conducting exercise intervention research. Certainly of importance is the finding that a primary motivator amongst participants was 'loyalty' to the principal investigator. This should be considered in future exercise interventions trials to enhance retention to the programmes. Whether this motivator would be applicable to male samples, or to different age ranges is questionable, and needs further evaluation.

The sample itself, comprising post-menopausal females, is not a 'new' cohort but is an under-studied group. Particularly with respect to cholesterol research which is controversial from the perspective of statin drug prescription, with under 30% of all trial participants to date having been female. In this context, statin drug prescription is controversial and the alternatives have not yet been adequately assessed, hence the dire need for more research into exercise and dietary interventions specifically in

post-menopausal females samples. Indeed, whether decreasing cholesterol is positive is also in question and should be investigated further.

The clinically significant decreases noted for waist circumference and diastolic blood pressure following 12 weeks of high intensity resistance training in middle aged females are not in themselves new findings, as other studies have reported similar changes in similar cohorts. What is noteworthy is the apparent 'independence' of these changes as, for example, the 5% decrease to waist circumference was not associated with other risk reductions such as reduced risk associated with plasma lipoproteins. The lack of association may be considered interesting, as existing literature does suggest relationships between variables, and as such, the inference that managing one risk factor (abdominal visceral fat deposits) improves another risk factor (dyslipidaemia). As association does not infer causation, it is possible that in this specific cohort these associations have been challenged as non-existent, and any inference of causation in previous literature exposed as misleading. The lack of notable changes in the other morphological measures and calculations (fat content, sum of skinfolds, BMI, WHR) is surprising at first glance, particularly in the context of the intensity and frequency of training, however with the body's drive toward homeostasis of energy balance in mind, this is perhaps not so surprising. Despite no overall change to dietary intake it is likely that appetite increased and diet did shift, even imperceptibly, to account for the increased energy demands. Ideally replication of this study design with enhanced dietary control would provide valuable insight into these mechanisms.

6.2 THE STATISTICAL HYPOTHESES

Table 6.1 presents the outcomes of the Statistical Hypotheses. The 'null' hypothesis is rejected for chest, back and leg strength; diastolic blood pressure; waist circumference; waist to hip ratio and waist to stature ratio in ExE. It is rejected for body mass index in CoN as this variable increased over time.

Table 6.1: Summary of outcomes of Statistical Hypotheses

Null Hypothesis	Variables	ExE	CoN
1) Strength			
	Chest, Back, Leg	**Reject**	N/A
2) Plasma Lipoproteins			
	LDL-C, HDL-C, TriG, TotC	Accept	Accept
3) Biochemical Measures			
	HbA1c, SHBG	Accept	Accept
4) Hormone Levels			
	Oestradiol, Testosterone	Accept	Accept
5) Blood Pressure			
	Systolic	Accept	Accept
	Diastolic	**Reject**	Accept
6) Anthropometry&Morphology			
	Body Mass, all girth measures,	Accept	Accept
	BMI	Accept	**Reject**
	Waist circumference, WHR, WSR	**Reject**	Accept
7) Dietary Intake			
	Total caloric intake, carbohydrate intake, protein intake and fat intake (per day)	Accept	Accept
8) Energy Expenditure (additional to intervention sessions)	Total energy expenditure (per day)	Accept	Accept

6.3 RECOMMENDATIONS

6.3.1 EXERCISE PROGRAMME: 'F.I.N.D' DESIGN

Studies engaging post-menopausal females often refer to the participants as "older" or "elderly" individuals. The nature and intensity of the exercise utilised in interventions is generally low to moderate whether aerobic or strength based. Menopause occurs at the age of 52 years on average, globally. It is the observation of this researcher that post-menopausal females are economically active, youthful, and in the current modern world, have a possible thirty years of life to live in the climacteric. The current sample enjoyed the higher intensity training and body composition changes were noted and in turn, motivating factors. Future research should consider higher intensity activity, and refrain from referring to the sample as "old" or "elderly".

The modern world is changing, with attendant time pressures. More research is required into the efficacy of strength training as can be undertaken at commercial wellness centres (in South Africa the commercial wellness centres are *VirginActive*® or *Planet Fitness*® facilities, as well as some smaller, privately owned gymnasiums). Many post-menopausal females (herewith acknowledgement of socio-economic

disparities in South Africa) in 2013 are willing and able to obtain membership at these facilities. Those unable to join an established centre could be assisted in more economically viable ways. Strength training can be completed effectively in thirty minute sessions, daily, to potentially greater effect than an endurance activity of similar duration.

6.3.2 YEARS POST-MENOPAUSE

The current sample were canvassed as to “years since menopause” however the sample was not stratified according to this criterion. The age range was minimised (55 to 65 years) to avoid an age-effect, but this may not have eliminated a potential menopause-age effect. It is posited that there is a ‘window of opportunity’ (the first five years post-menopause) and that changes to lifestyle and/or drug regimes need to be implemented during this time while the oestrogen receptors remain active, for the benefits to accrue (Stevenson, 2009). Future research should stratify samples according to ‘years since menopause’ in order to gain greater clarity on the ‘window of opportunity’.

6.3.3 MANNER OF MENOPAUSE

Surgical menopause occurs when a total hysterectomy has been performed, whereas natural menopause occurs when the ovaries are present, and fail naturally. Surgical menopause may take place at any point during the woman’s reproductive years, for a number of medical reasons. Individuals in this study had undergone surgical menopause but the sample was not stratified according to this factor: the fact that some participants had had hysterectomies in excess of twenty years prior to participation may indeed have affected the response to the intervention. It is recommended that research be devoted to extrapolating differences, if any, between natural and surgical menopause.

6.3.4 RESPONDERS VS NON-RESPONDERS

On an individual level ~50% of the participants responded positively to the intervention. This finding is not reflected in the mean data. A reason for this disparity in responses in a homogeneous sample requires further investigation. There is a need for research into possible genetic markers controlling response to interventions such as this one. Reporting of findings in similar trials should incorporate mean data and individual responses in all future reports.

6.3.5 COMPARISON OF ACUTE AND CHRONIC EFFECTS OF EXERCISE

This intervention focussed on the chronic effects of a resistance training programme. It would be interesting to compare the results of a chronic strength training intervention to acute effects of a strength training session in the same cohort, as it is known, for example, that the acute effects of exercise beneficial to glucose absorption in diabetic conditions are fundamental to utilising exercise as a means of managing the condition.

6.3.6 WAIST CIRCUMFERENCE FINDINGS

Waist circumference is an important anthropometric measure both in research settings and in the context of the layperson. It is an easy measure to take, requires no expensive equipment, and is reliable as an indicator of cardiovascular disease risk. The results of the current study are encouraging. The significant decrease to waist circumference over 12 weeks infers a direct drop in risk of associated cardiovascular disease. Replication of this methodology in a similar sample of post-menopausal females would be important to ratify this result.

6.3.7 THE WAIST TO STATURE RATIO

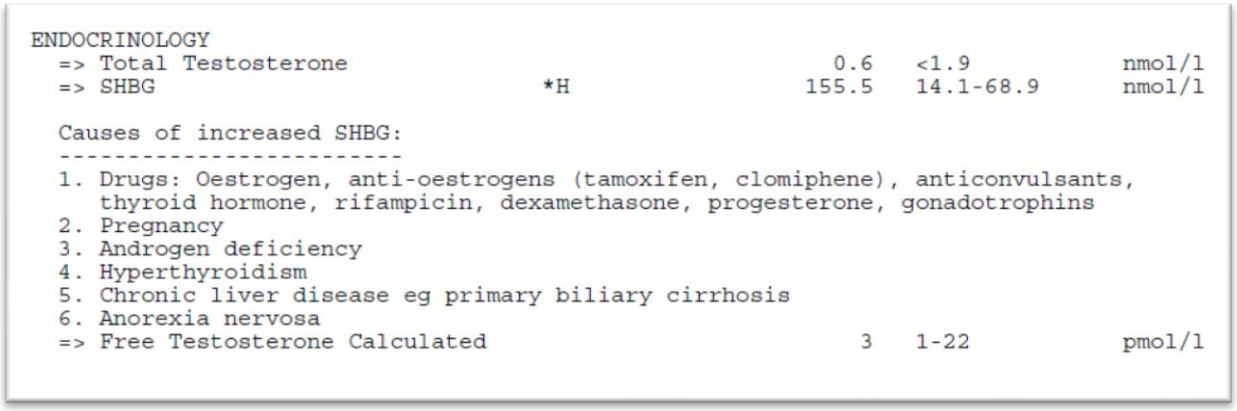
A measure used quite frequently with reference to child health, it is touted by some authors (Ho *et al.*, 2003; Hsieh & Muto, 2005) as one of the most effective anthropomorphic measures for predicting or identifying cardiovascular risk. The waist-to-stature ratio (WSR) was not found to correlate particularly well to cardiovascular risk factors in the current cohort. However, to the knowledge of the author it is not a measure that is frequently used in the available literature pertaining to post-menopausal females. Further research should include this ratio to ratify its usefulness as an accessible measure for assessing risk for chronic diseases of lifestyle related origin.

6.3.8 GLYCATED HAEMOGLOBIN

As HbA_{1c} is recognised as an important indicator of future cardiovascular risk as well as highlighting presence of or risk for diabetes, this biochemical marker warrants further attention. Few studies have evaluated the effect of exercise on the HbA_{1c} to date. Effect of strength training and endurance-type training, as well as combination training would add value to the knowledge-base. Analysis of exercise and HbA_{1c} in different populations would also provide valuable insight.

6.3.9 SEX HORMONE BINDING GLOBULIN

During the course of this research programme it became clear that there is a limited understanding of the potential applicability of SHBG to cardiovascular risk assessment. Medical practitioners were approached when the biochemical report pages were received from the laboratory with warning notes pertaining to either 'extremely high' or 'extremely low' levels of SHBG in the cohort (Figure 6.1). It was the researcher's ethical obligation to ensure that such warnings were conveyed to the participants so that medical advice could be sought if desired. The medical fraternity were, however, uncertain of how to address SHBG in the knowledge that no underlying disease-state (as itemised in Figure 6.1) was present in the affected individuals.



```
ENDOCRINOLOGY
  => Total Testosterone                              0.6    <1.9          nmol/l
  => SHBG                          *H              155.5    14.1-68.9     nmol/l

  Causes of increased SHBG:
  -------------------------
  1. Drugs: Oestrogen, anti-oestrogens (tamoxifen, clomiphene), anticonvulsants,
     thyroid hormone, rifampicin, dexamethasone, progesterone, gonadotrophins
  2. Pregnancy
  3. Androgen deficiency
  4. Hyperthyroidism
  5. Chronic liver disease eg primary biliary cirrhosis
  6. Anorexia nervosa
  => Free Testosterone Calculated                    3    1-22          pmol/l
```

Figure 6.1: Excerpt from biochemical report highlighting SHBG result warning

Anecdotally, one medical practitioner suggested that the researcher should report back to the participant that elevated SHBG suggested "greater sexiness". While this is a humorous response it is indicative of the sparse research connecting SHBG to cardiovascular risk: the link between menopause, greater androgenicity, lower SHBG and cardiovascular risk is apparent and further research is warranted in order to raise awareness of this biochemical risk marker. With apparently limited research to date, it is not yet clear how useful SHBG could be in identifying risk, nor whether lifestyle changes can ameliorate this risk.

6.3.10 INFLAMMATORY MARKERS

No investigation into biochemical markers of systemic inflammation was attempted during this research study. Prior research has indicated that physical activity may ameliorate subclinical inflammation in post-menopausal females (Hamer *et al.*,

2012). Inflammation, as indicated by serum levels of C-reactive protein and Interleukin-6 for example, has been implicated in the development of coronary heart disease, stroke and mortality there from (Esteghamati *et al.*, 2012). Research into the effect of exercise (both aerobic and resistive in nature) as well as dietary intake on inflammatory markers in specific populations, especially females both pre- and post-menopause, is warranted.

6.3.11 RESEARCHER-PARTICIPANT INTERACTION TIME

A significant drawback in the current design was that the exercise sample had daily face-to-face contact with the researcher at exercise sessions whereas the control group only met every four weeks for measurements. This differential in contact time may have influenced the results and future studies may benefit from a "placebo" activity to mirror the "face-time" in both samples.

6.4 CONCLUDING STATEMENT

This randomized controlled trial aimed to evaluate the effect of a progressive resistance training programme on the plasma lipoproteins in a cohort of post-menopausal females in the absence of hormone replacement therapy. ExE results (n=30) indicate that strength training over the course of 12 weeks did not positively affect plasma lipoproteins. Individual data analyses revealed, however, that positive lipoprotein outcomes were experienced in ~50.0% of ExE, suggesting the existence of "responders" and "non-responders" in this homogeneous sample.

PUBLICATIONS

JOURNAL ARTICLES

1. Viljoen JE and Christie CJ (2011). Resistance training and changes to plasma lipoproteins in post-menopausal women. *South African Journal of Sports Medicine*, 23 (2): 40-44.

Please note: The author's maiden name is Kelly, and some early publications may reflect this surname.

CONFERENCE PROCEEDINGS

*	Denotes an Oral Presentation
#	Denotes a Poster Presentation
*#	Denotes an Oral-Poster Presentation (5 minutes Oral, Poster on Display)

1. Kelly JE and Christie CJ (2009). *Factors affecting the compliance of post-menopausal women over the course of a 24 week progressive resistance training programme*#. South African Sports Medicine Association Congress.

2. Kelly JE and Christie CJ (2009). *Factors affecting the compliance of post-menopausal women over the course of a 24 week progressive resistance training programme*#. ASICS Conference of Science and Medicine in Sport, Hamilton Island, Australia.

3. Viljoen JE and Christie CJ (2010). *Post-menopausal cardiovascular health: a review*#. ASICS Conference of Science and Medicine in Sport, Port Douglas, Australia.

4. Viljoen JE and Christie CJ (2011). *Aging or chronic disease: which is the real culprit?**. Organisational Design and Management Conference, Grahamstown, South Africa.

5. Viljoen JE and Christie CJ (2011). *Excellent work-place quality: questionable socio-economics**. Organisational Design and Management Conference, Grahamstown, South Africa.

6. Viljoen JE and Christie CJ (2011). *The effect of progressive resistance training on the plasma lipoproteins in post-menopausal women**#. Medical Research Council Research Day, Cape Town, South Africa.

7. Viljoen JE and Christie CJ (2012). *Progressive resistance training and body composition in post-menopausal females**#. Medical Research Council Emerging Scientists Conference, Cape Town, South Africa.

8. Viljoen JE and Christie CJ (2012). *The effect of progressive resistance training on cardiovascular risk factors in post-menopausal women*. Rhodes University Inter-Disciplinary Postgraduate Conference, Grahamstown, South Africa.

9. Viljoen JE and Christie CJ (2013). *Does HbA_{1c} respond to strength training in post-menopausal females?**. European Congress of Sport Science, Barcelona, Spain.

10. Viljoen JE and Christie CJ (2013). *Does HbA_{1c} respond to strength training in post-menopausal females?**. Rhodes University Inter-Disciplinary Post-Graduate Conference, Grahamstown, South Africa.

11. Crymble T, Viljoen JE and Christie CJ (2013). *Efficacy of a 12 week walking intervention on blood pressure in previously sedentary black African females*. 15th Biennial South African Sports Medicine Association Conference, Wild Coast, South Africa.

12. Viljoen JE and Christie CJ (2013). *Does blood pressure respond to strength training in post-menopausal females?***.** 15th Biennial South African Sports Medicine Association Conference, Wild Coast, South Africa. *(Note: was unable to attend conference and Oral presentation was sent as a Poster presentation)*.

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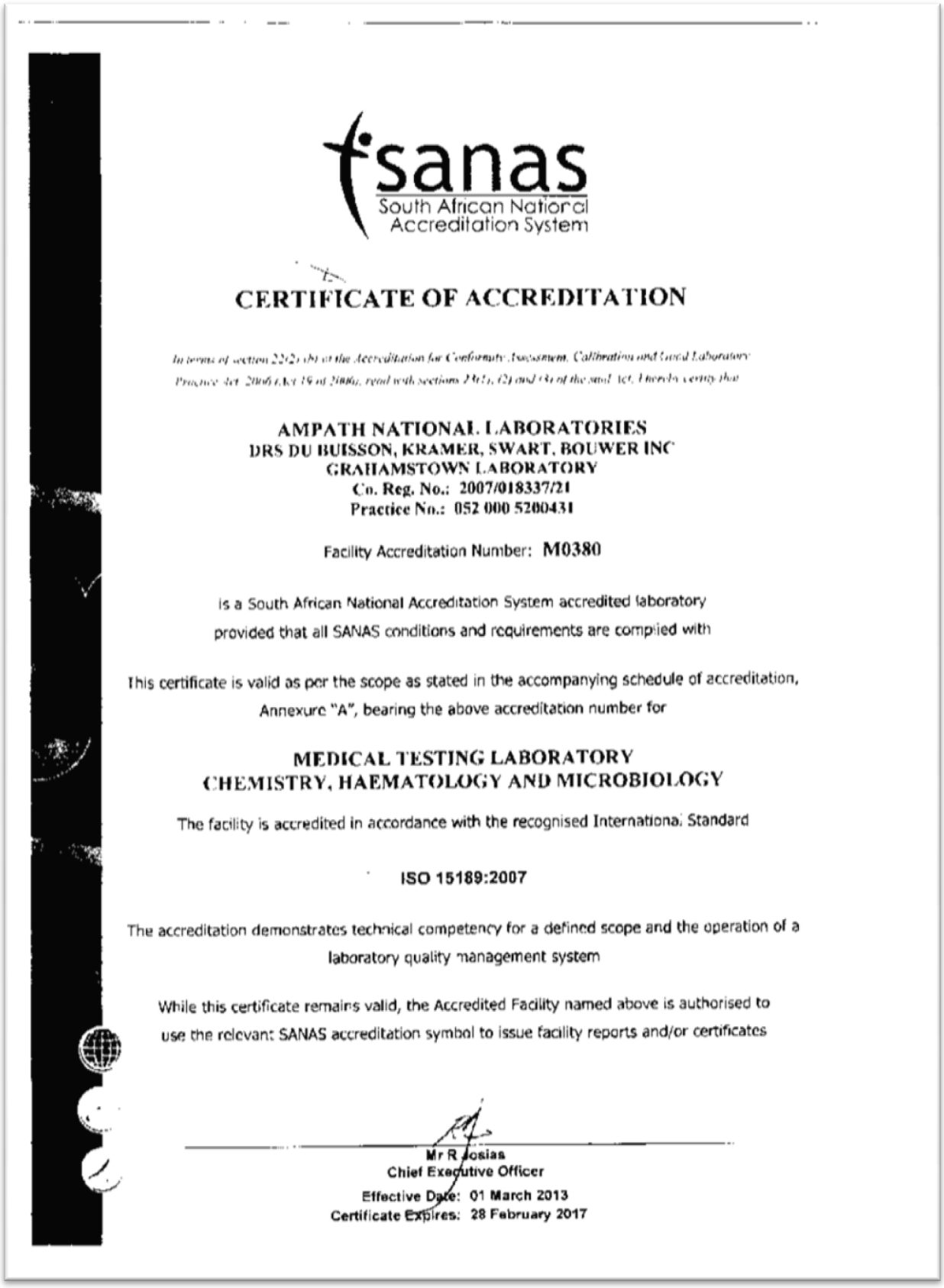
APPENDIX A: LABORATORY ACCREDITATION



sanas
South African National Accreditation System

CERTIFICATE OF ACCREDITATION

In terms of section 22(2) (b) of the Accreditation for Conformity Assessment, Calibration and Good Laboratory Practice Act 2006 (Act 19 of 2006), read with sections 23(1), (2) and (3) of the said Act, I hereby certify that

AMPATH NATIONAL LABORATORIES
DRS DU BUISSON, KRAMER, SWART, BOUWER INC
GRAHAMSTOWN LABORATORY
Co. Reg. No.: 2007/018337/21
Practice No.: 052 000 5200431

Facility Accreditation Number: **M0380**

is a South African National Accreditation System accredited laboratory provided that all SANAS conditions and requirements are complied with

This certificate is valid as per the scope as stated in the accompanying schedule of accreditation, Annexure "A", bearing the above accreditation number for

MEDICAL TESTING LABORATORY
CHEMISTRY, HAEMATOLOGY AND MICROBIOLOGY

The facility is accredited in accordance with the recognised International Standard

ISO 15189:2007

The accreditation demonstrates technical competency for a defined scope and the operation of a laboratory quality management system

While this certificate remains valid, the Accredited Facility named above is authorised to use the relevant SANAS accreditation symbol to issue facility reports and/or certificates

Mr R Josias
Chief Executive Officer
Effective Date: 01 March 2013
Certificate Expires: 28 February 2017

APPENDIX B: ETHICAL APPROVAL

Human Kinetics and Ergonomics

Ethics Committee Report

RHODES UNIVERSITY
Where leaders learn

Applicant's Name: Janet Kelly
Type of Research: PhD Thesis
Project Title: The effect of progressive resistance training on the cardiovascular health, body composition and quality of life in post-menopausal women.
Supervisor: Dr. C Christie
Report compiled: 12 January 2010

HKE Ethics Committee Comments

Reviewers	Comments
A	All suggestions have been effected – final application is approved
B	N/A
C	N/A

Approved	Approved, on condition that suggestions have been effected	Request for rework and resubmission	Rejected
✓			

Remark:
The application has unanimously been approved by the members of the Human Kinetics and Ergonomics (HKE) Ethics Committee.

Signed

Miriam Mattison.

Chairperson
Human Kinetics and Ergonomics Ethics Committee

RHODES UNIVERSITY
Where leaders learn

Rhodes University Ethical Standards Committee, Rhodes University, P O Box 94, Grahamstown, 6140
Tel: +27 46 603 8399 • Fax: +27 46 636 1205 • email: M.Goebel@ru.ac.za

29 May 2011

Dr C. Christie
Department of Human Kinetics and Ergonomics
Rhodes University
PO Box 94
GRAHAMSTOWN
6140

Dear Dr Christie,

Ethics Clearance 2011Q1-1: The effect of progressive resistance training on the blood lipid profile in post-menopausal women

This letter confirms that a research proposal with tracking number 2011Q1-1 and title: ***The effect of progressive resistance training on the blood lipid profile in post-menopausal women*** was given ethics clearance by the Rhodes University Ethical Standards Committee at its meeting of 6 May 2011 pending clarification of certain concerns. These concerns were subsequently satisfactorily addressed and include the latest recommendations conveyed to yourself.

Please ensure that the ethical standards committee is notified should any substantive change(s) be made, for whatever reason, during the research process. This includes changes in investigators. Please also ensure that a report is submitted to the ethics committee on completion of the research. The purpose of this report is to indicate whether or not the research was conducted successfully, if any aspects could not be completed, or if any problems arose that the ethical standards committee should be aware of.

Please be aware that Professor Dowse will remain available for consulting about any of the aspects of the study should such a need arise.

Yours sincerely

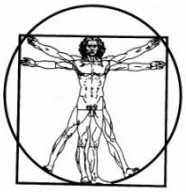
M. R. JOBSON

Former Chairperson Rhodes University Ethical Standards Committee (RUESC)
on behalf of Professor M. Goebel: present Chairperson RUESC.

Note:

1. This clearance is valid from the date on this letter to the time of completion of data collection.
2. The ethics committee cannot grant retrospective ethics clearance.
3. Progress reports should be submitted annually unless otherwise specified in the clearance letter.

APPENDIX C: PRELIMINARY FORMS AND CONSENT DOCUMENTATION



DEPARTMENT OF HUMAN KINETICS AND ERGONOMICS
RHODES UNIVERSITY, GRAHAMSTOWN

[This research has been cleared by the Ethics Committee for research involving human subjects through the Department of Human Kinetics and Ergonomics]

YOUR HELP NEEDED!

DO YOU FIT THE FOLLOWING CRITERIA??:

- **POST-MENOPAUSAL FEMALE**
- **AT LEAST 12 MONTHS POST-MENOPAUSE**
- **TAKING ESTROGEN REPLACEMENT**
- **OR A NON-HRT TAKER [BOTH CATEGORIES ARE NEEDED!]**
- **AGE 50 – 70**
- **HEALTHY [NO HEART, LUNG, LIVER, KIDNEY DISEASE]**
- **NON-SMOKER**
- **SEDENTARY [LESS THAN 30MIN OF MODERATE ACTIVITY DAILY]**

WOULD YOU LIKE TO:

- **HAVE FREE PERSONAL TRAINING SESSIONS?**
- **EMBARK ON A STRUCTURED EXERCISE PROGRAMME?**
- **DERIVE HEALTH BENEFITS?**
- **JOIN A GROUP OF LIKE-MINDED WOMEN, IN A SOCIAL SMALL GROUP SETTING, IN A 'PRIVATE' GYM?**
- **BE PART OF A SCIENTIFIC STUDY – CONTRIBUTING TO RESEARCH?**

CAN YOU COMMIT TO:

- **3 x WEEKLY SESSIONS OF 30-45MINS DURATION EACH?**
- **CONTINUE YOUR SESSIONS FOR 6 MONTHS [24 WEEKS]BETWEEN FEBRUARY AND JULY 2010?**

DON'T HESITATE! CONTACT JANET KELLY ON 072 180 7757 OR EMAIL JANET.KELLY78@GMAIL.COM NOW!

FREE exercise training...

FREE health testing...

WHO CAN APPLY?

Check these criteria:

- ***WOMEN*, age 55 – 65 years**
- **Post-menopause (**at least 1 year with no menstruation**)**
- **Inactive/sedentary** (*not sure? Check with Janet!*)
- **Healthy (**no heart, lung, liver, kidney disease**)**
- ***NOT* taking hormone replacement medication OR cholesterol medication**
- **Caucasian**
- **Non-smokers (**OR at least 1 year since smoked**)**

WHAT IS THIS ABOUT?

A PhD level research project investigating the link between exercise and heart health in women. As a participant you would be a part of a small group, exercising in a quiet and private environment, with qualified supervision.

Interested? Turn page over for more information!

HOW DO I GET INVOLVED?

There are LIMITED SPACES so contact JANET VILJOEN now to express interest:

EVEN IF YOU'RE NOT 100% SURE – LET'S CHAT!!

Email Janet on: janet.viljoen78@gmail.com
Call Janet on: 072 180 7757 (or SMS and I will be in touch)

WHEN IS THIS TAKING PLACE?

May/June 2012: starting with an information meeting – you won't be asked to commit until we've met & I've explained it all.

THREE months of health monitoring, THREE months of exercise... (Sound "hectic"? It really isn't!)

WHAT ARE THE BENEFITS TO ME?

FREE health screening and exercise sessions
IMPROVED health status = LOWER risk of heart disease
STRENGTH improvement ... LOSE CENTIMETRES.... ☺

This research takes place in the Department of Human Kinetics and Ergonomics at Rhodes University. Ethical approval for this research has been granted by the Rhodes University Ethical Standards Committee for research involving human participants.

For email distribution:
Department of Human Kinetics and Ergonomics, Rhodes University
PhD Research: Participants Required!

I am embarking on a study investigating the effects of progressive resistance training on health parameters in post-menopausal women.

The inclusion criteria are as follows:

- Women, age 55 – 65
- Post-menopausal (at least 12 months without menses)
- Healthy (no heart, lung, liver or kidney disease)
- Not taking (past or present) hormone replacement therapy (or any bio-identical derivative thereof)
- Not taking cholesterol lowering medication
- Sedentary (defined as being active for less than 20minutes on fewer than three days of the week)
- Non-smokers (defined as never having smoked, or having completely ceased smoking at least 12 months prior)
- Caucasian (Cholesterol is one of the parameters under investigation, the known and documented race-related differences in cholesterol profiles had to be considered. Goedecke *et al.* (2010) outline existing differences in South African race groups.)

If you think you fit the profile (and if you're not sure, please contact me to discuss your doubts!), and would be willing to participate in a programme of exercise for three months, with sessions on five days of the week (each session lasting 30-40minutes) please contact Janet Viljoen:

- Email: janet.viljoen78@gmail.com
- Mobile: 0721807757
- Home (a/h):0466224770

This research study has been approved by the Rhodes University Ethical Standards Committee for research involving human participants.

The research is funded by:

- **The South African MEDICAL RESEARCH COUNCIL (Self-Initiated Research Grant)**
- The National Research Foundation (NRF) (Incentive funding for rated researchers)
- Janet Viljoen is funded by an "In Country PhD Scholarship" from the "Deutsche Akademiese Austausch Dienst" (DAAD) via the NRF

INTRODUCTORY MEETING: PhD RECRUITMENT

1. **Introduce myself, Candice, Tegan**

2. **Reason for this meeting:**
   Spell out exactly what committing to this project entails
   Provide enough information for you to make an informed, voluntary decision
   Describe the exercise intervention, as well as measurements to be taken
   Provide a forum for questions

3. **What is this project about?**
   Health of post-menopausal women: specifically cardiovascular, or heart health
   Investigate an alternative to drug therapy, in a lifestyle alteration, and assess a "dose response" relationship between the intervention prescribed, and the reactions measured.

4. **What is the exercise intervention?**
   - The intervention is designed as follows:
   - Three months, or twelve weeks, of resistance training that will become gradually more difficult as you gradually improve in strength.
   - The format is exercise on 5 days of the week (Mon-Fri) for approximately 30-40 minutes.
   - The time of these sessions is something we will discuss, and I hope that we can offer a suitable range of times so as to suit all your lifestyle requirements.
   -

5. **What measurements will be taken?**
   - Before we begin the intervention, and then every four weeks, a batch of measurements will be taken:
   - I will do basic body composition and anthropometric measures, such as stature, mass, and selected girth measures. I will also use skinfold callipers to assess subcutaneous levels of adipose tissue.
   - Tegan will re-assess your 1-repetition maximum on selected exercises to assess the change in your musculo-skeletal strength over time, and also to ensure that we are 'pegging' the exercises at the correct intensity. Tegan will also conduct a 'bio-electrical impedance' analysis, to assess body composition.
   - The staff at Du Buisson's pathology laboratory will draw blood for the various biochemical analyses.
   - There are also two questionnaires that you will need to fill in every four weeks, and return to me. I will also require a dietary recall diary every four weeks, which you will soon become adept at completing!
   -

6. **Pre-screening:**
   - The first batch of measurements effectively determine for me whether or not you are eligible to be a part of this study. We will screen for latent diabetic conditions, as well as safety to exercise. Please consider this process entirely for your benefit, as you will not be charged for any of the testing, even if we cannot include you in the study.
   - Apart from initial blood work, there will be a short physical examination by Dr Jameson, and I will run a submaximal exercise ECG. Dr Jameson reviews the ECG printout and declares you healthy to exercise based on the functioning of your heart during that short, light bout of stationery cycling.
   -

7. **So, none of this has put you off: what now?**
   - Collect your participant pack; collect your participant code keyring.
   - Sign up for pre-screening slots: Jameson and Du Buissons.
   - Take information home, complete all documentation, and please bring back with you to pre-screening.
   -

8. **"Gym" etiquette**
   - Clothing: wear whatever is comfortable. Prefarably pants, shorts or culottes or split skirts.
   - Shoes: preferably some form of athletic shoe, closed.

- Hand towel and water bottle: please do bring a small hand towel with you to mop your brow, and a water bottle with your own water. This is important, and becomes more so if the weather is warmer! Its also a matter of hygiene.
- Each session will be supervised by a post-graduate student, myself or Candice.
- We are there to guide you in correct execution of exercises, ensure your continued safety, and please note that supervisors will have cellphones and access to emergency contact information.
-

9. Admin

- Participant codes: please only use your codes when you fill in any paperwork, including referencing at Du Buisson's and when I take your measurements.
- This ensures anonymity – should I need to refer to the individual I will have a master list but it will be stored separately to the data, thus, no-one can ever trace the results to you directly.
- For the purposes of objectivity – I am afraid I cannot share your results with you during the intervention. After the intervention, its all yours! If there are problematic results or your health is in jeopardy of course I will ensure that we discuss this, but otherwise, it'll remain a mystery for 12 weeks!

LETTER TO LOCAL DOCTORS:

1

June 2011

Dear Medical Professional

Re: PhD Research investigating the effect of resistance training on health parameters in post-menopausal women

I am embarking on research which has as its objective an investigation into the effect of progressive resistance training over the course of three months (12 weeks) on cardiovascular health parameters in a sample of post-menopausal women.

The parameters under investigation are plasma glucose, plasma lipoproteins, blood pressure, body composition and musculo-skeletal strength.

The criteria for inclusion into the study are as follows:

- Women, age 55 – 65
- Post-menopausal (at least 12 months without menses)
- Healthy (no heart, lung, liver or kidney disease)
- Not taking (past or present) hormone replacement therapy (or any bio-identical derivative thereof)
- Not taking cholesterol lowering medication
- Sedentary (defined as being active for less than 20minutes on fewer than three days of the week)
- Non-smokers (defined as never having smoked, or having completely ceased smoking at least 12 months prior)
- Caucasian (Cholesterol is one of the parameters under investigation, the known and documented race-related differences in cholesterol profiles had to be considered. Goedecke *et al.* (2010) outline existing differences in South African race groups.)

I will require 60 participants in total, and will in all probability run more than one "phase" of the exercise intervention in order to accommodate the sample. There will be one phase in 2011, and a further one in early 2012.

I would be most grateful if you would bear this study in mind and mention it to any clients/patients who you believe may benefit from this study, and who fit the inclusion criteria. Please do not hesitate to contact me with any queries.

Yours sincerely

Janet Viljoen

CONTACT DETAILS:

- Email: janet.viljoen78@gmail.com
- Mobile: 0721807757 / Home (a/h): 0466224770

APPENDIX D: INCLUSION CRITERIA, INFORMATION, AND PRE-SCREENING

THE EFFECT OF PROGRESSIVE RESISTANCE TRAINING ON CARDIOVASCULAR HEALTH, BODY COMPOSITION AND QUALITY OF LIFE IN POST-MENOPAUSAL WOMEN.

RESEARCH PARTICIPANTS: INFORMATION SHEET

Thank you for agreeing to participate in this testing programme. As titled, this research will investigate the effect of a progressive resistance training programme over the course of a 24 week period on the cardiovascular health, body composition and perceptions of quality of life in a sample of post-menopausal women.

If you are successfully selected to participate in this study I trust that it will be a mutually beneficial time. You will commence an exercise regime based on resistance training exercises, in a small group setting in the Human Kinetics and Ergonomics Department laboratory at Rhodes University, and I will gather data as you progress through the programme. During your initial sessions it is important that we establish that you are healthy enough to commence with an exercise programme. To that end, Dr Celia Jameson will be present at an ECG submaximal stress-test, during which you will be required to cycle on a stationary bicycle while your heart beat is monitored. Dr Jameson will also facilitate full physical examinations, again to ensure your safety prior to undertaking any physical activity.

We also need to ensure that you are not likely to develop any diabetic-related complications and will require you to undergo a 2-hour oral glucose tolerance test, again, this is non-invasive and requires only a standard blood withdrawal for blood glucose level analysis. A pre-test full blood lipid profile test will reveal your current cholesterol values, via withdrawal of a blood sample. Please note that that ALL blood sampling will be done by qualified Nursing Sisters, at an accredited laboratory (Du Buisson's). In addition, please note that all blood tests as well as the submaximal stress-test in Dr Jameson's care are paid for by the researcher's funds.

Once we have the results of the preliminary tests, we will commence with the next round of introductory sessions. You will be required to complete Consent forms, and provide information pertaining to your health and lifestyle history. Please rest assured that all information that is gathered is treated with great confidentiality, and is coded for use. You will never be identified by name nor recognised in the presentation of the results. The information may be kept for use for a period of 24 months after your participation is complete, and this is merely for the researcher's use. The results of this study may be published in recognised academic journals if accepted.

During the introductory sessions we will deal with the complex issue of diet. We are attempting to isolate the effects of exercise alone on the health indices to be monitored, and thus we will educate you accordingly regarding weight gain and loss. We will not require you to embark on any special diet, and we will not request you to lose weight during this study. During the course of the study you will be required to submit a 24-hour dietary recall diary at regular intervals to ensure that your dietary habits are remaining consistent.

Your exercise sessions will be supervised at all times. You will select your exercise session attendance at times suitable to you from a range of times provided by the principal researcher. The sessions will take place in the Department of Human Kinetics and Ergonomics, making use of standard commercially available gym equipment as well as "free" core training equipment such as exercise balls, medicine balls, 'bosu' balls and foam rollers. The exercise programme you will commence is generic, safe, and progressive, in other words as you get stronger and fitter, the difficulty level will increase. You will be required to attend three sessions weekly, of a duration of 30-40minutes each. You may occasionally encounter different supervisors, all of whom will be postgraduate students of the Department. All will have been properly briefed by the principal researcher. You are encouraged to ask questions at any time, and to contact the principal researcher at any time should you have any comment or query.

At four week intervals measurements will be taken. These will be as follows, including the equipment that will be used:

Cardiovascular Measures	Full Blood Lipid Profile [Including Estrogen levels] Blood Pressure	Blood test [blood is then stored and analysed according to laboratory directions] Sphygmomanometer
Body Composition Measures	Body Mass Fat/Fat Free Mass Girth Measures	Electronic Scale Skinfold Calipers Tape Measure
Quality of Life Perception	Profile of Mood States Questionnaire	Questionnaires to fill in

As knowledge of your results may influence motivation levels during the testing phase and thus influence the results obtained, I cannot share the results with you during the testing period. However, once the 24 week period is completed, you will be furnished with all your results in hard copy for your interest and records. During the 24 week period we will meet on a monthly basis to discuss questions and queries. These meetings will be social and informal, and will further facilitate you getting to know the other women in the group.

Please note that resistance training is recommended for pre- and post-menopausal women. Conditions of osteoporosis are greatly assisted by weight training, and the use of more muscle fibres increases metabolic rate. Resistance training does not encourage unsightly development of muscle, but strengthens the muscles, protecting the skeletal frame.

Please do not hesitate to contact me at any stage, and please ask as many questions as you would like to!

Janet Viljoen
Principal Researcher
072 180 7757
janet.viljoen78@gmail.com

Supervisor:
Dr Candice Christie
Tel [w]: 046 603 8470
Email: c.christie@ru.ac.za

Information For Control Participants

Research Study (PhD) – Janet Viljoen

Supervisor: Dr Candice Christie

Department of Human Kinetics and Ergonomics, Rhodes University

Note: This study obtained ethical clearance from the Ethical Standards Committee at Rhodes University for research involving human participants.

Support: This study is supported by a grant awarded to Dr Candice Christie from the Medical Research Council of SA (Self-Initiated Research grant, 2011-2013).

Janet Viljoen is supported by a PhD scholarship from the Deutscher Akademiescher Austausch Dienst (DAAD) (2010-2012).

1. Introduction

The study you have expressed interest in is entitled "Progressive resistance training and the plasma lipoproteins in post-menopausal females". Designed as an "academic clinical trial" it is designed to have two participating groups: the intervention group and the control group. The intervention group in this study undertook 12 weeks of strength training. The control group (of which you would be one) undertakes ONLY the measurements and does not engage in an intervention. This is so that the findings from the strength training can be compared to similar individuals who do NOT undertake any exercise to ensure that the findings are not affected by time, or any other factor other than the exercise that could have been experienced by individuals meeting the inclusion criteria.

The strength training intervention was completed in December 2012. Without the necessary control data this study cannot be presented in academic forums nor can the thesis be completed. In addition, this study may reveal important information for medical and allied fields that must be released into the public domain – this in turn may positively influence the medical care received by females – and your contribution would be pivotal in this. It is worth noting that, to date, 30% of clinical trials have included female participants, so whatever medical care we as females are receiving is far, far under-researched and it is also worth noting that males and females respond very differently and so super-imposing what works for men does not mean it will work for women.

2. Measurements

At week 0 (the first time we meet) and every four weeks thereafter for a total of 12 weeks (four measurement sessions) the following measurements will be taken:

Anthropomorphic:

- Stature (your height)
- Body mass
- Girth measures (using a tape measure) (upper arm, chest, waist, hip, thigh and calf)
- Body fat estimation (skinfold calliper technique and bio-electrical impedance technique)

Biochemical:

These measures will be taken by a qualified nurse at the commercial pathology laboratory by arrangement.

- Full blood lipid profile (cholesterol)
- Glycated haemoglobin measure (HbA1c) (to see how your body processed glucose)
- Hormones: estrogen and testosterone

Strength:

- Three measures of strength will be undertaken, two for the upper body (chest and back) and one for the legs.

Questionnaires:

I will give you a set of questionnaires to complete every measurement session, and you will return them to me the following session, so these are completed in your own time.

- *Profile of Mood States*: a quick, 60 question form which indicates how you're 'feeling' at the time of completion. I don't analyse these as a psychologist would, I merely record the findings and use them to see whether, as a group, any mood changes occur.
- *'CHAMPS' physical activity questionnaire*: this assesses the level of activity you usually experience in a week. It is an easy questionnaire and I use it to ensure that you are not exceeding the limits of activity as prescribed for the control group.
- *Diet recall*: I will require that on three days you record ALL that you eat and drink. This is to ensure that you maintain a relatively similar dietary pattern throughout the 12 week period. I ask that you be honest, and not embarrassed by what you write down – I really am not interested in WHAT you're eating, more in that you're not changing what you eat!!! ☺
-

The time requirements for each measurement are estimated as follows:

- Anthropomorphic: ~30minutes
- Biochemical: ~15minutes
- Strength: ~30minutes
- Questionnaires (in your own time): ~30-40minutes

3. Responsibility of the Participant

If you commit to the study you will be asked to sign a consent form, and your provision of this form is your indication that you understand the study completely and that you have read and understood the requirements of you, and those of me to you. Please note that you are encouraged to ask questions throughout the participation phase and if you are not happy with anything, to report it. You have the right to withdraw at any time.

I do ask that you commit to providing honest and true answers to all questionnaires, and that you do commit to returning all documentation to me, as required. The only other thing that I ask of you is to come along for measurements when we arrange the session – it's usually quite a fun few minutes anyway! ☺

4. Responsibility of the Researcher

I commit to providing you a professional environment and service and to upholding the confidentiality implicit in obtaining medical and other personal information. I commit to providing you with your full set of results on completion of the 12 weeks, and to answering any questions fully and honestly. Should any untoward or dangerous results be found in your biochemical tests I commit to alerting you to this immediately so that you can take any action you would like to. I commit to regular communication, good organisation, good time-management and to ensuring that your participation is a pleasant experience. I am grateful for your interest and commitment to the study and I appreciate every minute of your time, and every blood sample drawn.

I commit to ensuring that your involvement is entirely FREE and this includes ANY medical appointment that is associated with your participation in this study. We are partnered with Dr Celia Jameson, and if you require any medical attention whatsoever I would arrange for you to consult with her, free of charge. At the end of the study your participation will be honoured, and we will celebrate together socially, together with a short, informal presentation of the results of the group – thus, I commit to educating you along the way.

5. Dates to diarise

We commence the study in May 2013, and herewith are suggested dates to diarise – please note that as a group we may opt to change these by a day or a time according to availability. Please note there are two groups: one in Grahamstown and one in Port Alfred. Please align yourself to the one most suitable to you.

***Please note:* ALL blood tests must be taken in a FASTED condition. Please do not eat or drink anything from 22h00 the evening prior (except water, if required). Please do not take in tea,coffee,rooibos the morning of the test either. It thus makes most sense to head over to the**

lab first thing to have the test so that you can then get your morning cuppa and breakfast straight afterwards!

Date	Grahamstown	Port Alfred
22 May 2013		Measurements at Philli Dell's residence (P.A.) at ~16h00
23 May 2013	Blood tests at Du Buissons pathology lab at 08h15 Measurements at HKE at ~16h00	
24 May 2013		Blood tests at 09h00 at Philli Dell's house
19 June 2013	Blood tests at Du Buissons pathology lab at 08h15 Measurements at HKE at ~16h00	
20 June 2013		Blood tests at Philli's at 08h15 Measurements at Philli's at ~16h00
17 July 2013		Blood tests at Philli's at 08h15 Measurements at Philli's at ~16h00
18 July 2013	Blood tests at Du Buissons pathology lab at 08h15 Measurements at HKE at ~16h00	
20 August 2013		Blood tests at Philli's at 08h15 Measurements at Philli's at ~16h00
21 August 2013	Blood tests at Du Buissons pathology lab at 08h15 Measurements at HKE at ~16h00	

At our first session (May 2013) I will include a brief introductory session and please come armed with your questions and anything else you have thought of. I look forward to meeting each one of you and embarking on this little journey of discovery together.

Please record my contact details and keep them handy!

Kind regards
Janet Viljoen
PhD Scholar

Janet:
Email: janet@viljie.com
Mobile: 072 180 7757
Home: 011 467 1105

Candice:
Email: c.christie@ru.ac.za
Office: 046 603 8470

INFORMED CONSENT FOR PARTICIPATION IN AN EXERCISE PROGRAMME
PROGRESSIVE RESISTANCE TRAINING

1. Purpose and Explanation of the Test

You will embark on a 24 week programme of resistance training, beginning at a very low intensity and gradually increasing in intensity as your physical strength and condition increases and improves. The researcher may stop the you exercising at any time should you present with signs of fatigue, dizziness, changes in your heart rate, or signs of shortness of breath and fainting. It is important for you to realise that you must report any of these symptoms to the researcher immediately.

2. Attendant Risks and Discomforts

There exists the risk that certain changes may take place during participation in physical activity. These include: abnormal blood pressure, fainting, irregular heart beat rhythm, and in rare cases, heart attack, stroke, or death. Every effort will be made to minimise these risks by evaluation of preliminary information relating to your health and fitness and by careful observations during testing. Emergency equipment and trained personnel are available to deal with unusual situations that may arise.

3. Responsibilities of the Participant

Information you possess about your health status or previous experiences of heart-related symptoms (such as shortness of breath with low-level activity, pain, pressure, tightness, heaviness in the chest, neck, jaw, back and/or arms) with physical effort may affect the safety of your exercise test. Your prompt reporting of any of these feelings during the exercise test is important. You are responsible for fully disclosing your medical history, fully report all medications (including non-prescriptive) taken recently. Please rest assured that all information is treated confidentially by the researcher.

4. Benefits to be Expected

It is well documented that participation in regular physical activity has a wide variety of health benefits to individuals of all ages. In particular, post-menopausal women benefit from resistance training as it assists in preventing the development of osteoporotic conditions, and raises metabolic rate thus assisting in weight management. By participating in this research project you will also be exposed to information pertaining to your health status, and thus learn more about your body. The measurements that will be taken every four weeks will provide valuable health-related data that will be of value to you personally as well as to the research project.

5. Enquiries

Any questions about the procedures used in the exercise test are encouraged. If you have any concerns or questions, please feel free to approach the principal researcher [Janet Kelly] or supervisor to the degree [Dr Candice Christie] at any stage. [Contact details are provided in your participant information packs].

6. Use of Medical Records

The information obtained during this exercise programme at four weekly intervals will be treated as highly confidential. It will not be released or revealed to any other person without your written consent. The information will be used for scientific purposes and statistical analysis, but will be done so under an anonymous code at all times. The information will be stored for the researcher's reference for a period of 24 months following completion of the exercise testing phase. It will not be shared with any other individual, and when used for the purposes of academic research will always be coded.

7. Freedom of Consent

I hereby consent to voluntarily participate in an exercise test to determine my exercise capacity and state of cardiovascular health. My permission to perform this exercise test is given voluntarily. I understand that I am free to stop the test at any point, if I so desire.

I have read this form and I understand the test procedures that I will perform and the attendant risks and discomforts. I have had ample opportunity to ask questions, and these have been answered satisfactorily, and thus I consent to voluntarily participate in this test.

_____ _____

Signed [Participant] **Signed [Researcher] [as Witness]**

_____ _____

DATE **DATE**

INFORMED CONSENT FOR EXERCISE TESTING

SUBMAXIMAL CYCLE ERGOMETRY TEST [BRUCE PROTOCOL]

1. Purpose and Explanation of the Test

You will perform an exercise test on a cycle ergometer. The exercise intensity will begin at a low intensity and will be advanced in stages, depending on your fitness level (as monitored by carefully noting your heart rate). The researcher/medic may stop the test at any time due to signs of fatigue, dizziness, changes in your heart rate, electrocardiogram (ECG) or blood pressure. It is important for you to realise that you may stop at any stage due to discomfort or feelings of fatigue.

2. Attendant Risks and Discomforts

There exists the risk that certain changes may take place during the test. These include: abnormal blood pressure, fainting, irregular heart beat rhythm, and in rare cases, heart attack, stroke, or death. Every effort will be made to minimise these risks by evaluation of preliminary information relating to your health and fitness and by careful observations during testing. Emergency equipment and trained personnel are available to deal with unusual situations that may arise.

3. Responsibilities of the Participant

Information you possess about your health status or previous experiences of heart-related symptoms (such as shortness of breath with low-level activity, pain, pressure, tightness, heaviness in the chest, neck, jaw, back and/or arms) with physical effort may affect the safety of your exercise test. Your prompt reporting of any of these feelings during the exercise test is important. You are responsible for fully disclosing your medical history, fully report all medications (including non-prescriptive) taken recently, and in particular those taken on the day of the test, to the medical staff.

4. Benefits to be Expected

The results obtained from the exercise test may assist in diagnosis of illness, in evaluating effect of medications, or in evaluating what physical activity you may engage in with low risk.

5. Enquiries

Any questions about the procedures used in the exercise test or the results of your own test are encouraged. If you have any concerns or questions, please feel free to approach the medical staff or the researcher.

6. Use of Medical Records

The information obtained during this exercise testing will be treated as highly confidential. It will not be released or revealed to any other person without your written consent. The information will be used for scientific purposes and statistical analysis, but will be done so under an anonymous code at all times.

7. Freedom of Consent

I hereby consent to voluntarily participate in an exercise test to determine my exercise capacity and state of cardiovascular health. My permission to perform this exercise test is given voluntarily. I understand that I am free to stop the test at any point, if I so desire.

I have read this form and I understand the test procedures that I will perform and the attendant risks and discomforts. I have had ample opportunity to ask questions, and these have been answered satisfactorily, and thus I consent to voluntarily participate in this test.

_____ _____

Signed [Participant] Signed [Researcher]

INFORMED CONSENT FOR PARTICIPATION IN RESEARCH STUDY

CONTROL GROUP

1. Purpose and Explanation of the Programme

As a member of the 'control' group you are not required to undertake any form of lifestyle change (exercise or dietary). In order to compare the findings from the group who did engage in strength training I require a group of matched women who meet the same inclusion criteria and who I shall measure in the same way. By doing this we can assess whether the natural progression of time or any other 'life' factor over the course of 12 weeks could naturally affect the findings. Your role in this study is pivotal: without your group the value of the findings is reduced and the strength of the study weakened significantly.

2. Attendant Risks and Discomforts

2.1. Measurements

At week 0 (May 2013), and every four weeks thereafter (for 12 weeks – until August 2013), a battery of measurements will be taken. These measurements will provide the researcher with a measurable indication of any changes occurring as a result of the implementation of the exercise regime. Some of these tests require the withdrawal of blood samples. There is risk inherent in the procedure of blood withdrawal, such as infection of the puncture site on the skin, and adverse reaction to blood sampling such as feelings of dizziness and faintness. All blood samples will be drawn by professional nursing staff at a registered pathology laboratory, in a sterile environment. You are requested and advised to report any feelings of light headedness to the nurse on duty when your blood sample is drawn.

3. Responsibilities of the Participant

Information you possess about your health status. Your prompt reporting of any health changes or effects related to your participation in this study is of utmost importance at all times. The responsibility of full disclosure of medical records rests with you, the participant. You are advised that all information is treated as confidential.

4. Benefits to be Expected

As a member of the control group your role in this study is that of support: without your measurements the findings cannot be adequately reported. Thus, you may not directly benefit from the exercise intervention BUT your measurements will ensure that these findings can be reported adequately and this may inform future medical care of females over the age of 50.

It is well documented that participation in regular physical activity has a wide variety of health benefits to individuals of all ages. Post-menopausal women may benefit from resistance training in that the development of muscle strength assists in the prevention of osteoporotic conditions, which increased muscle mass raises metabolism, thus assisting in the management of body weight. By participating in this research project you will be afforded the chance to exercise under controlled and safe conditions, with reduced risk to your physical self which is especially important as you undertake "formal" exercise for the first time, or after a break of a number of years. You may expect feelings of improved wellness and overall health and wellbeing and you may experience an increase in daily energy levels. The measurements that will be taken every four weeks will offer you valuable insight into your own body and physiology, and being immersed in a scientific environment may offer you the opportunity to learn about your own body, physiological processes and health in general.

5. Enquiries

Questions related to the exercise programme and any measurements taken are encouraged. Please feel free to approach the researcher (Janet Viljoen) or the supervisor to the research (Dr Candice Christie) at any stage. Contact details for both individuals are included in your information packs.

6. Use of Medical Records

The information obtained at any point during this programme will be treated as highly confidential. It will not be released or revealed to any other person without your written consent. The information will be used for scientific purposes and statistical analysis, but will be used under anonymous code at all times. The information will be stored for the purposes of the researcher's reference for a period of no longer than five years following the completion of the exercise programme. The information will not be shared with any other person and when referred to, will always be coded.

7. Freedom of Consent

I hereby consent to participate in a 12 week CONTROL group, as part of the protocol for research investigating the "effects of exercise on the health of post-menopausal women". I confirm that I have read and understand the information given to me. I understand that I am free to question the protocol at any stage, and questions that I have asked have been answered satisfactorily to date. I am aware of the need to disclose any medical conditions fully, and I am happy that this information will remain confidential. My consent is willingly and freely given, and I understand that I am free to leave the study at any time should I wish to do so.

_____ _____

Signed [Participant] **Signed [Researcher]**

_____ _____

WITNESS 1 **WITNESS 2**

_____

DATE

Department of Human Kinetics and Ergonomics, Rhodes University

PARTICIPANT SCREENING

Phd Research Project: Principal Researcher: Mrs Janet Viljoen

Supervisor to Research: Dr Candice Christie

Please indicate your AGE in years and months:		This study requires females who are 55 - 65 years of age.
Please indicate how long you have been post-menopausal [defined as 12 consecutive months without regular menses]		Only women who are at least 1 year post-menopause can be accepted to this study.
Have you taken, or are you taking any form of HRT?		This study requires women who DO NOT currently take HRT and have not done so in the past, or any bio-identical derivative of HRT.
Have you ever been told that you have DIABETES?		This study precludes individuals who are diagnosed Diabetics, either Type I or II.
Do you SMOKE?		Smokers are excluded.
Do you do any "formal" EXERCISE?		This study requires individuals who are currently "sedentary". If you participate in more than 30 minutes of light activity daily, you are too active!
Are you of CAUCASIAN descent?		Health indices are affected by race. Standardisation for the research requires a homogenous sample.
Do you have any HEART problems?		For medical safety, and for the purposes of deriving the most reliable results from this study, we cannot select individuals with known complications of these organs.
Do you have any LUNG [or related breathing] problems or difficulties?		
Do you have any LIVER problems?		
Do you have any KIDNEY problems?		

I [full name] _____ declare that the information that I have provided above is truthful and correct.

_____ _____

Signed by participant Date

This research has been cleared as ethically sound by the Rhodes University Ethical Standards Committee for research involving human participants.

PAR-Q RISK STRATIFICATION FOR EXERCISE

PLEASE NOTE THAT THE INFORMATION YOU WILL PROVIDE ON THIS FORM REMAINS STRICTLY CONFIDENTIAL. THIS INFORMATION IS REQUIRED FOR YOUR SAFETY DURING EXERCISE.

Participant Code: _____
Participation in PhD Degree Research Project
Principal Researcher: Janet Viljoen [072 180 7757]

PERSONAL DETAILS

Full Name and Surname	
Date of Birth	
Emergency Contact Person [and relationship to you] [It is best if this individual is resident in Grahamstown] Emergency Contact Person's Mobile No.	
Physician [local] Physician Contact No.	

PREVIOUS EXERCISE EXPERIENCE

1.Please outline your previous involvement, if any:

None	Housework/ Gardening/ Active work Related tasks/ Walking dog	Regular walk/ Golf/ Swimming/ Tennis etc	Socially Competitive Sport/ Very regular Gym attendance	Competitive athlete

2. How often have you exercised [per week] in the last 6 months?

Never	1 x per week	2-4 x per week	Daily

3. How much time have you spent exercising per week in the last 6 months?

0-1 hour 1-2 hours 2-4 hours >4 hours

MEDICAL HISTORY [please place an X where appropriate]

1.Have you sustained any Motor Vehicle Accident related injuries (within the past five years)? Comment:	**Y**	**N**
2. Have you sustained any Sports Injuries (within the past five years)? Comment:	**Y**	**N**
3. Have you been diagnosed with any HEART related complications?	**Y**	**N**
4. Has your Doctor ever informed you that you should NOT enter into an exercise programme without medical consent?	**Y**	**N**
5. When was your last complete physical check up? Date:	**Y**	**N**
6. Do you experience Chest Pains while exercising?	**Y**	**N**
7. Do you have High Blood Pressure? Current Value:	**Y**	**N**
8. Do you have Diabetes?	**Y**	**N**
9. Do you suffer from Asthma?	**Y**	**N**
10.Do you have any Allergies? Comment:	**Y**	**N**
11.Are you currently taking any Chronic Medication? Comment:	**Y**	**N**
12. Do you have any family history of the following: Heart, lung, metabolic disease, stroke, sudden death Comment:	**Y**	**N**
13. What level of activity is required during your average daily work? Please specify if there is a lot of upper body activity required. Comment:	**Y**	**N**

ADDITIONAL INFORMATION

1. Have you undergone SURGERY within the last 12 months? Comment:	**Y**	**N**
2. Are you currently receiving treatment [ie Chemotherapy, Psychotherapy]? Comment:	**Y**	**N**
3. Are you currently PREGNANT?	**Y**	**N**

BASED ON THE INFORMATION PROVIDED, WE RESERVE THE RIGHT TO EXCLUDE YOU FROM THE CURRENT RESEARCH PROJECT, BASED ON THE REQUIREMENTS WHICH POTENTIAL SUBJECTS MUST FULFIL, AND FOR MEDICAL SAFETY.

I, _____ [full name] do confirm that the information here provided is complete and is correct.

_____	_____
Signed [Subject for Research Study]	Date
_____	_____
Signed [Researcher]	Date

Department of Human Kinetics and Ergonomics
Rhodes University

Please be advised that this research has been cleared as ethically sound by the Rhodes University Ethical Standards Committee for research involving human participants.

PHYSICAL EXAMINATION FOR PHYSICAL ACTIVITY

PARTICIPANT CODE: **DATE:**

ASPECT TO EXAMINE	**MEDICAL PRATICITIONER'S COMMENT AND RECOMMENDATIONS**
1. Apical pulse rate and rhythm	
2.Resting blood pressure: seated, supine and standing	
3.Auscultation of lungs [note: specific attention to absence of wheezes and other sounds]	
4.Auscultation of carotid, abdominal and femoral arteries	
5.Evaluation of abdomen for tenderness	
6.Palpation and evaluation of lower extremities for oedema and presence of arterial pulses	
7.Absence or presence of tendon xanthoma or skin xanthelasma	
8.Follow up examination of orthopaedic/other medical conditions that would limit exercise testing	
9.Tests of neuralgic function, including reflexes	
10.Inspection of the skin, especially lower extremities in known diabetics [note: no subject for the purposes of this study may be diabetic]	
SIGNED: Dr CP Jameson	

APPENDIX E: DATA FORMS AND QUESTIONNAIRES

DATA SHEET: ECG TEST AND SUBMAX BICYCLE PROTOCOL

PARTICIPANT CODE: _____

Pre Stage 1	Stage 1	Stage 2	Stage 3	Stage 4	Stage 5
Heart Rate [bpm]					
BP [mmHg]					
Cycle speed [rpm]					
RPE [Borg scale]					
Watts [bicycle]					

ECG DATA

	Reference / Pre	Activity	Post-Activity
ECG Trace			
Comment			
Physician			

ANTHROPOMETRIC AND BODY COMPOSITION MEASURES

DATE	
MEASURE No	
CODE	

CONTROL PHASE GROUP, 2013

AGE (yr)	
STATURE (m)	
MASS (kg)	

BIA	
%FAT	
BP(mmHg)	

GIRTHS (mm)	
TRICEP	
CHEST	
WAIST	
HIP	
THIGH	
CALF	

SKINFOLDS	
TRICEP	
SUBSCAP	
MID-AXIL	
CHEST	
SUPRA-IL	
ABDOMEN	
THIGH	

BMI	
WHR	

SS	
BODY DEN	
%FAT	

DIETARY RECALL TEMPLATE

To be completed by participants in Janet Viljoen's PhD research study.

Participant Code: _____

Instructions:

- This information is required as it is imperative that I can demonstrate that dietary intake of the participants did not change dramatically over time. I will not be analysing the diet, merely using this data for statistical correlations.
- There are no "good" or "bad" foods – please do not feel embarrassed about recording, truthfully, what you have consumed.
- Please record everything you eat and drink over a three-day period on the following days of the week: Tuesday, Thursday and Saturday. For each day, please note everything you consume from waking until going to sleep that night (effectively 24 hours).
- Please give your best estimate of portion sizes, and quantities. Amounts may be given in numbers, volume, or weight. Please consider one "portion" to be ½ cup or 'a handful'. Please specify when referring to spoons: teaspoon/dessert spoon/serving spoon.
- Be specific about substances (such as milk: was it full cream or 2%?)
- Record ALL alcoholic beverages (and please state how many glasses, or quantity, if possible)
- Record all non-alcoholic beverages: tea (was it rooibos or ordinary? How many sugars? Brown or white sugar?) / cooldrinks (coke light 330ml; fanta orange 330ml ; iced tea, peach, 250ml)
- Record all discrete components of a meal: fillet steak, grilled (250g); brown rice; green beans...
- Please also record all "snacks" eaten between meals

This research has been cleared by the Rhodes University Ethical Standards Committee for research involving human participants.
The research is funded by:
The MEDICAL RESEARCH COUNCIL OF SOUTH AFRICA
NRF Incentive Funding for rated researchers
PhD in-country scholarship from "DAAD"

Day 1: TUESDAY (complete for ONE Tuesday only) Date: _____

Example: **07h15: 1x small cup filter coffee (plunger) with 50ml milk (2%)** **1 x large wholemeal rusk (Ouma Brand) with raisins.**	**Example:** **13h00: Two thick-cut slices brown bread, butter spread (Flora light), peanut butter (two dessert spoons).** **One small yoghurt (plain, low fat, 250ml).**

Please return to Janet AS SOON as this recall is completed! Thank you.

To be completed by participants in Janet Viljoen's PhD Research Study.

The research has been cleared by the RHODES UNIVERSITY ETHICAL STANDARDS COMMITTEE for research involving human participants.

The research is funded by the MEDICAL RESEARCH COUNCIL OF SOUTH AFRICA (SIR Grant)

CHAMPS: Community Healthy Activities Model Program for Seniors
Institute for Health & Aging, University of California San Francisco
Stanford Center for Research in Disease Prevention, Stanford University

Contact: Anita L. Stewart, Ph.D., UCSF, anitast@itsa.ucsf.edu

Date:_____

This questionnaire is about activities that you may have done in the past 4 weeks. The questions on the following pages are similar to the example shown below.

INSTRUCTIONS

If you DID the activity in the past 4 weeks:

- **Step #1** **Check the YES box.**
- **Step #2** **Think about <u>how many</u> TIMES <u>a week</u> you usually did it, and write your response in the space provided.**
- **Step #3** **Circle how many TOTAL HOURS <u>in a typical week</u> you did the activity.**

Here is an example of how Mrs. Jones would answer question #1: Mrs. Jones usually visits her friends Maria and Olga <u>twice a week</u>. She usually spends <u>one</u> hour on Monday with Maria and <u>two</u> hours on Wednesday with Olga. Therefore, the total hours a week that she visits with friends is <u>3</u> hours a week.

In a typical week during the past 4 weeks, did you…							
1. Visit with friends or family (other than those you live with)? ☐ **YES** How many TIMES a week?_____ ➔ 2 ☒ **NO**	How many TOTAL <u>hours a week</u> did you usually do it? ➔	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours

If you DID NOT do the activity:

- **Check the NO box and move to the next question**

In a typical week during the past 4 weeks, did you …							
1. Visit with friends or family (other than those you live with)? ☐ **YES** How many TIMES a week?_____ ➔ ☐ **NO**	How many TOTAL <u>hours a week</u> did you usually do it? ➔	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
2. Go to the senior center/other centre for group activity? ☐ **YES** How many TIMES a week?_____ ➔ ☐ **NO**	How many TOTAL <u>hours a week</u> did you usually do it? ➔	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
3. Do volunteer work? ☐ **YES** How many TIMES a week?_____ ➔ ☐ **NO**	How many TOTAL <u>hours a week</u> did you usually do it? ➔	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
4. Attend church or take part in church activities? ☐ **YES** How many TIMES a week?_____ ➔ ☐ **NO**	How many TOTAL <u>hours a week</u> did you usually do it? ➔	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
5. Attend other club or group meetings? ☐ **YES** How many TIMES a week?_____ ➔ ☐ **NO**	How many TOTAL <u>hours a week</u> did you usually do it? ➔	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
6. Use a computer? ☐ **YES** How many TIMES a week?_____ ➔ ☐ **NO**	How many TOTAL <u>hours a week</u> did you usually do it? ➔	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
7. Dance (such as square, folk, line, ballroom) (do <u>not</u> count aerobic dance here)? ☐ **YES** How many TIMES a week?_____ ➔ ☐ **NO**	How many TOTAL <u>hours a week</u> did you usually do it? ➔	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
8. Do woodworking, needlework, drawing, or other arts or crafts? ☐ **YES** How many TIMES a week?_____ ➔ ☐ **NO**	How many TOTAL <u>hours a week</u> did you usually do it? ➔	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours

In a typical week during the past 4 weeks, did you …							
9. Play golf, carrying or pulling your equipment (count walking time only)? ☐ **YES** How many TIMES a week?_____ ➔ ☐ **NO**	How many TOTAL hours a week did you usually do it? ➔	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
10. Play golf, riding a cart (count walking time only)? ☐ **YES** How many TIMES a week?_____ ➔ ☐ **NO**	How many TOTAL hours a week did you usually do it? ➔	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
11. Attend a concert, movie, lecture, or sport event? ☐ **YES** How many TIMES a week?_____ ➔ ☐ **NO**	How many TOTAL hours a week did you usually do it? ➔	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
12. Play cards, bingo, or board games with other people? ☐ **YES** How many TIMES a week?_____ ➔ ☐ **NO**	How many TOTAL hours a week did you usually do it? ➔	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
13. Shoot pool or billiards? ☐ **YES** How many TIMES a week?_____ ➔ ☐ **NO**	How many TOTAL hours a week did you usually do it? ➔	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
14. Play singles tennis (do not count doubles)? ☐ **YES** How many TIMES a week?_____ ➔ ☐ **NO**	How many TOTAL hours a week did you usually do it? ➔	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
15. Play doubles tennis (do not count singles)? ☐ **YES** How many TIMES a week?_____ ➔ ☐ **NO**	How many TOTAL hours a week did you usually do it? ➔	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
16. Skate (ice, roller, in-line)? ☐ **YES** How many TIMES a week?_____ ➔ ☐ **NO**	How many TOTAL hours a week did you usually do it? ➔	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours

In a typical week during the past 4 weeks, did you …							
17. Play a musical instrument? ☐ **YES** How many TIMES a week?_____ ➔ ☐ **NO**	How many TOTAL <u>hours a week</u> did you usually do it? ➔	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
18. Read? ☐ **YES** How many TIMES a week?_____ ➔ ☐ **NO**	How many TOTAL <u>hours a week</u> did you usually do it? ➔	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
19. Do heavy work around the house (such as washing windows, cleaning gutters)? ☐ **YES** How many TIMES a week?_____ ➔ ☐ **NO**	How many TOTAL <u>hours a week</u> did you usually do it? ➔	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
20. Do light work around the house (such as sweeping or vacuuming)? ☐ **YES** How many TIMES a week?_____ ➔ ☐ **NO**	How many TOTAL <u>hours a week</u> did you usually do it? ➔	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
21. Do heavy gardening (such as spading, raking)? ☐ **YES** How many TIMES a week?_____ ➔ ☐ **NO**	How many TOTAL <u>hours a week</u> did you usually do it? ➔	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
22. Do light gardening (such as watering plants)? ☐ **YES** How many TIMES a week?_____ ➔ ☐ **NO**	How many TOTAL <u>hours a week</u> did you usually do it? ➔	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
23. Work on your car, truck, lawn mower, or other machinery? ☐ **YES** How many TIMES a week?_____ ➔ ☐ **NO**	How many TOTAL <u>hours a week</u> did you usually do it? ➔	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours

In a typical week during the past 4 weeks, did you …							
****Please note: For the following questions about running and walking, include use of a treadmill.**							
24. Jog or run? ☐ **YES** How many TIMES a week?_____ ➔ ☐ **NO**	How many TOTAL hours a week did you usually do it? ➔	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
25. Walk uphill or hike uphill (count only uphill part)? ☐ **YES** How many TIMES a week?_____ ➔ ☐ **NO**	How many TOTAL hours a week did you usually do it? ➔	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
26. Walk fast or briskly for exercise (do not count walking leisurely or uphill)? ☐ **YES** How many TIMES a week?_____ ➔ ☐ **NO**	How many TOTAL hours a week did you usually do it? ➔	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
27. Walk to do errands (such as to/from a store or to take children to school (count walk time only)? ☐ **YES** How many TIMES a week?_____ ➔ ☐ **NO**	How many TOTAL hours a week did you usually do it? ➔	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
28. Walk leisurely for exercise or pleasure? ☐ **YES** How many TIMES a week?_____ ➔ ☐ **NO**	How many TOTAL hours a week did you usually do it? ➔	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
29. Ride a bicycle or stationary cycle? ☐ **YES** How many TIMES a week?_____ ➔ ☐ **NO**	How many TOTAL hours a week did you usually do it? ➔	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
30. Do other aerobic machines such as rowing, or step machines (do not count treadmill or stationary cycle)? ☐ **YES** How many TIMES a week?_____ ➔ ☐ **NO**	How many TOTAL hours a week did you usually do it? ➔	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours

In a typical week during the past 4 weeks, did you …							
31. Do water exercises (do not count other swimming)? ☐ **YES** How many TIMES a week?_____ ➔ ☐ **NO**	How many TOTAL hours a week did you usually do it? ➔	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
32. Swim moderately or fast? ☐ **YES** How many TIMES a week?_____ ➔ ☐ **NO**	How many TOTAL hours a week did you usually do it? ➔	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
33. Swim gently? ☐ **YES** How many TIMES a week?_____ ➔ ☐ **NO**	How many TOTAL hours a week did you usually do it? ➔	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
34. Do stretching or flexibility exercises (do not count yoga or Tai-chi)? ☐ **YES** How many TIMES a week?_____ ➔ ☐ **NO**	How many TOTAL hours a week did you usually do it? ➔	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
35. Do yoga or Tai-chi? ☐ **YES** How many TIMES a week?_____ ➔ ☐ **NO**	How many TOTAL hours a week did you usually do it? ➔	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
36. Do aerobics or aerobic dancing? ☐ **YES** How many TIMES a week?_____ ➔ ☐ **NO**	How many TOTAL hours a week did you usually do it? ➔	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
37. Do moderate to heavy strength training (such as hand-held weights of more than 5 lbs.(11kg), weight machines, or push-ups)? ☐ **YES** How many TIMES a week?_____ ➔ ☐ **NO**	How many TOTAL hours a week did you usually do it? ➔	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
38. Do light strength training (such as hand-held weights of 5 lbs.(11kg) or less or elastic bands)? ☐ **YES** How many TIMES a week?_____ ➔ ☐ **NO**	How many TOTAL hours a week did you usually do it? ➔	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours

In a typical week during the past 4 weeks, did you …							
39. Do general conditioning exercises, such as light calisthenics or chair exercises (do not count strength training)? ☐ **YES** How many TIMES a week?_____ ➔ ☐ **NO**	How many TOTAL hours a week did you usually do it? ➔	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
40. Play basketball, soccer, or racquetball (do not count time on sidelines)? ☐ **YES** How many TIMES a week?_____ ➔ ☐ **NO**	How many TOTAL hours a week did you usually do it? ➔	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours
41. Do other types of physical activity not previously mentioned (please specify)? _____ ☐ **YES** How many TIMES a week?_____ ➔ ☐ **NO**	How many TOTAL hours a week did you usually do it? ➔	Less than 1 hour	1-2½ hours	3-4½ hours	5-6½ hours	7-8½ hours	9 or more hours

Thank You

SELF-REPORT QUESTIONS: GROUP ExE

1. What motivated you to undertake this study? (Why did you volunteer?)

2. What has kept you motivated during the 12 weeks... day in and day out?

3. Have you felt any physical (eg; muscles, bones, joints) changes as a result of this programme? If so, what?

4. Have you felt any systemic eg; (lung function, digestive function, energy levels) changes as a result of this programme? If so, what?

5. Have you been aware of any mood or emotional changes (good or bad!) that may be attributable to this participation?

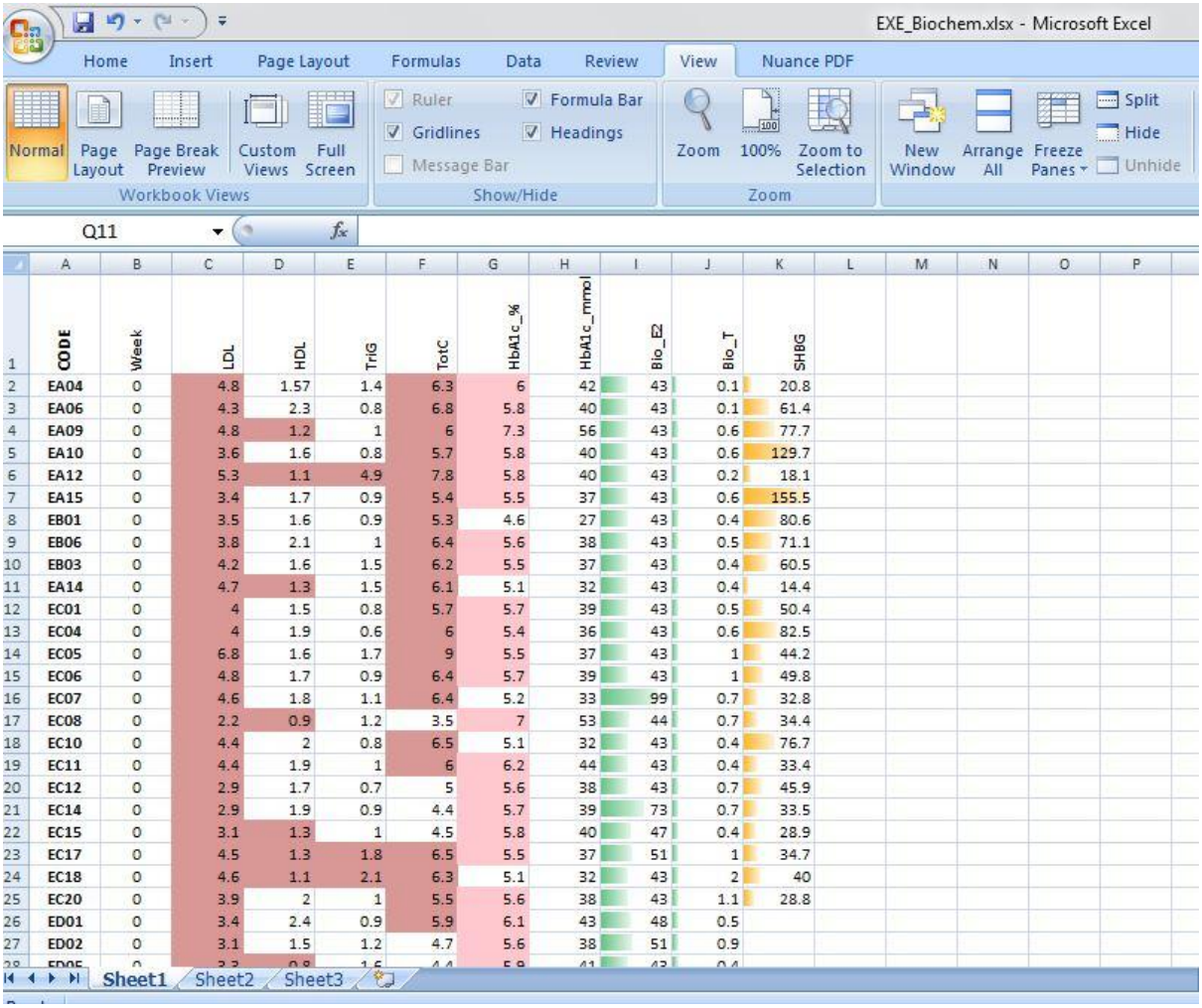
6. Would you consider continuing with activity beyond the 12 weeks... and why?

7. What is your impression of the structure of the programme - being a 5x/week session? (If you can relate this to a 3x/week design, please comment).

8. Please include general comments.

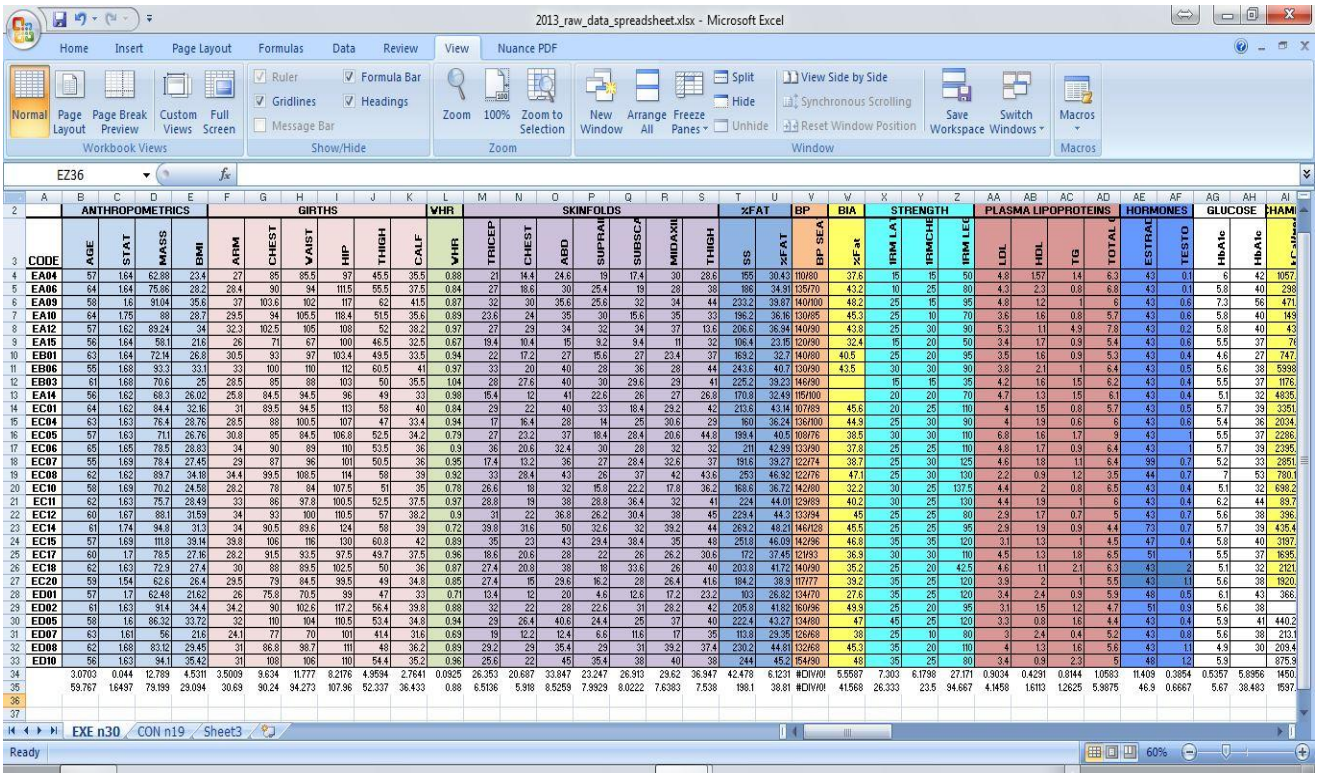
APPENDIX F: IMAGES OF RAW DATA AND DATABASE

1. Database Image



	A	B	C	D	E	F	G	H	I	J	K
1	CODE	Week	LDL	HDL	TriG	TotC	HbA1c_%	HbA1c_mmol	Bio_E2	Bio_T	SHBG
2	EA04	0	4.8	1.57	1.4	6.3	6	42	43	0.1	20.8
3	EA06	0	4.3	2.3	0.8	6.8	5.8	40	43	0.1	61.4
4	EA09	0	4.8	1.2	1	6	7.3	56	43	0.6	77.7
5	EA10	0	3.6	1.6	0.8	5.7	5.8	40	43	0.6	129.7
6	EA12	0	5.3	1.1	4.9	7.8	5.8	40	43	0.2	18.1
7	EA15	0	3.4	1.7	0.9	5.4	5.5	37	43	0.6	155.5
8	EB01	0	3.5	1.6	0.9	5.3	4.6	27	43	0.4	80.6
9	EB06	0	3.8	2.1	1	6.4	5.6	38	43	0.5	71.1
10	EB03	0	4.2	1.6	1.5	6.2	5.5	37	43	0.4	60.5
11	EA14	0	4.7	1.3	1.5	6.1	5.1	32	43	0.4	14.4
12	EC01	0	4	1.5	0.8	5.7	5.7	39	43	0.5	50.4
13	EC04	0	4	1.9	0.6	6	5.4	36	43	0.6	82.5
14	EC05	0	6.8	1.6	1.7	9	5.5	37	43	1	44.2
15	EC06	0	4.8	1.7	0.9	6.4	5.7	39	43	1	49.8
16	EC07	0	4.6	1.8	1.1	6.4	5.2	33	99	0.7	32.8
17	EC08	0	2.2	0.9	1.2	3.5	7	53	44	0.7	34.4
18	EC10	0	4.4	2	0.8	6.5	5.1	32	43	0.4	76.7
19	EC11	0	4.4	1.9	1	6	6.2	44	43	0.4	33.4
20	EC12	0	2.9	1.7	0.7	5	5.6	38	43	0.7	45.9
21	EC14	0	2.9	1.9	0.9	4.4	5.7	39	73	0.7	33.5
22	EC15	0	3.1	1.3	1	4.5	5.8	40	47	0.4	28.9
23	EC17	0	4.5	1.3	1.8	6.5	5.5	37	51	1	34.7
24	EC18	0	4.6	1.1	2.1	6.3	5.1	32	43	2	40
25	EC20	0	3.9	2	1	5.5	5.6	38	43	1.1	28.8
26	ED01	0	3.4	2.4	0.9	5.9	6.1	43	48	0.5	
27	ED02	0	3.1	1.5	1.2	4.7	5.6	38	51	0.9	

2. Raw Data Spreadsheet Image (sample sheet)



APPENDIX G: STATISTICS

Factors which had statistically significant (95% confidence interval) between group effects are presented here. For a complete set of the statistical worksheets please contact the author.

1. Between Group Analyses: ExE and CoN

Factor	Effect	*SS*	*DF*	*MS*	*F*	*p*
Body Mass	Intercept	1108277	1	1108277	1877.46	0
	Group	338	1	338	0.572	0.453305
	Error	27744	47	590		
	Period	2	3	1	0.613	0.607562
	Period*Group	30	3	10	11.202	0.000001
	Error	125	141	1		
Body Mass Index	Intercept	143493.3	1	143493.3	1685.055	0
	Group	56.3	1	56.3	0.662	0.420197
	Error	3917.2	46	85.2		
	Period	0.8	3	0.3	1.014	0.388807
	Period*Group	4.7	3	1.6	5.682	0.001067
	Error	38.3	138	0.3		
Waist Circumference	Intercept	1521487	1	1521487	2699.163	0
	Group	396	1	396	0.702	0.406427
	Error	26493	47	564		
	Period	83	3	28	3.216	0.024826
	Period*Group	151	3	50	5.861	0.000843
	Error	1207	141	9		
Estradiol	Intercept	485368.9	1	485368.9	1090.851	0
	Group	3255.5	1	3255.5	7.317	0.009548
	Error	20467.5	46	444.9		
	Period	747.1	3	249	1.304	0.275536
	Period*Group	438.4	3	146.1	0.765	0.515309
	Error	26345.5	138	190.9		
Energy Expenditure CHAMPS	Intercept	469555876	1	469555876	28.2565	0.000005
	Group	11324100	1	11324100	0.68145	0.41424
	Error	631469796	38	16617626		
	PERIOD	20577906	3	6859302	3.29333	0.02316
	PERIOD*Group	19969835	3	6656612	3.19601	0.026192
	Error	237437514	114	2082785		

Leg Strength	Intercept	848901.1	1	848901.1	353.1126	0
	Group	1900.5	1	1900.5	0.7905	0.380371
	Error	79333.7	33	2404.1		
	PERIOD	2100.7	3	700.2	2.381	0.074107
	PERIOD*Group	7355.5	3	2451.8	8.3373	0.000054
	Error	29113.9	99	294.1		
Back Strength	Intercept	72695.12	1	72695.12	328.2883	0
	Group	101.93	1	101.93	0.4603	0.502502
	Error	6864.54	31	221.44		
	PERIOD	1312.68	3	437.56	11.8081	0.000001
	PERIOD*Group	1049.81	3	349.94	9.4434	0.000017
	Error	3446.22	93	37.06		
Chest Strength	Intercept	35362.84	1	35362.84	166.164	0
	Group	1420.61	1	1420.61	6.6752	0.014715
	Error	6597.39	31	212.82		
	PERIOD	215.41	3	71.8	2.0712	0.109349
	PERIOD*Group	108.4	3	36.13	1.0423	0.37767
	Error	3223.99	93	34.67		
Glycated Haemoglobin	Intercept	255540.1	1	255540.1	5330.883	0
	Group	120.3	1	120.3	2.509	0.120074
	Error	2205	46	47.9		
	PERIOD	24.7	3	8.2	1.023	0.384381
	PERIOD*Group	95.6	3	31.9	3.959	0.009599
	Error	1111.3	138	8.1		
Thigh Girth	Intercept	477415.3	1	477415.3	5133.007	0
	Group	52.4	1	52.4	0.563	0.456806
	Error	4278.4	46	93		
	PERIOD	6.7	3	2.2	0.946	0.420222
	PERIOD*Group	20	3	6.7	2.834	0.040587
	Error	324	138	2.3		
Waist to Hip Ratio	Intercept	128.44	1	128.44	4170.711	0
	Group	0.0275	1	0.0275	0.893	0.349578
	Error	1.4166	46	0.0308		
	PERIOD	0.0078	3	0.0026	3.575	0.015695
	PERIOD*Group	0.0109	3	0.0036	4.987	0.002578
	Error	0.1008	138	0.0007		
Waist to Stature Ratio	Intercept	53.90643	1	53.90643	2348.202	0
	Group	0.01808	1	0.01808	0.787	0.379506
	Error	1.056	46	0.02296		

	PERIOD	0.00184	3	0.00061	2.283	0.081814
	PERIOD*Group	0.00763	3	0.00254	9.445	0.00001
	Error	0.03717	138	0.00027		

2. Within Group Analysis: ExE

Factor	Effect	*SS*	*DF*	*MS*	*F*	*p*
Body Mass	Intercept	739705.5	1	739705.5	1119.256	0
	Error	19165.8	29	660.9		
	PERIOD	22.6	3	7.5	7.104	0.000252
	Error	92.4	87	1.1		
Body Mass Index	Intercept	99490.76	1	99490.76	1231.708	0
	Error	2342.46	29	80.77		
	PERIOD	3.85	3	1.28	3.358	0.022422
	Error	33.27	87	0.38		
Waist Circumference	Intercept	1012848	1	1012848	1962.255	0
	Error	14969	29	516		
	PERIOD	290	3	97	12.369	0.000001
	Error	679	87	8		
Testosterone	Intercept	64.827	1	64.827	137.2325	0
	Error	13.69925	29	0.47239		
	PERIOD	0.38433	3	0.12811	4.8367	0.003679
	Error	2.30442	87	0.02649		
Energy Expenditure CHAMPS Data	Intercept	482091985	1	482091985	28.19377	0.000015
	Error	444580157	26	17099237		
	PERIOD	21322934	3	7107645	3.21016	0.02751
	Error	172700599	78	2214110		
Leg Strength	Intercept	1629486	1	1629486	690.8263	0
	Error	68404	29	2359		
	PERIOD	28537	3	9512	29.4255	0
	Error	28124	87	323		
Back Strength	Intercept	129098.3	1	129098.3	527.3668	0
	Error	6609.5	27	244.8		
	PERIOD	3512.2	3	1170.7	29.5309	0
	Error	3211.2	81	39.6		
Chest Strength	Intercept	84082.38	1	84082.38	368.2508	0
	Error	6164.89	27	228.33		
	PERIOD	991.56	3	330.52	8.4816	0.000058
	Error	3156.49	81	38.97		

Glycated Haemoglobin	Intercept	177831.5	1	177831.5	2827.659	0
	Error	1823.8	29	62.9		
	PERIOD	97.9	3	32.6	3.455	0.019895
	Error	822	87	9.4		
Waist to Hip Ratio	Intercept	88.15102	1	88.15102	3110.55	0
	Error	0.82184	29	0.02834		
	PERIOD	0.02438	3	0.00813	8.308	0.000064
	Error	0.0851	87	0.00098		
Abdominal Skinfold Site	Intercept	144171.7	1	144171.7	622.0226	0
	Error	6721.6	29	231.8		
	PERIOD	124.3	3	41.4	3.4016	0.021256
	Error	1060	87	12.2		
Waist to Stature Ratio	Intercept	37.26583	1	37.26583	1889.546	0
	Error	0.57194	29	0.01972		
	TESTS	0.01049	3	0.0035	12.049	0.000001
	Error	0.02525	87	0.00029		

3. Within Group Analysis: CoN

Factor	Effect	*SS*	*DF*	*MS*	*F*	*p*
Body Mass	Intercept	436888.5	1	436888.5	916.6992	0
	Error	8578.6	18	476.6		
	PERIOD	11.3	3	3.8	6.2526	0.00101
	Error	32.6	54	0.6		
Body Mass Index	Intercept	55145.29	1	55145.29	595.3191	0
	Error	1574.74	17	92.63		
	PERIOD	2.14	3	0.71	7.2941	0.000367
	Error	5	51	0.1		
Energy Expenditure CHAMPS Data	Intercept	124089026	1	124089026	7.967634	0.015383
	Error	186889639	12	15574137		
	PERIOD	19768765	3	6589588	3.66445	0.02108
	Error	64736915	36	1798248		
Back Strength	Intercept	19845	1	19845	311.2941	0.000061
	Error	255	4	63.75		
	PERIOD	765	3	255	13.0213	0.000441
	Error	235	12	19.58		
Upper Arm Girth	Intercept	63116.08	1	63116.08	1613.936	0
	Error	664.82	17	39.11		
	PERIOD	2.97	3	0.99	3.068	0.036029
	Error	16.46	51	0.32		
Thigh Girth	Intercept	186986.5	1	186986.5	2031.98	0
	Error	1564.4	17	92		
	PERIOD	17.2	3	5.7	3.478	0.022453
	Error	83.9	51	1.6		
Fatigue Score POMS Data	Intercept	1380.071	1	1380.071	18.09148	0.000941
	Error	991.679	13	76.283		
	PERIOD	58.964	3	19.655	4.84273	0.005848
	Error	158.286	39	4.059		

APPENDIX H: ADMINISTRATION

This appendix contains samples of documents required for the principal researcher to effectively administrate the research project.

Contents of this Appendix:

1. Attendance register for exercise sessions
2. Participant screening form (inclusion criteria)
3. PAR-Q risk stratification form (sample completed by participant)
4. Consent forms:
    a. For submaximal cycle test
    b. For participation in progressive resistance training programme
5. Medical examination form (completed by medical practitioner for participant)
6. ECG data sheet (completed during submaximal cycle ergometry test)
7. Time-slot allocation for baseline fasted blood withdrawal at Du Buisson's Laboratory
8. Time-slot allocation for ECG and submaximal cycle ergometry test as well as physical examination by medical practitioner
9. Coded biochemical report returned from Du Buisson's Laboratory
10. Anthropomorphic data collection sheet (sample is for participant EC11 at Week 8, completed on 26/03/2012)
11. CHAMPS scoring tool (following guidelines provided by questionnaire authors)
12. Dietary recall sample (completed by participant EC10 for submission at week 4 measurement)
13. Profile of Mood States scoring grid
14. Profile of Mood States Standard Form (completed by participant EB01 for submission at week 12 measurement)

EXERCISE GROUP ATTENDANCE REGISTER

PHASE 1/3

WEEKS 1 - 4

DATE:	20-06-2011:					27-06-2011:					04-07-2011:					08-07-2011:					
	1	2	3	4	5	1	2	3	4 (FEST?)	5	1	2	3	4	5 (END PEST)	1	2	3	4	5	
June	✓	✓	✓	✓	✓	✓	✓														
EA06 Brenda	✓	✓	✓	✓	O	✓	✓	O	O	✓	O	✓	O	✓	O	✓	✓	✓	✓	O	(missed 6)
EA04 CarolAnne	✓	✓	O	✓	O	✓	✓	✓	O	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	(missed 3)
EA09 Anne	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	O	✓	✓	✓	✓	✓	✓	✓	
EA15 Liz	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	O	O	O	✓	✓	✓	✓	✓	✓	✓	(missed 3)
X Jenny	✓	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	O	✓	✓	
Trish	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	O	✓	✓	✓	✓	O	✓	✓	✓	✓	
Gill	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	
[redacted]	✓ (Meanwell)	✓ (Meanwell)	✓ (EXL)																		

EXERCISE GROUP ATTENDANCE REGISTER

PHASE 2/3

WEEKS 5 - 8

DATE:	18-07-2011:					25-07-11:					01-08-2011					08-08-2011:					
	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	
June			✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓							
Brenda	✓	✓	✓	✓	O	O	✓	✓	✓	✓	O	O	O	✓	✓	O	✓	✓	✓	O	
CarolAnne	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	O	O	✓	✓	✓	✓	✓	
Anne	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	
Liz	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	
Jenny																					(missed 10)
Trish	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	
Gill	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	
[redacted]																					

2012 : GROUP (1)

EXERCISE GROUP ATTENDANCE REGISTER
PHASE 1/3
WEEKS 1 - 4

DATE:	30-Jan (1 FEB)						06-Feb						13-Feb						20-Feb				
	1	2	3	4	5		1	2	3	4	5		1	2	3	4	5		1	2	3	4	5
~~Roelien~~																							
EC12 Di																							
EC15 Carol																							
EC06 Steph																							
EC08 Denise																							
EC07 Agata			(AWAY)																				
EC10 Sally																							
EC05 Penny																							
EC01 June																							
EC04 Celia																							

EXERCISE GROUP ATTENDANCE REGISTER
PHASE 2/3
WEEKS 5 - 8

DATE:	27-Feb						05-Mar						12-Mar						19-Mar				
	1	2	3	4	5		1	2	3	4	5		1	2	3	4	5		1	2	3	4	5
~~Roelien~~																							
Di																							
Carol																							
Steph																							
Denise			(Fall)																				
Agata																							
Sally	(AWAY)																						
Penny																							
June																							
Celia																							

EXERCISE GROUP ATTENDANCE REGISTER
PHASE 3/3
WEEKS 9 - 12

DATE:	26-Mar						02-Apr						09-Apr						16-Apr				
DATE:	1	2	3	4	5		1	2	3	4	5		1	2	3	4	5		1	2	3	4	5
~~Roelien~~																							
Di																							
Carol																							
Steph																							
Denise																							
Agata																							
Sally																							
Penny																							
June																							
Celia																							

(+/ week)

Department of Human Kinetics and Ergonomics, Rhodes University

PARTICIPANT SCREENING

Phd Research Project: Principal Researcher: Mrs Janet Viljoen

Supervisor to Research: Dr Candice Christie

Please indicate your AGE in years and months:	59 yrs. 9 months	This study requires females who are 55 - 65 years of age.
Please indicate how long you have been post-menopausal [defined as 12 consecutive months without regular menses]	18 yrs.	Only women who are at least 1 year post-menopause can be accepted to this study.
Have you taken, or are you taking any form of HRT?	No. Not for at least 12-14 yrs.	This study requires women who DO NOT currently take HRT and have not done so in the past, or any bio-identical derivative of HRT.
Have you ever been told that you have DIABETES?	No	This study precludes individuals who are diagnosed Diabetics, either Type I or II.
Do you SMOKE?	No	Smokers are excluded.
Do you do any "formal" EXERCISE?	No	This study requires individuals who are currently "sedentary". If you participate in more than 30 minutes of light activity daily, you are too active!
Are you of CAUCASIAN descent?	Yes.	Health indices are affected by race. Standardisation for the research requires a homogenous sample.
Do you have any HEART problems?	No.	For medical safety, and for the purposes of deriving the most reliable results from this study, we cannot select individuals with known complications of these organs.
Do you have any LUNG [or related breathing] problems or difficulties?	No	
Do you have any LIVER problems?	No	
Do you have any KIDNEY problems?	No	

I [full name] VIRGINIA ANNE REED declare that the information that I have provided above is truthful and correct.

V.A.Reed.
Signed by participant

28 May 2013.
Date

This research has been cleared as ethically sound by the Rhodes University Ethical Standards Committee for research involving human participants.

PAR-Q RISK STRATIFICATION FOR EXERCISE

PLEASE NOTE THAT THE INFORMATION YOU WILL PROVIDE ON THIS FORM REMAINS STRICTLY CONFIDENTIAL. THIS INFORMATION IS REQUIRED FOR YOUR SAFETY DURING EXERCISE.

Participant Code: 06
Participation in PhD Degree Research Project
Principal Researcher: Janet Viljoen [072 180 7757]

PERSONAL DETAILS

Full Name and Surname	ELIZABETH DE WET
Date of Birth	23 NOVEMBER 1954
Emergency Contact Person [and relationship to you] [It is best if this individual is resident in Grahamstown] Emergency Contact Person's Mobile No.	CHRIS DE WET (Husband) 0764597358
Physician [local] Physician Contact No.	Dr. Geoff Bennett

PREVIOUS EXERCISE EXPERIENCE

1.Please outline your previous involvement, if any:

None ✓	Housework/ Gardening/ Active work Related tasks/ Walking dog	Regular walk/ Golf/ Swimming/ Tennis etc	Socially Competitive Sport/ Very regular Gym attendance	Competitive athlete

2. How often have you exercised [per week] in the last 6 months?

Never ✓	1 x per week	2-4 x per week	Daily

3. How much time have you spent exercising per week in the last 6 months?

0-1 hour ✓	1-2 hours	2-4 hours	>4 hours

MEDICAL HISTORY [please place an X where appropriate]

1.Have you sustained any Motor Vehicle Accident related injuries (within the past five years)? Comment:	Y	(N) X
2. Have you sustained any Sports Injuries (within the past five years)? Comment:	Y	N X
3. Have you been diagnosed with any HEART related complications?	Y	N X
4. Has your Doctor ever informed you that you should NOT enter into an exercise programme without medical consent?	Y	N X
5. When was your last complete physical check up? Date: Jan 2011	Y	N
6. Do you experience Chest Pains while exercising?	Y	N X
7. Do you have High Blood Pressure? Current Value:	Y	N X
8. Do you have Diabetes?	Y	N X
9. Do you suffer from Asthma?	Y	N X
10.Do you have any Allergies? Comment:	Y	N X
11.Are you currently taking any Chronic Medication? Comment:	Y	N X
12. Do you have any family history of the following: Heart, lung, metabolic disease, stroke, sudden death Comment:	Y	N X
13. What level of activity is required during your average daily work? Please specify if there is a lot of upper body activity required. Comment: quite a bit of walking, + lifting of awkward material eg very large bound newspapers, piles of bound registers etc. Occasionaly boxes.	Y	N

ADDITIONAL INFORMATION

1. Have you undergone SURGERY within the last 12 months? Comment:	**Y**	**N** X
2. Are you currently receiving treatment [ie Chemotherapy, Psychotherapy]? Comment:	**Y**	**N** X
3. Are you currently PREGNANT?	**Y**	**N** X

BASED ON THE INFORMATION PROVIDED, WE RESERVE THE RIGHT TO EXCLUDE YOU FROM THE CURRENT RESEARCH PROJECT, BASED ON THE REQUIREMENTS WHICH POTENTIAL SUBJECTS MUST FULFIL, AND FOR MEDICAL SAFETY.

I, Elizabeth de Wet [full name] do confirm that the information here provided is complete and is correct.

Signed [Subject for Research Study] — Date: 20:6:2012

Signed [Researcher] — Date: 20/06/2012

Department of Human Kinetics and Ergonomics
Rhodes University

Please be advised that this research has been cleared as ethically sound by the Rhodes University Ethical Standards Committee for research involving human participants.

INFORMED CONSENT FOR EXERCISE TESTING

SUBMAXIMAL CYCLE ERGOMETRY TEST [BRUCE PROTOCOL]

1. Purpose and Explanation of the Test

You will perform an exercise test on a cycle ergometer. The exercise intensity will begin at a low intensity and will be advanced in stages, depending on your fitness level (as monitored by carefully noting your heart rate). The researcher/medic may stop the test at any time due to signs of fatigue, dizziness, changes in your heart rate, electrocardiogram (ECG) or blood pressure. It is important for you to realise that you may stop at any stage due to discomfort or feelings of fatigue.

2. Attendant Risks and Discomforts

There exists the risk that certain changes may take place during the test. These include: abnormal blood pressure, fainting, irregular heart beat rhythm, and in rare cases, heart attack, stroke, or death. Every effort will be made to minimise these risks by evaluation of preliminary information relating to your health and fitness and by careful observations during testing. Emergency equipment and trained personnel are available to deal with unusual situations that may arise.

3. Responsibilities of the Participant

Information you possess about your health status or previous experiences of heart-related symptoms (such as shortness of breath with low-level activity, pain, pressure, tightness, heaviness in the chest, neck, jaw, back and/or arms) with physical effort may affect the safety of your exercise test. Your prompt reporting of any of these feelings during the exercise test is important. You are responsible for fully disclosing your medical history, fully report all medications (including non-prescriptive) taken recently, and in particular those taken on the day of the test, to the medical staff.

4. Benefits to be Expected

The results obtained from the exercise test may assist in diagnosis of illness, in evaluating effect of medications, or in evaluating what physical activity you may engage in with low risk.

5. Enquiries

Any questions about the procedures used in the exercise test or the results of your own test are encouraged. If you have any concerns or questions, please feel free to approach the medical staff or the researcher.

6. Use of Medical Records

The information obtained during this exercise testing will be treated as highly confidential. It will not be released or revealed to any other person without your written consent. The information will be used for scientific purposes and statistical analysis, but will be done so under an anonymous code at all times.

7. Freedom of Consent

I hereby consent to voluntarily participate in an exercise test to determine my exercise capacity and state of cardiovascular health. My permission to perform this exercise test is given voluntarily. I understand that I am free to stop the test at any point, if I so desire.

Signed [Participant]	Signed [Researcher]
WITNESS 1	WITNESS 2

INFORMED CONSENT FOR PARTICIPATION IN AN EXERCISE PROGRAMME

PROGRESSIVE RESISTANCE TRAINING

1. Purpose and Explanation of the Programme

You will embark on a progressive resistance training protocol which will continue for 12 weeks. Resistance training infers exercise that develops muscular strength rather than exercise which focuses on cardiovascular 'fitness'. Exercise that is 'progressive' in nature becomes more challenging as you participate and become stronger and more able to manage a more difficult routine. The difficulty will progress every four weeks, in line with documented strength and condition increases when undertaking resistance training. In order to maximise the benefits to you, the participant, a programme of "compound" exercises has been developed. This means that you will use multiple muscles for every exercise, thus increasing the effect of the exercise on your strength and condition. The researcher may stop you during the exercises at any time, should you exhibit signs of dizziness, faintness, shortness of breath, or should you experience chest pain or sudden changes to your heart rate. It is important to report any of these symptoms to the session supervisor immediately should you experience any of the listed symptoms, or feel generally unwell.

2. Attendant Risks and Discomforts

2.1. Exercise Sessions

There exists the risk that certain changes may take place during participation in physical activity. These include: abnormal blood pressure, fainting, irregular heart beat and rhythm, and in rare cases, heart attack, stroke or death. Every effort will be made to minimise these risks by evaluating preliminary information pertaining to your health status. In addition, a physical examination for readiness to exercise by the attendant Specialist Physician will further ensure that there are no identifiable underlying concerns that may endanger you during physical activity. Please be assured that all information will be considered confidential and will be treated as such.

2.2. Measurements

Prior to the commencement of the exercise sessions, and every four weeks thereafter, a battery of measurements will be taken. These measurements will provide the researcher with a measurable indication of any changes occurring as a result of the implementation of the exercise regime. Some of these tests require the withdrawal of blood samples. There is risk inherent in the procedure of blood withdrawal, such as infection of the puncture site on the skin, and adverse reaction to blood sampling such as feelings of dizziness and faintness. All blood samples will be drawn by professional nursing staff at a registered pathology laboratory, in a sterile environment. You are requested and advised to report any feelings of light headedness to the nurse on duty when your blood sample is drawn.

3. Responsibilities of the Participant

Information you possess about your health status, and reporting any experiences of heart-related symptoms (such as shortness of breath with low-level activity, pain, pressure, tightness, heaviness in the chest, neck, jaw, back and/or arms) with physical effort may affect the safety of your participation in the exercise programme. Your prompt reporting of any of these feelings is of utmost importance at all times during the exercise programme. The responsibility of full disclosure of medical records rests with you, the participant. You are advised that all information is treated as confidential.

4. Benefits to be Expected

It is well documented that participation in regular physical activity has a wide variety of health benefits to individuals of all ages. Post-menopausal women may benefit from resistance training in that the development of muscle strength assists in the prevention of osteoporotic conditions, which increased muscle mass raises metabolism, thus assisting in the management of body weight. By participating in this research project you will be afforded the chance to exercise under controlled and safe conditions, with reduced risk to your physical self which is especially important as you undertake "formal" exercise for the first time, or after a break of a number of years. You may expect feelings of improved wellness and overall health and wellbeing and you may experience an increase in daily energy levels. The measurements that will be taken every four weeks will offer you valuable insight into your own body and physiology, and being immersed in a scientific environment may offer you the opportunity to learn about your own body, physiological processes and health in general.

5. Enquiries

Questions related to the exercise programme and any measurements taken are encouraged. Please feel free to approach the researcher (Janet Viljoen) or the supervisor to the research (Dr Candice Christie) at any stage. Contact details for both individuals are included in your information packs.

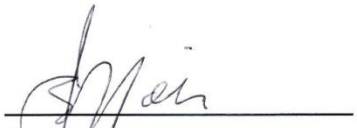
6. Use of Medical Records

The information obtained at any point during this programme will be treated as highly confidential. It will not be released or revealed to any other person without your written consent. The information will be used for scientific purposes and statistical analysis, but will be used under anonymous code at all times. The information will be stored for the purposes of the researcher's reference for a period of no longer than five years following the completion of the exercise programme. The information will not be shared with any other person and when referred to, will always be coded.

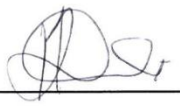
7. Freedom of Consent

I hereby consent to participate in a 12 week programme of progressive resistance training, as part of the protocol for research investigating the "effects of exercise on the health of post-menopausal women". I confirm that I have read and understand the information given to me. I understand that I am free to question the protocol at any stage, and questions that I have asked have been answered satisfactorily to date. I am aware of the need to disclose any medical conditions fully, and I am happy that this information will remain confidential. My consent is willingly and freely given, and I understand that I am free to leave the study at any time should I wish to do so.

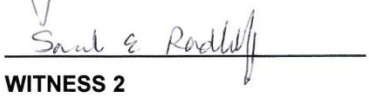
Signed [Participant]



Signed [Researcher]



WITNESS 1



WITNESS 2

6/6/12

DATE

PHYSICAL EXAMINATION FOR PHYSICAL ACTIVITY

PARTICIPANT CODE: EC 17 . **DATE:** 3-2-2012

ASPECT TO EXAMINE	MEDICAL PRATICITIONER'S COMMENT AND RECOMMENDATIONS
1. Apical pulse rate and rhythm	SINUS RHYTHM. APEX NAD. PULSE 94.
2.Resting blood pressure: seated, supine and standing	LYING: 123/98 SITTING 121/93 STANDING 111/94
3.Auscultation of lungs [note: specific attention to absence of wheezes and other sounds]	CLEAR.
4.Auscultation of carotid, abdominal and femoral arteries	NORMAL
5.Evaluation of abdomen for tenderness	NAD
6.Palpation and evaluation of lower extremities for oedema and presence of arterial pulses	NAD
7.Absence or presence of tendon,xanthoma or skin xanthelasma	NAD.
8.Follow up examination of orthopaedic/other medical conditions that would limit exercise testing	INJURY to (R) KNEE.
9.Tests of neuralgic function, including reflexes	REFLEXES NAD CEREBELLAR NAD PROPRIOCEPTION NAD
10.Inspection of the skin, especially lower extremities in known diabetics [note: no subject for the purposes of this study may be diabetic]	NORMAL
SIGNED: Dr CP Jameson	MRCP

DATA SHEET: ECG TEST AND SUBMAX BICYCLE PROTOCOL

PARTICIPANT CODE: ED07

Pre Stage 1	Stage 1 PRE	Stage 2	Stage 3	Stage 4	Stage 5 POST
Heart Rate [bpm]	81.	68	63.	108.	123.
BP [mmHg]					
Cycle speed [rpm]					
RPE [Borg scale]					
Watts [bicycle]					

ECG DATA

	Reference / Pre	Activity	Post-Activity
ECG Trace	NORMAL	NORMAL	NORMAL
Comment	NORMAL	NORMAL	NORMAL
Physician	[signature]	[signature]	[signature]

BLOOD TESTS AT DU BUISSON'S LABORATORY

TIME	MONDAY 13 JUNE	TUESDAY 14 JUNE	WEDNESDAY 15 JUNE
08H30	1 ~~EA 09~~ EA 08 2 EA 11 3 EA 09	1 EA 04 2 EA 01 3	1 EA 15 2 3
08H45	1 2 3	1 2 3	1 2 3
09H00	1 EA 10 2 3 ✓	1 EA 13 2 EA 06 3	1 2 3

THESE TESTS MUST BE TAKEN IN A FASTED CONDITION: PLEASE DO NOT EAT OR DRINK ANYTHING FROM 22H00 THE PREVIOUS EVENING!!

EA 12 → Saturday 8:30 ✓

ECG AND PHYSICAL EXAM: MONDAY 13 JUNE		
TIME	PARTICIPANT 1	PARTICIPANT 2
14H00	[redacted]	EA10
14H45	[redacted] EA 09	
15H30	[redacted]	
16H15	EA 12	EA01

(4)

The ECG and Physical Examination slots are 45minutes each, 2 participants per slot.

These pre-screening tests will take place at 60 Beaufort Street, Dr Jameson's Rooms.

ECG AND PHYSICAL EXAM: TUESDAY 14 JUNE		
TIME	PARTICIPANT 1	PARTICIPANT 2
14H00	EA13 [redacted]	EA04
14H45	EA06	EA15
15H30		
16H15	EA08	

The ECG and Physical Examination slots are 45minutes each, 2 participants per slot.
These pre-screening tests will take place at 60 Beaufort Street, Dr Jameson's Rooms.

PATHOLOGISTS · PATOLOË
Drs Du Buisson, Kramer, Swart, Bouwer Inc./Ing.
AMPATH

24 Uur kontaknommer / Hour contact number 082 787 0753

PATIENT:	DOCTOR:	SUBMITTING DR:
Rhodes-Kelly,EA12	Rhodes University-Viljoen Proj Dept of Human Kinetics & Ergon Rhodes University Grahamstown 6140 ROUTE:49500:10	Rhodes University-Viljoen Proj **COPY DR(s):**
Female/19540510/57 ID : H: C: **FOLIO:EA12** M/A : MEMB : NO :	**FINAL REPORT** **REQ NO : 13112552** SPEC :0815:AS02425S PT LOC :49500 BATCH # :5403425	**COLLECTED :15/08/11 0820** RECEIVED :15/08/11 0920 PRINTED :16/08/11 0818

ORDERED: Cholesterol Tot, Triglycerides, HDL Cholesterol, LDL Cholesterol, HbA1c Oestradiol, Free Testosterone

Test	ABN	Result	Reference	Units
LIPIDS				
=> Cholesterol Total	H	7.4	2.8-4.9	mmol/l
=> Triglycerides	H	4.8	0.4-1.6	mmol/l
=> HDL Cholesterol	L	1.0	1.2-1.9	mmol/l
=> LDL Cholesterol	H	4.7	1.5-2.9	mmol/l

Therapeutic targets: Category I risk Category II risk
Total-Chol <4.5 mmol/l <5.0 mmol/l
LDL-Chol <2.5 mmol/l <3.0 mmol/l

Category I risk: CVD, DM type 2, DM type 1 with microalbuminuria, T-Chol >8 or LDL >6, HT (BP >=180/110), Framingham risk score >20%
Category II risk: Above conditions absent, Framingham risk score <20%

Reference: European Heart Journal 2003; 24: 1601-1610.
SA Heart 2006 Supplement; 6(6): 13-20.

GLUCOSE METABOLISM				
=> HbA1c (DCCT/NGSP)		6.0	4.0-6.0	%
=> HbA1c (IFCC)		42	20-42	mmol/mol
ENDOCRINOLOGY				
=> Total Testos (Beckman)		0.8	< 2.7	nmol/l
=> SHBG (Beckman)		19.3	16.8-125.2	nmol/l
=> Free Testosterone Calculated		18.9	2.0-33.0	pmol/l
=> Oestradiol		43		pmol/l
=> Reference Range:		.		

	Oestradiol	*FSH*	*LH*	*Progesterone*
Post Menopausal	*<137*	*23-116*	*15.9-54*	*<2.4*

=>NUWE RESULTAAT SEDERT VORIGE VERSLAG / NEW RESULTS SINCE PREVIOUS REPORT
#BETEKENINGSVOLLE VERANDERING SEDERT VORIGE VERSLAG / SIGNIFICANT CHANGE SINCE PREVIOUS REPORT *L / *H HOOGS ABNORMALE RESULTATE / HIGHLY ABNORMAL RESULTS

ANTHROPOMETRIC AND BODY COMPOSITION MEASURES			
PARTICIPANT:	EC11	DATE:	26/3/2012
MEASUREMENT No.:	8		

%FAT FORMULA:	
AGE:	62
BD:	1.003
%FAT:	43.70

Stature (m)		
Mass (kg)		75.02
Blood Pressure (mmHg) (seated)		140/90
Girth Measures (mm)	Upper arm	32.5
	Chest	90.5
	Waist	94.3
	Hip	100.6
	Thigh	50.3
	Calf	37.5
Skinfold Measures (mm)	Tricep	29
	Chest	19.4
	Abdomen	39.6
	Supra-Iliac	21.4
	SubScapular	36
	Mid-Axillary	34.2
	Thigh	41.6

221.20

EA01 78.56 kg (0.39)

Week 4

CHAMPS SCORING TOOL

Variable	Question	Answer	Dur Var	Weight DV	Caloric Ex PER	Caloric Ex WEEK
ALL CALORIC	7	1	0.5	4.5	2.25	1211.54
	9					
	10					
	14					
	15					
	16					
	19					
	20	1	0.5	2.5	1.25	673.08
	21					
	22					
	23					
	24					
	25					
	26					
	27	1	0.5	2.5	1.25	673.08
	28					
	29					
	30					
	31					
	32					
	33					
	34					
	35					
	36					
	37					
	38					
	39					
	40					

Variable	Question	Answer	Dur Var	Weight DV	Caloric Ex PER	Caloric Ex WEEK
MOD ACT CALORIC	7					
	9					
	14					
	15					
	16					
	19					
	21					
	23					
	24					
	25					
	26					
	29					
	30					
	31					
	32					
	33					
	36					
	37					
	38					
	40					

Variable	Question	Answer
ALL FREQUENCY	7	1
	9	
	10	
	14	
	15	
	16	
	19	
	20	1
	21	
	22	
	23	
	24	
	25	
	26	
	27	1
	28	
	29	
	30	
	31	
	32	
	33	
	34	
	35	
	36	
	37	
	38	
	39	
	40	

Variable	Question	Answer
MOD FREQUENCY	7	
	9	
	14	
	15	
	16	
	19	
	21	
	23	
	24	
	25	
	26	
	29	
	30	
	31	
	32	
	36	
	37	
	38	
	40	

2557.7 →

3

✓

SOUTH AFRICAN MEDICAL RESEARCH COUNCIL

DIETARY RECALL TEMPLATE

To be completed by participants in Janet Viljoen's PhD research study.

Participant Code: EC 10 Wk 4

Instructions:

- This information is required as it is imperative that I can demonstrate that dietary intake of the participants did not change dramatically over time. I will not be analysing the diet, merely using this data for statistical correlations.
- There are no "good" or "bad" foods – please do not feel embarrassed about recording, truthfully, what you have consumed.
- Please record everything you eat and drink over a three-day period on the following days of the week: Tuesday, Thursday and Saturday. For each day, please note everything you consume from waking until going to sleep that night (effectively 24 hours).
- Please give your best estimate of portion sizes, and quantities. Amounts may be given in numbers, volume, or weight. Please consider one "portion" to be ½ cup or 'a handful'. Please specify when referring to spoons: teaspoon/dessert spoon/serving spoon.
- Be specific about substances (such as milk: was it full cream or 2%?)
- Record ALL alcoholic beverages (and please state how many glasses, or quantity, if possible)
- Record all non-alcoholic beverages: tea (was it rooibos or ordinary? How many sugars? Brown or white sugar?) / cooldrinks (coke light 330ml; fanta orange 330ml ; iced tea, peach, 250ml)
- Record all discrete components of a meal: fillet steak, grilled (250g); brown rice; green beans...
- Please also record all "snacks" eaten between meals

This research has been cleared by the Rhodes University Ethical Standards Committee for research involving human participants.

The research is funded by:

The MEDICAL RESEARCH COUNCIL OF SOUTH AFRICA

NRF Incentive Funding for rated researchers

PhD in-country scholarship from "DAAD"

Day 1: TUESDAY **Date:** 18th March.

Example: **07h15: 1x small cup filter coffee (plunger) with 50ml milk (2%)** **1 x large wholemeal rusk (Ouma Brand) with raisins.**	**Example:** **13h00: Two thick-cut slices brown bread, butter spread (Flora light), peanut butter (two dessert spoons).** **One small yoghurt (plain, low fat, 250ml).**
Wake up 1 cup boiled water, few slices of ginger + juice of ½ lemon. 1 glass water	
Breakfast 5 cm slice spansepek 2 Tbsp plain yoghurt. Small bowl of muesli ½ cup milk + 1 banana	
1 slice brown toast, ~~smear butter + marmalade~~ 1 cup filter coffee, splash milk + 1 tsp sugar	
Mid Morning 1 mango. 1 glass water	
Lunch 3 thin slices brown bread + ¼ avocado. + little butter.	
Evening Class 6 rice snacks + 2 tsps cream cheese ½ small glass red wine 1 Grapetiser	
Supper 1 sweet potato + blob butter 20 cm Boerewors 3 Cucumber slices	

Day 2: THURSDAY **Date:** 8th March.

Wake up: 1 x cup hot water, ½ lemon juice + sliced ginger 1 glass water	
Breakfast Scm slice spanspekk wide ½ mango + 2 Tbs plain yoghurt 1 bowl of muesli + milk 1 piece wholewheat toast + marmalade. 1 cup filter coffee + touch of milk 1 tsp sugar	
Mid Morning 1 glass water 1 cup green tea 6 Brazil nuts.	
Lunch 3 slices crispbread, smear of cream cheese + 1 thin slice salami. ½ mango. 1 small cup coffee + touch of milk + 1 tsp sugar.	
Afternoon 1 cup rooibos. Drawing Class: 2 glasses of grapefruit juice, handful of plain salted chips, 12 tsp of plain cream cheese.	
Supper 1 Kipper fillet fried in butter 1 fried egg + baby tomatoes ± 8	

Day 3: SATURDAY **Date:** 10th March

Wake up – 1 cup boiled water + ginger 1 mango + 5cm slice spanspek + 2 tbsp yoghurt 1 poached egg + toast 1 cup coffee (filter) + touch of milk + 1 tsp sugar	
Mid morning 1 glass water 1 mango 1 homegrown! tree tomato – the first one off the tree!!	
Afternoon 1 cup Green tea 3 glasses water	
Supper 1 bowl stirfry (± cup of noodles, onion, green pepper ± 150g beef strips, cabbage) 1 red grapefruit	
5cm wide slice of spanspek.	

POMS™ Standard Scoring Grid

BY DOUGLAS M. McNAIR, Ph.D., MAURICE LORR, Ph.D., JW P. HEUCHERT, Ph.D., & LEO F. DROPPLEMAN, Ph.D.

Client ID: EC06 Week 4 **Age:** _____ **Gender:** Male Female (Circle one)

Birth Date: ___/___/___ (Month Day Year) **Today's Date:** ___/___/___ (Month Day Year) **Name:** _____

For items 31–65, transfer each number below into the corresponding unshaded box. and For shared boxes, add the values when summing the column. 3 2 = 5 and For items 1–30, transfer each number below into the corresponding shaded box.

	T	D	A	V	F	C
1.	4	3	2	(1)		0
2.	4	3	2	(1)		0
3.	4	3	2	(1)		0
4.	4	3	2	(1)		0
5.	4	3	2	1		(0)
6.	4	3	2	1		(0)
7.	4	3	2	(1)		0
8.	(1)	3	2	1		0
9.	→	3	2	1		(0)
10.	4	3	2	(1)		0
11.	4	3	2	(1)		0
12.	4	3	2	1		(0)
13.	(4)	3	2	1		0
14.	4	3	2	1		(0)
15.	4	3	2	1		(0)
16.	4	3	2	(1)		0
17.	4	3	2	1		(0)
18.	4	3	2	1		(0)
19.	4	(3)	2	1		0
20.	4	(3)	2	1		0
21.	4	3	2	1		(0)
22.	4	3	2	1		(0)
23.	4	3	2	(1)		0
24.	4	3	2	1		(0)
25.	0	1	2	(3)		4
26.	4	(3)	2	1		0
27.	4	(3)	2	1		0
28.	4	3	2	1		(0)
29.	4	3	2	1		(0)
30.	(4)	3	2	1		0
31.	4	3	2	(1)		0
32.	4	3	2	1		(0)

Instructions:

Transfer circled numbers into boxes across each row, as indicated at the top of the scoring grid. Each circled number will be copied once. The seven unscored items indicated by an asterisk (*) are not transferred into the scoring boxes.

To obtain raw scores for factors T, D, A, V, F, and C, add the numbers in each column and enter the sum in the box at the bottom of the column.

0	1	2	3	(4)	1.*
0	(1)	2	3	4	2.
0	1	(2)	3	4	3.
0	(1)	2	3	4	4.
0	(1)	2	3	4	5.
0	1	(2)	3	4	6.*
0	1	2	3	(4)	7.
0	(1)	2	3	4	8.
0	(1)	2	3	4	9.
0	(1)	2	3	4	10.
(0)	1	2	3	4	11.
(0)	1	2	3	4	12.
0	1	2	(3)	4	13.*
0	(1)	2	3	4	14.
0	1	2	(3)	4	15.
0	(1)	2	3	4	16.
0	(1)	2	3	4	17.
0	(1)	2	3	4	18.
0	1	2	(3)	4	19.
0	(1)	2	3	4	20.
(0)	1	2	3	4	21.
4	(3)	2	1	0	22.
0	(1)	2	3	4	23.
(0)	1	2	3	4	24.
0	1	2	(3)	4	25.*
(0)	1	2	3	4	26.
(0)	1	2	3	4	27.
0	(1)	2	3	4	28.
0	(1)	2	3	4	29.
0	1	2	(3)	4	30.*

T	D	A	V	F	C
9	6	5	28	5	8

Sum T, D, A, F, and C and subtract V in the boxes below to obtain the Total Mood Disturbance (TMD) score. Plot the Raw Scores and TMD score on the appropriate profile contained in this QuikScore™ form.

Raw Score 9 + 6 + 5 + 5 + 8 − 28 = 5 **Total Mood Disturbance**

POMS™ Standard Form

BY DOUGLAS M. McNAIR, Ph.D., MAURICE LORR, Ph.D., JW P. HEUCHERT, Ph.D., & LEO F. DROPPLEMAN, Ph.D.

Client ID: EB01 W12 **Age:** 64 **Gender:** Male (Female) (Circle one)

Birth Date: 10 / 21 / 1947 (Month / Day / Year) **Today's Date:** 11 / 30 / 2011 (Month / Day / Year)

To the Administrator:

Place a checkmark ✔ in one box to specify the time period of interest.

To the Respondent:

Below is a list of words that describe feelings that people have. Please read each word carefully. Then circle the number that best describes

- ☐ how you have been feeling during the PAST WEEK, INCLUDING TODAY.
- ☐ how you feel RIGHT NOW.
- ☐ other: _____

If no box is marked, please follow the instructions for the first box.

POMS™

		Not at all	A little	Moderately	Quite a bit	Extremely
1.	Friendly	0	1	2	(3)	4
2.	Tense	0	(1)	2	3	4
3.	Angry	(0)	1	2	3	4
4.	Worn out	(0)	1	2	3	4
5.	Unhappy	(0)	1	2	3	4
6.	Clear-headed	0	1	(2)	3	4
7.	Lively	0	1	2	(3)	4
8.	Confused	(0)	1	2	3	4
9.	Sorry for things done	0	(1)	2	3	4
10.	Shaky	(0)	1	2	3	4
11.	Listless	(0)	1	2	3	4
12.	Peeved	(0)	1	2	3	4
13.	Considerate	0	1	(2)	3	4
14.	Sad	0	(1)	2	3	4
15.	Active	0	1	2	3	(4)
16.	On edge	(0)	1	2	3	4
17.	Grouchy	(0)	1	2	3	4
18.	Blue	(0)	1	2	3	4
19.	Energetic	0	1	2	(3)	4
20.	Panicky	(0)	1	2	3	4
21.	Hopeless	(0)	1	2	3	4
22.	Relaxed	0	1	2	(3)	4
23.	Unworthy	(0)	1	2	3	4
24.	Spiteful	(0)	1	2	3	4
25.	Sympathetic	0	1	2	3	(4)
26.	Uneasy	(0)	1	2	3	4
27.	Restless	(0)	1	2	3	4
28.	Unable to concentrate	(0)	1	2	3	4
29.	Fatigued	0	(1)	2	3	4
30.	Helpful	0	1	2	3	(4)

Please flip over.

Items continue on the back page...

POMS™ Standard Form

BY DOUGLAS M. McNAIR, Ph.D., MAURICE LORR, Ph.D., JW P. HEUCHERT, Ph.D., & LEO F. DROPPLEMAN? Ph.D.

POMS™

		Not at all	A little	Moderately	Quite a bit	Extremely
31.	Annoyed	(0)	1	2	3	4
32.	Discouraged	0	(1)	2	3	4
33.	Resentful	0	(1)	2	3	4
34.	Nervous	(0)	1	2	3	4
35.	Lonely	0	(1)	2	3	4
36.	Miserable	(0)	1	2	3	4
37.	Muddled	(0)	1	2	3	4
38.	Cheerful	0	1	2	(3)	4
39.	Bitter	0	(1)	2	3	4
40.	Exhausted	0	(1)	2	3	4
41.	Anxious	(0)	1	2	3	4
42.	Ready to fight	(0)	1	2	3	4
43.	Good natured	0	1	2	(3)	4
44.	Gloomy	(0)	1	2	3	4
45.	Desperate	(0)	1	2	3	4
46.	Sluggish	(0)	1	2	3	4
47.	Rebellious	(0)	1	2	3	4
48.	Helpless	(0)	1	2	3	4
49.	Weary	0	(1)	2	3	4
50.	Bewildered	(0)	1	2	3	4
51.	Alert	0	1	2	3	(4)
52.	Deceived	(0)	1	2	3	4
53.	Furious	(0)	1	2	3	4
54.	Efficient	0	1	2	3	(4)
55.	Trusting	0	1	2	(3)	4
56.	Full of pep	0	1	2	(3)	4
57.	Bad-tempered	(0)	1	2	3	4
58.	Worthless	(0)	1	2	3	4
59.	Forgetful	0	(1)	2	3	4
60.	Carefree	0	1	2	(3)	4
61.	Terrified	(0)	1	2	3	4
62.	Guilty	(0)	1	2	3	4
63.	Vigorous	0	1	2	(3)	4
64.	Uncertain about things	0	(1)	2	3	4
65.	Bushed	(0)	1	2	3	4

Please ensure you have answered every item.
Thank you for completing this questionnaire.

EPILOGUE: THE JOURNEY

"…Two roads diverged in a wood, and I –
I took the one less travelled by,
And that has made all the difference."
Robert Frost

The production and presentation of a thesis is but the pinnacle of the PhD experience. In carefully edited and structured pages the vastness of life experience gained on the journey toward the submission cannot be expressed, but each insight and each step taken informs the end product and indeed, the future. In this chapter I would like to share some of my journey taken over the five years in the fourth decade of my life during which my task at hand was working toward this submission.

I.

I began the journey as a full-time PhD scholar after resigning from my job following completion of my MSc, part-time. The realisation that research, teaching, thinking and writing was what I enjoyed best had been an enlightening – working a notice period was agony as I couldn't wait to get going. I was determined: three years, full-time, and I would have completed the doctorate, and be on with my career. I dove head first into the literature to gain insight into related topics – I knew that if I was to examine participants whose defining characteristic was that they were to be post-menopause, I needed to understand all there was about this transition. Similarly, I researched the basic physiological working of the plasma lipoproteins.

II.

Despite writing and developing the research methodology during 2009 (that first year) hindsight reveals that I lacked understanding of the need to focus the study. My literature review at the time reveals very little critical thinking and an apparently "apologetic" writing style. It would be four years before this humbling realisation could be verbalised – and today I am rather glad that the product submitted is not that first attempt. My understanding of the application of 'evidence based medicine' grew slowly with each year and with added insight from various sources: from one really inspiring meeting with a Professor of Pharmacy, attending conferences both

locally and internationally, conferring with peers, the consistently encouraging input of my supervisor, and, fundamentally, reading the works of Goldacre, Kahnemann, Taleb, and Taubes (among others).

III.

When I set out to undertake this research I had no understanding of what it takes to apply for and be awarded a financial grant. With an adequate review of related literature in hand, together with a methodology that seemed to make perfect sense, I sent a document off to the Departmental Ethical Standards Committee in early 2010. Departmental ethical approval thus granted, my supervisor engaged me in assisting her in completing applications for financial backing for the project. What a learning curve. We spent that year applying for every grant that we might qualify for and with the completion of each administrative form my understanding of my own research aim and project definition grew – exponentially. As frustrated as I may have been in my naïvete, that process was valuable. Dr Christie was successful in her application to the Medical Research Council in December 2010 – a feather in her cap as an academic, and the means to this research for the next three years.

IV.

I departed on the journey believing time was of the essence. I did not initially have financial support and so my own meagre savings and a good dose of faith were what I would survive on. I do have a long-suffering and supportive family who have stepped into the breach – and without whose support I doubt I would have realised this dream. Initial impatience as obstacles presented themselves has gradually given way to contented patience and in fact an ardent belief in the value of time: I no longer believe that a doctorate in philosophical thought with the concomitant personal development can be undertaken at any pre-determined speed.

V.

"Not all those who wander are lost."

JRR Tolkien

Insofar as my journey was as a "full-time" scholar, other facets of life certainly determined the route, and were in turn affected by the journey toward the doctorate.

Since committing to full-time study I met, and have married, my husband. The relationship could only have been nurtured and developed given my relative flexibility in those first two years: his geological exploration had him based in Mozambique and our infrequent meetings required that I drop everything (more or less) to give “us” the time we lacked during the other five weeks of a six week cycle. In those halcyon two years (2009 and 2010) we spent time in Mozambique, Malawi, Zimbabwe, South Africa and the Seychelles. None of those experiences and travels would have been possible had I not been working gradually on developing this study, and been communicating via email with Dr Christie. Once again I owe her a debt of gratitude as without her understanding and trust things may well have been far different. In addition, my appreciation of these opportunities and my awareness of the unique experiences I was afforded on each trip heightened my desire and resolve to learn, and to continue doing so. Each withdrawal from the task at hand gave me perspective and renewed my passion for research.

Attracted to physical challenges, it was during this journey that I diverged to train for and complete two Ironman 70.3 events in South Africa (2010 and 2012). Some might say that the self-motivation and single-minded focus required to prepare for an event such as that would enhance the similar dedication required to write a doctoral thesis: critics might say it is a detraction from the required focus. Whichever it was for me it certainly fed a need in me at the time.

Following the first event, but I believe not entirely related to it alone but to a lifetime’s worth of overtraining and not “listening to my body”, I fell prey to a virus and subsequently post-viral fatigue syndrome. The PhD journey was certainly altered by this, as three months were spent virtually bed-ridden, and recurrences of the PVFS are reminders to slow down in a world that keeps on spinning. Again, the initial reaction was frustration and fear, paralysing to the mind and to creative thought. Now, the reaction is to work with the situation, rather than against it, conserving rather than wasting energy.

VI.

It was as a much-changed individual that I navigated 2011. With financial backing from the MRC we felt that we were ready to go: but this was not to be the case quite yet. Further ethical approval (at the level of the institution) was required by the MRC and this process raised some 'red flags'. Six months later the approval was granted – six months during which both Dr Christie and I were challenged and in turn rose to these challenges, learning at every step of the way. I would go so far as to say that this was the first pivotal experience in my development as a junior academic. I had always understood the importance of the ethical process – or so I thought – but this period of consultations, critiques, drafts and fine-tuning projected my understanding forward in leaps. I now have an understanding of the need for ethical approval – and not simply for the purpose of ensuring that no obvious hard comes to participants: I have come to see that the methodological design is as much an ethical concern as the harm that may come to the volunteers may be. Today I look forward to research design and ethical application, and I enjoy sharing my understanding with junior post-graduates, encouraging them to see the process not as an administrative hassle, but as a period of unprecedented growth.

VII.

Scientific validation of inclusion criteria is a given to the researcher, but not to the intended participant pool. It was with some surprise that I received vitriolic notes via anonymous letters in the local print media and emails sent not to me, but to the administrator of our department following my public call for recruits. The context of South Africa's political past has left an indelible sensitivity over the issue of 'race' and my requirement that my sample be 'white' had offended individuals in the community. Despite the defence for this criterion (the race differences in expression of plasma lipoprotein levels, as confirmed in 2010 and again in 2012 by Goedecke *et al.* in Cape Town-based research) I felt very vulnerable to this kind of antagonism from individuals I did not know personally. I suppose I also feared that a negative connotation surrounding my study might affect others' impressions of the research and by implication, me, thus impacting the recruitment campaign. The naïve "me" had not yet learned the difference between personal and professional critique, and through these experiences I learnt not to 'take things personally'. Today, I would be glad of criticism: it is valuable to obtain external viewpoints in order to re-assess

one's own intent and decision. As far as the recruitment goes, participants were not affected by the minority who spoke negatively of the research: the small voice of doom did not penetrate too far.

VIII.

Recruitment was not as smooth as I had anticipated. My Masters research had also engaged a sample of older women, but the recruitment criteria were admittedly a lot weaker than the current research called for – another instance of academic maturity on my part was the awareness of limiting factors and a drive to eliminate them. I had anticipated engaging a group of 30 women quite easily: the reality was not that simple. Recruiting in the region of ten women per advertising drive, it took four different recruitment periods to engage the requisite sample of 30 for the exercising group. This required personal interaction with over 120 women, some of whom did not meet the inclusion criteria, others of whom did not commit to the study, and some of whom dropped out. The control group proved even tougher to engage: without the exercise programme as a motivation individuals were loathe to commit to assisting me on the basis that they wanted to undertake exercise (but were currently sedentary), that they wanted to go on a diet (which I would not have permitted), or that they had insufficient time. I respect these choices, but with the dawn of the fifth year and the danger of the data becoming "old" I did feel the pressure as each recruitment drive yielded two or three willing individuals, and in each instance, committed participants were inevitably lost to factors beyond their, and indeed my, control (in the control sample in 2013 a participant was lost to a superbug following a knee operation).

IX.

As much as recruitment was difficult, I learnt the sheer determination of those candidates who did commit. I was humbled by their commitment to me, the researcher, as this "social contract" was what served as perhaps their strongest external motivator for adhering to the 12 week study – as has been ratified by their own self-reports following the intervention. This sample was simply a pleasure to work with and the women displayed gritty determination to meet every one of my requirements. In turn, the knowledge of their commitment drove me to continue when times got tough, or when I felt tired, or lacked motivation. I know I paid more

attention to the groups because I'd learnt this fact than I may have done before I understood the magnitude of their conscientiousness.

X.

"No problem can be solved from the same level of consciousness that created it."

Albert Einstein

A turning point in my thinking, my critical reasoning and analyses, and my approach to academic research came in 2012. I became personally interested in an allied topic, the matter of the 'high fat low carbohydrate' diet. Perhaps because Professor Tim Noakes had become very vocal about this topic, and it had become quite a controversial standpoint and was afforded a lot of time in the media, and perhaps because my sample started asking me questions about this lifestyle choice I decided to find out more about it. So I read. Gary Taubes was the first author I chose and I devoured '*Good Calories, Bad Calories*' with equal measures of shock, horror, amazement and disbelief. I couldn't really believe what he was saying: that we had all been duped, yet he seemed to provide adequate evidence. I could believe the idea that insulin function is affected most significantly by carbohydrate intake and so I could understand that from that premise the low carbohydrate idea was sound. I couldn't wrap my head around the idea that eating meat would result in extreme weight loss in obese individuals and yet the anecdotes piled up. In the end, whether or not Taubes did 'cherry pick' (as some critics say), whether or not the high fat diet is the 'be all and end all' (trials are needed but anecdotes continue to pile on) is not the point: what happened was that I experienced a turning point in my own analytic mind, and my writing revealed this subtle shift. Suddenly my work was tighter, neater, focussed and logical. On reading drafts of sections of the literature review Dr Christie recognised this too and was commenting on it: I wanted to go back and delete the review to write it again, in this newfound understanding of what it really is to write critically and engage with the existing literature. Perhaps my mind was just right for the change, perhaps it was indeed my interest in the subject matter that led me to experience this shift, whatever it was, it was the second pivotal moment on the journey.

XI.

"We do not receive wisdom; we must discover it for ourselves
After a journey that no one can take for us or spare us."
Marcel Proust

No part of this journey has really been 'alone'. Dr Christie has patiently and consistently guided me every step of the way. As is her manner, she has never openly directed me and has allowed me to explore avenues which may, and may not have worked: ultimately, I believe that as much as this journey was my challenge, I believe that she and I took it together. Growing into the confidence to take 'ownership' of my work has taken the small research team to new levels: together Dr Christie and I can discuss new ideas, take the challenge of new projects and encourage junior post-graduates to become involved in large-scale projects. One aspect of Dr Christie's supervision has been outstanding: her selflessness. Opportunities to attend conferences, present papers, and further my own career never pass her by without her encouraging me, and in many instances supporting me financially through her own grants. Her belief in me has never waned and I know that this solid backing has defined my experienced as a doctoral candidate. I mean it quite sincerely when I say I owe her a debt of gratitude.

XII.

"We should not judge people by their peak of excellence:
But by the distance they have travelled from the point where they started."
Henry Ward Beecher

Five years ago the thought of being launched as an 'independent' academic, without the safety-net of a supervisor, was a rather frightening thought. I couldn't imagine how I would manage. Through the process of the PhD research I feel far better equipped to lead research, critique research designs, consider methodologies and engage with topics independently. I know I have a long way to go – but at least I know I'm moving along a trajectory rather than remaining static. I don't know where this journey is taking me, but I am eager to move on, as I am well aware that this research is but the beginning of whatever is to come.

“Now this is not the end. It is not even the beginning of the end.
But it is, perhaps, the end of the beginning.”
Winston Churchill