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**BODY COMPOSITION, METABOLIC PROFILE AND FITNESS IN MEN AND
WOMEN WITH TYPE 2 DIABETES MELLITUS FOLLOWING A 6-MONTH
EXERCISE INTERVENTION: A GENDER COMPARISON**

Rikst Attema

Thesis submitted to the
Faculty of Graduate and Postdoctoral Studies
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in partial fulfilment of the requirements
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ABSTRACT

We compared changes in thigh muscle cross sectional area (CSA), strength, VO_{2peak} , and HbA_{1c} following aerobic training (**A**), resistance training (**R**), or their added combination (**AR**) in 115 sedentary type 2 diabetic men and women. Participants aged 40 to 70 years, mean BMI of 33.5 kg/m^2 , were randomly assigned to 6 months of 3x/wk **A** only (17 M, 11 W), **R** only (17 M, 11 W), combined **AR** (17 M, 12 W), and waiting-list control (**C**) (17 M, 13 W). All exercising men increased mid-thigh CSA (all $p < 0.05$). Mean increases in VO_{2peak} were exhibited in **A** and **AR** men (8.4% and 7.3%; $p < 0.05$). Strength increases were similar for exercising men and women. Absolute HbA_{1c} decreased in **AR** men (1.22%) and women (0.62%), and **A** men (0.80%) (all $p < 0.05$). **R** men exhibited a greater relative reduction in HbA_{1c} as compared to **R** women ($p = 0.033$ between sexes). Exercising men had modestly greater improvements in HbA_{1c} than women.

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**BODY COMPOSITION, METABOLIC PROFILE AND FITNESS IN MEN AND
WOMEN WITH TYPE 2 DIABETES MELLITUS FOLLOWING A 6-MONTH
EXERCISE INTERVENTION: A GENDER COMPARISON**

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1. INTRODUCTION

1.1 General Problem

The prevalence of type 2 diabetes mellitus (T2DM) continues to rise at an astonishing rate and is now considered one of the most predominant illnesses to affect humans. According to the Canadian Diabetes Association (CDA) (2002), more than 2 million Canadians now have diabetes mellitus and approximately 90% of those are afflicted with the type 2 form. The seriousness of the disease is real as it is considered to be a primary cause of mortality by disease in Canadians (CDA, 2002).

This disease was formerly termed 'maturity-onset diabetes' because the disease generally sets in after the age of 40; however, more and more cases are surfacing in young adults, adolescents, and even children. While there is a genetic component to T2DM, the disease is also strongly associated with obesity, poor diet and a sedentary lifestyle (Hu et al., 2001; Bonen, 1995). Obesity is closely associated with increased insulin resistance, which increases risk of type 2 diabetes mellitus (Bjorntorp, 1991).

Hyperinsulinemia and hyperglycemia, two primary characteristics of T2DM, are the forerunners of the serious complications associated with this disease.

Hyperinsulinemia is associated with hypertension and dyslipidemia, which are both highly detrimental to one's health. Ultimately, individuals with T2DM are afflicted with various and often numerous micro- and macrovascular complications. While the seriousness of this disease is often neglected, it is the constellation of these complications that may eventually lead to death if uncontrolled (Bonen, 1995).

The treatment of T2DM seeks to control blood glucose. In the early stages of the disease, dietary manipulation is often sufficient to normalize glucose levels. In moderate

cases, a combination of a strict diet and the use of oral hypoglycemic medications are commonly used. Finally, insulin injections are often required in advanced stages of the disease. Since skeletal muscle is a major site of glucose uptake, physical activity is also recommended as an important therapeutic intervention of T2DM. Muscular contractions increase glucose uptake through enhanced translocation of GLUT-4, a glucose transporter in the muscle to the cell surface, thus decreasing serum glucose concentrations. This is one of several mechanisms by which exercise improves glycemic control and is further discussed in the literature review. Weight reduction is also an important goal through diet and/or exercise because research has shown that weight loss decreases serum glucose and improves insulin sensitivity (Ivy, Zderic & Fogt, 1999; Bonen, 1995).

While exercise is recommended in the treatment of T2DM, experts often cannot agree on a specific prescription. Additionally, it is not known to what extent improvements in glucose and insulin regulation are affected by exercise-induced weight loss. Traditionally, aerobic exercise has been recommended for people with T2DM, although recent evidence suggests that resistance training may also provide benefits in glycemic control. Recent research suggests that the additional benefits of resistance training make it comparable to aerobic training as a therapeutic intervention for those with T2DM (Castaneda et al., 2002; Dunstan et al., 2002). Aerobic exercise is generally associated with modest weight loss mainly from adipose tissue, while resistance training is associated with increased lean body mass and decreased fat mass without a significant change in body weight. This is further described in the review of literature.

While the prevalence of T2DM is comparable among men and women (Gale and Gillespie, 2001), there are several key gender differences that may have important

implications on the outcome parameters of exercise training as a means of a therapeutic intervention for T2DM. A highly important and obvious distinction between the genders is the influence of sex hormones and the differences in ratios between men and women; women primarily under the influence of estrogen and progesterone, and men under the primary influence of testosterone. The hormones exercise diverse metabolic and regulatory functions on the body and affect the response to exercise (Roberges & Roberts, 2000). This difference in hormones has been hypothesized to be a primary reason why men and women differ physiologically in terms of body composition, metabolic parameters, cardiorespiratory fitness and strength, although this hypothesis needs further clarification. It is also known that genetic and cultural factors also play a role in the physiological gender gap (Legato, 1997).

Consequentially to the differences between men and women, the response to exercise is influenced by gender. Therefore, it is of interest to examine these differences and how they compare to changes in body composition, metabolic profile and fitness parameters, and the implications these changes may have on the overall metabolic profile of individuals with T2DM.

1.2 Specific Problem

While experts agree that there is great potential in managing T2DM through exercise training, there is no consensus on specific guidelines and subsequently there is no universally accepted exercise prescription. Aerobic training has been recommended in the past, but more recent research has begun to explore resistance training and suggested that the benefits for T2DM may be comparable to that of aerobic training (Castaneda et

al., 2002; Dunstan et al., 2002). Furthermore, the combination of aerobic and resistance training should theoretically be of greatest benefit; yet this remains to be established.

In determining exercise guidelines, gender may be an important consideration. While the incidence of T2DM is comparable in men and women (Gale and Gillespie, 2001), there are many existing sex differences unrelated to the disease that may influence the therapeutic potential of exercise training. As such, men and women may require different exercise prescriptions to meet their individual needs.

Gender differences in body composition, glycemic control, lipid profile, fitness parameters, and responses to exercise are those differences of greatest relevance. The aging adult and role of menopause may also influence exercise-training responses. Wirth and Steinmetz (1998) noted 22% more visceral adipose tissue in men than women. At the same time, men bear more lean body mass than women mainly in the form of bone and according to Janssen, Heymsfield, Wang and Ross (2000) 36% more skeletal muscle mass. The accumulation of abdominal obesity commonly seen in men has negative consequences on lipid profile and glycemic control (Björntorp, 1991). Women tend to accumulate fat in the gluteal-femoral region under the influence of estrogen; however, some women and more frequently post-menopausal women accumulate visceral fat (Gambacciani et al., 1997), which causes predisposition to metabolic complications such as T2DM (Björntorp, 1991). Muscle mass, strength, and cardiorespiratory fitness are all lower in women than men. Conversely, women exhibit more favourable lipid profiles than men and appear to be protected from cardiovascular disease (CVD) by the effects of estrogen until menopause (Smith et al., 2001). In T2DM however, this apparent protection is no longer evident and diabetic women have twice the risk for a recurrence of

myocardial infarction and four times the risk of having heart failure as compared to diabetic men (Wenger, 2002).

Comparison of gender differences is a difficult and complex task because of the difficulty in controlling for sex hormones. Although this area of research has become more popular in recent years, there remains a large gap in the literature. To our knowledge, there is only one study by Vanninen, Uusitupa, Siitonen, Laitinen and Lansimies (1992) examining the effects of exercise training on T2DM where the results from men and women are evaluated separately (discussed in literature review). Research to date on the effects of exercise on T2DM have pooled results for men and women and gender comparisons are virtually absent in the literature thus requiring further exploration.

In order to optimize exercise prescriptions and maximize the exercise-related benefits on T2DM, there is a definite need for larger, well-controlled, clinical trials examining the modality of exercise (Boulé, Haddad, Kenny, Wells, & Sigal, 2001) and evaluation of gender responses to exercise in the diabetic population. A specific prescription or at the least, clear guidelines on exercise training are imperative for the medical community to implement exercise as a primary form of treatment in T2DM. A specific prescription, tailored to the individual is highly needed so that patients may reap the greatest benefits that exercise has to offer and ultimately improve under the best possible conditions abolish symptoms and retard the progression of their disease.

1.3 Objectives

The purpose of this study is to examine whether or not gender differences exist in body composition and fitness parameter changes following a 6-month exercise training

program in previously sedentary participants with T2DM and how these changes compare to metabolic profile. Type 2 diabetic participants are diagnosed as such by a physician according to CDA criteria and for the purposes of this study include those that are moderately controlled and treated with diet alone and/or in combination with oral agents.

More specifically, this research study will examine the occurrence of gender differences in type 2 diabetic adults with regards to changes in body weight, fat distribution [abdominal subcutaneous adipose tissue (SAT), visceral adipose tissue (VAT)] and muscle cross sectional area (CSA) of the thigh, as well as strength and cardiorespiratory fitness (VO_{2peak}) following a 6-month exercise intervention. Furthermore, it would be of interest to examine the changes in body composition and fitness parameters and how they compare to glycemic control, as reflected by HbA_{1c}, insulin resistance (using HOMA model) (Sakane et al., 1997), and lipid profile [HDL-C, LDL-C, total cholesterol, total cholesterol/HDL-C ratio and triglycerides (TG)]. Four groups will be assessed including; waiting list control (C), resistance-only (R), aerobic-only (A), and combined aerobic and resistance (AR) exercise.

1.4 Hypotheses

Because men have the greater propensity to build muscle mass from resistance training, and muscle mass is positively associated with improved glycemic control and may have additional benefits (Ivy et al., 1999), it was postulated that the R and AR men would exhibit greater improvements in body composition, glycemic control, lipoprotein lipid profile and fitness parameters [VO_{2peak} and strength by predicted 1-repetition max (RM)] as compared to women of the same groups following a 6-month exercise training

program. Furthermore, A men and women would improve similarly for these variables. More specifically, it was hypothesized that **R** and **AR** men would exhibit greater abdominal adipose tissue loss, greater increases in muscle cross sectional area, and increased improvements in strength and VO_{2peak} as compared to the women of the same groups.

1.5 Significance

Researchers have yet to agree on a specific exercise training program designed as a therapeutic intervention in the treatment of T2DM. Furthermore, it is known that men and women differ physiologically and while cardiorespiratory and strength improvements in response to training are comparable between the genders, it remains to be determined whether or not men and women reap similar health benefits from the same exercise training. Specifically, research examining the effects of different exercise modalities on T2DM has pooled results for men and women. The differences that exist between the sexes may have important implications when designing an exercise intervention in a population at high risk for micro- and macrovascular complications. The significance bears great importance considering that the relative mortality risk associated with having T2DM is greater in women than men (Wenger, 2002). Wenger (2002) also describes a poorer prognosis in terms of coronary events for women than men with T2DM as compared to healthy men and women. Abbott, Donahue, Kannel, and Wilson (1988) suggest that T2DM may predispose to a form of myocardial infarction having a greater probability of failure and further complications, and may occur more strongly in women. This study compares not only the different modalities of exercise on variables associated with health, but comparisons across genders will be made in order to help establish

appropriate exercise guidelines for men and women respectively. A specific prescription may allow men and women separately to reap greater benefits from the exercise intervention and ideally create an environment most able to control a disease that is progressive in nature.

1.6 Limitations and Delimitations

- It would be ideal to separate the female participants in terms of menopausal state, menstrual cycle phase, and users versus non users of hormonal supplements; however, this would require recruitment of a very large sample as each subgroup would be further divided into one of four intervention groups. Furthermore, it would be of benefit to measure sex hormone levels to evaluate and quantify the differences in hormonal milieu between men and women.

1.7 Definitions

1. *Type 2 diabetes mellitus (T2DM)* is based on a medical diagnosis by a licensed physician, following the 1998 Canadian Diabetes Association guidelines and standards. Under these standards, 7.0 mmol/L is the minimum value for a fasting plasma glucose test (CDA, 2002).
3. *Glycemic control* refers to glucose control. Good glycemic control is an attempt at reducing hyperglycemia and achieving ideal blood glucose levels of 4-6 mmol/L throughout the day.
4. *HbA_{1c}* is the term used to describe the hemoglobin with glucose attached to the beta chain and normally accounts for approximately 5% of total hemoglobin in non-diabetic individuals. Several hemoglobins with glucose derivatives attached have been isolated and two of these have been marked as HbA_{1a} and HbA_{1b} and make up approximately 1%

of total hemoglobins in non-diabetic individuals. HbA₁ is thus the term used to describe the collective hemoglobins with attached glucose or glucose derivatives (Davidson, 1998).

The attached glucose or glucose derivatives alters the charge properties of the HbA and consequently, the molecules move faster in particular chromatographic separation techniques including ion chromatography, electrophoresis, or high-performance liquid chromatography (HPLC). It has been shown that diabetic individuals have a greater percentage of fast hemoglobins than non-diabetics (Davidson, 1998). Measurement of hemoglobin A_{1c} reflects the average blood glucose concentration over the previous 8 to 12 weeks and thus is a good indicator of glycemic control (Boulé et al., 2001).

5. *Insulin resistance* refers to the impairment of glucose uptake by target tissues when stimulated by insulin (Corry, 2001). Using the homeostasis (HOMA) model of assessment proposed by Matthews et al. (1985) insulin resistance is evaluated as an index of resistance and is based on fasting insulin and glucose levels. Tissue insulin sensitivity is best measured by the euglycemic hyperinsulinemic clamp technique and is considered to be the gold standard. This technique however, is time consuming and not convenient for large clinical studies (Cervenakova, Ksinantova & Koska, 2002). Matthews et al. (1985) reported a correlation of insulin resistance calculated by HOMA to be correlated with estimates of insulin resistance attained via the euglycaemic clamp ($R_s = 0.88$, $P < 0.0001$), the fasting insulin concentration ($R_s = 0.81$, $P < 0.0001$), and the hyperglycaemic clamp, ($R_s = 0.69$, p less than 0.01). In their study, Cervenakova et al. (2002) further

noted that the use of the HOMA model to be more suitable in diabetic as compared to non-diabetic individuals. The formula is described in the methodology section.

6. *Fat mass (FM) and fat-free mass (FFM) (lean body mass)* follow the two-compartment model of the human body. In this model, the body is comprised of two components; fat mass, which includes essential and nonessential body fat; and fat-free mass, which refers to all of the body's non-fat tissue, including bone, muscle, organs and connective tissue (Wilmore & Costill, 1999). There are various techniques to assess FM and FFM including underwater weighing and bioelectric impedance.

7. *Resistance training* is performed through repeated exertion of the working muscles against a load or resistance. Resistance training is quantified by number of continuous repetitions to complete a set and successive sets may be completed with a given rest between sets. The goal of resistance training is to improve strength.

8. *Aerobic training* involves systematic repetitive, rhythmic contraction and movement of large body muscles that places a cardiorespiratory demand on the body and can be sustained over a period of time. The goal of aerobic training is to increase oxygen consumption and enhance cardiovascular and pulmonary functioning.

9. *Subcutaneous adipose tissue (SAT)* is the fat layer that lies directly under the skin layers, but does not surround the organs of the thorax nor is it found in the muscles or organ tissues of the body.

10. *Visceral adipose tissue (VAT)* is the fat tissue that lies deep to the subcutaneous adipose tissue inside the abdominal cavity and surrounds the main organs of the thoracic region. It does not include the fat inside the organs.

11. *Metabolic profile*, for the purposes of this study, includes blood lipoprotein lipid profile, insulin resistance and glycemic control (as defined above).

12. *Blood lipoprotein lipid profile* is comprised of measurements of total cholesterol, HDL-C, LDL-C, total cholesterol/HDL-C ratio, and TG.

2. LITERATURE REVIEW

2.1 Introduction

To date, research examining the effects of exercise on physiological factors in individuals with T2DM has pooled results for men and women. In their meta-analysis on the effects of exercise on T2DM, Boulé et al. (2001), found only one study that separated men and women in their analyses and met the inclusion criteria of a controlled clinical trial lasting 8-weeks or longer with a defined exercise intervention. This was the study by Vanninen et al., (1992) comparing a one year aerobic exercise intervention versus non-exercise control in newly diagnosed men and women with T2DM. Consequently, very little is known regarding the response of type 2 diabetic men versus women following different modalities of exercise. As such a standard exercise prescription for type 2 diabetic men and women is yet to be determined.

While the prevalence of T2DM in men and women is comparable (Gale & Gillespie, 2001), the gender differences that exist in terms of body composition, metabolic profile and response to exercise may impact the effectiveness of exercise training programs designed as therapeutic interventions for T2DM. Those gender differences of greatest relevance include peripheral versus central body fat distribution in women versus men respectively, greater lean body mass in men relative to body weight, estrogen effects on lipoprotein lipid profile and glycemic control, and the sex specific responses to exercise training. Research to date examining gender differences is limited and little research has explored the effects of exercise in women. Finally, it is of interest

to determine the respective responses of each gender to exercise and the implications any differences may have on the overall metabolic profile of individuals with T2DM.

2.2 Body Composition

Morphologically, men are bigger than women; they are typically taller and heavier. Looking more closely however, it is known that men and women exhibit marked differences in body composition in terms of both adipose tissue and lean muscle tissue; the major tissues for energy reserve and production of mechanical work, respectively. In absolute terms and relative body weight, not only do men bear more lean muscle tissue, while women carry more adipose tissue, but the distribution of tissues is also different between the sexes. The body composition differences of greatest significance include greater upper body muscle mass in men and greater lower body fat mass in women (Nindl, Scoville, Sheehan, Leone and Mello, 2002). In men, the greater proportion of FFM is reflective of higher levels of testosterone and is evidenced by greater bone and muscle mass (Tarnopolsky, 1999). Vague in 1947, was the first to describe the gender difference in body fat distribution and later (1956) attributed risk factors with male type body fat distributions. He stated that males typically exhibit a greater proportion of body fat in the abdominal (visceral) region, while women have a tendency to store more adipose tissue in the gluteal-femoral region. These fat deposition types are termed android or central and gynoid type distributions respectively (Vague, 1947). It is thought that these fundamental differences in body composition reflect evolutionary development in that women are designed to conserve energy in times of starvation so they may still bear and support offspring (Tarnopolsky, 1999).

Aging is associated with major changes in body composition that can ultimately be detrimental to health. Both men and women experience considerable increases in total body fat mass that accumulates mainly in the upper body. Conversely, lean body mass decreases substantially with loss of both muscle and bone mass, an undesirable combination. While these changes are typical with age, they are largely due to physical inactivity and reduced energy intake and may be retarded through exercise training (Schuit et al., 1998).

It appears that men achieve greater weight loss through diet and/or exercise than do women. Van Gaal, Vansant, Moeremans and De Leeuw (1995), noted that following 6 months of a hypocaloric, protein-enriched diet, the abdominally obese men decreased their waist to hip ratio (WHR) by 11% while the women experienced a 6% decrease. As noted previously, Andersson et al. (1991) reported greater weight loss in men as compared to women of similar body fat following 3 months of aerobic exercise despite only slight negative shift in energy balance. According to Tarnopolsky (1999), women are much more resistant to weight loss reflecting a protective mechanism against fat and protein loss potentially through compensatory increased energy intake not seen in men. Conversely, Janssen and Ross (1999) found that obese men and obese pre-menopausal women who lost ~10% body weight by diet alone or in combination with exercise, had similar reductions in total adiposity, subcutaneous and visceral adipose tissue. In the study by Janssen and Ross (1999), adherence to diet and exercise was controlled. Diet therefore, may play a crucial role for women to experience similar weight loss as compared to men following the analogous exercise regimens as a consequence of their tendency for dietary compensation.

2.3. Gender Differences in Adipose Tissue

The distribution of body fat is of great importance considering the influence on both metabolic and endocrine parameters (Legato, 1997). In pre-menopausal women, estrogen is responsible for greater fat deposition in the thighs and hips and appears to protect women against increased risk for cardiovascular disease and T2DM (Smith et al., 2001). Cefalu et al. (1998) noted that the women in their study had significantly greater subcutaneous fat than the men and subsequently totalling in greater overall body fat. More specifically, Wirth and Steinmetz (1998) found that women had a 35% wider subcutaneous fat layer and 22% lower visceral fat as compared to men matched for height, weight and age. As men and women age, there is a continued increase in central body fat distribution and eventually by the 7th decade, absolute amount of VAT is comparable between genders (Hunter et al., 1997; Hunter et al., 1996).

In early postmenopausal women there is a redistribution of body fat towards android (central) adiposity as estrogen levels plummet. Fat mass begins to fall and continues to do so in post-menopausal decades and is consistent with the notion that estrogen influences fat mass (Aloia, Vaswani, Ma & Flaster, 1996). It has been postulated that estrogen reduces postprandial lipid oxidation, although the mechanism remains unknown (O'Sullivan, Martin & Brown, 2001). Furthermore, estrogen may influence body fat through direct effects via estrogen receptors found in adipocytes where different regions of adipose tissue may respond differently to lipolytic agents (Rebuffé-Scrive et al., 1985). Finally, there may be other effects of estrogen on fat mass that are still unknown.

Results from a study by Gambacciani et al. (1997) confirmed the notion that early menopause is associated with an increase in body weight and a redistribution of body fat. Women experienced increased adiposity in trunk and arms while there was no change observed in the legs. Furthermore, hormones rather than individual differences were clearly isolated as the independent factor resulting in body fat changes following menopause. These body composition changes are relevant because there is a clear association between abdominal fat, especially visceral fat and impaired glucose metabolism and the increased risk for development of T2DM (Rönnemaa et al., 1997; Fujioka, Matsuzawa, Tokunaga, & Tarui, 1987).

At the level of the cell however, Mauriège et al. (2000), found no difference between premenopausal and early postmenopausal women in terms of changes in adipose cell mobilization and/or storage capacities. Nor did they find changes in basal lipolytic rate, or lipoprotein lipase activity (LPL) in comparison of abdominal and gluteal-femoral adipose regions in pre- and postmenopausal women. These findings are in contrast to previous research, but it should be noted that all adipose cells in this study were similar in size.

2.4. The Influence of Obesity on Hormone Levels in Men and Women

It is common for obese men and women to display disturbances in hormone levels. A relative hyperandrogenicity is characteristic in abdominally obese women. Consequently, abdominal obesity has been associated with increased concentration of free testosterone and estradiol (Goodman-Gruen & Barrett-Connor, 2000) and decreased serum sex hormone binding globulin (SHBG) (Björntorp, 1991). While the cause of this abnormality is poorly understood, it has been postulated that this change in hormonal

milieu may have a causal effect on muscle tissue insulin resistance in women (Björntorp, 1991). Obese women often but not always become infertile and experience loss of menses. Interestingly, obese women who do not have cessation of menses display normal testosterone levels (Legato, 1997).

In contrast, abdominally obese men exhibit hypogonadism resulting in decreased testosterone levels (Björntorp, 1991). Couillard et al. (2000) found that visceral obesity was correlated with decreased C₁₉ adrenal steroid hormones (DHEA, DHEA-FA and DHEA-S), androgen levels (testosterone and DHT) and decreased SHBG. These authors further noted that the association of body fatness to testosterone was largely independent of the aging process while levels of C₁₉ androgens decreased with age. Research has suggested that glucocorticoids alter testosterone secretion by the testis and obese individuals frequently display increased plasma glucocorticoid concentrations (Björntorp, 1991). Alternatively, it has been proposed that adipose tissue contains the enzymes which aromatize adrenal steroids (precursors to androgens or estrogens) to estradiol, a conversion that is more potent in obese individuals (Tarnopolsky & Cortright, 1999). The mechanism by which body fatness is related to a reduction in testosterone concentrations in men but not in women remains uncertain and requires further study (Couillard et al., 2000). Goodman-Gruen and Barrett-Connor (2000) found that in men, total testosterone was inversely related to fasting plasma glucose, while in women bioavailable estradiol and testosterone were positively associated with glycemia.

Insulin resistance typically follows castration in male rats and in abdominally obese men hypogonadism has been linked to insulin resistance. Furthermore, abdominally obese men and women typically experience low levels of SHBG; an

independent predictor of T2DM. Low levels of SHBG are also associated with increased plasma insulin and abdominal obesity. As such, it is likely that the additive effects of hyperandrogenicity/hypogonadism, decreased SHBG and excess visceral body fat distribution contribute to the development of T2DM. The role of female sex-steroid hormones on glucose-insulin metabolism is much less studied and thus poorly understood (Björntorp, 1991).

2.5 Central Obesity and the Link to T2DM

It has long been established that obesity is associated with metabolic complications including dyslipidemia, hyperinsulinemia and T2DM (Björntorp, 1991). The importance of body fat was demonstrated by Abate et al. (1996), who found that while both healthy control and T2DM participants had similar BMIs (28.5 ± 7.7 vs. 28.6 ± 5.1), the healthy control group had significantly lower body fat mass. Control participants were recruited as having the same range of BMI as those participants with T2DM. Furthermore, after adjusting for percentage body fat, the T2DM participants had significantly lower sums of peripheral skinfolds than the healthy control group. More specifically, central body fat accumulation is a strong and independent predictor of insulin sensitivity (Cefalu et al., 1995; Rönnemaa et al., 1997; Fujioka et al., 1987)). While central fat patterning was associated with age, insulin sensitivity revealed only a modest correlation to age (Abate et al., 1996).

In an attempt to understand the mechanisms underlying this phenomenon, Björntorp (1991) published a review postulating a possible cause-and-effect relationship between VAT and the ultimate development of T2DM. Research has found increased FFA concentrations and turnover rate in generalized obesity that was even more

pronounced in abdominal obesity. This elevation is consequential of several factors including enhanced sensitivity of enlarged obese adipocytes to lipolytic stimuli. Subcutaneous abdominal adipocytes are highly sensitive to lipolytic activity in comparison to other subcutaneous adipose cells, while visceral portal adipose tissue contains the most sensitive adipose cells, particularly in the abdominally obese (Björntorp, 1991). It is interesting to note that visceral adipose cells are the least sensitive of adipose cells to the antilipolytic action of insulin consequentially due to a low density of insulin receptors. Visceral adipose tissue, with its high sensitivity to lipolytic stimuli and low sensitivity to antilipolytic effects of insulin, therefore contributes a considerable amount of FFAs into systemic circulation (up to 50% or greater of total circulating FFA). Furthermore, since SAT is sensitive to insulin effects on lipolysis, the proportion of FFAs mobilized into systemic circulation by visceral adipocytes is further augmented (Björntorp, 1991).

When FFA concentrations are elevated in systemic circulation, there are several negative effects on blood glucose. In muscle tissue, excess FFAs appear to decrease insulin-stimulated muscle glucose clearance. FFAs may also accumulate in muscle causing insulin resistance (Ivy et al., 1999). Furthermore, excess FFAs in the liver results in FFA-stimulated gluconeogenesis and therefore increased hepatic glucose output (Ivy et al., 1999). In an attempt to control increasing levels of blood glucose, insulin secretion is increased via the pancreatic β -cells. Ultimately, the increased demand and production of insulin can cause β -cell exhaustion and therefore, decreased insulin production. β -cell impairment intensifies the insulin resistance, decreases FFA clearance, accelerates hepatic glucose output and develops into T2DM (Ivy et al., 1999) It is important to note

however, that hyperinsulinemia itself may result in diminished insulin sensitivity in muscle and liver (Björntorp, 1991).

There is an alternate mechanism leading to decreased insulin sensitivity but not specific to fat depots. In this theory, an increase in fat mass leads to adipocyte hypertrophy. When adipocytes increase in size, there is a decrease in density of insulin receptors and consequently insulin sensitivity decreases. Adipocytes then eventually become deficient in α -glycerophosphate, a glucose product that is required for FFA esterification and reducing plasma FFA clearance by adipocytes (Ivy et al., 1999). Again, we see an increase in circulating FFAs that have negative effects on blood glucose as previously described.

Increased cortisol levels as well as decreased SHBG are also characteristic of abdominally obese men and women. The combination of these abnormal hormone levels is associated with a high density of glucocorticoid receptors in VAT, directing cortisol effects to the visceral adipose area, enhancing fat deposition in this area. In premenopausal women, it appears that progesterone interacts with the glucocorticoid receptors protecting this area from the effects of cortisol. This is one explanation for the observed increase in abdominal fat distribution in women as progesterone secretion ceases with menopause (Björntorp, 1991).

It is quite apparent that obesity and clearly abdominal obesity predispose one to the development of T2DM. It is the VAT that increases FFA levels in the circulation and begins a cascade of events promoting hyperglycemia and ultimately T2DM. It is this type of fat distribution that needs to be reduced in high-risk individuals and those already affected by the disease to reduce the risk and complications that accompany excess VAT.

2.6. The Effect of Exercise on Fat Mass and Distribution

Both aerobic and resistance exercise result in favourable body composition changes, although outcomes and mechanisms are different, reflecting the nature of the activity. A large amount of energy may be expended during a single bout of aerobic activity thus increasing total daily energy expenditure. When the total daily energy expended is greater than energy intake of the diet, there is a negative energy balance causing the body to utilize stored energy predominately from adipose tissue. Ultimately, if the aerobic activity is continued regularly, weight loss may occur.

In resistance training, the muscles are taxed and muscle proteins are essentially catabolized and resynthesized, ultimately resulting in greater muscle mass through skeletal muscle hypertrophy. Research to date examining the effects of resistance training on changes in FFM, body fat percentage and resting metabolic rate remain controversial. While a bout of resistance training does not result in a substantial amount of energy expenditure, one theory suggests that the resultant increase in active muscle mass increases resting metabolic rate (RMR) (Lemmer et al., 2001). Another theory proposes that following resistance training, individuals increase their spontaneous physical activity increasing total daily energy expenditure (Castaneda et al., 2002). Both theories result in increases in total daily energy expenditure that may eventually cause a negative shift in energy balance ultimately resulting in fat loss. Other studies show no change in body fat following a resistance training program (Hurley et al., 1988). Resistance training has also been shown to improve muscle quality (strength per unit of trained muscle mass). Tracy et al. (1999) demonstrated similar improvements in muscle

quality in elderly men and women following a 9-week resistance training program. There were however, no changes in percent body fat or FFM.

In a gender comparison by Andersson et al. (1991), it was concluded that middle-aged men and women of comparable body fat percentages respond differently to the same exercise program. Following three months of physical training (mainly aerobic in nature but with some strength component), men exhibited significant decreases in body weight, body mass index (BMI), waist and hip circumferences, and body fat (kg), while a reduced waist circumference was the only significant change noted in the women. The authors further compared the men and women to a group of obese women who displayed body composition changes more similar to the group of men, as compared to the leaner women. Following the exercise training, the obese women demonstrated a similar loss of body fat and comparable increase in lean body mass as compared to the men. Andersson et al. (1991) concluded that the women with similar body fat as the men (the lean women) reacted to the stimulus of exercise with dietary overcompensation as been described in rats, protecting their body fat. Furthermore, the obese women had more fat to lose.

Wirth and Steinmetz (1998) noted that although the men and women in their study had similar reductions in body weight (13.4 kg and 12.8 kg respectively) and fat mass following 15 weeks of dieting and aerobic exercise, the men displayed a greater reduction in VAT (measured through ultrasonography) and less reduction in SAT as compared to the women. The men and women were matched for weight, height and age for a total of 16 pairs. This gender difference, however, is likely consequential of differences in VAT and SAT at baseline, where men had 22% more VAT and a 35%

thinner subcutaneous layer. Overall, reduction in waist to hip ratio, however, was greater in men than women. It appears that initial levels of VAT and SAT are more crucial in preferential adipose tissue loss than gender following weight loss.

In a study examining the effects of endurance training on fat metabolism in lean women, Horowitz, Leone, Feng, Kelly and Klein (2000) noted a progressive increase in glycerol mobilization from abdominal SAT during endurance exercise. This increased mobilization however, did not occur in the femoral SAT where glycerol release did not change. This study illustrates the finding that abdominal adipose tissue is the preferred site of fat mobilization during aerobic exercise over peripheral SAT.

In gender comparisons, initial levels of VAT and abdominal SAT must be taken into consideration since men have higher VAT and less abdominal SAT than women. It is likely that differences in initial values of VAT and abdominal SAT between men and women account for gender differences in fat loss following weight loss. Doucet et al. (2002) demonstrated an eradication of gender differences in specific fat loss following weight loss when initial levels were accounted for.

The results of studies examining the effects of resistance training on body fat distribution remain conflicting. Two studies have reported a significant reduction in VAT in women following 16 weeks of resistance training (Treuth et al., 1995) and 25 weeks of resistance training (Hunter, Bryan, Wetzstein, Zuckerman & Bamman, 2002). In the same study by Hunter et al. (2002) the men did not show any changes in VAT following training. Conversely, men have been shown to decrease fat mass while women exhibited no change in fat mass following 12 weeks of resistance training (Joseph, Davey, Evans, & Campbell, 1999) and 6 months of resistance training (Hurlbut et al.,

2002). Hunter et al. (2002) hypothesized that hormones may influence changes in body fat distribution following resistance training. All resistance programs mentioned were fairly similar in that exercises were performed 3 times a week, with 2 sets of 10-15 repetitions except for the study by Joseph et al. (1999) where participants completed 3 sets of exercises but only twice a week. Furthermore, body composition was determined through various techniques. Treuth et al. (1995) used several precise techniques including dual x-ray absorptiometry (DEXA) as well as magnetic resonance imaging (MRI) and underwater weighing. The other authors relied on a single method to assess body composition. Hurlbut et al. (2002) chose DEXA, Hunter et al. (2002) examined a CT slice of the abdomen and Joseph et al. (1999) used the underwater weighing technique to determine body composition. The study by Joseph et al. (1999) was not able to examine body fat distribution as the other authors had. The use of different techniques and slight variations in exercise regimens may have contributed to the conflicting results noted.

2.7. Gender Differences in Lean Body Mass

It has been well documented that men have greater lean body mass as compared to women. Even when matched for age and height, trained men had greater FFM as compared to trained women (Abe, Brechue, Fujita, & Brown, 1998). More specifically, Gallagher et al. (1996) found that men had more total appendicular skeletal muscle as compared to women.

Abe et al. (1998) noted that muscle thickness was greater in men as compared to women at 12 sites with the exception of the anterior thigh. It was determined that the women had approximately 94% of muscle thickness for the lower body versus

approximately 73% and 74% the muscle thickness for the arm and trunk respectively, as compared to the men. These men and women were matched for age and height. Janssen et al. (2000), who studied healthy but untrained adults, also noted this difference in upper and lower body muscle mass between genders. These researchers determined that men averaged 36% more total skeletal muscle mass than women. More specifically, the men displayed 40% more upper body and 33% more lower body muscle mass in comparison to the women. Consequently, the women had approximately 70% of the lower body strength and approximately 50% of the upper body strength as compared to the men.

Abe et al. (1998) found that in trained individuals, muscle fibre number, fascicle length, and proportion of connective tissue are similar between men and women. The limit of FFM accumulation appears to be governed by the upper limit of muscle fibre growth capacity; a capacity that appears to be greater in men although this theory remains to be resolved and is discussed later.

While it is well established that men exhibit greater skeletal muscle mass in comparison to women, it appears that men also experience greater losses with age. It has been hypothesized that the hormonal differences described earlier are responsible, although mechanisms remain unclear (Doherty, 2001). Morphological studies have come to the agreement that it is the type II muscle fibres that decrease with age (20-50%), while the type I muscle fibre type remain much less altered by age (1-25% decline) (Doherty, 2001). The difference in fibre type loss may be largely due to age-related decreased physical activity. Lack of large explosive movements results in decreased recruitment of larger type II muscle fibres while type I muscle fibre are required for day-to-day living (eg. posture).

2.8. The Effects of Exercise on Muscle Mass

As mentioned previously, skeletal muscle response to aerobic and resistance training is different and as such, exercise modality bears important training outcome implications. Furthermore, there is limited research on the effects of combined aerobic and resistance training.

In men, the physiological response to resistance training promotes a hormonal milieu that is highly favourable to muscle protein synthesis and much more so than is experienced by women (Staron et al., 1994). Testosterone is a major anabolic hormone that favours protein synthesis in muscle and it is known that men have higher testosterone levels in the blood at rest. In response to resistance training, men exhibit a greater absolute increase in testosterone level following a single resistance exercise bout (Kraemer et al., 1991), and display greater absolute increase in resting level following a resistance training regimen as compared to women (Staron et al., 1994). In resistance training, testosterone and growth hormone are the major hormones responsible for protein synthesis, ultimately building muscle mass. Cortisol is a catabolic hormone that also plays a role. Although resting levels are similar in men and women at rest, following a resistance training program, the level of cortisol is decreased in men but remains unchanged in women (Staron et al., 1994). The ratio of testosterone to cortisol is therefore further heightened in men following training and is thought to be important for muscle protein synthesis (Florini, 1985).

Lemmer et al. (2000) demonstrated that men increased their muscle mass twice as much as the women following a 9-week resistance training program. Their program, however, was focused on unilateral leg extension, whereby participants performed 5 sets

3 times a week. The heavy resistance, high volume and focused nature of the training program may understandably demonstrate impressive results. Significant increases in muscle thickness were also apparent following 6 weeks of resistance training in a study by Abe, DeHoyos, Pollock, and Garzella (2000). While the percentage increase in muscle hypertrophy was similar for men and women in this study, the absolute increase in cross sectional area was greater in men. Total FFM may also be examined, and a study by Joseph et al. (1999) demonstrated that following a 12-week resistance training program, men increased their FFM (2.2 ± 0.5 kg) while the women saw no change (0.0 ± 0.3 kg).

Staron et al. (1994) concluded that muscle fibre type conversions and muscle fibre hypertrophy were similar in men and women following an intense 8-week resistance training program. However, they noted that only the men exhibited significant increases in testosterone and decreases in cortisol levels, fostering an environment for increased protein synthesis. Long-term changes were not examined.

In a meta-analysis, Ballor and Keesey (1991) noted that cycling training and resistance training in men resulted in increased FFM while walk/run training did not. Training frequency and duration was longer for the cycling group as compared to the other exercising treatments and the resistance training groups had significantly greater increases in FFM than the cycling groups. In the women, there was no increase in FFM for either cycling or run/walk training groups. All men in exercising groups lost fat mass while only those women in the run/walk training groups experienced fat loss. Studies examining resistance training in women were not included because the literature was

scarce. Little is known regarding the effects of a combined aerobic and resistance training program on muscle mass.

2.9. Gender Differences in Strength and Cardiorespiratory Fitness

Sex differences in strength and cardiorespiratory fitness exist in large part due to the differences in body composition between men and women. Women carry around more fat mass using a smaller amount of functional skeletal muscle mass and are consequently at a disadvantage. The gender gap is greatly reduced when accounting for these differences in body composition and minimizes the difference between genders and with exercise training.

Strength differences between the sexes have long been documented (Hoffman, Stauffer & Jackson, 1979), and are primarily reflective of the greater skeletal muscle mass exhibited in men. Frontera, Hughes, Lutz, and Evans (1991), found that in isokinetic testing of the knee, women had 59.8% the strength at slower speeds and 58.7% the strength at higher speeds as compared to the men. In examination of elbow flexion and extension, the women averaged between 50.2 and 46.1% the strength at slower and higher speeds respectively of the men. While the differences observed between sexes were expected, gender differences were significantly reduced or completely eradicated when muscle strength was corrected for muscle mass. This also held true for the observed age-related differences, and as such, Frontera et al. (1991) concluded that the decline of strength with age was related to a decrease in muscle mass rather than function.

In the absence of physical activity, muscle mass begins to decline in the beginning of the third decade. Strength declines at a rate of 10-15% every ten years so that by the

time an adult is into their 70's and 80's they have approximately 50% of the strength they had as young adults (Doherty 2001). In his review, Doherty (2001) concludes that while women may demonstrate a slight premature decline in strength as compared to the men, general strength losses are comparable across the genders. In physically active individuals, this decline in strength is delayed.

Following resistance training, it is expected that both men and women increase strength significantly, with men having greater total strength before and after training. Relative increases in strength following training have been found to be similar in men and women although absolute strength gains are often greater in men (Joseph et al., 1999; Cureton, Collins, Hill & McElhannon, 1988).

Following puberty, males exhibit greater muscle mass and cardiac size, directly putting them at a cardiorespiratory fitness advantage in comparison to women. Finally, women exhibit lower blood haemoglobin concentration (13.8 g/dL for women vs. 15.6 g/dL for men) resulting from several variables including iron losses through menstruation and lower blood androgenic steroid levels. When expressed per kg of body weight, both sedentary and elite athletic women average 20% lower aerobic power as compared to men (Shephard, 2000).

Aerobic capacity is related to body composition, in that higher body fat and lower muscle mass is associated with lower aerobic capacity, putting women at a disadvantage in comparison to men based solely on this criterion. Even when VO_{2max} is expressed relative to body weight, women have a lower aerobic capacity, unless they are extremely lean (Tarnopolsky, 1999). Ideally, aerobic power should be expressed per kg of lean body mass, reducing this gender gap even further.

According to Shephard (2000), research examining the training responses of women is very limited. Under the same training conditions, men and women have similar percentage increases in aerobic capacity however; absolute values remain higher for men due to higher initial values (Shephard, 2000). According to Cowan and Gregory (1985), postmenopausal women respond similarly to aerobic conditioning as pre-menopausal women.

2.10. Lipoprotein Lipid Profile and Gender

Individuals with T2DM often have unfavourable lipoprotein lipid profiles. Specifically, T2DM individuals often exhibit low levels of HDL, higher TG levels, and small LDL particles (Resnick & Howard, 2002), increasing the risk for CVD in those with T2DM as compared to non-diabetic individuals. However, there are distinct gender differences that have important implications on lipid profiles. Estrogen has long been thought to reduce cardiovascular risk factors including peripheral fat distribution, higher HDL, lower LDL and lower blood pressure in pre-menopausal women (Resnick and Howard, 2002). This protective effect accounts for significantly greater risk factors attributed to males as compared to pre-menopausal women (Smith et al., 2001). This apparent protection in women is not fully understood and quite possibly not fully explained by hormonal factors (Collins, Stevenson & Mosca, 2002).

It is well established that women generally have higher HDL-C levels than men do, particularly before women reach menopause (Joseph et al., 1999; Cefalu et al., 1998; Gardner, Tribble, Young, Ahn, & Fortmann, 2000). Up until puberty, HDL-C levels are the same in both sexes and Gardner et al. (2000) found that gender, menopausal status,

and use of sex hormones all had significant effects on several lipoprotein lipid variables in non-diabetic individuals.

The accumulation of visceral fat has been associated with increased TG and total cholesterol levels (Fujioka et al., 1987). Similarly, Cefalu et al. (1998) noted the correlation of overall obesity, abdominal fat accumulation and glucose metabolism with HDL-C and TG. The strongest predictor of TG in this study was the insulin area under the curve.

Insulin resistance is frequently exhibited for some time before the development of T2DM. Interestingly, women with insulin resistance typically have low estrogen and higher androgen levels, two factors that are attributed to increased CVD risk factors (Resnick & Howard, 2002). Consequently, women with T2DM typically exhibit relatively poorer dyslipidemia as compared to men with T2DM when adjusted for other CVD risk factors including increased dense LDL cholesterol particles (Resnick & Howard, 2002; Haffner et al., 1997) and decreased HDL cholesterol in the women as compared to the men (Haffner et al., 1997). Haffner et al. (1997) noted that the change in lipoprotein lipid profile is already apparent in the stages preceding the development of T2DM.

Carr et al. (2001) determined that gender was highly significantly related to hepatic lipase (HL) activity. HL is the enzyme that hydrolyzes TG and phospholipids in HDL-C and LDL-C and has been associated with abdominal fat, genetic factors, age, sex steroid hormones and gender. The higher the HL activity, the smaller, denser, and more atherogenic the LDL and HDL particles are. Carr et al. (2001) clearly demonstrated an unmistakable association between gender and HL activity independent of abdominal

adipose tissue and genetic factors. The men had significantly greater HL activity as compared to the pre-menopausal women.

2.11. Exercise Effects on Lipoprotein Lipid Profile

While aerobic exercise has been shown to improve lipoprotein lipid profile by increasing HDL-C and lowering LDL-C, total cholesterol and TG, there remain conflicting results. Furthermore, this improvement may be largely due to weight loss accompanied by aerobic training. Following a resistance training program there is usually no change in body weight; nevertheless little research has examined the effects of resistance training on lipoprotein lipid profile.

In a study by Schuit et al. (1998), healthy older (60 to 80 years) men and women exhibited favourable but small changes in total cholesterol, HDL-C and LDL-C following six months of aerobic training. Unexpectedly, only the women exhibited a significant reduction in TG levels. All improvements were independent of body composition changes. Conversely, lipoprotein lipid profiles did not change following a 40-week brisk walking program in women aged 22 to 40 years, despite a 22% increase in VO_{2max} (Santiago, Leon & Serfass, 1995).

Wirth and Steinmetz (1998) concluded that following similar weight loss through diet and aerobic exercise men showed greater favourable improvements in TG and HDL-C as compared to women. This well-controlled study clearly demonstrated this sex difference and further noted that while the men exhibited a continuous increase in HDL-C, the women initially displayed a brief drop in HDL-C before values started to climb. This trend was previously documented by Wing & Jeffrey, (1995).

Joseph et al. (1999) reported significant increases in HDL-C following 3 months of RT in men, while the women had decreases in their HDL-C. Total cholesterol, LDL-C, and TG did not change for either men or women. In this study, the men showed significant increases in FFM and decreases in body fat percentage, while the women did not exhibit any changes in body composition.

A meta-analysis by Lokey and Tran (1989), focusing on studies with female participants, revealed that while the literature is sparse, research up until the mid 1980's revealed that both aerobic and resistance exercise training result in favourable lipoprotein lipid profile changes in both men and women. Exercising women exhibited lower total cholesterol and TG levels compared to sedentary controls. HDL-C and LDL-C were no different following training but the total cholesterol to HDL-C ratio did decrease significantly. Lokey and Tran (1989) further noted that those groups with greater dyslipidemia concentrations exhibited more favourable changes. Weight loss was positively correlated with the decline in total cholesterol and TG levels. In those studies where body weight was maintained throughout the exercise intervention, TG and total cholesterol did not change significantly.

In comparing genders, Lokey and Tran (1989) noted that women exhibited smaller lipoprotein lipid profile improvements following exercise training as compared to men. This difference, however, was largely due to the fact that pre-menopausal women have more favourable lipoprotein lipid profiles to begin with.

2.12. Sex Differences in Glycemic Control

Nuutila et al. (1995) were the first researchers to show a gender difference in skeletal but not heart muscle in terms of insulin sensitivity of glucose uptake. They

determined that in healthy men and women, whole body glucose uptake was 41% higher in the women as compared to men. When expressed per FFM, women exhibited 64% greater whole body glucose uptake. Women also had 47% greater femoral glucose uptake as compared to the men however, heart glucose uptake was similar between men and women when expressed per heart muscle mass. The women in the study were all pre-menopausal.

In a healthy population, HbA_{1c} begins to increase in the third decade rising throughout adulthood in both men and women. Before they reach menopause however, women have a lower average HbA_{1c} as compared to men (Yang, Lu, Wu & Chang, 1997). Pre-menopausal women were also found to be less insulin resistant as compared to men (Donahue et al., 1997). When insulin areas under the curve (AUC) were not adjusted for body fat percentage, men and women exhibited similar responses, although women had a higher body fat percentage. Adjusted AUC revealed that women are more insulin sensitive (Donahue et al., 1997). Clausen et al. (1996) established that VO_{2max} and use of oral contraceptives to be the prime determinants of the insulin sensitivity index in healthy men and women. They concluded however, that the gender difference in glycemic control requires further investigation.

In their review of literature on diabetes and cardiovascular disease, Resnick and Howard (2002), concluded that lack of differences in prevalence of T2DM between men and women when adjusted for risk factors suggests that the inherent differences in men and women do not contribute to worsening glycemic control and development of T2DM.

2.13. Weight loss and Glycemic Control

Weight loss is often the first recommendation in the treatment of T2DM. Since obesity is a major risk factor in developing the disease by contributing to decreased insulin sensitivity, weight loss is effective in improving glycemic control by reversing this decreased sensitivity. While diet alone may be sufficient in achieving the weight loss necessary to improve glycemic control, exercise should be used as an adjunct therapy due to its promising effects on weight loss maintenance (Perri, Sears & Clark, 1993) and conservation of lean body mass (Janssen and Ross, 1999).

A study by Blonk, Jacobs, Biesheuvel, Weeda-Mannak, and Heine (1994), compared a conventional diet and counselling method of weight loss with a weight loss technique that incorporated the conventional dietary counselling in addition to behavioural modification and exercise in 19 men and 35 women. While a strong correlation between body weight and HbA_{1c} was found at 6 months into both programs, it no longer persisted at 12 months. The HbA_{1c} levels of those participants who used the conventional method returned to baseline values at 12 months and climbed even modestly higher by 24 months despite the fact that weight loss was maintained. The HbA_{1c} levels of the exercise and behaviour modification group, however, reached an all time low at 6 months, and slowly ascended reaching baseline levels at 24 months. The authors suggest that a negative energy balance and subsequent weight loss rather than a balance in energy and therefore weight maintenance (which occurred between 6 and 24 months) is needed to improve glycemic control. It is likely that weight maintenance does not induce any further improvements in HbA_{1c} levels but rather may reduce the deterioration that would have occurred otherwise. However, these findings do propose that exercise may slow the

regression of HbA_{1c} back towards pre-weight loss values following improvement after weight loss. The exercise program included 60 minutes of aerobic activity twice a week from 3 months to 6 months time and then once a week from 9 months to 12 months time and then again months 15 to 18. A more clear distinction between diet alone and diet in combination with exercise may have been seen had the exercise program been more intense.

From a systematic review and meta-analysis of current literature, Boulé et al. (2001) determined that the improvements in HbA_{1c} exhibited in exercise groups were independent of variability in weight loss, exercise intensity, or exercise volume. Boulé et al. (2001) further concluded that exercise reduces insulin resistance and increases glucose uptake through various mechanisms that are not necessarily related to changes in body weight.

The effect of weight loss on T2DM was clearly demonstrated by Dixon and O'Brien (2002), who looked at the effects of laparoscopic adjustable gastric banding in severely obese T2DM men and women one year after surgery. Body weight decreased from 137±30 kg to 110±24 kg one year following the surgery and HbA_{1c} decreased from 7.8±3.2 % to 6.2±1.5 %. All other measures of glycemic control including fasting plasma glucose, fasting plasma insulin, C-peptide, HOMA%S (measure of percentage of insulin sensitivity from adapted HOMA model) and HOMA%B (measure of percentage β-cell function from adapted HOMA model) improved significantly from baseline with weight loss. Overall, they found that many of the patients experienced a remission in their T2DM and 94% had exceptional glycemic control following the weight loss. This improvement was a reflection of both enhanced insulin sensitivity and improved β-cell

function (measured indirectly by the HOMA model). The authors conclude however, that β -cell function was correlated with duration of diabetes and not weight loss implicating that the capability for the dysfunction of β -cells to reverse is variable and influenced by duration of T2DM

2.14. Exercise and Glycemic Control

Several mechanisms have been proposed to explain how exercise improves glycemic control. Exercise enhances glucose uptake because of changes within the contracting muscle itself; increased capillary blood flow, improved glucose transport at the membrane, and oxidative and glycolytic enzyme activation (those responsible for glucose disposal). The GLUT-4 glucose transporter found in skeletal muscle facilitates membrane glucose transport via stimulation by insulin and/or muscular contractions (McConnell, McCoy, Proietto, & Hargreaves, 1994). In their study, however, McConnell et al. (1994) found an inverse relationship of glucose uptake during 40 minutes of high intensity exercise ($72\% \text{VO}_{2\text{peak}}$) to total muscle GLUT-4 protein level, suggesting that total GLUT-4 protein levels do not explain glucose uptake regulation during exercise. Instead, the acute effect of muscular contraction stimulates GLUT-4 translocation to the cell membrane during exercise (McConnell et al., 1994).

An adaptive response to aerobic training is improved insulin-stimulated glucose transport. This is a consequence of increased protein expression of GLUT-4 (Dohm, 2002) and insulin signalling molecules including insulin receptor substrate 1 and 2 (IRS-1, IRS-2) and phosphatidylinositol 3-kinase (PI3 kinase) (Thomas, Zorzano & Ruderman, 2002) that enhance insulin sensitivity.

Resistance training can also improve insulin sensitivity and/or glucose tolerance (Castaneda et al., 2002; Hurley et al., 1988; Miller, Sherman & Ivy, 1984). It is thought that the increase in muscle mass accompanied by resistance training increases glucose storage area (Miller et al., 1984). Furthermore, the increase in lean body mass following resistance training may be related to enhanced insulin binding and a subsequent augmented insulin clearance. Therefore, less insulin would be required to maintain comparable glucose uptake (Miller et al., 1984).

Overall, physical activity has been shown to reduce resting hepatic glucose output and decrease fasting glycemia. Furthermore, physical activity can decrease postprandial hyperglycemia and enhance insulin sensitivity up to 48 hours after a single exercise bout (Davidson, 1998). Exercise can also reduce vascular complications due to increased blood flow and enlarged muscular capillary areas in the body (Kemmer, Gudat, & Berger, 1997).

In a meta-analysis on exercise and glycemic control, Boulé et al. (2001) concluded that while there are many studies that examine the effects of exercise on glycemic control, well-controlled and well-designed studies are scarce. A general consensus was found in the existing literature; that exercise intervention groups clearly exhibit significant decreases in HbA_{1c} levels. Furthermore, it was determined that studies with diet and exercise intervention displayed similar results to those with exercise alone. Ultimately, Boulé et al. (2001) determined that from the literature, exercise reduced HbA_{1c} values by 0.66%, a sufficient decrease that could likely lessen potential diabetic complications tremendously.

Several authors postulate that while aerobic exercise is traditionally prescribed in the treatment of T2DM, resistance training may be as beneficial as aerobic training for this population in terms of glycemic control as well as other health aspects (Castaneda et al, 2002; Dunstan et al., 2002). Eriksson et al. (1997) also suggested that an exercise regimen geared toward muscle hypertrophy, thus improving muscle function and strength, should theoretically improve peripheral resistance, a significant metabolic deficiency in T2DM. In their study, Honkola et al. (1997) examined the effects of circuit-type resistance training, which induces aerobic-like effects due to the nature of the activity. This notion should be addressed as resistance training in a circuit manner may actually induce the greatest changes due to the aerobic nature of the workout. After the 5-month resistance training intervention, the difference in HbA_{1c} between the intervention and control groups was significant at 0.5% with no change in body weight. It was also noted that resistance training has great potential because aging results in a decline in muscle mass and long-term glycemic control is strongly correlated to muscle mass.

In a recent study of nondiabetic individuals by Hurlbut et al. (2002), men exhibited favourable reductions in fasting insulin levels and total insulin area under the curve following resistance training while the women did not. Conversely and unexpectedly, the older women (65-75 years) demonstrated worsened glucose tolerance following strength training. The men did not exhibit significant improvements in glucose tolerance. The researchers concluded that body composition changes and strength gains did not explain the sex differences that were displayed and that further research is needed to establish any gender differences as this was the first study of its kind.

As mentioned previously, there is only one known study that examined the effects of diet and exercise on metabolic control in T2DM where results were not pooled for men and women. The study by Vanninen et al. (1992) looked at an intensified diet and exercise education program over a 1-year period in men and women who were newly diagnosed with T2DM. Participants in the intervention group were encouraged to engage in aerobic activities 30-60 minutes in duration, 3-4 times per week. The diet therapy was individualized but with the goal of weight loss through energy and fat restriction and increased consumption of complex carbohydrates. Both exercising men and women improved glycemic control, but it was the exercising women who were the only group to demonstrate continued improvement in fasting blood glucose and HbA_{1c} over the course of the year. The women started with higher levels of body fat as compared to the men, and both men and women lost a significant amount of body weight over the year. This program, however, was not a structured exercise program, so activity was variable.

2.15. Implications of Menopause and Hormone Replacement Therapy (HRT)

The major consequence of menopause is a decline in estrogen levels. There is a gradual and persistent decrease in ovarian steroidogenesis that precedes the cessation of menstruation by about 15 years and continues for another 15 years (Shangold & Merkin, 1994). As estrogen levels plummet, there are changes in body composition in terms of lean body mass as well as a redistribution of fat mass (as discussed previously). As such, menopause is associated with increased risk of several metabolic complications. Shangold and Merkin (1994) noted that serum cholesterol and TG levels are significantly higher in post-menopausal women in comparison to pre-menopausal women. Menopause is also associated with a decline in muscle mass. This change coincides with a decline in

endogenous growth hormone (GH), a decline in pituitary responsiveness to growth hormone releasing hormone (GHRH), loss of muscle fibres, neuromuscular alterations, inactivity and other factors. Pre-menopausal women have significantly greater pituitary response to GHRH than do men of the same age, but post-menopausal women do not. Therefore, it is likely that estrogen deficiency accelerates the age-related decline in GH secretion and may also accelerate the loss of muscle tissue that occurs as women age (Shangold & Merkin, 1994).

As such, the implications of hormone replacement therapy (HRT), which aims to increase estrogen and progesterone levels, work to minimize the changes related with the decline in female sex hormones associated with menopause. Gardner et al. (2000) noted that hormone users [oral contraceptives and estrogen replacement therapy (ERT)] exhibited significantly higher HDL-C and Apo A-I despite menopausal status. Post-menopausal women using ERT had significantly higher HDL₂-C as compared to nonusers. Additional benefits of HRT use include; decreased waist circumference, waist-to-hip ratio, central abdominal fat, HbA_{1c}, LDL and total cholesterol (Samaras, Hayward, Sullivan, Kelly, & Campbell, 1999). Conversely, use of HRT has also been associated with increased risk of stroke, coronary heart disease and thrombosis (Writing Group for the Women's Health initiative Investigators, 2002). Other adverse effects have also been reported and as such it has been recommended that individuals with cardiovascular disease not use HRT (Nelson, 2002). Menopausal status and use of hormone replacement therapies have a significant impact on various health parameters in aging women. Furthermore, the extent to which post-menopausal T2DM women respond differently to exercise as compared to pre-menopausal T2DM women is not known.

2.16. Conclusion

While literature has explored the relationship between exercise and T2DM, there remain many gaps and inconsistencies. Researchers have only begun to examine the effects of different exercise modalities on T2DM and concrete conclusions have yet to be established. Research to date has almost always pooled results for men and women and to our knowledge there is only one study by Vanninen et al. (1992) that examines the effects of exercise on T2DM in men and women separately.

Morphologically, men and women differ in many ways. While men bear more lean body mass, a more metabolically active tissue, they also exhibit increased visceral adiposity putting them at risk for metabolic complications. Conversely, women carry more overall body fat but prior to menopause, this fat is primarily SAT and less VAT than men, and reduces their metabolic risk. Pre-menopausal women also exhibit more favourable lipoprotein lipid profiles than men, again in part reflecting lower visceral adiposity. It is important to note however, that those women with T2DM often have increased VAT as compared to non-diabetic women. The major differences in body composition between men and women are also reflected by the differences in strength and cardiorespiratory fitness between genders. However, relative strength and fitness improvements following training are similar between men and women but it is not known to what extent these exercise related gains impact health parameters such as lipoprotein lipid profile and glycemic control in T2DM. Men appear to lose more body fat and show greater absolute gains in muscle mass in response to exercise training as compared to women. It may be that men and women experience greater benefits from different exercise modalities. As such, there is a definite need for more research in this area, as the

implications may lead patients towards better control of their disease, and ideally reduce the morbidity and mortality associated with T2DM.

3. ARTICLE

Body composition, metabolic profile and fitness in men and women with type 2 diabetes mellitus following a 6-month exercise intervention: A gender comparison

ABSTRACT

We compared changes in visceral adipose tissue (VAT), abdominal subcutaneous adipose tissue (SAT), thigh muscle cross sectional area (CSA), strength, VO_{2peak} , lipoprotein lipid profile and HbA_{1c} following aerobic training (A), resistance training (R), or their added combination (AR) in 115 previously sedentary type 2 diabetic men and women. **METHODS:** Participants aged 40 to 70 years and BMI of 25-50 (mean 33.5) kg/m^2 were randomly assigned to 6 months of 3x/wk A only (17 M, 11 W), R only (17 M, 11 W), combined AR (17 M, 12 W), and waiting-list control (C) (17 M, 13 W). A was increased to 45 min. at 75% of HR max, while 2-3 sets of 8-RM for 7 exercises was completed for R. The AR group completed both workouts. **RESULTS:** VAT declined 7.5% in AR men ($p=0.003$) and AR women exhibited a decrease in abdominal SAT (5.5%; $p=0.021$). All exercising men increased mid-thigh CSA with no change observed in the women. Absolute increases in CSA were greater in the R men than the R women ($p<0.05$ between sexes). Mean increases in VO_{2peak} were exhibited in A and AR men (8.4% and 7.3%; $p<0.05$). Strength increases were similar for men and women in all groups. AR men displayed a 19.3% decrease in triglycerides ($p=0.044$). Absolute HbA_{1c} decreased in AR men (1.22%) and women (0.62%), and A men (0.80%) ($p<0.05$). R men exhibited a greater relative reduction in HbA_{1c} as compared to R women ($p=0.033$ between sexes). **CONCLUSIONS:** Exercising men had increases in muscle CSA that women did not. Men and women had similar strength gains from R exercise, but men increased VO_{2peak} from A exercise while women did not. Exercising men had modestly greater improvements in HbA_{1c} . For the women, R training provided no benefits in glycemic control.

BACKGROUND

To date, research examining the effects of exercise on physiological factors in individuals with T2DM has typically pooled results for men and women. In their meta-analysis on the effects of exercise on T2DM, Boulé et al. (2001), found only one clinical trial examined men and women separately in their analyses and met the inclusion criteria of an 8-week or longer defined exercise intervention. The study by Vanninen, Uusitupa, Siitonen, Laitinen and Länsimies (1992) assessed a one-year diet and aerobic exercise education intervention on newly diagnosed men and women with T2DM. Consequently, very little is known regarding the response of type 2 diabetic men versus women following aerobic exercise and thus far it appears that no studies have examined the effects of resistance training in women with T2DM.

While the prevalence of T2DM in men and women is comparable (Gale & Gillespie, 2001), the gender differences that exist in terms of body composition, metabolic profile and response to exercise may impact the effectiveness of exercise training programs designed as therapeutic interventions for T2DM. Those gender differences of greatest relevance include peripheral versus central body fat distribution in women versus men respectively, greater lean body mass in men, estrogen effects on lipoprotein lipid profile and glycemic control, and the sex specific responses to exercise training. Research to date examining gender differences is limited. Little research has explored the effects of exercise in women and the validity of the studies that have involved both men and women are easily hindered, as it is difficult to make direct comparisons between genders due to the physiological differences in body composition and sex hormones. The extent to which exercise alone and/or improvements in body

composition improves glycemic control and metabolic profile also needs to be confirmed. Finally, it is of interest to determine the respective responses of each gender to exercise and the implications any differences may have on the overall metabolic profile of individuals with T2DM. The differences that exist between the sexes may have important implications when designing an exercise intervention in a population at high risk for micro- and macrovascular complications. The significance bears great importance considering that the relative mortality risk associated with having T2DM is greater in women than men (Abbott et al., 1988).

The primary goal of this study was to examine whether or not gender differences exist in body composition and fitness parameter changes following a 6-month exercise training program in previously sedentary men and women with T2DM and how these changes relate to metabolic profile.

More specifically, this research study examined the occurrence of gender differences in type 2 diabetic adults with regards to changes in body weight, fat distribution [abdominal subcutaneous adipose tissue (SAT), visceral adipose tissue (VAT) and SAT of the thigh] and muscle cross sectional area (CSA) of the thigh, as well as strength and cardiorespiratory fitness (VO_{2peak}) following a 6-month exercise intervention. We also examined the extent to which changes in body composition and fitness parameters related to glycemic control, insulin resistance (using HOMA model) (Sakane et al., 1997), and lipoprotein lipid profile [HDL-C, LDL-C, total cholesterol/HDL-C ratio and triglycerides (TG)].

RESEARCH DESIGN AND METHODS

Study population

Type 2 diabetic participants are diagnosed as such by a physician according to CDA criteria and for the purposes of this study include those that are moderately controlled and treated with diet alone and/or in combination with oral agents.

The sample of this substudy comes from the larger ongoing DARE study population. For the DARE study, 256 volunteers will be recruited through local radio and newspaper advertisements of the Ottawa region over a four year span. Recruitment campaigns are held as needed to meet the demands of the study. For this substudy, data from the first 17 men of each of the four experimental groups were evaluated and the corresponding number of women who have completed the study at the time of analysis.

After completing a four-week aerobic and resistance training run-in period, compliant patients were randomized to one of four groups: aerobic training only (**A**), resistance training only (**R**), both aerobic training and resistance training (**A-R**), or waiting-list control (**C**). Once randomized, data from participants were included in the analyses despite some participants who dropped out of the study before completion of the 6 month intervention. Only one woman (**R** only) was eliminated from all analyses due to a hyperactive thyroid which presented itself after her randomization.

Inclusion criteria for DARE study

All participants were diagnosed as having T2DM according to 1998 CDA guidelines and were being treated with diet alone or in combination with oral medication but not taking insulin. Hemoglobin A_{1c} values were between 0.066 and 0.099 and participants were between the age of 40 and 70 years.

Exclusion criteria for DARE study

Participants had not participated in any regular physical activity a minimum of twice a week for 20 minutes or longer during the previous 6 months. They were not taking insulin nor had unstable hyperglycemia (fasting plasma glucose > 15mM, HbA_{1c} > 0.099). Participation of the study excluded those with significant renal disease (serum creatinine \geq 200mEq/l or proteinuria > 1 g/24 hours) and uncontrolled hypertension as measured in sitting position (systolic blood pressure >160 mmHg or diastolic blood pressure >95 mmHg). Individuals were not accepted into the study if they had limitations in physical activity due to illness such as intermittent claudication, severe peripheral neuropathy or active proliferative retinopathy, unstable pulmonary or cardiac disease, disabling stroke, severe arthritis. Those who had \geq 5% change in body weight within 2 months prior to starting in study or changes in diabetes, blood pressure or lipid medication within 2 months before screening process of study were excluded. Any other disease or ailment as determined by participant or study physician to render participation difficult or make study participation not recommended was also a determinant of exclusion to this study. Failure to comprehend or follow instructions due to a significant cognitive deficit and pregnancy or plan to become pregnant within the following year of starting the study were also conditions for exclusion. Finally, those who were unable to communicate in English or French adequately or those who were reluctant in signing informed consent were excluded from participation in the DARE study.

Initial assessment

Baseline assessment took place at various locations including, the Ottawa Hospital Civic Campus, the Ottawa Health Research Institute, the University of Ottawa,

and the University of Ottawa Heart Institute according to test assessment. Following telephone screening, the research coordinator (registered nurse or MA in Human Kinetics) assessed potential participants to ensure that all inclusion and exclusion criteria were met. A medical history was taken, including medication and physical activity history. For the women, a questionnaire regarding menstrual cycle and menopause also administered (See Appendix A). A physical examination was conducted and anthropometric measurements were taken including height, weight, waist circumference, and sagittal abdominal diameter. These measurements provided additional data to assess body composition changes.

Outcome measures

Compliance and Activity Level

Compliance of the aerobic only, resistance only and combination aerobic and resistance training groups was also examined from examination of both exercise logs and sign-in binders that were kept at all gyms and had to be initialled by a trainer or gym staff member. Compliance was calculated as percentage of sessions that were attended out of the number of sessions that were prescribed over the 6 month periods at 3 times per week. If a participant dropped out of the study, the compliance for the subsequent weeks was zero and calculated into the total. Data from all participants that were randomized were used for the analyses regardless of whether or not they completed the study. All baseline or 3 month data was carried forward for those who did not complete the study.

At baseline and 6 months time, all participants wore a pedometer (Yamax Digiwalker; Japan, 2000) at the hip. Participants wore the pedometer from the time they got up until the time they retired for bed and recorded the number of daily steps for 7

days. If participants were engaging in a prescribed exercise workout as part of the DARE study, the pedometer was removed during the workout or the number of steps during the workout was subtracted from the total daily steps.

Body composition

Computed tomography (CT) scans (General Electric, Milwaukee, WI) of abdominal area and upper thigh were taken at baseline and 6 months to evaluate adipose tissue and muscle cross sectional area of the thigh. The scan was taken with participants lying supine with both arms stretched above their heads and without any restrictive clothing. An initial scout film was used to determine positioning of abdominal and thigh images. A single 5 mm slice was taken at L4-L5 to examine abdominal adipose tissue and at midway between the anterior iliac spine and base of the patella to examine the thigh.

CT images were analyzed using SliceOmatic (v.4.2, 2001) image analysis software (Tomovision Inc., Montreal, QC) using an attenuation range of -190 to -30 Hounsfield units for adipose tissue. In a validation study by Lemieux, Prud'homme, Tremblay, Bouchard and Després (1996) a correlation of 0.99 was found between abdominal fat using this method derived by using all 22 cuts of an abdominal CT scan. Matsuzawa (1997) concludes computed tomography as the "most useful method for measuring fat volume and fat distribution, which enables the analysis of intra-abdominal visceral fat" (p. 4). Abdominal fat is of interest because it is correlated with metabolic complications such as insulin resistance, dyslipidemia, and T2DM (Lehmann, Vokac, Niedermann, Agosti & Spinass, 1995).

The muscle cross sectional area was calculated from the CT slice of the mid-thigh as the sum of both high density and low density muscle areas and the added total for both legs (attenuation range from 0 to 100 Hounsfield units). Changes in muscle cross sectional area may be indicative of muscle hypertrophy or atrophy as well a change in lean body mass. All areas were determined using a highlighting technique.

Muscle strength

At baseline and 6 months, all participants performed an 8-RM for 3 exercises at the University of Ottawa using a universal gym (EXM-2000S, Body Solid, USA). The exercises were seated row, leg press, and bench press. The tester was blind to previous results and allowed the participant a warm-up set for each exercise. Furthermore, the participant was given a minimum of 1 minute of rest between sets. The same tester performed both 8-RM tests when possible to control for tester interaction. Strength testing data was also used to help assess compliance of the control group. All 8-RM values were converted to predict 1-RM in lbs using Wathan's (1994) 1-RM prediction tables. According to Knutzen, Brilla and Caine (1999), the Wathan prediction equation reliably predicted values nearest the actual 1-RM for all exercises of the upper body as well as the leg press and dorsiflexion exercise in older adults (70.7 ± 6.1 years). All of the other equations that were compared by Knutzen et al. (1999) consistently had predicted values that were lower than the actual 1-RM.

Aerobic capacity

Following initial screening and signed informed consent, all potential candidates returned on a separate day, non-fasted, for a cardiopulmonary stress test at the University of Ottawa Heart Institute. This test was repeated at 6 months time. The test followed a

slow ramp treadmill protocol and was performed in the presence of a physician. Those administering the test were certified in Basic (BCLS) and Advanced (ACLS) Cardiac Life Support. All required equipment and materials were present at the testing site. The use of a metabolic cart (MedGraphics CPX-D Metabolic Cart, St-Paul, MN, USA) permitted continuous breath-by-breath analysis of inspired and expired oxygen and carbon dioxide. Constant monitoring of a 12-lead electrocardiogram (v.4.03, GE Marquette Medical Systems Inc.) was also conducted.

Three different continuous ramp protocols were used based on what the tester perceived to be the ability of the participant. Each ramp protocol started at a different speed so that there was a slow, medium and fast protocol. At 6 months time, the participant would complete the same protocol as was completed at baseline. The speed was then progressively increased at 2-minute intervals until volitional fatigue or when VO_2 and heart rate attained a steady state. The highest VO_2 from raw 30 second samples was considered to be the VO_{2peak} . Subjects showing abnormalities on the stress test were sent for additional cardiac evaluation, and were permitted to continue in the study only if cleared by the consulting cardiologist.

Lipoprotein lipid profile

Lipoprotein lipid profile included the evaluation of total cholesterol, HDL-cholesterol, LDL-cholesterol, and TG in mmol/l. The ratio of total cholesterol to HDL-C was also calculated. All blood collection was done at baseline and 6 months in the morning following a 12-hour fast and a minimum of 48 hours following the last exercise bout. Total cholesterol was measured using the BMC method and using cholesterol esterase/oxidase. BMC was also used to measure TG but using lipase/glycerol

kinase/oxidase enzymes. HDL-cholesterol was measured using the Randox technique and direct HDLC (cyclodextrin buffer/polyethylene modified cholesterol oxidase). Finally, LDL-cholesterol was calculated with the Friedewald equation.

Glycemic control

Blood samples were collected to examine complete blood count, hemoglobin A_{1c}, fasting plasma glucose and insulin and was taken as described above. Analysis for HbA_{1c} was conducted using ion exchange chromatography (BioRAD Diastat®). Measurement of hemoglobin A_{1c} reflects the average blood glucose concentration over the previous 8 to 12 weeks and thus is a good indicator of glycemic control (Boulé et al., 2001). Since HbA_{1c} is a measure of the average blood glucose concentrations over the previous 2-3 months, the values are not affected by daily fluctuations. A euglycemic clamp was not used in this study because of the additional costs and the inconvenience it bears on participants who must already devote a substantial amount of time to this study.

The Homeostasis (HOMA) Model is used to estimate insulin sensitivity and β -cell function based on fasting plasma glucose and insulin. This model is based on the glucose-insulin feedback system in the homeostatic (12 hour fasted) state. An estimate is given by the formula: insulin resistance index = $FI \times G / 22.5$, where FI is the fasting insulin (U/ml) and G is the fasting glucose (mmol/l) (Sakane et al., 1997), while computer analysis can provide a more accurate calculation.

Dietary intake

All participants met with a registered dietitian at baseline, 3 months and 6 months. The dietitian explained and demonstrated 3-day dietary records that participants were to document. Energy intake was determined through breakdown of the diet and analyzed

using the NUTRIBASE software (v.3.05, Cybersoft Inc., USA). The dietitian also prescribed a diet according to Canadian Diabetes Association guidelines. The recommended diet was comprised of 50-55% carbohydrate, 15-20% protein and <30% fat. Participants were encouraged to consume no lower than 90% of estimated requirements for maintenance of body weight. Dietary adjustments and encouragement were provided at follow-up at 3, 6, and 12-month visits. Both total caloric intake and macronutrient intake were assessed and used to evaluate the dietary intake of the participants and to explore the nutrition of participants over the course of the study.

Run-in period

Following baseline assessments, all participants began a 4-week run-in period. During this time, participants were able to familiarize themselves with the exercises and compliance was assessed. Exercise was prescribed 3 times a week and participants had to attend a minimum of 10 out of 12 sessions during the 4-week run-in period in order to be randomized. Participants engaged in aerobic training on all three sessions in a week and on two out of three occasions they completed resistance training as well. The specific training program is outlined under "Exercise training". During the run-in period, a student trainer from the University of Ottawa supervised participants twice a week and subjects trained on their own for the third weekly session. Training was completed at one of 6 Ottawa-area YMCA's or at the University of Ottawa Sports Complex. Availability of multiple exercise facilities was intended to enhance compliance by minimizing the need to spend time commuting to exercise facilities.

Student exercise specialists were trained by Dr. Glen Kenny (exercise physiology specialist, a leader in the Canadian Society for Exercise Physiology) and/or Rikst Attema

and Katherine Dittmann (Masters students of exercise physiology working on the study, Certified Fitness Consultants). All trainers were 3rd and 4th students of the University of Ottawa, School of Human Kinetics and under the close supervision of Dr. Kenny and his exercise physiology masters students assisted the participants in their familiarization of the gym and understanding of the training process. They also ensured that all participants followed proper breathing, techniques and adjusted equipment properly. Close supervision occurred during the run-in period (2 times a week) to ensure workouts were done in a safe and correct manner, and good habits could be established. Following randomization, supervision was reduced depending on the needs of the participant.

Ideally, the trainer supervised the participant twice a week up until 8 weeks from the first training session. After this, the trainer was present once a week and finally once every two weeks as the participant became more independent in the gym and the trainer was confident that the participant was progressing appropriately.

Randomization

Following 4 weeks of exercise training and having attended a minimum of 10 training sessions all participants were randomized to one of the four groups: **A**, **R**, **AR**, or **C**. Randomization was done as needed and stratified by gender and age (40-54 and 55-70). Once ready to be randomized, participant data including name, date of birth and sex were emailed from a researcher at the University of Ottawa to the Clinical Epidemiology Unit (CEU) data center at the Ottawa Hospital, Civic Campus. There, a data specialist who was blind to other aspects of the study ran the randomization program, which generated randomization assignment. The CEU data specialist documented the study ID of the individual to be randomized prior to running the software. The randomized group

assignment for that participant was then documented and information was emailed back to a researcher at the University of Ottawa. Following their 12th training session, Dr. Kenny, Ms. Dittmann, or Ms. Attema informed the participant of their randomization and gave instructions on changes to their program. A complete randomization package was also mailed to that participant, giving details on their group assignment and what was required of them for the subsequent 5-month period.

Exercise Training

Tables 3.1 and 3.2 describe the training protocol including both aerobic and resistance components. The aerobic portion is described in terms of frequency, intensity and duration, while the resistance program is determined by set, number of repetitions, weight (by repetition max), and frequency. At each workout, participants completed a 5-minute aerobic warm-up (at a low intensity), followed by whole body stretching. A cool-down similar to the warm-up was also completed after each workout. All participants kept detailed exercise of each log so that progression could be evaluated by the trainer and adjusted if needed.

Resistance training

The resistance training protocol was divided into three phases and was followed by the resistance only group as well as the combination group. Table 3.1 depicts the first two phases. After the run-in period, participants were required to complete 3 sets of 8 repetitions at an 8-RM for all exercises (Table 3.2). Participants performed the exercises in a circuit manner or more commonly performed all 3 sets successively with a minimum of 1 minute 30 seconds of rest between sets to ensure recovery. All exercises were performed on weight machines or through a pulley system to ensure safety. The

resistance training program was divided into two workouts: A and B. The workouts were always alternated each training session and were as follows:

- **Workout A:** abdominal crunches, seat row, seated biceps curl, seated bench press, leg press, shoulder press, and leg extension.
- **Workout B:** abdominal crunches, latissimus pulldown, chest fly, leg press, upright row, triceps pushdown, and leg curls.

Participants were instructed to exhale upon exertion (e.g. while lifting a weight) and inhale upon returning to starting position. They were also instructed to perform each repetition slowly and to take a very minimum of 1 minute (preferably 1 minute 30 seconds to 2 minutes) between sets. Participants were told to exert themselves in a manner whereby they were not able to perform a 9th repetition with proper form. Once the participant was capable of performing 10 repetitions, the weight was increased for the following set. The exercise had to be performed with proper form before the weight was increased.

Aerobic Training

Once randomized, those individuals in the aerobic only group or combination group followed the progression in Table 3.2 under aerobic training. Aerobic exercise was completed on a cycle ergometer or treadmill. The participant could choose an apparatus during the run-in period but then had to continue using that apparatus for the remainder of the study to facilitate consistent progression in intensity. Treadmill incline had to 1% or greater in order to calculate work. Heart rate was also monitored during each exercise training session. Working intensity started at 60% of max heart rate (as determined from stress test) and was increased until 75% of max heart rate during weeks 17 to 26 (see

Table 3.2). During each training session, participants were required to maintain a constant intensity.

Combination aerobic and resistance training

Those participants randomized to the combination group followed the progression outlined in Table 2 for both aerobic and resistance training. Participants completed both aerobic and resistance portions of their training during the same exercise bout on all 3 days.

Control group

Following randomization, the control group was asked to resume pre-study physical activity levels and to maintain this level for the following 5 months of the study. Their gym memberships were cancelled, and they were asked to complete a daily activity log for 7 consecutive days of every month to ensure their activity levels returned to baseline levels.

Statistical analysis

Data are presented as group means \pm standard error (SE). For any participants who did not complete the study, but had been randomized, baseline or 3 month data was carried forward as their 6 month value. This substudy was a randomized, controlled clinical trial with a 4x2x2 (group x sex x time) factorial repeated measures design. A four (group) by two (sex) way multivariate analysis of variance (ANOVA) was employed to evaluate all initial dependent variables to assess any gender or group differences at baseline. Baseline to 6 month data was analyzed using a four (group) by two (sex) repeated measures ANOVA. Analysis of absolute and relative (%) changes were also conducted via a multivariate ANOVA to assess main effects and interaction of treatment.

Analysis of relative changes may give additional insight to the repeated measures design analysis that may have been confounded by variables, such as strength and VO_{2peak} , that were different between men and women at baseline. A Tukey's B *post hoc* test was employed when $P < 0.05$ for the multifactorial or repeated measures ANOVA comparison tests to isolate particular baseline differences and main treatment effects. To account for baseline differences between men and women, each of the eight groups was further subdivided as above and below the calculated median BMI for the entire sample population. The same analysis as described above was used to see if less obese and more obese individuals responded differently to the exercise intervention.

Intervention group and sex were the independent variables in this study while dependent variables were relative compliance (%), 7-day total of steps (#), body weight (kg), BMI (kg/m^2), abdominal SAT (cm^2), VAT (cm^2), mid-thigh CSA (cm^2), predicted 1-RM for seated row, bench press and leg press (all in lbs), VO_{2peak} (ml/kg/min), HDL-C (mmol/l), LDL-C (mmol/l), total-C (mmol/l), total-C:HDL, TGs (mmol/l), HbA_{1c} (%) and HOMA. Analyses were performed using SPSS v11.0 (SPSS, Evanston, IL) for Windows software. Results were considered statistically significant if the two-tailed $P < 0.05$.

RESULTS

Baseline participant characteristics

Participants, who failed to complete the 6 month study, did so for various reasons including, medical conditions that interfered with their ability to complete the study, loss of interest, lack of time, work/family problems and relocation out of the Ottawa area.

The numbers of dropouts are distributed as follows: **A** only, 5 men and 2 women; **R** only, 2 men and 2 women; **AR**, 4 women; and **C**, 2 men.

Table 3.3 represents the baseline characteristics of the men and women divided into the 4 intervention groups. There were no differences in age or baseline HbA_{1c} between any of the groups or genders. The 68 men differed from the 49 women in terms of body weight ($p=0.04$), BMI ($p=0.028$) and VO_{2peak} ($p=0.000$). The men were heavier but had lower BMIs and higher VO_{2peak} values. More specifically, **R** and **A** men were heavier than the women of the same groups ($p=0.029$ and $p=0.039$). Control men tended to be heavier than **C** women but this difference was not significant ($p=0.057$). Surprisingly, the men and women of the **AR** group were very similar in body weight (94.4 ± 4.7 kg and 96.9 ± 4.1 kg respectively), with the women even slightly heavier. Oddly, the women of the **AR** group were slightly but non-significantly heavier than the women of the other three groups, and the **AR** men were, although not significantly, lighter than the men of the other groups. Consequentially, **AR** women had a significantly higher BMI as compared to **AR** men ($p=0.008$).

As expected, the men in each of the four groups had a higher peak oxygen consumption per kg compared to the women of the same groups respectively (**R**, $p=0.047$; **A**, $p=0.002$; **AR**, $p=0.000$; and **C**, $p=0.000$). Interestingly, the **C** men had significantly higher VO_{2peak} values than the men in the **R** group.

Finally, VAT was no different between the men and women of any of the four groups. Likewise, the men and women also had similar baseline values for abdominal SAT except for the **AR** group, where the women had more abdominal SAT than the **AR** men ($p=0.002$).

Compliance and daily activity

Overall compliance for exercising men was higher than for the women at $82.9 \pm 2.6\%$ versus $69.6 \pm 5.0\%$ respectively ($p=0.012$) and is presented in Figure 3.4.

When compliance was examined by group (Figure 3.5), there was no difference between men and women in the **A** group with adherence values of $76.3 \pm 5.4\%$ and $75.6 \pm 7.4\%$ for men and women respectively. In the **R** group, the men had modestly higher compliance values than the women at $83.7 \pm 4.2\%$ versus $73.3 \pm 5.3\%$ respectively. The difference between men and women was significant ($p=0.002$) in the **AR** group where men were $88.7 \pm 3.3\%$ compliant, while the women were only $60.8 \pm 10.0\%$ compliant.

At baseline, the only difference in activity level was seen between **C** men and women, where the **C** men took significantly more step over 7 days than did the **C** women ($p=0.044$) (Table 3.6). This difference however, was no longer significant at 6 months time. The only group to exhibit increased levels of daily activity as measured by 7-day pedometer readings were the men in the **A** group who had a $31.74 \pm 15.0\%$ increase in their activity level ($p=0.022$). The women in the **R** group had a similar increase of $36.4 \pm 35.9\%$ although, this was not significant and there was a high degree of variability ($p=0.134$).

Body composition outcomes

Body weight and BMI

Table 3.7 represents results for both body weight and BMI. Over the 6 month period there was an overall loss of body weight in all participants ($p=0.030$), but significance was not evident in any of the individual groups. With men and women combined, the **A** group had a significant weight loss of $2.11 \pm 1.2\%$ ($p=0.034$) while the

AR group had a similar weight loss of $2.00 \pm 0.78\%$ ($p=0.061$) and **R** and **C** groups experienced no change in body weight. When subdivided further by gender, we saw the greatest weight loss in men of the **A** ($2.75 \pm 1.9\%$) and **AR** ($2.25 \pm 1.1\%$) groups, although not significant ($p=0.070$ and $p=0.061$ respectively). Both **A** and **AR** women had very modest decreases in body weight, while **C** men and women had no change in body weight.

BMI also decreased over the 6-month intervention ($p=0.035$). When grouped by sex, the men had a significant decrease ($p=0.006$), while the women did not ($p=0.145$). The greatest change in BMI was noted in the **A** group (from $34.11 \pm 1.03 \text{ kg/m}^2$ to $33.27 \pm 0.95 \text{ kg/m}^2$; $p=0.032$) followed by a modest decrease in the **AR** group (from 33.3 ± 1.08 to $32.7 \pm 1.09 \text{ kg/m}^2$) as a reflection of the weight loss exhibited in these groups. Looking at all 8 groups in Table 3.6, it is evident that the only significant improvements in BMI were noted by the men in the **A** and **AR** groups ($p=0.008$ and $p=0.05$ respectively). While men in these groups did not display significant decreases in body weight in their groups, the differences in body weight were such that mean changes in BMI were significant.

Visceral adipose tissue

There were no statistically significant differences in VAT between men and women at baseline or at 6 months (see Table 3.8). Overall, VAT decreased modestly in all exercising groups except for the **R** men as illustrated in Figure 3.9. Both men and women in the **AR** group displayed the greatest VAT loss at $7.52 \pm 7.2\%$ and $9.78 \pm 3.7\%$ reductions respectively, although this change was significant only in the **AR** men ($p=0.003$). The **A** group also displayed modest decreases in VAT at $6.40 \pm 5.3\%$ and

4.41±3.2% for men and women respectively. These decreases were not statistically significant. Finally, we saw no change in VAT of the men in the **C** group and a small increase (3.27±5.6%) in VAT in the **C** women.

Abdominal SAT

Combination men and women were significantly different in terms of abdominal SAT at both baseline ($p=0.002$) and at 6 months time ($p=0.003$), with the women having significantly more abdominal SAT than the men (Table 3.10). When men and women were grouped together, reductions in abdominal SAT were exhibited by the **A** group ($p=0.044$), **R** group ($p=0.041$) and **AR** group ($p=0.004$). In examination of men versus women, we see that both the men ($p=0.016$) and the women ($p=0.001$) separately demonstrated significant reductions in this fat depot. By examining Table 3.10 and Figure 3.11, it is clear that only the **AR** women displayed a significant reduction (5.50±3.0%, $p=0.021$) in abdominal SAT. Conversely, the **AR** men demonstrated very little change in abdominal SAT with only a 1.76±3.0% reduction. Men and women in the **R** group displayed a moderate reduction of 3.96±1.3% and 5.08±3.6% respectively in abdominal SAT following training. And in the **A** group, men and women displayed modest losses in abdominal SAT of 2.67±2.5% and 4.06±2.8% respectively. Finally, the **C** men did not exhibit any change in abdominal SAT while the **C** women had a slight reduction 2.59±2.4%.

Mid-thigh CSA

As expected, baseline thigh muscle cross sectional area was significantly ($p=0.000$) higher in men (491.6±8.77 cm²) as compared to women (393.7±17.6 cm²) as indicated in Table 3.12. In particular, the men in the **R**, **A**, and **C** groups had higher cross

sectional areas ($p=0.032$, $p=0.000$ and $p=0.003$) than the women in corresponding groups. The men in the combined aerobic and resistance group had modestly higher muscle CSA but this difference was not significant at baseline ($p=0.154$).

Following the training intervention, the men had a significant increase ($p=0.000$) in their muscle cross sectional area while the women did not ($p=0.79$). Overall, there was an effect of time ($p=0.003$), an interaction of time and sex ($p=0.009$) as well as an interaction of time and resistance training ($p=0.006$). The effect of sex on thigh muscle cross sectional area was also apparent in examination of absolute ($p=0.009$) and percent ($p=0.029$) changes in comparing all men versus all women.

At six months time, the men of the **R**, **A**, and **C** groups still had significantly higher muscle cross sectional area ($p=0.016$, $p=0.00$ and $p=0.006$). Relative changes in muscle CSA are depicted in Figure 3.13. While the **AR** men displayed a significant $2.57\pm 0.56\%$ increase in muscle CSA ($p=0.001$) versus a decrease of $0.031\pm 1.36\%$ in muscle CSA in the **AR** women, this difference did not result in a significant difference between genders at 6 months time. The absolute difference over 6 months however, was significantly different between genders ($p=0.033$) of the **AR** group.

In the **R** group, a $3.17\pm 0.72\%$ increase in muscle CSA was significant in the men ($p=0.000$) versus only a modest increase of $1.15\pm 1.81\%$ in the women ($p=0.494$). The absolute difference in muscle CSA over the 6-month exercise intervention was significantly different for men and women in the **R** group ($p=0.048$).

The **A** men also had a significant increase in muscle CSA of $1.15\pm 0.55\%$ ($p=0.011$) while the women displayed no real change ($0.007\pm 1.19\%$). This difference in absolute change however, was not quite significant ($p=0.062$). Finally, as expected,

neither men nor women in the **C** group displayed any changes in muscle CSA following 6 months time.

Muscle strength

All 8-RM strength data is presented as predicted 1-RM values in Table 3.14 as well as relative changes in strength are depicted in Figures 3.15, 3.16 and 3.17.

Bench Press

Data for bench press was collected for 96 participants and presented in Table 3.14 and Figure 3.15. Data from several participants was not used because of difficulty in lifting the lowest weight on the bench press machine; adjustments were made to the equipment later on in the study. As such data from 61 men versus 35 women was analyzed.

Women in all four groups lifted a consistently lower weight for the bench press as compared to the men at both baseline and 6 months time ($p=0.000$ each at baseline and at 6 months time except for 6 month **R** men versus women, $p=0.011$ and **A** men versus women, $p=0.001$). The **AR** and **R** groups (men and women together) displayed significant improvements in bench press strength ($p=0.000$ for both). Similarly, men increased their strength following the intervention as did the women ($p=0.000$ for both). In the **R** group, men and women separately improved their strength by $39.3\pm 9.8\%$ and $88.3\pm 33.6\%$ respectively ($p=0.000$ for both). Likewise, in the **AR** group, we saw increases of $43.1\pm 7.52\%$ ($p=0.000$) and $54.4\pm 17.2\%$ ($p=0.003$) for men and women respectively.

In the **A** group, men and women improved their strength modestly by $7.59\pm 5.7\%$ (NS) and $18.31\pm 15.2\%$ (NS). Finally, in the **C** group, the men displayed a small

decrement in strength ($-4.89 \pm 4.6\%$) while the women had a moderate improvement of $9.83 \pm 12.7\%$.

In the analysis of percent change in strength, there was both an effect of sex and group on percent change in strength. In the comparing groups, both **R** and **AR** groups increased their strength on the bench press significantly more than **A** (**AR** versus **A**, $p=0.025$; **R** versus **A**, $p=0.001$) and **C** groups (**AR** versus **C**, $p=0.001$; **R** versus **C**, $p=0.000$). Overall, women had greater relative gains in strength on the bench press as compared to the men ($p=0.016$). As demonstrated in Figure 3.14, **R** women improved significantly more than **R** men ($p=0.010$).

Seated Row

Data for strength when performing the seated row was analyzed for 95 participants and is presented in Table 3.14 and Figure 3.16. Men were consistently stronger than the women at baseline and 6 months time in all groups ($P < 0.05$). Seated row strength improved with the intervention ($p=0.000$) and there were several interactions of time-by-group ($p=0.000$), time-by-sex ($p=0.002$) and time-by-group-by-sex ($p=0.028$). Both **R** and **AR** groups improved their strength for seated row ($p=0.000$ for both) while **A** and **C** groups did not. The gains attained by the **AR** and **R** groups were significantly different from that of the **A** and **C** groups. Separately, **AR** men ($p=0.000$) and women ($p=0.007$), and **R** men ($p=0.000$) and women ($p=0.000$) exhibited strength gains. Men in the **AR** group had significantly greater improvements ($44.23 \pm 4.5\%$) in strength for seated row than did the **AR** women (23.49 ± 7.1) ($p=0.032$). Resistance only women showed modestly greater improvements in strength ($32.45 \pm 11.6\%$) following

training than the **AR** women and improvements were not statistically lower than that of **R** men.

Leg Press

Strength test data for the leg press was analyzed for 107 participants and is presented in Table 3.14 and Figure 3.16. There were significant effects of time ($p=0.000$) as well as a time-by-group interaction ($p=0.048$). Baseline and 6 month absolute strength was again greater in the men as compared to the women, but significance was attained in **A** ($p=0.035$ and $p=0.010$ respectively) and **C** groups ($p=0.000$ and $p=0.001$ respectively), but not **R** and **AR** groups. When men and women were grouped together, each of the four treatment groups displayed significant improvements on the leg press following the intervention period. Men and women separately saw similar improvements over time ($p=0.000$ for both). More specifically, the greatest strength gains were noted by **R** men and women with $68.88\pm 22.7\%$ ($p=0.000$) and $76.83\pm 17.9\%$ ($p=0.000$) gains respectively.

VO_{2peak}

Cardiorespiratory fitness data for all 115 participants is presented in Table 3.18 and Figure 3.19. In examination of baseline to 6 month data, there is an effect of time ($p=0.031$) as well as time-by-group ($p=0.000$) and time-by-sex interactions ($p=0.043$). Men had consistently higher **VO_{2peak}** values at baseline and 6 months time in all groups as compared to the women ($p<0.05$). Furthermore, men as a group improved their **VO_{2peak}** following the intervention ($p=0.001$), while women did not ($p=0.930$). We saw improvements in cardiorespiratory fitness in both **A** ($p=0.000$) and **AR** groups ($p=0.006$), but more specifically it was the **A** men ($p=0.000$) and **AR** men ($p=0.001$) that had significant improvements. In the analysis of relative (%) changes in **VO_{2peak}**, we saw that

both **AR** and **A** groups improved significantly more than the **C** group. Overall, men improved significantly more than women ($p=0.047$), although this significance was no longer apparent when divided into 8 intervention groups.

Specifically, we saw the greatest improvements for men and women in the **A** group with increases in VO_{2peak} of $8.34\pm 2.9\%$ ($p=0.000$) and $3.77\pm 1.9\%$ (NS) respectively. Men and women in the **AR** group displayed similar increases of $7.28\pm 2.8\%$ ($p=0.001$) and $2.74\pm 3.14\%$ (NS) respectively. Men in **R** and **C** groups saw no real change in VO_{2peak} following the intervention while women in **R** and **C** groups saw slight decrements in their cardiorespiratory fitness of $2.50\pm 1.5\%$ and $3.19\pm 2.6\%$ respectively.

Lipoprotein lipid profiles

All data for lipoprotein lipid profiles is presented in Table 3.20 and relative changes are depicted subsequently in Figures 3.21, 3.22, 3.23, 3.24 and 3.25. At baseline, the only difference that existed between men and women was higher HDL-cholesterol level in **R** women as compared to the **R** men ($p=0.035$), but this difference was no longer significant following the intervention ($p=0.088$). The only significant change in lipoprotein lipid profile occurred in the **AR** men who saw a decrease in their TGs.

HDL-cholesterol

Over the six month intervention period, HDL-cholesterol levels decreased for all groups combined ($p=0.015$) although when separated, this decrease was significant in men ($p=0.012$) but not women and there were no significant changes in any of the 8 groups. The **AR** women were the only group to exhibit an increase in HDL-cholesterol. The increase of $1.23\pm 3.3\%$ however, was only modest and thus insignificant.

Conversely, the **R** group with men and women combined had a significant decrease in HDL-C ($p=0.037$).

LDL-cholesterol

None of the changes in LDL-C were significant in any of the 8 groups, although slight decreases in LDL-C were noted in exercising groups. More specifically, modest decreases in LDL-C were noted in **A** men ($1.87\pm 6.8\%$) and women ($4.97\pm 6.7\%$), **R** men ($3.97\pm 4.5\%$) and **AR** men ($2.64\pm 5.4\%$). Conversely, the **R** women saw no change in their LDL-C and the **AR** women displayed very slight increase ($2.53\pm 6.0\%$) in their LDL-C. Similarly, both **C** men and women displayed increases in their LDL-C following the 6 month period by $6.07\pm 4.2\%$ and $12.65\pm 10.9\%$ respectively.

Total cholesterol

No significant differences in total cholesterol were noted for any of the groups following the intervention, nor were there any differences between the sexes. All groups displayed modest increases in total cholesterol except for the **R** women who exhibited no change and the **C** men who exhibited very small decreases ($3.21\pm 2.4\%$) following the intervention.

Total cholesterol: HDL cholesterol

In men, the ratio of total cholesterol to HDL-C did not change for the **A** group, increased slightly for the **R** group ($2.2\pm 5.2\%$), significantly for the **C** group ($13.21\pm 7.7\%$) ($p=0.044$) and finally, a modest improvement of $-2.22\pm 5.2\%$ was exhibited by the **AR** group. In the women, the ratio of total cholesterol to HDL-C changed only modestly over the 6 month period with increases exhibited by the **A** ($13.0\pm 14.7\%$), **R** ($7.37\pm 4.6\%$) and **C** groups ($5.62\pm 4.7\%$) and a slight decrease in

the **AR** group ($-1.83 \pm 4.8\%$). None of the changes experienced by the women were significant.

Triglycerides

Finally, TGs did not improve following training as a whole group, but there was a time-by-group interaction ($p=0.017$). The greatest improvement was noted in the **AR** group ($p=0.010$) where TGs decreased by $19.3 \pm 7.5\%$ in men ($p=0.044$) and $13.2 \pm 7.9\%$ in women (NS). In men, improvements in TGs were also noted modestly in the **A** ($-8.29 \pm 11.5\%$) and slightly in **R** ($-1.47 \pm 9.2\%$) groups. Conversely, in women **A** and **R** groups had increases in TGs following training at $18.4 \pm 18.3\%$ and $9.55 \pm 4.3\%$ respectively; although these were still insignificant. In the **C** group, TGs increased by $16.6 \pm 12.0\%$ in men and $19.3 \pm 15.4\%$ in women.

Glycemic and metabolic outcomes

Hemoglobin A_{1c}

The HbA_{1c} and was presented for all participants in both Table 3.26 and Figure 3.27. From baseline to 6 months, we saw a main effect of time ($p=0.000$), as well as time-by-group ($p=0.001$) and time-by-sex ($p=0.015$) interactions. The greatest improvements in HbA_{1c} for both men and women were demonstrated following **AR** training ($p=0.000$), followed by **A** training ($p=0.001$) alone. Separately, we saw an improvement in men ($p=0.000$) but not women ($p=0.234$).

At baseline, we saw no differences between men and women within each group for HbA_{1c}. At 6 months time however, men in the **R** group had a lower HbA_{1c} than the **R** women ($p=0.005$) owing to the changes that occurred to HbA_{1c} during the intervention for both men and women.

For both men and women, the **AR** groups saw the greatest improvements in HbA_{1c} with decreases of $14.6 \pm 2.5\%$ ($p=0.000$) and $7.7 \pm 3.4\%$ ($p=0.028$) for men and women respectively. Aerobic men and women had improvements of $-9.6 \pm 3.1\%$ ($p=0.001$) and $-5.5 \pm 3.3\%$ (NS) respectively.

When we analyzed relative (%) and absolute changes in HbA_{1c}, it was clear that the **R** men responded more favourably to the intervention than the **R** women ($p=0.033$). Resistance men had a modest decrease of $5.7 \pm 2.5\%$ ($p=0.051$) in HbA_{1c} while the women had an increase of $4.1 \pm 2.2\%$. We also saw that the **AR** group responded better than both the **R** group ($p=0.009$) and **C** groups ($p=0.001$) and that the **A** group responded better than the **C** group ($p=0.049$).

HOMA model

Results for HOMA values can be found in Table 3.28 and Figure 3.29. No differences between men and women were observed at baseline or 6 months time in any of the groups for HOMA values. In all groups combined, there was an effect of time ($p=0.000$) with a reduction in HOMA values over the 6 month intervention period. Similarly, both men ($p=0.011$) and women ($p=0.001$) saw reductions in HOMA. The greatest decrease in HOMA was exhibited by the **A** group ($p=0.000$) followed by the **AR** training group ($p=0.052$). Specifically, we saw the greatest reduction of $20.0 \pm 13.7\%$ in **A** women ($p=0.001$), followed by a $12.9 \pm 11.3\%$ reduction in **A** men ($p=0.073$), $10.9 \pm 12.5\%$ decrease in **AR** men (NS) and an $8.6 \pm 19.5\%$ reduction in **AR** women ($p=0.068$). Resistance men had a modest decrease of $7.4 \pm 15.4\%$ while **R** women saw no change. Finally, **C** men and women saw $10.1 \pm 7.2\%$ and $7.7 \pm 9.4\%$ reductions.

Dietary intake

All nutritional data is presented in Table 3.30. On the whole, men consumed more energy than women at baseline (2259 ± 64 kcal/day versus 1872 ± 88 kcal/day) but in particular, baseline differences were significant only in **R** and **C** groups (see Table 3.29). We saw no difference between men and women at baseline in terms of proportion of either carbohydrates, proteins or fats to total caloric intake. It was recommended that participants consume 50-55% of their total daily energy intake from carbohydrates, 15-20% from proteins and <30% from fat. At baseline men had a ratio of carbohydrate to protein to fat as percentages of total daily caloric intake of 46.5:18.8:32.7 and women had a similar baseline ratio of 49.4:18.4:32.7. Over the 6 month intervention, we saw an improvement in this ratio towards what was recommended by the dietitian. At 6 months time, men consumed a macronutrient ratio of 48.6:20.3:31.0, while women similarly had a consumption ratio of 51.4:19.0:31.3.

Over the 6 month intervention period, men reduced their caloric intake by 260 ± 66 kcal/day while the women decreased their intake by 188 ± 51 kcal/day which accounted for a ~10% reduction in caloric intake. Similarly, we saw significant reductions in total caloric intake for **A** ($p=0.038$), **R** ($p=0.003$) and **C** men ($p=0.004$) and for **R** women ($p=0.005$). The men the in **A** group also increased their relative carbohydrate intake from $44.8\pm 1.8\%$ of total caloric intake to $50.3\pm 1.9\%$ of total caloric intake ($p=0.007$) over the 6 month period towards as was recommended. The **C** women also increased the relative carbohydrate consumption from $48.3\pm 1.4\%$ to $53.3\pm 1.3\%$ over time ($p=0.027$). In the **AR** group, the men had a significant increase in their relative protein intake from

17.5±1.6% of total caloric intake to 20.0±1.2% (p=0.038) at the upper limit of what was recommended.

Menopausal Status

Menopausal status was determined from the women's responses to the Menopausal Questionnaire (Appendix). Unfortunately, this questionnaire was designed and administered long after some participants had completed the study and we were unable to get their results. If participants were over the age of 55, it was assumed that they were post-menopausal based on age. Also, menopausal status was also undetermined if a participant had a hysterectomy and did not specify whether it was a partial or full hysterectomy. The number of women in each group is predicted as being pre- or post-menopausal or undetermined and the data is presented in Table 3.31. The questionnaire also evaluated the use of hormone replacement therapy (HRT), although no participants indicated use of HRT.

In the **A** group, six of the women had an undetermined menopausal status, four were considered to be post-menopausal and one was pre-menopausal. In the **R** group, eight of the women were considered post-menopausal and 1 was pre-menopausal. For six of the **AR** women, menopausal status could not be determined, while four and two were considered to be pre- and post-menopausal respectively. Finally, in the **C** group, ten of the women were considered to be post-menopausal the status of four was undetermined and none of these women were considered to be pre-menopausal.

DISCUSSION

The influence of gender in response to 6 months of aerobic, resistance or combination aerobic and resistance training was examined in previously sedentary

participants with T2DM in terms of fitness, body composition, lipoprotein lipid profile and glycemic control. Furthermore, compliance to exercise training, dietary data and menopausal status were evaluated.

At baseline, the men were heavier and displayed greater cardiorespiratory fitness as compared to women and this has been well documented (Shephard, 2000).

In contrast to previous research (Cefalu et al., 1998; Doucet et al., 2002) where men typically exhibit greater VAT and less abdominal SAT than women, baseline levels of VAT were not significantly different between men and women in any of the four groups. VAT in the men did appear to be slightly higher than in the women. According to Han, Feskens, Lean and Seidell (1998), increased VAT is evident in individuals with T2DM and may account for more similar VAT between men and women in our study as compared to healthy men and women.

Compliance and Activity level

There was a substantial difference between men and women in terms of exercise compliance where exercising men attended ~83% of prescribed sessions while women attended only ~70% of what was prescribed. In the meta-analysis on T2DM and exercise, Boulé et al. (2001) found mean compliance to be >80% in the 14 trials that were evaluated and is similar to what was found in our men. If those participants who dropped out of the study before 6 months were excluded from the compliance data, compliance was similar in men and women although men in **R** groups were still modestly more compliant than the women. It is interesting to note that there were no **AR** men who had dropped out of the study while there were four women in this group who did not finish the program.

When the compliance was examined in terms of exercise groups, it becomes evident that it is only when **R** training is included in the training regimen that women were less compliant than men. It is possible that the women do not enjoy this type of exercise or that they had preconceptions of resistance training that deterred them from engaging in this type of activity since resistance training has not been traditionally performed by women until recent years. Vanninen et al. (1992), suggests that motivation and compliance with instructions are the primary difficulties with exercise training in T2DM. And furthermore, they suggest that obesity and cardiovascular morbidity hinder effective exercise training.

The greatest difference in compliance was in the **AR** group where the men were ~89% compliant versus ~61% compliance in the women. Since the exercise workout for this program was the added combination of the aerobic program plus the resistance program, the time requirement for this program was also double that of the other two groups. This is also the group where the men were somewhat more compliant than the other groups and the women were oppositely less compliant than the women in the other exercise groups. It is important to note that compliance of dropouts (N=15 out of exercising groups, 8 M and 8 W) was included in the analyses. The number of dropouts for women was proportionally higher in women versus men (17% versus 12% respectively).

Overall, daily activity levels were increased only by the **A** men. An increase in daily activity level may have had confounding effects on metabolic and body composition parameters in this group. Castaneda et al. (2002) reported increased levels of spontaneous physical activity following resistance training that was not observed in

our participants. It is possible that we did not see the observed improvements that Castaneda et al. (2002) reported because again, the increased physical activity may have confounded the results. Except for the **A** men, we can therefore attribute changes in the variables that were examined to the exercise program without a change in spontaneous activity.

Anthropometrics and abdominal fat

The exercise intervention at hand was not designed for weight loss and as anticipated, weight loss was minimal following the 6-month intervention period for all participants. With minimal weight loss, we hoped to explain any physiological changes as a consequence of the exercise that was performed. In response to exercise alone, men have been reported to lose more weight than women even despite only slight negative shift in energy balance (Andersson et al., 1991). According to Tarnopolsky (1999), women are much more resistant to weight loss reflecting a protective mechanism against fat and protein loss potentially through compensatory increased energy intake not seen in men. When adherence to both diet and exercise is tightly controlled as in the study by Janssen and Ross (1999) weight loss was similar between men and women.

With the change in weight loss, we saw the subsequent decrease in BMI in the **A** and **AR** men. This change in BMI is a direct consequence of weight loss and while weight loss was not significant in these groups, mean BMI values for **A** and **AR** men decreased following the intervention period.

As previously mentioned, all exercising groups experienced modest losses in VAT except for the men in the **R** group. The percent change in VAT of the men in the **R** group was largely driven by two individuals who were very non-compliant (in terms of

exercise and diet) and had increases in their VAT of 56.7% and 40.6% respectively following the intervention. It is also possible that there may have been some error in these particular scans. When these two participants are omitted from the analysis, the mean percent change in VAT for this group was $-3.10 \pm 3.1\%$, which is similar to the VAT loss exhibited by the women in the same group ($-4.75 \pm 4.0\%$).

The modest changes in VAT exhibited by our participants following the intervention were not surprising since overall weight loss was not significant. Modest VAT loss occurred in exercising groups as described earlier and no differences between men and women were apparent in response to the training. Baseline VAT was similar for men and women, which may explain the similar VAT loss following training. Doucet et al. (2002) also found that when baseline differences in VAT were taken into account, VAT loss was similar for men and women following weight loss. In this study, there were no differences at baseline, which may be characteristic of this T2DM population, who according to Han et al. (1998) display increased VAT as compared to a healthy population.

The only significant reduction in VAT was experienced by the **AR** men and conversely, the only significant reduction in abdominal SAT occurred in the **AR** women. The **AR** women did experience similar VAT loss as the **AR** men (9.8% and 7.5% for women and men respectively) but their loss was not significant. Significant reductions in adipose tissue could be expected to be seen in the **AR** group since this group performed the most volume of exercise.

This significant improvement in abdominal SAT experienced by the **AR** women may be a reflection of the higher initial abdominal SAT in this group of women. While

the abdominal SAT of the **AR** women was only significantly different from the men in the **AR** group at baseline, the abdominal SAT of these women was modestly higher than the other women. Doucet et al (2002) noted that in their study population, those with higher initial VAT had greater reduction in VAT with weight loss. Likewise, it is plausible to think that this may also apply to abdominal SAT.

Overall, the men seemed to lose slightly more VAT and women seemed to lose slightly more abdominal SAT, which again may be reflective of somewhat slightly different amounts of abdominal fat depots. Furthermore, VAT loss appeared to be modestly greater than abdominal SAT loss, but again, this is likely a reflection of greater initial levels of VAT versus abdominal SAT.

Janssen and Ross (1999) found that VAT was preferentially decreased in comparison to abdominal SAT and no different between obese men and women following ~10% weight loss induced by either diet alone or diet and aerobic exercise. With diet and resistance training, Janssen and Ross reported greater abdominal SAT loss than the other treatments. Aerobic only and **AR** men in our study seemed to lose modestly more VAT even when the 2 outliers in the **R** group were omitted. Conversely, **A** and **R** women had similar reductions in VAT. The men in the **R** group displayed the greatest abdominal SAT loss for the men and this is also consistent with the findings of Janssen and Ross (1999) although our findings were not significant. Overall there did not appear to be a preferential loss of either abdominal adipose tissue depot in response to exercise.

In comparing abdominal SAT to VAT loss, there does not appear to be a preferential loss in response to exercise. But, looking at baseline values for both fat

depots, we see that both men and women carried substantially more of adipose tissue in the subcutaneous compartment than the visceral compartment. There is likely no preferential loss of abdominal SAT over VAT, as can be noted by the smaller discrepancies in adipose tissue loss when expressed as a percent change.

Muscle cross sectional area

Following the training intervention, all exercising men saw significant increases in mid-thigh muscle CSA, while none of the women experienced any significant changes over the 6-month period. The men in the **R** training groups increased their absolute muscle CSA significantly more than the women who completed 6 months of strength training. Previous researchers have noted greater changes in muscle hypertrophy in men as compared to women following resistance training including Lemmer et al. (2000), who found that the men in their study increased their muscle mass twice as much as the women following a 9-week RT program. Similarly, in their study on resistance training in older men and women, Hunter et al. (2002) found that following the 25 week training program, the 4.7% increase in FFM in men approached significance over the 2.3% increase in women ($p=0.06$).

Furthermore, Abe, DeHoyos, Pollock, and Garzella (2000) found that while the percentage increase in muscle hypertrophy was significant and similar for men and women following 6 weeks of resistance training, as found in our study, the absolute increase in CSA was greater in men. Likewise, Staron et al. (1994) noted similar significant increases in muscle hypertrophy of the lower body in men and women following heavy resistance training. The participants in their study however, were in their early twenties and healthy.

Not surprisingly, among the women, the **R** group exhibited the greatest change in muscle CSA, although modest at 1.15% and non-significant. Similarly in the men, we saw the greatest improvement of 3.2% in the **R** group, followed by a 2.6% increase in the **AR** men. Aerobic only men had a 1.15% increase in mid-thigh muscle CSA, which was equivalent to that of the **R** women. While muscle mass is thought to be maintained but not increased following aerobic training in their meta-analysis, Ballor and Keeseey (1991) noted that cycling training in men did result in increased FFM while walk/run training did not. All aerobic training in our study was performed as lower body activities of treadmill walking or stationary cycling, and over a 6 month intervention period may account for the increase in muscle CSA in the men.

With significant increases in muscle CSA in exercising men and relatively no change in the exercising women, the difference between men and women in muscle CSA that was seen at baseline was augmented following training. The **AR** men and women, however, were no different in terms of their mid-thigh muscle CSA at both baseline and 6 months time. While different from the other groups, this similarity in thigh muscle CSA has been documented by Abe et al. (1998) who noted that muscle thickness was greater in men as compared to women at 12 sites with the exception of the anterior thigh. It was determined that the women had approximately 94% of muscle thickness for the lower body versus approximately 73% and 74% the muscle thickness for the arm and trunk respectively, as compared to the men. As discussed earlier, this group was an anomaly in our study, in that body composition patterns in this group were different from the other groups. Since participants were randomly assigned to the groups, this is likely coincidental.

Muscle hypertrophy is thought to be related to a hormonal environment that promotes protein synthesis. In men, the physiological response to resistance training promotes a hormonal milieu that is highly favourable to muscle protein synthesis and much more so than is experienced by women. Testosterone is a major anabolic hormone that favours protein synthesis in muscle and it is known that men have higher resting levels of testosterone in the blood. Following a single bout of resistance training, men have been shown to exhibit a greater absolute increase in testosterone level (Kraemer et al., 1991), and display greater absolute increase in resting level following a resistance training regimen as compared to women (Staron et al., 1994). Growth hormone is another major anabolic hormone that may promote muscle protein synthesis and finally, cortisol is a catabolic hormone that also plays a role in the muscle metabolism. Although resting cortisol levels are similar in men and women at rest, the level of cortisol is decreased in men but remains unchanged in women following a heavy 8-week resistance training program (Staron et al., 1994). The ratio of testosterone to cortisol is therefore further heightened in men following training and is thought to be important for muscle protein synthesis (Florini, 1985). While hormone levels were not measured in our study, the changes in testosterone and cortisol that are documented by others may be hypothesized to explain the gender difference in muscle hypertrophy that was observed in response to exercise training.

In their study, Charette et al. (1991) found that older (69 ± 1 yr) women who completed 12 weeks of lower body resistance training, exhibited a $20.1 \pm 6.8\%$ increase in CSA of type II muscle fibers although no change in type I muscle fibers in the vastus lateralis muscle. They performed a muscle biopsy to examine muscle CSA and it is

possible that a muscle biopsy may be more sensitive to changes in muscle hypertrophy that are not observable through examination of a CT slice.

Following six months of training, men and women exhibited similar changes in body weight and abdominal fat deposition. As intended, the exercise interventions were not designed to induce weight loss, but exercising groups did see small non-significant decreases in body weight which were slightly although not significantly greater in the men as compared to the women. Conversely, when examining mid-thigh muscle CSA, the men in the **R** training groups exhibited significantly greater increases in absolute muscle CSA as compared to the women.

Evaluation of body fat percentage, fat mass and FFM may have been beneficial in providing a more clear and complete interpretation of body composition changes. Since muscle CSA increased in the exercising men and they lost slightly more body weight than the women, it is probably that overall body fat loss was greater in men than women, although we cannot draw this conclusion.

Strength

Strength differences between the sexes have long been documented (Hoffman, Stauffer & Jackson, 1979), and are primarily reflective of the greater skeletal muscle mass exhibited in men. The men in our study were significantly stronger than our women for all three exercises at both baseline and 6 months time. The difference in strength between men and women has been documented before and after training, with similar relative strength gains following resistance training (Joseph et al., 1999; Cureton, Collins, Hill & McElhannon, 1988).

There were two gender differences in relative strength gains in upper body exercises following strength training. For the bench press, the women in the **R** group had greater relative improvements (88.3%) in strength following training as compared to the men (39.3%), although at both baseline and 6 months time, the women lifted significantly less weight. Conversely, the **AR** men improved similarly to that of the **AR** women as well as the **R** men. Improvements in strength of 43.1% and 54.4% for **AR** men and women respectively were not significantly different from each other although the women appeared to have slightly greater improvements.

When we compared the absolute increases in strength for bench press in the **R** group, the gains were similar for men and women. The analysis of bench press strength included the data of only 96 participants (61 M and 35 W) with only 7 women in the **R** group. As such, the variability in the results for the women is quite high and may have been driven by a few individuals who displayed exceptional improvements.

For the seated row exercise, we saw an opposite gender difference where **AR** men exhibited greater strength gains as compared to the **AR** women. Once again, men were stronger for seated row at both baseline and 6 months time in all groups as could be expected. It is possible that in the **AR** group this difference may reflect the poor compliance by the women in this group although, the gender difference in strength in the **AR** group was not observed for bench press strength. Resistance only and **AR** men had similar improvements in strength, but **R** women displayed modestly higher strength gains following training as compared to the **AR** women for this exercise.

Exercising men and women responded similarly to **R** training in their relative lower body strength gains in strength as documented by others (Shephard, 2000).

Surprisingly, in both the **AR** and **R** groups, men and women were not statistically different in terms of strength at baseline and at 6 months time. In the **R** group 266.5±21.9 lbs was the predicted 1-RM for the men versus 196.5±41.4 lbs for the women at baseline. While not statistically different, the men of the **R** group did appear to be somewhat stronger than the corresponding women. Conversely, in the **AR** group, the men had a predicted 1-RM value of 249.7±19.0 lbs at baseline, while the women had a very similar predicted value of 232.8±35.4 lbs. The men and women in the **AR** group again, appear to have different baseline gender comparisons as the other groups in the study. Perhaps, in an obese population, women have more leg strength than lean women because they must carry more body weight around in their daily living.

Furthermore, we saw increases in strength of the leg press in all groups, including the **C** group and especially the **C** women (55.11±20.1%, p=0.031)). It is possible that the **C** group experienced some strength gains during the first month of the study when they engaged in both aerobic and resistance activities during the run-in period. It is also probably that following the run-in period, participants in the **C** group became motivated by the first month of exercise and increased their activities of daily living enough to maintain leg strength. Finally, it is also possible that some individuals in the **C** group were non-compliant to the boundaries of this group.

What was also different about strength gains in the leg press as compared to the upper body exercises was that for the leg press, both men and women in both **A** and **AR** groups all displayed very similar improvements. Following the combination aerobic plus resistance training, modestly greater improvements in strength would be expected consequential to the resistance training, but this was not the case. Since aerobic exercise

was performed on the treadmill or stationary bike, it is plausible that lower body strength would improve. The **A** men also experienced increased mid-thigh muscle CSA and this may coincide with the increase in muscle strength, although an increase in muscle CSA was not exhibited in the **A** women. It is also possible that the **AR** group experienced difficulty in pushing themselves through both portions of the workout as the lower body was targeted twice in the same day and they may have compensated by reducing intensity in either portion of the workout. As such, the potential for strength gains from the resistance training portion of the **AR** program may not have been reached.

Cureton et al. (1988) suggested that a similar training response in men and women would be revealed by the comparable relative increases in the two sexes, but greater absolute increases in the men. Likewise, we saw significantly greater bench press strength in the women over that of the men, although absolute changes were similar. Therefore, in accordance to Cureton's proposed notion, the women did in fact display a greater response to training for the bench press. Likewise, the **AR** men saw a significantly greater response to training than **AR** women for the seated row.

VO_{2peak}:

As expected and well-documented, men were consistently more fit in terms of VO_{2peak} both prior to and following training (Shephard, 2000). Improvements were highest in the **A** group for both men and women, although significant only in the men. Combination men and women both saw similar increases in VO_{2peak} as compared to the **A** men and women but again the improvement was significant only in the men and very modest in women.

Overall, men improved more than women following aerobic training. Because women started with a lower VO_{2peak} values at baseline and their gains were lower following training, the difference between genders of VO_{2peak} is greater following training. Similarly, Keteyian et al. (2003), noted a +20% improvement in peak oxygen consumption in men following 14-24 week exercise training program and only a +2% improvement in women. The participants in their study all had had heart failure. Conversely, Shephard (2000) found that men and women improved their oxygen consumption similarly in response to the same training. Shephard's finding is conclusive only towards healthy men and women and is not specific to particular populations. It may be that responses in VO_{2peak} of men and women with T2DM to aerobic training may be different than that of healthy men and women. While the difference in VO_{2peak} between men and women (~8% versus ~3% for men and women respectively) following aerobic training were not as striking as what was found by Keteyian et al. (2003), there is no underlying reason for us to believe that our training stimulus was inadequate for the women in our study.

Likewise, the study by Vanninen et al. (1992) did compare T2DM men and women and the authors found that the exercising men improved VO_2 at anaerobic threshold (ml/kg/min) although did not increase their VO_{2max} following a year of exercise, while the women did not show any changes in oxygen consumption. The participants in this study however, were only encouraged to exercise, although self-reported activity increased similarly in men and women.

Finally, it has been proposed that increases in peak oxygen consumption may be directly related to improvement in other metabolic parameters, Wilmore et al. (2001)

found that high responders (greatest improvements in VO_{2max}) did not display more favourable changes in lipids and lipoproteins.

Lipoprotein lipid profile

Our exercise intervention did not induce any significant improvements in lipoprotein lipid profile, except following the **AR** program in men where TGs were reduced by 19%. Knowing that only one group displayed a significant improvement in TGs, it could be hypothesized that it would be the **AR** men, since this group completed the most volume of exercise and previous research has shown men to display greater improvements in lipoprotein lipid profile following exercise training (Wirth & Steinmetz, 1998). Vanninen et al. (1994) also reported a significant decrease in serum TGs in T2DM men, but not women after a year of increased exercise.

There were no apparent gender differences in any of the changes in lipoprotein lipid profile that occurred following exercise training. Previous research has shown aerobic training or resistance training to induce some favourable changes in lipoprotein lipid profile in men and women, although some of the results have been conflicting (Lokey & Tran, 1989). Unlike our findings, Honkola, Forsén and Eriksson (1997), found that a 5-month resistance training program of the circuit type had a significant effect on the lipoprotein lipid profiles in men and women with T2DM. Total cholesterol dropped by 12%, LDL-C fell 14% and TG decreased by 20%. It should be noted that while this program was a resistance training program, it was done in a circuit type manner, adding an aerobic component to the training.

In a study by Schuit et al. (1998), healthy older (60 to 80 years) men and women exhibited favourable but small changes in total cholesterol, HDL-C and LDL-C following

six months of AT. Unexpectedly, only the women exhibited a significant reduction in TG levels. All improvements were independent of body composition changes. Conversely, lipoprotein lipid profiles did not change following a 40-week brisk walking program in women aged 22 to 40 years, despite a 22% increase in VO_{2max} (Santiago, Leon & Serfass, 1995).

Lokey and Tran (1989) noted that those groups with greater dyslipidemia concentrations exhibited more favourable changes. Weight loss was positively correlated with the decline in total cholesterol and TG levels. In those studies where body weight was maintained throughout the exercise intervention, TG and total cholesterol did not change significantly

In comparing genders, Lokey and Tran (1989) noted that women exhibited smaller lipoprotein lipid profile improvements following exercise training as compared to men. This difference, however, was largely due to the fact that pre-menopausal women have more favourable lipoprotein lipid profiles to begin with.

It appeared that the exercising men displayed greater improvements in TGs following training as compared to the women. While improvements were similar in men and women for the **AR** group, men and women appeared to respond differently to **A** training and **R** training interventions. In the **A** group, the men displayed a modest decrease of ~8% while women displayed the opposite effect with an increase of ~18%. And following **R** training, the men displayed no real change (-1.47%) while the women again, had increased levels of TGs of ~9.5 % following training. It may be that women require a greater volume of training to induce any reductions in TGs as exhibited in the **AR** group but not in either **R** training alone or **A** training alone. On the other hand, **A**

training alone had somewhat of a positive effect on TGs in men, although not significant, while with **R** training, TGs remained relatively stable from baseline (~ -1.5%). All exercising men did show some improvement in TGs while in women, only the **AR** exercise program may have been sufficient to induce any favourable changes. It is important to note that both **C** men and women exhibited worsening levels of TGs with increases of ~17% and ~19% respectively following the 6-month period. It is plausible to say that exercise may be one way to prevent a worsening TG profile in this population in both men and women, although women may need a more rigorous program induce improvements.

The exercise intervention in this study did not appear to be sufficient to affect lipoprotein lipid profiles and no gender differences were observed in lipoprotein lipid profiles in response to exercise. A more rigorous program may be needed to induce improvements in lipoprotein lipid profiles in men and women with T2DM.

Glycemic Control

To our knowledge, this is the first study of its kind to demonstrate that T2DM men displayed significantly greater improvements in HbA_{1c} following **R** training as compared to women. Furthermore, **A** and **AR** men also appeared to exhibit slightly greater improvements in HbA_{1c} as compared to the women in corresponding groups, although the differences between genders were not significant. Resistance training in combination with aerobic training appeared to have an added benefit in glycemic control in men but only modestly in women.

It was surprising to see that although baseline values for HbA_{1c} were no different between men and women, that following training in the **R** group, men had significantly

lower values of HbA_{1c} as compared to the women. The glycemic control of these women did not only not decrease, but instead it increased by $4.05 \pm 2.2\%$, indicating that the resistance training provided no benefit whatsoever to the glycemic control in these women. On the flip-side, the women in the **AR** group seemed to display some, although modest, added benefit of the resistance training to the aerobic training, as we saw modestly greater improvements in the **AR** women ($-7.73 \pm 3.4\%$, $p=0.028$) as compared to the **A** women ($-5.46 \pm 3.2\%$, $p=0.150$).

Similarly, Hurlbut et al. (2002) found that men had favourable improvements in insulin response to an oral glucose tolerance test following strength training, while the women showed no improvements following training. Both younger (20-30 years) and older (65-75 years) men and women were examined with the same finding in both younger and older participants. Two of the older men had T2DM, but this was a relatively healthy group. Furthermore neither changes in strength, FFM, nor body fat could explain the observed sex difference.

It is possible that women did not have any improvements in glycemic control from **R** training, because of a lack of muscle hypertrophy. All groups of exercising men displayed significant improvements in mid-thigh muscle CSA and as such increased the muscle mass for glucose disposal. This may also be why **A** men displayed modestly greater improvements in glycemic control as compared to women. Eriksson et al. (1997) reported a strong correlation between thigh muscle size and glycemic control in T2DM participants but results were pooled for men and women (4 men and 4 women).

Castaneda et al. (2002) reported a 1.2% absolute reduction in HbA_{1c} following a high intensity 16-week progressive resistance training program. These researchers

reported a considerably greater improvement in glycemic control than the $0.46 \pm 0.1\%$ absolute reduction in HbA_{1c} noted in the **R** men in our study. Both training interventions used the same number of sets and repetitions, but Castaneda et al. (2002) used hydraulic resistance machines in their study. Compliance in the Castaneda study was extremely high ($90 \pm 10\%$), partly because participants were transported by taxi to and from each exercise session, and had one-on-one supervision at each session. The participants in Castaneda et al.'s study included 40 women and 22 men. They were older (66 ± 8 yrs) than our participants and were all Latino, whereas our population was primarily Caucasian.

Since there were no real changes in body fat or weight following the interventions, the differences in changes of muscle CSA between men and women following training, therefore likely bears greater relevance to the differences seen in glycemic control. Furthermore, men in the **A** groups seemed to display slightly greater improvements in VO_{2peak} , which may be related to the modestly greater improvements in glycemic control in the men of these groups as compared to the women of these groups. Vanninen et al. (1992) reported that the decrease in HbA_{1c} in their participants was not associated with a change in aerobic capacity.

Dietary Analysis

The higher energy consumption in men was expected to support a greater body weight. The overall caloric reduction ($\sim 10\%$ for men and women combined) was also not surprising since the dietitian closely monitored each participant at baseline, 3 and 6 months and encouraged consumption of 90% of energy required for body maintenance. Conversely, we did not see reductions in caloric intake for either **AR** men or women, or **A** women possibly because this group also experienced the greatest caloric deficit from

the exercise and may have maintained their baseline caloric intake as a compensation for the caloric expenditure via exercise. Tarnopolsky (1999) suggests that this is commonly seen in exercising women to conserve fat mass. The change in relative carbohydrate intake for the **A** men as well as **C** women increased over the 6 month intervention period, both towards the recommended relative consumption. Similarly, the **AR** men increased their relative consumption of protein, although at 6 months time, their relative protein intake was at the upper limit of what was recommended. Overall, there were no surprising changes in diet that would appear to influence primary outcomes of the study.

It is important to note that may have underreported nutritional intake and since the dietary log was only three days, it could be subject to a great deal of variability.

Differences in season may have also influenced dietary habits over the course of the intervention period.

Limitations

There are several limitations to this substudy. The level of compliance was variable among participants, with greater non-compliance seen in the women as compared to the men, and data from certain individuals may have driven the results of some variables, although major outliers were examined.

Because the combination aerobic and resistance training program consisted of the added combination of the two modalities, volume of training and therefore energy expenditure was much greater in the **AR** group. Similarly, energy expenditure between **A** and **R** training programs also differed, with a higher caloric expenditure from **A** training therefore limiting our ability to make direct comparisons between exercise modalities.

Supervision of exercise was somewhat variable among participants. Because participants could exercise at any of the five designated locations and at any time that the facilities were open, it was difficult to accommodate to the needs of certain participants. There was also a high turnover in exercise trainers who were students from the University of Ottawa. Certain participants were demanding or required extra supervision while others preferred to work on their own with minimal intervention. The level of competency and ability of the trainer to motivate participants was also highly variable.

Menopausal status was undetermined for 17 participants and it was difficult to draw any conclusions based on the data that was available. Furthermore, we did not measure sex hormone levels in men or women. The N values for the women in each of the four groups were smaller than those of the men and they were less compliant, reducing the statistical power of this substudy.

CONCLUSIONS

Men and women with T2DM responded similarly to aerobic and combination aerobic and resistance training in terms of glycemic control, although men displayed modestly greater improvements than the women. For the women in our study, resistance training provided no benefit in terms of glycemic control, and men had modest improvements in HbA_{1c}. To our knowledge, this has not been previously reported and may suggest that R training may be beneficial for T2DM men but not women. However, when resistance training was in combination with aerobic training, women did have slightly greater improvements as compared to A training and may reap additional benefits of resistance training. Likewise, the intensity and/or volume and/or motivation may not have been sufficient enough for the women in our study to see similar improvements as

the men, as compliance for women was also lower in resistance groups as compared to the men.

The most probable reason for the gender difference in glycemic control changes following training is the gender difference in muscle CSA whereby all exercising men had increases in muscle CSA, while none of the female groups exhibited any differences. Muscle mass has been previously correlated to glycemic control (Ivy et al., 1999). Furthermore, other changes in body composition including body weight and abdominal adipose tissue were similar in men and women as were changes in total caloric and macronutrient consumption

Moreover, our exercise program did not induce improvements in lipoprotein lipid profile except in the **AR** men where TGs were reduced, suggesting that the volume and or intensity of our training program may not have been sufficient to affect lipid control. This was also evidenced by only moderate increases in VO_{2peak} following **A** training in women. Men and women did have similar improvements in both upper and lower body strength following training.

Furthermore, the data from all participants who were randomized, except that of one woman, were included in the analyses and as such, the data from non-compliant participants were included in the analyses. Results may have been more striking had only highly compliant participants been included in the analysis.

Finally, the notion of responders versus non-responders to training was not examined and it is possible that a greater proportion of women were non-responders to the exercise intervention; displaying little changes that would be expected in response to exercise training.

4. GENERAL CONCLUSIONS

This study was a gender comparison of the changes in body composition, metabolic profile and fitness in previously sedentary participants with T2DM. The only other study to be found evaluating the effects of exercise on T2DM and not pooling results was carried out by Vanninen et al. (1992). This study, however, did not examine the effects of a structured program, nor did they examine the effects of resistance training. Because men have a greater propensity to build muscle, it was hypothesized that men could respond differently than women to resistance training and therefore, also to combination aerobic and resistance training. Because T2DM is a progressive disease and exercise training has been shown to improve blood glucose control in those with T2DM (Ivy et al., 1999), examining the gender specific responses may bear important implications when prescribing exercise as a therapeutic intervention in the treatment of T2DM.

In our study, the men and women in the combination aerobic and resistance training showed the greatest improvements in HbA_{1c}. Because this group experienced the greatest volume of training, this could be expected. Conversely, we expected similar changes for men and women in the aerobic only group, but in this group the men saw significant improvements in HbA_{1c} while the women exhibited only modest improvements. For the women in our study, resistance training provided no benefits in terms of glycemic control, and men had modest improvements in HbA_{1c}. The response of resistance men was significantly better than that of the women. To our knowledge, this has not been previously reported and suggests that resistance training may be beneficial for T2DM men but not women.

The most probable reason for the gender difference in glycemic control changes following training is the gender difference in muscle CSA whereby all exercising men had increases in muscle CSA, no changes occurred for the women. Muscle mass has been previously correlated to glycemic control (Ivy et al., 1999). Furthermore, other changes in body composition including body weight and abdominal adipose tissue were similar in men and women as were changes in total caloric and macronutrient consumption. Moreover, our exercise program did not induce improvements in lipoprotein lipid profile except in the combination men where TGs were reduced, suggesting that the volume and or intensity of our training program may not have been sufficient to affect lipid control. This was also evidenced by only moderate increases in VO_{2peak} following aerobic training in women. Men and women also displayed similar improvements in both upper and lower body strength following training.

While from our findings we cannot yet determine a specific exercise prescription for men and women with T2DM, we can conclude that the combination aerobic and resistance training proved beneficial to both men and women in terms of improved HbA_{1c} , a important marker for long term glycemic control. Furthermore, the difference in HbA_{1c} between men and women in the resistance group warrants the need for further research to clarify the greater improvements seen in our men. Finally, a direct comparison of exercise modalities, whereby energy expenditure is equivalent in all modalities would provide the greatest insight to the effects of the different exercise modalities on T2DM. For now, we can say that a higher volume of aerobic and combination exercise is beneficial to those with T2DM.

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TABLES

Table 3.1 Aerobic and resistance training protocol during run-in period

Week	AEROBIC TRAINING			RESISTANCE TRAINING			
	Duration (min/day)	Intensity (%Hrmax)	Frequency (days/wk)	Sets	Reps	Weight (RM)	Frequency (days/wk)
1-2	15	60	3	1	15	15	2
3-4	20	60	3	2	15	15	2

**RM (repetition maximum): 15 RM is the weight used so that the 15th repetition is the last repetition that can be performed properly.

Table 3.2 Aerobic and resistance training protocol for weeks 5 to 26

Week	AEROBIC TRAINING			RESISTANCE TRAINING			
	Duration	Intensity	Frequency	Sets	Reps	Weight	Frequency
	(min/day)	(%Hrmax)	(days/wk)			(RM)	(days/wk)
5-6	25	70	3	3	8	8	3
7-8	30	70	3	3	8	8	3
9-10	35	70	3	3	8	8	3
11-12	40	70	3	3	8	8	3
13-16	45	70	3	3	8	8	3
17-19	40	75	3	3	8	8	3
20-26	45	75	3	3	8	8	3

Table 3.3 Baseline descriptive characteristics of participants. Data are means \pm SE. **** significant gender difference between men and women with the same group at $P < 0.05$, 0.01 and 0.001 respectively. For CT analysis of VAT and SAT, some participants were excluded from the data and the N values were as follows: Aerobic only, 16 M and 11 W; Resistance only, 16 M and 10 W; Combination A+R, 17 M and 10 W; and Control, 17 M and 11 W.

<i>Dependent Variable</i>	<i>Aerobic Only</i>	<i>Resistance Only</i>	<i>Combination (A+R)</i>	<i>Control</i>
N	28	28	29	30
Men (n)	17	17	17	17
Women (n)	11	11	12	13
Age (yrs)				
Men	54.5 \pm 1.9	53.7 \pm 2.1	54.3 \pm 1.6	54.7 \pm 0.8
Women	53.8 \pm 2.1	56.0 \pm 2.4	52.6 \pm 2.0	55.9 \pm 2.0
BMI (kg/m²)				
Men	33.8 \pm 1.4	33.2 \pm 1.5	30.9 \pm 1.2	32.2 \pm 1.2
Women	34.5 \pm 1.6	33.7 \pm 2.3	36.7 \pm 1.5**	34.8 \pm 1.6
Weight (kg)				
Men	104.7 \pm 4.4	101.3 \pm 4.5	94.4 \pm 4.7	100.8 \pm 3.7
Women	90.4 \pm 4.9*	86.1 \pm 7.3*	96.9 \pm 4.1	88.3 \pm 3.9
HbA_{1c} (%)				
Men	7.74 \pm 0.24	7.55 \pm 0.18	7.84 \pm 0.28	7.64 \pm 0.21
Women	7.26 \pm 0.17	7.85 \pm 0.35	7.62 \pm 0.2	7.88 \pm 0.28
VO_{2peak} (ml/kg/min)				
Men	25.0 \pm 1.1	23.7 \pm 1.1	25.6 \pm 0.99	26.3 \pm 0.82
Women	20.1 \pm 1.3**	20.6 \pm 1.4*	19.6 \pm 0.80***	18.9 \pm 0.89***
VAT (cm²)				
Men	213.9 \pm 21.7	210.3 \pm 22.8	209.9 \pm 23.6	230.8 \pm 20.3
Women	216.9 \pm 40.2	177.4 \pm 22.0	197.5 \pm 17.8	190.6 \pm 19.8
Ab. SAT (cm²)				
Men	392.7 \pm 36.2	380.7 \pm 46.4	302.6 \pm 34.6	333.4 \pm 27.6
Women	429.1 \pm 35.2	407.2 \pm 37.9	474.1 \pm 29.6**	417.6 \pm 33.8

Table 3.6 Total number of steps as read by pedometer over 7-day period at baseline and 6 months and percent change over the 6-month period. Data was analyzed for 13 men and 10 women in **A**; 17 men and 11 women in **R**; 13 men and 10 women in **A**; and 11 men and 12 women in **C**. *, $P < 0.05$ between men and women of the same group

Group	Baseline (total steps)	6 Month (total steps)	Percent Change (%)	P (0-6 months)
Aerobic Only				
Men	37281±4074	47828±7024	31.74±15.0	0.022
Women	39726±7125	38542±7406	4.88±13.3	NS
Resistance Only				
Men	40435±6875	40845±5421	18.92±16.0	NS
Women	35338±6750	34108±4659	36.4±35.9	NS
Combination				
Men	39791±5615	45834±6119	16.84±6.57	NS
Women	45574±7117	47053±6406	15.27±17.4	NS
Control				
Men	47668±5839	48357±6909	2.96±7.41	NS
Women	29538±3675*	34421±5999	11.45±9.39	NS

Table 3.7 Baseline, 6 month body weight (kg) and BMI (kg/m²) and absolute change in body weight (kg). Data is presented as means \pm SE. *, **, *** P<0.05, 0.01 and 0.001, respectively between men and women of the same group.

Group	Baseline Body Weight (kg)	6 Month Body Weight (kg)	Absolute change in weight (kg)	Baseline BMI (kg/m²)	6 Month BMI (kg/m²)	P (0-6)
A Only						
Men	104.7 \pm 4.4	101.2 \pm 3.7	-3.6 \pm 2.6	33.8 \pm 1.4	32.7 \pm 1.2	0.008
Women	90.4 \pm 4.9*	89.5 \pm 5.0	-0.89 \pm 0.60	34.5 \pm 1.6	34.2 \pm 1.6	NS
R Only						
Men	101.3 \pm 4.5	100.1 \pm 4.4	-1.12 \pm 0.66	33.2 \pm 1.5	32.8 \pm 1.5	NS
Women	86.1 \pm 7.3*	86.3 \pm 7.6	0.23 \pm 0.57	33.7 \pm 2.3	33.7 \pm 2.4	NS
A+R						
Men	94.4 \pm 4.7	91.9 \pm 4.3	-2.5 \pm 1.4	30.9 \pm 1.2	30.1 \pm 1.1	0.050
Women	96.9 \pm 4.1	95.6 \pm 4.5	-1.4 \pm 0.98	36.7 \pm 1.5	36.4 \pm 1.7	NS
Control						
Men	100.8 \pm 3.7	100.7 \pm 3.9	-0.09 \pm 0.91	32.2 \pm 1.2	32.2 \pm 1.2	NS
Women	88.3 \pm 3.9	88.6 \pm 4.0	-0.42 \pm 0.46	34.8 \pm 1.6	35.0 \pm 1.6	NS

Table 3.8 Visceral adipose tissue (VAT) area at baseline and 6 months, and the absolute and percent changes following the 6 month training intervention in 108 participants.

Data is presented as means \pm SE. N=108, A (16 M, 11 W), R (16 M, 10 W), AR (17 M, 11 W) and C (17 M, 11 W).

Group	Baseline VAT (cm²)	6 Month VAT (cm²)	Absolute Change (cm²)	Percent Change (%)	P (0-6)
Aerobic Only					
Men	213.9 \pm 21.7	199.3 \pm 22.1	-14.5 \pm 9.79	-6.40 \pm 5.25	NS
Women	216.8 \pm 40.2	207.5 \pm 38.9	-9.39 \pm 7.42	-4.41 \pm 3.19	NS
Resistance Only					
Men	210.3 \pm 22.8	211.6 \pm 22.2	1.32 \pm 8.67	3.37 \pm 5.22	NS
Women	177.4 \pm 22.0	173.1 \pm 26.8	-4.31 \pm 6.83	-4.75 \pm 3.99	NS
Combination					
Men	209.9 \pm 23.9	183.5 \pm 21.2	-26.5 \pm 10.7	-7.52 \pm 7.17	0.003
Women	197.5 \pm 17.8	179.2 \pm 20.0	-16.6 \pm 5.96	-9.78 \pm 3.73	NS
Control					
Men	230.8 \pm 20.3	216.1 \pm 17.3	-14.7 \pm 11.7	-0.690 \pm 7.12	NS
Women	190.6 \pm 19.8	195.2 \pm 20.2	4.56 \pm 7.22	3.27 \pm 5.58	NS

Table 3.10 Abdominal subcutaneous adipose tissue (SAT) area at baseline and 6 months, and the absolute and percent changes following the 6 month training intervention in 108 participants. Data is presented as means \pm SE. *, **, *** P<0.05, 0.01 and 0.001, respectively between men and women of the same group.

Group	Baseline SAT (cm ²)	6 Month SAT (cm ²)	Absolute Change (cm ²)	Percent Change (%)	P (0-6)
Aerobic Only					
Men	392.7 \pm 36.2	382.5 \pm 36.2	-10.14 \pm 7.62	-2.67 \pm 2.52	NS
Women	429.1 \pm 35.2	412.7 \pm 35.0	-16.39 \pm 12.6	-4.06 \pm 2.83	NS
Resistance Only					
Men	380.7 \pm 46.4	365.2 \pm 45.0	-15.50 \pm 4.96	-3.96 \pm 1.28	NS
Women	407.2 \pm 37.9	395.0 \pm 45.1	-12.23 \pm 10.7	-5.08 \pm 3.62	NS
Combination					
Men	302.6 \pm 34.6	288.5 \pm 30.6	-14.13 \pm 9.19	-1.76 \pm 2.96	NS
Women	474.1 \pm 29.6**	449.6 \pm 35.2**	-22.32 \pm 11.4	-5.50 \pm 2.99	0.021
Control					
Men	333.4 \pm 27.6	333.2 \pm 28.4	-.222 \pm 5.93	.159 \pm 1.82	NS
Women	417.6 \pm 33.8	402.6 \pm 28.5	-15.05 \pm 12.2	-2.59 \pm 2.41	NS

Table 3.12 Mid-thigh cross sectional area (CSA) at baseline and 6 months, and the absolute and relative (%) changes following the 6 month training intervention in 103 participants. Data is presented as means \pm SE. *, **, *** P<0.05, 0.01 and 0.001, respectively between men and women of the same group. Data was collected for 13 M and 11 W in A, 14 M and 10 W in R, 17 M and 10 W in AR, and 17 M and 10 W in C.

Group	Baseline CSA (cm²)	6 Month CSA (cm²)	Absolute Change (cm²)	Percent Change (%)	P (0-6 m)
Aerobic Only					
Men	502.3 \pm 19.4	512.6 \pm 19.5	3.08 \pm 2.62	1.15 \pm 0.55	0.011
Women	346.5 \pm 18.6***	345.3 \pm 16.7***	-1.16 \pm 3.89	.007 \pm 1.19	NS
Resistance Only					
Men	474.7 \pm 13.1	489.5 \pm 13.1	14.75 \pm 3.72	3.17 \pm 0.72	0.000
Women	393.3 \pm 39.9*	396.4 \pm 39.3*	3.08 \pm 5.33*	1.15 \pm 1.81	NS
Combination					
Men	470.9 \pm 16.1	482.2 \pm 15.2	11.31 \pm 2.23	2.57 \pm 0.56	0.001
Women	419.2 \pm 34.8	418.3 \pm 34.7	-0.94 \pm 4.77*	-0.031 \pm 1.36	NS
Control					
Men	519.6 \pm 18.9	516.1 \pm 19.4	-3.27 \pm 3.10	-0.69 \pm 0.61	NS
Women	416.1 \pm 42.1**	417.4 \pm 45.5**	1.32 \pm 6.60	-0.23 \pm 1.35	NS

Table 3.14 Baseline, 6 month and relative (%) change in predicted 1 RM strength for bench press, seated row and leg press exercises. Men and women for all groups were different at baseline and 6 months time for bench press and seated row absolute strength (P<0.05). Data is presented as means. *, **, *** P<0.05, 0.01 and 0.001, respectively between men and women of the same group

Variable	Men				Women			
	Baseline	6 Months	Relative	P (0-6m)	Baseline	6 Months	Relative	P (0-6m)
	(lbs)	(lbs)	(%)		(lbs)	(lbs)	(%)	
Aerobic Only			Change				Change	
Bench Press	81.0±5.0	87.9±7.7	7.6±5.7	NS	36.0±3.4	42.5±7.1	18.3±15.2	NS
Seated Row	110.0±6.1	116.5±8.7	5.3±4.4	NS	83.3±8.4	90.1±5.9	13.9±7.9	NS
Leg Press	280.0±35.7	381.3±41.0	47.1±12.7	0.000	191.1±40.5*	241.4±52.5*	54.6±25.5	0.085
Resistance Only								
Bench Press	76.2±5.6	101.2±6.2	39.9±9.8	0.000	35.8±3.8	66.7±13.6	88.3±33.6*	0.000
Seated Row	112.1±7.8	152.5±8.0	40.4±8.2	0.000	80.2±5.1	105.5±10.5	32.5±11.6	0.000
Leg Press	266.5±21.9	398.1±26.9	68.9±22.7	0.000	196.5±41.4	317.2±58.6	76.8±17.9	0.000
Combination (A+R)								
Bench Press	79.9±5.8	113.3±9.5	43.1±7.5	0.000	39.1±3.7	59.6±8.4	54.4±17.2	0.003
Seated Row	114.0±4.3	164.7±8.6	44.2±4.4	0.000	82.0±6.6	99.3±6.8	23.5±7.1*	0.007
Leg Press	249.7±19.0	364.1±27.7	49.1±8.6	0.000	232.8±35.4	318.1±34.6	52.7±17.0	0.006
Control								
Bench Press	91.6±7.3	86.7±7.8	-4.89±4.6	NS	35.7±3.3	37.1±3.8	9.83±12.3	NS
Seated Row	122.8±4.2	130.9±5.9	7.32±4.5	NS	75.1±4.0	77.3±2.4	6.2±6.1	NS
Leg Press	318.3±22.1	371.0±33.3	18.7±9.0	0.036	143.6±14.6***	202.0±15.6**	55.1±20.1	0.031

Table 3.18 Baseline, 6 month and relative changes in VO_{2peak} in 115 participants. Data is presented as means \pm SE. *, **, *** $P < 0.05$, 0.01 and 0.001, respectively between men and women of the same group.

Group	Baseline VO_{2peak}(ml/kg /min)	6 Month VO_{2peak}(ml/kg /min)	Percent Change (%)	P (0- 6months)
Aerobic Only				
Men	25.0 \pm 1.1	27.1 \pm 1.3	8.36 \pm 2.9	0.000
Women	20.1 \pm 1.3**	21.1 \pm 1.6**	3.77 \pm 1.9	NS
Resistance Only				
Men	23.7 \pm 1.1	23.5 \pm 1.2	1.24 \pm 2.8	NS
Women	20.6 \pm 1.4*	20.0 \pm 1.3*	-2.50 \pm 1.5	NS
Combination				
Men	25.6 \pm 0.99	27.3 \pm 1.1	7.28 \pm 2.8	0.001
Women	19.6 \pm 0.80***	20.1 \pm 0.86***	2.74 \pm 3.1	NS
Control				
Men	26.3 \pm 0.82	26.0 \pm 0.87	-0.96 \pm 1.8	NS
Women	18.9 \pm 0.89***	18.2 \pm 0.81***	-3.18 \pm 2.6	NS

Table 3.20 Pre-, post-intervention (mmol/L) and relative (%) change for lipoprotein lipid profile including; HDL-C, LDL-C, total-C, the ratio of total cholesterol to HDL-C and TG. N was 115 for all measurements and divided as previously described, except for measurement of LDL (N=110) where participants were distributed as follows: aerobic (16 M, 11 W), resistance (16 M, 10 W), combination (17 M, 11 W) and control (16 M, 13 W). Data is presented as means \pm SE. ****P<0.05, 0.01 and 0.001, respectively between men and women of the same group.

Variable	Men			Women				
	Base	6 Month	Relative (%) Change	P (0-6m)	Base	6 Month	Relative (%) Change	P (0-6m)
Aerobic Only								
HDL (mmol/L)	1.16 \pm 0.07	1.16 \pm 0.11	-0.64 \pm 5.1	NS	1.30 \pm 0.12	1.23 \pm 0.11	-3.97 \pm 4.4	NS
LDL (mmol/L)	3.02 \pm 0.21	2.84 \pm 0.21	-1.87 \pm 6.8	NS	2.99 \pm 0.23	2.82 \pm 0.26	-4.97 \pm 6.7	NS
Total-C (mmol/L)	5.11 \pm 0.26	4.89 \pm 0.24	5.84 \pm 4.5	NS	5.20 \pm 0.27	5.38 \pm 0.51	3.00 \pm 7.7	NS
Total:HDL-C	4.61 \pm 0.30	4.66 \pm 0.44	0.80 \pm 6.9	NS	4.19 \pm 0.25	4.71 \pm 0.74	13.0 \pm 14.7	NS
TG (mmol/L)	2.28 \pm 0.28	2.16 \pm 0.42	-8.29 \pm 11.5	NS	2.01 \pm 0.22	2.30 \pm 0.48	18.4 \pm 18.3	NS
Resistance Only								
HDL (mmol/L)	1.10 \pm 0.05	1.04 \pm 0.05	-5.69 \pm 3.5	NS	1.22 \pm 0.04*	1.18 \pm 0.04	-4.64 \pm 3.7	NS
LDL (mmol/L)	2.75 \pm 0.12	2.63 \pm 0.15	-3.97 \pm 4.5	NS	2.85 \pm 0.20	2.89 \pm 0.26	0.99 \pm 6.4	NS
Total-C (mmol/L)	4.80 \pm 0.16	4.58 \pm 0.23	-7.00 \pm 3.8	NS	5.05 \pm 0.25	5.12 \pm 0.28	-0.35 \pm 3.2	NS
Total:HDL-C	4.44 \pm 0.22	4.52 \pm 0.28	2.20 \pm 4.1	NS	4.07 \pm 0.31	4.36 \pm 0.37	7.37 \pm 4.6	NS
TG (mmol/L)	2.03 \pm 0.22	1.92 \pm 0.26	-1.47 \pm 9.2	NS	2.27 \pm 0.34	2.45 \pm 0.39	9.55 \pm 4.3	NS
Combination (A+R)								
HDL (mmol/L)	1.22 \pm 0.04	1.18 \pm 0.04	-2.65 \pm 2.7	NS	1.25 \pm 0.10	1.24 \pm 0.09	1.23 \pm 3.3	NS
LDL (mmol/L)	2.95 \pm 0.16	2.82 \pm 0.18	-2.64 \pm 5.4	NS	3.11 \pm 0.23	3.10 \pm 0.18	2.53 \pm 6.0	NS
Total-C (mmol/L)	5.09 \pm 0.17	4.71 \pm 0.19	-10.0 \pm 4.5	NS	5.28 \pm 0.30	5.10 \pm 0.20	3.74 \pm 4.6	NS
Total:HDL-C	4.23 \pm 0.20	4.07 \pm 0.25	-2.22 \pm 5.2	NS	4.50 \pm 0.38	4.33 \pm 0.34	-1.83 \pm 4.8	NS
TG (mmol/L)	2.04 \pm 0.20	1.55 \pm 0.18	-19.3 \pm 7.5	0.044	2.25 \pm 0.48	1.76 \pm 0.31	-13.2 \pm 7.9	NS
Control								
HDL (mmol/L)	1.17 \pm 0.06	1.14 \pm 0.08	-3.85 \pm 4.0	NS	1.24 \pm 0.05	1.18 \pm 0.05	-3.86 \pm 3.6	NS
LDL (mmol/L)	2.83 \pm 0.20	2.94 \pm 0.21	6.07 \pm 4.2	NS	2.78 \pm 0.32	2.85 \pm 0.29	12.6 \pm 10.9	NS
Total-C (mmol/L)	5.02 \pm 0.26	5.18 \pm 0.23	-3.21 \pm 2.4	NS	5.10 \pm 0.30	5.12 \pm 0.34	1.26 \pm 3.6	NS
Total:HDL-C	4.36 \pm 0.24	4.96 \pm 0.48	13.2 \pm 7.7	0.044	4.22 \pm 0.28	4.42 \pm 0.31	5.62 \pm 4.7	NS
TG (mmol/L)	2.21 \pm 0.31	2.39 \pm 0.27	16.6 \pm 12.0	NS	2.35 \pm 0.26	2.86 \pm 0.52	19.3 \pm 15.4	NS

Table 3.26 Baseline, 6 month, absolute change and percent change of HbA_{1c} for 115 participants divided into 4 randomized groups. Data is presented as means \pm SE. *,** P<0.05 and 0.01 between men and women of the same group.

Group	Baseline HbA_{1c} (%)	6 Month HbA_{1c} (%)	Absolute Change	Percent Change	P value (0-6m)
Aerobic Only					
Men	7.74 \pm 0.24	6.94 \pm 0.23	-.80 \pm 0.25	-9.55 \pm 3.12	0.001
Women	7.26 \pm 0.17	6.85 \pm 0.22	-.42 \pm 0.23	-5.46 \pm 3.27	NS
Resistance Only					
Men	7.55 \pm 0.18	7.09 \pm 0.20	-0.46 \pm 0.19	-5.72 \pm 2.47	0.051
Women	7.85 \pm 0.35	8.16 \pm 0.40**	0.32 \pm 0.16*	4.05 \pm 2.15*	NS
Combination					
Men	7.84 \pm 0.28	6.62 \pm 0.20	-1.22 \pm 0.25	-14.6 \pm 2.53	0.000
Women	7.62 \pm 0.2	7.00 \pm 0.21	-0.62 \pm 0.28	-7.73 \pm 3.40	0.028
Control					
Men	7.64 \pm 0.21	7.64 \pm 0.24	0.00 \pm 0.30	.91 \pm 3.74	NS
Women	7.88 \pm 0.28	7.92 \pm 0.34	0.046 \pm 0.27	.93 \pm 3.16	NS

Table 3.28 Baseline, 6 month and relative change in HOMA values for aerobic (16 M, 11 W), resistance (17 M, 10 W), combination (17 M, 12 W) and control (16 M, 13 W) groups following 6 months of intervention. Data is presented as means \pm SE. *, **, *** P<0.05, 0.01 and 0.001 between men and women of the same group.

Group	Baseline HOMA (%)	6 Month HOMA (%)	Percent Change	P value (0-6m)
Aerobic Only				
Men	7.13 \pm 1.1	5.68 \pm 0.92	-12.92 \pm 11.3	0.073
Women	10.16 \pm 2.4	6.84 \pm 1.31	-20.04 \pm 13.7	0.001
Resistance Only				
Men	6.89 \pm 1.09	5.68 \pm 0.96	-7.39 \pm 15.4	NS
Women	6.93 \pm 1.57	6.25 \pm 1.31	0.27 \pm 10.7	NS
Combination				
Men	4.87 \pm 0.48	4.20 \pm 0.77	-10.87 \pm 12.5	NS
Women	6.79 \pm 1.23	5.09 \pm 1.01	-8.62 \pm 19.5	0.068
Control				
Men	6.96 \pm 0.83	6.22 \pm 0.94	-10.14 \pm 7.2	NS
Women	5.47 \pm 0.98	4.64 \pm 0.79	-7.70 \pm 9.4	NS

Table 3.30 Baseline, 6 month and relative changes in dietary intake in terms of total kcal, contribution (%) of carbohydrate (CHO), protein, and fat to total caloric intake. Nutritional data was available for 111 participants. Missing data was as follows: 2 AR men, 1 A woman, and 1 AR woman. Data presented as means \pm SE. *, **, *** P<0.05, 0.01, 0.001 respectively between men and women of the same intervention group.

Variable	Men			Women				
	Base	6 Month	Relative (%) Change	P (0-6m)	Base	6 Month	Relative (%) Change	P (0-6m)
Aerobic Only								
Total kcal	2080 \pm 82	1844 \pm 103	-9.75 \pm 5.7	0.038	1723 \pm 105	1795 \pm 140	5.48 \pm 6.9	NS
% CHO	44.8 \pm 1.8	50.3 \pm 1.9	15.2 \pm 6.3	0.007	44.8 \pm 2.3	50.3 \pm 1.4	15.2 \pm 3.0	NS
% Protein	20.2 \pm 0.86	20.8 \pm 1.5	4.0 \pm 7.0	NS	19.1 \pm 0.68	18.3 \pm 0.85	-4.05 \pm 4.2	NS
% Fat	33.3 \pm 1.7	29.3 \pm 2.1	-8.0 \pm 7.5	NS	31.5 \pm 2.1	32.0 \pm 1.3	4.24 \pm 5.1	NS
Resistance Only								
Total kcal	2386 \pm 110	2044 \pm 114	-11.6 \pm 5.8	0.003	1845 \pm 104*	1448 \pm 76**	-20.3 \pm 3.6	0.005
% CHO	46.7 \pm 2.5	48.6 \pm 1.6	7.14 \pm 5.2	NS	49.3 \pm 3.1	51.5 \pm 2.4	6.27 \pm 4.4	NS
% Protein	19.3 \pm 0.91	20.9 \pm 0.90	9.98 \pm 5.0	NS	20.0 \pm 1.26	19.6 \pm 0.92	-0.43 \pm 3.8	NS
% Fat	32.9 \pm 1.9	30.3 \pm 1.5	-2.67 \pm 7.3	NS	31.6 \pm 2.5	32.4 \pm 5.0	0.58 \pm 8.1	NS
Combination (A+R)								
Total kcal	2030 \pm 134	1916 \pm 116	-4.68 \pm 3.5	NS	2111 \pm 308	1948 \pm 323	-7.61 \pm 5.4	NS
% CHO	46.4 \pm 2.1	47.7 \pm 2.1	4.32 \pm 4.7	NS	49.8 \pm 2.6	48.9 \pm 1.7	0.42 \pm 5.3	NS
% Protein	17.5 \pm 1.6	20.0 \pm 1.2	48.1 \pm 38.1	0.038	16.2 \pm 0.83	18.5 \pm 1.1	14.1 \pm 5.2	NS
% Fat	33.8 \pm 2.0	32.6 \pm 1.77	1.30 \pm 8.0	NS	33.1 \pm 2.5	31.4 \pm 2.3	-1.88 \pm 8.6	NS
Control								
Total kcal	2511 \pm 149	2182 \pm 106	-8.75 \pm 6.0	0.004	1808 \pm 102**	1575 \pm 107**	-12.8 \pm 3.4	NS
% CHO	48.1 \pm 2.5	47.7 \pm 2.1	0.88 \pm 4.0	NS	48.3 \pm 1.4	53.3 \pm 1.3	11.3 \pm 3.6	0.027
% Protein	19.1 \pm 0.72	18.3 \pm 1.1	-4.05 \pm 5.4	NS	18.1 \pm 0.92	19.3 \pm 0.83	9.8 \pm 7.3	NS
% Fat	31.5 \pm 2.2	32.0 \pm 1.7	4.24 \pm 9.1	NS	34.1 \pm 1.3	29.7 \pm 1.3	-11.4 \pm 5.2	NS

Table 3.31 Number of women in the four different treatment groups according to menopausal status as determined from responses of the Menopausal Questionnaire (see Appendix). Status was determined as pre-menopausal, post-menopausal, or undetermined (due to missing or questionable data). Use of hormonal replacement therapy (HRT) was also indicated.

Group	N	Pre-menopausal (n)	Post- Menopausal (n)	Undetermined (n)	HRT (n)
Aerobic	11	1	4	6	0
Resistance	11	2	8	0	0
Combination	12	2	4	6	0
Control	13	0	10	3	0

Figure Legends

Figure 3.4 Compliance data presented as a percentage calculated as sessions attended out of sessions prescribed for exercising men (N=51) versus exercising women (N=34) Data is presented as means \pm SE. * $P < 0.05$ between men and women.

Figure 3.5 Compliance data presented as a percentage calculated as sessions attended out of sessions prescribed for aerobic (17 M, 11 W), resistance (17 M, 11 W), combination (17 M, 12 W) participants following 6 months of intervention. Data is presented as means \pm SE. * $P < 0.05$ between men and women of the same group. Men are depicted by black bars and women are depicted by white bars.

Figure 3.9 Percent changes in visceral adipose tissue (VAT) area for aerobic (16 M, 11 W), resistance (16 M, 10 W), combination (17 M, 10 W) and control (17 M, 11 W) men and women following 6 months of intervention. Data is presented as means \pm SE. ** $P < 0.01$ from baseline. Men are depicted by black bars and women are depicted by white bars.

Figure 3.11 Relative changes in abdominal SAT after 6 months for aerobic (16 M, 11 W), resistance (16 M, 10 W), combination (17 M, 10 W) and control (17 M, 11 W) men and women following 6 months of intervention. Data is presented as means \pm SE. * $P < 0.05$ from baseline. Men are depicted by black bars and women are depicted by white bars.

Figure 3.13 Relative (%) changes in mid-thigh muscle CSA following the 6-month intervention period in 103 participants. Data is presented as means. *, **, *** $P < 0.05$, 0.01 and 0.001 respectively from baseline. † $P < 0.05$ between men and women of the same group. Data was collected for 13 M and 11 W in **A**, 14 M and 10 W in **R**, 17 M and 10 W in **AR**, and 17 M and 10 W in **C**. Men are depicted by black bars and women are depicted by white bars.

Figure 3.15 Relative (%) changes in predicted 1-RM strength for bench press for aerobic (14 M, 8 W), resistance (15 M, 7 W), combination (14 M, 8 W) and control (16 M, 10 W) following 6 months of intervention. Data is presented as means \pm SE. *, **, *** $P < 0.05$, 0.01 and 0.001, respectively from baseline. † $P < 0.001$ between men and women of the same group. Men are depicted by black bars and women are depicted by white bars.

Figure 3.16 Relative (%) changes in predicted 1-RM strength for seated row for aerobic (14 M, 10 W), resistance (12 M, 9 W), combination (13 M, 10 W) and control (14 M, 13 W) following 6 months of intervention. Data is presented as means \pm SE. *, **, *** $P < 0.05$, 0.01 and 0.001, respectively from baseline to 6 months time. † $P < 0.001$ between men and women of the same group. Men are depicted by black bars and women are depicted by white bars.

Figure 3.17 Relative (%) changes in predicted 1-RM strength for leg press for aerobic (16 M, 11 W), resistance (16 M, 11 W), combination (15 M, 10 W) and control (15 M, 13 W) following 6 months of intervention. Data is presented as means \pm SE. *, **, ***

$P < 0.05$, 0.01 and 0.001, respectively between men and women of the same group. Men are depicted by black bars and women are depicted by white bars.

Figure 3.19 Relative changes in VO_{2peak} for aerobic (17 M, 11 W), resistance (17 M, 11 W), combination (17 M, 12 W) and control (17 M, 13 W) following 6 months of intervention. Data is presented as means \pm SE. *, **, *** $P < 0.05$, 0.01 and 0.001 from baseline. Men are depicted by black bars and women are depicted by white bars.

Figure 3.21 Relative (%) changes in HDL cholesterol for 115 participants in aerobic, resistance, combination, and control men over the 6 month intervention period. Data is presented as means. None of the changes in HDL cholesterol were significant. Men are depicted by black bars and women are depicted by white bars.

Figure 3.22 Relative (%) changes in LDL cholesterol for 110 participants in aerobic, resistance, combination, and control groups over the 6 month intervention period. There were no values for LDL cholesterol for one man in each of A, R and C groups and one woman in each R and AR groups, because the absolute values for these individuals were too high. Data is presented as means. There were no significant changes in LDL-cholesterol. Men are depicted by black bars and women are depicted by white bars.

Figure 3.23 Relative changes in total cholesterol for 115 participants in aerobic, resistance, combination, and control groups over the 6 month intervention period. Data is

presented as means. There were no significant changes in total cholesterol. Men are depicted by black bars and women are depicted by white bars.

Figure 3.24 Relative changes in the ratio of total cholesterol to HDL-C for 115 participants in aerobic, resistance, combination, and control groups over the 6 month intervention period. Data is presented as means. * $P < 0.05$ from baseline. Men are depicted by black bars and women are depicted by white bars.

Figure 3.25 Relative (%) changes in TGs of 115 participants in aerobic, resistance, combination, and control men over the 6 month intervention period. Data is presented as means. * $P < 0.05$ from baseline. Men are depicted by black bars and women are depicted by white bars.

Figure 3.27 Relative (%) changes in HbA_{1c} for aerobic (17 M, 11 W), resistance (17 M, 11 W), combination (17 M, 12 W) and control (17 M, 13 W) following 6 months of intervention. Data is presented as means \pm SE. *, **, *** $P < 0.05, 0.01$ and 0.001 , from baseline and † $P < 0.05$ between men and women of the same group. Men are depicted by black bars and women are depicted by white bars.

Figure 3.29 Relative (%) changes in HOMA for aerobic (16 M, 11 W), resistance (17 M, 10 W), combination (17 M, 12 W) and control (16 M, 13 W) following 6 months of intervention. Data is presented as means \pm SE. *, **, *** $P < 0.05, 0.01$ and 0.001 from

baseline to 6 month respectively. Men are depicted by black bars and women are depicted by white bars.

FIGURES

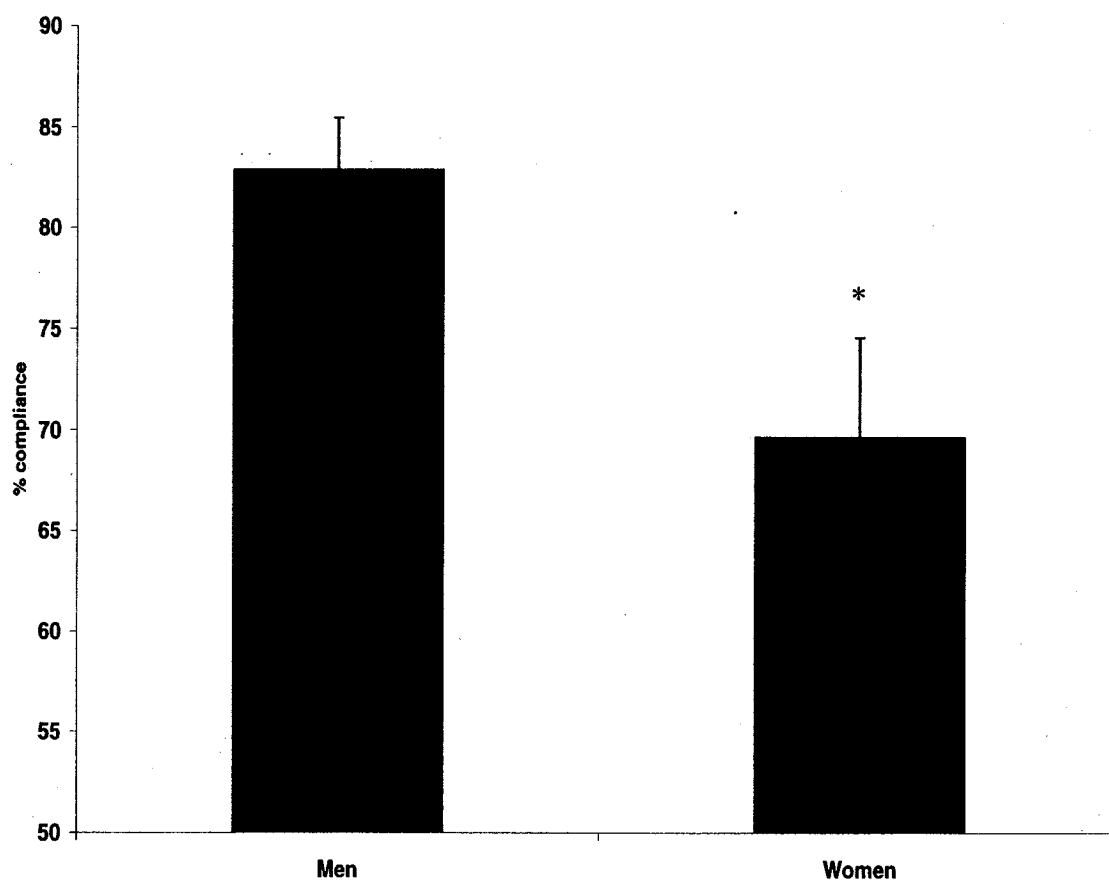


Figure 3.4 Compliance data presented as a percentage calculated as sessions attended out of sessions prescribed for exercising men (N=51) versus exercising women (N=34) Data is presented as means \pm SE. * $P < 0.05$ between men and women.

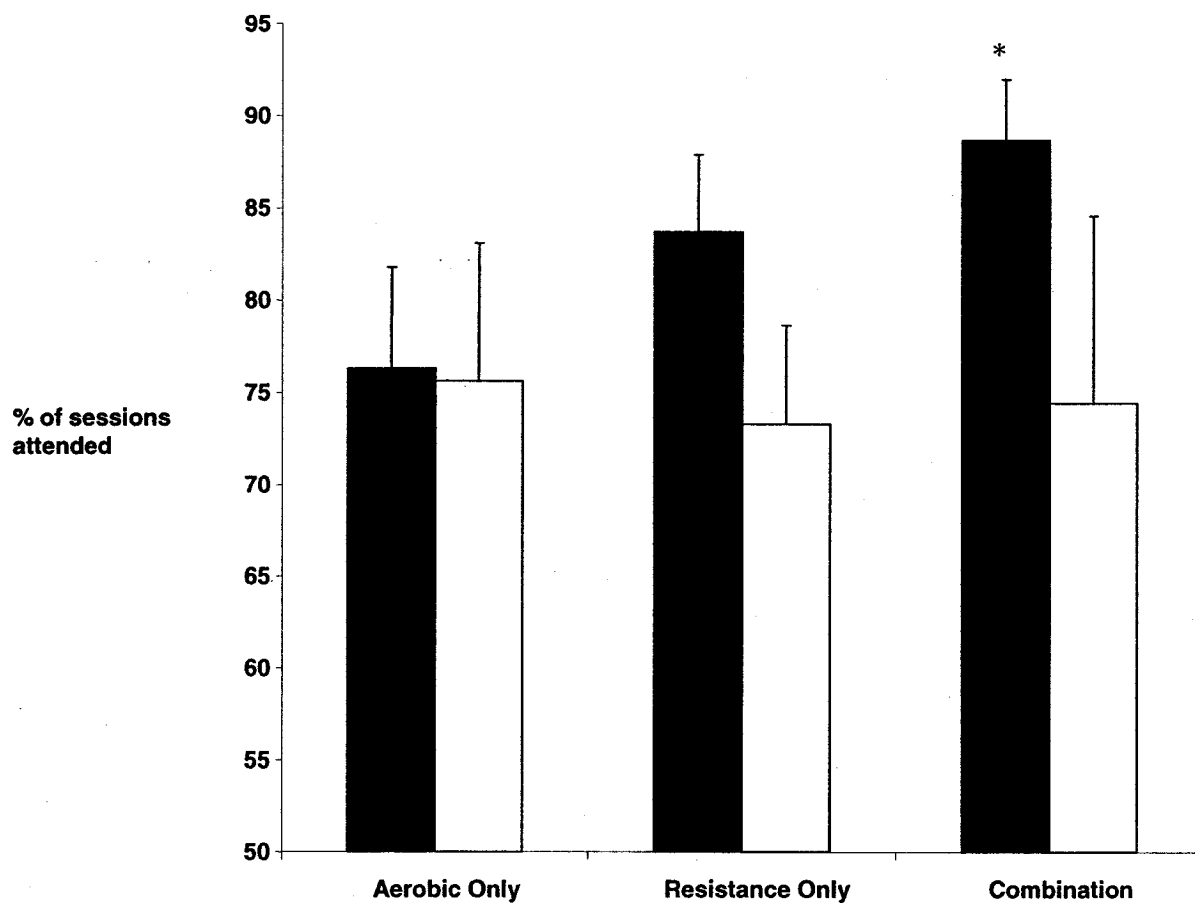


Figure 3.5 Compliance data presented as a percentage calculated as sessions attended out of sessions prescribed for aerobic (17 M, 11 W), resistance (17 M, 11 W), combination (17 M, 12 W) participants following 6 months of intervention. Data is presented as means \pm SE. * $P < 0.05$ between men and women of the same group. Men are depicted by black bars and women are depicted by white bars.



Figure 3.9 Percent changes in visceral adipose tissue (VAT) area for aerobic (16 M, 11 W), resistance (16 M, 10 W), combination (17 M, 10 W) and control (17 M, 11 W) men and women following 6 months of intervention. Data is presented as means \pm SE.

** $P < 0.01$ from baseline. Men are depicted by black bars and women are depicted by white bars.

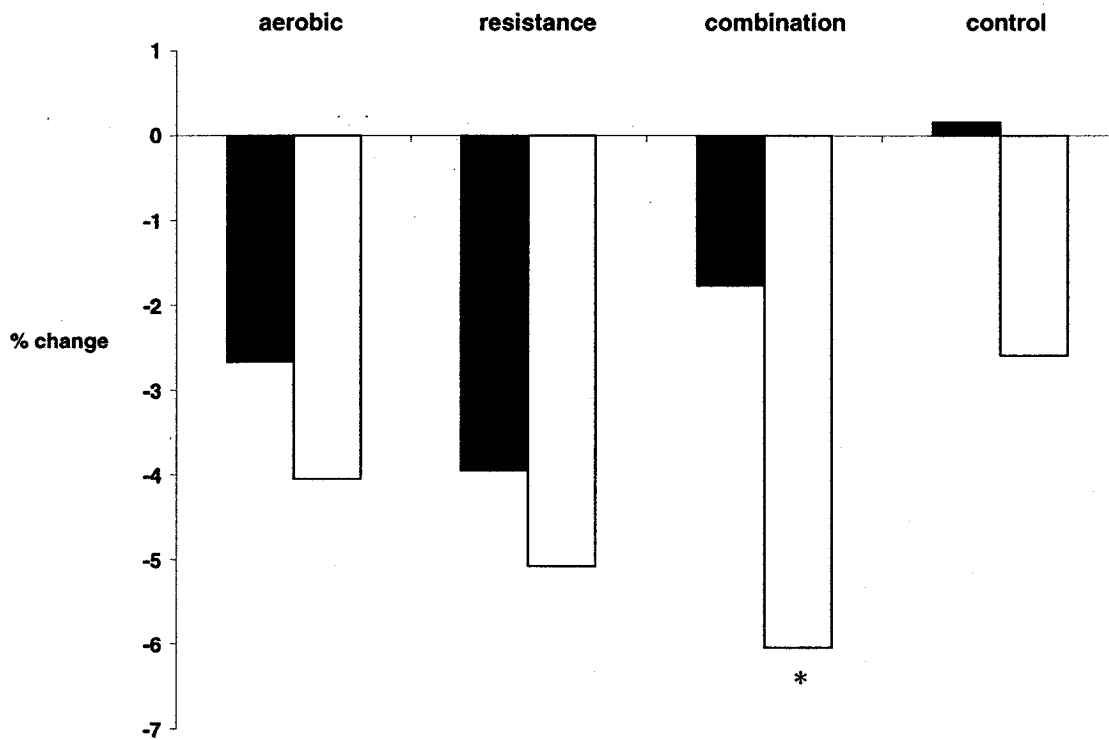


Figure 3.11 Relative changes in abdominal SAT after 6 months for aerobic (16 M, 11 W), resistance (16 M, 10 W), combination (17 M, 10 W) and control (17 M, 11 W) men and women following 6 months of intervention. Data is presented as means \pm SE.

* $P < 0.05$ from baseline. Men are depicted by black bars and women are depicted by white bars.

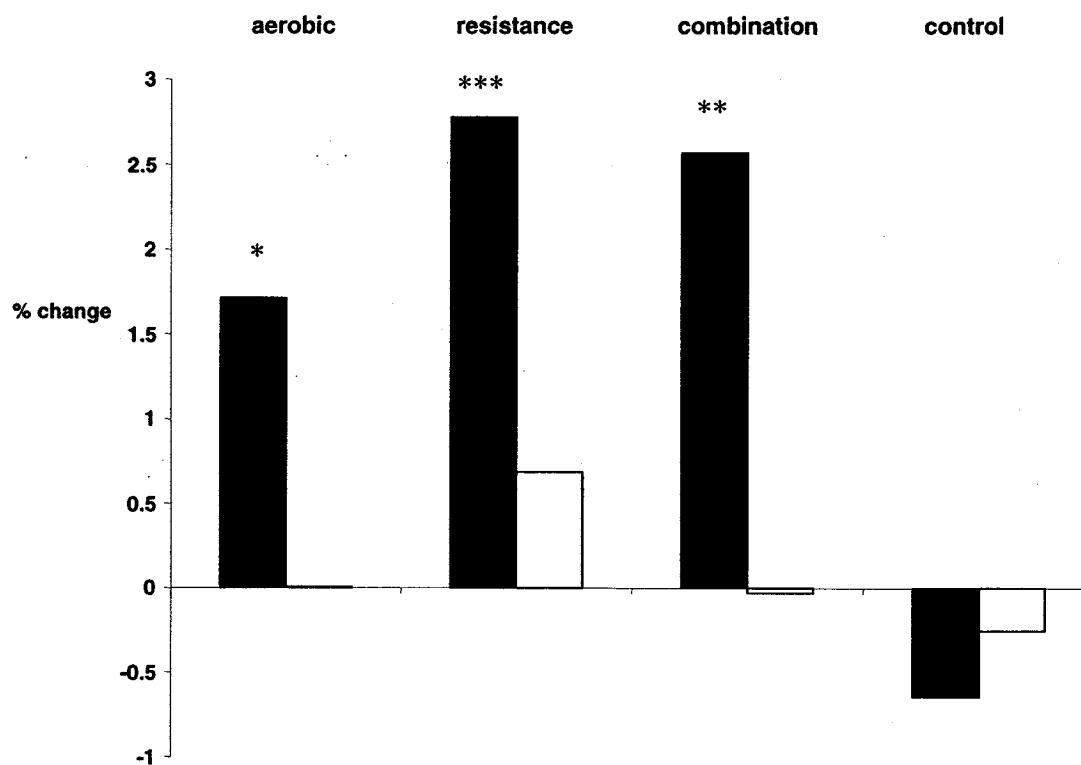


Figure 3.13 Relative (%) changes in mid-thigh muscle CSA following the 6-month intervention period in 103 participants. Data is presented as means. *, **, *** $P < 0.05$, 0.01 and 0.001 respectively from baseline. † $P < 0.05$ between men and women of the same group. Data was collected for 13 M and 11 W in **A**, 14 M and 10 W in **R**, 17 M and 10 W in **AR**, and 17 M and 10 W in **C**. Men are depicted by black bars and women are depicted by white bars.

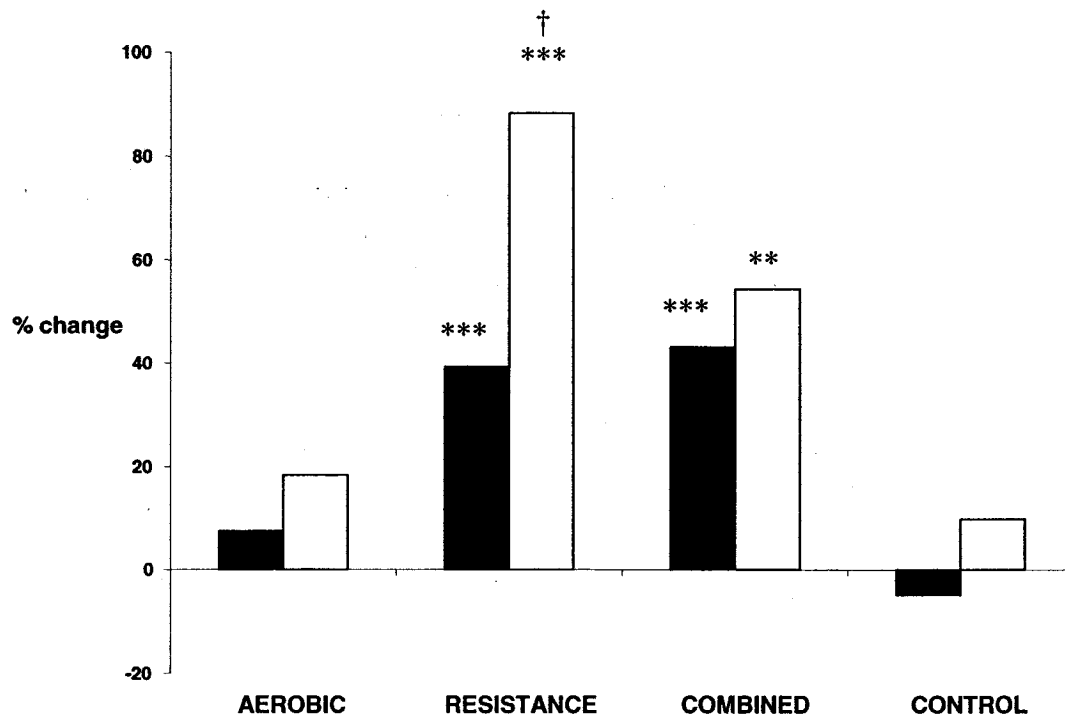


Figure 3.15 Relative (%) changes in predicted 1-RM strength for bench press for aerobic (14 M, 8 W), resistance (15 M, 7 W), combination (14 M, 8 W) and control (16 M, 10 W) following 6 months of intervention. Data is presented as means \pm SE. *, **, *** P<0.05, 0.01 and 0.001, respectively from baseline. †P<0.001 between men and women of the same group. Men are depicted by black bars and women are depicted by white bars.

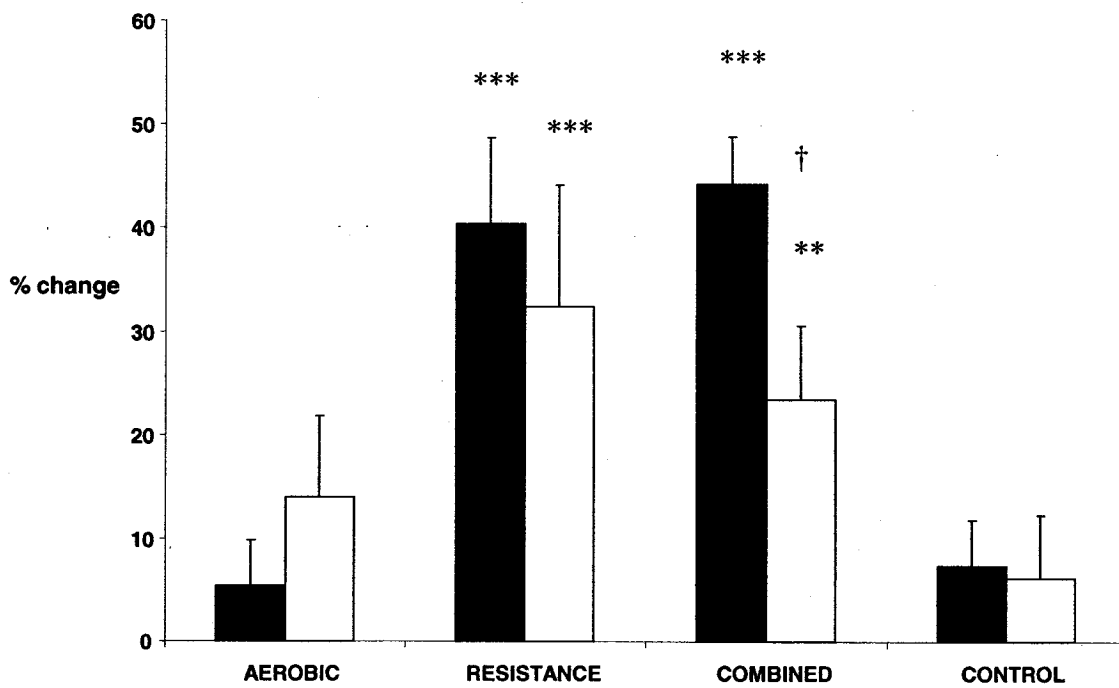


Figure 3.16 Relative (%) changes in predicted 1-RM strength for seated row for aerobic (14 M, 10 W), resistance (12 M, 9 W), combination (13 M, 10 W) and control (14 M, 13 W) following 6 months of intervention. Data is presented as means \pm SE. *, **, *** $P < 0.05$, 0.01 and 0.001, respectively from baseline to 6 months time. † $P < 0.001$ between men and women of the same group. Men are depicted by black bars and women are depicted by white bars.

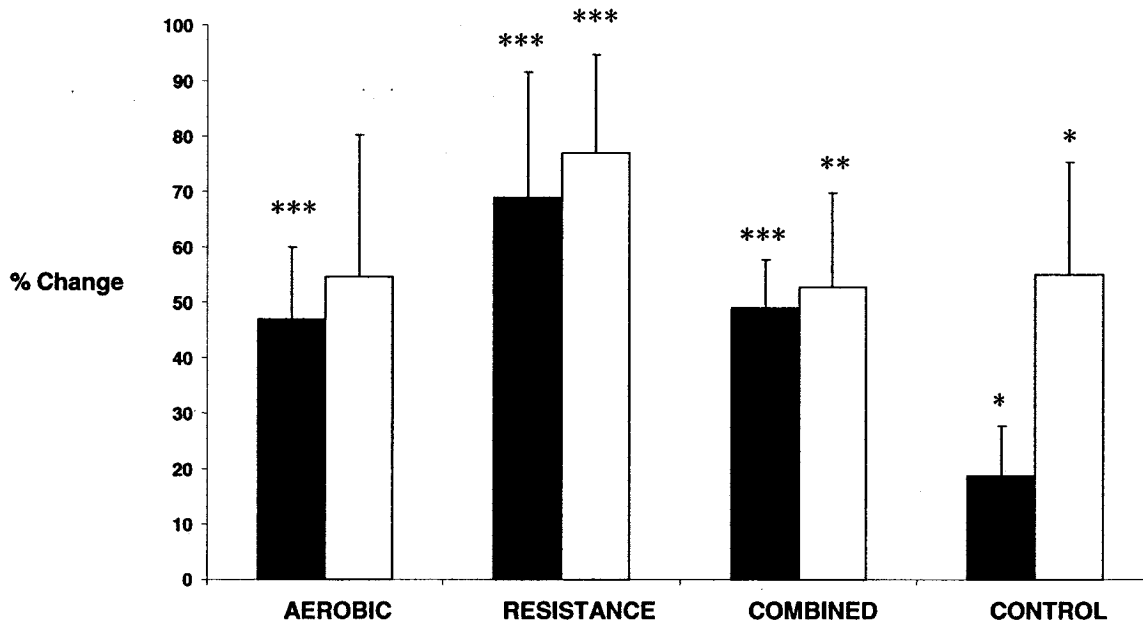


Figure 3.17 Relative (%) changes in predicted 1-RM strength for leg press for aerobic (16 M, 11 W), resistance (16 M, 11 W), combination (15 M, 10 W) and control (15 M, 13 W) following 6 months of intervention. Data is presented as means \pm SE. *, **, *** $P < 0.05$, 0.01 and 0.001, respectively between men and women of the same group. Men are depicted by black bars and women are depicted by white bars.

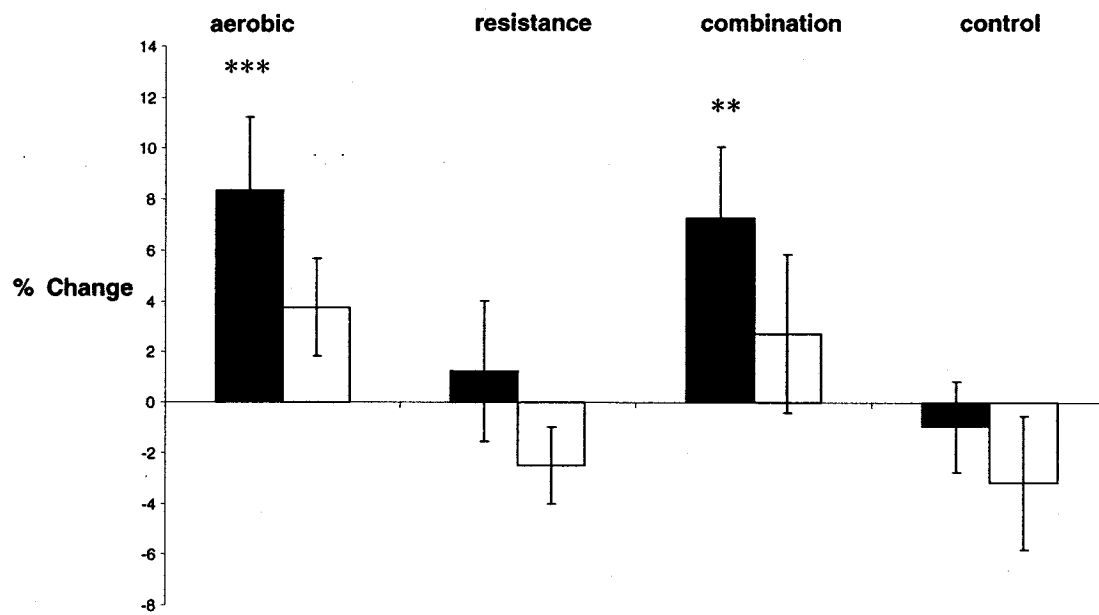


Figure 3.19 Relative changes in VO_{2peak} for aerobic (17 M, 11 W), resistance (17 M, 11 W), combination (17 M, 12 W) and control (17 M, 13 W) following 6 months of intervention. Data is presented as means \pm SE. *, **, *** $P < 0.05$, 0.01 and 0.001 from baseline. Men are depicted by black bars and women are depicted by white bars.

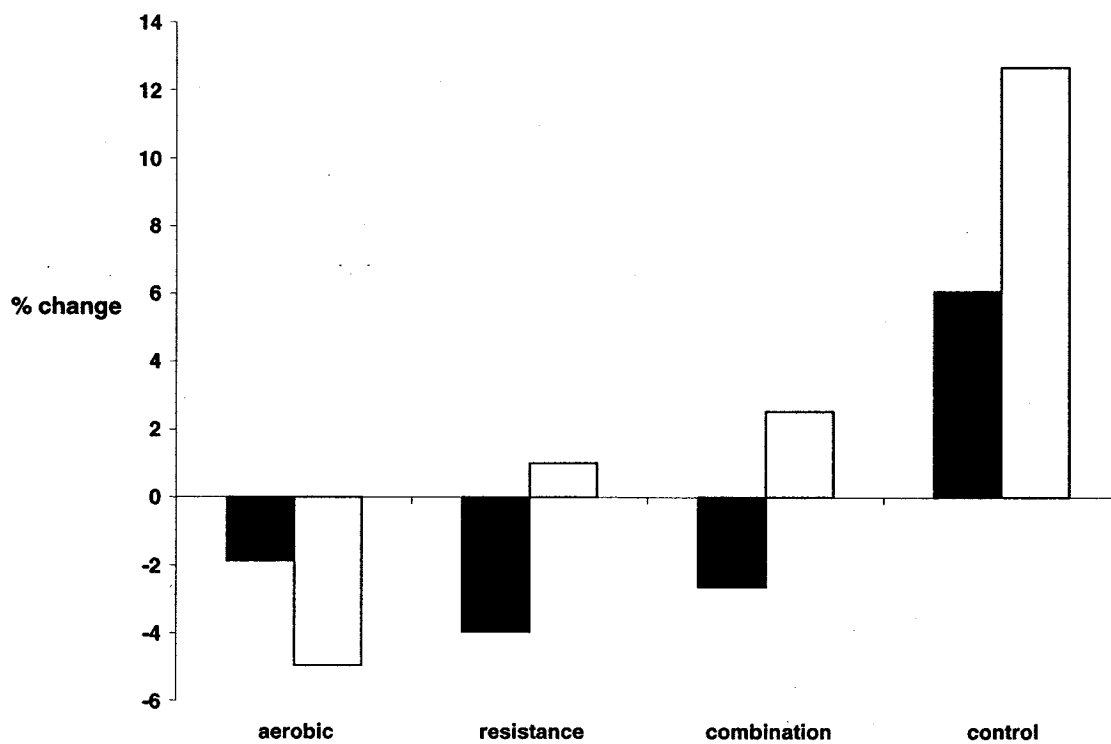


Figure 3.21 Relative (%) changes in HDL cholesterol for 115 participants in aerobic, resistance, combination, and control men over the 6 month intervention period. Data is presented as means. None of the changes in HDL cholesterol were significant. Men are depicted by black bars and women are depicted by white bars.

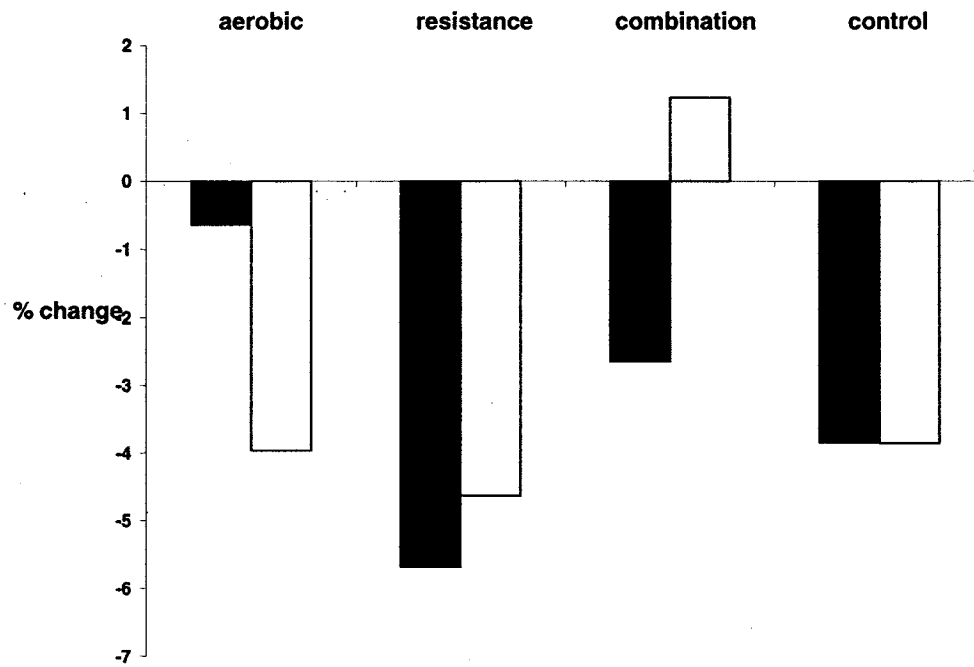


Figure 3.22 Relative (%) changes in LDL cholesterol for 110 participants in aerobic, resistance, combination, and control groups over the 6 month intervention period. There were no values for LDL cholesterol for one man in each of **A**, **R** and **C** groups and one woman in each **R** and **AR** groups, because the absolute values for these individuals were too high. Data is presented as means. There were no significant changes in LDL-cholesterol. Men are depicted by black bars and women are depicted by white bars.

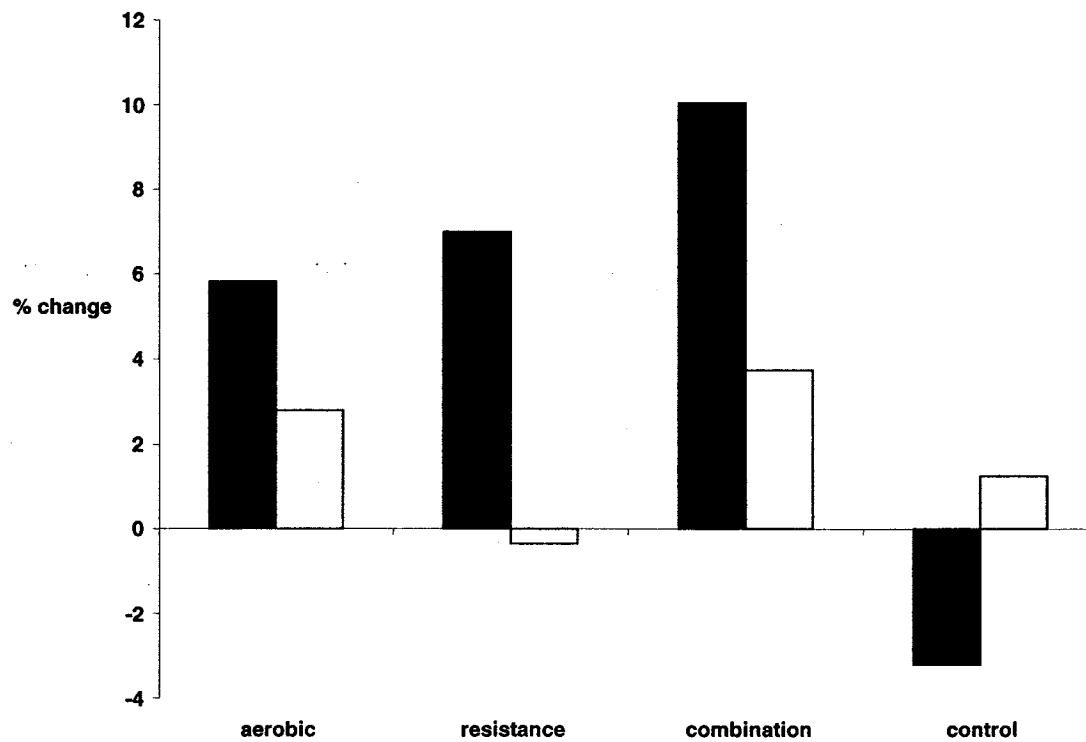


Figure 3.23 Relative changes in total cholesterol for 115 participants in aerobic, resistance, combination, and control groups over the 6 month intervention period. Data is presented as means. There were no significant changes in total cholesterol. Men are depicted by black bars and women are depicted by white bars.

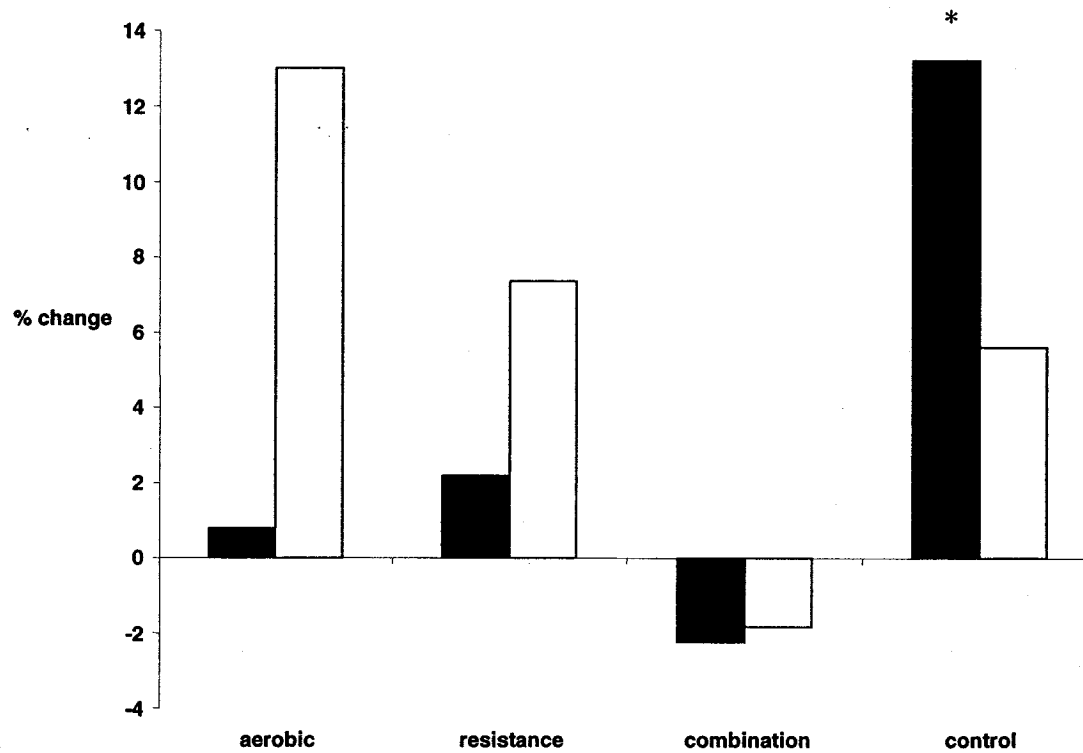


Figure 3.24 Relative changes in the ratio of total cholesterol to HDL-C for 115 participants in aerobic, resistance, combination, and control groups over the 6 month intervention period. Data is presented as means. * $P < 0.05$ from baseline. Men are depicted by black bars and women are depicted by white bars.

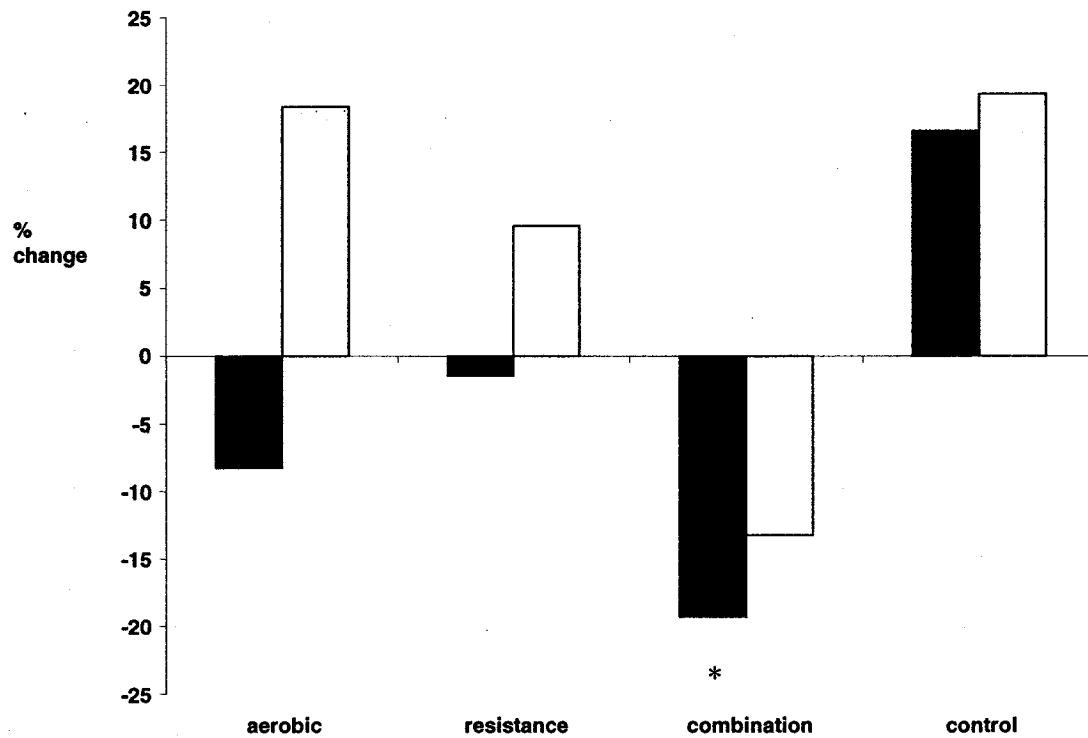


Figure 3.25 Relative (%) changes in TGs of 115 participants in aerobic, resistance, combination, and control men over the 6 month intervention period. Data is presented as means. * $P < 0.05$ from baseline. Men are depicted by black bars and women are depicted by white bars.

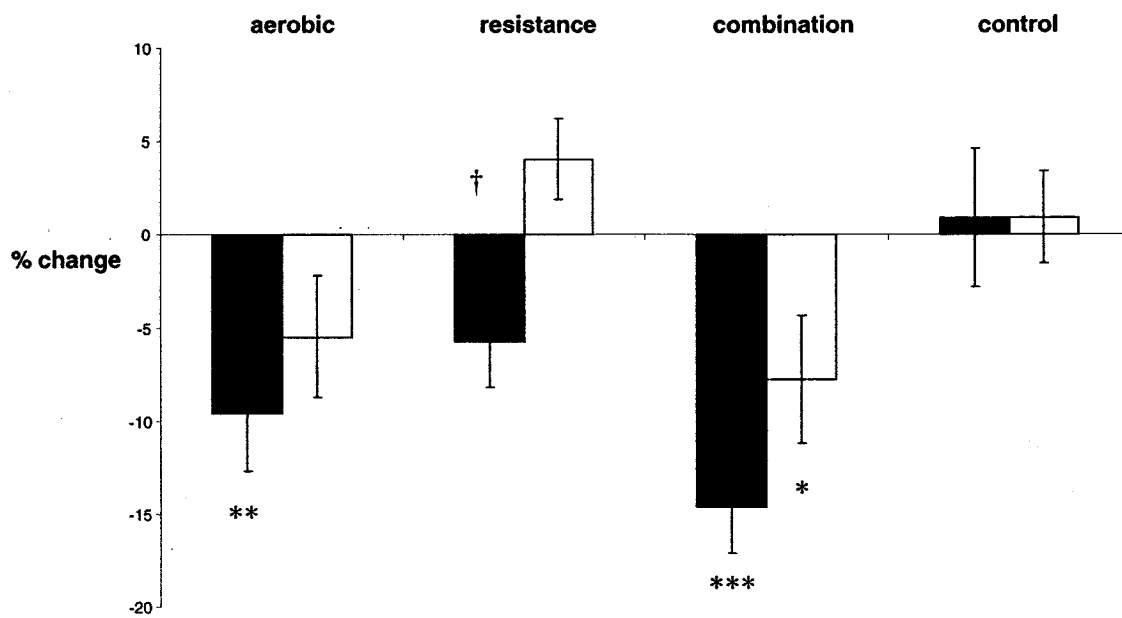


Figure 3.27 Relative (%) changes in HbA_{1c} for aerobic (17 M, 11 W), resistance (17 M, 11 W), combination (17 M, 12 W) and control (17 M, 13 W) following 6 months of intervention. Data is presented as means \pm SE. *, **, *** P<0.05, 0.01 and 0.001, from baseline and † P<0.05 between men and women of the same group. Men are depicted by black bars and women are depicted by white bars.

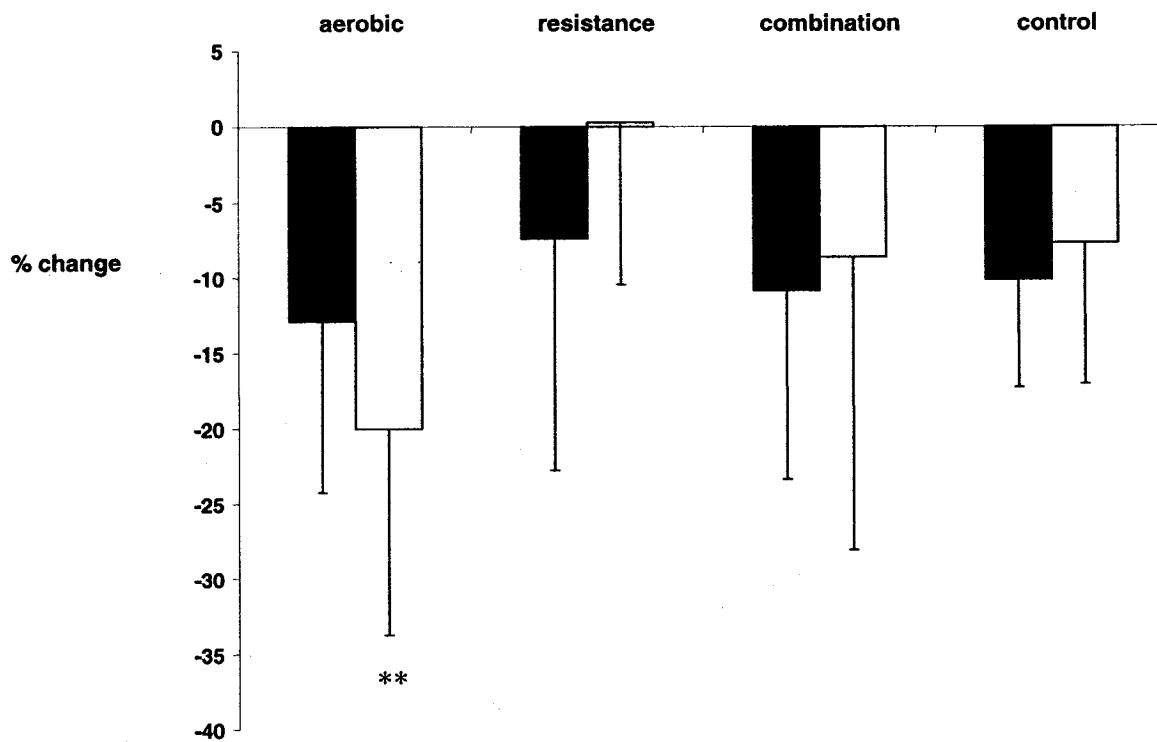


Figure 3.29 Relative (%) changes in HOMA for aerobic (16 M, 11 W), resistance (17 M, 10 W), combination (17 M, 12 W) and control (16 M, 13 W) following 6 months of intervention. Data is presented as means \pm SE. *, **, *** $P < 0.05$, 0.01 and 0.001 from baseline to 6 month respectively. Men are depicted by black bars and women are depicted by white bar.

APPENDIX

Menopausal Questionnaire

Name: _____

Date: _____

When was the first day of your last period? (exact date) _____

What is the average length of your menstruation (number of days)? _____

What is the length of a typical cycle? (From first day of menstruating until the next first day of menstruating-eg. 28 days) _____

Has your cycle been regular over the past 12 months? (circle) Yes No

Are you currently taking oral contraceptives? _____

What kind? _____

How long have you been taking this particular kind? _____

How long have you been taking oral contraceptives? _____

If you are currently not taking oral contraceptives, have you taken them in the past?

Yes No

If yes, when did you last take them and for how long? _____

If you have not been menstruating recently, when was your last menses? (be as specific as you can) _____

Are you currently undergoing hormone replacement therapy? Yes No

If yes, what are you taking and how long have you been taking them? _____