Influence of Supervised Training and a Hypocaloric Macronutrient Scheduled Diet vs a Hypocaloric Macronutrient Scheduled Diet Alone on Energy Regulating Hormones in Overweight and Obese Men Ages 35-55: A Randomized Control Trial

by

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ABSTRACT

Context: Adiponectin is a hormone involved in energy metabolism. However, its response to weight loss achieved through Exercise + Diet as compared to Diet Alone, is not fully understood. In addition, the impact of Exercise and Diet on adiponectin related hormones has not been thoroughly investigated in the specific cohort of men ages 35-55 years of age who are overweight and obese.

Objectives: To determine; (1) the influence of 12 weeks of supervised resistance training combined with a hypocaloric macronutrient scheduled diet (Exercise + Diet) on fasting adiponectin in overweight and obese men, (2) the influence of the above modalities on TNF-α, leptin, ghrelin, and testosterone, and (3) the relationship of regional adiposity and body fat topography with these hormones.

Design, Setting, Participants: The study was a randomized control trial of fifty-one healthy inactive males (35-55 years old), with a BMI of 25-35 kg/m^2, in St. John's NL between August 2011 and August 2014.

Intervention: Subjects received either a 12 weeks of Exercise + Diet or a Diet Alone weight loss intervention.

Main Outcome Measure: Biochemical analysis to determine energy regulating hormones including adiponectin, TNF-α, leptin, ghrelin and total testosterone, as well as metabolic risk factors, anthropometrics, and physical fitness measurements were collected at baseline and following the interventions.

Results: There was no difference in adiponectin or weight loss (~4.5%) between interventions however, when controlling for regional adiposity, adiponectin decreased in the Exercise + Diet and increased in the Diet Alone group. Leptin changed with body weight loss ($p<0.001$), with no difference between groups. TNF-α, testosterone, and ghrelin showed no significant changes with either intervention. When controlling for lean body mass, ghrelin showed a decrease in the Diet Alone group ($p=0.05$). Lastly, visceral fat was positively associated with adiponectin ($p<0.04$), leptin ($p<0.003$) and ghrelin ($p<0.01$), while exercise increased lean body mass ($p<0.001$) and decreased triglycerides ($p<0.007$), and diastolic blood pressure.

Conclusions: Exercise + Diet improved body composition, cardiometabolic risk factors and fitness. Irrespective of these health improvements, this investigation could not determine whether Exercise + Diet induced weight loss provided additional benefit from adiponectin over diet induced weight loss alone.

When controlling for body composition, adiponectin did increase through Diet Alone, but it decreased in the Exercise + Diet induced weight loss. It is possible that this altered response with exercise may be due to the insulin sensitizing effects of physical activity, however further research is needed to clearly identify this phenomenon. The decrease in appetite suppressing hormone leptin, coupled with the increase in appetite regulating hormone ghrelin in the Exercise + Diet group indicates that exercise may increase the stimulus for food consumption. Lastly, subcutaneous adipose tissue is not correlated to energy regulating hormone concentration in this population. The current Exercise + Diet program provides a clinical prescription for effective weight loss and health improvements.

However, more substantial weight loss, or adjustments to insulin sensitivity, may be required to elicit a significant adjustment in adiponectin concentration. Consequently, further investigations of the influences of resistance training in combination with diet on adiponectin are necessary.

Trial Registration: This study was approved by the Health Research Ethics Authority (HREA), Memorial University of Newfoundland and Labrador (#11.327).

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List of Symbols, Nomenclature or Abbreviations

ACSM – American College of Sports Medicine

ANCOVA – Analysis of Covariance

ANOVA – Analysis of Variance

β – Beta Cell Function

BMI – Body Mass Index

CDC – Center for Disease Control

CDV – Cardiovascular Disease

CSEP – Canadian Society of Exercise Physiology

CT – Computed Tomography

DXA – Dual-Energy X-Ray Absorptiometry

GI – Glycemic Index

HDL – High Density Lipoprotein

HF – Heart Failure

HOMA – Homeostatic Model Assessment

HMW- High Molecular Weight Adiponectin

IR – Insulin Resistance

LDL – Low Density Lipoprotein

LMW – Low Molecular Weight Adiponectin

MHO – Metabolically Healthy Obese

MMW – Medium Molecular Weight Adiponectin

MUO – Metabolically Unhealthy Obese

NL – Newfoundland and Labrador

NSCA – National Strength and Conditioning Association

RR – Relative Risk

SD – Standard Deviation

TNF - α – Tumor Necrosis Factor Alpha

Trig – Trigylcerides

VLCD – Very Low Calorie Diet

WHO – World Health Organization

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Introduction

Obesity is a complex multifaceted condition consisting of environmental and physiological factors (P. Patel & Abate, 2013). It is defined as the abnormal or excessive accumulation of fat tissue which is the result of energy imbalance between calories consumed and calories expended (World Health Organization, 2015) Obesity status has been grouped as overweight (BMI 25.00–29.99), and obese (BMI ≥ 30-34.99), as recommended by the World Health Organization (WHO) (World Health Organization, 2015). Centralized obesity has been associated with metabolic disorders such as hypertension, diabetes mellitus, hypertriglyceridemia, hypertension and early mortality (Kaur, 2014). These disease states and processes of energy regulation are controlled by various hormones, including adipokines (hormones produced by adipose tissue) such as adiponectin, and TNF-α, as well as those responsible for energy intake such as leptin, ghrelin, and insulin, in addition to other hormones that promote muscle anabolism including the androgen testosterone.

Managing obesity has traditionally revolved around the achievement of weight loss. However, a growing understanding of the role of energy regulating hormones is providing important insights into the cause of and associated health risks related to obesity.

A growing understanding of the relationship between these hormones, weight loss and regional adiposity has emerged as a new aspect of obesity research due to the advent of

advanced adipose tissue imaging techniques (De Lorenzo et al., 2013). Of particular relevance to the current study is that obesity impacts populations differently, as middle aged men are more susceptible to obesity-related diseases then women (Yim, Heshka, Albu, Heymsfield & Gallagher, 2008). In addition, regional adiposity has sex specific differences, where the central fat patterning which is characteristic of men has a greater impact on the incidence of disease then the peripheral fat patterning of women (Despres, 2007; Gautier et al., 1998; Geer & Shen, 2009; Katsuki et al., 2003a; Machann et al., 2005; P. Patel & Abate, 2013; Smith et al., 2001; Taksali et al., 2008; Wajchenberg, Giannella-Neto, da Silva, & Santos, 2002; Yim, Heshka, Albu, Heymsfield, & Gallagher, 2008). Obesity is strongly associated with cardiometabolic diseases, however these disease states are more closely attributed to the dysregulation of energy regulating hormones than obesity itself (Blüher, 2014). Although obesity-related diseases account for 1 in 5 deaths per year in North America, obesity is one of the most preventable diseases (Raine et al., 2014). Therefore, studies focusing on the management of obesity must investigate metabolic disease associated clinical markers, including energy regulating hormones, along with weight loss to develop better understanding of obesity management interventions.

Current obesity interventions include pharmacology, bariatric surgery, exercise and diet weight management interventions.

The most popular and accessible of these interventions are diet and exercise (Miller, Koceja, & Hamilton, 1997). If adequate exercise is performed on a regular basis, physical activity can increase metabolism and reduce the risk of developing obesity and its co-morbidities, including protection from loss of lean body mass, improved cardiorespiratory fitness, and an increase in overall quality of life (Okay, Jackson, Marcinkiewicz, & Papino, 2009). There are various forms of exercise, ranging from cardiovascular to resistance training, and within each category there are varying levels of intensity, volume and duration (ACSM, 2014). Exercise in isolation has shown limited results with respect to weight loss, however has been shown to be more effective with respect to reducing body fat when when aerobic training is employed and when exercise training is supervised versus unsupervised (Conn, Hafdahl, Phillips, Ruppar, & Chase, 2014). A goal of this research was determine if high intensity resistance training designed to increase energy expenditure to a greater extent than traditional resistance training was sufficient to achieve the same impact as combined aerobic and resistance training at improving weight loss outcomes.

Similar to exercise, diet is also a broadly defined term some of which is more successful than others. A variety of approaches have been employed to successfully reduce body fat in a range of populations (Miller et al., 1997). Countless dietary protocols exist with some approaches restricting total calories, others restricting specific macronutrients and others which restrict both calories and macronutrients (Miller et al., 1997).

The literature suggests that the macronutrient content of meals as well as meal frequency are important aspects of diet (Astrup, 1999; Dansinger, Gleason, Griffith, Selker, &

Schaefer, 2005; Ebbeling et al., 2012; Foster et al., 2003; Lambert, Frank, & Evans, 2004; Mansoor, Vinknes, Veierod, & Retterstol, 2016; Rees et al., 2013; Sofi, Cesari, Abbate, Gensini, & Casini, 2008). Whether calories are consumed in the form of protein, carbohydrates or fats impacts an individual's satiety, energy metabolism, and body composition (Bowen, Noakes, Trenerry, & Clifton, 2006; Erdmann, Topsch, Lippl, Gussmann, & Schusdziarra, 2004; Niwano et al., 2009). Although diet alone may be effective for weight loss, it is not as effective as when it is combined with exercise, nor is it as effective at maintaining weight loss (Miller et al., 1997). Although these approaches have benefits, what is not clear is the most effective way to combine specific modes of diet and exercise for both weight loss and weight management. Investigations into supervised resistance training programs combined with a hypocaloric macronutrient scheduled diet may help to address this gap in current obesity management and add to the literature. Thus, the assessment of intervention effectiveness should not be limited to weight loss and changes in adiposity. Such assessments should also measure metabolic biomarkers, including hormones associated with energy regulation.

Adiponectin is one of several hormones that is related to obesity, and has been inversely associated with insulin resistance (Weyer et al., 2001). The response of adiponectin to weight loss achieved through diet and exercise has been quite variable, as circulating concentrations have been observed to increase, decrease, and remain the same (S. Bluher et al., 2014; Boudou, Sobngwi, Mauvais-Jarvis, Vexiau, & Gautier, 2003; Bruun, Helge, Richelsen, & Stallknecht, 2006; Christiansen, Paulsen, Bruun, Pedersen, & Richelsen, 2010; Esposito et al., 2003; Fatouros et al., 2005; Giannopoulou et al., 2005; Golbidi & Laher, 2014; Hulver et al., 2002; Kim, Cho, Kang, Choi, & Park, 2012; Klimcakova et

al., 2006; Kondo, Kobayashi, & Murakami, 2006; R. R. Kraemer et al., 2003; R. R. Kraemer & Castracane, 2007; Marcell, McAuley, Traustadottir, & Reaven, 2005; Markofski et al., 2014; Miyazaki et al., 2010; Polak et al., 2006; Ryan, Nicklas, Berman, & Elahi, 2003; Saunders et al., 2012a; Shadid, Stehouwer, & Jensen, 2006; Taksali et al., 2008; Van Berendoncks et al., 2011; Yatagai et al., 2003). The current study hypothesized that a supervised resistance training program and a structured hypocaloric macronutrient scheduled diet would result in a greater increase in adiponectin then through diet alone. This hypothesis assumed that adiponectin would increase in the diet and exercise group due to the greater weight loss achieved previously through combined diet and exercise interventions as opposed to diet in isolation (Ballor, 1994). Furthermore, adiponectin was expected to increase as a result of chronic exercise. Resistance training exercise results in metabolic adaptations, including increased muscle mass, greater cardiovascular fitness and improved insulin sensitivity, all of which are associated with improvements in adiponectin (Hakkinen et al., 2002; Ritchie, Wright, & Dyck, 2014).

TNF-α is an inflammatory cytokine that is inversely related to adiponectin and positively associated with the degree of adiposity (Hivert et al., 2010; Hotamisligil, Arner, Caro, Atkinson, & Spiegelman, 1995). TNF- α is also inversely related to insulin sensitivity, and has been recognized as a relevant clinical biomarker for diabetics (Chaldakov, Stankulov, Hristova, & Ghenev, 2003). Weight loss achieved through diet and exercise has shown mixed results with respect to changes in TNF-α (Dandona et al., 1998a;

Plaisance & Grandjean, 2006a). What is broadly accepted is that TNF-α is reduced with weight loss as well as with participation in physical activity (Greiwe, Cheng, Rubin, Yarasheski, & Semenkovich, 2001). It is proported that exercise, and specifically resistance training, may offset TNF-α related chronic inflammation and muscle atrophy (Greiwe et al., 2001). Resistance training has been shown to reduce TNF-α even when no change in weight or body composition was has taken place, indicating an independent effect outside of weight loss (Phillips et al., 2012).

The effect of diet on TNF-α has not yet been fully elucidated. What is known is that the macronutrient composition of food intake can attenuate obesity related adipose tissue dysregulation and circulating TNF-α concentration (Cassani, Fassini, Silvah, Lima, & Marchini, 2015). Therefore, the current study employs resistance training in conjunction with a diet emphasizing a specific macronutrient content of meals consumed at frequent intervals as compared to the diet intervention alone. This approach was chosen to determine whether weight loss achieved via exercise combined with diet has a greater impact on TNF-α than diet in isolation.

Appetite regulating hormones leptin and ghrelin also show mixed results with respect to their response to diet and exercise. Leptin is strongly associated with body fat and is reduced during weight loss, however, it has shown inconsistent responses to exercise (Ozcelik, Celik, Ayar, Serhatlioglu, & Kelestimur, 2004; Polak et al., 2006). The majority of studies indicate that leptin reduces with weight loss regardless of the method

by which it is achieved (Ozcelik et al., 2004; Polak et al., 2006). As a result, the current study hypothesized a greater decrease in leptin following the exercise and diet intervention as opposed to the diet alone due to the greater weight loss expected due to increased energy expenditure from exercise in the combined intervention.

Ghrelin plays an important role in energy regulation and increases during weight loss, in particular as a response to caloric restriction (Cummings, 2006). Ghrelin has been shown to respond differently to energy intake depending on the macronutrient content of meals (Erdmann et al., 2004; Overduin, Frayo, Grill, Kaplan, & Cummings, 2005; Tannous dit El Khoury, Obeid, Azar, & Hwalla, 2006). Additionally, ghrelin has shown an independent response to the increased energy expenditure associated with exercise (Schubert, Sabapathy, Leveritt, & Desbrow, 2014). These increases in ghrelin could contribute to an increased energy intake, thereby hindering weight loss due to physical activity. The current study utilized a high intensity supervised resistance training program, designed to increase energy expenditure to a greater extent then traditional resistance training (Vingren 2010), as well as a dietary approach which emphasised frequent feeding and macronutrient ratios previously shown to augment ghrelin concentration. It was hypothesized that the exercise and diet intervention would result in a greater increase in ghrelin concentration as compared to diet alone due to the greater energy demand created by physical activity as well as the greater weight loss expected from the combined intervention. In addition to weight loss, resistance training has been shown to increase lean body mass and improve basal metabolism (Okay et al., 2009).

These exercise related changes are hypothesized to result in an increase in ghrelin to compensate for the associated increase in metabolism and energy expenditure (Bajer, Vlcek, Galusova, Imrich, & Penesova, 2015). If demonstrated, this would illustrate the importance of assessing energy regulating hormones in the treatment of obesity and support further research in this area.

Testosterone is a steroid hormone that is responsible for muscle protein synthesis and which reduces muscle protein degradation, while playing a significant role in energy expenditure (Tajar et al., 2012). Specifically, testosterone enhances lipolysis and reduces triglyceride uptake in human abdominal adipose tissue (Tajar et al., 2012). A reciprocal relationship exists between obesity status and testosterone, where elevated testosterone helps prevent weight gain and lowered testosterone helps promote weight gain (Grossmann, 2011). Additionally, increases in visceral fat, a patterning associated with male obesity, elevates circulating TNF-α, insulin and leptin, all of which may downregulate the hypopituitary gonadal axis, resulting in reductions in testosterone (Sharman & Volek, 2004). Changes in basal testosterone concentration during resistance training have been inconsistent, showing increases in some studies (Hakkinen, Pakarinen, Alen, Kauhanen, & Komi, 1988a; Hakkinen, Pakarinen, Alen, Kauhanen, & Komi, 1988b; W. J. Kraemer et al., 1999; Marx et al., 2001; Staron et al., 1994), while others have shown no change (Alen, Pakarinen, Hakkinen, & Komi, 1988; Hakkinen et al., 1988b; Hakkinen & Pakarinen, 1994; Hakkinen, Pakarinen, Kraemer, Newton, & Alen, 2000a; Hickson, Hidaka, Foster, Falduto, & Chatterton, 1994; McCall, Byrnes,

Fleck, Dickinson, & Kraemer, 1999). Testosterone is believed to be augmented by exercise prescription variables, including volume, intensity and duration of exercise (Hakkinen et al., 1988a; Hakkinen et al., 1988b).

The impact of diet on circulating testosterone has not been investigated extensively. This investigation controlled for diet in order to determine if there was an independent effect of exercise on fasting testosterone concentration. The exercise protocol employed in the current study was similar to other interventions previously shown to elicit changes in energy regulating hormones (Gotshalk et al., 1997; Hakkinen, Pakarinen, Kraemer, Newton, & Alen, 2000b; R. R. Kraemer et al., 2003; W. J. Kraemer et al., 1998; W. J. Kraemer et al., 1999; Linnamo, Pakarinen, Komi, Kraemer, & Hakkinen, 2005; Migiano et al., 2010). Therefore, one objective of this research was to determine the exercise and diet associated changes in testosterone during weight loss in a population susceptible to obesity-associated decrease in androgens. Additionally, changes in regional adiposity were investigated to determine whether testosterone concentration was associated with fat patterning in an overweight and obese (body mass index (BMI) between 25-35 kg/m^2) male cohort.

In summary, the current investigation into the adiponectin response to weight loss achieved through structured supervised resistance training and a hypocaloric macronutrient scheduled diet versus a hypocaloric macronutrient scheduled diet alone may provide greater understanding into the behaviour of this adipokine in overweight

and obese, aging males. Investigation into the response of our secondary energy regulating hormones, leptin, ghrelin, TNF-α, and testosterone may also provide a better understanding of their response to weight loss accomplished using diet and exercise versus diet alone. Additional analysis of biochemical measures and metabolic risk factors, physical fitness and anthropometry adds insight into the effectiveness of resistance training and diet in this overweight and obese male cohort. Finally, the exploratory analysis into the relationship between regional adiposity and energy regulating hormones provides additional understanding of how fat influences the endocrine system and body fat topography.

To our knowledge, this is the first study to compare a weight loss program involving supervised resistance training interventions in conjunction with a hypocaloric macronutrient scheduled diet versus a hypocaloric macronutrient scheduled diet alone to investigate it's impact on energy regulating hormones in an overweight and obese, 35-55 year old male population. This diet and exercise prescription could provide practitioners with an effective intervention for weight loss and obesity management in aging males in both clinical and non-clinical settings.

Hypotheses and Objectives

Primary Objective – To determine the influence of supervised resistance training in conjunction with a hypocaloric macronutrient scheduled diet as opposed to the influence of a hypocaloric macronutrient scheduled diet alone on fasting adiponectin concentration in overweight and obese men ages 35-55.

Hypothesis 1 – Adiponectin concentration will be inversely associated with body fat and will increase to a greater extent as a result of weight loss achieved through supervised resistance training and a hypocaloric macronutrient scheduled diet rather than through weight loss achieved by a macronutrient scheduled diet alone.

Secondary Objective – To determine how both supervised resistance training in conjunction with a hypocaloric macronutrient scheduled diet, and a hypocaloric macronutrient scheduled diet alone effects fasting energy regulating hormones TNF-α, leptin, ghrelin and testosterone in overweight and obese men ages 35-55.

Hypothesis 2 –TNF-α concentration will decrease with weight loss in both the Exercise + Diet and Diet alone groups and TNF-α will decrease to a greater extent in the Exercise + Diet group due to the independent effect of physical activity.

Hypothesis 3 – Leptin concentration will decrease with weight loss in both the Exercise + Diet and Diet alone groups, and TNF-α will decrease to a greater extent in the

Exercise + Diet group due to the greater energy expenditure resulting from physical activity.

Hypothesis 4 – Ghrelin concentration will increase with weight loss in both the Exercise + Diet and Diet alone groups, and will increase to a greater extent in the Exercise + Diet group due to the greater energy expenditure resulting from physical activity.

Hypothesis 5 – Testosterone concentration will increase with weight loss in both the Exercise + Diet and Diet alone groups, and will increase to a greater extent in the Exercise + Diet group due to the resistance training protocol.

Exploratory Analysis – To determine the relationship between resting circulating concentrations of energy regulating hormones and regional adiposity including body fat topography.

Hypothesis 6 – Weight loss will be greater as a result of supervised resistance training in conjunction with a hypocaloric macronutrient scheduled diet, rather that through a hypocaloric macronutrient scheduled diet alone.

Hypothesis 7 – Measures of regional adiposity, including visceral fat, subcutaneous fat, as well as circumferential and DXA measures, will decrease to a greater extent as a result of weight loss achieved through supervised resistance training in conjunction with

a hypocaloric macronutrient scheduled diet, rather than weight loss achieved through a hypocaloric macronutrient scheduled diet alone.

Hypothesis 8 – Measures of central adiposity, including visceral fat and abdominal subcutaneous fat, will be associated with fasting energy regulating hormone concentration.

Outline for Review of Literature

Obesity and Body Fat Distribution will review obesity and obesity-related co-morbidities, illustrate the impact of regional adiposity on general health, and will demonstrate the role played by energy regulating hormones.

Weight and Health Management through Exercise will explore the effectiveness of exercise as a means of weight loss and treatment for obesity. A specific focus will be placed upon the frequency, intensity, time, and types of exercise to determine the most appropriate use of physical activity for managing weight-loss.

Weight and Health Management through Diet will discuss the effectiveness of various diets as a means of weight loss and treatment for obesity. Specifically, this chapter will isolate the differences between fasting, caloric restriction, low-fat and feeding frequency diets, and will identify the current best practices for safe and effective diet induced weight loss for obese individuals.

Weight and Health Management through Diet & Exercise will discuss the importance of diet and exercise for obese individuals who wish to archive weight loss and manage their health.

The Role of Energy Regulating Hormones in Obesity and Weight-loss Through Diet and/or Exercise is the last section of the review. This chapter will discuss the association of energy regulating hormones adiponectin, TNF-α, leptin, ghrelin and

testosterone with obesity, and will investigate their impact and role in exercise and diet induced weight loss.

The Summary of Literature Review will provide a succinct overview of the literature to show the logical steps taken to perform the current study which can address the hypotheses of this thesis. In addition, a brief overview highlighting the specific study design considerations and rationale for this thesis will be provided.

3.1 Obesity and Body Fat Distribution

3.1.1 Overview of Obesity

Obesity is the result of a higher daily energy intake than the energy expenditure, achieved through excess caloric intake, insufficient physical activity or a combination of both (Oh et al., 2014). With the increased availability of high calorie, convenience foods coupled with a trend towards a more sedentary lifestyle, the energy balance is shifting to one which promotes weight gain and results in obesity (Kumanyika et al., 2008). To date, the obesity epidemic affects over 500 million people globally including 18.3% of Canadians (Twells 2014). The rate of obesity in Canada has nearly doubled between 1978 and 2008, rising from 13.8% to 24.3% (Raine et al., 2014). In addition, there has been a disproportionate increase in people demonstrating severe obesity in Canada (Katzmarzyk & Mason, 2006). Specifically, the province of Newfoundland and

Labrador has the highest prevalence of obesity in the country with 29% and 40% of its population recognized as obese and overweight, respectively (Twells, Gregory, Reddigan, & Midodzi, 2014). Numerous studies have demonstrated that obesity increases the risk of developing type 2 diabetes, hypertension and dyslipidemia (Bogl et al, 2016, Kaur, 2014, Kissebah & Perris, 1989, Oh et al., 2014). In addition the social stigma often reported by individuals living with obesity can cause psychological stress (Bogl et al., 2016; Despres, 2007; Kaur, 2014; Kissebah & Peiris, 1989; Oh et al., 2014; P. Patel & Abate, 2013). For example, type 2 diabetes comprises 90% of all diabetic cases and has become an ever increasing healthcare challenge as the number of people affected climbs concordantly with obesity to epidemic proportions (World Health Organization, 2015). Moreover, the prevalence of type 2 diabetes is expected to reach over 438 million people globally by the year 2030 and, like most cardiometabolic diseases, carries with it a significant fiscal burden (Canadian Diabetes Association, 2013).

Obesity is a multifaceted condition resulting from a variety of physiological and environmental conditions, including education, income, social class, age, gender, ethnicity, and genetic predisposition (Dutton & McLaren, 2011; McLaren, 2007; Shields & Tjepkema, 2006; Y. Wang & Beydoun, 2007). Males between the ages of 35-55, are at particular risk of developing obesity and represent 14.2% of Newfoundland and Labrador's (NL) population (Twells et al., 2014). The obese male population has a higher risk of developing cardiovascular disease, sleep apnea, and osteoarthritis, and

also has a greater risk of developing certain cancers than their normal weight counterparts (Glintborg 2014). In fact, it has been suggested that obesity contributes as much as, if not more than, smoking to the onset of disease (Jia & Lubetkin, 2010), that it decreases quality of life, and that it increases the risk of premature death (Katzmarzyk & Mason, 2006). Within the last decade, the direct and indirects costs of obesity in Canada has been estimated to be $4.3 billion (Katzmarzyk, Gledhill, & Shephard, 2000). This estimate includes the cost of hospital care, pharmaceuticals, and lost work days due to short and long-term disability (Katzmarzyk et al., 2000). Therefore, the rapid increase in obesity, where obesity rates have doubled in the last 20 years, is both a health and economic concern (Katzmarzyk et al., 2000). Currently, there are no interventions shown to prevent the development of obesity, however, lifestyle modifications (such as increased physical activity, moderate weight loss, and eating behavior modifications) have been shown to attenuate the onset of obesity and obesity related conditions (World Health Organization, 2015).

The functional relationship of energy regulating hormones with obesity and obesity-related conditions is a significant and growing field. At present, however, very little is understood regarding the role that energy regulating hormones play in obesity development, specifically how these hormones are affected by weight loss induced through lifestyle modifications.

3.1.2 Obesity and Energy Regulating Hormones

Obesity has a very complex multidimensional etiology. Generally, obesity is the result of weight gain caused by a chronic positive caloric balance, where the total daily energy intake is greater than the total daily energy expenditure. However, although a lack of activity and/or the increased accessibility/consumption of calorie dense foods are the primary factors which contribute to obesity development, genetics, diet composition and the environment also play important roles in the development of energy regulation and body weight maintenance (Cahill 2016). For example, animal studies have shown that the genetically modified *ob/ob* or obese mouse is deficient in leptin, an energy regulating hormone that acts upon the hypothalamus to regulate energy expenditure and eating behavior (Y. Zhang et al., 1994). The administration of leptin to this phenotype of mice ameliorated the reduction of energy expenditure and excessive food intake (Halaas et al., 1995). Additionally, a study by Montague and Farooqi et al. which examined obese children found a very low circulating leptin concentration and that they were leptin deficient (Montague et al., 1997). The administration of recombinant leptin increased energy expenditure and significantly reduced food intake and body fat in these children (Montague et al., 1997).

These studies provided the first evidence that genetics, and its subsequent influence on endocrinology, is an important factor in body fat management. Furthermore, a study by Frayling et al. showed that a common variant of the FTO gene was significantly

associated with BMI in children and adults (Frayling et al., 2007). The study found that adults who were homozygous for the risk allele weighed about three kilograms heavier. The researchers found that adults who were homozygous for the risk allele had significantly greater odds of being obese as compared with those without the risk allele. It appears that genetics can significantly affect endocrine function, and that the optimal performance of various energy regulatory pathways results in an increased susceptibility to weight gain (**Figure 1 & 2 – role of energy regulating hormones in obesity**).

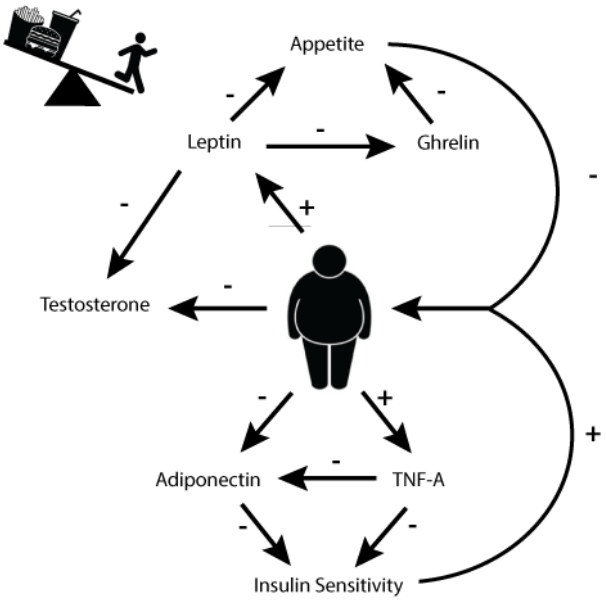

Figure 1: Impact of obesity on and from energy regulating and sex hormones: Obesity is characterized by changes in several hormones associated with energy regulation, metabolism and body composition. These include a proportional increase in leptin in association with increases in body fat, and a subsequent decrease in ghrelin to reduce food intake. Additionally, both leptin and adipose tissue result in

decreases in circulating testosterone through down regulation of the hypopituitary gonadal axis and the aromatization of testosterone to estrogen via adipose tissue respectively. Adiponectin is reduced under conditions of obesity resulting from increases in TNF-α and mechanisms not fully elucidated. This subsequent decrease in adiponectin and increase in TNF-α results in reduced insulin sensitivity which consequently increases the likelihood of additional weight gain.

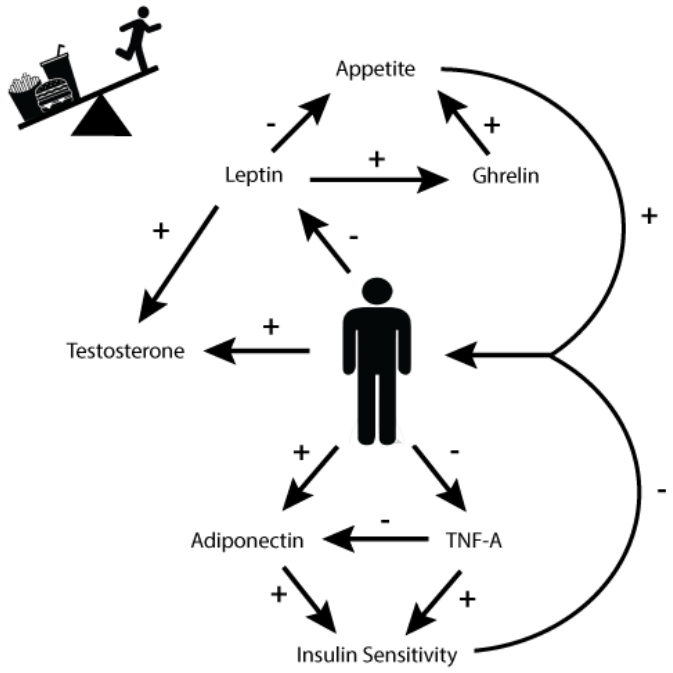

Figure 2: The impact of normal weight homeostasis on and from energy regulating and sex hormone: Normal weight homeostasis is characterized by the regulation of body weight via several

hormones associated with energy regulation, metabolism and body composition. These include leptin which is produced in proportion to body fat, and ghrelin which assists in both short and long term regulation of body weight through acute and chronic increases in appetite stimulation. Testosterone concentration is not augmented by body composition under conditions of normal weight due to the removal of inhibitory stimuli associated with the obese state. Adiponectin concentration is higher in normal weight versus obese individuals while TNF-α is reduced leading to improved insulin sensitivity as compared to obese individuals.

This can lead to obesity and obesity-related conditions. Therefore, energy regulating hormones have significant influence over glucose/lipid metabolism and body weight homeostasis. For example, some of the energy regulating hormones which enter circulation can act directly on the CNS, and can influence eating behavior (Konturek et al., 2005). These hormones include ghrelin, a gut-derived hormone which stimulates appetite in an attempt to regulate energy intake and restore body fat during weight loss (Ueda et al., 2009), glucagon like peptide one (GLP-1), which is secreted by the L-cells of the distal ileum in response to food intake to suppress hunger, and polypetide YY (PYY), another gut derived appetite suppressing hormone which inhibits gastrointestinal motility and pancreatic hormone secretion (Batterham 2002). In response to increases in body fat resulting from disturbances in energy balance, the inflammatory cytokine TNF-α is elevated and promotes insulin resistance (Hotamisligil, Shargill, & Spiegelman, 1993a). Furthermore, adipose tissue derived hormones adiponectin and leptin, when

released into circulation, can also significantly affect insulin sensitivity, energy expenditure, and eating behavior. For instance, adiponectin has been shown to attenuate insulin resistance and effectively increase the disposal of circulating glucose (Hotta et al., 2001; Moreno-Aliaga, Lorente-Cebrian, & Martinez, 2010). Since adiponectin has been recognized as a significant insulin sensitizer it would be reasonable to anticipate that circulating adiponectin levels would be elevated in the presence of an insulin resistant state such as obesity. However, the research to date suggests that adiponectin is inversely associated with both obesity (Arita et al., 2012; Cnop et al., 2003) and insulin resistance (Hotta et al., 2001; Yamauchi, Iwabu, Okada-Iwabu, & Kadowaki, 2014). The majority of cross-sectional studies show that circulating adiponectin is diminished among the obese population (Arita et al., 2012; Yang et al., 2001), and is significantly promoted after weight reduction in cross-sectional studies (Christiansen et al., 2010; Yang et al., 2001). However, hormones like TNF-α have been observed to inhibit adiponectin release, while adiponectin has been shown to inhibit TNF-α in adipose tissue (N. Maeda et al., 2002). Adiponectin also reduces the expression of adhesion molecules in endothelial cells and elicits its anti-inflammatory properties by decreasing cytokine production from macrophages (Salmenniemi et al., 2004). Furthermore, it promotes insulin sensitivity and inhibits the inflammatory mediators (Yang et al., 2001). Due to the significant influence of energy regulating hormones on metabolism, and their potential role in the development of adiposity and adiposity-related health conditions, the current study aims to investigate a number of these hormones to explore the benefits

of a weight loss program based on supervised resistance training and diet as opposed to a weight loss program based on diet alone. In addition, this study also aims to explore the relationship between body fat distribution and circulating energy regulating hormone concentration. Although exercise and diet are still the most recommended approaches for managing obesity, there remains a great deal of controversy regarding the most effective diet and exercise modalities for health improvement. These modalities are especially difficult to decipher when outcomes are primarily body-weight based, and often neglect to measure the success of the intervention on health-based outcomes.

3.1.3 Body Fat Distribution and Health Outcomes

The majority of epidemiological studies/reports attempting to evaluate the association of cardiometabolic disease with obesity make the assumption that BMI can accurately predict adiposity. Over the past few decades, however, the measurement of body fat distribution has demonstrated that BMI is a poor predictor of adiposity and obesity status (Kennedy, Shea, & Sun, 2009; Shea, Randell, & Sun, 2011; Shea, King, Yi, Gulliver, & Sun, 2012). More importantly, the current literature has demonstrated that BMI significantly over estimates the association of obesity with cardiometabolic disease (Bennasar-Veny et al., 2013; de Lima, Nobrega, & de Souza, 2012; Melmer et al., 2013). In addition, it was shown that despite a normal BMI, individuals with an elevated BF% are more susceptible to cardiometabolic disease (Kennedy et al., 2009; Shea et al., 2011; Shea et al., 2012). Due to the poor predictability of BMI for adiposity,

an increasing number of studies have investigated the influence of more accurate and cost effective methods for assessing adiposity along with body fat distribution, to determine a more precise link between body fat accumulation and cardiometabolic risk factors (De Lorenzo et al., 2013). In addition, various low cost and easy to administer techniques such as predictive equations, girth measurements, and skin fold thickness measurements, have been employed to quantify these relationships. Advances in technology have also led to a greater understanding of regional adipose tissue depositions, including dual-energy x-ray absorptiometry (DXA). To date, few studies have attempted to explore the impact of both supervised resistance training and diet vs. diet alone on the changes in body distribution and its association with energy regulating hormones (Christiansen et al., 2010; Dutheil et al., 2010; Geliebter, Ochner, Dambkowski, & Hashim, 2014; Kelly et al., 2011; Kim et al., 2012; Mason et al., 2015; Ryan et al., 2003) and even fewer studies have included both insulin resistance and other cardiovascular disease risk factors such as HDL cholesterol, LDL cholesterol, and triglycerides (Bravata et al., 2003; Bueno, de Melo, de Oliveira, & da Rocha Ataide, 2013; Mansoor et al., 2016). These biochemical risk factors are not only associated with total adiposity, but also with the region in the body where body fat is stored.

Central, or android, obesity has been associated with metabolic disorders such as hypertension, diabetes mellitus, hypertriglyceridemia, hypertension and mortality (Kaur, 2014). Meanwhile, peripheral or gynoid obesity has a significantly lower risk of cardiovascular disease as compared with central deposits and in some cases is

considered cardio protective (Bogl et al., 2016; Samsell, Regier, Walton, & Cottrell, 2014; Selyatitskaya, Pinkhasov, Karapetyan, & Kuz'minova, 2015). The use of girth measurements, including waist and hip circumference, have been used to determine regional adiposity, particularly trunk fat (van der Kooy et al., 1993). Much of what is known regarding the relationship between central fat patterning and disease is due to this simple circumferential measure. What girth measurements are not able to determine is whether central fat is stored in the subcutaneous or visceral compartment, both of which have unique physiological characteristics.

Elevated trunk fat is a characteristic of android obesity and is comprised of both subcutaneous and visceral fat (Kissebah&Peiris, 1989). There is controversy about the functional role of these fat depots, particularly, their relationship with insulin resistance. It was initially thought that trunk subcutaneous fat content had a stronger correlation with insulin sensitivity than visceral fat among non-insulin dependent diabetic men (Goodpaster et al., 2005). It was therefore believed that the stronger relationship between subcutaneous adipose tissue and insulin resistance observed in the non-diabetic population could be related to larger volumes of subcutaneous adipose tissue mass, which is estimated to be four to five times greater than visceral fat mass (Abate, Garg, Peshock, Stray-Gundersen, & Grundy, 1995a; Abate et al., 1996; Garg, 2004). Because of its larger volume, subcutaneous fat mass is considered to be a major contributor to systemic free fatty acid flux and therefore, to insulin resistance (Cnop et al., 2002).

Due to the advent of advanced imaging techniques, such as DXA, which

accurately assess the intra-abdominal fat compartment, it has been determined that the impact of visceral fat on metabolism is greater than was previously thought. The majority of research now demonstrates that abdominal visceral fat has a stronger correlation with insulin resistance than to the subcutaneous fat compartment, in both diabetic and non-diabetic subjects (Cnop et al., 2003). Similarly, visceral adipose tissue and the centralization of adipose tissue is frequently correlated with a number of related metabolic variables, including plasma glucose and lipid concentrations (Abate et al., 1995a; Bogl et al., 2016; Frayn, 2000; Smith et al., 2001). Intraabdominal adipose tissue in the visceral compartment also has increased metabolic (both lipogenesis and lipolysis) activity as compared to subcutaneous fat.

Under the conditions of excess caloric intake resulting in increased adiposity, it is suspected that adipose tissue may become dysfunctional due to fat cell hypertrophy, decreased adipogenesis, and increased angiogenesis (Patel& Abate, 2013). This is demonstrated by the inverse nonlinear relationships between glucose disposal and visceral fat and is independent of gender (Banerji, Chaiken, Gordon, Kral, & Lebovitz, 1995). Visceral fat explains a significant portion (34%) of variance in the insulin-mediated glucose disposal, whereas total or subcutaneous fat does not (Banerji et al., 1995). The negative implications of elevated visceral fat mass are further supported by the portal vein theory, which states that free fatty acids, as a product of lipolysis, directly enter the liver via the portal , causing increased lipid synthesis, gluconeogenesis, and insulin resistance. This can result in hyperlipidemia, glucose intolerance, hypertension

and ultimately atherosclerosis (Garg, 2004). As well, excess circulating free fatty acids can inhibit skeletal muscle glucose uptake, leading to peripheral insulin resistance (Arnlov, Ingelsson, Sundstrom, & Lind, 2010). To demonstrate the aforementioned metabolic outcomes, this theory would require that the majority of free fatty acids would reside in the visceral compartment. However, visceral fat represents only a small proportion of total fat in men at ~15%–18% (Arnlov et al., 2010). It is therefore thought that other mechanisms must be involved which make visceral fat phenotypically unique as compared with other fat deposits. One such explanation is that adipose tissue is not merely a dormant fat storage site, as was once believed. Instead it is a complex, essential, and highly active metabolic and endocrine organ. It has been shown that in excess it can lead to systematic inflammation, assists in energy regulation and plays a significant role in reproduction.

Visceral fat has shown a consistent negative association with the insulin sensitizing hormone adiponectin (Yang et al., 2001). In vitro studies show that visceral adipocytes have increased the expression of adiponectin as compared to subcutaneous adipose tissues (Fain, Madan, Hiler, Cheema, & Bahouth, 2004). The nature of the inverse relationship between adiponectin and visceral fat is believed to occur because adiponectin is down regulated by the inflammatory cytocine TNF-α, whose primary production and secretion site is the visceral adipose tissue (Clement et al., 2004). As visceral fat increases, so does inflammation, resulting in a subsequent suppression of adiponectin. It has been shown that even small changes in visceral fat may influence

changes in TNF-α in both overweight and obese males (Kirwan, Krishnan, Weaver, Del Aguila, & Evans, 2001). These findings indicate that although the visceral compartment is relatively small in comparison with the larger subcutaneous depot, its role with respect to metabolism and energy regulation may be significantly greater than other fat depots.

The role played by visceral fat in metabolism is further supported by studies that contract central and peripheral obesity. It has been demonstrated that subjects with higher trunk fat, specifically visceral fat, are more insulin resistant than subjects with peripheral or lower body obesity (Bogl et al., 2016; Samsell et al., 2014; Selyatitskaya et al., 2015). Regardless of mechanism, be it energy regulating hormones or the portal vein transmission of fat to neighboring organs, what is certain is that trunk fat (visceral and subcutaneous fat) has a higher free fatty acid concentration than the peripheral gluteofemoral region. A study by Goodpaster et al found that thigh subcutaneous fat, as an indicator of fat deposition in peripheral tissue, can significant predict insulin sensitivity (Goodpaster et al., 2005). It is thought that gluteofemoral fat has a protective role, and that adipocytes in that region are relatively insensitive to lipolysis stimulus and sensitive to anti-lipolysis stimulus (Manolopoulos, Karpe, & Frayn, 2010).

3.1.4 Chapter 1 Summary

The traditional view of adipose tissue as a passive reservoir for energy storage is no longer valid. As early as 1987, adipose tissue was identified as an endocrine organ and a major site for the metabolism of sex steroids, as well as for energy regulating hormones.

As a result, adipose tissue is systemically involved in coordinating a variety of biological processes, including energy metabolism, growth and reproduction, in addition to immune function. Research into the effects of diet and exercise on energy regulating hormones has revealed limited information on how these factors influence obesity. Furthermore, the relationships between energy regulating hormonal concentrations and regional adipose tissue is not well understood. Therefore, the current study provides an opportunity to examine the relationship between exercise, diet, and energy regulating hormones under conditions of weight loss, as well as the associations, if any, between these hormones and regional adiposity in an overweight and obese male cohort.

3.2 3 Weight and Health Management through Exercise

The recommendation to participate in regular exercise and physical activity is one of the most broadly prescribed lifestyle modifications in the treatment of obesity. Exercise has been defined as activity requiring physical effort, carried out especially to sustain or improve health and fitness (ACSM, 2014). If appropriate exercise is performed on a regular basis, physical activity can increase metabolism and reduce the risk of developing obesity and its co-morbidities. Exercise can also prevent the loss of lean body mass, improve cardiorespiratory fitness, and increase one's overall feeling of well-being (Okay et al., 2009). The impact of exercise on weight loss and health improvement is complex, which can be attributed, in part, to the effects of hormones responsible for insulin sensitivity, appetite and muscle anabolism. The following chapter will review exercise related weight loss and health benefits, and will give particular attention to the hormonal response to resistance training.

3.2.1 Exercise Modalities:

The terms "aerobic", "anaerobic", and "resistance training" do not have universal definitions throughout academic and popular media due to the broad variety of modalities which encompass these types of exercise. Aerobic exercise is commonly defined as exercise involving large muscle groups in dynamic activities, which can result in substantial increases in heart rate and energy expenditure (Powers, Howley, & Cox, 1985). Anaerobic exercise, in contrast, is completed at very high intensities such that a

large portion of energy is provided by glycolysis and stored phosphocreatine. Resistance training is exercise that causes muscles to contract against an external resistance, with an expectation of increases in strength, tone, mass, and/or endurance (Howley, 2001).

3.2.2 Weight Loss and Body Fat Distribution

Exercise intervention studies show conflicting results with respect to weight loss. This is not surprising, given the broad spectrum of modalities that are considered exercise. The term exercise is often broadly used in physical activity research, where the differences between approaches such as cardiovascular training and resistance training are not always clearly identified (American College of Sports Medicine, 2009). Due to the varied physiological and adaptive responses that occur as a result of different activities, it is important that the characteristics of the exercise intervention are clearly explained (American College of Sports Medicine, 2009). Because of the uncontrolled nature of many exercise intervention studies, researchers are often unable to determine the participants' energy expenditure during an exercise session (Conn et al., 2014). This difficulty is compounded by the standardization of training programs administered in research studies, which can result in individuals working at varying levels of intensity based upon physical fitness and exercise experience. Furthermore, the lack of supervision in many trials results in an over or under reporting of total activity

performed and does not control for possible modifications in exercise performance, including lower time under tension, increased rest intervals between sets, and a reduced range of motion (Ballor & Poehlman, 1994; Garrow & Summerbell, 1995; Miller et al., 1997).

In a meta-analysis on the effect of exercise on weight loss, participants who engaged in exercise lost an average of 2.4 kg more than the sedentary control groups (Wing & Phelan, 2005). In six out of the ten studies reviewed, the difference in the amount of weight loss was significant, leading reviewers to conclude that exercise alone produces moderate weight loss (Wing & Phelan, 2005). However, the small sample sizes used in several of these studies limits generalizations for the larger population. The sample sizes for three out of the ten studies were as follows: five participants in the control and experimental group, n=10 (Verity & Ismail, 1989), 13 participants in both the control and experimental group, n=26 (Ronnemma,1988), and eight participants in the experimental group and four in the control group, n=12 (Hammer, 1989). This meta-analysis was pursued in order to increase the sample size and derive a more accurate picture of the relationship between exercise therapy and obesity.

Although caloric restriction remains the most efficacious method for weight loss, exercise and physical activity are integral components of long-term weight maintenance and do lead to additional, although modest, weight loss when combined with diet. In a meta-analysis on weight loss approaches performed by Miller et al. weight loss achieved

through exercise in isolation resulted in only a 2.9 kg weight loss, where diet resulted in 10.7 kgs, and diet combined with exercise resulted in 11 kg (Miller et al. 1997). When performed in isolation, the difference in weight loss between diet and exercise is substantial, therefore it is recommended that diet or diet and exercise be performed to achieve healthy body weight for obese patients (Miller et al. 1997). As significant heterogeneity exists within the definition of exercise the opportunity to determine effective approaches which provide additional weight loss when exercise is combined with diet would contribute to the current literature.

The average energy deficits created by exercise are estimated at ~28% of daily energy intake (Ross et al., 2000). When combined with caloric restriction, exercise results in additional benefit, demonstrating a 30% greater energy deficit than that observed in individuals who rely on dieting alone (Ross et al., 2000). Ross et al. concluded that more controlled studies are required whereby energy deficits induced by dieting and exercise are carefully matched to determine whether exercise alone is beneficial for weight loss (Ross et al., 2000). These previous investigations have helped define the current study's approach towards the use of exercise and diet for weight loss.

The increased energy expenditure achieved with exercise may be more important to weight loss outcomes then the modality of exercise itself (Sedlock, Fissinger, & Melby, 1989). In two out of the ten studies reviewed, energy deficits are approximately equal between exercise in isolation versus dieting alone (Ross et al., 2000; Sopko et al., 1983).

Sopko et. al found that weight loss for exercise in isolation is comparable to that of the diet only under conditions of matched energy deficits (Sopko et al., 1983). The authors believe that the magnitude of the energy deficit is a more important factor than the manner in which the energy deficit is achieved (Sopko et al., 1983). Ross et. al also found that body weight decreased by 7.5 kg (8%) in both the diet and exercise groups when equal energy restrictions were administered, while total fat decreased by 1.3 kg more in the exercise only group (Ross et al., 2000). Exercise itself, even without weight loss, has been shown to reduce specific regional adipose deposits including those in the visceral region (Ohkawara, Tanaka, Miyachi, Ishikawa-Takata, & Tabata, 2007). The reduction in visceral fat associated with exercise demonstrates specific benefits for men, as intra-abdominal fat is associated with a higher risk of metabolic disease, including diabetes, in this population (Smith et al., 2001). The preferential reduction in visceral fat associated with exercise indicates that visceral fat is more sensitive than subcutaneous fat to lipolytic stimulation and less is resistant to insulin suppression (Fried, Leibel, Edens, & Kral, 1993). In contrast, Egger et. al concluded that physical activity on its own is not effective for weight loss unless the individual is participating in approximately 3-3.5 hours of physical activity a day, which is an un-realistic expectation for most obese populations (Egger, 2008). However, exercise effectiveness can be improved via several prescription variables to yield effective interventions, while reducing overall time required for exercise (Ross et al., 2000). It is clear that more research is needed to employ evenly matched energy restrictions in order to determine

the effects of exercise in isolation on weight loss. Also, studies need to take a broader view on physiological responses to exercise that are not limited to weight loss, such as the biochemical and hormonal variables specific to the obese phenotype (D. L. Williamson & Kirwan, 1997).

Exercise can lead to weight loss. However, the type and intensity of the activity dictates the degree (Ross et al., 2000; Wing & Phelan, 2005). Structured exercise is a complex arrangement of movements where numerous variables can be modified to elicit a variety of training effects ranging from strength to endurance. The practitioner must differentiate between the benefits of aerobic, anaerobic, and resistance training, as well as between low, moderate, and high intensity training regimens in order to accomplish the desired training effect (Howley, 2001).

The literature focusing on the weight loss effects of exercise often considers all exercise to be equivalent. The incorporation of exercise prescription principles in the development of exercise interventions aimed at weight loss would help reduce the heterogeneity in exercise interventions currently existing in the literature. The current investigation incorporates a series of important training specificity variables into its resistance training protocol prescription.

Research involving exercise as a means of weight loss must carefully consider the prescription of resistance training programming. In order to optimize training effect, recommendations for exercise should include attention to contraction speed, sufficient to

recruit fast twitch muscle fibers, the use of a variety of contraction types, and an assortment of closed chain, multi-joint free weight exercises. Although these exercise prescription principles have been well established in younger athletic populations, their benefit for aging and overweight/obese populations is not clear.

3.2.3 Physiological and Biochemical Changes

Approximately 20 years ago, the importance of exercise as a therapy was investigated by a panel of experts representing the National Heart, Lung, and Blood Institute as well as the National Institute of Diabetes and Digestive and Kidney Disease in an attempt to identify, evaluate, and treat overweight and obese adults (Wing & Phelan, 2005). Since those seminal studies, exercise has played an important role in the treatment of weight gain in the general and clinical population.

It is well established that acute energy expenditure attained via exercise is not the only effect of physical activity. Chronic exercise results in metabolic adaptation, increased muscle mass, cardiovascular fitness and insulin sensitivity, all of which impact obesity (Hakkinen et al., 2002; Ritchie et al., 2014). Therefore, studies that focus solely on energy expenditure during exercise are limited, and may lack a larger view of exercise adaptation.

Resistance training as an exercise modality for cardiovascular disease risk factors has shown success with improving cholesterol (Kukkonen-Harjula, Borg, Nenonen, &

Fogelholm, 2005) and triglycerides (Cornelissen, Fagard, Coeckelberghs, & Vanhees, 2011). Additionally, resistance training may slightly improve diastolic blood pressure (Cornelissen et al., 2011; Pattyn, Cornelissen, Eshghi, & Vanhees, 2013), waist circumference (Christiansen et al., 2010; Lemes et al., 2016) and glucose disposal (Roberts, Hevener, & Barnard, 2013).

Exercise-associated improvements in insulin sensitivity and glucose tolerance have been found in a variety of populations, including younger individuals (Poehlman, Dvorak, DeNino, Brochu, & Ades, 2000) and older individuals (Zachwieja, Toffolo, Cobelli, Bier, & Yarasheski, 1996), those with hypertension (Reynolds, Supiano, & Dengel, 2004) and people who have type II diabetes (Ishii et al., 2001).

Resistance training, regardless of prescription has shown consistent evidence that it improves insulin sensitivity (Roberts et al., 2013). However, there were two identified studies involving resistance training that failed to achieve significant changes. The first study showed an increase of ~10% and did not achieve statistical significance ($P<0.06$) (Davidson et al., 2009) and the second used 60 minutes of physical activity per week, suggesting that a minimum level of activity is warranted to elicit change (Ryan et al., 2001). The latter study supports guidelines from exercise physiology governing bodies, which recommend 60 minutes of physical activity per day. It is therefore not surprising that with only 60 minutes per week, no significant change in insulin sensitivity was detected (ACSM, 2014).

Resistance training can show health benefits in the absence of weight loss (Klimcakova et al., 2006). In obese, middle-aged men, a 24% increase in glucose disposal rate, without any change in body weight, fat mass or $VO_{2max,}$ was demonstrated (Klimcakova et al., 2006). Other research noted a modest increase in insulin sensitivity, which occurred in the absence of changes in total body, subcutaneous or visceral fat (Poehlman et al., 2000).

In summary, a recent systemic review of 20 studies found that supervised resistance exercise training improved glycemic control and insulin sensitivity in a wide variety of study groups (Gordon, Benson, Bird, & Fraser, 2009). However, without supervision, resistance training compliance and glycemic control are generally less, suggesting either the need for supervision or additional motivation to maximize training-induced benefits. Lastly, the addition of a calorically restricted diet, as was employed in the current study, improves insulin sensitivity in exercise participants to a greater degree than exercise in isolation (Gordon et al., 2009).

3.2.4 Energy Regulating Hormones

Exercise is capable of altering hormones responsible for insulin sensitivity, metabolism, appetite and muscle anabolism. The insulin sensitizing adipokine, adiponectin, the primary hormone of interest in the current study, has been the focus of several studies (Boudou et al., 2003; Christiansen et al., 2010; Dutheil et al., 2010; Esposito et al., 2003; Hulver et al., 2002; Ryan et al., 2003; Yatagai et al., 2003). These studies have used various modalities, frequencies and intensities of exercise in a variety

of populations. To date, however, there is a relatively small amount of research using the current study population of overweight and obese aging males (Simpson & Singh, 2008).

The adiponectin response to exercise has been unpredictable. Where some studies show an increase in adiponectin (Saunders et al., 2012b), others show no changes (Yatagai et al., 2003), or in one example, an adiponectin decrease (Christiansen et al., 2010).

The inflammatory cytokine TNF-α increases under conditions of obesity and decreases with regular participation in physical activity (Plaisance & Grandjean, 2006b). Research has also shown that regular physical activity can negate or reverse TNF-α's association with obesity status, which reduces the health risk associated with both obesity and inflammation (Mattusch, Dufaux, Heine, Mertens, & Rost, 2000). The physical activity associated with increases in insulin sensitivity is accomplished, in part, by suppressing TNF-α, which in turn upregulates the production/secretion of the insulin sensitizing hormone adiponectin (Kasapis & Thompson, 2005). The exercise induced reduction in circulating concentrations of TNF-α is not limited to chronic exercise, but is also acutely reduced following a single exercise session (Mattusch et al., 2000).

Weight loss also reduces the size and number of TNF-α producing fat cells, which demonstrates the importance of exercise in creating a decrease in energy balance (Hotamisligil, Shargill, & Spiegelman, 1993b). Currently, there is limited research as to which modes of exercise are the most effective at reducing chronic inflammation

resulting from TNF-α. This gap in the literature provides an opportunity for investigations into specific exercise prescriptions and their effect on obesity related inflammatory hormones.

The appetite regulating adipokine leptin has been observed to decrease in response to exercise. However, these findings have been inconsistent. It is well established that leptin is directly correlated to adiposity status and, as a result, the majority of research indicates that exercise associated changes in leptin are in response to weight loss resulting from exercise, rather than exercise itself (Ozcelik et al., 2004; Polak et al., 2006). Studies showing the independent effects of exercise on leptin have involved various modalities and intensities of exercise, often in an uncontrolled setting, leading to uncertainties about the true impact of exercise on leptin. There is a need for highly controlled, supervised exercise research using well defined protocols which can provide definite answers about leptin's relationship with physical activity.

Ghrelin, an energy and appetite regulating hormone, has been observed to increase in response to weight loss (Leidy et al., 2004). Similar to leptin, ghrelin consistently fails to show an independent change in circulating concentrations in response to chronic exercise (Foster-Schubert et al., 2005; R. R. Kraemer & Castracane, 2007; Leidy et al., 2004; Schubert et al., 2014; Thomas et al., 2012; Ueda et al., 2009). Due to the energy demands of exercise, ghrelin has shown an acute post exercise increase, which is believed to stimulate energy intake which restores the energy depleted during exercise

(Schubert et al., 2014). Additionally, ghrelin is thought to increase in response to the secondary benefits of exercise, in particular, the lower inhibitory effects of leptin associated with weight loss, and the increased energy demand from improvements in lean body mass (Schubert et al., 2014). It is well established that exercise protocols lead to food cravings and increased appetite due to the increased energy demands of exercise activity, and that ghrelin stimulates these responses (Thomas et al., 2012).

Testosterone is an androgen hormone which plays an important role in muscle protein synthesis (W. J. Kraemer et al., 1998). Changes in resting testosterone concentrations during resistance training have been inconsistent. Testosterone concentrations have shown increases in some studies (Hakkinen et al., 1988a; Hakkinen et al., 1988b; W. J. Kraemer et al., 1999; Marx et al., 2001; Staron et al., 1994) while others have shown no change (Alen et al., 1988; Hakkinen et al., 1988b; Hakkinen & Pakarinen, 1994; Hakkinen et al., 2000a; Hickson et al., 1994; McCall et al., 1999). Additionally, the majority of research involves younger individuals, or subjects who are highly trained (Hakkinen & Pakarinen, 1993; L. Hansen, Bangsbo, Twisk, & Klausen, 1999; Linnamo et al., 2005). The goal of the current investigation is to determine whether protocols previously shown to increase testosterone in more athletic populations result in similar changes for overweight and obese aging male population.

3.2.5 Chapter 2 Summary

It has been shown consistently that exercise without dietary restrictions does not show significant weight loss in obese individuals (Ross et al., 2000). However, this connection is subject to limitations, and must be interpreted cautiously. Studies that prescribe adequate intensity, duration and loading of exercise has been shown to elicit a greater weight loss and training adaptation (Ross et al., 2000). In eight out of the ten studies reviewed, the negative energy balance created through the amount and intensity of exercise prescription was small, to the point where results showed that large weight losses are not attainable (Ross et al., 2000). Additionally, exercise interventions must focus on outcomes outside of weight loss including both biochemical and physical changes in cardiovascular risk factors. In particular studies must investigate the changes in energy regulating hormones, many of which are associated with the aforementioned changes in adiposity and cardiovascular risk factors. The current investigation implemented a structured, supervised resistance training protocol, based on those previously shown to augment energy regulating hormones while providing sufficient metabolic demand to elicit weight loss, in an overweight and obese aging male population. Finally, exercise has been shown to be most effective when combined with caloric restriction (Miller et al., 1997). The following chapter highlights the most current approaches for effective weight loss through diet, and discusses the impact of nutrition on weight loss, health risk reduction and energy regulating hormones.

3.3 Weight and Health Management through Diet

Dietary restriction remains the most common method of weight loss prescribed by physicians (D. F. Williamson, Serdula, Anda, Levy, & Byers, 1992). However, no single diet plan has been universally successful at achieving weight loss and improving clinically relevant health measures (Matarese & Pories, 2014). In fact, there is a surprising lack of consistent weight loss outcomes associated with dietary restriction. Diets emphasizing reduced calorie intake typically characterize most approaches; however, the exclusion of various nutrients including low fat or low carbohydrate diets add complexity to dietary prescriptions. Additionally, the unique characteristics of the various macronutrients, specifically saturated versus unsaturated fats and complex versus simple carbohydrates, have been considered to be important factors when determining the impact of diet on energy regulating hormones, including adiponectin (Esposito et al., 2003), leptin (Barkoukis et al., 2007; Bouche et al., 2002; Ebbeling et al., 2012; Niwano et al., 2009)., ghrelin (Erdmann et al., 2004; Overduin et al., 2005; Tannous dit El Khoury et al., 2006), and TNF-α (Kelly et al., 2011). The following chapter reviews the weight loss, health, and energy regulating hormone outcomes shown in previous research and provides the rationale behind the hypocaloric macronutrient scheduled diet employed in the current study.

With a growing emphasis on weight loss in society stemming from an increased awareness of obesity related health risks, significant efforts have been made to validate the best approach to achieving and maintaining a healthy body composition. The past six decades have led to several distinct approaches to weight loss via diet, all of which vary in effectiveness, macronutrient content or quantity and health impact.

The very low calorie diet (VLCD), which was popularized in the 1980s, promotes the ingestion of liquids which are low in energy (Kaplan, Miller, & Anderson, 1992). Although an effective modality for weight loss, the practicality of these diets is limited due to the strict guidelines which leads to a lack of patient adherence (Miller et al., 1997). Within one year after dieting, 75% of dieters were shown to re-gain the weight lost and, after two years over 90% were unsuccessful (Safer, 1991). VLCD diets typically provide 20% of their energy from protein, 20% from fat, and 60% from carbohydrates and limit individuals to only 400-800 calories a day, which is a significantly lower caloric intake in comparison to normal eating habits (Cowburn, Hillsdon, & Hankey, 1997). For these reasons, the use of the VLCD was not employed in the current study.

In contract to pure caloric restriction, the reduction of certain macronutrients has been investigated extensively. These diets are commonly known as the low fat and low carbohydrate diets (Bravata et al., 2003; Bueno et al., 2013; Matarese & Pories, 2014).

The low fat diet has been the most commonly prescribed weight loss approach with respect to caloric restriction (Matarese & Pories, 2014). The popularity of this approach is thought to be related to the reduction in caloric intake due to the higher caloric content of dietary fat versus protein and carbohydrate.

Low carbohydrate diets promote a reduced or restricted carbohydrate intake that leads to a ketogenic state (Bravata et al., 2003; Bueno et al., 2013). This approach provides more nourishment as compared to VLCD, while still leading to significant weight loss (Brehm, Seeley, Daniels, & D'Alessio, 2003; Tay, Brinkworth, Noakes, Keogh, & Clifton, 2008). Consuming a low carbohydrate diet redirects substrate utilization from glucose to ketone bodies in an attempt to fuel the central nervous system due to the inability of the brain to metabolize fatty acids in the absence of glucose (Bueno et al., 2013). What is known is that the low-carbohydrate diet decreases appetite, even during periods of caloric restriction and weight loss (Gibson et al., 2015). It has been proposed that the state of ketosis is partly responsible for this decrease in hunger (Gibson et al., 2015). It has been well established that the macronutrient content of meals can influence energy intake in the post meal period, with protein exerting a stronger satiety influence over appetite than carbohydrates (Blundell, Stubbs, Hughes, Whybrow, & King, 2003). The low-carbohydrate approach may inadvertently benefit from a disproportional intake of protein, which may lead to reduced hunger (Gibson et al., 2015).

The understanding of the role of the various macronutrients with respect to energy metabolism, as well as the understanding of the importance of frequent feeding, has led to effective and sustainable approaches to weight loss via diet without excessive macronutrient or caloric restriction. Moderate energy restriction typically recommends that caloric intake be limited to approximately 1,200 calories a day. However, these restrictions allow for increases or decreases in energy intake depending upon body size, metabolic needs, activity levels, gender, and age (Cowburn et al., 1997). Due to the known effect of various macronutrients on weight loss and satiety, the efficacy of "calorie counting" may be oversimplified and requires attention with respect to macronutrient scheduling and type (Frost, 2007). Although macronutrients have a specific caloric content that can be measured, they exert different effects on satiety independent of their caloric value (Matarese & Pories, 2014). Furthermore, the assumption that all individuals function equally under the same caloric restriction is highly variable. The traditional calorie counting approach has been shown to underestimate the amount of energy required by each individual, leading to lower adherence due to increased appetite resulting from reduced nutrient intake (Frost, 2007). It has been shown that the most effective approach for moderate caloric restriction should be no more than 500 kcal below their estimated energy expenditure (James, 1983). This is the approach that was employed in the current study.

Although it is well established that the amount of calories ingested is a crucial variable in the effectiveness of a weight loss diet, it is not the only consideration. In particular,

within moderate energy restriction diets there are several variables which can be adapted to optimize caloric intake including feeding frequency and quality of macronutrients, such as the glycemic index of carbohydrates and the proportion of saturated versus unsaturated fats in food sources (Schoenfeld, Aragon, & Krieger, 2015). The glycemic index (GI) is a measure of the ability of individual foods to elevate blood sugar over two hours compared to eating a simple sugar such as glucose and has been hypothesized to impact the satiety of an individual during caloric restriction (Sacks et al., 2014). High-GI foods digest rapidly and have various negative health effects while low-GI foods digest slower and are believed to be beneficial to our health (Sacks et al., 2014). In a review by Niwano, the GI was investigated to determine its impact on appetite, hunger and satiety (Niwano et al., 2009). It was found that high-GI foods were generally found to increase hunger and lower satiety over the short term, possibly due to a resulting state of hypoglycemia (Niwano et al., 2009). Consequently, high-GI test meals resulted in individuals eating more at subsequent meals (Ball et al., 2003; Ludwig et al., 1999; Warren, Henry, & Simonite, 2003).

Understanding the role of various nutrients, their combinations, as well as the recommended timing of nutrient intake are all important variables in the prescription of diet. The following sections summarize the impact of these various dietary approaches on outcomes of interest investigated in the current study, including weight loss, cardiovascular risk factors and energy regulating hormones.

3.3.1 Weight Loss and Body Composition

The degree of weight loss achieved through caloric restriction varies greatly depending upon the approach employed. The average weight loss results with VLCD range anywhere from 1.5-2.5 kg/week within the first six to ten months; however, it is broadly recommended that ranges of 0.5-1.0 kg/week are safe and desirable for long term weight loss (Weinsier, Wilson, & Lee, 1995). As time passes, the rate at which people lose weight on VLCD diminishes, owing to a reduction in basal metabolic rate by an average of 15% (Cowburn et al., 1997).

With respect to macronutrient restriction, low fat diets emphasize reduced caloric intake through the avoidance of high calorie dietary fats, and demonstrate significant weight loss. However, low fat diets are generally considered to be less effective than other caloric restriction approaches (Ajala, English, & Pinkney, 2013). Randomized control trials which prescribe low fat and high carbohydrate interventions show a mean weight loss ranging between 0 and 10 kg (Astrup, Toubro, Raben, & Skov, 1997). Meanwhile, a recent systematic review in human obesity and dietary fat consumption found that a reduction of 10% in dietary fat intake results in a reduction in weight of 16g/d, corresponding to a weight loss of 2.9 kg over six months (Bray & Popkin, 1998). To determine the impact of restricting dietary fat, Ebbeling et al. evaluated the effects of different macronutrient diet compositions of diets on energy expenditure during weight loss (Ebbeling et al., 2012). They developed a three-way crossover study of overweight

and obese young adults (n = 21) which included a run-in phase in which calories were restricted to achieve a 10% to 15% weight loss (Ebbeling et al., 2012). The diet was composed of 45% carbohydrate, 30% fat, and 25% protein and subjects were randomly assigned iso-caloric diets for four weeks: either a low fat, high–glycemic load (60% carbohydrate, 20% fat, 20% protein); low–glycemic index (40% carbohydrate, 40% fat, 20% protein); or a very-low-carbohydrate, low–glycemic load (10% carbohydrate, 60% fat, 30% protein) diet (Ebbeling et al., 2012). During each phase energy expenditure was measured. The researchers found that the reduction in both resting and total energy expenditures was highest in the low-fat group, indicating that weight loss was more difficult (Ebbeling et al., 2012).

Additionally, low carbohydrate diets gained popularity following research showing that when obese individuals consumed a high-fat, high-protein diet, they experienced significant weight loss, even when there was no negative caloric balance (Foster et al., 2003). In contrast, recent comparisons of the low carbohydrate diet to other caloric reducing diets, have shown that macronutrient composition is not the sole determining factor in the effectiveness of losing weight when energy intake is also decreased (Matarese & Pories, 2014). It is therefore assumed that the weight loss observed amongst low carbohydrate dieters is mainly due to a reduction in energy intake rather than macronutrient composition (Dansinger et al., 2005; Foster et al., 2003; Morgan et al., 2009; Yancy, Olsen, Guyton, Bakst, & Westman, 2004). In general, low carbohydrate diets are not associated with significantly greater weight loss then other

diets. However, all diets that have a long duration and a high caloric restriction result in greater weight loss then those with of shorter duration and less caloric restriction (Mansoor et al., 2016).

With respect to body composition, an increased frequency of feeding (three meals and three snacks per day versus three meals per day) is positively associated with reductions in fat mass and body fat percentage, as well as with an increase in lean body mass (Schoenfeld et al., 2015). Lean body mass has been shown to be maintained or increased with greater feeding frequency, as protein synthesis and growth are heightened when protein-containing meals are consumed frequently throughout the day (Moore et al., 2012). The ingestion of protein scheduled every three hours has been determined as the most beneficial frequency for increasing net protein balance, in particular following resistive exercise (Moore et al., 2012). These findings are relevant for overweight populations, as many weight loss interventions combine both diet and exercise, in particular resistance training (Moore et al., 2012). The increase in anabolism that results in increases in lean mass would conceivably aid in weight management due to enhancements in resting metabolic rate (Areta et al., 2013).

Changes in body composition are not the only clinically relevant outcomes of dietary restriction. Changes in physiological and biochemical measures resulting from caloric restrictions have made diet an appealing therapy for metabolic disease and lifestyle related illnesses.

3.3.2 Physiological and Biochemical Changes

Dietary restriction has led to both positive and negative health effects. Diets emphasizing excessive caloric restriction have led to warnings from governing medical associations, and are therefore not recommended for individuals seeking a healthy approach towards weight loss (Miller, et al., 1997). For example, a common risk factor with rapid weight loss resulting from VLCD is cholelithiasis (the formation of gallstones), partly due to patients losing more than 1.5 kg/week (Weinsier et al., 1995). In addition, VLCDs include significant challenges around patient adherence, loss of lean body tissue and weight regain following cessation (Miller et al., 1997).

With respect to positive health benefits, the low fat diet is an appealing approach as it encourages low saturated fat intake which results in a decreased risk of elevated cholesterol and triglycerides (Mansoor et al., 2016). Alternately, studies using the combination of a high fat and a low carbohydrate diet have been associated with a greater weight loss, as well as a greater reduction of both total cholesterol and triglycerides and increased HDL cholesterol, compared with their low fat diet counterparts (Bravata et al., 2003; Bueno et al., 2013). However, these studies also show a significant increase or lack of reduction in LDL cholesterol, which is credited to the high fat content of the low carbohydrate diet (Bueno et al., 2013; Nordmann et al., 2006; Schwingshackl & Hoffmann, 2013a; Schwingshackl & Hoffmann, 2013b; Tay et al., 2008). High LDL cholesterol can be harmful, as it is an important risk factor for CVD

morbidity and mortality (Krauss & Siri, 2004). Therefore, concerns have been raised about the use of a low carbohydrate diet that does not discourage the excessive consumption of saturated fats, especially by patients with known CVD, type 2 diabetes, dyslipidemia and/or hypertension, many of which fall into the category of overweight and obese individuals seeking to lose weight (Bravata et al., 2003). It is therefore essential to identify the form of fat consumed during a low carbohydrate diet and to reduce the consumption of saturated fats, while maintaining higher levels of mono and polyunsaturated fats which have been shown to benefit those patients (Bravata et al., 2003; Bueno et al., 2013).

Significant research has been conducted regarding the use of low glycemic index carbohydrates in place of simple carbohydrates for the control of blood glucose. After a low-GI breakfast, adolescents ate less lunch than those eating a high-GI breakfast due to the lowering of the post prandial insulin response from the low-GI meal (Warren et al., 2003). The response to a rapid increase in blood glucose is an increased insulin action (Warren et al., 2003). Therefore individuals ingesting a high-GI food are more likely to experience mild hypoglycemia (Warren et al., 2003). As blood glucose drops below the person's base level, satiety ends and appetite returns. Therefore, the greater glycemic control offered by low-GI foods provides a greater opportunity for stable blood sugar as compared with high-GI food. For example, various forms of low glycemic carbohydrates, including fructose, glucose, sucrose and maltodextrins serve to suppress appetite, and reduce the later intake of energy by approximately the same amount of

calories that was ingested (Astrup, 1999). For this reason, low-GI foods have been promoted for the treatment of obesity, and are included frequently in current dietary recommendations. Low-GI foods were therefore employed in the current study.

In a five week study, which included moderately overweight men undergoing a low-GI diet, subjects effectively ameliorated some plasma lipid parameters, decreased total fat mass and tended to increase lean body mass without changing body weight (Bouche et al., 2002). These authors proposed possible mechanisms to explain why the lower GI diet induced a selective decrease in fat and an increase in lean body mass, including the difference in nitrogen balance and protein metabolism (Bouche et al., 2002). Due to the negative nitrogen balance associated with the high GI diet, it was suggested that fat tissue is oxidized to a lesser degree and muscle to a greater degree with the high-GI diet (Bouche et al., 2002). Another possible mechanism they proposed is that a low-GI diet utilization, which reduces carbohydrate oxidation and increases fat oxidation (Bouche et al., 2002).

To date, the results of long-term studies showed varying responses of appetite/satiety to foods of various glycemic indices, and there is inadequate evidence to support the widespread use of low-GI foods in the treatment of obesity (Kelly et al., 2011). Specifically, long-term studies do not show that low-GI diets reduce appetite or hunger unless, there is a definite change in blood glucose level (Kelly et al., 2011). Therefore, the current study aims to clarify the use of low glycemic index carbohydrates in

conjunction with scheduled feeding and food log supervision in overweight and obese males.

In addition, the benefit of feeding frequency, moderate energy restriction and a low GI diet extends to more than cardiovascular risk factor improvement and changes in body composition, but also to changes in energy regulating hormones (Bowen, Noakes, & Clifton, 2006). Hormonal response to specific dietary approaches is not a novel concept, and has been the focus of significant study due to the relationship between energy regulating homrones, obesity, and weight loss.

3.3.3 Energy Regulating Hormones

Energy regulating hormones show a variety of responses to nutritional intake. The adipose tissue derived hormone adiponectin showed a significant improvement in adiponectin concentration following a comprehensive multidisciplinary approach towards nutrition, employing whole grains, mono and poly unsaturated fats, and a balanced macronutrient intake (Esposito et al., 2003). Other hormones respond directly, both acutely and chronically, to total energy intake as well to the quality of macronutrients.

Post prandial increases in insulin and glucose stimulate the release of leptin (Barkoukis et al., 2007). As a result, the consumption of low glycemic index carbohydrates and their impact on leptin have been studied extensively, with the majority of studies showing that

low glycemic index meals result in a post prandial environment that is favorable to satiety and which increases leptin post prandially (Barkoukis et al., 2007; Bouche et al., 2002; Ebbeling et al., 2012; Niwano et al., 2009).

The benefits of increased feeding frequency can be impacted by the macronutrient content of meals, in particular when considering the appetite stimulating hormone ghrelin. It is well established that the type of macronutrient ingested dictates the magnitude of ghrelin suppression (Erdmann et al., 2004; Overduin et al., 2005; Tannous dit El Khoury et al., 2006) where carbohydrates demonstrate the greatest satiety, followed by protein and fat respectively (Tannous dit El Khoury et al., 2006). Ingestion of carbohydrates and proteins decreases ghrelin by approximately 70% during the post prandial period, while fats result in an approximate decrease of 50% (Bowen et al., 2006). The higher concentration of ghrelin associated with dietary fat intake is one of the proposed mechanisms of weight gain related to high fat diets due to the reduced humoral signal to consume additional calories (Tannous dit El Khoury et al., 2006). Therefore, meals which contain higher protein or complex carbohydrates ingested at regular intervals have been shown to maintain the post prandial elevation of ghrelin, potentially assisting in the inhibition of additional feeding and the maintenance of diet adherence.

A low-glycemic index diet has also been shown to reduce the inflammatory adipokine TNF-α in older, obese adults and it is believed that the normalization of plasma glucose resulting from a low GI diet can help halt the cycle of hyperglycemia, which contributes

to insulin resistance, adipose tissue dysfunction, and pro-inflammatory cytokine production (Kelly et al., 2011). Researchers confirmed that a low glycemic index diet improved glucose tolerance, and that a low-GI diet can reduce the inflammation that is associated with obesity (Kelly et al., 2011). These findings are supported by longer-term dietary interventions, which suggest that carbohydrate intake modification may influence the protein or mRNA expression of inflammatory markers in adipose tissue (Kirwan et al., 2001). Of particular significance in prescription of diet is that increasing age leads to an exacerbated response of the inflammatory cytokine TNF-α to hyperglycemia and hyperinsulinemia resulting from high glycemic index carbohydrates, which has been shown to reduce insulin sensitivity (Kirwan et al., 2001). Therefore the relevance of the low GI dietary approach for older individuals becomes an important consideration during the design of dietary restrictions for overweight and obese populations (Kirwan et al., 2001).

Based on this promising evidence, future studies should investigate the impact of low-GI foods, frequent feeding and a balanced macronutrient intake on weight loss, long term health, and obesity related energy regulating hormones.

3.3.4 Chapter 3 Summary

In summary, the evolution of dietary protocols aimed at weight loss has undergone a variety of iterations since its initial mainstream adoption over five decades ago. Countless dietary approaches have since been developed, which have yielded significant insights into strategies involving various caloric intakes, macronutrient ratios and timing of food intake. These approaches have shown both benefits and risks for individuals, and in some cases have yielded significant weight loss while also constituting significant health risks (Miller et al., 1997). Other approaches have shown improvements in body composition, while demonstrating significant long term health benefits relevant to overweight and obese populations seeking meaningful outcomes from weight loss (Miller et al., 1997). The current study has adopted the approach of utilizing a moderate calorie restriction focused on reduced carbohydrate intake in the form of low GI and high fiber sources, coupled with a low saturated fat intake and characterized by frequent feedings. Significant work is still required to determine more refined dietary approaches, in particular the development of strategies that lead to long term weight loss, and of how these strategies can impact energy regulating hormones in an overweight and obese aging male population.

3.4 Weight and Health Management through Diet & Exercise

There is a growing understanding in the field of health and wellness that even small amounts of weight reduction can lead to increased health benefits (Bajer et al., 2015; Herring, Wagstaff, & Scott, 2014; Mansoor et al., 2016; Stuart et al., 2016). A weight loss of 10% is associated with marked reductions in the risk for chronic diseases associated with obesity (Christiansen et al., 2010). As a result, health practitioners are promoting small and gradual change to lifestyle, including the addition of exercise and improving eating habits. Safer et al concluded that those who do not combine a restrictive diet with an exercise routine as in, they only participate in one or the other tend to increase the amount of weight lost for the first two years, but decrease weight maintenance after three to five years versus individuals who incorporated both exercise and diet together into their lifestyle (Safer, 1991).

Even when effective diet and exercise approaches are employed adherence remains a challenge. The application of behaviour change theory (BCT) has been shown to improve the effectiveness of exercise and diet interventions in obese and overweight individuals. In a meta-analysis, Olander et al. aimed to identify which BCTs increase individual's self-efficacy and physical activity behaviour of obese adults (Olander et al., 2013). They found that the BCTs that were associated with significant increases in these variables included; action planning, reinforcing of effort or progress towards behaviour, and provided instruction. It appears that some BCT approaches were more effective with

obese populations than others therefore it was concluded that to develop effective lifestyle interventions it may be important to consider tailoring intervention techniques to this population (Olander et al., 2013). These approaches include that goal setting, compliance tracking and logging of food intake and exercise participation are effective means at improving healthy lifestyle adherence (Samdal, Eide, Barth, Williams, & Meland, 2017). Additionally, the degree of support provided to an individual dictates weight loss success (Conn, Hafdahl, Phillips, Ruppar, & Chase, 2014). Supervised exercise complimented with generic nutrition advice, including information on weight loss delivered via booklets, brochures, weight loss manuals, or even by a one-time personal session with a dietitian, did not result in successful weight loss (Conn et al., 2014). It appears that exercise and diet require regular monitoring and ongoing support, as unsupervised education results in negligible outcomes with respect to weight loss as compared to higher attention interventions (Franz et al., 2007; Herring, Wagstaff, & Scott, 2014; Yoshida et al., 2010). In a systematic review by Samdal et al. two theoretical themes emerged of importance in the maintenance of lifestyle change; BCTs facilitating behaviour self-regulation, including skills and functional aspects of behaviours ("how to"), combined with a communication style that addresses the underlying nature of motivation ("the why") in order to maintain the new behaviour over time (Samdal et al., 2017). It was highlighted that these perspectives are not opposites, but complement each other. Without the first, there would be lack of competence. Without the second, there is lack of meaning, value, and satisfaction of psychological

needs. Therefore addressing behaviour change as part of a diet or exercise intervention is an important aspect of any intervention in order to maintain positive behaviour over time (Samdal et al., 2017). The current study employed several of these established BCT approaches to ensure adherence and compliance in the exercise and diet interventions.

Those following a moderate diet in combination with exercise have the best results, with more weight loss occurring after two years than through dieting alone. Those who continue to exercise regularly have the best weight loss maintenance after six years (Safer, 1991). In one study completed by Katahn et al., forty-four people who were considered massively obese (approximately 82.5% over their ideal weight) were administered a six month treatment program which included guidance in nutrition and reversing undesirable eating habits, along with information pertaining to a physically active lifestyle (Wallston, McMinn, Katahn, & Pleas, 1983). Results demonstrated that participants lost 28.1 pounds during the treatment and gained other significant health benefits such as a reduction in blood pressure and increased cardiorespiratory endurance (Wallston et al., 1983). This behavior education/modification technique of combined diet and exercise was considered successful, as long-term follow up results showed that twelve to eighteen months later, the majority of subjects involved were able to maintain the weight loss (Wallston et al., 1983). The researchers found that the combination of both diet and exercise was important as those who only followed the diet modification regained at least 40% of the weight they had lost during the treatment (Wallston et al., 1983). In another study completed by Svendsen, Hassager, and Christiansen (1994),

half of the participants followed a moderate energy restriction diet of 1,200 calories, and the other half followed an exercise routine along with a 1,200 calorie diet. With the diet alone, participants maintained a 6.6 kg weight loss after nine months. Participants who followed the diet and exercise routine, in contrast, maintained a weight loss of 10.6 kg. Previous research has demonstrated that using dieting techniques alone has not shown conclusive efficacy. Therefore, it has been proposed that in order to successfully lose weight and maintain weight loss, multiple lifestyle changes, including both diet and physical activity levels, must occur (Svendsen, Hassager, & Christiansen, 1995). There are more effective means of exercise than others to improving health and fitness, and the application of these prescription principles may be a means to improve the outcomes of future weight loss studies.

The beneficial impact of exercise on weight loss becomes more apparent when investigating its effectiveness in combination with diet. Individuals show greater long-term weight loss with diet and exercise in combination as compared to either exercise or diet in isolation (Franz et al., 2007). Furthermore, the combined approach of diet and exercise indicates that individuals maintain weight loss for longer periods of time as compared to the use of weight reducing diet alone (Curioni & Lourenco, 2005). Reduction of weight by as little as 10% is associated with significant health benefits for individuals, particularly when that weight loss is the result of decreased adipose storage in the visceral compartment (Christiansen et al., 2010).

As obesity rates continue to increase, it is clear that a better understanding of the impact of diet on weight loss is required. Studies that implement dietary restrictions without the incorporation of exercise regimens have not provided strong evidence for long term weight loss within obese patients (Franz et al., 2007). In addition, more long-term studies using moderate energy restriction diets that have been shown to benefit clinically significant outcomes are necessary (Mancini, Filion, Atallah, & Eisenberg, 2016). While weight loss can average up to 1.5-2.5 kg/week on very low calorie diets, there is mounting evidence to suggest that 0.5-1.0 kg/week is a safe and maintainable weight loss goal (Weinsier, Wilson, & Lee, 1996). Moderate energy restriction diets can lead to this degree of weight loss, and were found to be easier to adhere to (Wadden et. al, 1994). Therefore, moderate energy restriction which accounts for individual differences in energy requirements based on one's age, sex, and physical activity level should be considered as an effective and safe approach for those seeking weight loss (Frost, 2007).

Exercise and physical activity assist in controlling obesity, and can significantly reduce the risk of developing co-morbidities associated with excess adiposity (Okay, 2009). However, results have varied as to whether exercise is recommended for use in weight loss on its own (Wing, 1999, Ross, Freeman, &Jannsen, 2000, Sopko et. al, 1995, & Egger et. al, 2008). When aerobic training is compared to strength training, subjects in strength training groups generally do not decrease their body weight or fat free mass but have significant decreases in percentage of body fat, while participants in aerobic training groups tend to have decreases in body weight and fat free mass, but no

differences in percentage of body fat (Ballor, 1996, &Geliebter et. al, 1997). Body composition is not the only clinically relevant end point and research into the effectiveness of exercise training should include clinically relevant biomarkers into their outcome measures (Okay et. al, 2009).

3.4.1 Chapter 4 Summary

Previous studies suggest that a one dimensional approach to weight loss has not been effective (Tyler, Johnston, &Foreyt, 2007). It is recommended that people aim to lose weight by focusing on lifestyle modifications in diet and exercise to promote weight loss maintenance (Tyler, Johnston, &Foreyt, 2007). Individuals who are given education and training in moderate energy restriction diets in combination with exercise routines have shown the best weight loss management over six year periods (Safer, 1991). Adopting lifelong habits conducive to weight control and overall health rather than temporary measures for weight loss should be emphasized in patients seeking a long term weight loss solution (tyler, Johnston, &Foreyt, 2007). For these reasons, the current study compared Diet + Exercise to Diet Alone to determine their various impact on weight loss, health outcomes and energy regulating hormones in overweight and obese aging males.

3.5 Role of Energy Regulating Hormones in Obesity and Weight-loss Through Diet and/or Exercise

Exercise and dietary intervention effectiveness has typically involved a general assessment of anthropometric and body composition measures. The current study acknowledges the relevance of weight loss and changes in body composition due to diet and exercise and expands on these outcome measures to include the assessment of specific molecular health variables. Molecular measures including cholesterol, blood glucose and triglycerides have been well established biomarkers of health associated with diet and exercise interventions (Bravata et al., 2003; Bueno, de Melo, de Oliveira, & da Rocha Ataide, 2013; Mansoor et al., 2016), however, there has been limited investigation as to the impact of these interventions on hormones associated with body composition, metabolism and food intake (Simpson & Singh, 2008).

The classification of hormones as energy regulating has traditionally been reserved for those hormones which control appetite through the promotion or inhibition of energy intake (Williams 2016). In the current study, the definition of energy regulating hormones has been expanded to not only include those hormones considered to be responsible for appetite regulation, namely leptin and ghrelin, but also include hormones involved in metabolism; specifically, those impacted by obesity that have been shown to be altered by exercise and diet. These candidate hormones include adiponectin, TNF-α and testosterone.

The following chapter will discuss the interplay of these hormones with diet and exercise and their relevance to the current study population. For example, adiponectin is inversely associated with obesity (S. Bluher et al., 2014; Boudou, Sobngwi, Mauvais-Jarvis, Vexiau, & Gautier, 2003; Bruun, Helge et. Al 2006; Christiansen et. Al 2010; Esposito et al., 2003; Fatouros et al., 2005; Giannopoulou et al., 2005; Golbidi & Laher, 2014; Hulver et al., 2002) while leaner individuals demonstrate elevated concentrations of adiponectin that are believed to improve insulin sensitivity and metabolism (Weyer et al., 2001). TNF-α is positively correlated with degree of adiposity, inversely associated with insulin sensitivity and is believed to down regulate adiponectin (Hivert et al., 2010; Hotamisligil, Arner, Caro, Atkinson, & Spiegelman, 1995). Specifically, the visceral fat depots, characteristic of overweight and obese men, have been shown to exhibit higher TNF-α concentration (Clement et al., 2004). Appetite regulating hormone leptin shows a strong positive association with degree of adiposity and in animal models has been considered to control long term energy intake (Bouassida et al., 2010). Ghrelin, a gut derived peptide hormone, controls short term regulation of energy intake and shows a subsequent inverse relationship with obesity and increases during weight loss in an attempt to promote increased food intake and weight regain (Foster-Schubert et al., 2005). Lastly testosterone, which is has shown a reciprocal relationship with obesity status in men and decreases with age, is involved with lipolysis and muscle anabolism, two important outcome variables of the current study (Camacho, 2013). Additionally, testosterone has been shown to be improved during high intensity resistance training

protocols like those employed in the current study (Hakkinen et al., 1988a; Hakkinen et al., 1988b; W. J. Kraemer et al., 1999; Marx et al., 2001; Staron et al., 1994) and preferentially reduce visceral fat (Camacho et al., 2013; Tajar et al., 2012).

3.5.1 Adiponectin

Adiponectin is an adipose tissue derived adipokine. Adiponectin was independently characterized in 1995 and 1996 by four groups using different methods, and given alternative names of apM1 (adipose most abundant gene transcript 1), Acrp30 (adipocyte complement-related protein of 30 kDa), adipoQ, and GBP28 (gelatin binding protein of 28 kDa) (Kershaw & Flier, 2004). Adiponectin is a protein hormone that modulates a number of metabolic processes, including glucose regulation and fatty acid catabolism (Chandran, Phillips, Ciaraldi, & Henry, 2003). This hormone plays an important role in the suppression of metabolic illnesses that can result in type 2 diabetes, obesity, artherosclerosis, non-alcoholic fatty liver disease and an independent risk factor for metabolic syndrome (You, Arsenis, Disanzo, & Lamonte, 2013). Although adiponectin is exclusively secreted from adipose tissue into the blood stream, and is abundant in plasma relative to many hormones, circulating concentrations are inversely correlated with body fat percentage in adults (Kershaw & Flier, 2004). There appears to be a gender specific difference in circulating levels between men and women, with females displaying a higher basal concentrations than males. As stated, adiponectin is

inversely associated with insulin resistance and as a result, is markedly lower in diabetics than non-diabetics. However, weight reduction can increase levels in this population and others (Chandran et al., 2003).

Adiponectin is found in circulation in several multimeric forms, which have different physiological actions (Waki et al., 2003; Wang et al., 2006). These include High, Medium and Low–molecular weight (HMW) adiponectin. It is believed that HMW adiponectin is the biologically active form and is a stronger predictor of metabolic parameters then total adiponectin (Hara et al., 2006). Several studies have reported an association between HMW adiponectin and insulin sensitivity (Bobbert et al., 2005; Lara-Castro, Luo, Wallace, Klein, & Garvey, 2006), however, whether HMW is a stronger predictor of insulin sensitivity than total adiponectin is still debated (Bluher et al., 2006; Christiansen, Paulsen, Bruun, Pedersen, & Richelsen, 2010).

Changes in the adiponectin multimeric complexes have shown varied responses to diet-induced weight loss (Polak et al., 2007). It is unknown whether this heterogeneity in the research is due to unexplained biological actions of adiponectin or methodological challenges with the small number of studies investigating adiponectin isoforms during weight loss. Of relevance to the current study, Bluher et al. did not detect any clinically significant difference between HMW adiponectin and total adiponectin at predicting insulin sensitivity and metabolic variables following an exercise treatment program (Bluher et al., 2006). In agreement, Christiansen et al. found that changes in the three

adiponectin complexes were comparable in all groups undergoing an exercise and diet intervention (Christiansen et al., 2010). Therefore, based on the heterogeneity in the research, the current investigation did not investigate these different isoforms but instead relied on the assessment of total adiponectin.

Adiponectin exerts itself centrally via the brain in conjunction with its upstream partner leptin (Kershaw & Flier, 2004). Adiponectin binds to its own specific receptors, which are inversely correlated with insulin. In animal models, these receptors are found in lower numbers in the skeletal muscle and adipose tissue of diabetic mice (Yamauchi et al., 2003). Investigations into varying degrees of glucose tolerance demonstrated that hypo-adiponectinemia is strongly associated with insulin resistance (Weyer et al., 2001). Adiponectin replacement therapy has been shown to dramatically reverse insulin resistance and glucose intolerance in obese, diabetic mice (Arita et al., 2012) and in adiponectin-knock out mice (K. Maeda et al., 2012). Adiponectin replacement therapy for humans has not yet been studied, and current methods to increase circulating adiponectin levels involve patient lifestyle intervention. Simple lifestyle interventions aimed at decreasing excess body fat and restoring a healthy body weight have been shown to be effective at increasing circulating levels of adiponectin and improving insulin resistance (Yang et al., 2001). This indicates that lifestyle change is an appealing, safe and long term solution to controlling the morbid effects of hypoadiponecetinemia.

3.5.1.1 Adiponectin and Obesity

Despite being produced by adipose tissue, adiponectin concentration is inversely correlated to body fat and is lower in obese patients as compared to normal weight individuals (Esposito et al., 2003). The mechanism responsible for this down regulation in the obese has not been fully elucidated. It could be assumed that increased volumes of adipose tissue would be related to increased adipokine production; however, this is not the case with adiponectin.

Although some studies have not shown a significant change in circulating adiponectin levels in obese subjects (Hotta et al., 2001), research indicates that following weight loss, adiponectin concentration is improved significantly and demonstrates an inverse relationship with circulating leptin as compared to pre-weight loss values (Calvani et al., 2004). Reports investigating the magnitude of this relationship have shown that weight loss influences leptin to a greater degree than adiponectin (Shand, Scott, Elder, & George, 2003). Both are strongly correlated to the degree of adiposity and its location in the body, especially the visceral and subcutaneous abdominal deposits (Shand et al., 2003). Furthermore, hypoadiponectinemia is associated with hyperinsulinemia and is an independent risk factor for type 2 diabetes (Lindsay et al., 2002; Spranger et al., 2003).

Alterations in adiponectin pulsatility may also be associated with the Hypothalamic-Pituitary Axis (HPA). The action of these counter regulatory hormones has been shown to be over active in obese individuals, potentially limiting adiponectin release (Rosmond & Bjorntorp, 1998). Furthermore, it has been hypothesized that swollen fat cells produce and secrete quantities of the inflammatory cytokine TNF-α, which interacts with adiponectin by mutually inhibiting each other's production in adipose tissue (K. Maeda et al., 2012).

Adiponectin has several specific roles within the body, one of which is its effect on endothelial cell function. Adiponectin has also been shown to reduce the expression of adhesion molecules in these endothelial cells, and results in an anti-inflammatory response by decreasing cytokine production from macrophages (Salmenniemi et al., 2004). It is well established that adiponectin promotes insulin sensitivity (Yang et al., 2001) and that circulating concentrations have been found to decline concurrently with the development of insulin resistance. Additionally, and of relevance to the current study, adiponectin decreases in obese middle-aged subjects to a greater extent than in younger, leaner individuals (Hotta et al., 2001).

3.5.1.2 Adiponectin and Exercise

Exercise has historically been used as a tool for sport performance or weight loss, However, its role in improving health status is now broadly recognized. Individuals

suffering with illnesses ranging from diabetes to cardiovascular disease are universally encouraged to engage in regular physical activity as part of their treatment (Kaur, 2014). With this new acceptance in the medical community comes confusion regarding the efficacy of different modes of exercise. It is apparent that the medical community will require validated exercise and nutrition prescriptions to ensure health benefits for patients.

The ability of exercise to alter adiponectin has been the focus of several studies (Boudou et al., 2003; Christiansen et al., 2010; Dutheil et al., 2010; Esposito et al., 2003; Hulver et al., 2002; Ryan et al., 2003; Yatagai et al., 2003). Studies have used various modalities, frequencies and intensities of exercise in a variety of populations. To date, however, there is a relatively small amount of research using overweight and obese aging males (Simpson & Singh, 2008).

The studies reported in the adiponectin literature thus far have shown inconsistency, with some showing that plasma adiponectin levels can increase (Saunders et al., 2012b), remain the same (Yatagai et al., 2003), or decrease (Christiansen et al., 2010) in response to exercise. Yatagai et. al attempted to elucidate the effect of exercise on adiponectin by controlling for weight reduction, and by using an active cohort who did not experience a decrease in body fat (Yatagai et al., 2003). This approach, although effective for controlling weight loss, lacks the pragmatic nature of evaluating adiponectin response to exercise interventions due to its well established relationship with increased body fat and reduced insulin sensitivity. Therefore, investigators must take a more practical approach to the impact of lifestyle on adiponectin including both diet and exercise whenever

possible. Both diet and exercise behaviors have been shown to exhibit the most robust decreases in body fat and increases in adiponectin when used in tandem. (Simpson & Singh, 2008).

In a well-designed lifestyle intervention undertaken by Faturouros et. al, adiponectin increased in response to diet and exercise in elderly individuals (Fatouros et al., 2005). Specifically, these participants demonstrated an increase in adiponectin in response to the exercise prescription in a dose response manner. These results have been mirrored in a recent study using mice, suggesting that there is a dose effect for exercise training intensity (Garekani et. al 2011). Exercise intensity may be an important factor when investigating the adiponectin response to physical activity. Similarly, when investigating non-diabetic obese adults, nineteen weeks of diet and exercise showed an improvement in total body fat, visceral fat, and insulin resistance as well as increased adiponectin (Shadid et al., 2006). Of the adipokines measured, only adiponectin was consistently related to insulin sensitivity and body fat distribution (Shadid et al., 2006). Conversely, resistance training was employed for a span of twelve weeks with obese male subjects. Exercise training was conducted using a progressive training model that increased intensity over the intervention relative to the individual's baseline strength tests (Klimcakova et al., 2006). After training, total body mass and adiponectin remained the same even in the presence of improved insulin resistance and reduced leptin. It is possible that the small sample size of only twelve individuals was an explanation for the lack of change in adiponectin (Klimcakova et al., 2006). Furthermore, as adiponectin appears to

follow a dose response, the progression of exercise which began with a single set for each exercise may not have been sufficient to result in a significant training effect. Similarly, in obese but elderly men and women, twelve weeks of aerobic training improved overall fitness, insulin resistance and reduced fat mass in both the subcutaneous and visceral regions. Humoral markers, including leptin, reduced; however, there was no statistically significant change in adiponectin (O'Leary et al., 2006).

Adiponectin has also been shown to decrease in response to exercise, even when suitable intensity is achieved (Christiansen et al., 2010). Christiansen et al., found a decrease in adiponectin during weight loss resulting from exercise by using a randomized sample of overweight and obese individuals on a hypocaloric diet who engaged in high intensity aerobic exercise (Christiansen et al., 2010). It was shown that not only was significant weight loss achieved of greater than 10% of body weight, but there was a significant decrease in adiponectin as a result of exercise (Christiansen et al., 2010). This decrease in adiponectin was not seen in the diet only group of the study, indicating that there is an exercise-mediated effect on adiponectin via a mechanism that has not yet been elucidated.

3.5.1.3 Nutrition and Adiponectin

In a review of popular diets by Freedman et al., it was demonstrated that only 10% of dieters maintain their specific “popular diet” program of choice (Freedman et al., 2014). This high attrition rate coupled with the confusion and broad definition of nutrition

recommendations in popular media warrants important attention while developing dietary protocols, particularly where adiponectin is concerned.

Esposito et al's study (2003) showed a significant improvement in adiponectin concentration following a comprehensive multidisciplinary approach towards lifestyle including structured exercise and nutrition guidelines proposed by the Mediterranean Diet (Esposito et al., 2003). Results demonstrated an increase in adiponectin and a reduction in markers of vascular inflammation and insulin resistance (Esposito et. al 2003). Additionally, adiponectin increased in response to a diet and exercise intervention in subjects with metabolic syndrome (Dutheil et al., 2010). It was highlighted that although this intervention was successful, compliance to the new healthy lifestyle was not optimal and the intervention still constituted significant challenges for the clinical population, who may not be motivated to modify diet and incorporate exercise into their daily schedule (Dutheil et al., 2010). The need for rigorously designed investigations that involve a multidisciplinary approach and which utlize effective and documented interventions would help clarify the potential impacts of diet on adiponectin in overweight and obese cohorts. These interventions must utilize techniques which are not only scientifically founded, but are pragmatic enough in application to be useful to the medical community and general population in day to day life.

3.5.1.4 Summary of Adiponectin

Adiponectin and its relationship to obesity and insulin resistance has been extensively investigated (Kershaw & Flier, 2004; Chandran et al., 2003). However, the way in which weight loss achieved through exercise and diet impacts adiponectin remains unclear (Boudou et al., 2003; Christiansen et al., 2010; Dutheil et al., 2010; Esposito et al., 2003; Hulver et al., 2002; Ryan et al., 2003; Yatagai et al., 2003). Recent investigations have provided greater insight into the response of adiponectin to various modalities and intensities of physical activity, indicating that the nature of exercise intervention is a relevant factor. Additionally, a greater understanding of the impact of diet on adiponectin, including the approach utilized in the current investigation shows that weight loss achieved through caloric restriction yields positive results (Esposito et. al 2003). Therefore, the goal of the current study is to determine the influence of supervised resistance training and a hypocaloric macronutrient scheduled diet as compared to a hypocaloric macronutrient scheduled diet alone on fasting adiponectin concentration in overweight and obese men ages 35-55.

3.5.2 TNF-α

Tumor necrosis factor alpha (TNF-α), a proinflammatory cytokine, is expressed and secreted into circulation by a variety of cells (Mohan et al., 2002). TNF-α has been

shown to be positively associated with adiposity (Warne, 2003), and significantly higher levels of circulating TNF-α have been found amongst obese individuals compared to normal weight individuals (Kern, Ranganathan, Li, Wood, & Ranganathan, 2001). TNF-α gene expression is greater in the adipose tissue of obese individuals then in normal-weight individuals and, more specifically, this expression is much higher in visceral adipose tissue than subcutaneous adipose tissue (Kern et al., 2001). In fact, among obese individuals, macrophage-infiltrated visceral fat is one of the primary sites of TNF-α production (Clement et al., 2004). TNF-α is also positively correlated with the degree of obesity and the level of hyperinsulinemia (Hotamisligil et al., 1993a; Hotamisligil et al., 1995). Diabetic patients have also been shown to have a much higher level of TNF-α activity both in circulation and in skeletal muscles (Saghizadeh, Ong, Garvey, Henry, & Kern, 1996) Accumulating data suggests that the prevalence of insulin resistance increases concordantly with circulating TNF-α concentrations in the blood, and is inversely associated with circulating adiponectin (Hivert et al., 2010).

3.5.2.1 TNF-α and Obesity

In obese individuals there are marked increases in the secretion of pro-inflammatory adipokines like TNF-α, and a decreased production of anti-inflammatory adipokines such as adiponectin (de Carvalho, Colaco, & Fortes, 2006). This change in adipokine balance is a key component of pathogenic metabolic and immune responses and impacts

angiogenesis, blood pressure and lipid metabolism, all of which are linked with cardiovascular disease (de Carvalho et al., 2006). Accumulating data suggests that during high lipolytic activity, more fatty acids are released from visceral adipose tissue than subcutaneous adipose tissue (Katsuki et al., 2003b). This is may be due to the higher metabolic rate and increased susceptibility of lipolytic enzymes in visceral adipose tissue (Wajchenberg et al., 2002). TNF-α has been shown to stimulate fatty acid uptake while simultaneously attenuating fatty acid oxidation (Wajchenberg et al., 2002). During stages of adiposity development it has been theorized that adipocyte degeneration begins with a significant increase in TNF-α levels (Chaldakov et al., 2003). Therefore, persistent chronic inflammation and increased levels of TNF-α play a role the development of obesity and obesity-related commodities (Chaldakov et al., 2003).

3.5.2.2 TNF- α and Exercise

Over the past ten years, a growing body of evidence has shown that TNF-α is positively associated with obesity status and inversely associated with physical activity (Plaisance & Grandjean, 2006b). Research has also shown that regular physical activity can attenuate, or even ameliorate, this association with obesity and its subsequent negative health effects (Mattusch et al., 2000). For example, it has been shown that physical activity increases insulin sensitivity by suppressing the reduction of resting levels of TNF-α,

which in turn augments the production/secretion of insulin sensitizers like adiponectin (Kasapis & Thompson, 2005). In addition, overall exercise induced weight loss is effective in reducing circulating concentrations of inflammatory markers, where even acute episodes of physical activity can have strong positive influence (Mattusch et al., 2000). Weight loss through exercise decreases the volume/number of adipocytes as well as the number of endothelial and macrophage cells that produce TNF-α (Hotamisligil et al., 1993b). However, very little is currently known about which modes of exercise are the most effective at attenuating/ameliorating chronic inflammation due to biomarkers such as TNF-α. Therefore, investigations such as this thesis, are important to further understand the role that diet and exercise plays in body fat management and the related management of obesity related health risks. In fact, a study by Timmerman et al. revealed that the combination of a moderate to high intensity aerobic and resistant training program was able to significantly reduce TNF-α (Timmerman, Flynn, Coen, Markofski, & Pence, 2008). The exercise program was twelve weeks (three days/week) in duration, and consisted of 20 min of aerobic exercise at 70–80% of heart-rate reserve, and resistance exercise training (eight exercises, two sets) at 70–80% of maximal effort (Timmerman et al., 2008). Interestingly, a study by Balsucci et al. found that resistance training is only able to reduce circulating TNF-α in combination with aerobic exercise (Balducci et al., 2010). In this study 23 participants, underwent 40 min of aerobic exercise at 70-80% Vo2 max, and 20 min of resistance training at 80% of their maximum effort. Neither low intensity aerobic exercise alone or high intensity aerobic

exercise alone were able to effect TNF-α levels. This would suggest that resistance training may be the more important mode of physical activity to help reduce the chronic inflammation caused by TNF-α in the obese. Resistance training may also be so effective in attenuating TNF-α that even a change in weight or body composition is not necessary. Eleven participants underwent a twelve week resistance training program (three sets, 8-12 repetitions, for 10 exercises, three times per week), and although they did not see any significant changes in body composition, TNF-α was significantly reduced (Phillips et al., 2012). This is a novel finding which supports a growing body of literature which states that resistance training may have more physiological and lifestyle benefits then traditional aerobic exercise programs. This is especially true for those in aging populations, where muscle atrophy is a serious issue.

The reduction in muscle strength and endurance is one of the most deleterious effects on the quality of life for men (McGregor, Cameron-Smith, & Poppitt, 2014). It is believed that resistance training may offset TNF-α related chronic inflammation and muscle atrophy (Greiwe et al., 2001). Muscle TNF-α mRNA and protein levels significantly decreased in those elderly individuals who undertake resistance training exercise as opposed to those who do not (Greiwe et al., 2001). These findings also later supported by a study from Bruunsgaard et al., which revealed that baseline TNF-α was inversely associated with an increase in muscle strength after twelve weeks of resistance training (Bruunsgaard, Bjerregaard, Schroll, & Pedersen, 2004). Overall, recent studies have established that resistance training has significant benefits for building muscle strength

and assisting in weight management, especially for the aging population (Winett & Carpinelli, 2001). However, it would appear that resistance training may have a more direct impact on circulating TNF-α than aerobic exercise, which may also be independent of significant weight loss.

3.5.2.3 TNF-α and Nutrition

Obesity and insulin resistance are strongly associated with metabolic dysregulation and chronic inflammation (Kaur, 2014). A proper diet that maintains or decreases body weight may provide a strong stimulus for improving both issues (Dandona et al., 1998b). Although a reduction in body weight amongst obese individuals results in significant reductions in TNF-α production, and the amelioration of insulin resistance (Dandona et al., 1998b), very little is known about whether diet induced weight loss has the same positive influence on inflammation and circulating TNF-α (Dandona et al., 1998b).

A study by Moller et al. placed 42 obese men and women on an eight week diet, which resulted in a loss of body weight (~ 7 kg) and a reduction in circulating TNF-α (Moller et al., 2016). However, a study by Rosc et al., did not find any change in TNF-α for diet induced weight loss amongst morbidly obese men and women (Rosc et al., 2015). Although the investigators discovered significantly higher levels of TNF-α in the

morbidly obese subjects (BMI > 40 kg/m^2) compared to their normal-weight (BMI < 24 kg/m^2) subjects at baseline, there was not a significant change in TNF-α after a 9.4% reduction in body weight. Investigators hypothesized that the reduction in body weight may not have been great enough to elicit the restoration of normal adipocyte function. This would suggest that there is a specific set point regarding weight loss and the reduction in TNF-α production.

Investigations into the dietary approaches indicate that the macronutrient composition of food intake may be the critical factor regarding the attenuation/reversal of adipose tissue dysregulation (Cassani et al., 2015). A study by Cassani et al found that while circulating TNF-α was significantly reduced (25%) after 42 days on a low carbohydrate diet, those who also ingested 60g of flaxseed powder per day saw a much great reduction in TNF-α (46%) (Cassani et al., 2015). Although weight loss should eventually attenuate adipose tissue dysregulation, it would appear that the composition of one's diet could be more effective then weight loss in achieving this goal. Overall, diet induced weight loss plays an important role in circulating TNF-α, and there is a significant need to further investigate the impact of nutritional composition.

3.5.2.4 Summary of TNF-α

Adipose tissue clearly plays a critical role in the inflammatory process. The clinical objective of identifying lifestyle factors that may affect the obesity-immune system dynamic is therefore very important. Although physical activity and nutrition are very

well known lifestyle factors for weight loss/management, very little is currently known about how these factors influence the deleterious inflammatory profile for the overweight and the obese. Ultimately, both aerobic and resistance exercise may be effective in attenuating obesity related inflammation, in addition to having significant implications to preventing obesity. Mechanistic studies in humans demonstrate that moderate exercise exerts an inhibition of TNF-α (N. Maeda et al., 2002). Moreover, indirect anti-inflammatory effects of exercise may be mediated via improvements in body composition. It should be emphasized that physical activity and proper nutrition constitute a natural, strong, anti-inflammatory and metabolism-improving strategy with minor side effects. TNF-α may be an important co-factor to consider in response to the primary question of this thesis. The alterations in circulating adiponectin amongst obese individuals may also be directly associated with the expression/circulation of TNF-α (Rosmond & Bjorntorp, 1998). This hypothesis would suggest that TNF-α interacts with adiponectin by inhibiting both its production and secretion from adipose tissue (N. Maeda et al., 2002). Since adiponectin plays a role in both the attenuation of insulin resistance and inflammation it may be possible that the presence of TNF-α could potentially exacerbate these affects amongst obese males, while also negatively affecting the role adiponectin plays in the reversal of insulin resistance and inflammation during weight loss due to exercise. Therefore, the current investigation aims to determine the influence of supervised resistance training and a hypocaloric macronutrient scheduled

diet versus a hypocaloric macronutrient scheduled diet alone on TNF-α in overweight and obese men ages 35-55.

3.5.3 Appetite Regulating Hormones

The control of food intake is complex and consists of neural and hormonal signals between the pancreas, gut and central nervous system. In additional hormones related to adipose tissue volume, as well as individual genetic factors are involved with energy regulation and the signal to consume nutrients. These hormones act within key brain areas such as the hypothalamus and brainstem which adjusts food intake accordingly (Simpson & Bloom, 2010).

3.5.3.1 Leptin

Leptin, is one of the first identified adipocytokines, and is produced in proportion to body fat. Leptin demonstrates higher concentrations in obese individuals, and is associated with energy balance, appetite and adiposity status in both animals and humans (Bouassida et al., 2010). The role of leptin was first discovered in the *ob/ob* mouse model (Campfield, Smith, Guisez, Devos, & Burn, 1995). The gene coding for leptin, having been mutated in this animal model, resulted in an obese phenotype. This work eventually led to an understanding of leptin's involvement in appetite suppression (M. Bluher, 2013). Later studies demonstrate that the administration of recombinant

leptin reduces body weight by decreasing food intake and increasing energy metabolism in animals (Reseland et al., 2001).

Human studies investigating leptin have identified that obese individuals generally have high leptin concentrations (Teerds, de Rooij, & Keijer, 2011). Since leptin's primary function appears to be the suppression of hunger for body weight regulation, elevated leptin in the presence of obesity may indicate that a resistance to leptin is occurring (Thong, Hudson, Ross, Janssen, & Graham, 2000). The concept of leptin resistance has been supported by the administration of recombinant leptin in humans, which has led to weight loss and decreased food intake in only a small subset of obese patients with genetic leptin deficiency (Savage & O'Rahilly, 2002). Leptin has also been associated with insulin and insulin resistance in both animals and humans, and demonstrates a consistent relationship with improved insulin sensitivity during weight loss (M. Bluher, 2013).

3.5.3.1.1 Leptin and Obesity

Leptin concentration increases during weight gain and decreases during weight loss (Teerds et al., 2011). Leptin has also shown regionally specific expression, with subcutaneous adipocytes expressing greater concentrations when compared with visceral adipocytes (Taksali et al., 2008). It has been shown that the decrease in leptin associated

with visceral fat reflects an unfavorable metabolic profile characterized by higher insulin resistance and lower adiponectin (Taksali et al., 2008). These regional characteristics are of particular importance in the current study population who are characterized by greater visceral adipose deposits as compared to female and younger male populations (Fain et al., 2004; Polak et al., 2006).

In circumstances of weight loss, leptin concentration is reduced in proportion to weight loss. Although leptin concentration is diminished in weight loss, its anticipated inhibitory effect on satiety in humans does not consistently translate into reducing food intake, as will be discussed in the following sections (Bouassida et al., 2010).

3.5.3.1.2 Leptin and Exercise

Leptin has been shown to decrease in response to exercise. However, these findings are inconsistent. The majority of research indicates that exercise associated changes in leptin are in response to weight loss resulting from exercise, rather than in response to exercise itself (Ozcelik et al., 2004; Polak et al., 2006). Studies showing the independent effects of exercise on leptin involve various modalities and intensities of exercise, often in an uncontrolled setting, leading to uncertainties about the true impact of exercise on leptin.

In obese females, for example, leptin has been shown to consistently decrease after aerobic training. However, leptin remains strongly correlated to decreases in fat mass, and demonstrates no independent effect from exercise (Ozcelik et al., 2004; Polak et al.,

2006). Similar results have been shown in overweight men following a one year exercise program (Miyatake et al., 2004). These men had a reduced circulating leptin concentration in accordance with their percentage body fat. Again the investigators concluded that there was no independent effect on circulating leptin resulting from exercise (Miyatake et al., 2004). Older men, ages 65-78, were divided into one of four resistant training groups, consisting of a control group as well as a low, moderate and high intensity training group (Fatouros et al., 2005). It was found that measures of physical fitness improved in all exercise groups, as did anthropometric values including subcutaneous skinfold measures and BMI. The greatest decrease in leptin occurred in the highest intensity training group. However, that group also experienced the greatest decrease in body fat (Fatouros et al., 2005). The authors concluded that leptin may have a dose response to exercise. Due to the strong correlation with changes in body composition, however, it would appear that, similar to others, leptin decreases in proportion to weight loss.

In summary, exercise training has disparate effects concerning leptin concentration. Exercise training protocols that result in reduced fat mass are generally accompanied by lower leptin concentrations. Reductions in leptin levels have also been attributed to alterations in energy balance, insulin sensitivity and lipid metabolism. However, the majority of research indicates that leptin concentration is correlated to the amount of body fat the individual possesses. It is possible that the dose response regarding exercise intensity may elicit the independent leptin response as proposed by Fatouros (Fatouros et

al., 2005). Concurrently, the types of exercise and training programs must be carefully considered, and researchers should build on previous studies that focus on well designed exercise intervention research.

3.5.3.1.3 Leptin and Nutrition

The true impact of leptin on food consumption may be overestimated in overweight and obese individuals (Thong et al., 2000). Due to high levels of circulating leptin which occur in most cases of obesity in humans, as well as rodents fed a high-fat diet, it is likely that a state of leptin resistance is occurring (Thong et al., 2000). As a result, the effect of leptin on satiation may be minimal unless leptin sensitivity is improved through either weight loss or change in energy balance. It has been hypothesized that adipocytes can detect energy balance. Therefore, hypocaloric diets can be expected to demonstrate augmented leptin in overweight and obese individuals (Considine, 1997).

Post prandial increases in insulin and glucose stimulate the release of leptin (Barkoukis et al., 2007). As a result the consumption of low glycemic index carbohydrates and their impact on leptin has been studied extensively, with the majority of studies showing that low glycemic index meals result in a post prandial environment that is favorable to satiety and which increases leptin post prandially (Barkoukis et al., 2007; Bouche et al., 2002; Ebbeling et al., 2012; Niwano et al., 2009). In a long term study investigating moderately overweight men, a low glycemic index diet resulted in the improvement of blood lipid concentrations, reduced body fat and improved lean body mass (Bouche et

al., 2002). Leptin decreased in accordance with body fat, but food intake was not altered (Bouche et al., 2002). The role of leptin in humans appears to be very modest in adults who are overweight or obese. Although leptin concentration appears to be improved during hypocaloric diets that are low in fat and which consist of low glycemic index carbohydrates, leptin's strong relationship with adiposity status appears to be the determining factor in its circulating concentration.

3.5.3.1.4 Summary Leptin

Leptin is strongly correlated to body fat and is suppressed during weight loss in a variety of populations (Teerds et al., 2011). Leptin's role with respect to appetite suppression is well established in animal models, but elevated circulating concentrations in obese men and women indicates that leptin resistance occurs in humans (Thong et al., 2000). Diet and exercise have shown inconstant effects on leptin unless accompanied by a change in body fat mass, indicating that irrespective of how weight loss is achieved, leptin follows obesity status (Ozcelik et al., 2004; Polak et al., 2006). However, promising insights regarding the role of low glycemic diets indicate that a diet that controls for insulin response to feeding and which maintains glucose homeostasis results in beneficial changes with respect to both leptin and body fat in overweight and obese individuals (Barkoukis et al., 2007; Bouche et al., 2002; Ebbeling et al., 2012; Niwano et al., 2009). Consequently, the current investigation will determine the influence of supervised

resistance training and a hypocaloric macronutrient scheduled diet versus a hypocaloric macronutrient scheduled diet alone on leptin in overweight and obese men ages 35-55.

3.5.3.2 Ghrelin

Ghrelin is the only known circulating orexigen which is implicated in both the short term control of food intake and the long term control of body weight (Foster-Schubert et al., 2005). Circulating ghrelin has been shown to increase in response to weight loss resulting from hypocaloric diets, cancer cachexia, anorexia nervosa, and chronic failure of the heart, kidneys and liver (Foster-Schubert et al., 2005).

3.5.3.2.1 Ghrelin and Obesity

Body weight is maintained within a narrow, individualized range by a process known as "energy homeostasis" (Cummings, 2006). In an attempt to maintain body weight, hormones such as ghrelin are engaged to improve or reduce appetite in response to both caloric restriction, and caloric surplus, respectively (Cummings, 2006). Weight loss has been shown to trigger an increase in circulating ghrelin concentrations as part of an adaptive response to energy deficits (Crujeiras et al., 2010). The associated increase in ghrelin has been associated with changes in leptin which are diminished when levels drop in accordance with fat loss (Crujeiras et al., 2010). Furthermore ghrelin levels have

been shown to increase in response to resistance training and exercise to compensate for associated increases in energy expenditure.

Ghrelin is a meal patterning hormone which triggers acute food intake. Additionally, there is growing evidence which suggest that it plays a significant role in obesity. Circulating ghrelin consistently correlates negatively with measures of adiposity, and demonstrates low concentrations in overweight individuals (Cummings, 2006; Ravussin, Tschop, Morales, Bouchard, & Heiman, 2001; Tschop et al., 2001).

Ghrelin has been said to impact all aspects of energy regulation in order to achieve weight gain for the individual. This has been evidenced by the consistent increase in ghrelin during weight loss. Obese individuals who achieve a 5% decrease in body weight demonstrate significant increases in ghrelin (T. K. Hansen et al., 2002). It has been hypothesized that this relationship may not be entirely associated with adiposity, and instead may be linked to the nutrient restriction related to weight loss (T. K. Hansen et al., 2002).

3.5.3.2.2 Ghrelin and Exercise

Ghrelin has been shown to increase in response to weight loss achieved through exercise. However, physical activity has not consistently shown an independent effect on circulating concentration (Foster-Schubert et al., 2005; R. R. Kraemer & Castracane, 2007; Leidy et al., 2004; Schubert et al., 2014; Thomas et al., 2012; Ueda et al., 2009).

Exercise has been shown to acutely suppress post workout ghrelin. There appears to be a compensatory effect in ghrelin stemming from the increased energy expenditure resulting from exercise. Additionally, exercise may result in chronic changes in ghrelin due to the lower inhibitory effects of leptin associated with weight loss, and the increased energy demand from improvements in lean body mass (Schubert et al., 2014). It is well established that exercise protocols lead to food cravings and increased appetite due to the increased energy demands of these activities (Thomas et al., 2012)

Chronic changes in circulating ghrelin concentrations have not mirrored acute post workout responses. Leidy et al. demonstrated only a modest and non-clinically significant increase in ghrelin during twelve weeks of exercise training without changes in body weight for women (Leidy et al., 2004). Additionally, Foster-Schubert failed to show exercise-associated changes in ghrelin where increases in circulating concentrations were related to weight loss alone (Foster-Schubert et al., 2005). Conversely, a study by Markofski et al. showed the independent effects of exercise on ghrelin concentrations. This investigation showed elevated ghrelin when no significant changes in body composition had occurred, indicating that the change was related to the intensity of the exercise intervention (Markofski et al., 2014). One of the challenges with exercise intervention studies is monitoring adherence, especially during subject self-reporting (Wing & Phelan, 2005). In the aforementioned study, exercise participants were exercising unsupervised and at a self-selected intensity, which limits the reliability of the results due to self-reporting (Timonen et al., 2002).

A recent systematic review of the effects of exercise on appetite regulation indicates that what is currently missing are studies which investigate the impact of long-term (greater than six weeks) exercise on appetite-related hormones, and which determine how any changes observed relate to weight loss and prevention of weight regain in response to exercise in the obese population. We feel this study helps answer this gap in the literature.

3.5.3.2.3 Ghrelin and Nutrition

Diet and nutrition have a clear impact on ghrelin. Previous work has demonstrated that ghrelin suppression occurs post-prandially when specific ratios of macronutrients are consumed (Erdmann et al., 2004; Overduin et al., 2005; Tannous dit El Khoury et al., 2006). High protein diets have been shown to promote weight loss as compared with high fat diets. The suppressive effect of protein on ghrelin is considered to be an important factor in the success of high protein, hypocaloric diets (Bowen et al., 2006). Furthermore, due to a 3-4 hour feeding frequency, the diet protocol used in both groups of the current study was designed to reduce ghrelin concentration between feedings. This reduction was expected to take place in the presence of weight loss as well.

Ghrelin response to dietary restriction has shown conflicting results. However, studies which have employed nutrition protocols that control for timing and the macronutrient content of meals have better demonstrated a decrease in ghrelin, as they address post prandial responses by suppressing ghrelin release (Bowen et al., 2006; Bowen et al.,

2006). Specifically, carbohydrates demonstrate the greatest suppressive effect on ghrelin, followed by protein and fat, respectively (Erdmann et al., 2004; Overduin et al., 2005; Tannous dit El Khoury et al., 2006) The lack of ghrelin suppression demonstrated by fat intake is hypothesized as one of the causes of weight gain associated with high fat diets (Tannous dit El Khoury et al., 2006). Furthermore, diets which are higher in low glycemic index carbohydrates and lean protein sources have shown encouraging results with respect to weight loss (Ajala et al., 2013; Mancini et al., 2016; Nordmann et al., 2011; Rees et al., 2013; Sofi et al., 2008). It is likely that the reduction in ghrelin following the feeding of these nutrients helps with hunger during periods of weight loss and caloric restriction which typically results in increased ghrelin and subsequent hunger (Bowen et al., 2006). Therefore, ghrelin release appears to occur in response to the ingested macronutrients and, as a result, helps dictate subsequent hunger and food intake. Ghrelin also shows strong relationships with adiposity status in overweight individuals, and appears to respond acutely to weight loss specifically achieved through caloric restriction.

3.5.3.2.4 Ghrelin Summary

Ghrelin concentration is increased during weight loss in an attempt to maintain energy intake and preserve body fat stores (Cummings, 2006). This relationship has been demonstrated in a variety of populations, and is considered an important factor in weight maintenance and weight loss (Cummings, 2006; Ravussin et al., 2001; Tschop et al.,

2001). Ghrelin has not been shown to be effected by exercise itself, but rather through the weight loss achieved through increases in caloric expenditure (Foster-Schubert et al., 2005; R. R. Kraemer & Castracane, 2007; Leidy et al., 2004; Schubert et al., 2014; Thomas et al., 2012; Ueda et al., 2009). Nutrition has shown a much more consistent impact on ghrelin. Higher carbohydrate and protein intake, relative to fat intake, has shown a measurable reduction in circulating ghrelin concentration, as has frequent feedings every 3-4 hours (Bowen, Noakes, & Clifton, 2006; (Erdmann et al., 2004; Overduin et al., 2005; Tannous dit El Khoury et al., 2006). Ghrelin increases to encourage food intake with even small decreases in body fat, and therefore plays an important role in body weight regulation (T. K. Hansen et al., 2002). The current study investigates the response of ghrelin to both exercise and diet compared to diet alone in order to determine the ghrelin response to weight loss achieved through these approaches in aging overweight and obese males.

3.5.3.3 Insulin

Insulin is a peptide hormone produced by beta cells of the pancreatic islets and is an anabolic hormone whose functions are manifested during the fed state. Insulin is secreted in response to meals and acts on its key target tissues, skeletal muscle, liver, and adipose tissue, to stimulate the uptake of glucose and to store calories predominantly in the form of glycogen and fat. Circulating insulin also affects the synthesis of proteins in a wide variety of tissues (Kaur, 2014) and are proportional to degree of adiposity (Rocha et al.,

2011). Animal studies have shown that exogenous administration of insulin in rodents reduces food intake and body weight (Air, Benoit, Blake Smith, Clegg, & Woods, 2002). Insulin works to suppress food intake and maintain energy balance similar the adipokine leptin (Garcia-San Frutos et al., 2007). Insulin has been found to stimulate the synthesis and secretion of leptin from white adipose tissue through the adipoinsular axis (Kieffer & Habener, 2000). As insulin is increased during obesity, chronically high circulating concentrations of insulin can lead to insulin resistance (Adam et al., 2009). As a result it has been hypothesized that obesity is a product of insulin resistance and not the cause of insulin resistance (Morrison, Huypens, Stewart, & Gettys, 2009).

Insulin is believed to impact food intake through insulin receptors located in the central nervous system. It is well established that, in addition to a sufficient supply of insulin to the brain, insulin receptor function is vital for energy homeostasis (Figlewicz, 2003).

Insulin has been considered to be a potential regulator of leptin, because plasma insulin concentrations decrease during fasting and increase after refeeding in parallel with plasma leptin levels (Kolaczynski et al., 1996). Current evidence suggests that insulin plays a chronic role in the regulation of leptin gene expression and production by white adipose tissue and that hyperinsulinemia increases plasma leptin levels and gene expression in both rodents and humans (Kolaczynski et al., 1996). As fat stores increase, rising plasma leptin concentrations reduce insulin levels, in an attempt to direct less energy to the formation of adipose tissue. In the event that adipose stores diminish, falling plasma

leptin levels would permit increased insulin production, thereby resulting in the deposition of additional fat. Therefore, it has been hypothesized that leptin helps regulates insulin levels based on the extent of adiposity. This interplay with insulin is reciprocal in nature as part of a bidirectional adipoinsular axis (Kieffer, Heller, & Habener, 1996).

3.5.3.4 Glucagon-like Peptide-1

Glucagon-like peptide-1 (GLP-1), a 30-amino acid peptide hormone secreted from the L-cells of the distal ileum (Holst, Schwartz, Lovgreen, Pedersen, & Beck-Nielsen, 1983), GLP-1 is released into circulation in response to food intake in proportion to the amount of calories consumed (Verdich et al., 2001a). GLP-1 is lowest in the fasted state, while the concentration rises postprandially in response to feeding (Wadden et al., 2013).

GLP-1 binds to its own receptors that are present in a variety of tissues which help facilitate the glucose dependent release of insulin from the pancreatic beta-cells (Meier & Gressner, 2004), decrease appetite and decrease gastric motility (Wadden et al., 2013).

GLP-1 has been associated in many chronic metabolic diseases and thought to be involved in obesity as morbidly obese subjects demonstrate a decreased diurnal L-cell secretion (Holst et al., 1983). Fasting GLP-1 has shown inconsistencies in its relationship with obesity but has been found to be lower in obese diabetic patients as compared to healthy controls (Greenfield et al., 2009). Morbidly obese individuals have a lower postprandial secretion of GLP-1 that improves after weight loss (Naslund et al., 1998).

Although previous studies have suggested that obese individuals have a lower GLP-1 secretion as compared to lean individuals (Holst et al., 1983; Mannucci et al., 2000; Naslund et al., 1998; Verdich et al., 2001b). Research has shown no significant difference in fasting GLP-1 concentration between overweight/obese and normal weight subjects. Wadden et al. found that no significant relationship between baseline GLP-1 concentration and markers of adiposity including BMI and percent body fat in normal weight and obese 19-29 year old males (Wadden et al., 2013). In an attempt to determine the relationship between overfeeding and weight gain in this population it was found that the rise in GLP-1 concentration resulting from caloric challenge was independent of adiposity status in these normal weight and overweight/obese groups (Wadden et al., 2013). Gynoid obesity was the only measure of adiposity that was associated with a change in GLP-1 at baseline in the overweight/obese group. In general, women are more likely to have greater gynoid fat distribution, and having this distribution is thought to oppose cardiovascular diseases through more efficient fat storage/lipoprotein lipase functionality (McCarty, 2003).

As recent evidence suggests that GLP-1 is more closely related to caloric intake then adipose tissue the current study did not assess this energy regulating hormone however it is clear that GLP-1 plays a significant role in appetite regulation during periods of caloric restriction and overfeeding.

3.5.3.5 PYY

Peptide YY (PYY), a 36-amino acid appetite suppressing gut hormone, is secreted from the L-cells of the gastrointestinal tract. Circulating PYY increases satiety and decreases food intake via gut-brain communication (Batterham et al., 2002; Chaudhri, Small, & Bloom, 2006; Karra & Batterham, 2010), inhibits gastrointestinal motility (Imamura, 2002) and pancreatic hormone secretion (Pfluger et al., 2007; Yang, 2002). PYY plays an integral part in maintaining energy homeostasis (P. C. Konturek, Konturek, Czesnikiewicz-Guzik, Brzozowski, Sito, & Konturek, 2005b; S. J. Konturek, Konturek, Pawlik, & Brzozowski, 2004) but its role in obesity development and its relationship with adiposity has shown contrasting evidence (Boggiano et al., 2005; Cahill et al., 2013).

Appetite is an important factor in energy homeostasis and hormones including PYY significantly influences the regulation of body weight (Boggiano et al., 2005). Therefore investigating appetite regulating hormones, such as PYY, may provide valuable insight into the underlying mechanisms responsible for weight loss intervention effectiveness.

Animal studies have shown that PYY knockout mice developed significant hyperphagia (an abnormal increased appetite for food) and that that exogenous replacement of PYY significantly ameliorated this condition (Batterham et al., 2002; Batterham et al., 2003). These initial investigations indicated that PYY was inversely associated with obesity-related phenotypes (Batterham et al., 2002). These studies demonstrated that a deficiency

in circulating PYY could be a significant contributing factor toward the promotion of increased food intake and subsequent weight gain. However, many successive PYY knockout (Boey et al., 2006; Wortley et al., 2007), studies have failed to reproduce the strong association of PYY with appetite and diet-induced obesity or demonstrate any significant association between circulating PYY and adiposity (Cahill et al., 2013; Kim, Cho, Kang, Choi, & Park, 2012; Pfluger et al., 2007).

Current research has investigated the association of circulating PYY concentration with obesity and body composition, measured by dual-energy x-ray absorptiometry, in a large population adjusting for major confounding factors. Cahill et. al investigated whether PYY was associated with obesity classification and body composition by comparing fasting serum PYY between normal-weight (NW), overweight (OW) and obese (OB) men and women. They found that that serum PYY is not negatively associated with obesity status defined by BMI or %BF as was currently accepted (Cahill 2013). Additionally, an extensive review in 2005, exploring the anorexigenic effect of PYY, revealed 84% studies produced among 41 independent research groups were unable to reaffirm the claim proposed by the initial investigations (Batterham et al., 2003). Data from human studies are limited, inconsistent, contain small sample sizes and have utilized less accurate obesity measures (such as BMI) in place of more accurate measures of body fat such as DXA. Therefore the inaccurate measurement of adiposity and the misclassifications of obesity status could be the factor attributing to the contradictory reports concerning the association of PYY with obesity. Cahill et al found that circulating PYY was not

significantly different among normal-weight, overweight and obese participants and these findings were consistent whether obesity status was defined either by %BF or BMI. With over 2000 subjects, these results indicate that circulating PYY concentration is not likely a significant factor affecting obesity status at the population level (Newfoundland), in particular with respect to men (Cahill 2013).

Due to the apparent lack of relationship between adiposity status, in particular with men, PYY was not investigated in the current study as normal, overweight and obese individuals do not demonstrate differing circulating concentrations of PYY.

3.5.5 Testosterone

The aging overweight and obese male population is at significant risk of developing cardiovascular disease, sleep apnea, osteoarthritis, certain cancers and gonadal dysfunction (Glintborg et al., 2014). Specifically, the androgen hormone testosterone naturally decreases with age following full maturity in men, and this decline is further amplified by obesity (Allan, Strauss, Burger, Forbes, & McLachlan, 2008; Allan & McLachlan, 2010; Camacho et al., 2013; Glass, Swerdloff, Bray, Dahms, & Atkinson, 1977; Wu et al., 2012). Due to testosterone's involvement in the promotion of muscle protein synthesis, and that it is reduced by the obese state, its response to weight loss achieved through resistance training exercise is of particular relevance to our current study population (Camacho et al., 2013).

3.5.5.1 Testosterone and Obesity

Obesity's role in lowering testosterone was evidenced by the Massachusetts Male Aging Study (MMAS), which demonstrated that moving from a non-obese to an obese state resulted in a decline of testosterone levels comparable to that of advancing ten years in age (Travison, Araujo, Kupelian, O'Donnell, & McKinlay, 2007). Conversely, obesity may also be compounded by low testosterone levels. Testosterone enhances lipolysis and reduces triglyceride uptake in human abdominal adipose tissue. There is a reciprocal relationship between obesity status and testosterone where elevated testosterone helps prevent weight gain, and lowered testosterone helps promote weight gain (Grossmann, 2011). Testosterone is also susceptible to conversion into estrogen by excess adipose tissue via the fat derived enzyme aromatase (Camacho et al., 2013). Additionally, increases in visceral fat which is a fat storage pattern associated with male obesity, also increases circulating TNF-α, insulin and leptin, all of which may down regulate the hypopituitary gonadal axis and result in reductions in testosterone (Sharman & Volek, 2004).

Testosterone has been shown to increase with both lifestyle intervention and surgical approaches, though the latter yields more significant results (Botella-Carretero et al., 2013; Corona et al., 2013; Hakkinen et al., 1988b; Hammoud et al., 2009; W. J. Kraemer et al., 1999; Marx et al., 2001; Staron et al., 1994). During these interventions, the degree of weight loss was predictive of testosterone response, with the largest percent of

body weight lost yielding the greatest increase in testosterone (Camacho et al., 2013). It is believed that the magnitude of weight loss required to augment testosterone levels must amount to 15% of one's body weight. As typical weight loss interventions yield between a 6-17% decrease in body weight, only the weight loss interventions which yield the greatest results are successful at augmenting testosterone (Camacho et al., 2013).

3.5.5.2 Testosterone and Exercise

Changes in resting testosterone concentrations during resistance training have been inconsistent. Testosterone concentrations have shown increases in some studies (Hakkinen et al., 1988a; Hakkinen et al., 1988b; W. J. Kraemer et al., 1999; Marx et al., 2001; Staron et al., 1994) while others have shown no change (Alen et al., 1988; Hakkinen et al., 1988b; Hakkinen & Pakarinen, 1994; Hakkinen et al., 2000a; Hickson et al., 1994; McCall et al., 1999). It is believed that the current state of lean body mass corresponds to resting concentrations of testosterone in that increases or decreases may occur depending upon both the volume and the intensity of exercise performed (Hakkinen et al., 1988a; Hakkinen et al., 1988b).

Resistance exercise and its corresponding acute testosterone response have been the focus of several investigations (Gotshalk et al., 1997; Hakkinen et al., 2002; Izquierdo et al., 2006; R. R. Kraemer et al., 2006; W. J. Kraemer et al., 1998; Linnamo et al., 2005). Acute elevations in testosterone have been attributed to adrenergic stimulation, lactate-

stimulated secretion, and potential adaptations in the testosterone synthesis of leydig cells in the testes (Durand et al., 2003). Hormonal response to resistance training is dependent upon several variables including volume, number of sets, order of exercise, intensity, rest intervals, and choice of exercise.

Exercises which encompass large muscle groups including Olympic lifts (W. J. Kraemer et al., 1998), deadlifts (Heavens et al., 2014), squats and squat jumps (Volek, Kraemer, Bush, Incledon, & Boetes, 1997) demonstrate the highest acute testosterone response. The addition of large muscle group exercises at the beginning of a resistance training routine has been shown to increase the hormonal response from smaller muscle group exercises, which would not typically elicit an acute testosterone response had the larger exercise not been performed initially (L. Hansen et al., 1999). Therefore the design of structured resistance training programs aimed at producing increases in circulating testosterone should incorporate the use of large muscle exercises at the start of an exercise sessions.

In order to stimulate a testosterone response from exercise there appears to be a required level of intensity which must be achieved. This intensity is closely tied to training volume. Low intensity exercise which is characterized by loads that are less than 50% of an individual's one repetition maximum and a low number of repetitions, have not been shown to elicit a testosterone response (W. J. Kraemer & Ratamess, 2005). Kreamer demonstrated that when total volume is unchanged, a reduction in training intensity can

prompt a lower testosterone response (W. J. Kraemer & Ratamess, 2005). Similarly, when repetitions are kept constant, higher load and the resulting higher volume exercise protocols bring about a greater testosterone release post exercise (Hakkinen & Pakarinen, 1993). It has been shown that working at or close to an individual's repetition maximum yields the highest testosterone response. However, there appears to be a ceiling on intensity. Hakkinen showed that ten sets was needed to increased testosterone; however, increasing the number of sets to twenty did not significantly increase testosterone levels indicating that there is a ceiling effect with resistance exercises (Hakkinen & Pakarinen, 1993).

3.5.5.3 Testosterone and Nutrition

The impact of diet on testosterone is unclear. It appears that reducing total fat intake and drastically increasing polyunsaturated to saturated fat intake ratios results in a decrease in total testosterone in women (Allen, Appleby, Davey, & Key, 2002). Whether men respond accordingly, however, has not yet been investigated to our knowledge. It is also unclear how diet related decreases in total testosterone influences muscle mass, if at all. It has been recommended that to improve testosterone, 25% of dietary calories should be in the form of protein, which allows for adequate carbohydrate intake to provide energy during resistance-training sessions and adequate fat to maintain circulating testosterone levels (Lambert et al., 2004). The impact on testosterone as a result of reducing dietary saturated fat must be balanced with the potential beneficial effects of these changes on

cardiovascular risk factors (Lambert et al., 2004). Clearly, more research on these relationships needs to be conducted.

3.5.5.4 Testosterone Summary

In summary, resistance training programs seeking to improve testosterone in overweight and obese aging males should incorporate methodologies from previous research which demonstrates improvements in androgens. This would include the use of large full body movement exercises, performed at a high relative load for upwards of ten sets, with moderate to low rest intervals. This exercise, coupled with a caloric restriction diet aimed at reducing body weight, may foster a physiological environment which promotes improved testosterone in a population susceptible to its decline. Lastly, it is expected that weight loss achieved through resistance exercise would not only promote testosterone as a result of physical activity, but would also reduce the inhibitory effects of counter regulatory hormones TNF-α, leptin and insulin. Therefore, we believe that the assessment of testosterone in the current investigation is an important biomarker in the current study cohort due to testosterone's relationship with other energy regulating hormones, obesity and resistance training.

3.5.5 Energy Regulating Hormones Summary

Obesity is a complex condition that is controlled in part by adipose tissue related hormones which play an important role in energy regulation (Fasshauer & Bluher,

2015). Adipose tissue produces, interacts with, and augments these hormones, which in turn effects insulin sensitivity (Chandran et al., 2003), inflammation (de Carvalho et al., 2006), appetite (Schubert et al., 2014) and protein synthesis (Camacho et al., 2013). Traditional approaches to assessing weight loss intervention effectiveness have focused on weight loss, with some approaches addressing changes in biochemical and physiological health (Simpson et al. 2008). Recent advances in the understanding of adipose tissue as an endocrine organ have led to an improved understanding of the impact of weight loss on energy regulating hormones (Fasshauer & Bluher, 2015). This research has also demonstrated that where fat is stored also impacts these hormones and causes resulting health risks (P. Patel & Abate, 2013). Therefore, the objective of this research is to determine the influence of supervised resistance training and a hypocaloric macronutrient scheduled diet vs a hypocaloric macronutrient scheduled diet alone on the fasting energy regulating hormones adiponectin, TNF-α, leptin, ghrelin and testosterone in overweight and obese men ages 35-55. Additionally, this research will investigate the relationship between these energy regulating hormones and body fat topography, including total and regional adiposity.

4. Methods

This chapter outlines the eligible study population, the study sample including the setting for the study and the primary sample size, the intervention and control,

definitions of outcomes of interest (primary and secondary), data analysis, and ethical considerations.

4.1 Ethics Statement

This study was approved by the Health Research Ethics Authority (HREA), Memorial University of Newfoundland and Labrador (#11.327). All subjects provided written informed consent prior to participation in the research study. HREA approval letter (including renewal application), and consent form are included in Appendix 9 and 10.

4.2 Study Design

This was a randomized control trial (RCT) that lasted twelve weeks. Subjects were randomized to either a Resistance Training and Diet (Exercise + Diet) or Diet (Diet Alone) intervention group. Individuals in the Exercise + Diet group underwent strength training sessions at a local fitness facility (Definitions Health and Wellness) supervised by a certified kinesiologist for the duration of the intervention (see below for details). The kinesiologist was provided with comprehensive training by the primary investigator and a manual (**Appendix 1 – Research Assistant Handbook**) to ensure that he understood the exercise intervention as well as the study protocols and processes surrounding their role in the research. To ensure that exercise sessions were implemented correctly, the primary investigator reviewed workout logs and met with the kinesiologist weekly. All subjects in both groups met with a registered dietitian (RD) in

order to review the dietary guidelines of the intervention and to provide food logs, as well as to take home information regarding nutrition planning.

As part of the RCT design, blinding was ensured whenever possible. Subjects, as well as the certified kinesiologist and registered dietitian (RD) directly involved with the intervention were aware of group allocation due to the nature of the study, which required structured exercise for some (Exercise + Diet) and not others (Diet Alone). The primary investigator was not aware of group allocation to avoid potential measurement bias during skinfold and girth measurement assessment. Assessment of fitness testing was performed at the School of Human Kinetics and recreation by the resident laboratory kinesiologist who was unaware of group allocation, however the kinesiologist performing the physical training was unable to be blinded due to their involvement with the training. Similarly, the RD who audited food logs was required to be aware of group allocation due to the various timing of nutrients pre and post exercise for the Exercise + Diet group. The RD was not involved with any data collection this did not impose any bias in the assessment of diet using the food intake questionnaire **(Appendix 12)** and the diet assessment **(Appendix 13)** provided at the Complex Diseases Laboratory at Memorial University.

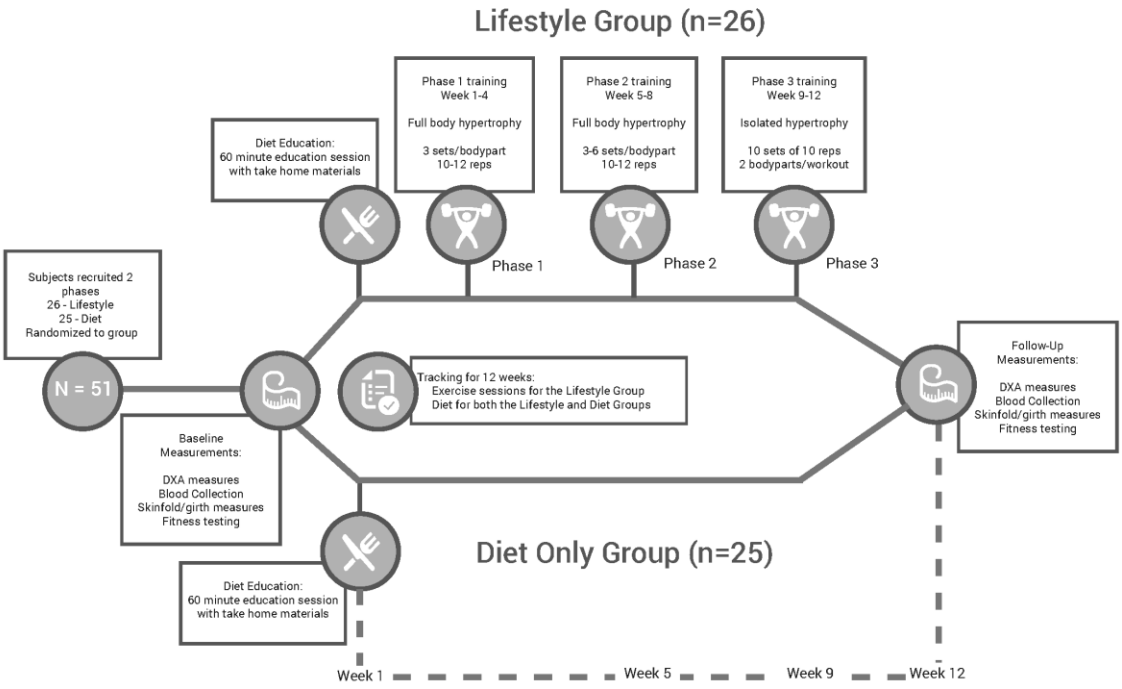

Figure 3*: Study design: Randomized trial to either the Exercise + Diet or Diet Alone intervention groups*

Each stage of the exercise training was designed based on previously established protocols shown to elicit muscular hypertrophy in similar populations (Vingren et al., 2010). All subjects underwent nutritional education and submitted weekly food logs which were monitored for compliance to the nutrition protocol (see below for details).

4.3 Study Population

Fifty-one 35-55 year old males participated in this study. Inclusion criteria 1) male; 2) BMI in the overweight (BMI > 25 < 30); or obese category I (BMI ≥ 30 < 35); 3) 35-55 years of age; 4) not currently engaging in physical activity. Physical activity was self-reported and had to describe their activity level as sedentary and not currently participating in structured or intentional physical activity (i.e. walk regularly, play sports, go to gym) were excluded. Subjects were recruited through at businesses in the city of St. John's (NL, Canada) and surrounding areas. These businesses were in a variety of locations and included blue and white collar workplaces to ensure a variety of potential subjects. Potential subjects were verbally informed on the upcoming study and if interested were sent a recruitment email which outlined enrollment and inclusion criteria (Appendix 11). Recruitment for the initial phase of the research (initial 30 subjects) took approximately four weeks, from the beginning of November to start of December 2013 and, during the second phase of the research, recruitment occurred much more quickly with the second phase of recruitment (n=21) taking only a week. The second phase of recruitment occurred the same time the following year, consisting of the first week of November 2014. Seventy-eight individuals volunteered for the study, however, 27 were excluded for various reasons including: having a pre-existing metabolic condition, a BMI of either below the overweight BMI category (BMI < 30) or greater than the obese class I category (BMI>34.99), or inability to attend the full twelve week intervention in succession.

4.4 Study Interventions

4.4.1 Resistance Training Protocol

Participants were instructed to follow the Canadian Society for Exercise Physiology (CSTF 1995) preliminary instructions (no smoking, caffeine or alcohol) prior to exercise (CSTF 1995). Subjects in the Exercise + Diet group underwent supervised (certified kinesiologist) strength training sessions three times per week for twelve weeks. The kinesiologist was trained by the primary investigator, and was provided with a standardized research assistant manual (**Appendix 1**) developed by the primary investigator. The manual provided guidance on proper workout facilitation and coaching. Exercise was divided into three separate, four week progressive resistance training programs. The initial four week protocol involved three sets of fifteen repetitions of eight different exercises (**Appendix 2**) including an exercise for each of the following muscle groups: full body compound movement, chest, back, legs, biceps, triceps, shoulders and core. All eight exercises were performed in succession with a sixty second break following the eighth exercise. The second phase of resistance training involved nine sets of twelve repetitions of three body parts, such as chest, back, and core, shoulders, legs, and core, and triceps, biceps and core. Exercises were divided into groups of two that involved opposing muscle groups, and were performed in succession with a sixty second rest interval between sets. A total of nine exercises were

performed each day (three for each primary muscle group and three for the core) (**Appendix 3**). During the final phase individuals performed ten sets of ten repetitions for two body parts per day. Examples of these routines are as follows; chest & back – bench press, latissimus dorsi pulldown. shoulders & legs – shoulder press, barbell squat; and biceps & triceps – dumbbell curls, db triceps extensions. One set of each exercise was performed in succession, which was followed by a sixty second rest period. This was repeated until all ten sets were completed for both exercises in the routine (**Appendix 4**). Tempo was controlled by the kinesiologist, and included a three second eccentric movement, a one second pause and a one second concentric movement. All workouts were tracked and recorded in order to progressively overload the subjects and improve strength over the course of the training. Subjects booked all of the exercise sessions through the kinesologist using a fitness facilities booking system (Mindbody.com). Workout attendance for the Exercise + Diet group was tracked by the primary investigator via the online booking system to ensure that all participants completed their required exercise training. At the end of twelve weeks, it was determined that all Exercise + Diet subjects completed their prescribed workouts and completed the protocol. Subjects who missed scheduled exercise sessions were provided with an alternative time during the same week to make up for the missed session. Verbal encouragement was also provided to all participants during exercise sessions.

4.4.2 Diet Protocol

Baseline energy requirements were determined from 24-hr diet recalls and a thirty day dietary inventory. Participants were instructed to consume approximately sixteen hundred calories per day (hypocaloric diet), and to adhere to a macronutrient contribution of 30% protein, 30% fat, and 40% carbohydrates to mimic guidelines shown to be effective in weight loss studies, and which impact energy regulating hormones (Bowen et al., 2006; Niwano et al., 2009; Tannous dit El Khoury et al., 2006). Subjects were encouraged to eat three meals and three small snacks each day. A nutrition education session was completed with each subject, where macronutrients, timing of food intake and recommendations for meal selection were taught by a registered dietitian. The primary investigator was also in attendance to answer questions surrounding food log requirements. This one hour session included a take home and online education manual that clearly outlined healthy options and recommended dietary selections for each period of the day, in order to ensure a balance of nutrients at each meal (**Appendix 5 – Meal Planner**). All subjects participated in the nutrition intervention; however the Diet Alone was encouraged to follow the nutrition guidelines while maintaining their previous level of physical activity during the course of the study. This separation was reinforced by restricting fitness facility access to only those in the Exercise + Diet group. Exercise avoidance was assessed as part of the food log, which required subjects to record all physical activity or exercise during the week. Food logs required individuals to record meals and snacks for each day of the week (3 meals and 3

snacks/day). As part of this reporting foods were recorded under a specific macronutrient category that represented the primary macronutrient that the food consisted of (e.g. Peanut butter = fat, fish = protein, apple = carbohydrate). Lists of food categories and their respective serving sizes were included in the education manual and this ongoing education and macronutrient awareness created through food tracking was an intentional design of the study in an attempt to re-enforce RD coaching (Appendix 5). These food logs were subjective in nature and did not utilize a validated measurement tool. Therefore, no data analysis was performed on these tracking sheets, rather they were used to coach subjects to dietary change.

All subjects from both the Exercise + Diet and Diet Alone groups received a handbook following the education session with key nutrition principles, recipes and sample meal plans. As part of the research design, the dietitian was aware of group allocation of all subjects during the education session in order to reinforce maintenance of physical activity levels in the Diet Alone group. All nutrition education sessions and submitted food log reviews were conducted by the same Registered Dietitian during the course of the study.

4.4 Randomization

Subjects were block randomized in groups of 8 via sealed envelope to that were prepared and shuffled by the primary investigator. Subjects chose an envelope following baseline testing with the kinesiologist in the Human Kinetics and Recreation Physiology

Lab. Regardless of group allocation, all subjects were booked to meet with the RD to undergo diet education. Subjects allocated to the Exercise + Diet group were also provided instructions on exercise training and booked their initial session in the fitness facility using the online booking tool (mindbody.com).

4.5 Study Outcomes

Anthropometric, body composition, physical and biochemical measurements were collected, at baseline and after twelve weeks, following a twelve hour fast. Each subject completed a questionnaire to obtain baseline information regarding lifestyle and physical activity. Girth measurements and skin fold thickness measurements were assessed the following day at baseline and after twelve weeks by the primary investigator, who was blinded to group allocation. Variables and their assessment scales are included in Table 1 and testing and the data collection process is included in Figure 4. All subjects completed the intervention, and were tested at baseline and after twelve weeks. There were no drop outs or missing data from the subjects at either baseline or follow-up.

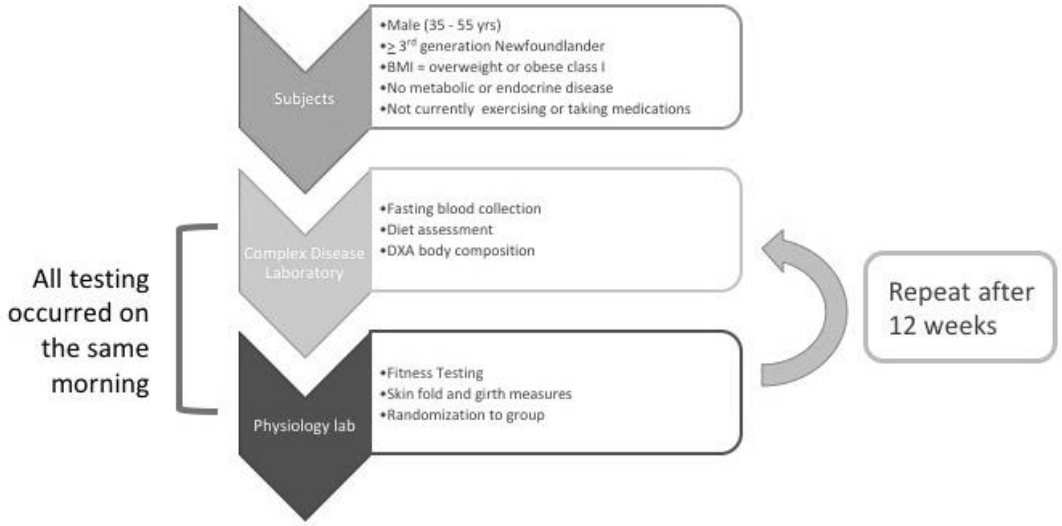

Figure 4. Baseline and post intervention testing was performed at the Complex Diseases Laboratory in the School of Medicine and Physiology Laboratory at the School of Human Kinetics and Recreation at Memorial University. Trained laboratory technicians conducted DXA and anthropometric measures, blood collection, sample analysis, dietary questionnaires at the Complex Diseases Laboratory. Subjects then went to the Human Kinetics and Recreation Physiology Laboratory where they participated in fitness testing, skin fold and girth measurements.

Table 1. Variable Definitions and Measurement Scales

Body Composition Characteristics	**Variable Type**	**Assessment Method**
Age (yr)	Objective	Recall
Height (m)	Objective	Medical scale
Weight (kg)	Objective	Medical scale
Waist (cm)	Objective	Measuring tape
Hip (cm)	Objective	Measuring tape
Total Body Fat (kg)	Objective	DXA
Total Lean Tissue (kg)	Objective	DXA
Body Fat (%)	Objective	DXA
Trunk Fat (%)	Objective	DXA
BMI (kg/m^2)	Objective	Predictive equation
Visceral Fat (kg)	Objective	DXA
Metabolic Characteristics		
HDL Cholesterol (mmol/L)	Objective	Blood sample
LDL Cholesterol (mmol/L)	Objective	Blood sample
Total Cholesterol (mmol/L)	Objective	Blood sample
Triacylglycerol (mmol/L)	Objective	Blood sample
Insulin (pmol/L)	Objective	Blood sample
HOMA-IR	Objective	Predictive equation
HOMA-β	Objective	Predictive equation
Glucose (mmol/L)	Objective	Blood sample
Systolic Blood Pressure (mmhg)	Objective	Blood pressure cuff
Diastolic Blood Pressure (mmhg)	Objective	Blood pressure cuff
Heart Rate (bpm)	Objective	Blood pressure cuff
Energy Regulating Hormones		
Adiponectin (ug/ml)	Objective	Blood sample
Leptin (ug/ml)	Objective	Blood sample
TNF-α (pg/ml)	Objective	Blood sample
Total Testosterone (pg/ml)	Objective	Blood sample
Free Testosterone (pg/ml)	Objective	Blood sample
Ghrelin (pg/ml)	Objective	Blood sample
Fitness Tests		
Pushups	Objective	Standardized fitness test
Sit and Reach	Objective	Standardized fitness test
Partial Curl-Up	Objective	Standardized fitness test
Back Extension	Objective	Standardized fitness test

4.5.1 Serum Hormone and Biochemical Measurements

All hormonal blood measurements and analysis were performed by a trained laboratory technician in the Complex Diseases Laboratory, located in the Faculty of Medicine at Memorial University.

Fasting serum was collected from subjects in the morning between 9 am and 11 am following a twelve hour fast, and was stored at -80 °C for subsequent analysis. Adiponectin, (EMD Millipore, Austin, TX, USA), and testosterone (Phoenix Pharmaceuticals, Belmont, California) were measured in duplicate utilizing, enzyme-linked immunosorbent assays. Leptin, ghrelin, and TNF-α were also measured in duplicate using a magnetic bead-based quantitative immunoassay via the MAGPIX system (EMD Millipore, Austin, TX, USA). The intra-assay CV for adiponectin (n=3, average of Plate 1, Plate 2 and Plate 3 = 2.8 + 3.8 + 3.1) was 3.2% while the inter-assay CV (n=3, Average of High and Low control 7.1% and 1.2%) was 4.2%. The TNF-α intra-assay CV (n=3, Average of Plate 1, Plate 2 and Plate 3 = 6.9%, 5.5% and 5.6%) was 6.0% and the inter-assay CV (n=3, Average of High and Low control = 5.3% and 5.2%) was 5.3%. Leptin demonstrated an intra-assay CV (n=3. Average of Plate 1, Plate 2 and Plate 3 = 6.7%, 5.7% and 5.4%) of 5.9% and an inter-assay CV (n=3, Average of High and Low control = 7.4% and 2.7%) of 5.1%. Ghrelin showed an intra-assay CV (n=3, Average of Plate 1, Plate 2 and Plate 3 = 6.6%, 5.6% and 4.4%) of 5.3% and an inter-assay CV (n=3, Average of High and Low control = 6.1% and 4.1%) of

5.1%. The intra-assay CV of total testosterone (n=3, Average of Plate 1, Plate 2 and Plate 3 = 3.6%, 2.9% and 3.4%) was 3.3% while the inter-assay CV (n=3, Average of High and Low control = 1.4% and 3.6%) was 2.5%

Serum insulin concentrations were measured with the use of an immunoassay analyzer (Immulite; DPC, Los Angeles, CA). The homeostasis model assessment (HOMA) was used to measure insulin resistance and β-cell function (Matthews et al., 1985).

$$HOMA - IR = ((Fasting\_Insulin[\mu U / ml] \times Fasting\_Glucose[mmol / L]) / 22.5)$$

$$HOMA - \beta = ((20 \times Fasting\_Insulin[\mu U / ml] / (Fasting\_Glucose[mmol / L] - 3.5))$$

The homeostatic model assessment (HOMA) is a method used to quantify insulin resistance and beta-cell function. It was first described under the name HOMA by Matthews et al. (Matthews et al., 1985)

Serum concentrations of glucose, triacylglycerols (TG), high-density lipoprotein cholesterol (HDLc) and total cholesterol were measured by an Lx20 analyzer (Beckman Coulter Inc, Fullerton, CA). Low-density lipoprotein cholesterol (LDLc) was calculated with the following formula which is reliable in the absence of severe hyperlipidemia.

LDLc = [Total Cholesterol(mmol/L) – HDL Cholesterol (mmol/L) – (Triacylglycerol (mmol/L/2.2)]

The samples were analyzed in batches at the end of the study. Upon the completion of the study the samples are thawed and analyzed. All of the samples were measured in batches were as many participant samples, both pre and post, could be measured on a single plate. For example, when doing ELISA on a 96 well plate 16 wells were used to build the standard curve in duplicate and another 4 wells were used for 2 standard controls. Since both the pre and post samples were measure in duplicate on the same plate 4 wells were required per subject. Therefore 19 subjects (with both pre and post samples) were measured on each ELISA plate. Sample analysis for glucose, triglycerides and lipids was performed in a similar fashion following the completion of the study at the Memorial University Medical School biochemistry laboratory run by Dr. Edward Randell.

4.5.2 Anthropometric and Body Composition Measurements

Height (nearest 0.1 cm) and weight (nearest 0.1 kg) measurements were collected, repeated twice, and averaged for subjects who were wearing a standard hospital gown without footwear, using a platform balance weigh scale (Health O Meter, Bridgeview, IL). BMI was calculated as weight divided by height squared (kg/m^2) from these measurements. Obesity status has been grouped as overweight (BMI 25.00–29.99), and obese (BMI ≥ 30-34.99), as recommended by the World Health Organization (WHO) (World Health Organization, 2015). Percent trunk fat was measured utilizing dual x-ray

absorptiometry (DXA) (Lunar Prodigy, GE Medical Systems, Madison, WI, USA). Measurements were performed on subjects in a supine position after the removal of all metal accessories. The enCORE software package (version 12.2, GE Medical Systems, Madison, WI, USA) was used for DXA data acquisition.

Skin fold and girth measurements were taken following the American College of Sports Medicine's (ACMS) guidelines for fitness testing (ACSM, 2014). Skin fold sites included the chest, triceps subscapularis, mid-axillary, suprailiac, abdominal and thigh. Girth measurements included the biceps (flexed and relaxed), neck, chest, waist, hip, and thigh. The specific standardized protocols of skin fold/girth measurements are included in **Appendix 6**. All measurements were taken in triplicate and averages of the scores were recorded as the site value.

The sum of the skin fold's body fat percentage was calculated using the Jackson Pollock 7 site skin fold protocol that determines body fat using the various skin fold sites listed above. This protocol was developed from the research of Dr. Andrew Jackson and M. L. Pollock (Jackson & Pollock, 2004). The primary investigator, who was blinded to group allocation, took all anthropometric measurements, and is certified by the Canadian Society of Exercise Physiology to perform these tests.

4.3 Fitness Testing

Fitness testing was completed according to the Canadian Society of Exercise Physiology's (CSEP) guidelines for fitness testing and included tests for muscular strength, endurance and flexibility. This testing was performed at the Human Kinetics and Recreation laboratory at Memorial University by the resident certified kinesiologist. These tests included a push up test, partial curl-up, back extension, and sit and reach flexibility (fitness testing protocols included in **Appendix 7)**. All baseline and post intervention fitness testing was performed by the kinesiologist.

4.6 Sample Size and Statistical Analysis

Preliminary sample size calculation was based on the Fatourous study which measured the adiponectin response to high intensity exercise training (Fatourous et al., 2005). Therefore, using a mean difference of 18% in adiponectin, shown to be statistically significant by the Fatourous study, and a mean total adiponectin concentration of 8.1 ug/ml with a SD of 2 ug/ml, an alpha of 0.05, and a power set to 0.8, a total of 15 subjects were needed in the intervention group.

Following completion of the initial study an interim analysis was performed. Based on preliminary data analysis it was decided to to increase the sample size. This resulted in additional recruitment of subjects and a re-running of the study. The final sample size

was determined from a power calculation on adiponectin from the initial fifteen subjects who were recruited in each group.

When setting the minimum mean difference to 25% for the Exercise + Diet group (n=15) with the Standard Deviation (SD) of the adiponectin measurement from the interim analysis of 13.1 ug/ml , an alpha of 0.05, and a power set to 0.8, a total of 26 people are needed. Therefore, we recruited eleven more subjects for this group.

When setting the minimum mean difference to 25% for the Diet Alone group (n=15), with the Standard Deviation of the adiponectin measurement from the interim analysis of 12.0 ug/ml, an alpha of 0.05, and a power set to 0.8, a total of 22 people are needed. In total, 11 more subjects were recruited to the Exercise + Diet group and, due to the block randomization approach employed in the current study, 10 additional subjects were recruited to the Diet Alone group.

Data are presented as means ± SD, unless otherwise stated. Before any statistical analysis was performed, data that were not normally distributed were logarithmically transformed (TG, insulin, HOMA-IR and HOMA-β) to approximate normal distribution. Baseline values between the two groups were analyzed using an independent student's t-test and a Bonferonni adjustment was used to control for multiple comparisons. Within groups analysis in response to the Exercise + Diet and Diet Alone groups was performed using a student paired t-test to ensure similarity between groups. Differences in variables between the two groups were analyzed using a two-way repeated measures analysis of

variances test (ANOVA). The Main Effect P-value was reported along with interaction (Intervention * Group) P-Value if it was found to be significant ($p < 0.05$). An interaction effect is a change in the simple main effect of one variable over levels of the second. For example, if the differences (due to the interventions) describing the simple main effects are not parallel, an interaction would exist. Therefore, a simple main effect can be found without differential influences from the two interventions. Pearson's correlation analysis was also performed to identify potential factors related to the variables of interest. Additionally, two correlation analyses were performed as follows: 1) Adiponectin, leptin, TNF-α, testosterone, and ghrelin at baseline were compared with all physical and biochemical phenotypes at baseline 2) Adiponectin, leptin, TNF-α, testosterone, and ghrelin at baseline were compared with changes in physical and biochemical phenotypes in response to the interventions. A two-way ANCOVA analysis was also performed while controlling for variables which may influence the response of adiponectin, leptin, TNF-α, testosterone, and ghrelin regarding the interventions. SPSS software version 20.0 (SPSS Inc, Chicago, IL, USA) was used for all analyses. Statistical analyses were 2-sided and $p < 0.05$ was considered to be statistically significant.

5 Results

5.1 Study Baseline Characteristic and Adherence:

Of the seventy eight individuals who responded to the study advertisements, twenty seven did not meet inclusion criteria. Six were excluded because of serious metabolic conditions, twelve had a BMI that was not within the overweight or obese class I range, and eight were excluded due to age, as they were either below the 35 year old minimum or above the 55 year old maximum (Figure 5- subject flow diagram demonstrating recruitment, group randomization and follow-up).

Fifty-one males, aged 35-55 years old, classified by BMI as either overweight or obese, who self-reported as physically inactive (not engaging in regular or structured physical activity) and not suffering from a serious metabolic, cardiovascular, or endocrine disease met the inclusion criteria (Figure 5). Of the fifty one subjects recruited to the study twenty six were randomized to the Exercise + Diet group and twenty five were randomized to the Diet Alone group. All subjects completed the intervention, and were tested at baseline and after twelve weeks and the study was stopped after all subjects completed their respective interventions (Figure 5). There were no significant differences between groups at baseline for any anthropometric or biochemical measurements **(Table 2).**

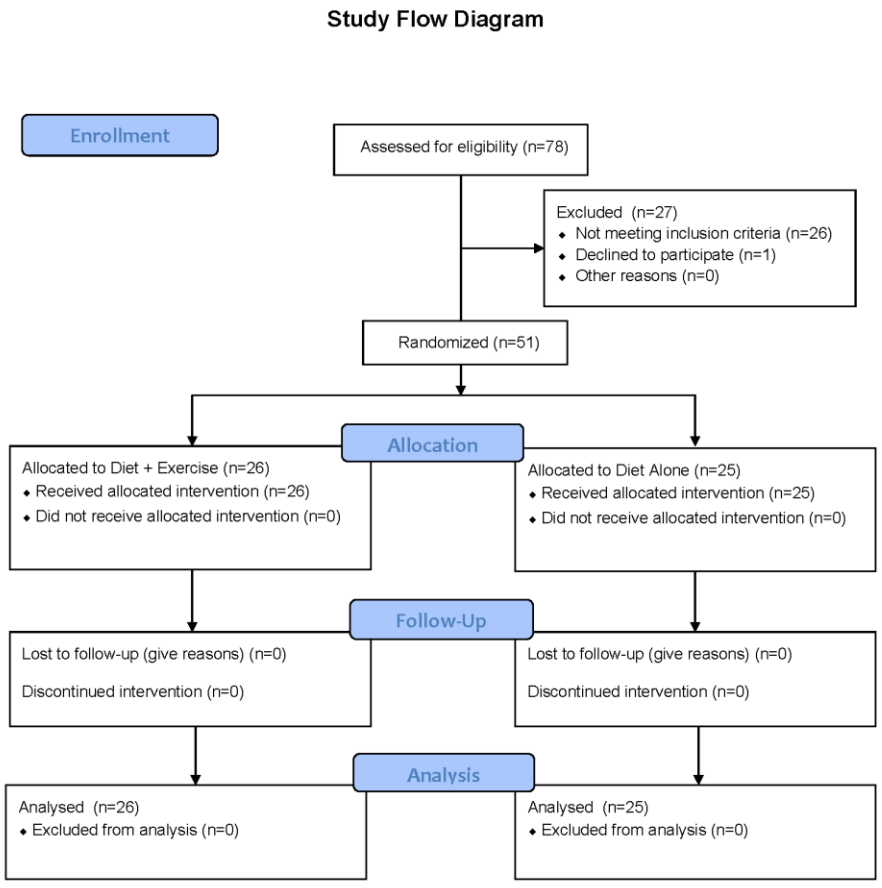

Figure 5: Study flow diagram: Include a flow diagram that would also show the disposition of subjects into the two arms, and how many completed each time point.

Table.2 - Body Composition and Metabolic Characteristics for the Exercise + Diet and Diet Alone Groups at Baseline (n=51)

	Exercise + Diet (n=26) Baseline		Nutrition (n=25) Baseline			
Body Composition Characteristics	Mean	SD	Mean	SD	p	Sig
Age (yr)	43.45	± 5.8	45.73	± 7.1	0.217	NS
Height (m)	179.00	± 6.5	176.68	± 5.1	0.164	NS
Weight (kg)	102.90	± 13.4	99.00	± 17.2	0.372	NS
Waist (cm)	111.99	± 10.2	110.22	± 11.8	0.579	NS
Hip (cm)	109.83	± 8.8	108.09	± 11.5	0.56	NS
Total Body Fat (kg)	34.28	± 10.0	31.56	± 10.3	0.344	NS
Total Lean Tissue (kg)	64.99	± 6.3	64.25	± 8.8	0.731	NS
Body Fat (%)	32.83	± 6.0	31.23	± 5.0	0.306	NS
Trunk Fat (%)	40.28	± 5.8	38.29	± 5.5	0.216	NS
BMI (kg/m2)	32.09	± 3.6	31.62	± 4.7	0.689	NS
Visceral Fat (kg)	2.13	± 0.8	1.89	± 0.8	0.318	NS
Metabolic Characteristics						
HDL Cholesterol (mmol/L)	1.13	± 0.2	1.11	± 0.2	0.798	NS
LDL Cholesterol (mmol/L)	3.61	± 0.9	3.89	± 0.9	0.258	NS
Total Cholesterol (mmol/L)	5.42	± 1.1	5.83	± 1.1	0.188	NS
Triacylglycerol (mmol/L)	1.50	± 0.7	1.57	± 0.7	0.735	NS
Insulin (pmol/L)	59.36	± 35.9	76.43	± 40.1	0.129	NS
HOMA-IR	2.15	± 1.4	2.84	± 1.8	0.143	NS
HOMA-ß	86.53	± 54.7	110.43	± 75.0	0.225	NS
Glucose (mmol/L)	5.61	± 0.8	6.04	± 2.6	0.451	NS
Systolic Blood Pressure (mmhg)	128.27	± 9.0	130.22	± 15.5	0.601	NS
Diastolic Blood Pressure (mmhg)	84.96	± 6.0	86.78	± 12.0	0.516	NS
Heart Rate (bpm)	67.35	± 7.0	69.43	± 12.3	0.478	NS

5.2 Physical Fitness Response to Intervention:

All fitness test scores improved within both the Exercise + Diet and Diet Alone groups. The magnitude of these differences was in favor of the Exercise + Diet group. The Exercise + Diet group demonstrated a significantly greater increase in fitness testing scores ($p<0.001$) including push-ups (# of repetitions), partial curl-ups (# of repetitions), sit and reach flexibility (distance in cms), and back extensions (time holding position), with improvements of 22%, 30%, 51%, 40%, respectively **(Table 4&5)**. The Diet Alone group also showed significant improvements of 6%, 11.5%, 34.5%, and 22%. Flexibility improved the most in the Diet Alone group, which could be a result of changes in regional adiposity, specifically that of the trunk. These changes could lead to a greater range of motion due to a reduction in fat mass (**Table 3**).

5.3 Nutritional Intake Response to Intervention:

The average caloric intake per day at baseline was 2171.3 ± 705.2 kcal, where average protein intake was determined to be 97.6 ± 42.4 g, carbohydrate intake was 274.6 ± 96.1 g (fiber at 22.6 ± 10.8 g), total fat intake was 75.0 ± 29.0 g;, saturated fats intake was 21.5 ± 11.2 g. This constitutes a macronutrient intake ratio of approximately 18% protein, 55% carbohydrate, and 31% fat. Following the nutrition education session, both groups had their food intake re-assessed at twelve weeks, and showed a decrease of 30% in total calories and a 40% reduction in carbohydrate intake per day (g) (**Table 6&7**). As a result the macronutrient intake was 26% and 27% protein, 42% and 44%

Table. 3 - Differences With-In The Exercise + Diet and Diet Alone Groups - Body Composition, Metabolic Characteristics and Energy Regulating Hormones Differences (n=51)

	Exercise + Diet (n=26)					**Diet Alone (n=25)**				
	Pre		**Post**			**Pre**		**Post**		
Body Composition Characteristics	Mean	SD	Mean	SD	p	Sig	Mean	SD	Mean	SD	p	Sig
Age (yr)	43.45	± 5.8	--	--	--	--	45.73	± 7.1	--	--	--	--
Height (m)	179.00	± 6.5	--	--	--	--	176.68	± 5.1	--	--	--	--
Weight (kg)	102.90	± 13.4	98.13	± 12.1	**0.000**	**SIG**	99.00	± 17.2	94.83	± 16.9	**0.000**	**SIG**
Waist (cm)	111.99	± 10.2	105.75	± 10.6	**0.000**	**SIG**	110.22	± 11.8	105.89	± 12.8	**0.001**	**SIG**
Hip (cm)	109.83	± 8.8	105.31	± 8.8	**0.000**	**SIG**	108.09	± 11.5	104.80	± 11.0	**0.017**	**SIG**
Total Body Fat (kg)	34.28	± 10.0	28.34	± 9.7	**0.000**	**SIG**	31.56	± 10.3	27.43	± 10.1	**0.000**	**SIG**
Total Lean Tissue (kg)	64.99	± 6.3	66.16	± 6.9	**0.000**	**SIG**	64.25	± 8.8	64.39	± 8.0	0.629	NS
Body Fat (%)	32.83	± 6.0	28.35	± 6.6	**0.000**	**SIG**	31.23	± 5.0	28.07	± 5.6	**0.000**	**SIG**
Trunk Fat (%)	40.28	± 5.8	35.11	± 7.3	**0.000**	**SIG**	38.29	± 5.5	34.54	± 6.6	**0.000**	**SIG**
BMI (kg/m^2)	32.09	± 3.6	30.62	± 3.3	**0.000**	**SIG**	31.62	± 4.7	30.30	± 4.6	**0.000**	**SIG**
Visceral Fat (kg)	2.13	0.8	1.52	± 0.8	**0.000**	**SIG**	1.89	± 0.8	1.53	± 0.8	**0.001**	**SIG**
Metabolic Characteristics												
HDL Cholesterol (mmol/L)	1.13	± 0.2	1.15	± 0.2	0.498	NS	1.11	± 0.2	1.19	± 0.2	0.114	NS
LDL Cholesterol (mmol/L)	3.61	± 0.9	3.22	± 0.7	**0.011**	**SIG**	3.89	± 0.9	3.61	± 0.8	0.086	NS
Total Cholesterol (mmol/L)	5.42	± 1.1	4.87	± 0.8	**0.005**	**SIG**	5.83	± 1.1	5.60	± 1.1	0.214	NS
Triacylglycerol (mmol/L)	1.50	± 0.7	1.10	± 0.5	**0.001**	**SIG**	1.57	± 0.7	1.60	± 0.9	0.771	NS
Insulin (pmol/L)	59.36	± 35.9	58.92	± 32.2	0.939	NS	76.43	± 40.1	70.69	± 49.5	0.404	NS
HOMA-IR	2.15	± 1.4	2.07	± 1.2	0.674	NS	2.84	± 1.8	2.57	± 1.6	0.251	NS
HOMA-β	86.53	± 54.7	101.46	± 66.1	0.236	NS	110.43	± 75.0	79.99	± 46.5	**0.009**	**SIG**
Glucose (mmol/L)	5.61	± 0.8	5.42	± 0.7	0.199	NS	6.04	± 2.6	6.24	± 2.5	0.251	NS
Systolic Blood Pressure (mmhg)	128.27	± 9.0	121.06	± 9.0	**0.001**	**SIG**	130.22	± 15.5	132.13	± 17.6	0.607	NS
Diastolic Blood Pressure (mmhg)	84.96	± 6.0	78.40	± 7.6	**0.000**	**SIG**	86.78	± 12.0	85.91	± 10.1	0.196	NS
Heart Rate (bpm)	67.35	± 7.0	62.18	± 9.2	**0.005**	**SIG**	69.43	± 12.3	63.30	± 11.3	**0.006**	**SIG**
Energy Regulating Hormones												
Adiponectin (ug/ml)	24.05	± 13.1	21.34	± 12.2	0.304	NS	23.51	± 12.0	25.93	± 16.8	0.422	NS
Leptin (ug/ml)	7.43	± 4.5	4.77	± 3.7	**0.002**	**SIG**	7.09	± 6.1	5.56	± 4.9	**0.023**	**SIG**
TNF-α (pg/ml)	5.83	± 3.6	5.07	± 3.0	0.108	NS	6.73	± 3.8	6.69	± 3.8	0.931	NS
Total Testosterone (pg/ml)	8.32	± 5.6	7.63	± 3.7	0.497	NS	6.49	± 4.6	7.26	± 4.3	0.312	NS
Free Testosterone (pg/ml)	8.02	± 4.2	8.97	± 5.5	0.386	NS	7.54	± 3.4	8.89	± 5.7	0.106	NS
Ghrelin (pg/ml)	47.41	± 46.4	49.76	± 35.7	0.749	NS	60.13	± 38.7	41.91	± 23.8	0.063	NS

Table. 4 - Fitness Measure Differences Within Groups (n=51)

	Exercise + Diet (n=26)						Diet Alone (n=25)					
	Pre		Post		T-Test		Pre		Post		T-Test	
	Mean	SD	Mean	SD	p	Sig	Mean	SD	Mean	SD	p	Sig
Curl-Ups (repetitions)	36.53 ±	7.4	47.53 ±	9.6	0.001	**SIG**	25 ±	6.41	40.76 ±	6.36	0.001	**SIG**
Push-Ups (repetitions)	19.65 ±	7.8	23.94 ±	9.5	0.001	**SIG**	24 ±	7.78	18.65 ±	8.15	0.001	**SIG**
Flexibility (cm)	15.12 ±	5.1	22.88 ±	7.7	0.001	**SIG**	16 ±	5.2	20.24 ±	8.15	0.001	**SIG**
Back Extension (seconds)	41.71 ±	13.7	58.41 ±	19.1	0.001	**SIG**	35 ±	12.4	52.29 ±	14.9	0.001	**SIG**

Table. 5 - Fitness Measure Differences Between Groups ANOVA (n=51)

	Two-Way ANOVA			
	Main Effect		Interaction	
	p	Sig	p	Sig
Curl-Ups (repetitions)	0.001	**SIG**	0.001	**SIG**
Push-Ups (repetitions)	0.001	**SIG**	0.001	**SIG**
Flexibility (cm)	0.001	**SIG**	0.001	**SIG**
Back Extension (seconds)	0.001	**SIG**	0.001	**SIG**

Table. 6 - Nutritional Intake Differences Within Groups (n=51)

	Exercise + Diet (n=26)						Diet Alone (n=25)					
	Pre		Post		T-Test		Pre		Post		T-Test	
	Mean	SD	Mean	SD	p	Sig	Mean	SD	Mean	SD	p	Sig
Total Calories	2135.1 ±	750	1555.21 ±	162	0.001	**SIG**	2208.9 ±	669	1512.1 ±	161	0.001	**SIG**
Protein (grams)	98.12 ±	49.4	100.4 ±	24.6	0.48	NS	97.06 ±	34.6	101.9 ±	28.8	0.57	NS
Carbohydrates (grams)	266.89 ±	104	164 ±	30.1	0.001	**SIG**	282.72 ±	88.1	168.7 ±	26.9	0.001	**SIG**
Dietary Fiber (grams)	22.35 ±	10.6	20 ±	8.5	0.71	NS	22.91 ±	11.3	21 ±	5.32	0.65	NS
Fat (grams)	65.95 ±	29.7	54.4 ±	16.7	0.74	NS	64 ±	28.7	45.9 ±	13.4	0.63	NS

Table. 7 - Nutritional Intake Differences Between Groups (n=51)

	Two-Way ANOVA			
	Main Effect		Interaction	
	p	Sig	p	Sig
Total Calories	**0.021**	**SIG**	0.222	NS
Protein (grams)	0.527	NS	0.648	NS
Carbohydrates (grams)	**0.001**	**SIG**	0.135	NS
Dietary Fiber (grams)	0.167	NS	0.661	NS
Fat (grams)	0.683	NS	0.505	NS

carbohydrates and 30% and 27% fat intake for the Exercise + Diet and Diet Alone groups, respectively. As a result no statistically significant differences were found between groups with respect to total calories per day, as well as with respect to total protein, carbohydrate, saturated fat and dietary fiber (g) intake at baseline and twelve weeks. These results suggest that the intervention was adhered to equally by both groups (**Table 6&7**). Adherence to the nutrition program was monitored by the registered dietitian, who received weekly food logs from all participants. Food logs were submitted an average of eleven times over twelve weeks, and no subjects went longer than one week without submitting a food log. There was no statistically significant difference in participation between groups with both the Exercise + Diet and Diet Alone groups submitting food logs 90% of the time (**Table 8**).

5.4 Physical & Biochemical Response to Intervention

Although the Exercise + Diet group had two interventions that could cause weight loss as opposed to the single intervention experienced by the Diet Alone group, both groups lost a similar amount of weight after twelve weeks (~5 kg and ~ 4 kg, respectively). This modest weight loss was significantly lower than baseline ($p<0.001$) for each group, but there was no statistically significant difference between the groups after twelve weeks.

Table 8. Food Log Compliance during 12 Week Intervention (n=51)

	Group	
	Exercise + Diet (n=26)	**Diet Alone (n=25)**
Week 1	25	24
Week 2	24	20
Week 3	24	22
Week 4	22	20
Week 5	22	22
Week 6	24	24
Week 7	23	23
Week 8	22	21
Week 9	24	23
Week 10	23	23
Week 11	24	24
Week 12	26	24
	91%	90%

Table. 9 - Differences Between Exercise + Diet and Diet Alone Groups - Body Composition, Metabolic Characteristics and Energy Regulating Hormones

	Two Way ANOVA			
	Main Effect		Interaction	
Body Composition	p	Sig	p	Sig
Weight (kg)	**0.000**	**SIG**	0.601	NS
Waist (cm)	**0.000**	**SIG**	0.191	NS
Hip (cm)	**0.000**	**SIG**	0.424	NS
Total Body Fat (kg)	**0.000**	**SIG**	0.137	NS
Total Lean Tissue (kg)	**0.002**	**SIG**	**0.016**	**SIG**
Body Fat (%)	**0.000**	**SIG**	0.135	NS
Trunk Fat (%)	**0.000**	**SIG**	0.209	NS
BMI (kg/m^2)	**0.000**	**SIG**	0.692	NS
Visceral Fat (kg)	**0.000**	**SIG**	**0.050**	**SIG**
Metabolic Characteristics				
HDL Cholesterol (mmol/L)	0.080	NS	0.318	NS
LDL Cholesterol (mmol/L)	**0.003**	**SIG**	0.627	NS
Total Cholesterol (mmol/L)	**0.004**	**SIG**	0.235	NS
Triacylglycerol (mmol/L)	**0.007**	**SIG**	**0.025**	**SIG**
Insulin (pmol/L)	0.483	NS	0.547	NS
HOMA-IR	0.235	NS	0.507	NS
HOMA-β	0.352	NS	**0.009**	**SIG**
Glucose (mmol/L)	0.926	NS	0.084	NS
Systolic Blood Pressure (mmhg)	0.179	NS	0.024	NS
Diastolic Blood Pressure (mmhg)	**0.000**	**SIG**	**0.041**	**SIG**
Heart Rate (bpm)	**0.000**	**SIG**	0.992	NS
Energy Regulating Hormones				
Adiponectin (ug/ml)	0.942	NS	0.197	NS
Leptin (ug/ml)	**0.000**	**SIG**	0.266	NS
TNF-α (pg/ml)	0.207	NS	0.251	NS
Total Testosterone (pg/ml)	0.946	NS	0.253	NS
Free Testosterone (pg/ml)	0.093	NS	0.765	NS
Ghrelin (pg/ml)	0.187	NS	**0.039**	**SIG**

This trend continued for circumferential measurements of the waist ($p<0.001$) and hips ($p<0.001$), which reduced by ~5 cm and ~4 cm respectively in both groups.

Measurement of adiposity including total body fat (in kg), body fat percentage (%BF), trunk fat percentage (%TF), and BMI also reduced ($p<0.001$), all of which was expected given the similar reduction in weight for both groups. The Exercise + Diet group displayed a moderate increase in lean body mass of 1.2 kg ($p=0.016$) most likely as a result of the resistance training intervention. Additionally, visceral fat, which decreased in both groups, showed a 42% greater reduction in fat mass in the Exercise + Diet group as compared to the Diet Alone group ($p=0.05$) (**Table 9**).

In addition to weight loss and anthropometric changes, cardiovascular and blood lipid measurements demonstrated overall and intervention specific responses within and between groups **(Table 9&10)**

Baseline and follow-up assessment was conducted to determine the total number of subjects in the study, and in each intervention group, who possess diabetes, hypertension and dyslipidemia (**Table 10**). With respect to blood pressure, 9 subjects in the study were normotensive, 31 were pre-hypertensive and 7 subjects were classified as hypertensive at baseline. Following the twelve week interventions the total number of normotensive individuals increased from 9 to 19, where the Exercise + Diet group saw an increase in normotensive individuals from 4 at baseline to 14 at follow-up. The Diet Alone group showed 5 individuals who were classified as normotensive at baseline and

Table.10 - Blood pressure, glucose and lipid risk classifications of study participants (n=51)

Blood Pressure

	Entire Cohort		Exercise		Nutrition	
	Pre	Post	Pre	Post	Pre	Post
Normal	9	19	4	14	5	5
Prehypertension	31	21	18	11	13	10
Hypertension	7	7	3	0	4	7

Normal = Systolic Blood Pressure < 120 mm Hg

Prehypertension = Systolic Blood Pressure 121 - 139 mm Hg

Hypertension = Systolic Blood Pressure > 140 mm Hg

Blood Glucose

	Entire Cohort		Exercise		Nutrition	
	Pre	Post	Pre	Post	Pre	Post
Normal	41	38	22	23	19	15
Prediabetic	5	8	3	2	2	6
Diabetic	3	3	1	1	2	2

Normal = Fasting Blood Glucose < 6.0 mmol/L

Prediabetic = Fasting Blood Glucose 6.0 - 7.0 mmol/L

Diabetic = Fasting Blood Glucose > 7.0 mmol/L

Blood LDLc

	Entire Cohort		Exercise		Nutrition	
	Pre	Post	Pre	Post	Pre	Post
Normal	17	28	11	19	6	9
Boarderline	15	12	8	4	7	8
Dyslipidemia	16	8	7	3	9	5

Normal = LDL < 3.3 mmol/L

Boarderline = LDL 3.3 - 4.1 mmol/L

Dyslipidemia = LDL > 4.1 mmol/L

Table.11 - Differences in Energy Regulating Hormones Between Exercise + Diet and Diet Alone Groups Analyzed by BMI Classification (n=51)

Overweight			
Exercise + Diet (n = 6)			
		Mean	SD
Adiponectin	Pre	25.35	± 7.4
	Post	26.06	± 8.9
Diet Alone (n = 10)			
		Mean	SD
Adiponectin	Pre	25.64	± 16.6
	Post	21.78	± 11.7
P = 0.326			
Interaction = P = 0.249			

Obese			
Exercise + Diet (n = 6)			
		Mean	SD
Adiponectin	Pre	23.66	± 14.5
	Post	19.92	± 12.9
Diet Alone (n = 10)			
		Mean	SD
Adiponectin	Pre	22.09	± 8.1
	Post	28.70	± 19.4
P = 0.954			
Interaction = P = 0.301			

Overweight			
Exercise + Diet (n = 6)			
		Mean	SD
TNF-α	Pre	5.18	± 4.1
	Post	3.73	± 3.1
Diet Alone (n = 10)			
		Mean	SD
TNF-α	Pre	7.17	± 4.3
	Post	6.63	± 3.9
p = 0.123			
Interaction = p = 0.162			

Obese			
Exercise + Diet (n = 6)			
		Mean	SD
TNF-α	Pre	6.02	± 3.5
	Post	5.48	± 2.9
Diet Alone (n = 10)			
		Mean	SD
TNF-α	Pre	6.41	± 3.6
	Post	6.73	± 3.8
p = 0.973			
Interaction = p = 0.742			

Overweight			
Exercise + Diet (n = 6)			
		Mean	SD
Leptin	Pre	3.32	± 1.6
	Post	3.09	± 1.7
Diet Alone (n = 10)			
		Mean	SD
Leptin	Pre	4.27	± 2.4
	Post	2.22	± 1.0
p < 0.03			
Interaction = p = 0.120			

Obese			
Exercise + Diet (n = 6)			
		Mean	SD
Leptin	Pre	8.72	± 4.4
	Post	5.31	± 4.1
Diet Alone (n = 10)			
		Mean	SD
Leptin	Pre	8.96	± 7.1
	Post	7.78	± 5.1
p < 0.001			
Interaction = p < 0.004			

Overweight			
Exercise + Diet (n = 6)			
		Mean	SD
Ghrelin	Pre	81.61	± 77.3
	Post	60.61	± 49.6
Diet Alone (n = 10)			
		Mean	SD
Ghrelin	Pre	84.38	± 39.3
	Post	47.02	± 29.0
p = 0.201			
Interaction = p = 0.296			

Obese			
Exercise + Diet (n = 6)			
		Mean	SD
Ghrelin	Pre	34.25	± 19.6
	Post	45.59	± 30.3
Diet Alone (n = 10)			
		Mean	SD
Ghrelin	Pre	42.50	± 28.3
	Post	38.19	± 19.9
p = 0.422			
Interaction = p = 0.113			

Overweight			
Exercise + Diet (n = 6)			
		Mean	SD
Testosterone	Pre	11.34	± 7.1
	Post	10.40	± 5.6
Diet Alone (n = 10)			
		Mean	SD
Testosterone	Pre	7.30	± 4.2
	Post	6.86	± 4.6
p = 0.936			
Interaction = 0.896			

Obese			
Exercise + Diet (n = 6)			
		Mean	SD
Testosterone	Pre	7.42	± 4.9
	Post	6.80	± 2.5
Diet Alone (n = 10)			
		Mean	SD
Testosterone	Pre	5.89	± 5.0
	Post	7.55	± 4.3
p = 0.115			
Interaction = p = 0.631			

5 who classified as normotensive at follow-up. The number of individuals classified as pre-hypertensive also decreased from baseline to twelve weeks, dropping from 31 pre-hypertensive subjects to 21 following the interventions. The Exercise + Diet group dropped from 18 individuals at baseline to 11 individuals at twelve weeks who were pre-hypertensive, while the Diet Alone group saw a decrease from 13 to 10 individuals following the study. The number of subjects with hypertension remained the same from baseline to follow-up, however, it was characterized by a decrease of 3 to 0 individuals in the Exercise + Diet group while the Diet Alone group saw an increase of subjects with hypertension increasing from 4 to 7 individuals at twelve weeks.

With respect to diabetes 41 subjects were considered to have normal fasting glucose, while 7 were considered pre-diabetic and 3 were classified as diabetic at baseline. Following the respective interventions, the total number of individuals with normal fasting blood glucose dropped to 40. The Exercise + Diet group saw an increase in individuals classified as normal blood glucose, increasing from 22 subjects at baseline to 23 at twelve weeks. The diet alone group had 2 less individuals classified as normal blood glucose at twelve weeks dropping from 19 to 17 subjects in this category. The number of individuals classified as pre-diabetic increased at twelve weeks, from 7 subjects at baseline to 8 following the interventions. Of these the Exercise + Diet group dropped from 3 individuals at baseline to 2 individuals at twelve weeks while the Diet Alone group saw an increase from 4 to 6 individuals following the study. The number of

subjects with diabetes remained the same from baseline to follow-up where 1 individuals in the Exercise + Diet group and 2 individuals in the Diet Alone group had diabetes.

Seventeen subjects in the study displayed normal blood cholesterol, 15 were classified as borderline dyslipidemia, while 16 were considered to have dyslipidemia. Following the respective interventions, the total number of individuals with normal cholesterol was 28, where the Exercise + Diet group saw an increase from 11 subjects at baseline to 19 at twelve weeks. The diet alone group went from 6 to 9 individuals at twelve weeks who displayed normal blood lipids. The number of individuals classified as borderline hyperlipidemia decreased at twelve weeks, dropping from 15 subjects at baseline to 12 following the interventions. Of these, the Exercise + Diet group dropped from 8 individuals at baseline to 4 individuals at twelve weeks while the Diet Alone group saw an increase from 7 to 8 individuals following the study. The number of subjects with dyslipidemia dropped from 16 at baseline to 8 at follow-up, where 3 individuals in the Exercise + Diet group had dyslipidemia post study as compared to 7 at baseline and the Diet Alone group had 5 individuals with dyslipidemia following the study as compared to 9 at baseline.

Between baseline and follow-up, equivalent reductions in heart rate of approximately ~5 and ~6 bpm ($p=0.006$), LDL cholesterol of between ~11% and ~7% ($p=0.011$), and total cholesterol of ~10% and ~4% ($p<0.005$) were shown in both the Exercise + Diet and Diet Alone groups, respectively. Although results showed a significant difference within

groups, they did not show between groups differences when compared using an ANOVA. However, the Exercise + Diet group demonstrated a significant reduction in both diastolic and systolic blood pressure (mm Hg) of ~6 mm/hg ($p<0.001$) and ~7 mm/hg ($p<0.001$) respectively, which can be considered to be of clinical benefit, in the presence of no change in either value for the Diet Alone group.

Similarly, fasting triacylglycerol was reduced in the Exercise + Diet group by approximately 27% ($p<0.001$), while the Diet Alone group intervention showed no effect. With respect to insulin resistance, HOMA-IR did not respond to either the Exercise + Diet or Diet Alone protocols even under conditions of significant weight loss. HOMA-β was significantly reduced in the Diet Alone group by nearly 28% ($p=0.009$), however, the Exercise + Diet group saw an unexpected non-significant increase of ~15% under conditions of similar weight loss, suggesting that nutrition in isolation improved Beta cell function, while exercise in conjunction with diet (Exercise + Diet) resulted in no statistically significant change (**Table 3**).

5.5 Primary Outcome

5.5.1 Adiponectin response to the intervention

The primary outcome of this study was to determine the adiponectin response to an Exercise + Diet intervention as compared to a Diet Alone intervention. Student paired t-tests revealed that adiponectin did not change significantly in response to the twelve

week intervention for either the Exercise + Diet or the Diet Alone groups (**Table 3**). Furthermore, ANOVA demonstrated there was no significant difference between groups in response to either the Exercise + Diet or Diet Alone intervention (**Table 9**) indicating that neither a twelve week Exercise + Diet or Diet Alone intervention elicited a change in adiponectin for overweight and obese 35-55 year old males. Adiponectin results were graphed in a forest plot for the entire cohort **(Figure 6)** the Exercise + Diet group **(Figure 7)**, and the Diet Alone Group **(Figure 8)**.

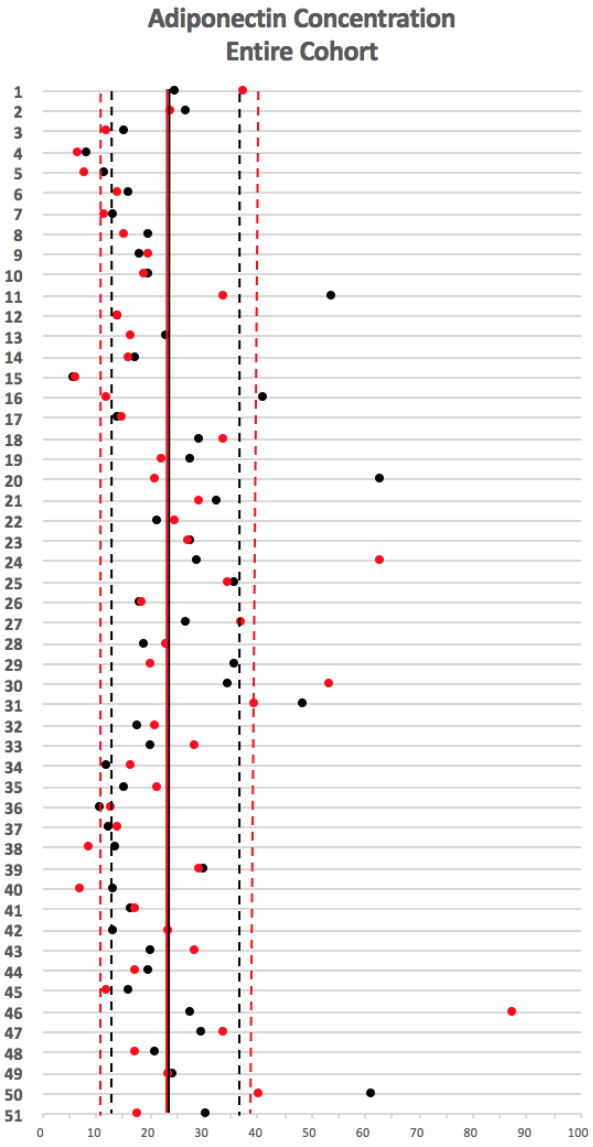

Figure 6: Adiponectin Response to intervention by subject for entire cohort

- Black - Baseline adiponectin by subject
- Red - Post intervention adiponectin by subject

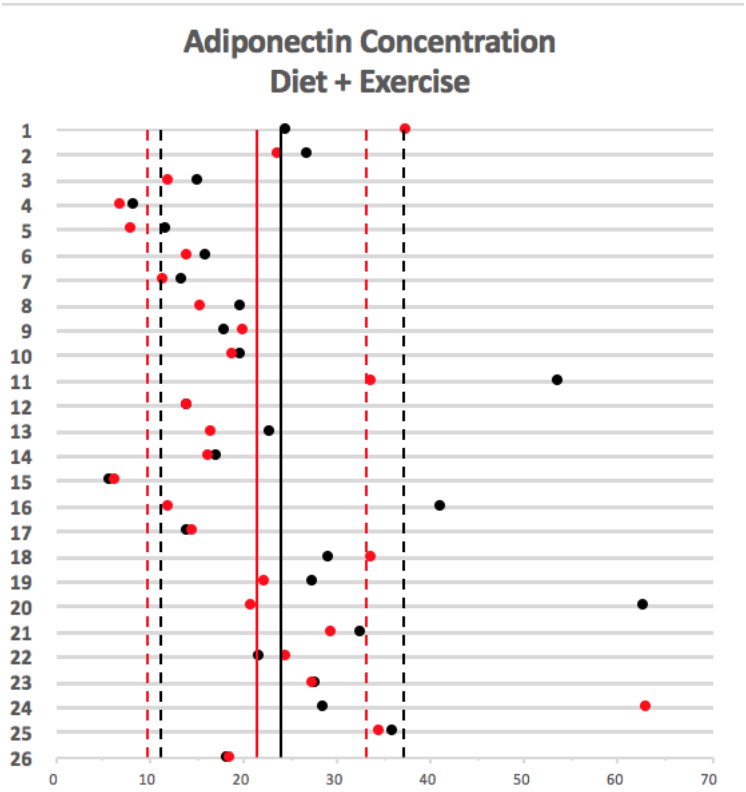

Figure 7: Adiponectin Response to intervention by subject for Exercise + Diet group

- Black - Baseline adiponectin by subject
- Red - Post intervention adiponectin by subject

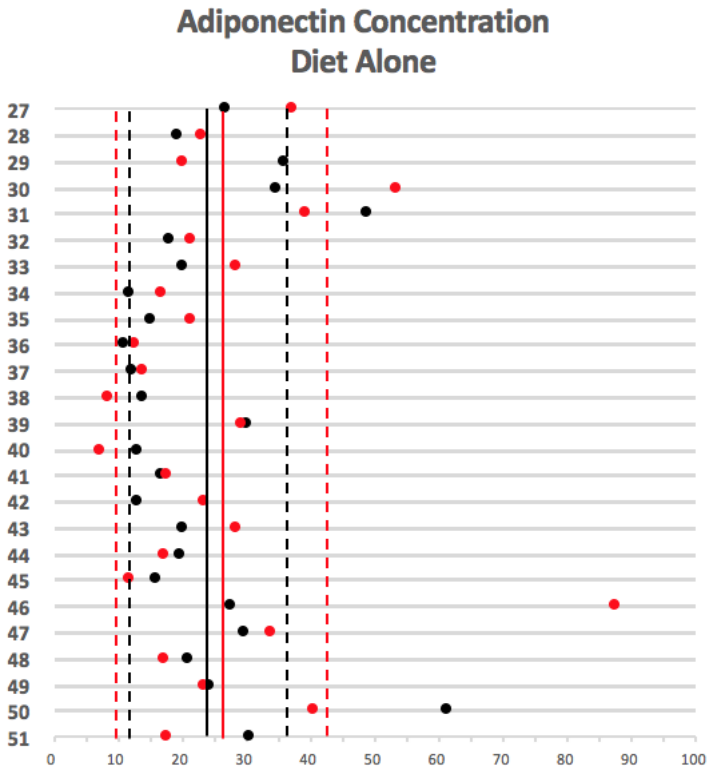

Figure 8: Adiponectin Response to intervention by subject for Diet Alone group

- Black - Baseline adiponectin by subject
- Red - Post intervention adiponectin by subject

5.6 Secondary Results

5.6.1 Adiponectin's relationship with Anthropometric and Biochemical Measures:

To determine adiponectin's relationship with anthropometric (e.g. %BF, %TF, waist circumference) and biochemical measures (e.g. Glucose, LDL, HDL) associated with obesity and metabolic disease, a correlation analysis was conducted. Baseline fasting adiponectin demonstrated an inverse association with visceral fat percentage %VF ($p=0.04$), which is a key adipose storage site with respect to metabolic health. Baseline assessments also showed an inverse relationship between adiponectin and biochemical measures, including triacylglycerol ($p<0.001$), (a known risk factor for diabetes and stroke), and the glucose mediating hormone insulin ($p=0.003$) **(Table 13)**. Furthermore, HOMA-IR ($p=0.003$) showed a strong correlation with adiponectin at baseline, indicating that adiponectin may interplay with insulin resistance in overweight and obese populations **(Table 13)**. With respect to humoral variables (adiponectin, TNF-α, leptin, ghrelin, testosterone), our results demonstrated a statistically significant inverse relationship between TNF-α and adiponectin at baseline ($p=0.02$), indicating that this hormone may be associated (**Table 14**).

Additionally, subgroup analysis was performed to determine if overweight and obese subjects responded differently to either the Exercise + Diet and Diet Alone interventions. This subgroup analysis divided by subjects with a BMI in the overweight or obese category indicated that adiponectin as well as other hormones of interest responded to

Table. 12 - Baseline Pearson Correlation of Body Composition Characteristics with Circulating **Adiponectin, Leptin, TNF-α, Total Testosterone,** and **Ghrelin** (n=51)

	Adiponectin		Leptin		TNF-α		Total Testosterone		Ghrelin	
	r	P	r	P	r	P	r	P	r	P
Age (yr)	0.95	NS	-0.10	NS	0.25	NS	-0.35	**0.01**	-0.01	NS
Height (cm)	1.00	NS	0.12	NS	-0.09	NS	0.16	NS	-0.16	NS
Weight (kg)	-0.09	NS	0.58	**0.00**	-0.21	NS	-0.08	NS	-0.42	**0.01**
Waist (cm)	0.12	NS	0.67	**0.00**	-0.22	NS	-0.12	NS	-0.48	**0.00**
Hip (cm)	0.01	NS	0.65	**0.00**	-0.28	NS	-0.06	NS	-0.45	**0.01**
Total Body Fat (kg)	0.03	NS	0.69	**0.00**	-0.29	**0.04**	-0.11	NS	-0.36	**0.03**
Total Lean Tissue (kg)	0.10	NS	0.27	NS	-0.02	NS	-0.02	NS	-0.40	**0.01**
Body Fat (%)	0.00	NS	0.67	**0.00**	-0.31	**0.03**	-0.13	NS	-0.31	NS
Trunk Fat (%)	0.04	NS	0.63	**0.00**	-0.28	**0.04**	-0.15	NS	-0.32	NS
BMI (kg/m2)	-0.06	NS	0.62	**0.00**	-0.20	NS	-0.17	NS	-0.44	**0.01**
Visceral Fat (kg)	0.02	**0.04**	0.42	**0.00**	-0.04	NS	-0.34	NS	-0.43	**0.01**

Table. 13- Baseline Pearson Correlation of Metabolic Characteristics with Circulating **Adiponectin, Leptin, TNF-α, Total Testosterone, Free Testosterone** and **Ghrelin** (n=51)

	Adiponectin		Leptin		TNF-α		Total Testosterone		Ghrelin	
	r	P	r	P	r	P	r	P	r	P
HDL Cholesterol (mmol/L)	-0.02	NS	-0.20	NS	-0.28	NS	0.05	NS	0.15	NS
LDL Cholesterol (mmol/L)	-0.11	NS	0.17	NS	0.05	NS	-0.18	NS	-0.34	NS
Total Cholesterol (mmol/L)	-0.21	NS	0.10	NS	0.07	NS	-0.21	NS	-0.35	**0.04**
Triacylglycerol (mmol/L)	-0.36	**0.01**	0.26	NS	0.23	NS	-0.20	NS	-0.44	**0.01**
Insulin (pmol/L)	-0.31	**0.03**	0.50	**0.00**	-0.04	NS	-0.09	NS	-0.55	**0.00**
HOMA-IR	-0.31	**0.03**	0.41	**0.00**	-0.10	NS	-0.10	NS	-0.55	**0.00**
HOMA-β	-0.15	NS	0.36	**0.01**	0.11	NS	-0.20	NS	-0.23	NS
Glucose (mmol/L)	0.05	NS	-0.04	NS	-0.17	NS	0.02	NS	-0.19	NS
Systolic Blood Pressure (mmhg)	-0.09	NS	0.38	**0.01**	0.00	NS	0.07	NS	-0.19	NS
Diastolic Blood Pressure (mmhg)	0.00	NS	0.17	NS	-0.07	NS	-0.15	NS	-0.16	NS
Heart Rate (bpm)	-0.18	NS	0.30	**0.04**	0.07	NS	-0.18	NS	-0.21	NS

Table. 14 - Baseline Pearson Correlation of Circulating **Adiponectin, Leptin, TNF-α, Total Testosterone, Free Testosterone** and **Ghrelin** (n=51)

	Adiponectin		Leptin		TNF-α		Total Testosterone		Ghrelin	
	r	P	r	P	r	P	r	P	r	P
Adiponectin (ug/ml)			-0.14	NS	-0.32	**0.02**	0.07	NS	0.28	NS
Leptin (ug/ml)	-0.14	NS			-0.13	NS	0.09	NS	-0.40	**0.02**
TNF-α (pg/ml)	-0.32	**0.02**	-0.13	NS			-0.38	**0.01**	-0.24	NS
Total Testosterone (pg/ml)	0.07	NS	0.09	NS	-0.38	**0.01**			0.08	NS
Ghrelin (pg/ml)	0.28	NS	-0.40	**0.02**	-0.24	NS	0.10	NS		

Table. 15 - Pearson Correlation of Change in Body Composition with Baseline with Circulating Adiponectin, Leptin, TNF-α, Total Testosterone, and Ghrelin (n=51)

	Adiponectin		Leptin		TNF-α		Total Testosterone		Ghrelin	
Exercise + Diet (n=26)	r	P	r	P	r	P	r	P	r	P
Weight (kg)	0.01	NS	-0.41	**0.04**	0.02	NS	0.00	NS	0.20	NS
Waist (cm)	-0.21	NS	-0.07	NS	-0.06	NS	-0.12	NS	0.42	NS
Hip (cm)	-0.01	NS	-0.02	NS	-0.08	NS	-0.11	NS	0.52	**0.03**
Total Body Fat (kg)	-0.12	NS	-0.15	NS	0.07	NS	-0.04	NS	0.24	NS
Total Lean Tissue (kg)	0.28	NS	-0.19	NS	-0.11	NS	0.34	NS	0.29	NS
Body Fat (%)	-0.19	NS	0.10	NS	-0.01	NS	-0.14	NS	-0.06	NS
Trunk Fat (%)	-0.24	NS	0.15	NS	-0.05	NS	-0.19	NS	0.35	NS
BMI (kg/m2)	0.06	NS	-0.41	**0.04**	0.00	NS	0.02	NS	0.33	NS
Visceral Fat (kg)	-0.05	NS	0.07	NS	0.19	NS	0.04	NS	0.27	NS
Diet Alone (n=25)										
Weight (kg)	0.00	NS	-0.23	NS	0.36	NS	-0.12	NS	-0.11	NS
Waist (cm)	0.00	NS	0.03	NS	-0.03	NS	0.01	NS	-0.07	NS
Hip (cm)	0.00	NS	-0.15	NS	0.30	NS	-0.10	NS	-0.20	NS
Total Body Fat (kg)	0.00	NS	-0.22	NS	0.18	NS	-0.05	NS	0.11	NS
Total Lean Tissue (kg)	0.00	NS	-0.22	NS	0.19	NS	-0.28	NS	-0.07	NS
Body Fat (%)	0.00	NS	-0.07	NS	0.08	NS	-0.02	NS	0.37	NS
Trunk Fat (%)	0.00	NS	0.03	NS	0.09	NS	0.02	NS	-0.24	NS
BMI (kg/m2)	0.00	NS	-0.24	NS	0.39	NS	-0.13	NS	-0.33	NS
Visceral Fat (kg)	-0.16	NS	-0.47	**0.02**	-0.01	NS	0.03	NS	0.11	NS

Table. 16 - Pearson Correlation of Change in Metabolic Characteristics with Baseline Circulating **Adiponectin, Leptin, TNF-α, Total Testosterone,** and **Ghrelin** (n=51)

	Adiponectin		Leptin		TNF-α		Total Testosterone		Ghrelin	
Exercise + Diet (n=26)	r	P	r	P	r	P	r	P	r	P
HDL Cholesterol (mmol/L)	0.12	NS	0.09	NS	0.53	**0.01**	-0.08	NS	-0.32	NS
LDL Cholesterol (mmol/L)	0.12	NS	-0.07	NS	0.12	NS	0.28	NS	0.26	NS
Total Cholesterol (mmol/L)	0.20	NS	-0.12	NS	0.14	NS	0.18	NS	0.19	NS
Triacylglycerol (mmol/L)	0.26	NS	-0.22	NS	-0.14	NS	-0.15	NS	0.15	NS
Insulin (pmol/L)	0.09	NS	-0.46	**0.02**	0.23	NS	-0.20	NS	0.23	NS
HOMA-IR	0.24	NS	-0.55	**0.00**	0.34	NS	-0.12	NS	0.21	NS
HOMA-β	-0.38	NS	-0.19	NS	0.13	NS	-0.35	NS	0.04	NS
Glucose (mmol/L)	0.41	**0.04**	-0.17	NS	0.21	NS	0.15	NS	0.01	NS
Systolic Blood Pressure (mmhg)	0.29	NS	-0.16	NS	-0.54	**0.01**	0.14	NS	0.51	**0.03**
Diastolic Blood Pressure (mmhg)	0.16	NS	-0.10	NS	0.13	NS	-0.23	NS	0.20	NS
Heart Rate (bpm)	0.06	NS	-0.05	NS	0.29	NS	-0.04	NS	-0.01	NS
Diet Alone (n=25)										
HDL Cholesterol (mmol/L)	-0.24	NS	-0.24	NS	0.26	NS	-0.36	NS	-0.12	NS
LDL Cholesterol (mmol/L)	-0.19	NS	0.25	NS	0.07	NS	0.08	NS	-0.06	NS
Total Cholesterol (mmol/L)	-0.27	NS	0.25	NS	0.17	NS	-0.15	NS	0.02	NS
Triacylglycerol (mmol/L)	-0.28	NS	0.24	NS	0.24	NS	-0.42	NS	0.21	NS
Insulin (pmol/L)	0.03	NS	-0.05	NS	-0.01	NS	-0.61	**0.00**	0.42	NS
HOMA-IR	0.03	NS	0.26	NS	0.15	NS	-0.66	**0.00**	0.19	NS
HOMA-β	0.13	NS	-0.03	NS	-0.39	NS	0.01	NS	0.39	NS
Glucose (mmol/L)	-0.34	NS	0.03	NS	0.50	**0.02**	-0.39	NS	0.01	NS
Systolic Blood Pressure (mmhg)	0.07	NS	-0.12	NS	0.18	NS	-0.52	**0.01**	-0.26	NS
Diastolic Blood Pressure (mmhg)	0.02	NS	-0.05	NS	-0.09	NS	-0.19	NS	-0.37	NS
Heart Rate (bpm)	0.17	NS	-0.36	NS	-0.26	NS	-0.05	NS	0.16	NS

both the Exercise + Diet and Diet Alone interventions similarly regardless of BMI classification and reflect the results of the combined (overweight and obese) group analysis **(Table 11)**.

To determine the relationship between baseline adiponectin and the changes in physical and biochemical characteristics due to the interventions, correlation analysis was performed **(Table 15, 16 & 17)**. Subgroup investigation revealed that fasting baseline adiponectin was positively associated with a change in glucose ($p<0.04$), which was expected. As well, it appears that baseline adiponectin is negatively associated with a change in adiponectin within the Exercise + Diet group ($p<0.05$), indicating that those with lower adiponectin at baseline experience the greatest increase in adiponectin in response to exercise and diet ,while higher baseline adiponectin results in a smaller increase in adiponectin in response to the intervention (**Table 15 & 16**). In the Diet Alone group, baseline adiponectin was not associated with changes in any of the physical (**Table 15**) or biochemical characteristics (**Table 16 & 17**).

Table. 17 - Pearson Correlation of Change in **Adiponectin, Leptin, TNF-α, Total Testosterone,** and **Ghrelin** with the Baseline Energy Regulating Hormones (n=51)

	Adiponectin		Leptin		TNF-α		Total Testosterone		Ghrelin	
Exercise + Diet (n=26)	r	P	r	P	r	P	r	P	r	P
Adiponectin (ug/ml)	-0.39	**0.05**	0.38	NS	-0.32	NS	0.05	NS	-0.12	NS
Leptin (ug/ml)	0.06	NS	-0.56	**0.003**	0.09	NS	0.11	NS	0.42	NS
TNF-α (pg/ml)	-0.01	NS	0.00	NS	-0.45	**0.02**	0.21	NS	0.13	NS
Total Testosterone (pg/ml)	0.04	NS	0.13	NS	0.19	NS	-0.71	**0.00**	-0.30	NS
Free Testosterone (pg/ml)	-0.02	NS	-0.08	NS	0.21	NS	-0.44	**0.03**	-0.44	NS
Ghrelin (pg/ml)	0.26	NS	0.26	NS	0.38	NS	-0.15	NS	-0.52	**0.03**
Diet Alone (n=25)										
Adiponectin (ug/ml)	-0.14	NS	0.31	NS	0.11	NS	-0.02	NS	-0.25	NS
Leptin (ug/ml)	-0.04	NS	-0.60	**0.00**	-0.15	NS	-0.31	NS	0.09	NS
TNF-α (pg/ml)	0.29	NS	-0.03	NS	-0.24	NS	-0.29	NS	-0.10	NS
Total Testosterone (pg/ml)	0.38	NS	-0.12	NS	-0.18	NS	-0.57	**0.00**	0.02	NS
Free Testosterone (pg/ml)	0.02	NS	0.03	NS	-0.05	NS	-0.33	NS	-0.21	NS
Ghrelin (pg/ml)	0.00	NS	0.25	NS	0.10	NS	-0.01	NS	-0.68	**0.00**

Table 18. Baseline Pearson Correlation Skinfold Measurements with Circulating Adiponectin, Leptin, TNF-α, Total Testosterone, and Ghrelin (n=51)

	Adiponectin		Leptin		TNF-α		Total Testosterone		Ghrelin		Insulin	
Skin Folds	r	P	r	P	r	P	r	P	r	P	r	P
Pectoralis	0.04	NS	0.42	**0.001**	-0.04	NS	-0.36	NS	-0.47	**0**	0.25	NS
Tricep	0.06	NS	0.27	NS	0.04	NS	-0.20	NS	-0.30	NS	0.50	**0.001**
Sub	-0.02	NS	0.46	**0.001**	-0.28	NS	-0.11	NS	-0.27	NS	0.22	NS
Mid	-0.11	NS	0.54	**0.001**	-0.09	NS	-0.19	NS	-0.25	NS	0.26	NS
Supra	-0.02	NS	0.28	NS	-0.23	NS	-0.19	NS	-0.03	NS	0.19	NS
Umb	-0.02	NS	0.19	NS	-0.04	NS	-0.22	NS	-0.01	NS	0.19	NS
Quad	0.12	NS	0.35	**0.01**	-0.09	NS	-0.06	NS	-0.16	NS	0.17	NS
Girth Measurements												
Right Bicep Flex	0.00	NS	0.33	**0.02**	-0.27	NS	-0.07	NS	-0.20	NS	0.01	NS
Left Bicep Flex	0.04	NS	0.37	**0.01**	-0.37	**0.01**	-0.02	NS	-0.26	NS	0.16	NS
Right Bicep	0.09	NS	0.29	**0.04**	-0.37	**0.01**	-0.07	NS	-0.11	NS	0.08	NS
Left Bicep	0.06	NS	0.42	**0.001**	-0.40	**0.001**	-0.02	NS	-0.26	NS	0.19	NS
Neck	-0.05	NS	0.56	**0.001**	-0.22	NS	0.23	NS	-0.39	**0.02**	0.48	**0.001**
Shoulders	-0.13	NS	0.49	**0.001**	-0.30	**0.04**	-0.14	NS	-0.31	NS	0.29	NS
Chest	-0.21	NS	0.51	**0.001**	-0.24	NS	-0.15	NS	-0.40	**0.02**	0.28	NS
Waist	-0.13	NS	0.74	**0.001**	-0.13	NS	-0.08	NS	-0.51	**0.001**	0.44	**0.001**
Hip	-0.05	NS	0.69	**0.001**	-0.36	**0.01**	0.06	NS	-0.33	**0.05**	0.35	**0.02**
Right Thigh	0.12	NS	0.11	NS	-0.43	**0.001**	0.19	NS	0.11	NS	0.15	NS
Left Thigh	0.12	NS	0.16	NS	-0.39	**0.01**	0.15	NS	-0.01	NS	0.21	NS

Table. 19 - HOMA-β & HOMA-IR For Non-Diabetic Normal-Weight, Overweight, and Obese Men (Ages 35-55) From The General Population (n=317)

	Entire Cohort	NW	OW	OB
	(n = 317)	(n = 71)	(n = 143)	(n = 103)
	Mean SD	Mean SD	Mean SD	Mean SD
HOMA-β	120.76 ± 66.3	88.48 ± 48.7	109.72 ± 55.6	158.04 ± 73.0
HOMA-IR	2.60 ± 1.7	1.80 ± 1.6	2.38 ± 1.2	3.51 ± 1.9

5.6.2 Exercise associated and energy regulating hormonal response to intervention

Student paired t-tests were performed to determine if the twelve week Exercise + Diet or Diet Alone interventions resulted in a change in fasting TNF-α, testosterone, leptin and ghrelin (**Table 3**).

Paired t-test revealed that energy regulating hormone leptin decreased in response to both the Exercise + Diet (36.5%) ($p=0.002$) and Diet Alone (21.6%) ($p=0.023$) interventions and after conducting ANOVA it was demonstrated that there were no significant differences between the groups. This indicated that other factors may be responsible for the change in leptin outside of Exercise + Diet (**Table 9**). Similarly, ANOVA was conducted between groups for ghrelin, testosterone and TNF-α, which determined that there were no differences between groups as a result of the intervention (**Table 9**). Leptin, ghrelin, testosterone and TNF-α did not respond differently to the Exercise + Diet, and Diet Alone interventions.

Baseline anthropometric and biochemical variables were compared with our secondary hormone measures to determine if pre-established or novel associations were present (**Table 12, 13, 14**). To increase statistical power in all baseline correlations, subjects from both groups were pooled at baseline for Pearson's Correlation analysis.

As expected, baseline fasting leptin was found to be positively correlated with several anthropometric variables related to obesity. These variables included global measures of

obesity including weight ($p<0.001$), total body fat ($p<0.001$) and body fat percentage ($p<0.001$). Of particular interest to this study were regional measures of adiposity, specifically those representative of central fat patterning including trunk fat % ($p<0.001$), visceral fat % ($p<0.001$), waist circumference ($p<0.001$), and hip circumference ($p<0.001$), which all showed a statistical association. Leptin showed the highest correlation with anthropometrics compared to any other hormone, indicating that leptin is strongly related to adiposity.

Biochemical markers of insulin sensitivity including insulin ($p<0.001$), HOMA-IR ($p<0.001$), and HOMA-β ($p<0.01$), all of which showed moderate correlations with leptin at baseline. Additionally, systolic blood pressure ($p=0.01$) and heart rate ($p=0.04$) also showed statistically significant correlations (**Table 13**).

When compared to changes in anthropometric and biochemical markers following the twelve week intervention, baseline leptin was negatively associated with a change in weight ($p=0.04$) and BMI ($p=0.04$) in the Exercise + Diet group. These results suggest that leptin is not just related to bodyweight and BMI at baseline, but also during changes occurring as a result of weight loss achieved through exercise. Furthermore, leptin was correlated to insulin ($p=0.02$) and HOMA-IR ($p=0.04$), but only in the Exercise + Diet group. Regardless of group, baseline leptin was inversely correlated with the change in leptin (**Table 17**). Finally, for the Diet Alone group, baseline leptin was associated with a change in %VF ($p=0.02$) (**Table 15**).

Baseline fasting ghrelin was found to be negatively correlated with several measurements related to adiposity and body composition, including weight ($p=0.01$), waist circumference ($p<0.001$), hip circumference ($p=0.01$), %TF ($p=0.03$), and %VF ($p=0.01$) (**Table 12**). These results were expected due to ghrelin's inverse relationship with obesity. As hypothesized, metabolic variables related to energy metabolism including insulin ($p=0.04$) and HOMA-IR ($p=0.01$), also demonstrated inverse relationships with ghrelin. Moreover, biochemical variables of total cholesterol ($p<0.001$), and tricylglycerol ($p<0.001$) were correlated to ghrelin for the entire cohort (**Table 13**). In the Exercise + Diet group, baseline ghrelin was positively associated with changes in hip circumference ($p=0.03$) and systolic blood pressure ($p=0.03$) (**Table 15, 16**). Baseline ghrelin, however, is predictive of change in ghrelin in both the Exercise + Diet ($p=0.03$) and Diet Alone ($p<0.001$) groups where higher baseline ghrelin indicates a smaller change in ghrelin when weight loss is achieved (**Table 17**).

Total testosterone was negatively associated with age ($p=0.01$) (**Table 12**). Additionally, baseline testosterone is inversely related to TNF-α ($p=0.01$), which was predicted due to its well established reciprocal relationship with testosterone status (**Table 14**).

Baseline total testosterone was inversely associated with changes in insulin ($p<0.001$) and HOMA-IR ($p<0.001$), as well as with systolic blood pressure ($p=0.01$) in the Diet group only. It was expected that these results would be present in both cohorts due to their similar weight loss (**Table 16**). Similar to the other measured hormonal variables

in our study, baseline testosterone predicted the change in testosterone resulting from the Exercise + Diet protocol (p=0.05). However, this correlation was not present in the Diet Alone group (**Table 16**).

Lastly, it was hypothesized that baseline fasting TNF-α would be negatively associated with adiposity. Results suggest that baseline total body fat (p=0.04), %BF (p=0.03), and %TF (p=0.04) support this hypothesis (**Table 12**). Furthermore, as stated previously, the hormones adiponectin (p=0.02) and total testosterone (p=0.01) were both correlated with TNF-α (**Table 14**). Baseline TNF-α was positively associated with the change in HDL cholesterol due to Exercise + Diet (p=0.01) and negatively associated with the change in systolic blood pressure (p=0.01), which confirms the previously identified associations between TNF-α and cardiovascular health. (**Table 16**). Baseline TNF-α was only positively associated with the change in glucose in the Diet Alone group (p=0.02), (**Table 13**) which, along with the lack of correlation with HOMA-IR, did not show the anticipated relationship with insulin resistance.

5.6.3 Exploratory Analysis of Endocrine Response to Intervention:

An analysis of covariance (ANCOVA) was performed, controlling for percentage or trunk fat at baseline, which is an established confounding variable for adiponectin (Cahill et al., 2013). The ANCOVA suggests that adiponectin significantly decreased in the Exercise + Diet group and increased in the Diet Alone group ($p < 0.036$) (**Table 9**). Additionally, we conducted an ANCOVA on TNF-α, which controlled for percentage of

trunk fat. The ANCOVA revealed that TNF-α significantly decreased in both the Exercise + Diet and Diet Alone groups between baseline and twelve weeks by a similar magnitude. However, there was no difference between the groups.

To control for the impact of changes in body composition, specifically the increase in lean body mass in the Exercise + Diet group, on the energy regulating hormone ghrelin, an ANCOVA was performed. Lean body mass has been shown to be a confounder for ghrelin (Bajer et al., 2015). This analysis revealed that ghrelin decreased significantly in the Diet Alone group ($p=0.05$) compared to the Exercise + Diet group ($p=0.04$) when controlling for increases in lean body mass (**Table 9**).

5.6.4 The Association of Baseline Adiponectin, Leptin, Ghrelin, Total Testosterone, and TNF-α Concentration with Adiposity Characteristics

To investigate the possible association between endocrine variables and regional adiposity, Pearson correlations were performed between hormones and regional measurements of girth, as well as for regional subcutaneous skin fold thickness **(Table 18)**.

Leptin, shown to be elevated in conditions of obesity and reduced when decreases in adiposity occur during weight loss, was associated with several skinfold sites including the pectoralis ($p<0.001$), mid-axillary ($p<0.001$), subcapularis ($p<0.001$), the quadriceps ($p<0.001$), and all girth measurements ($p<0.05$) except thighs. Leptin was also

associated with %BF ($p<0.001$), BMI ($p<0.001$), TF% ($p<0.001$), and VF% ($p<0.001$), as mentioned previously. Due to leptin's previously established relationship with regional adiposity, all skinfold and girth measurements were used in the analysis (**Table 18**).

Ghrelin was shown to be inversely associated with the pectoralis skinfold as well as with girth measurements for the chest, waist and hips, and was negatively associated with BMI and VF% when a correlation analysis was performed (**Table 18**).

Correlation analysis revealed that sex hormones showed no significant association with subcutaneous skinfold sites, girth measurements or regional body fat measures. Skinfold and girth measurement sites related to gynoid and android obesity were chosen for analysis with testosterone to reduce the potential number of comparisons, and to maintain statistical power. These included the triceps, pectoralis, suprailiac, umbilical and quadriceps skin fold sites, as well as arm, waist, hip and thigh girth measurements (**Table 18**).

Correlation analysis was also performed for adiponectin, which did not show a relationship with skinfold sites. However, as previously reported, adiponectin was negatively associated with percentages of visceral fat ($p=0.04$) determined by DXA. TNF-α failed to demonstrate correlations with any regional skinfold or girth measurements, but it did show a positive association with the TF% and BF% determined by DXA. Skin fold and girth measurements associated with gynoid fat patterning were

also chosen for analysis, including the subscapularis, mid axillary, suprailliac and umbilical skinfold sites, the waist and hip girth measures, and DXA measures of adiposity (**Table 18**).

5.6.5 The Association of Baseline Adiponectin, Leptin, Ghrelin, Total Testosterone, and TNF-α Concentration with the Change in Adiposity Characteristics

Insulin was positively associated with the triceps skinfold site, as well as several DXA measures of adiposity including BF%, TF%, and visceral fat in our correlation analysis (**Table 18**).

In an attempt to determine if the change in adiposity measures, either through skin fold, girth or DXA measures, were associated with baseline endocrine concentration, a correlation analysis was performed. Due to the lack of change in several endocrine variables in the presence of significant changes in adiposity, the correlation analysis failed to show any significant associations between changes in adiposity variables and baseline hormones (**Table 18**).

6 Discussion

The obesity epidemic affects over 500 million people globally (Center for Disease Control, 2016). The prevalence of obesity in Canada is nearly 20%, and Newfoundland and Labrador is the most significantly impacted, with an estimated 29-40% of the population affected (Twells et al., 2014). Middle aged overweight and/or obese males possess specific risk factors for metabolic disease, including hypertension, coronary heart disease, stroke, type 2 diabetes and certain cancers (Camacho et al., 2013). To mitigate obesity and its comorbidities, diet and exercise interventions have been extensively employed; however, there is inconsistency in their adherence and training prescription, leading to heterogeneity in the research.

This research sought to investigate the benefits of structured exercise and nutrition (Exercise + Diet) on increasing levels of adiponectin and metabolic risk factors such as obesity and energy regulating hormones (specifically TNF-α, leptin, ghrelin and testosterone). The relationship between such energy regulating hormones and regional adiposity as a result of structured exercise and nutrition was also explored. Specifically, the primary goal of this study was to compare the effectiveness of a twelve week structured exercise and nutritional-intervention program (Exercise + Diet) to a program of nutritional intervention alone (Diet Alone) on adiponectin levels.

Several hypotheses were considered throughout this study. The primary hypothesis was that adiponectin levels would increase as a result of weight loss from a combined modification of Exercise + Diet rather than through Diet Alone. Additionally, it was hypothesized that the Exercise + Diet group would have greater improvements in energy regulating hormones, such as ghrelin and testosterone, and a decrease in both leptin and TNF-α, compared to modification of Diet Alone. Lastly, it was hypothesized that central adiposity, as determined by DXA, would have a significant relationship with energy regulating hormones, while skin-fold thickness, determined by callipers, would not demonstrate a similar relationship.

6.1 Body Composition and Biochemical Response to Intervention:

At baseline, anthropometric and body composition was determined in participating middle aged males (44.59 ± 6.45yrs), indicating that they were overweight and/or obese (BMI – 31.85 ± 4.1), yet free from metabolic disease with respect to elevated cholesterol, blood pressure, glucose and insulin resistance. Following the twelve week intervention, body weight decreased by 4.5% in both the Exercise + Diet and Diet Alone groups. In addition, waist circumference, hip circumference, BMI, total mass, fat mass, trunk fat, visceral fat and percent body fat all decreased between 3-9% in both groups.

Changes in weight are affected by the amount of energy expended versus the amount of energy consumed (Swift, Johannsen, Lavie, Earnest, & Church, 2014). Overall, the

changes in weight in response to exercise training without caloric restriction are highly heterogeneous and individual differences can span weight gain to clinically significant weight loss (Swift et al., 2014). Based on the present literature, unless the overall volume of exercise training is very high, clinically significant weight loss is unlikely to occur (Swift et al., 2014). The current exercise intervention was considered high intensity and resulted in approximately 1800 calories in exercise expenditure per week, however, this may have been insufficient to result in additional weight loss.

Wing et al. reported that, although exercise training and caloric restriction together may promote greater weight loss compared to caloric restriction alone, the differences in weight loss are not statistically significant (Wing & Phelan, 2005). Miller et al. performed a meta-analysis of weight loss interventions and determined that rate of weight loss was similar after exercise training and caloric restriction (1.0 kg/week) and caloric restriction alone (0.98 kg/week) (Miller, Koceja, & Hamilton, 1997). Thus, the present study supports the majority of literature which indicates that the weight loss from combined exercise and caloric restriction can be attributed to caloric restriction (Wing & Phelan, 2005). Although body weight was also reduced regardless of intervention, the Exercise + Diet group experienced the greater improvement in fitness, lean body mass, and metabolic profile. Exercise may offset potential weight loss because of its tendency, as demonstrated in the current study, to build lean body mass. This increase in muscle resulting from exercise would result in less weight loss, however is beneficial for long term health and fitness (Wing & Phelan, 2005).

Metabolic measures including LDL, total cholesterol, triglycerides, systolic and diastolic blood pressure all decreased in the Exercise + Diet group but were not altered in the Diet Alone group. With respect to insulin resistance, HOMA-β improved by 28% in the Diet Alone group but not the Exercise + Diet group. The relevance of this measure is demonstrated by others who have shown that defects in islet β-cell function is predictive of the development of type 2 diabetes and is present long before the diagnostic criterion for diabetes has been met (Matthews, 1996; Pimenta et al., 1995).

Typically, the western diet, which is characterized by an increased proportion of dietary fat and lower amounts of carbohydrates negatively impacts β-cell function (Rosenbaum & Leibel, 2010). A shift to a diet lower in fat and higher in carbohydrates has been shown to ameliorate this dysfunction function (Rosenbaum & Leibel, 2010). These results were mirrored in the current study where significant decrease in HOMA-β as a result of the 12-week Diet Alone intervention. It is possible that the reduced intake of saturated fats and simple carbohydrates associated with the Diet Alone protocol was responsible for this change. This improved β-cell function was not shared by the Exercise + Diet group. This finding was unexpected given exercises established benefit to insulin sensitivity (Babraj et al., 2009; Potteiger, Jacobsen, Donnelly, Hill, & Midwest Exercise Trial, 2003; Whyte, Gill, & Cathcart, 2010).). In comparison to non-diabetic normal weight, overweight and obese men ages 35-55 years old from the general population of Newfoundland the Diet Alone groups baseline HOMA-β more closely

resembled that of the overweight category while the Exercise + Diet group baseline value was closer to that of a normal weight population (**Table 19**). This baseline difference, although not statistically significant may explain the lack of change in HOMA-β in the Exercise + Diet group. Additionally, the lack of change in HOMA-β is likely due to the absence of insulin resistance among the study population who were generally metabolically healthy, where 22 of the 26 subjects in the Exercise + Diet group displayed normal blood glucose. These conclusion are based on speculation the explanation as to why the Exercise + Diet group did not respond similarly to Diet Alone group after both undergoing the same dietary protocol is unanswered and warrants further investigation.

The results indicate that the two interventions were largely similar in terms of weight loss and change in regional adiposity, but that there were statistically significant differences in metabolic parameters, fitness and lean body mass within the Exercise + Diet group. Although greater quantities of lean body mass has been associated with improved insulin sensitivity and glucose disposal when comparing men and women, it is unlikely that the modest change in lean body mass in the Exercise + Diet group would have demonstrated an increased insulin sensitivity (Rattarasarn, Leelawattana, & Soonthornpun, 2010).

Although resistance training shows a positive impact on lean body mass, cardiovascular risk factors and insulin sensitivity, a recent meta-analysis suggest that in subjects with a BMI $\geq$25 kg/m^2, aerobic exercise is more efficient in reducing measures

of obesity including body weight, waist circumference and fat mass as well as in increasing VO_2max uptake when compared to resistance training (Schwingshackl et. al., 2013).

Furthermore, the meta-analysis results provide evidence that a combined intervention seems to be the most promising tool for management of overweight and obesity (Schwingshackl 2013). Combined aerobic and resistance training was more powerful in reducing anthropometric risk factors like body weight, waist circumference, fat mass and increasing lean body mass when compared to exercise training (either aerobic or resistance training) in isolation (Schwingshackl 2013). The American College of Sports Medicine recommends either moderate-intensity aerobic physical activity for a minimum of 30 min on five days each week or vigorous-intensity aerobic activity for a minimum of 20 min on three days each week for healthy adults (ACSM 2014). In addition, these authorities encourage regular resistance training (RT) for a minimum of two days per week performing 8 exercises with eight to twelve repetitions (ACSM 2014). The goal of this research was to investigate whether the high intensity supervised resistance training program utilized in this study and designed to increase energy expenditure to a greater extent than traditional resistance training was sufficient to achieve the same impact as combined aerobic and resistance training. Additionally, due to the equipoise which remains regarding the impact of resistance training on the hormones of interest which relate to energy metabolism, body composition and energy intake, the

current study used a single exercise approach to clearly delineate the exercise mediated impact on these hormones.

The current study did not find a difference in degree of weight loss between groups despite suspected increased energy demands in the structured Exercise + Diet group. It is likely that the frequency of exercise sessions was not sufficient to create a large enough energy deficit that could translate into greater weight loss between the Exercise + Diet and Diet Alone groups. Although the sample size calculation was based on similar work (Simpson & Singh, 2008) and increased based on interim analysis, the small sample size may help explain the lack of hypothesized change between groups, and the difference between baseline and twelve weeks.

6.2 Primary Outcome: The response of adiponectin to a structured fitness and nutrition program compared to nutrition alone

6.2.1 Adiponectin: Obesity

Although the adiponectin response to weight loss as a result of diet and exercise in humans is uncertain, adiponectin has been shown to be inversely related to obesity status in a large number of studies (Blüher, 2014; Fasshauer & Bluher, 2015; Hui, Lam, Vanhoutte, & Xu, 2012; Kern, Di Gregorio, Lu, Rassouli, & Ranganathan, 2003; Kishida, Funahashi, & Shimomura, 2014a; Lindsay et al., 2002; Selyatitskaya et al., 2015; Yamauchi et al., 2014). In addition, levels of adiponectin have increased in the presence

of significant weight loss (Varady, Tussing, Bhutani, & Braunschweig, 2009; Yang et al., 2001).

This study's hypothesis assumes that adiponectin would be inversely associated with body fat, and would increase in response to decreases in adiposity resulting from a highly controlled Exercise + Diet intervention. The current study failed to find an association between adiponectin and any of the obesity-related body composition measurements. However, adiponectin was negatively associated with triacylglycerol, insulin, insulin resistance, and TNF-α at baseline. The lack of association and change in adiponectin in the presence of significant reductions in total and regional body fat in the current study was unexpected. Several studies have examined changing adiponectin concentrations in response to weight reduction with contradictory results. Some groups showed no concordance between adiponectin status and change in adiposity (Cahill et al., 2013; Cnop et al., 2003), whereas others demonstrated that adiponectin levels significantly increased after weight reduction (Varady et al., 2009; Yang et al., 2001). The degree of weight loss in the current investigation was modest at ~5% and ~4% for the Exercise + Diet and Diet Alone groups, respectively. This result was similar to other studies using exercise in overweight and/or obese populations (M. Bluher, 2013; Boudou et al., 2003; Fatouros et al., 2005; Giannopoulou et al., 2005; Hara et al., 2005; Marcell et al., 2005; Oberbach et al., 2006; O'Leary et al., 2006; Polak et al., 2006; Ryan et al., 2003). Not only was weight loss expected in both groups, the current study hypothesized a greater degree of weight loss in the Exercise + Diet group due to increases in energy

expenditure. Weight loss and change in regional adiposity was similar between groups, with only lean body mass showing a physiologically significant difference in the Exercise + Diet group.

Only total adiponectin was measured in the current study. The choice to measure total adiponectin was due to the inconclusive response of different isoforms of adiponectin to weight loss achieved via diet and exercise. Weight loss by caloric restriction appears to be associated with an increase in HMW adiponectin (Acharya, Brooks, Evans, Linkov, & Burke, 2013; Bobbert et al., 2005). Regarding exercise alone, one study showed that, irrespective of any associated weight loss, there was a shift in the adiponectin multimer distribution toward LMW (Auerbach et al., 2013); two other studies showed no changes in HMW adiponectin after exercise training (Ando, Hosaka, Suzuki, & Yamagata, 2009; Christiansen et al., 2010); yet, another study showed that HMW adiponectin concentration increased (Kelly et al., 2012). Thus, with current evidence, we could not determine whether exercise training and caloric restriction induced weight loss have different effects on adiponectin multimer complex composition a decision was made not to measure adiponectin multimer distribution in this study. However, because HMW adiponectin may be more closely associated with insulin resistance than total plasma adiponectin concentration (Hara et al., 2006b), it would have been prudent to measure this as part of the current study's methodology. It is likely that the inconsistent findings from the current and previous studies is related to the lack of assessment of the

adiponectin multimer distribution changes in response to interventions and is a limitation of the current research.

The degree of weight loss between groups was expected to be greater in the current study, due to the increased energy demand from the structured exercise protocol, but this was not the case. It has been proposed that to increase circulating adiponectin, a weight loss of at least 10% of one's initial body weight is needed (Christiansen et al., 2010). Although the current study's weight loss was statistically significant (4.5%), and the population was overweight and/or obese, it may not have been realistic for these individuals to achieve the magnitude of weight loss necessary to impact adiponectin within the twelve week study period. Furthermore, studies which have shown increases in adiponectin in response to weight loss have done so by using a more obese population than subjects who displayed a BMI of between 25-35 kg/m^2 (Hulver et al., 2002; Kondo et al., 2006; Polak et al., 2006).

Several modalities have been employed to demonstrate changes in adiponectin in obese individuals, including the use of a very low calorie diet (VLDL) (Hotta et al., 2001; Manigrasso et al., 2005), exercise (Brekke et al., 2005; Giannopoulou et al., 2005; Hsieh & Wang, 2005; Hulver et al., 2002; Marcell et al., 2005; Oberbach et al., 2006) and gastric bypass surgery (Faraj et al., 2003; Hulver et al., 2002). The current study utilized moderate-to-high intensity resistance training exercise, which may not be achievable or safe for morbidly obese subjects (Gotshalk et al., 1997). As a result it was most appropriate to use overweight and obese subjects in this study. Although it is likely that

morbidly obese subjects may have been more capable of losing weight in twelve weeks as compared to the study sample population, the resistance training exercise intervention was more appropriate to an overweight and obese population.

Due to the intensity and energy requirements of the resistance training protocol, the nutrition protocol, which used a moderate decrease in caloric intake of approximately 25% of total calories, was determined to be most appropriate for subjects. An overly restrictive diet, such as those employed by other VLDL studies (Christiansen et al., 2010; Hotta et al., 2001; Manigrasso et al., 2005), was not considered to be adequate to meet exercise demands, as it could limit exercise adaptation and foster an energy restricted state which would confound the exercise programs effectiveness. Studies using individuals sharing a similar obesity profile as the current investigation's subjects have shown that adiponectin can be altered with weight loss (Balagopal, George, Yarandi, Funanage, & Bayne, 2005; Christiansen et al., 2010; Fatouros et al., 2005; Marcell et al., 2005). It is possible that there are differences in sample populations, and degrees of adiposity that could explain differences in adiponectin response between studies. In the current investigation, however, under conditions of moderate and clinically significant weight loss combined with highly controlled interventions, a statistically or clinically significant difference in adiponectin concentration was not observed in either group.

6.2.2 Adiponectin: Response to Exercise

Adiponectin levels have been studied extensively in exercise-related research (Bajer et al., 2015; Geliebter et al., 2014; Herring et al., 2014; W. J. Kraemer et al., 1998; Linnamo et al., 2005; Oliver et al., 2015). Based on previous reports, it was hypothesized that adiponectin would improve in response to a progressive, highly controlled resistance training protocol in combination with diet (Exercise + Diet), as compared to diet in isolation (Diet Alone).

The twelve week intervention failed to demonstrate a measurable change in adiponectin from baseline in the presence of a significant weight loss of 5% in the Exercise + Diet group, and 4% in the Diet Alone group. Despite these conflicting results, some studies have found similar results when using obese but otherwise healthy populations (Kondo et al., 2006; Ryan et al., 2003). The majority of studies which have shown an increase in adiponectin in overweight and obese populations have typically been performed on subjects who have glucose intolerance or insulin resistance, but who may not necessarily be diabetic (M. Bluher, 2013; Hsieh & Wang, 2005; Oberbach et al., 2006).

The effect of exercise on adiponectin is still unclear, with some studies showing that exercise improves adiponectin (Fatouros et al., 2005; Marcell et al., 2005) while others show no change (Kondo et al., 2006; Ryan et al., 2003) or a decrease (Christiansen et al., 2010; Christiansen et al., 2010; Yatagai et al., 2003). The lack of clearly defined

exercise protocols involves a variety of modalities, including aerobic training (Christiansen et al., 2010; Hsieh & Wang, 2005; Kondo et al., 2006; Oberbach et al., 2006) anaerobic training (Fatouros et al., 2005), supervised training (Boudou et al., 2003; Fatouros et al., 2005; Giannopoulou et al., 2005; Hara et al., 2005; Marcell et al., 2005) and unsupervised training (Hsieh & Wang, 2005; Yatagai et al., 2003). These modalities have all resulted in diverse findings. Furthermore, secondary outcome variables including weight/adipose tissue change, regional adipose location, impact of diet and the effects of other cytokines are not measured in many studies, making interpretation challenging, and comparisons difficult.

A systematic review by Simpson et al. highlighted the need for more studies which directly compare responses in healthy, sedentary, lean, obese, and clinical cohorts to clarify whether subject characteristics define exercise adaptation (Simpson & Singh, 2008). This exercise intervention study sought to address this issue, and based the resistance training protocol on previously established guidelines involving exercise progression models (Issurin, 2010). This approach prepared the study's inactive subjects for high intensity resistance exercise shown to result in improved fitness (Vingren et al., 2010). High intensity exercise was chosen for the structured exercise portion of this study, as both aerobic and anaerobic high intensity exercise demonstrates consistent findings with respect to improving adiponectin levels (Fatouros et al., 2005). It has also been shown that adiponectin changes resulting from high-intensity exercise are not lost

with short-term detraining, suggesting that a small amount of training may have a positive effect on adiponectin (Fatouros et al., 2005).

Sample populations may be a factor in the discrepancy between these results and those of others who have demonstrated an increase in adiponectin. Although adiponectin responses have been observed in populations with characteristics similar to the current study's subjects, it appears that no study has used such a population with a moderate to high intensity resistance training intervention (Ferguson et al., 2004; R. R. Kraemer et al., 2003; St-Pierre, 2006; Yatagai et al., 2003).

The specificity of the exercise intervention has been identified as an important study metric, as demonstrated in two contrasting studies. Fatourous et al. randomized subjects to four different exercise conditions: sedentary control, low intensity, moderate intensity and high intensity resistance training exercise, all of which lasted 24 weeks (Fatouros et al., 2005). A similar study used an intervention that lasted 16 weeks, and which included moderate and intense exercise as compared to sedentary controls (Marcell et al., 2005). Similar to this study, Fatourous incorporated baseline fitness testing that was used to determine training intensity for each subject during the intervention. This approach to tailored prescription was not used by Marcell, who measured baseline aerobic capacity with a generalized aerobic prescription, not accounting for baseline performance (Marcell et al., 2005). Furthermore, it is recommended that a variety of exercises be incorporated into an exercise progression model that increases the volume and intensity of training while matching strength improvements of the subjects (Budnar, Duplanty, Hill,

McFarlin, & Vingren, 2014; Hakkinen & Pakarinen, 1995; Klimcakova et al., 2006; W. J. Kraemer et al., 1998; Linnamo et al., 2005). The determination of training intensity provides insights into exercise prescription responses between exercise sessions, which is a significant benefit for individuals undergoing monitored training. Although the current study's intervention was similar to the aforementioned studies with respect to intervention and outcome measures, a change in adiponectin concentration was not identified. It is likely that differences in population demographics, in particular age as well as training duration could be a factor in the disagreement between these findings and those of others.

The interplay between nutrition and exercise may also play a role in adiponectin response to a specific intervention. For example, the lack of caloric restriction and resulting weight loss by Fatourous (1.2-1.7% over 24 weeks) could be a factor. In addition, several studies have not reported regional adiposity and lean mass, either due to a lack of imaging assessment or because they chose not to report these variables (Fatouros et al., 2005). An important finding of this intervention was the increase in lean body mass which results from resistance training. As muscle is a powerful regulator of insulin resistance, it would have been valuable to compare the change in lean body mass with previous studies to determine its impact on insulin sensitivity during exercise participation.

The length of the training intervention was shorter than some studies, which potentially impacted the adiponectin response and adaptations observed by others. The majority of exercise studies showed an improvement in adiponectin, which suggests that

training lasting longer than two months, that employs a sufficient exercise volume (frequency, intensity, and duration), results in a reduction in body weight, and improves insulin sensitivity increases adiponectin (Simpson & Singh, 2008). These criteria were applied to the study design; however, longer exposure to the exercise stimulus may have been necessary in the currents study's population. Although this study was twelve weeks in duration, and the supervised Exercise + Diet intervention was adequate in intensity, and resulted in improvements in muscle mass, fitness measures and a modest yet statistically significant weight loss, it is likely that the weight loss was not significant enough to demonstrate the hypothesized changes. Another possible explanation for why this cohort did not demonstrate a change in adiponectin is because they were not insulin resistant at baseline. However, this hypothesis requires further investigation involving the use of populations with and without insulin resistance.

A recent study by Christiansen et al. demonstrated a decrease, rather than an increase, in circulating adiponectin with exercise (Christiansen et al., 2010). They used a similar randomized sample size, involving a population of overweight and obese individuals, and also employed imaging techniques to capture anthropometric data (Christiansen et al., 2010) . Differences between the current study design and Christiansen et al. are evidenced by the protocols employed. The Christiansen group used aerobic training rather than resistance training and incorporated the use of a very low calorie diet (VLDL) of approximately 1/3 of the subject's baseline caloric intake (Christiansen et al., 2010). The goal of their intervention was to achieve weight loss

through the manipulation of energy balance, resulting from increases in energy expenditure from aerobic exercise and decreases in energy intake as a consequence of restricted caloric intake (Christiansen et al., 2010). Results demonstrated a weight loss of 11% ($p<0.05$) and a 19% ($p<0.1$) increase in adiponectin in the diet only group and a non-significant adiponectin reduction of 6% ($p=0.1$) in the combined exercise and diet group (Christiansen et al., 2010). In comparison with the aforementioned study, the intention of the present exercise protocol was two-fold: to increase energy expenditure, and to elicit muscular hypertrophy through the employed resistance training program. Unlike the Christiansen et al. study, this study also aimed to show improvements in the androgen hormone testosterone. The dramatically reduced caloric intake resulting from a VLDL used by Christiansen et al. was not applicable to this study's population, as it would not have provided necessary energy intake for hypertrophic adaptation to the resistance training intervention. Furthermore, it is possible that this high volume aerobic training program may have placed different physiological demands on subjects than a resistance training program, with respect to energy systems and training effect (Christiansen et al., 2010). The mixed gender cohort of subjects may also help explain the discrepancy between results, as it is well documented that men and women respond differently to exercise, particularly resistance exercise (Lewis, Kamon, & Hodgson, 1986). Gender differences may also help explain discrepancies in adiponectin levels in response to weight loss through controlled diet and exercise. It is also likely that the modest decrease in body weight (~4-5%) observed in the current study, as compared to the Christiansen,

group (>10%) could help explain the inconsistencies in these findings. As opposed to the current study, these studies may have achieved the required magnitude of weight loss necessary to elicit an increase in adiponectin (Simpson & Singh, 2008). Interestingly, under conditions of exercise adiponectin unexpectedly decreases, while under conditions of diet in isolation adiponectin increases (Christiansen et al., 2010). After adjustment for trunk fat using an analysis of covariance, the current study's results demonstrated that, similar to Christiansen et al., there was a statistically significant increase of adiponectin in the Diet Alone group and a corresponding decrease of adiponectin in the Exercise + Diet group.

Adiponectin is a significant insulin sensitizer that is more concordant with changes in glucose metabolism and insulin resistance than changes in adiposity (Weyer et al., 2001). Several studies have reported that the use of insulin-sensitizing agents markedly increase adiponectin concentrations, even in the absence of, or after adjustment for changes in weight (Fasshauer & Bluher, 2015; K. Maeda et al., 2012). The current study's baseline results demonstrate a relationship between adiponectin and insulin resistance, rather than adiposity, which is consistent with previous findings (Cnop et al., 2003; Hotta et al., 2001; Weyer et al., 2001). Similar weight loss interventions increase circulating levels of adiponectin; however, these changes occur in the presence of improved insulin resistance (Yang et al., 2001).

The present study's cohort was made up of overweight and/or obese, but otherwise healthy, individuals with normal insulin sensitivity and cardiovascular health. It

is important to recognize that obesity classification does not necessarily indicate the health of an individual. It is well established that obesity is associated with insulin resistance, inflammation and metabolic disease; however, it is estimated that 10-30% of the obese population is considered to be metabolically healthy obese (MHO) (M. Bluher, 2014). Although these MHO individuals have excess fat mass, they are insulin sensitive, normotensive and display a healthy blood lipid profile (Roberson et al., 2014). It is likely that there was little insulin sensitivity to be gained through the modest weight loss achieved by the current study's subjects. The assumption that adiposity status is predictive of health status may be a contributing factor to the gap in the literature regarding the adiponectin response to weight loss interventions.

6.2.3 Adiponectin: Exploratory Analysis

To explore whether regional adiposity was a confounding factor in the adiponectin response, an exploratory analysis was performed after controlling for trunk fat. A statistically significant ($p<0.002$) paradoxical response between interventions was discovered, where adiponectin was lowered in the Exercise + Diet group by ~12% and elevated in the Diet Alone group by ~8% (Christiansen et al., 2010).

The decrease in adiponectin demonstrated in the Exercise + Diet group relative to the Diet Alone group suggests that when controlling for the impact of regional adiposity physical activity suppresses adiponectin. Furthermore, it was demonstrated that only

diet-induced weight loss in the absence of exercise (Diet Alone group) increased adiponectin among overweight/obese subjects. These findings are in agreement with Christiansen et al., who found that adiponectin concentration was reduced whether weight loss was achieved through exercise alone or in combination with dieting, and that it increased when weight loss was achieved through diet without exercise (Christiansen et al., 2010).

To isolate the impact of exercise on adiponectin and determine its independent effect, one study controlled for weight reduction by using an active, normal-weight cohort who would not experience a significant decrease in body fat as a result of exercise training (Yatagai et al., 2003). This group used a smaller sample size of twelve non-obese subjects between the ages of 18-33 who were free of diabetes and not on any medications (Yatagai et al., 2003). Researchers conducted a six week intervention involving cycle ergometer aerobic training without caloric restriction (Yatagai et al., 2003). Body fat was measured using hydrostatic weighing and did not determine regional adiposity, unlike the DXA technique used in the current study. Investigators determined insulin sensitivity at baseline, sixteen hours following the subject's final exercise session, and one week after the final exercise session (Yatagai et al., 2003) After six weeks of lactate threshold ergometer exercise training, researchers discovered that insulin sensitivity improved independent of adiponectin, and that adiponectin levels decreased slightly as a result of this training (Yatagai et al., 2003) They concluded that adiponectin was suppressed due to an acute improvement in insulin action resulting from exercise (Yatagai et al., 2003). The

post-testing protocol involved blood collection that occurred forty-eight to seventy-two hours following the participants' final exercise session. It is therefore likely that enhanced insulin action as a result of exercise was not detected. This was previously supported by other studies, and found to be correlated with suppressed adiponectin levels (Christiansen et al., 2010). Therefore, future research using a similar cohort to those in this study would benefit from a close examination of the relationship between insulin and adiponectin shortly after exercise participation.

Another possible explanation for the suppression of adiponectin seen in exercise, was identified by Christiansen et al., who also measured the mRNA expression of adiponectin and its receptors in adipose tissue and muscle tissue, respectively. They found that diet-induced weight loss increased the mRNA expression of adiponectin in adipose tissue and increased adiponectin receptors in muscle tissue, but found that introducing physical activity soley resulted in an increase in adiponectin receptors in muscle tissue (Christiansen et al., 2010). Despite suggesting that mRNA expression could be responsible for the reduction of adiponectin through exercise and diet, this study did not provide evidence that changes in the expression of adiponectin receptors was associated with changes in the receptor protein and/or its subsequent biological effects. Similar to the current study's findings, it was determined that adiponectin is not concordant with adiposity but instead with other factors, some of which are related to exercise (Christiansen et al., 2010).

The results of the exploratory analysis of adiponectin were not pre-specified and relied on subgroups. Therefore, these results must be considered tentative rather than definitive, despite being statistically significant. Although results were adjusted for multiple comparisons and remained statistically significant, this was a post-hoc, unplanned analysis, and further investigations should be made into the relationship between specific regional adiposity and the adiponectin response to weight loss achieved through Exercise + Diet.

6.2.4 Association between regional adiposity and adiponectin:

Adiponectin's relationship to insulin sensitivity is well established. However, its association with adiposity remains uncertain within the literature (Cahill et al., 2013; Cnop et al., 2003). Visceral fat has shown a consistent negative association with adiponectin (Yang et al., 2001), as in vitro studies show that visceral adipocytes have increased the expression of adiponectin as compared to subcutaneous adipose tissues (Fain et al., 2004). The current study's findings show that adiponectin concentration is not associated with subcutaneous adipose tissue measured via skinfold thickness, but rather is negatively associated with visceral fat as measured by DXA. These findings reaffirm the findings of previous studies, which show that an elevation in visceral fat depresses adiponectin secretion (Cnop et al., 2003). Based on the literature, there was little expectation to see as strong of a relationship with regional subcutaneous fat as is observed

with visceral deposits. However, the lack of association with any skin fold sites was unexpected due to the understanding that adiponectin is associated with adiposity (Galic, Oakhill, & Steinberg, 2010; Guerre-Millo, 2004; Kern et al., 2003).

Although an easy to perform, skin fold caliper test that predicts adiponectin concentration could provide novel insights into its relationship with regional adiposity, a biochemical analysis is necessary to predict changes (Fasshauer & Bluher, 2015). Of relevance is that adiponectin has an acute and chronic response to rapid changes in body weight, and increases during periods of rapid weight gain in an attempt to improve energy regulation (Cahill et al., 2013). Therefore, adiponectin may be difficult to predict due to its response to various acute lifestyle scenarios associated with obesity (Cahill et al., 2013). It may be valuable to investigate adiponectin changes with respect to regional body fat distribution in a cohort diagnosed with insulin resistance, as the relationship between insulin resistance to body fat and adiponectin has been well established (Haluzik, Parizkova, & Haluzik, 2004; Kaur, 2014; Kishida, Funahashi, & Shimomura, 2014b; Lindsay et al., 2002; Spranger et al., 2003). It could be hypothesized that changes in adipose tissue may reflect changes in adiponectin. However, this speculation would most likely be due to changes in insulin sensitivity, rather than the interplay between adiponectin and body fat.

6.2.5 Adiponectin: Summary and Interim Conclusions

The present study's results indicate that the adiponectin response to the Exercise + Diet intervention is dependent upon insulin resistance rather than adiposity status. Although the current study was able to demonstrate significant changes in total and regional adiposity, it did not show an associated change in adiponectin, without controlling for regional adipose depots. Furthermore, the lack of change in insulin, insulin resistance and adiponectin in response to the intervention reinforces the relationships between these variables. In agreement with others (Christiansen et al. 2010), post hoc analysis revealed a reciprocal response of adiponectin in the intervention groups, where Exercise + Diet reduced and Diet Alone increased circulating concentration. Both groups displayed similar weight loss and the Exercise + Diet group demonstrated addition cardiovascular health benefits. Therefore, the current study indicates that the assessment of adiponectin may be irrelevant in the prediction of health improvement resulting from exercise, in a population which is not insulin resistant. Therefore, future research should clearly identify subjects with impaired insulin resistance when investigating the impact of diet and exercise on adiponectin.

6.3 Energy Regulating Hormones and Cytokines

The concentration of cytokine/hormones TNF-α, leptin and ghrelin are influenced by energy balance, and maintain homeostasis under conditions of reasonable food intake, energy consumption and normal metabolic rate (Considine, 1997; Golbidi & Laher, 2014; Kelly et al., 2011; R. R. Kraemer & Castracane, 2007; Leidy et al., 2004; Martins, Robertson, & Morgan, 2008; Ueda et al., 2009). Conversely, conditions of obesity resulting from excessive energy intake leads to a disruption of these energy regulating hormones/cytokines (Castaneda, Tong, Datta, Culler, & Tschop, 2010; Fasshauer & Bluher, 2015; Oh et al., 2014; Selyatitskaya et al., 2015; Tschop et al., 2001). Obese individuals express elevated basal concentrations of the adipokine leptin, which has been associated with the inhibition of food intake and increases in energy for both animals and humans (Bouassida et al., 2010), and TNF-α, which is associated with inflammation and decreased insulin sensitivity (Nikseresht, Sadeghifard, Agha-Alinejad, & Ebrahim, 2014). In addition, the gut peptide hormone ghrelin, which increases food intake and reduces fat metabolism, decreases in response to increases in adiposity (Hill, Murphy, & Singer, 2012). The behaviour of these hormones is associated with adiposity status as well as with changes in body composition under conditions of weight loss (Considine, 1997; Sharman & Volek, 2004; Tschop et al., 2001; Varady et al., 2009). As a result, this study investigated the response of TNF-α, leptin and ghrelin to weight loss achieved through an Exercise + Diet intervention in overweight and obese middle aged males, a population

which possesses significant risk for obesity related health conditions such as energy regulation and metabolism.

6.3.1 TNF-α

TNF-α has been shown to exhibit higher circulating levels in obese individuals, potentially promoting insulin resistance by inhibiting adiponectin release (Rosmond & Bjorntorp, 1998). Although physical activity and nutrition are well established lifestyle factors for weight loss/management, very little is known about how these factors influence the inflammatory profile for overweight and obese men, particularly the impact of structured, supervised, high intensity resistance training. Therefore, it was hypothesized that circulating TNF-α concentrations would reduce with weight loss in both the Exercise + Diet and Diet alone groups and that TNF-α would decrease to a greater extent in the Exercise + Diet group due to participation in physical activity.

6.3.1.1 TNF- α: Obesity

The current study's findings show a statistically significant, inverse relationship between TNF-α and total adiposity ($p<0.03$), as well as with trunk fat ($p<0.04$) at baseline. This inverse association supports the findings of others who state that even modest changes in adiposity may influence changes in TNF-α in overweight and obese

males (Kirwan, Kohrt, Wojta, Bourey, & Holloszy, 1993) and that the primary site related to increases in TNF-α production and secretion is the abdominal/visceral adipose tissue (Clement et al., 2004).

In both the Exercise + Diet and Diet Alone groups, TNF-α was inversely associated with adiponectin ($p<0.02$) as is currently understood in the literature (Hivert et al., 2010). This relationship with adiponectin is an important factor in the pathogenic impact of TNF-α on angiogenesis, blood pressure and lipid metabolism, all of which are linked with cardiovascular disease (Golbidi & Laher, 2014). Furthermore, it has been proposed that poor weight management could potentially promote an increase in TNF- α concentration, which can lead to chronic insulin resistance (Diehl, 2004). The current study population was not diabetic and did not demonstrate a significant change in insulin resistance in either the Exercise + Diet or Diet Alone group. Therefore, this intervention may have failed to demonstrate a change in TNF-α, because the subject's baseline health status did not include impaired insulin resistance, or because the intervention resulted in no difference in insulin resistance parameters, and only resulted in modest weight loss. Another possible consideration for the lack of change in TNF-α is the age of the subjects. It has been shown that plasma TNF-α increases with advancing age; however, the magnitude of this effect has not been clearly established (Kirwan et al., 2001). Thus, there exists a growing body of literature investigating the relationships between aging, glucose tolerance, changes in body composition, and modulatory factors such as TNF-α, particularly with respect to overweight and obese aging males.

6.3.1.2 TNF- α: Response to Exercise

The current study detected an inverse association between the baseline TNF-α concentration and the change in TNF-α concentration resulting from the Exercise + Diet intervention. An inverse relationship between the plasma levels of inflammatory adipokines and the amount of physical activity was found (Dutheil et al., 2010). Exercise has been shown to be protective against TNF- α induced insulin resistance while also increasing anti-inflammatory substances such as adiponectin (Plaisance & Grandjean, 2006b). This is of particular relevance to the current study population, as the expression of TNF- α in adipose tissue is highest in obese subjects (Kern et al., 2001), and that TNF-α interacts with adiponectin by inhibiting its production and secretion from adipose tissue (N. Maeda et al., 2002). No change in TNF-α levels was observed after the Exercise + Diet intervention, indicating that there is no apparent independent effect of high intensity resistance training in this overweight/obese male cohort.

6.3.1.3 TNF- α: Response to Nutrition

TNF-α did not change in response to the Diet Alone intervention in the current study. This finding was unexpected and contradicts other results, which show that TNF-α responds favourably to nutrition interventions aimed at weight loss (Kallio et al., 2008;

Kelly et al., 2011; Kirwan et al., 1993; Qi et al., 2006). Investigations into the use of a low-glycemic index diet, similar to the one employed in this study, show that TNF-α reduces in older, obese adults (Kelly et al., 2011). It is believed that the consumption of a low-glycemic index diet and its resulting normalization of plasma glucose can halt the cycle of hyperglycemia, which contributes to insulin resistance, adipose tissue dysfunction, and pro-inflammatory cytokine production (Kelly et al., 2011). Using a highly controlled dietary intervention, researchers confirmed that a low glycemic index diet improved glucose tolerance and provided novel evidence that diet can reduce obesity associated inflammation (Kelly et al., 2011). These results are supported by longer-term dietary interventions, which suggest that carbohydrate intake modifications may influence the protein or mRNA expression of inflammatory markers in adipose tissue (Kirwan et al., 2001). Because this study's population did not suffer from insulin resistance or impaired glycemic control, and demonstrated TNF-α concentrations that were inverse to those typically expressed in males suffering from obesity, these findings are not unexpected. In order for weight loss resulting from diet and exercise to reduce TNF-α, a baseline inflammatory profile may be necessary, which may not have been present in this cohort. Of particular significance is the impact of increasing age, which leads to an exacerbated TNF-α response to hyperglycemia and hyperinsulinemia resulting from high glycemic index carbohydrates (Kirwan et al., 2001). When compared with a group of healthy young men (22 ± 1 yr), older men (67 ± 2 yr) show a "normal" suppression in TNF-α production under post-prandial-like conditions, supporting the role of TNF- α as a

modulator of insulin-mediated glucose metabolism (Kirwan et al., 2001). TNF- α may be a factor in the decline in insulin action observed among older men, due to the relatively greater total body and abdominal fat mass witnessed in this population (Kirwan et al., 2001). The measurement of post-prandial TNF-α would be a valuable addition for future research employing the current study's dietary protocol, due to its effectiveness in reducing total adiposity and visceral fat in both the Exercise + Diet and Diet Alone groups.

The employed nutrition protocol not only involved the consumption of low glycemic carbohydrates, but encouraged their consumption in the form of whole grains, including dietary fiber. It was found that fiber intake was associated with lower inflammatory markers in both diabetic and non-diabetic individuals (Qi et al., 2006). It is possible that the inhibition of inflammation by whole grain and cereal fiber may be secondary to their effects of lowering glycaemia (Qi et al., 2006). This is supported by the observation that dietary glycemic index is positively related to inflammatory markers, as was also noted in a previous study among nondiabetic subjects similar to ours (Kallio et al., 2008).

6.3.1.4 Association between regional adiposity and TNF-α:

TNF- α is elevated in obese individuals, and is associated with systematic inflammation and insulin resistance (Cawthorn & Sethi, 2008). Although associated with

subcutaneous fat mass, the visceral adipose compartment is credited as the major source of TNF-α production and secretion (Clement et al., 2004). TNF-α concentration has been predicted by anthropometric measures including BMI, waist circumference and percent trunk fat, as determined by DXA (Clement et al., 2004). TNF-α did not show a significant relationship to any regional skin fold or girth measurements. However, it did show a positive association with total body fat, trunk fat percentage and body fat percentage as determined by DXA in the current study. This data does not reflect the relationship between TNF-α and adipose tissue, which consistently demonstrates a greater fasting concentration of TNF-α which is positively associated with visceral adipose tissue mass in obese humans (Clement et al., 2004). Of particular relevance is that most TNF-α release is due to non-fat cells, but shows an enhanced release by adipocytes isolated from subcutaneous adipose tissue of massively obese individuals (BMI of 45) as compared to their leaner counterparts (Ruan & Lodish, 2003). The study population of overweight and obese participants may not have met the necessary obesity threshold to demonstrate the previously established TNF-α relationship with subcutaneous adipose tissue (Fain et al., 2004). Furthermore, the relevance of skinfold caliper assessments for morbidly obese individuals becomes less relevant due to the lack of sensitivity associated with larger skin fold thickness measurements. These findings indicate that the use of skinfold thickness as a possible predictor of fasting TNF-α concentrations is unlikely to be of value during obesity management. It appears that the population who may best demonstrate the necessary resolution between TNF- α and subcutaneous skinfold thickness is likely those

who are obese. However, the use of this measurement technique is not accurate for these populations.

6.3.2 Leptin and Ghrelin:

6.3.2.1 Leptin, Ghrelin and Obesity

Leptin is an appetite regulating hormone produced in proportion to body fat, demonstrating higher concentrations in obese individuals (Bouassida et al., 2010). In circumstances of weight loss, circulating leptin concentration is reduced, which diminishes its inhibitory effect on satiety and leads to an increase in appetite and feeding (Bouassida et al., 2010). Therefore, it was hypothesized that circulating leptin levels would reduce with weight loss in both the Exercise + Diet and Diet Alone groups and that leptin would decrease to a greater extent in the Exercise + Diet group due to the increased energy expenditure resulting from physical activity.

The association between leptin and adiponectin observed at baseline was not maintained after weight loss, most likely because of the demographics of the study population. As stated previously, the baseline characteristics of the study population confirms that while subjects were overweight or obese according to the BMI scale and demonstrated various elevated measurements of regional adiposity as compared with their normal weight counterparts, their overall metabolic profile did not resemble that of those suffering from obesity associated metabolic conditions including hypertension,

hyperlipidemia or diabetes. It is likely that the significant change in adiposity, without a change in insulin resistance, is responsible for the uncoupling of the adiponectin-leptin relationship demonstrated at baseline. These results further reinforce the understanding that leptin is strongly associated with adiposity in humans (Teerds et al., 2011), while adiponectin is more closely related to insulin resistance than the degree of adiposity (Weyer et al., 2001). Interestingly, the fasting leptin concentration at twelve weeks maintained its relationship with insulin and insulin resistance after weight loss, although not as strongly. Neither of these variables demonstrated significant changes in response to either the Exercise + Diet or Diet Alone interventions. Another possibility for the lack of association between leptin and adiponectin may be due to the study power. However, sample size was addressed in the study design of the current experiment and was determined to be sufficient for demonstrating the relationships in this study's primary variables. It is more likely that these results mirror those of previous studies, which show that weight loss influences leptin to a greater degree than adiponectin, even though both are strongly associated with adiposity (Shand et al., 2003; Stefanyk & Dyck, 2010) .

Leptin receptors are also present in testicular tissue, and it is believed that leptin may exert a direct negative action on androgen production and play a role in the reduction of androgens among obese males (Isidori et al., 1999). The relationship between leptin and testosterone was not found at baseline or after twelve weeks for either the Exercise + Diet or Diet Alone groups (Table 11). The lack of change in total testosterone in the presence of both decreased leptin and weight loss may be a result of the relatively small

degree of weight loss or, more likely, the lack of obesity related derangement in sex hormones at baseline for these subjects. Baseline analysis revealed that subjects did not suffer from hypogonadism. Therefore, it would be expected that the inhibitory effects of leptin did not significantly impact sex hormones and, consequently, are not susceptible to improvements or changes resulting from either the Exercise + Diet or Diet Alone intervention.

Ghrelin is a peptide hormone, and is one of the only hormones known to increase appetite (Ahima, 2006; Nakazato, 2003). Unlike most other gut-derived, meal patterning peptides, ghrelin increases food intake and reduces fat utilization, and is therefore associated with long term body weight regulation (Foster-Schubert et al., 2005). Weight loss has been shown to trigger an increase in circulating ghrelin concentrations as part of an adaptive response to energy deficits (Cummings, 2006). It was therefore hypothesized that ghrelin would increase in response to weight loss and demonstrate greater positive change in the Exercise + Diet group, due to the high intensity exercise and its associated increase in energy expenditure.

The current study's results did not show a statistically significant change in ghrelin in response to either the Exercise + Diet or Diet Alone protocols. In the Diet Alone group, ghrelin demonstrated a statistically significant inverse association with anthropometric measures of obesity including weight ($p<0.01$), waist circumference ($p<0.001$), hip circumference ($p<0.001$) and total body fat ($p<0.003$). Of particular relevance is that this relationship between ghrelin and adiposity was not maintained

following weight loss for either the Exercise + Diet or Diet Alone groups. The current study suspected that the nature of the intervention that controlled for macronutrient content of meals and only required a reduction of daily caloric intake of approximately 25% for subjects is a factor in the discrepancies in the results and those of others who have shown an increase in ghrelin with weight loss (R. R. Kraemer & Castracane, 2007; Leidy et al., 2004; Markofski et al., 2014; Schubert et al., 2014; Thomas et al., 2012). As stated previously, ghrelin has an inverse relationship with leptin in both circulating concentrations and function, and is related to adiposity status, increasing appetite in order to restore energy balance during periods of weight loss (Hill et al., 2012). However, baseline associations were not maintained following both interventions in the current study. Both ghrelin and leptin have the same regulating system, and both inform the central nervous system about acute and chronic energy balance (Castaneda et al., 2010). Results from the current investigation indicate that ghrelin may be more closely linked to nutritional intake and energy balance than leptin, which is more strongly correlated with adiposity (Castaneda et al., 2010)..

6.3.2.2 Leptin and Ghrelin: Response to Exercise

Previous studies have shown that leptin decreases independently in response to exercise (Pasman, Westerterp-Plantenga, & Saris, 1998; Sakurai et al., 2012). These studies lack

methodological rigor, and have involved various modalities and intensity of exercise, often in an uncontrolled setting (Pasman et al., 1998; Sakurai et al., 2012). In the current study, both Exercise + Diet and Diet Alone groups displayed similar, modest weight loss. It was anticipated that changes in leptin concentration would only be apparent in the high intensity exercise training if significant weight loss was achieved. Studies have reported that fasting concentrations of leptin may decline with endurance and/or resistance training (Sakurai et al., 2013). However, the majority of investigations point to the inverse relationship of leptin with adiposity, and show no apparent impact from exercise (Bouassida et al., 2010; Golbidi & Laher, 2014; Markofski et al., 2014; Mason et al., 2015). The inability of previous studies to detect an independent effect of exercise on leptin concentration may be due to the exercise prescription itself and/or the lack of training supervision, which ensures that exercise intensity is maintained during activity sessions. A highly controlled exercise prescription could elicit a change in circulating leptin independent of the weight loss achieved through nutrition intervention alone, due to leptin's relationship with energy regulation and the sympathetic nervous system. Results from previous exercise studies have been hindered by their inability to disassociate the effects of exercise itself from the confounding effects of energy balance (Fatouros et al., 2005). Although intensity and hours of exercise have claimed to have independent effects on leptin, the strong association between adiposity and leptin makes interpretation of the change mechanisms difficult (Fatouros et al., 2005; Pasman et al., 1998). Findings of this study mirrored those of others, which have shown that weight loss, independent of

modality, results in an associated decrease in leptin, and that leptin does not change in response to long term exercise training when controlling for adiposity status (Bouassida et al., 2010; Kim et al., 2012; Sakurai et al., 2012).

With respect to ghrelin, there was an increase in the Exercise + Diet group of approximately 5% and a decrease in the Diet Alone group of ~30% between baseline and twelve weeks. However, these results were not statistically significant, and do not provide evidence that either intervention affected circulating ghrelin concentrations. These results provide further insight into the impact of exercise on ghrelin concentrations, as research to date has been inconclusive. Ghrelin has shown an acute suppressive response to the concentric action of resistance training. However, ghrelin does not change in response to running or cycling in humans (Takano et al., 2005). In an attempt to identify the role of chronic exercise on ghrelin, Markofski et. al controlled for body fat loss and showed significant increases in circulating ghrelin and adiponectin, as well as a trend towards reduced leptin following exercise training (Markofski et al., 2014). Study design considerations, such as lack of supervision and self-selected exercise intensity may explain the difference in outcomes from the current study. The fact that the highly controlled Exercise + Diet and Diet Alone prescriptions were supervised by a certified kinesiologist and registered dietitian in this study provides greater control over possible confounding variables, including exercise adherence and caloric intake. Furthermore, the assessment of adiposity using skin fold calipers used by Markofski et al., in lieu of gold standard adiposity imaging such as DXA, further reduces the reliability of subcutaneous

body fat measurements, and does not allow for the assessment of important regional adiposity sites including visceral fat. With respect to the Exercise + Diet group, it was hypothesized that the increase in ghrelin is related to the greater energy requirements of enhanced baseline lean muscle tissue, coupled with the increase in energy demanded by the resistance training protocol.

Ghrelin has shown a significant increase during weight loss via exercise, where those individuals with the highest degree of weight loss exhibit the greatest increase in ghrelin (Foster-Schubert et al., 2005; Leidy et al., 2004). One review concluded that in the absence of weight loss, exercise has no significant impact on the fasting plasma levels of ghrelin (R. R. Kraemer & Castracane, 2007). Of particular relevance is the current investigation's unplanned exploratory analysis that when controlling for lean body mass demonstrated a higher fasting ghrelin concentration in the Exercise + Diet group at twelve weeks compared to baseline. This finding supports a minority consensus in the literature that ghrelin is elevated in response to exercise to compensate for associated increases in energy expenditure (Bajer et al., 2015).

6.3.2.3 Leptin and Ghrelin: Response to Nutrition

With respect to nutrition, leptin concentration is associated with dietary reductions in total energy and dietary fat intake under conditions of caloric restriction and weight loss (Reseland et al., 2001). Lifestyle changes, including diet and exercise are similar to

those in this randomized trial, and have been reported to improve carbohydrate metabolism, reduce insulin resistance and improve metabolic profile (Erdmann et al., 2004; Overduin et al., 2005; Tannous dit El Khoury et al., 2006). Results from the present study indicate that there is a significant change in leptin after twelve weeks, however this was not independent of group. Both the Exercise + Diet and Diet Alone groups underwent a hypocaloric diet designed to promote weight loss and improve satiety through the use of a low glycemic index, high protein and low saturated fat nutrition protocol that has been shown to impact appetite regulating hormones (Mason et al., 2015; S. X. Zhang, Guo, Wan, & Xue, 2011). A study by Considine et. al. hypothesized that changes in energy intake or expenditure may be detected by adipocytes, which in turn influence the synthesis of leptin (Considine, 1997). Nutrition guidelines were provided to subjects by a registered dietitian, which included particular emphasis on the selection of low glycemic index (GI) foods. The relationship between glycemic response and leptin has been specifically investigated with respect to appetite control and satiety (Barkoukis et al., 2007; Bowen et al., 2006). One group reported that low glycemic meals promote a postprandial metabolic environment that is favourable for reduced food consumption in young, healthy volunteers (Barkoukis et al., 2007). In a separate five week study, using moderately overweight men undergoing a low-GI diet, subjects effectively ameliorated some plasma lipid parameters, decreased total fat mass and tended to increase lean body mass without changing body weight (Bouche et al., 2002). Similar to the current study, the decrease in fat mass was accompanied by a significant decrease in leptin; however,

the decrease in food intake was not confirmed (Bouche et al., 2002). These authors proposed possible mechanisms to explain why the lower GI diet induced a selective decrease in fat and an increase in lean body mass, including the difference in nitrogen balance and protein metabolism (Bouche et al., 2002). It was suggested that fat tissue was oxidized to a lesser degree and muscle to a greater degree with the high-GI diet due to the greater negative nitrogen balance associated with the high GI diet (Bouche et al., 2002). Another possible mechanism they proposed is a shift in substrate utilization for a low-GI diet which reduces carbohydrate oxidation and increases fat oxidation (Bouche et al., 2002). It is possible that the increase in lean mass observed in the Exercise + Diet group was enhanced by these proposed mechanisms. However, this theory is speculative, and warrants further investigation.

Diet and nutrition have a much clearer impact on ghrelin than leptin. It is well established that the type of macronutrient ingested dictates the magnitude of ghrelin suppression, with carbohydrates demonstrating the greatest suppressive effect, followed by protein and fat, respectively (Erdmann et al., 2004; Overduin et al., 2005; Tannous dit El Khoury et al., 2006). Ingestion of carbohydrates and proteins decreases ghrelin by approximately 70% during the post prandial period, while fats demonstrate an approximate decrease of 50% (Bowen et al., 2006). The higher post-prandial circulating concentration of ghrelin that is associated with dietary fat intake, as compared to carbohydrate or protein, is one of the proposed mechanisms of weight gain associated with high fat diets due to ghrelin's resulting stimulation of appetite (Tannous dit El

Khoury et al., 2006). Therefore, ghrelin release appears to occur in response to the ingested macronutrients and, as a result, helps dictate subsequent hunger and food intake. Both the Exercise + Diet and Diet Alone groups were required to ingest macronutrient ratios outlined by previous work that have demonstrated post-prandial ghrelin suppression (Erdmann et al., 2004; Overduin et al., 2005; Tannous dit El Khoury et al., 2006). Higher protein diets have been shown to promote weight loss more effectively than higher fat diets, and the implications is that the suppressive effect of protein on ghrelin is considered an important factor in the success of high protein, hypocaloric diets (Bowen et al., 2006). Because of the feed frequency that occurred every 3-4 hours, both the Exercise + Diet and Diet Alone protocols were designed to reduce ghrelin concentration between feedings, even in the presence of weight loss.

When controlling for lean body mass at baseline, ghrelin showed a statistically significant decrease ($p<0.001$) in the Diet group of ~30% and an increased in the Exercise + Diet group of ~5%. Although the post-prandial suppression of ghrelin has been established by previous work, the chronic effect of dietary protocols leading to decreased fasting ghrelin, as evidenced by the Diet Alone group in the current study, could be considered to be a novel finding. These results conflict with the results of others, which have shown that ghrelin is elevated in response to weight loss (Leidy et al., 2004). It should be noted that this was an exploratory analysis and although the result remains significant, even when adjusting for multiple comparisons, this was a post-hoc, unplanned analysis. This result therefore warrants further investigations into the relationship

between lean body mass and ghrelin under conditions of weight loss achieved through diet and exercise.

Of particular relevance is the lack of change or slight increase in circulating ghrelin, and the associated drop in leptin for the Exercise + Diet group. These results may create a scenario which fosters negligible weight loss and potential weight regain following exercise cessation. It has been established that restrained eaters, or successful dieters, are efficient at reducing energy intake in response to the elevated energy expenditure associated with exercise. Unrestrained eaters, or unsuccessful dieters, on the other hand, respond to increased energy expenditure by compensating with elevated energy intake (Geliebter et al., 2014; Mason et al., 2015). In lifestyle prescription, adherence to exercise and nutrition protocols is a limiting factor in intervention effectiveness (Anderson, Konz, Frederich, & Wood, 2001; Curioni & Lourenco, 2005; Franz et al., 2007; Martins et al., 2008; Mason et al., 2015; Poirier & Despres, 2001; Swift, Johannsen, Lavie, Earnest, & Church, 2014). With a decrease in satiety resulting from lowered leptin, coupled with the appetite stimulating characteristics of ghrelin, restrained eating may be more difficult for those in the Exercise + Diet group as compared to the Diet Alone group. Therefore, the results of the current study indicate that there may be a benefit to establishing restrained eating behaviours similar to those in the Diet Alone group prior to starting high intensity exercise. Although both groups showed high compliance in the current study, this may be due to the supervision aspect of the interventions, and may not be the case for individuals outside of the research setting.

As weight loss was comparable between the Exercise + Diet and Diet Alone groups over the twelve week intervention, and ghrelin was only reduced in the Diet Alone group, participants may display greater adherence to a hypocaloric dietary protocol in the absence of increased energy demands from exercise. Once initial weight loss is achieved and restrained eating is habitual, it may be beneficial to implement exercise to achieve the benefits of physical activity, particularly the cardio-protective attributes of the resistance training protocol employed in the current study. There are a lack of studies investigating the impact of long-term (greater than six weeks) exercise on appetite-related hormones which show how changes observed in these hormones relate to weight loss or prevention of weight regain in the obese population (Schubert et al., 2014). This study reveals important insights with respect to appetite regulating hormones associated with exercise and diet, which must be considered when prescribing lifestyle interventions to overweight and obese aging male patients, particularly where adherence and susceptibility to weight regain dictate long term success.

The weight loss threshold needed to elicit a change in fasting ghrelin has yet to be established. However, previous research has shown it is individuals experiencing the highest degree of weight loss that ghrelin concentration increases most profoundly (Kim et al., 2012; Markofski et al., 2014; Mason et al., 2015). The present research indicates that the adiposity-ghrelin relationship may be uncoupled by nutrition protocols designed to increase satiety and reduce post-prandial ghrelin. This Diet Alone protocol may have a protective effect for weight loss through its suppression of ghrelin in the absence of

increased energy expenditures resulting from exercise. Further investigation is therefore warranted into the potential beneficial impact of ghrelin concentration on appetite resulting from diet and exercise prescriptions for this demographic of 35-55 year old overweight and obese males.

6.3.2.4 Association between Regional Adiposity and Leptin and Ghrelin:

Leptin signals the central nervous system with respect to adiposity status and energy regulation (Blüher, 2014). The larger, subcutaneous fat deposits, rather than visceral fat deposits, have collectively been associated with leptin concentration and expression (Taksali et al., 2008). This relationship was demonstrated in the current study between leptin and skin fold measures, where statistically significant correlations were found for the pectoralis ($p<0.001$), mid-axillary ($p<0.001$), subscapularis ($p<0.001$), and the quadriceps ($p<0.01$). Additionally the current study also observed a strong association between visceral fat mass and leptin ($p<0.001$). It is believed that subcutaneous deposits, and not visceral fat, may be responsible for leptin signally to the CNS (Taksali et al., 2008). In the current study, both subcutaneous and visceral adipose deposits displayed statistically significant associations with leptin, where all of the subcutaneous skin fold sites showed a marginally stronger relationship with leptin. These results indicate that leptin changes with overall adiposity, and is not associated with any specific subcutaneous skin fold sites. That said, the overall measure of percent body fat,

determined by skinfold thickness, may be a useful tool for the predicting circulating leptin concentrations during weight loss.

Ghrelin has been shown to be associated with BMI. However, the majority of research indicates that it has a stronger relationship with leptin and nutritional intake, both of which are implicated in adiposity status (Bowen et al., 2006; Havel, 2001; Popovic & Duntas, 2005; Ueno, Dube, Inui, Kalra, & Kalra, 2004). The current investigation's results indicate a negative association between several measures of adiposity and ghrelin, including BMI ($p<0.01$), waist ($p<0.02$) and hip circumference ($p<0.001$), as well as with total body fat ($p<0.03$) and visceral fat mass (0.01) as determined by DXA. Of particular interest is ghrelin's statistically significant, inverse relationship with lean body mass ($p<0.01$), and its resulting, potential implications for energy regulation and metabolism. Research on energy expenditure increases achieved through exercise has been inconclusive with respect to its impact on ghrelin concentration. However, the increased basal and exercise associated energy demands related to increased lean body mass may show the promising, predictive capabilities of ghrelin (Kojima & Kangawa, 2008; Muccioli et al., 2004; A. D. Patel et al., 2006). The current study shows an inverse correlation with lean body mass that is stronger than ghrelin's relationship with total fat mass. As ghrelin informs the CNS about acute and chronic energy balance, the positive association of ghrelin with lean body mass provides important insights into the relationship between body composition and ghrelin (Castaneda et al., 2010). This is an important finding in the prescription of diet and exercise for obese populations, as

individuals who possess greater lean body mass at baseline, or who gain lean body mass as the result of lifestyle intervention, may be predisposed to increased appetite. Coupled with an inverse relationship with leptin, a scenario which fosters weight regain may become apparent. The assessment of lean body mass, either through imaging or through predictive equations such as skin fold caliper methods, may prove useful in the counselling of individuals with respect to caloric intake during weight loss and in populations with higher relative lean body mass irrespective, of obesity status. Furthermore, the lack of an association between ghrelin and regional skin fold thickness is likely not significant, particularly in the presence of several well established adiposity measures such as girth measures and body fat imaging. The secondary benefits of determining lean body mass using low cost assessment tools, such as skinfold thickness equations, may be more insightful than traditional BMI measures, which fail to determine body composition.

6.3.2.5 Summary of Energy Regulating Hormone Findings:

In summary, weight loss resulting from caloric restriction, with or without the increases in energy expenditure or improved lean body mass achieved through exercise, results in an associated decrease in circulating leptin for overweight and obese middle-aged men. Comparatively, ghrelin concentrations may be impacted by the nature of the weight loss intervention and their relationship with lean body mass. With respect to

inflammatory adipokines, it appears that either the Exercise + Diet or Diet Alone protocols failed to produce a change in TNF-α, in the absence of improvements to insulin sensitivity. Furthermore, it is likely that weight loss was not substantial enough to result in modified TNF-α in the current study. These results are therefore inconclusive with respect to others who have found that short term changes in inflammatory markers and energy-restricted low-fat and low-carbohydrate diets are primarily related to weight loss, rather than dietary intervention (Sharman & Volek, 2004). However, baseline relationships between adiposity, in particular visceral adiposity, indicate that the employed intervention may be an effective strategy at improving inflammatory profile if significant weight loss is achieved.

It appears that exercise has no significant effect on circulating TNF-α or leptin under the conditions of long term resistance training in this population, and that the demonstrated decrease in circulating leptin is weight loss-induced and associated with a reduction in adipose tissue. In addition, the reduction in ghrelin, coupled with the lower leptin concentration observed under conditions of caloric restriction in the Diet Alone group, indicates that current understandings of the ghrelin-obesity, ghrelin-leptin relationship may be disrupted through nutrient timing and the macronutrient content of meals. Leptin has been shown to suppress the secretion of ghrelin, and increases in ghrelin levels have been reported during diet-induced weight loss in obese individuals, suggesting that ghrelin contributes to appetite, responding to energy restriction and lower

leptin levels (Ueno et al., 2004). However, the current study's findings did not see the predicted associated increase in ghrelin under conditions of lowered leptin.

It is believed that the timing and macronutrient content of meals used in the employed nutrition protocol may have augmented this association. The significant reduction in ghrelin in the Diet Alone group coupled with the significant change in both measures of adiposity and leptin, indicates that the current nutrition protocol was successful in mitigating the previously established leptin-obesity-ghrelin relationship.

6.3.3 Testosterone:

6.3.3.1 Total Testosterone: Obesity

Testosterone is a steroid hormone that is responsible for muscle protein synthesis and which reduces muscle protein degradation, while playing a significant role in energy expenditure (Tajar et al., 2012). Testosterone circulates in the bloodstream, bound mostly to the sex hormone binding globulin and, to a lesser extent, serum albumin and corticosteroid-binding globulin (Tajar et al., 2012).

Previous research demonstrates that testosterone is impacted by several variables, and reduces in response to increasing obesity, and increases in response to exercise (Tajar et al., 2012) . Therefore, the current study hypothesized that weight loss achieved through diet and exercise would demonstrate an increase in total testosterone for the inactive, overweight and obese, middle aged male cohort.

The current study was unable to detect a measurable response to either the Exercise + Diet or Diet Alone interventions between baseline and twelve weeks. These preliminary results were not anticipated due to the inverse association between obesity and testosterone that has been well established in the literature (Camacho et al., 2013; Glass et al., 1977; Wu et al., 2012). However, upon further investigation into the baseline circulating testosterone levels observed in the current study's subjects, as well as the degree of weight loss, the explanation for the lack of change becomes evident. Obesity is associated with an 8.7 fold increase in the relative risk of hypogonadism (testosterone < 10.5mml and normal LH) and to date, the most significant predictor of low testosterone is obesity status (Frost, 2007; Tajar et al., 2012) . Additionally, obesity status is one of the major contributors to age-associated decline in testosterone levels in men (Tajar et al., 2010). In an obese state, adipose tissue expresses aromatase, which converts testosterone into estrogen. Furthermore, the increases in visceral fat associated with male pattern obesity promote increased TNF-α, insulin and leptin, all of which may down regulate the HPT axis (Sharman & Volek, 2004). Although the current study's population was classified as obese or overweight, and displayed elevated visceral fat stores in comparison to their normal weight counterparts, they did not demonstrate hypogonadism, as the mean total testosterone values fell within normal ranges for age matched males. Therefore, the lack of change in testosterone, although hypothesized to improve in response to weight loss and exercise, is not unexpected because of the baseline testosterone concentration, which fell within a normal range.

In humans, the degree of weight loss is predictive of testosterone response with individuals who experience the largest percent of body weight lost yielding the greatest increase in testosterone (Camacho et al., 2013). Weight loss of greater than 15% of body weight has shown a favorable impact on testosterone levels in overweight males. However, typical weight loss interventions using a hypocaloric diet results in between a 6-17% reduction in body weight (Camacho et al., 2013). The current study showed an average weight loss of 4.5% in the intervention groups within the twelve week period, which may not have been sufficient to result in any significant changes in fasting total testosterone.

6.3.3.2 Exercise and Testosterone:

Total testosterone response to resistance training is dependent upon several variables including volume, number of sets, order of exercise, intensity, rest intervals, choice of exercise and pre/post workout nutrition (Vingren et al., 2010). Based on previous research, resistance training protocols were employed that have been shown to consistently improve total testosterone in a variety of populations including young, old, active and inactive individuals (Beaven, Gill, & Cook, 2008; Beaven, Cook, & Gill, 2008; Budnar et al., 2014; W. J. Kraemer et al., 1998; Linnamo et al., 2005; Vingren et al., 2010). It was expected that these resistance exercise protocols would elicit a similar response in an overweight and obese, but otherwise healthy male cohort, as demonstrated

in similar non-obese populations (Hakkinen et al., 1988a; Hakkinen et al., 1988b; W. J. Kraemer et al., 1999; Marx et al., 2001; Staron et al., 1994). The basis for this hypothesis was twofold; first, it was anticipated that the training effect of the Exercise +Diet intervention would be amplified by the previously inactive status of the subjects, and secondly, it was anticipated that weight loss resulting from the Exercise +Diet protocol would have a beneficial and complimentary impact on total testosterone. However, this did not occur in the current study.

Contractile loading of skeletal muscle through resistive-type exercise and protein ingestion acts as a strong stimulus for muscle protein synthesis and, when combined can induce a net positive protein balance and muscle hypertrophy, as witnessed by the increase in lean body mass in the Exercise + Diet group of the current study. This investigation utilized protocols more suitable for an older population, where contraction can be manipulated. The study used moderate-load weight lifting to stimulate rates of muscle protein synthesis to a level comparable to traditional high-loads, which is an approach with important implications for older adults interested in undertaking resistance exercise (Breen & Phillips, 2012). The resulting increase in lean body mass, coupled with the improved muscle cross sectional area of the Exercise +Diet group, indicates that hypertrophy occurred. Although the fasting total testosterone did not change in response to the intervention, the goal of muscular hypertrophy was achieved in a population who has been shown to possess specific challenges with respect to improved muscle protein synthesis due to obesity and age (Camacho et al., 2013). Changes in acute total

testosterone may be responsible for this hypertrophic response in the Exercise +Diet group. However, the lack of acute post exercise measurement makes this hypothesis speculative, and should be addressed in future studies.

6.3.3.3 Testosterone and Nutrition:

Testosterone response to dietary intake and the effect of specific macronutrients on androgens has yet to be extensively investigated. It is also unclear how diet related decreases in total testosterone influences muscle mass. The results of this study indicate that a hypocaloric diet, with or without resistance training exercise that results in modest but statistically significant weight loss, does not impact total testosterone in the studied population. These results must be interpreted with caution, as the relatively small degree of weight loss and the lack of significant change in weight between groups was a limitation for determining whether a change in circulating total testosterone concentration took place as a result of diet.

6.3.3.4 Testosterone and Regional Adiposity:

Testosterone is inversely associated with obesity status (Allan & McLachlan, 2010). The impact of massive obesity on testosterone is well established; however, the impact of mild to moderate obesity on the hypopituitary gonadal axis is less clear (Tajar

et al., 2012). According to the Massachusetts Male Aging Study, testosterone concentration correlates with a number of abdominal fat parameters (Travison et al., 2007). It was therefore hypothesized that total testosterone was negatively associated with fat mass, in particularly the visceral compartment.

Results of the current study showed that testosterone concentration demonstrated the predicted statistically significant ($p<0.01$) inverse relationship with visceral fat. This finding is in agreement with other research, which has shown that circulating testosterone is negatively correlated with DXA measures of intra-abdominal fat in middle-aged men with BMIs ranging from 18-43 kg/m2 (Camacho et al., 2013; Tajar et al., 2012). Visceral fat has a high density of androgen receptors that, when exposed to testosterone, up-regulates in number (Blouin, Boivin, & Tchernof, 2008). This up-regulation inhibits the expression of free fatty acid uptake in the omental, but not subcutaneous, adipose tissue (Bjorntorp, 1997). The significance of this interaction is lipid mobilization, resulting in a reduction of visceral fat mass and a decrease in omental adipocyte size, as well as a decrease in leptin expression (Bjorntorp, 1997). The effects of testosterone on adipocyte metabolism would be expected to markedly inhibit triglyceride uptake and stimulate their mobilization as witnessed in in vivo studies in men, suggesting that testosterone is an important regulator of central and peripheral adipose tissue in human males (Wajchenberg et al., 2002).

Although no novel findings with respect to testosterone's relationship with subcutaneous adipose deposits were found, the addition of further research supporting the

inverse relationship between visceral fat mass and total testosterone adds to an understanding of obesity's impact on androgens in a population susceptible for obesity related sex hormone derangement.

6.3.3.5 Testosterone: Summary of Findings

In summary, total testosterone does not demonstrate significant change in response to diet in isolation, or in combination with high intensity resistance training in previously inactive, aging, overweight and obese men. These results support the understanding that significant weight loss must be achieved in order to elicit an increase in basal testosterone. Previous studies using similar protocols, but of a longer duration and exhibiting greater weight loss, have shown an increase in testosterone (Ahtiainen, Pakarinen, Alen, Kraemer, & Hakkinen, 2003; W. J. Kraemer et al., 1999; Marx et al., 2001; Staron et al., 1994). Obesity and its associated downregulation of the HPG axis is a powerful mechanism which appears to have a strong suppressive effect on androgens that cannot be controlled for through diet and physical activity unless significant weight loss is achieved or baseline androgen derangement is present. In addition, the assessment of bioavailable testosterone would be an important measure to add to this research, and would help determine the impact of obesity on testosterone. Bioavailable testosterone should therefore be added to future research investigating exercise and diet interventions in overweight and obese men.

Obesity status may augment the testosterone response to resistance exercise in an overweight population as compared to leaner individuals. Based on the results, it can therefore be concluded that moderate weight loss resulting from a hypocaloric diet, with or without exercise training, does not improve fasting total testosterone in aging, overweight and obese men.

6.4 Summary Regional Adiposity: Skin Fold Thickness

It appears that regional adiposity, as determined by skinfold thickness, yields limited insights into fasting circulating levels of the energy regulating and exercise associated hormones measured in this study. The multiple comparisons with these hormones of interest yielded some statistically significant correlations; however, these correlations are most likely due to chance. The phenotypical characteristics of adipose tissue are complex, and although there appears to be some regional predictive capabilities when employing skin fold thickness, the majority of depot specific associations have been previously demonstrated via other more reliable measurement techniques. These relationships include the interaction between visceral fat deposits, insulin resistance and associated adipokines, as well as leptins association with total adipose tissue (regardless of location). Furthermore, the application of skin fold testing during exercise training to predict changes in exercise related hormones, including testosterone, appears to be inconsequential. However, skin fold calipers provide researchers with an easily

administered, sensitive measure of subcutaneous skin fold thickness which is low cost, and which yields a more reliable prediction of obesity status as compared to many widely used techniques, including prediction formulas such as BMI. Although regional skin fold sites may not predict fasting circulating levels of hormones related to Exercise + Diet interventions, they do provide an effective means for assessing body composition outside of a clinical setting, which can be performed by a variety of allied health professionals in a standardized and easily replicable fashion.

6.5 Association between Adiposity and Biochemical Measures

Adiposity can be determined by a variety of techniques, including predictive equations, physical measurements and imaging techniques. As stated in the introduction, BMI is a widely debated means of assessing obesity. However, it has shown consistent reliability in the prediction of cardiovascular and metabolic risk factors. Regardless of the BMI measures limitations, the current study's results mirror the results of others which show the BMI's association with cardiovascular and diabetes risk, demonstrating a significant negative association with HDL cholesterol, and positive associations with insulin and insulin resistance. BMI is used frequently in population research, which was the basis for implementing it in the inclusion criteria in the current study. Based on previous research, the assumptions made during this study's design were that individuals falling within the overweight or obese BMI categories would possess an increased

likelihood of insulin resistance (even in the absence of diagnosed metabolic condition), which is an important biochemical characteristic with respect to the endocrine interplay of energy regulating and exercise related hormones associated with obesity. Although the relationship between BMI and insulin resistance was demonstrated in this study's population, it is likely that the use of solely obese individuals instead of those in the overweight category would have provided greater resolution with respect to changes in insulin resistance. Furthermore, it is possible that some subjects classified as overweight may have had body compositions which were characterized by greater lean body mass, which would elevate BMI and misclassify individuals as having excess adipose tissue.

These results coincide with the results of previous works, and demonstrate a relationship between waist and hip circumference, cardiovascular markers and diabetes. Both waist and hip circumference showed a statistically significant negative association with HDL cholesterol, and positive associations with insulin and insulin resistance in the study cohort.

Some studies demonstrate that abdominal subcutaneous fat has a stronger correlation with insulin resistance than the visceral fat compartment in both diabetic and non-diabetic subjects (Cnop et al., 2003). In agreement with other studies, these results show that DXA measurements, including total body fat percentage and visceral fat mass, have a strong positive association with insulin resistance and fasting insulin. Both waist and hip circumference, which are used to determine trunk fat non-invasively, demonstrated a negative association with HDL, while visceral fat, measured using the

gold standard DXA method, did not. Furthermore, subcutaneous skin fold thickness of the suprailiac and umbilical region also failed to demonstrate a significant correlation with cholesterol, indicating that it may be a combination of both visceral and subcutaneous fat deposits that result in the inverse association between HDL and the android obesity phenotype in this overweight, middle-aged male cohort. In addition, visceral adipose tissue and the centralization of adipose tissue is frequently correlated strongly with a number of related metabolic variables, including plasma glucose and lipid concentrations. However, statistical analysis did not demonstrate this relationship (Abate, Garg, Peshock, Stray-Gundersen, & Grundy, 1995b; Bogl et al., 2016; Frayn, 2000; Smith et al., 2001). This lack of association between adiposity and metabolic measures is likely the result of this study's sample population, who were required to be absent of metabolic disease while being categorized as overweight or obese. This exclusion criteria introduces a significant selection bias when comparing the current study's population to individuals of similar age and adiposity matched norms from studies without this rigorous exclusion criteria related to metabolic health (Roberson et al., 2014).

Visceral fat has been correlated to a greater extent with insulin resistance then total and subcutaneous fat (Banerji et al., 1995). Conversely, it is believed that subcutaneous trunk adipose tissue may impact insulin resistance (Cnop et al.,2002). This relationship was demonstrated in this research, as the subscapularis was associated with insulin resistance. Subcutaneous skinfold thickness has been used historically to predict

metabolic health risk (Kissebah & Peiris, 1989), and these results show that skin fold thickness may remain a useful tool in the non-invasive assessment of insulin resistance.

In previous comparisons between central and peripheral obesity, it has been shown that subjects with higher trunk fat are more insulin resistant than subjects with peripheral or lower body obesity (Bogl et al., 2016; Samsell et al., 2014; Selyatitskaya et al., 2015). Results from this study agree with these findings, as several measures of central obesity showed positive associations with insulin resistance in these middle aged overweight and obese males. The underlying mechanism is still vague, however it has been shown that trunk fat, including visceral and subcutaneous fat, has a higher free fatty acid concentration than the peripheral subcutaneous depots (Bogl et al., 2016). A study by Goodpaster et al found that thigh subcutaneous fat, as one indicator of fat deposition in peripheral tissue, is a significant predictor of insulin sensitivity (Goodpaster et al., 2005). Studies have found that the peripheral thigh subcutaneous fat compartment had no correlation with insulin sensitivity, while others show that thigh intramuscular fat, assessed using CT, had a negative correlation with insulin sensitivity (Fried & Kral, 1987; Karastergiou, Smith, Greenberg, & Fried, 2012). It is believed that gluteofemoral fat has a cardio-protective role, and that adipocytes in that region are relatively insensitive to lipolysis stimulus, and sensitive to anti-lipolysis stimulus (Manolopoulos et al., 2010). Although not measured in the current study, lipoprotein lipase (LPL) has an important role for free fatty acid uptake in circulation. Previous studies have found that femoral fat depot have a relatively high LPL activity and lower lipolysis-stimulated activity (Fried &

Kral, 1987). Therefore, the gluteofemoral fat depot may be more effective in releasing free fatty acid into circulation and tend to release less free fatty acid into the circulation (Fried & Kral, 1987). Gluteofemoral subcutaneous fat was negatively associated with HDL ($p<0.03$) in the current study, however unlike other subcutaneous sites it failed to demonstrate any significant relationship with insulin resistance. The concept of gluteofemoral subcutaneous adipose tissue that is physiologically different from other subcutaneous adipose sites is controversial, and the current study was unable to detect any associations with these biochemical measures of interest. Interestingly, this study was able to demonstrate similar findings to others which determined that the peripheral skin fold thickness of the triceps and subscapularis regions are associated with fasting insulin resistance (Kissebah & Peiris, 1989). Furthermore, both the triceps and subscapularis skin fold sites showed a positive association with fasting triglycerides, while the subscapularis showed an association with fasting glucose concentration as well. The explanation as to why these associations exist may relate to the overall adiposity and storage of body fat in the subcutaneous compartment. As body fat is stored preferentially from central to peripheral depots in men, the increase in peripheral stores may act as an indicator of overall adiposity as suggested by the body build continuum (Mueller & Wohlleb, 1981). Exploratory analysis found a significant correlation between both the triceps and subscapularis skin fold sites with regards to several measures of overall adiposity. Therefore, unlike other regions of adipose depots including the gluteofemoral region and visceral compartment, which may have unique adipose tissue characteristics or behavior,

it is likely that the triceps and subscapularis sites are primarily indicators of overall adiposity and that they behave similarly to other measures of obesity including girth measurements and prediction formulas in the assessment of metabolic health.

6.6 Limitations

Intervention studies using volunteer subjects possess several inherent limitations and challenges. Sample size would have been a limitation in our study without our interim analysis, which demonstrated that an increase in the number of subjects was required in order to detect a difference in our primary outcome, adiponectin.

The volunteer nature of our subject population is a limitation of the study, making it difficult to generalize the findings to the general population of overweight and obese males who fall within the 35-55 year old age range. The volunteers for this study were highly motivated, and were likely to possess a greater concern and awareness for their own health. Furthermore, participation in an exercise study may appeal more readily to a population who is familiar with exercise, especially resistance training.

Subject demographic was an intentional limitation of the study, nonetheless, it further restricted comparisons to others falling within the same age range, gender and obesity classification. Our subjects were required to be free of metabolic disease, and were

considered metabolically healthy and overweight/obese. This subject demographic reduces application to those of other age groups, as well as to the female population.

The small sample size of the study may be a factor in the negative findings of this investigation. Although interim sample size calculations were performed and additional subjects added, the variance in the adiponectin response was larger than expected, therefore the current study may be underpowered.

An additional limitation of the research was the lack of blinding by the primary investigator as to the group allocation of the subjects during the post test period. Although blinded to group allocation, the participation of the primary investigator in many aspects of the study implementation is a limitation of the current work.

With respect to the intervention, there is not yet a method for the accurate determination of dietary intake. Physical and psychological characteristics of study participants play an important role reporting bias and the degree of misreporting (Westerlep et al. 2002). A potential solution to unreliable reporting is to encourage subjects with earlier results of food reporting which occurred weekly in our intervention. The current study attempted to reduce this limitation by regular reporting of food logs to a registered dietitian which assists in diet coaching effectiveness.

The exercise intervention posed significant challenges in maintaining uniform exercise intensity amongst the various subjects, who ranged in fitness levels and previous

experience with resistance training. The study attempted to reduce these challenges by performing baseline fitness testing, which was used to determine the appropriate load for exercises using predictive tables available through the American College of Sports Medicine (ACSM, 2014). Furthermore, fitness testing was performed by a certified kinesiologist to ensure consistency in pre and post exercise testing measures.

Although a lengthier study may have allowed for great weight loss, the current study opted for a twelve week study due to cost and potential threats to subject adherence. Consideration of previous research helped determine the length of the study which indicated that this study was of sufficient length, but a longer intervention may have led to greater weight loss and a clearer signal with respect to the outcomes of interest related to weight loss.

Study adherence was a challenge in this intervention study. Our subjects all completed the required interventions, but some changes in the scheduling of workouts were required and 10% of food logs were not submitted. Because adherence is a vital aspect of a study such as this, the research team placed significant effort on ensuring participation in both the nutrition and exercise components of the study, allowing all fifty one subjects to complete the intervention, and to complete baseline and follow-up testing as per the study protocol.

The assessment of appetite regulating hormones PYY and GLP-1 would have contributed to this body of work due to their role in energy regulation. These hormones

in conjunction with ghrelin and leptin would have provided enhanced resolution on the role of Exercise + Diet and Diet Alone on the hormonal interplay of appetite regulation. Additionally the assessment of the various molecular weight adiponectin isoforms would have provided insight into the change of total adiponectin to its active form HWM in response to the current intervention.

For our secondary outcomes, testosterone was chosen as a hormone of interest due to its relationship with resistance training. However, the interpretation of these findings is limited due to several considerations specific to testosterone assessment. Much of the decline in testosterone linked to overweight/obesity is due to the lower bound levels of the hormone while the bioavailable levels are often maintained. We did not measure the bio-available testosterone in the current investigation, which does not allow for full resolution on the impact of obesity on testosterone. Furthermore, although the diurnal variation of testosterone was addressed through standardized sample collection in the morning, testosterone has superimposed spikes every ninety minutes. Consequently, the rigorous way to measure testosterone is by taking samples on three separate mornings which are then averaged, or by taking three separate measurements on one morning that are averaged. Due to cost constraints and subject availability this testing was not employed, which limits the resulting interpretation of the testosterone findings.

A final limitation of the current study was the lack of previous research from which to base the intervention, particularly with respect to moderate-high intensity resistance training, for a non-athletic population.

The lack of general population research utilizing highly controlled exercise interventions developed based on training specificity principles results in heterogeneity in ongoing research. Furthermore, no study to our knowledge has employed both periodized resistance training and a moderate caloric restriction diet to encourage weight loss in this overweight and obese population, while investigating energy regulating and exercise associated hormones.

6.7 Generalizability

This study provides greater insight into the response of hormones associated with body composition, metabolism and appetite to resistance training and diet in the aging (35-55 years old) overweight and obese male population. The findings of this study agree with others that demonstrate that exercise in combination with diet does not result in greater weight loss then diet alone (Miller 1997). Exercise does, however, provide added health benefits including increased lean body mass, improved cholesterol, triglycerides and blood pressure. Therefore, overweight and obese 35-55 year old men seeking weight loss can achieve this through caloric restriction and diet while those looking for additional benefits including greater lean body mass and cardiovascular health risk

reduction should be encouraged to incorporate resistance training exercise into their lifestyle.

7 Conclusions

Weight loss in overweight and obese 35-55 year old males achieved through twelve weeks of structured resistance training and diet (Exercise +Diet) or through Diet Alone does not result in a significant change in circulating adiponectin. The Exercise + Diet intervention led to a similar significant weight loss as the Diet Alone intervention and it appears that exercise has independent improvements in measures of cardiovascular health. The current study indicates that the assessment of adiponectin during weight loss in a non-insulin sensitive population may not provide any additional value or insight into health status Furthermore, the energy regulating hormones ghrelin and TNF-α, along with testosterone, do not change in response to weight loss achieved through Exercise +Diet and Diet Alone interventions, while circulating leptin concentration decreased in response to weight loss for all subjects, regardless of group assignment. When fat in the trunk region, a known confounder for adiponectin, was controlled for, adiponectin elevated in response to weight loss achieved through diet in isolation and reduced in response to weight loss achieved through resistance training exercise. Our results mirror other studies which have utilized different exercise modalities, including cardiovascular training, to elicit this response (Christiansen et al., 2010, Yatagai et al., 2003).

Although the weight loss and cardiovascular measures demonstrated statistically significant changes, our outcomes suggest that the length of the study may not have been sufficient for demonstrating the hypothesized humoral change. Additional exposure to resistance training and/or diet may have resulted in further weight loss and opportunities to observe changes in energy regulating and exercise associated hormones. Research using the current study's exercise and diet protocols should ensure a longer exposure of subjects to the respective interventions. Due to the small number of studies investigating the impact of structured resistance training on adiponectin and other humoral variables, this research indicates that short term exposure to resistance training is unlikely to impact this study's hormones of interest when resistance training is employed.

Well established relationships between circulating hormone concentrations and regional body composition were observed in this study. These included adiponectin, TNF-α's and testosterone's relationship with visceral fat, leptin's association with total body fat, and ghrelin's relationship with lean body mass.

The current study suggests that subcutaneous skin fold sites do not share the predictive capability of regional body composition with respect to circulating adiponectin, TNF-α, leptin, ghrelin and testosterone. This study is the first, to the best of our knowledge, to investigate the relationship between regional subcutaneous skin fold measures and circulating hormones on energy regulation and exercise. Although these results do not demonstrate any significant insights regarding subcutaneous skin fold thickness and

circulating hormone concentrations, our outcomes validate the skin fold caliper as an effective means for assessing body composition when imaging techniques are not available.

Obesity is a multi-factorial condition that is impacted by both environmental and genetic conditions. Weight loss achieved through changes in physical activity and diet are important approaches to improving and maintaining health. Our study provides insights into the impact of structured resistance training on the middle aged overweight and obese male demographic. Furthermore, this work provides an exercise and diet intervention which leads to healthy moderate weight loss in a relatively short period of time, while demonstrating measurable improvements in cardiovascular health benefits in overweight and obese middle aged males.

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Appendix

Appendix 1 – Research assistant handbook

Appendix 2 – Resistance Training Phase 1

Appendix 3 – Resistance Training Phase 2

Appendix 4 – Resistance Training Phase 3

Appendix 5 – Meal Planner

Appendix 6 – Body Fat Assessment Techniques

Appendix 7 – Anthropometric Testing Protocol

Appendix 8 – Fitness Testing Protocol

Appendix 9 – HREA Approval Letters

Appendix 10 – Subject Consent Form

Appendix 11 – Subject Recruitment Email

Appendix 12 – Food Intake Questionnaire

Appendix 13 – Dietary Assessment

Appendix 1

Research Assistant

Handbook

Influence of Supervised Resistance Training and a Hypocaloric Macronutrient Scheduled Diet vs a Hypocaloric Macronutrient Scheduled Diet Alone on Energy Regulating Hormones in Overweight and Obese Men Ages 35-55.

Research Assistants Handbook

Table of Contents

Introduction:

In order to organize all necessary components of the research project a comprehensive procedures manual has been develop to assist future research assistants. This manual will cover everything they need to know to be a successful research assistant for the study “Hormonal Adaptation to Lifestyle Interventions”. Please review this manual prior to engaging in any research activities and keep for reference when necessary during the course of your work.

Starting out:

Meet with the team at the training facility and the other researchers involved in the study

- Attend meetings with key partners with the primary investigator

Read and understand:

- Study protocol available in the intelligencebank.ca website
- Study consent forms
- Nutrition Questionnaire
- Previous subject files

Important material

The first important pieces of reading material you should make yourself aware of are the Thesis Protocol, and the Subject Handbook. The Thesis Protocol will inform you of the specifics for the study so you can have a strong grasp on the work you are completing. The Subject Handbook is the informational booklet that your test subjects will be reading and referencing concerning dietitian designed nutrition plan and their work outs. Therefore as their guide you should know everything in this book from front to back. There is a study e-mail that you will be using as your primary means of communication. The study e-mail is how you will contact all potential subjects and others involved in the study.

Procedures that you should know about

A DEXA Scan

A DEXA scan is a scan taken at the Health Science that measures your bone density at the beginning and end of the study at a couple of locations in the body. This scan will show you what percentage of your body is bone, and what percent is fat. The individual will have to fast for 12 hours before getting this scan done. While at the DEXA scan they will have a small sample of blood taken. They will then be brought to a room where a DEXA machine is located and will lie on the machine as it scans their body. The entire process should take no more than 1 hour to complete.

Meeting with Primary Investigator

The subjects should have the option to meet with the primary investigator the same day as both the DEXA and the blood test if at all possible. This ensures that the subject does not have to go out of their way to travel to The fitness facility twice when all of this could have happened in one day. If however this is too much for one day it is suggested that the client is given the option to make two trips and fast twice. This means they will get the DEXA completed one day and fast, and then have to fast again another day for their blood test and meet with the primary investigator that same day. When they meet with the primary investigator he will discuss with them proper nutrition, take their measurements, weigh them, and test there different skin fold sites. The meeting with the primary investigator takes half an hour. At this point the primary

investigator will give the subjects all needed documentation to make sure that it is all ready before the subject begins there first training session.

Training Sessions

There will be 3 training sessions per week for each subject lasting an hour. In this time frame they will do a light 5 minute warm up and dynamic stretching to prepare their body for the workout. The structured supervised strength training is a strict program that is designed to keep your body guessing to help increase weight loss. It finishes with a special type of workout called GVT or German Volume Training that will push the subjects to give them optimal results towards the end of the study. They will finish with a foam roll at the end performed by the trainer or they can foam roll themselves once they have been taught the proper technique. The entire process will last a total of 12 weeks.

Adding Clients to the study

Important forms and documents for the study participants

There are certain forms that must be given to the subjects before they begin their first training session. The first of these forms is a consent form and is found in the study materials filing cabinet. This form requires the consent of the participant to take part in the study and explains to them what this entails. The next form is the PAR-Q which asks the participant to check yes or no to any medical concerns that could cause them to need a Doctor's note. The remainder of the necessary forms include a Personal & Parental History Questionnaire, Physical Activity Questionnaire, a Food Groups and Serving Size Survey. Ensure that each client also has a Subject Hand book either e-mailed to them or given to them during their initial visits at the fitness facility. This will make the process much more efficient for everyone involved if they have something to refer to in the early stages.

File Folders

The next step is to make up a file folder for each client. There are blue folders located in the top shelf of the desk in the office. These folders are from previous or existing clients and you may need them for reference or you may need to add to the existing folders at some point. You can add your new folders by printing the individuals name clearly on a white tab and store these in the file cabinet next to the others. Remember to double check these folders to make sure that all

needed forms are there. If all forms are not there you must make a list indicating what you need and from which subject. The forms that must be in each folder are located in the “Needed forms Checklist” sheet which is found in Appendix J .You can then go to your “Personal Information “Excel sheet which will give you the subjects contact so you can notify them of the forms you need. These files are then provided to the primary investigator for locked storage.

Daily Follow up

Following up when dealing with the public is a VERY important part of a research assistants job. It is the responsibility of the work term student to get in contact with every person that is given to them at any point in time.

E-mail Records Document

The ``E-mail Records`` document, found in Appendix K, can be very helpful in organizing your e- mails. This document lets you know how many times you have sent an e-mail to a particular person. If you have e-mailed someone numerous times and there is no reply try to find a telephone number you can reach them at. This ensures that no one gets left behind in an over flux of e-mails.

Structure of the first e-mail

The first email must be very detailed identifying what personal information we need from the subjects, what the study is all about, and what the requirements are as a subject. An e-mail template can be found in Appendix L. This e-mail must include all of the different tests explained in detail and what is needed for each one. For example a Doctor`s note is a necessity for participation in the study and fasting is required for both the DEXA scan and the blood test at the lab. Also these e-mails must be simplistic, for example: some people may not know where the lab is in the Health Sciences Center. You must assume they do not know anything about the information you are giving them, this will ensure there are no surprises for the test subjects.

Role as the Kinesiologist

How to greet a client on their first day

Greet them with a welcoming smile; explain to them what is going to happen within the next hour (for example you will be using a foam roller) , show them the change rooms, offer them a glass of water at the beginning and provide them with a shake at the end. Explain to them the importance of having protein by itself after a workout when trying to lose weight.

Having good insight

As a trainer you must be aware of the vulnerability that these men may be experiencing. Some of them may have never exercised in their lives and others may have been strong athletes who are embarrassed to have reached this point. You must explain things in steps and with care. You can do this by thinking about the individual separate from the rest and explain things in a way that is easy to understand.

Progress sheet

You are responsible to fill in the portion of the Study Handbook that has the subject's workouts. This includes how much weight each client is lifting at the beginning to how much they can lift by the end. This will also help you in tracking where each client is from week to week.

Client and Trainer schedule

You must also do up a schedule to be used by you, your clients, and others at the gym in case they need to schedule someone in for you. This schedule should be done weekly and sent to the primary investigator so is aware of who is at what stage of their training and how many sessions you are doing each week. There is an example shown in Appendix N.

Follow up at the end of the 12 weeks

Following the 12 week intervention the subjects will be required to return for follow up measures including the outlined tests and questionnaires to determine activity status and lifestyle. All participants will receive results from tests and be informed about them once they are extrapolated. Subjects will also be required to attend blood collection for an additional 12 weeks following the end of the intervention to determine trends and adaptation associated with decreases in activity. It is your responsibility to ensure that all of these tests are scheduled in a time sensitive manor. You must refer to the personal training book indicating what stage each participant is at so that once they get to the 11^{th} and 12^{th} week you can start arranging there DEXA scan , Blood test, and meeting with the primary investigator.

Conclusion:

As a research assistant you must review all important material such as the "Thesis Protocol" and make yourself familiar with all of the different procedures such as a Vo2max test. You must become efficient at organizing when adding clients to the study and following up daily to make sure everyone is aware of what is happening. It is important to have a solid foundation for the structure of your first e-mail as this is the client's first impression of us as a company and the study as a project. We want the client to receive all of the information clearly at the beginning to make sure they have a set path to follow. This will make organizing appointments such as the

blood work at the Nexus clinic and DEXA scan at the Health Science run smoothly. We need to keep track of each client's progress so we can be ready for all of the follow up appointments that happen at the end of the 12 week period. This booklet will be a valuable reference for everything that you or your clients could need in terms of the study.

Appendix 2

Resistance Training Phase 1

Appendix 2

Name: Fullbody Phase 1 Workouts

Category: Fullbody **Intensity:** 3
Notes: a great medium intensity workout for gyms

Exercise name: Goblet Squat

Grouping: *A* ***Sets:*** *3* ***Reps:*** *10* ***Tempo:*** *Medium* ***Rest:*** *0*
Muscles: Quadriceps
Tools: DB
Description: Hold one Dumbbell by its end with the base of your two hands under your chin. It should look like you are taking about to take a drink out of a big goblet like glass using both hands. Descend into a deep squat while maintain an upright posture with your upper body - chin up the whole time.

	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
Date	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**

Exercise name: DB Press

Grouping: *A* ***Sets:*** *10* ***Reps:*** *10* ***Tempo:*** *Medium* ***Rest:*** *60*
Muscles: Chest
Tools: DB
Description: Lying on a flat bench. Press weights over chest until arms are extended. Lower until there is a stretch in the chest

	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
Date	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**

Exercise name: Cable Woodchop

Grouping: *B* ***Sets:*** *3* ***Reps:*** *10* ***Tempo:*** *Medium* ***Rest:*** *0*
Muscles: Abdominals
Tools: DB
Description: Grab high cable with both hands. Keeping arms straight bring the cable from the upper part of your body to the lower, rotating the hips and legs slightly contracting abdominals

	Set 1	Set 2	Set 3	Set 4	Set 5	Set 6	Set 7	Set 8	Set 9	Set 10

Date	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R

Exercise name: Seated Row

Grouping: *B* ***Sets:*** *3* ***Reps:*** *10* ***Tempo:*** *Medium* ***Rest:*** *60*
Muscles: Back
Tools: CB
Description: Lean forward to grab narrow grip, keeping a slight bend in the knees. Feet should be in contact with foot pads. Lean back while holding Narrow grip with straight arms. Pull the bar towards your stomach while maintaining a straight lower back. Return to position

	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
Date	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R

Exercise name: Tricep Rope Extensions

Grouping: *C* ***Sets:*** *3* ***Reps:*** *10* ***Tempo:*** *Medium* ***Rest:*** *0*
Muscles: Triceps
Tools: CB
Description: Grab bar attached to cable at about chest height holding the rope attachment. With elbows closely at your side push down on the bar with until arm is fully extended.

	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
Date	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R

Exercise name: Hammer Curls

Grouping: *C* ***Sets:*** *3* ***Reps:*** *10* ***Tempo:*** *Medium* ***Rest:*** *60*
Muscles: Biceps
Tools: DB
Description: Hold dumbbells, with palms facing your sides. keep elbows near your sides and bring the forearm up until it is vertical, maintaining upper arm position. Return back to normal

Date	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R

Exercise name: SB Crunch

Grouping: *D* ***Sets:*** *3* ***Reps:*** *15* ***Tempo:*** *Medium* ***Rest:*** *0*
Muscles: Abdominals
Tools: SB
Description: Start by sitting on a SB. Walk your feet out and roll your body with them until the SB is supporting your lumbar spine. Your feet should be firmly grounded and shoulder-width apart. From this position curl your upper torso upwards by contracting the abdominal muscles from the top down to the bottom. Repeat for the prescribed number of repetitions and then roll back up into the sitting position using your legs to safely get off the ball.

Date	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R

Exercise name: Plank

Grouping: *D* ***Sets:*** *3* ***Reps:*** *1* ***Tempo:*** *Slow* ***Rest:*** *60*
Muscles: Abdominals
Tools: BW
Description: Get into push up position but instead of being on your hands and toes place your weight on your elbows and toes. From here you want to maintain this position by trying to pull your belly button to your spine for the duration of the exercise. this exercise turns on a deep abdominal muscle called the Transverse Abdominals which aids in our posture and balance.

Date	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R

Name: Fullbody Phase 1 Workouts

Category: Fullbody **Intensity:** 4
Notes:

Exercise name: Step Ups

Grouping: *A* ***Sets:*** *3* ***Reps:*** *12* ***Tempo:*** *Medium* ***Rest:*** *40*
Muscles: Quadriceps
Tools: DB
Description: Start with one foot on the step and the other foot on the ground

	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
Date	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**

Exercise name: SB Leg Curl

Grouping: *A* ***Sets:*** *3* ***Reps:*** *12* ***Tempo:*** *Medium* ***Rest:*** *40*
Muscles: Hamstrings
Tools: SB
Description: Lie on your back with your heels and lower calves on a SB. First lift your hips up until your body forms a ramp

	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
Date	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**

Exercise name: Lat Pulldown

Grouping: *A* ***Sets:*** *3* ***Reps:*** *12* ***Tempo:*** *Medium* ***Rest:*** *40*
Muscles: Back
Tools: MA
Description: Palms facing, narrower than shoulder width grip. Lean back as you pull the bar to the sternum. Return to the starting position at the dictated tempo.

	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
Date	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**

Exercise name: Incline DB Press

Grouping: *A* ***Sets:*** *3* ***Reps:*** *12* ***Tempo:*** *Medium* ***Rest:*** *40*
Muscles: Chest
Tools: DB
Description: Incline an adjustable bench to between 30 and 60 degrees. Start with the DB's at your shoulders and press directly over your chest, perpendicular to the ground. Rotate the DB's from palms facing your feet in the bottom position to palms facing at the top.

	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
Date	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**

Exercise name: Arnold Press

Grouping: *B* ***Sets:*** *3* ***Reps:*** *10* ***Tempo:*** *Medium* ***Rest:*** *40*
Muscles: Shoulders
Tools: DB
Description: Grasp a dumbbell in each hand and raise the weights to top position of a dumbbell curl. As you raise the dumbbells overhead, rotate the hands in so that the palms face forward at the top of the movement. Remember to not lockout the arms. Reverse the movement on the way down.

	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
Date	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**

Exercise name: Cable Curls

Grouping: *B* ***Sets:*** *3* ***Reps:*** *10* ***Tempo:*** *Medium* ***Rest:*** *40*
Muscles: Biceps
Tools: BB
Description: Hold Low pulley at shoulder length, keep elbows at sides, lift with forearms until forearms are vertical.

	Set 1	Set 2	Set 3	Set 4	Set 5	Set 6	Set 7	Set 8	Set 9	Set 10

Date	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R

Exercise name: Tricep Rope Extensions

Grouping: *B* ***Sets:*** *3* ***Reps:*** *10* ***Tempo:*** *Medium* ***Rest:*** *40*
Muscles: Triceps
Tools: CB
Description: Grab bar attached to cable at about chest height holding the rope attachment. With elbows closely at your side push down on the bar with until arm is fully extended.

	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
Date	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R

Exercise name: Torso Twist

Grouping: *B* ***Sets:*** *3* ***Reps:*** *15* ***Tempo:*** *Medium* ***Rest:*** *40*
Muscles: Abdominals
Tools: CB
Description: Step out laterally while holding the bands out to the side. Establish a balanced stance with feet slightly wider than shoulder-width then rotate from the torso pulling the CB across to the other side of the body in a semi-circular pattern, then return along the same path.

	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
Date	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R

Name: Fullbody Phase 1 Workouts

Category: Fullbody **Intensity:** 3
Notes:

Exercise name: Leg Press

Grouping: *A* ***Sets:*** *3* ***Reps:*** *12* ***Tempo:*** *Medium* ***Rest:*** *60*
Muscles: Quadriceps
Tools: MA
Description: Sit with back against the seat and feet place firmly on the pad. Legs should be at hips width and legs should be bent at 90 degrees. Press pad with heels until extended but don't lock at the knees.

	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
Date	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**

Exercise name: Lat Pulldown

Grouping: *A* ***Sets:*** *3* ***Reps:*** *12* ***Tempo:*** *Medium* ***Rest:*** *60*
Muscles: Back
Tools: MA
Description: Palms facing, narrower than shoulder width grip. Lean back as you pull the bar to the sternum. Return to the starting position at the dictated tempo.

	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
Date	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**

Exercise name: Push Up

Grouping: *A* ***Sets:*** *3* ***Reps:*** *12* ***Tempo:*** *Medium* ***Rest:*** *60*
Muscles: Chest
Tools: BW
Description: Lie face down to the ground, with palms touching the ground and elbows at 90 degrees. Arms should be soulder width apart, then try to raise yourslef by pushing the ground. Legs and back shouls be straight for the whole movement with toes touching the ground.

	Set 1	Set 2	Set 3	Set 4	Set 5	Set 6	Set 7	Set 8	Set 9	Set 10

Date	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R

Exercise name: Torso Twist

Grouping: *A* ***Sets:*** *3* ***Reps:*** *12* ***Tempo:*** *Medium* ***Rest:*** *60*
Muscles: Abdominals
Tools: CB
Description: Step out laterally while holding the bands out to the side. Establish a balanced stance with feet slightly wider than shoulder-width then rotate from the torso pulling the CB across to the other side of the body in a semi-circular pattern, then return along the same path.

	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
Date	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R

Exercise name: Hip Extension

Grouping: *B* ***Sets:*** *3* ***Reps:*** *12* ***Tempo:*** *Medium* ***Rest:*** *60*
Muscles: Hamstrings
Tools: BW
Description: Lay on your back place your feet on a chair with a 90 degree angle. Lift hips until fully extended and then return to the starting position with a slow movement.

	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
Date	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R

Exercise name: DB Row

Grouping: *B* ***Sets:*** *3* ***Reps:*** *12* ***Tempo:*** *Slow* ***Rest:*** *60*
Muscles: Back
Tools: DB
Description: Grab a DB and a bench. Putting the opposite foot forward and having your palm facing you while holding DB, pull the DB to the side of the waist. Make sure you keep your back flat and strong throughout the movement and keep your shoulder level.

Date	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R

Exercise name: Tricep Rope Extensions

Grouping: *B* ***Sets:*** *3* ***Reps:*** *12* ***Tempo:*** *Slow* ***Rest:*** *60*
Muscles: Triceps
Tools: CB
Description: Grab bar attached to cable at about chest height holding the rope attachment. With elbows closely at your side push down on the bar with until arm is fully extended.

Date	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R

Exercise name: Back Extensions

Grouping: *B* ***Sets:*** *3* ***Reps:*** *12* ***Tempo:*** *Slow* ***Rest:*** *60*
Muscles: Back
Tools: BW
Description: Lie prone with your feet hooked under the foot supports of a back extension MA. Allow your body to bend forward at the waist and round your back slightly then extend your back up until your torso is just past parallel to the floor.

Date	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R

Appendix 3

Resistance Training
Phase 2

Appendix 3

Name: Full Body Phase 2 Workouts

Category: Fullbody **Intensity:** 5
Notes:

Exercise name: Incline Flys

Grouping: *A* ***Sets:*** *3* ***Reps:*** *12* ***Tempo:*** *Slow* ***Rest:*** *0*
Muscles: Chest
Tools: DB
Description: While lying on an incline bench hold dumbells with palms facing each other and arms extended above the chest. Rotate the shoulders back until Upper arms are parallel to the body and there is a slight strech in the chest. Bring weights forward the opposite way and squeeze the chest during contraction. arms are slightly bent throughout the movement

	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
Date	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**

Exercise name: Push Up

Grouping: *A* ***Sets:*** *3* ***Reps:*** *12* ***Tempo:*** *Slow* ***Rest:*** *0*
Muscles: Chest
Tools: BW
Description: Lie face down to the ground, with palms touching the ground and elbows at 90 degrees. Arms should be soulder width apart, then try to raise yourslef by pushing the ground. Legs and back shouls be straight for the whole movement with toes touching the ground.

	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
Date	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**

Exercise name: Dumbbell Bent Over Row

Grouping: *A* ***Sets:*** *3* ***Reps:*** *12* ***Tempo:*** *Slow* ***Rest:*** *60*
Muscles: Back
Tools: DB
Description: Opposite foot forward, palm facing you while holding DB, pull the DB to the side of the waist.

	Set 1	Set 2	Set 3	Set 4	Set 5	Set 6	Set 7	Set 8	Set 9	Set 10

Date	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R

Exercise name: DB Curls

Grouping: *B* ***Sets:*** *3* ***Reps:*** *12* ***Tempo:*** *Slow* ***Rest:*** *0*
Muscles: Biceps
Tools: DB
Description: Hold Dumbbells, with underhand grip. keep elbows near your sides and bring the forearm up until it is vertical, maintaining upper arm position. Return back to normal

	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
Date	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R

Exercise name: Tricep Rope Extensions

Grouping: *B* ***Sets:*** *3* ***Reps:*** *30* ***Tempo:*** *Slow* ***Rest:*** *60*
Muscles: Triceps
Tools: CB
Description: Grab bar attached to cable at about chest height holding the rope attachment. With elbows closely at your side push down on the bar with until arm is fully extended.

	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
Date	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R

Exercise name: 1 Arm Cable Row

Grouping: *C* ***Sets:*** *3* ***Reps:*** *10* ***Tempo:*** *Slow* ***Rest:*** *0*
Muscles: Back
Tools: CB
Description: Similar to a seated row, attach the single handle and row your arm towards your stomach. It is important to keep a straight back position and slightly bent knees to protect your back. Keep head up and body aligned forward, pull the single handle to your side. Complete the

dictated number of reps and then switch hands and repeat.

	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
Date	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**

Exercise name: Pallof Press

Grouping: *C* ***Sets:*** *3* ***Reps:*** *5* ***Tempo:*** *Slow* ***Rest:*** *0*
Muscles: Abdominals
Tools: CB
Description: Stand with feet shoulder-width apart. Set a pulley to chest height and grip handle with both hands. Move hands to chest and then straight out to extended position. Be sure to stand far enough away from the MA to ensure tension is maintained throughout the movement.

	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
Date	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**

Exercise name: Bicycle crunch

Grouping: *C* ***Sets:*** *3* ***Reps:*** *30* ***Tempo:*** *Slow* ***Rest:*** *60*
Muscles: Abdominals
Tools: BW
Description: Lying on your back with your hands behind your head, alternate between bringing your right and left knees to your chest . Have the elbow touch the opposite knee

	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
Date	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**

Name: Full Body Phase 2 Workouts

Category: Fullbody **Intensity:** 5
Notes:

Exercise name: BB Bench Press

Grouping: *A* ***Sets:*** *3* ***Reps:*** *10* ***Tempo:*** *Slow* ***Rest:*** *0*
Muscles: Chest
Tools: BB
Description: Grip bar less than shoulder width. Lower the bar to the sternum.

	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
Date	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**

Exercise name: High Row

Grouping: *A* ***Sets:*** *3* ***Reps:*** *10* ***Tempo:*** *Slow* ***Rest:*** *0*
Muscles: Back
Tools: MA
Description: Using a seated row with the rope attachment, grab on to the rope with thumbs facing each other and palms down. Keeping the back straight and knees slightly flexed, pull your hands up towards your ears, flexing the tops of your shoulders and squeezing your shoulder blades together. Pause for a second on top and lower at dictated tempo.

	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
Date	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**

Exercise name: Seated Row

Grouping: *A* ***Sets:*** *3* ***Reps:*** *10* ***Tempo:*** *Slow* ***Rest:*** *60*
Muscles: Back
Tools: CB
Description: Lean forward to grab narrow grip, keeping a slight bend in the knees. Feet should be in contact with foot pads. Lean back while holding Narrow grip with straight arms. Pull the bar towards your stomach while maintaining a straight lower back. Return to position

	Set 1	Set 2	Set 3	Set 4	Set 5	Set 6	Set 7	Set 8	Set 9	Set 10

Date	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R

Exercise name: Reverse Curls

Grouping: *B* ***Sets:*** *3* ***Reps:*** *10* ***Tempo:*** *Slow* ***Rest:*** *0*
Muscles: Biceps
Tools: DB
Description: Palms down, shoulder width grip

	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
Date	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R

Exercise name: Bench Dips

Grouping: *B* ***Sets:*** *3* ***Reps:*** *10* ***Tempo:*** *Slow* ***Rest:*** *0*
Muscles: Triceps
Tools: BW
Description: Using a bench place you back against the side with your hands shoulder width apart.keeping you elbows tight and your back against the bench bend your knees slightly and press up through your hands working your triceps. Remember to keep your chest out and head straight during this movement in order to isolate the triceps.

	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
Date	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R

Exercise name: Cable Woodchop

Grouping: *B* ***Sets:*** *3* ***Reps:*** *10* ***Tempo:*** *Slow* ***Rest:*** *60*
Muscles: Abdominals
Tools: DB
Description: Grab high cable with both hands. Keeping arms straight bring the cable from the upper part of your body to the lower, rotating the hips and legs slightly contracting abdominals

	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
Date	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**

Exercise name: Front Raises

Grouping: *C* ***Sets:*** *3* ***Reps:*** *10* ***Tempo:*** *Slow* ***Rest:*** *0*
Muscles: Shoulders
Tools: DB
Description: Hold dumbbells in front of legs with an overhand grip. Raise dumbells up and away from the body, maintaining hand position and keeping arms relatively straight. Lower back to original position and repeat

	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
Date	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**

Exercise name: Goodmornings

Grouping: *C* ***Sets:*** *3* ***Reps:*** *10* ***Tempo:*** *Slow* ***Rest:*** *0*
Muscles: Hamstrings
Tools: BB
Description: Wide grip on the bar, feet wider than shoulders, knees flexed 20°, back arched, lower the bar by pivoting throught the hips.

	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
Date	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**

Exercise name: Side Lunges

Grouping: *C* ***Sets:*** *3* ***Reps:*** *10* ***Tempo:*** *Slow* ***Rest:*** *0*
Muscles: Quadriceps
Tools: DB
Description: hold DB's to side, lunge to side keeping both feet straight forward. When in bottom position one db should be on either side of knee

Date	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R

Name: Full Body Phase 2 Workouts

Category: Fullbody **Intensity:** 5
Notes:

Exercise name: Incline DB Press

Grouping: *A* ***Sets:*** *3* ***Reps:*** *12* ***Tempo:*** *Slow* ***Rest:*** *0*
Muscles: Chest
Tools: DB
Description: Incline an adjustable bench to between 30 and 60 degrees. Start with the DB's at your shoulders and press directly over your chest, perpendicular to the ground. Rotate the DB's from palms facing your feet in the bottom position to palms facing at the top.

	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
Date	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**

Exercise name: Lat Pulldown

Grouping: *A* ***Sets:*** *3* ***Reps:*** *12* ***Tempo:*** *Slow* ***Rest:*** *0*
Muscles: Back
Tools: MA
Description: Palms facing, narrower than shoulder width grip. Lean back as you pull the bar to the sternum. Return to the starting position at the dictated tempo.

	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
Date	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**

Exercise name: Lat Raise and Pour

Grouping: *A* ***Sets:*** *3* ***Reps:*** *12* ***Tempo:*** *Slow* ***Rest:*** *60*
Muscles: Shoulders
Tools: DB
Description: Complete a standard side raise and at the top range of motion rotate thumbs from a neutral position to a downward pointed position and then return to the starting position and lower the arms to complete the reps.

	Set 1	Set 2	Set 3	Set 4	Set 5	Set 6	Set 7	Set 8	Set 9	Set 10

Date	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R

Exercise name: DB Curls

Grouping: *B* ***Sets:*** *3* ***Reps:*** *12* ***Tempo:*** *Slow* ***Rest:*** *0*
Muscles: Biceps
Tools: DB
Description: Hold Dumbbells, with underhand grip. keep elbows near your sides and bring the forearm up until it is vertical, maintaining upper arm position. Return back to normal

	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
Date	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R

Exercise name: BB Overhead Tricep Extensions

Grouping: *B* ***Sets:*** *3* ***Reps:*** *12* ***Tempo:*** *Slow* ***Rest:*** *0*
Muscles: Triceps
Tools: BB
Description: Shoulder width grip. Point elbows directly at ceiling. Bend at the elbows.

	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
Date	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R

Exercise name: Cable Woodchop

Grouping: *B* ***Sets:*** *3* ***Reps:*** *12* ***Tempo:*** *Slow* ***Rest:*** *60*
Muscles: Abdominals
Tools: DB
Description: Grab high cable with both hands. Keeping arms straight bring the cable from the upper part of your body to the lower, rotating the hips and legs slightly contracting abdominals

	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
Date	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**

Exercise name: Lunges

Grouping: *C* ***Sets:*** *3* ***Reps:*** *12* ***Tempo:*** *Slow* ***Rest:*** *0*
Muscles: Quadriceps
Tools: DB
Description: With Feet shoulder width apart hold dumbells at side of the body. Step forward with one leg , landing on the heel of that leg, keeping the back leg extended and heel raised. Lower back knee to the floor as you bend the lead leg at 90 degrees in the knee.

	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
Date	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**

Exercise name: DB Crunches

Grouping: *C* ***Sets:*** *3* ***Reps:*** *12* ***Tempo:*** *Slow* ***Rest:*** *0*
Muscles: Abdominals
Tools: DB
Description: hold db at chin. slowly lower using proper tempo and do not fully relax at bottom. hold and crunch until shoulders are off of bench

	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
Date	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**

Exercise name: Plank

Grouping: *C* ***Sets:*** *3* ***Reps:*** *1* ***Tempo:*** *Slow* ***Rest:*** *60*
Muscles: Abdominals
Tools: BW
Description: Get into push up position but instead of being on your hands and toes place your weight on your elbows and toes. From here you want to maintain this position by trying to pull your belly button to your spine for the duration of the exercise. this exercise turns on a deep abdominal

muscle called the Transverse Abdominals which aids in our posture and balance.

	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
Date	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**

Appendix 4

Resistance Training
Phase 3

Appendix 4

Name: Body Part Phase 3 Workouts

Category: Split-Arms **Intensity:** 5
Notes:

Exercise name: DB Shoulder Press

Grouping: *A* ***Sets:*** *10* ***Reps:*** *10* ***Tempo:*** *Slow* ***Rest:*** *0*
Muscles: Shoulders
Tools: DB
Description: Performed while standing, begin by taking 2 dumbbells at a 90 degree elbow position by the head and pressing them directly up through the full range of motion.

	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
Date	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**

Exercise name: Close Grip Benchpress

Grouping: *A* ***Sets:*** *10* ***Reps:*** *10* ***Tempo:*** *Slow* ***Rest:*** *90*
Muscles: Triceps
Tools: BB
Description: Grip bar less than shoulder width (10-14"). Lower the bar to the sternum from a bench press position. Pause at the bottom and press back to the starting position quickly.

	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
Date	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**

Exercise name: DB Side Raises

Grouping: *B* ***Sets:*** *3* ***Reps:*** *10* ***Tempo:*** *Slow* ***Rest:*** *0*
Muscles: Shoulders
Tools: DB
Description: Hold dumbbells with palms facing your legs. Raise arms until upper arms are parallel to shoulders. Lower and repeat

	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
Date	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**

Exercise name: Hammer Curls

Grouping: *B* ***Sets:*** *3* ***Reps:*** *10* ***Tempo:*** *Slow* ***Rest:*** *90*
Muscles: Biceps
Tools: DB
Description: Hold dumbbells, with palms facing your sides. keep elbows near your sides and bring the forearm up until it is vertical, maintaining upper arm position. Return back to normal

	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
Date	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**

Name: Body Part Phase 3 Workouts

Category: Split-ChestandBack **Intensity:** 5
Notes:

Exercise name: Wide grip Pull-up

Grouping: *A* ***Sets:*** *10* ***Reps:*** *10* ***Tempo:*** *Slow* ***Rest:*** *0*
Muscles: Back
Tools: MA
Description: Use a palms down, wider than shoulder width grip. Lean back as you pull the lower sternum to the bar.

Date	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R

Exercise name: DB Press

Grouping: *A* ***Sets:*** *10* ***Reps:*** *10* ***Tempo:*** *Slow* ***Rest:*** *90*
Muscles: Chest
Tools: DB
Description: Lying on a flat bench. Press weights over chest until arms are extended. Lower until there is a stretch in the chest

Date	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R

Exercise name: Push Up

Grouping: *B* ***Sets:*** *3* ***Reps:*** *10* ***Tempo:*** *Slow* ***Rest:*** *0*
Muscles: Chest
Tools: BW
Description: Lie face down to the ground, with palms touching the ground and elbows at 90 degrees. Arms should be soulder width apart, then try to raise yourslef by pushing the ground. Legs and back shouls be straight for the whole movement with toes touching the ground.

Date	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R

Exercise name: BB Row

Grouping: *B* ***Sets:*** *3* ***Reps:*** *10* ***Tempo:*** *Slow* ***Rest:*** *90*
Muscles: Back
Tools: BB
Description: Shoulder width palms down grip

	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
Date	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**

Name: Body Part Phase 3 Workouts

Category: Split-LegsandShoulders **Intensity:** 5
Notes:

Exercise name: Squats

Grouping: *A* ***Sets:*** *10* ***Reps:*** *10* ***Tempo:*** *Slow* ***Rest:*** *0*
Muscles: Quadriceps
Tools: BB
Description: Bend knees forward while allowing hips to bend back behind,knees should be in same direction as feet and back should be straight lower yourself until thighs are past parallel to the floor Extend legs pushing with the heels until legs are straight

	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
Date	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**

Exercise name: Leg Curl

Grouping: *A* ***Sets:*** *10* ***Reps:*** *10* ***Tempo:*** *Slow* ***Rest:*** *90*
Muscles: Hamstrings
Tools: MA
Description: Lying on the bench with knees slightly off, and lever pad in contact with the back of the ankles, lift the pad with the lower legs by flexing at the knee.

	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
Date	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**	**W**	**R**

Exercise name: Lunges

Grouping: *B* ***Sets:*** *3* ***Reps:*** *10* ***Tempo:*** *Slow* ***Rest:*** *0*
Muscles: Quadriceps
Tools: DB
Description: With Feet shoulder width apart hold dumbells at side of the body. Step forward with one leg , landing on the heel of that leg, keeping the back leg extended and heel raised. Lower back knee to the floor as you bend the lead leg at 90 degrees in the knee.

	Set 1	Set 2	Set 3	Set 4	Set 5	Set 6	Set 7	Set 8	Set 9	Set 10

Date	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R

Exercise name: Step Ups

Grouping: *B* ***Sets:*** *3* ***Reps:*** *10* ***Tempo:*** *Slow* ***Rest:*** *90*
Muscles: Quadriceps
Tools: DB
Description: Start with one foot on the step and the other foot on the ground

	Set 1		Set 2		Set 3		Set 4		Set 5		Set 6		Set 7		Set 8		Set 9		Set 10	
Date	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R	W	R

Appendix 5

Subject Handbook

Influence of Supervised Resistance Training and a Hypocaloric Macronutrient Scheduled Diet vs a Hypocaloric Macronutrient Scheduled Diet Alone on Energy Regulating Hormones in Overweight and Obese Men Ages 35-55.

Nutrition and Exercise Guidelines

WELCOME TO THE STUDY

As you already know the following research program requires your commitment to a healthy lifestyle including regular resistance training, cardiovascular training and proper nutrition.
Your training in the gym will be guided by the study's certified kinesiologist and our registered dietitian as well as the primary investigator Mike Wahl. It is the rest of the time you will need guidance in and primarily in the area of nutrition and proper eating.

The following book will provide you with all of the information you need to succeed in nutrition and training. Please review the book in the following steps...

Then, read the nutrition section of this manual to give you the fundamentals of what nutrients do what and how to tackle healthy eating at meal and snack times.

Next, read the section on typical nutrition days for you as a study subject depending on your activity and review the sample meal plans at the back and we will provide you a food log book to take with you each day to record your meals.
You will also notice your workouts are included in the back of this manual and include your three phases of resistance training and cardiovascular activity incase you are unable to attend a training session at anytime.

We hope this information teaches you how to live healthy and remember that you can ask questions at anytime. The results of this research and the impacts it will have on those like yourselves will depend on you. We appreciate your dedication to this research and look forward to seeing the end result!

Yours in Health!

Micheal Wahl
Primary Investigator

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KEYS TO SUCCESS...

Resistance Training:

You are required to book times to train with the Research Assistant/Kinesiologist 3 times each week. She is available between 6am and 8pm mon- day to Friday and from 7 until 3 pm on Saturday.

If you are not in town or unable to make a session please follow the workouts provided at the end of this manual for you do on your own at Definitions or another gym. Videos on how to complete the exercises can be found on www.definitionsonline.com using your personalized login provided by Mike Wahl or the Research Assistant/ Kinesiologist

Nutrition:

You must follow the guidelines dictated by our registered dietitian in this manual in order to lose weight. The following section involves a very comprehensive outline of how to eat and record your nutrition in a daily log.

Research staff will review this log weekly to ensure you are on track however, please don't hesitate to ask questions should they arise.

MACRONUTRIENTS 101

Protein

Protein stems from Greek origin, meaning "of primary importance." This is fitting, as protein plays a major role in building and maintaining of your body structure. It helps in:

- Building Muscles, Blood Cells, Bones, Teeth, Skin, Nails, and Internal Organs
- Composing Enzymes and Hormones
- Maintaining Blood Pressure
- Regulating Blood Sugar Levels
- Speeding Up Metabolism

Proteins are tiny chemical compounds composed of building blocks known as amino acids; it is the amino acids that the body utilizes to synthesize tissue. There are 20 amino acids in total, some are celled essential and some are called non-esential. Basically we need to eat some in our food and the rest we can make ourselves.

Protein is the crucial nutrient for those exercising as over time our bodies wear down, muscle degrades and injuries form when protein is not ingested in appropriate amounts.

Examples of Proteins…

- Fish
- Seafood
- Beef
- Ham
- Pork
- Turkey
- Chicken
- Wild game
- Beans (pulse crops)
- Dairy
- Eggs
- Whey protein

Notes for Eating Right…

Always have a lean protein source on hand for salad salads such tuna, turkey, chicken, chickpeas, cottage cheese, hardboiled eggs, almonds, chopped steak, etc.

Choose a protein source during each meal

When cooking casseroles or entrees make sure protein is at least 30% of content

Diversify protein offering so you are getting the various benefits from the different sources

To reduce costs choose large cuts of meat including roasts, hips, whole fish, turkeys and chickens and cook them in bulk for use in sandwiches, omelets, snacks and for "leftover" meals.

CARBOHYDRATES

Carbohydrates are sugars. There are good ones and there are bad ones and the bad ones taste better to most people. Unfortunately the carbohydrates which most people ingest are the bad ones and these are classified as simple sugars. Carbohydrates that are good for you are called complex sugars and are necessary in the following ways…

As a primary energy source - the brain can only use carbohydrates for fuel
To regulate blood sugar level (maintain energy) and increase fat burning in the body

Glycemic Index (GI)

Glycemic index (GI) refers to the ease at which carbohydrates from a food source can be digested into your cells. The GI index is a system ranking foods from 1-100.

Lower numbers mean that the food breaks down slower in your body and is more favorable for sustaining energy. Higher numbers approaching 100 mean the food does not take a lot of time to enter your system.

As a rule, foods with a lower GI are more desirable to eat than foods with a higher GI, as they are generally complex carbohydrates and can contain more fiber.

The general rule in choosing carbohydrates to eat are that the most complex sources come from nature. These include fruits, vegetables and whole grains, and rices.

On the next pages, are examples of common foods and their glycemic indexes. Remember the lower the number the better but some foods like potato chips, banana cake and chocolate although not high on the glycemic index are loaded with bad fats. This will take time to learn but any questions you have will be answered immediately by your definitions representative…

HIGH Glycemic Index Foods...

white breads, potatoes and sugars from foods like these break down very quickly and create energy faster than we can use it. If you can't use it, you store it, which is why fast food causes weight gain.

LOW Glycemic Index Foods...

Fruit, veggies, whole grains and dairy contain healthy carbohydrates that break down slowly in the body and give us a sustained release of energy. This energy release is slow enough for us to use all of the energy as it becomes available. This means we aren't tired and we won't store fat like we would with High GI foods.

Star * Point…

If your protein source isn't bigger than your carbohydrate source than you are eating too much carbohydrates

Vegetables should be consumed as much as possible with meals. Fruit contains fructose, a very complex sugar which can offer sustained energy in periods between meals. This makes fruit a great option for snack time.

Carbohydrate Sources:

Fruit – all kinds
Vegetables – all kinds
Breads, Grains and Rices

Veggies with the least amount of energy (carbs) are…

- Leafy vegetables (spinach, lettuce, cabbage)
- Flowering vegetables (broccoli, cauliflower)
- Colored Vegetables (peppers, tomato, carrots)
- Stalk vegetables (bok choy, celery, asparagus)
- Sprouts
- Onions

Highest energy (carb) content for vegetables are…

- Potato
- Yams/sweet potato
- Corn
- Peas

Bread, Grains and Rices…

- Multigrain
- Whole grain
- Whole wheat
- Oats
- Millett
- Brown Rice
- Basmati Rice
- Cuscus
- Steamed Rice (long grain)

Examples include…

- Whole wheat pasta
- Whole wheat/multi grain bread/wraps/pita's/bagels/English muffins
- cereals
- Are the preferred choices over white
- All bran
- Granola
- Fiber One
- Shredded Wheat
- Multi Grain Cheerios
- Muslix
- Whole Wheat Bread
- Multi Grain Bread
- Whole Wheat Bagels
- Whole Wheat English Muffins
- Oatmeal
- Porridge

FATS

While nobody wants to be fat, everybody needs to eat it.

Good Fats - Essential Fats

Appearing on labels as Mono-unsaturated or poly-unsaturated, or Omega 3, these fats are a part of a healthy diet and should be consumed in daily nutrition.

Essential fats function to…

Aid in metabolism
Transport oxygen from red blood cells to the tissues
Promote brain development
Prevent blood cells from clumping together (blood clots can be a cause of heart attacks and strokes, among others)
Act as an anti-inflammatory (rheumatoid arthritis, ulcerative colitis, Chron's disease)
Reduces blood pressure
Regulate the inflow and outflow of substances to and from cells
Direct hormones in the right direction
Support cardiovascular health

Bad Fats – Saturated Fats

Saturated fats (animal fats and) are solid at room temperature. Saturates fats in excess amounts, along with Trans fats can lead to many health problems including high cholesterol and hypertension which lead to even bigger problems. Saturated fats come in fatty cuts of meat (filet mignon, prime rib, bacon, and sausages), high fat cheeses, butter, coconut oil and palm oil. These fats although necessary to survival should be eaten in moderation and used sparingly when cooking.

Trans fats (hydrogenated or partially hydrogenated) come in the form of vegetable shortening, crackers candies and bars, baked goods, condiments, cereals, canned foods, and many others. The reason for their broad appeal with food manufacturers is that they are used to preserve the food and add flavor. These fats should never be consumed in any amounts and all foods containing them should be removed from the food orders and the food line. The pose serious health risks to the crew and yourself.

Notes for Eating Right…

Only use good fats to cook with and if you do use bad fats use them in moderation

Make fish a part of atleast one meal each day

Almonds or any nuts should be eaten as snacks but in moderation (16 nuts / serving)

Cook with canola oil (it has the highest heat threshold)

Extra virgin olive oil can be used for home-made dressings and salads as it contains the most beneficial essential fats of any oil

Natural peanut butter should be used on toast instead of jam and in moderation… 1tsp is enough

Omega 3s, where they went, and why we need them…

Omega 3 Fatty Acids are amazing nutrients that are becoming extinct in modern nutrition. They aid in all metabolic processes in the body and actually prevent diseases such as heart disease, cancer, depression, and Alzheimer's. Omega 3 has also been shown to treat rheumatoid arthritis, diabetes, ulcerative colitis, and Raynaud's disease to name a few. The question remains what are they and what do they do?

Omega 3 essential fats are anti-inflammatory in the body meaning they stop inflammation, as well they…

- Increases fat burning
- Helps decrease sugar cravigs
- Make you think better
- Improves skin and hair quality
- Helps you sleep
- Keeps you lean by preventing causes of diabetes

One of the most important things you can do for all of these conditions is to increase your intake of the omega-3 fats found in fish oil, and reduce your intake of omega-6 fats.

These two types of fat; omega-3 and omega-6, are both essential for human health. However, the typical American consumes far too many omega-6 fats in their diet while consuming very low levels of omega-3. The ideal ratio of omega-6 to omega-3 fats is 1:1. Our ancestors evolved over millions of years on this ratio. Today, though, our ratio of omega-6 to omega-3 averages from 20:1 to 50:1! That spells serious danger for you, and as is now (finally!) being reported throughout even the mainstream health media.

OMEGA 6	OMEGA 3
Nuts	Salmon
Cereals	Fish Oils
Whole Grain Breads	Shrimp
Vegetable Oils	Winter Squash
Poultry	Sardines
Red Meat	Herring
Almonds	Mackerel
Flax	Walnuts

*Star * Point*

It is important to remember that essential fats are still better for people than saturated or bad fats, so regardless of Omega 3 or 6, make them available to the crew so they can attain maximum health

For New and Existing Recipes try these Guidelines...

Whole milk	Skim milk
Condensed Milk	Low-fat/fat-free condensed milk
Ice Cream	Low-fat/fat-free yogurt, ice milk or Sorbet
Cheese	Reduced-fat cheese
Pasta with cream based sauce	Multi-grain pasta with tomato-based sauce
Bacon or sausage	Turkey bacon, Canadian bacon, lean ham or 95% fat-free sausage
1 Large egg	2 large egg whites or 1/4 cup egg substitute
White flour	Whole wheat flour
White bread	Multigrain, whole wheat bread/ wraps/pita
Mayonnaise	Reduced-fat / Fat-free mayo or Mustard
Regular salad dressing	Reduced-fat/calorie dressing
Creamed soups	Broth-based soups
Butter or shortening	Extra virgin olive oil, canola oil
Cream cheese	Light or fat-free cream cheese
Sour cream	Light or fat-free sour cream, Plain low-fat yogurt, or 1/2 cup cottage cheese blended with 1 1/2 tsp lemon juice
Whipped cream	Chilled, whipped evaporated skim milk
White rice	Long grain brown or wild rice

BREAKFAST

Breakfast is truly the most important meal of the day. A well balanced breakfast serves many purposes. Breakfast helps avoid…

- Weight Gain
- Headaches
- Poor Concentration
- Mood Swings
- Poor Energy Levels
- Cravings and Snacking
- Increased Chance of Illness

Breakfast Ideas…

Proteins:
- Egg white egg scrambled eggs combo (2 egg whites to every egg)
- Egg/Egg white Omelets (veggies, low fat cheese)
- Hard boiled eggs
- Lean Breakfast Ham

Carbohydrates:
- Oatmeal
- Steal cut oats
- Porridge

Star * Point

Instead of flavored oatmeal use cinnamon, honey, raisins, berries or maple and vanilla extract to flavor oatmeal

Or you could try from the Definitions Recipe Book…

- French toast with sugar free natural maple syrup
- Breakfast burrito's
- Breakfast casserole

Cold Ideas....
- Fresh fruit
- Frozen berries
- Cottage Cheese
- Low Fat Cheese
- Low Fat Yogurt

Cereals and Breads…
- All Bran
- Granola
- Fiber One
- Shredded Wheat
- Multi Grain Cheerios
- Muslix
- Whole Wheat Bread
- Multi Grain Bread
- Whole Wheat Bagels
- Whole Wheat English Muffins

From the Fridge…
- Smoothies
- Definitions Bars

Healthier Condiments…
- Salsa
- Natural peanut butter
- Sugar free maple syrup

Star * Point

***All Other choices should have healthy ingredients to make them "better" although they may not be good enough to be a "Definitions Choice."
For example French toast with whole wheat bread, hash browns baked not fried etc.

LUNCH

Frequent healthy meals are vital to individual's energy and success. Eating the right foods in the right amounts will allow you to maintain energy throughout the 2nd half of your day. You must build your plate as they would for supper and as indicated on the following pages

1/3 Protein, 1/3 Vegetables, 1/3 Carbohydrates

Lunch Ideas...

Protein (atleast one)

- Chicken
- Turkey
- Steak
- Fish
- Pork
- Lean cold meats

Vegetables any mix or salad every meal too!

Carbohydrate (Starch) (1 At least)

- Brown rice/wild rice
- Sweet potato
- Baked potato
- Whole wheat pasta
- Whole wheat bread
- Healthy mashed potato

Other choices for pre-made lunch meals are as follows and are in the recipe book (optional)

- Turkey burgers
- BLT wraps
- Spicy turkey cheddar melt
- Tuna melts
- Chicken curry in a hurry

A definitions soup as outlined in soup section

DINNER

Dinner Ideas...

Protein (1 At least)
- Chicken
- Turkey
- Steak
- Fish
- Pork
- Lean cold meats
- etc - see best foods by category list

Vegetables any mix

Carbohydrate (Starch) (1 serving maximum or no starch at all)
- brown rice/wild rice
- sweet potato
- baked potato
- whole wheat pasta
- whole wheat bread
- healthy mashed potato

Or from the Definitions Recipe Book…(optional)
- Tuna casserole
- Grilled salmon
- Asian beef stir-fry
- Spaghetti and meatballs
- Vegetable stew with broiled chicken
- Turkey meatloaf
- Hot pepper steak stir fry

MANDARIN CHICKEN
SERVES 2

- 2 tbsp rice wine vinegar
- 1 tsp sesame seed oil
- 1/2 tbsp garlic, minced
- 1 tbsp light soy sauce
- 2 chicken breast, cooked and chopped
- 3/4 cup drained mandarin orange segments
- 1/4 cup blanched snow peas
- 1/4 cup drained water chestnuts
- 2 cup shredded lettuce
- 1 tsp toasted sesame seeds

Mix the vinegar, sesame oil, garlic, and soy sauce thoroughly. Add chicken and orange segments, marinate for about 10 minutes. Add snow peas and water chestnuts. Place lettuce on plates, top with chicken mixture and sesame seeds.

SALADS

A great way to start a meal. It is also a good way to get extra fiber, vitamins and minerals.

Salads ... you gotta eat them...

Make sureyou have greens for your salad (spinach is the best choice)

Make sure vegetables are fresh whenever possible

Use extra virgin olive oil and low fat condiments when preparing salads

It is ok to add protein (i.e. chicken, turkey, eggs, ham) to salads

Make sure you use low calories salad dressings or balsamic vinegar and extra virgin olive oil (1tbsp olive oil in dressing)

Options for a tasty salad:

- Olives
- Eggs
- Chicken
- Tuna
- Ham
- Crab
- Left over proteins from meals
- Peppers
- Mushrooms
- Dried bananas
- Nuts
- Almonds
- Sunflower seeds
- Onions
- Tomato
- Cucumber
- Broccoli
- Cauliflower
- Mixed cheese
- Pickles
- Cottage cheese

Definitions pre-made salads could also be available

- Mandarin chicken salad
- Warm spinach chicken salad
- Non Caesar Caesar salad
- Mediterranean chicken salad
- Salmon with spinach and mustard

SOUPS

When cooking your own soups please focus on hearty soup with light broths. Include lots of vegetables, some seasoning and protein and try to stay away from cream based broths.

Definitions recipes are as follows:

- Chicken soup
- Oriental chicken linguine soup
- Broccoli soup
- Minestrone with whole wheat pasta
- Bean soup
- Pea soup with ham

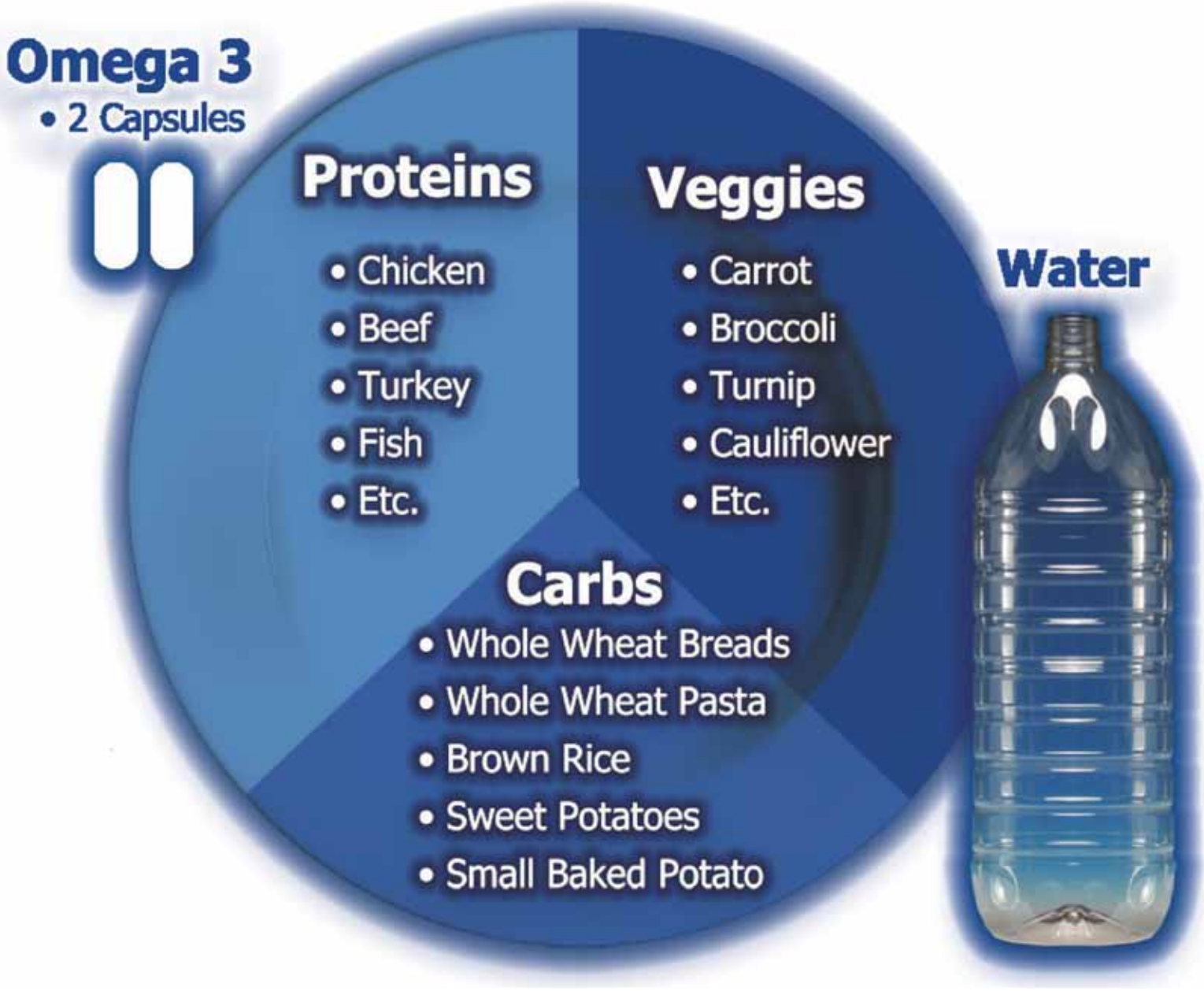
Star * Point - For your own recipes...
Add proteins to soup (i.e. 2 times the meat) Noodle soups use the whole wheat noodles. Add barley, brown/wild rice, beans and chick peas to soups

EASY SOUP

- 1/2 pound chicken breast
- 1/2 cup minced carrots
- 1 cup chopped onions
- 1 cup corn
- 1/2 cup canned peeled tomatoes
- 1 tsp olive oil
- 2 cloves of garlic, minced
- 2 tbsp chopped basil or parsley
- 1 cup canned navy beans, drained
- 1/4 tsp ground black pepper

In a large saucepan over low heat, cook the chicken and onion in the oil for about 10 minutes or until the onion is golden brown. Add the garlic and cook for 1 minute. Then add the stock, beans and carrots, bring to a boil. Finally add the corn and tomatoes (with juice) and cook for 15 minutes.

Perfect Power Eating Day



SNACKS

Snacks are critical in Power Living. Hearty snacks are the key here as foods with hollow calories (i.e. simple sugars) such as crackers and jam lead to blood sugar drops, low energy, and obesity. All snacks should be hearty and use natural ingredients and well rounded nutrient profiles (protein, fats and carbs) thus keeping energy up, fat burning and muscle building environments working in the body.

Typical Snacks should include...

- Wraps (approved protein source, veggies and low fat condiments)
- Whole wheat sandwiches (same as wraps)
- Any fruit
- Definitions bars
- Definitions cookies
- Yogurt
- Cheese
- Nuts
- Chili
- Soups

Star * Point

For snack stations bring out and mark Diet Pop and water as Definitions Choices to encourage their consumption versus high sugar beverages

Definitions Cookies - For Emergencies only!

Non-stick cooking spray
1 cup firmly packed light or dark brown sugar
3/4 cup trans-fat-free soft tub margarine spread
2 large egg whites
1 cup chocolate protein powder
2 tsp. pure vanilla extract
1 can chick peas drained and rinsed
2 cups semisweet chocolate chips
3/4 cup chopped walnuts (optional)
3/4 cup raisins (optional)
2 cups flour
1/2 cup oatmeal
1 tsp baking soda
1/4 tsp salt

Preheat oven to 350F. Coat a baking sheet with cooking spray. In a large mixing bowl, beat the sugar and margarine with a wooden spoon or on medium speed with a mixer until smooth. Beat in the egg whites and vanilla, then the chickpeas and chocolate chips. Add the flour, oats, baking soda, and salt, and mix on low speed until a thick dough forms. Drop the dough by the tablespoonful onto the baking sheet, spacing the cookies about 2 inches apart. Press gently with a fork to flatten. Bake until the cookies are golden brown and just set, 11 to 13 minutes; do not over bake. Transfer to a rack to cool. Store in an airtight container for up to 3 days.

SNACKS

Snacks can be tricky so let's remember on simple saying when it comes to the sugary stuff.

Star * Point

"You can't turn straw into gold!"

This study does not encourage sugary snacks but at the same time realizes that people love their treats. That being said, if an individual chooses a well rounded meal including protein, carbohydrates and essential fats, their body has received the nutrients necessary to give them energy and rebuild their body until their next meal. If this individual chooses to have dessert several interesting things happen if they have eaten a well rounded meal first.

- They have increased satiety from the healthy meal
- They have a properly elevated blood sugar so cravings decrease
- They don't have room for more than one dessert
- They understand that it is ok occasionally but their meal is where their nutrition comes from

It is imperative that you do not cheat on your nutrition by eating too much and the wrong types of foods... you can however make sure your snacks still give you the chance to be healthy and have taste

Definitions Desserts…

- Berry Parfait
- Definitions Bars (not before bed)
- Definitions Cookies (not before bed)

Most times we want you to stick to the snacks listed in the previous section however as the study runs 14 weeks you made need some of these foods to help cravings for the sweet stuff.

Definitions Bars

2 cups chocolate protein powder
1 1/4 cups oatmeal
1/2 cup wheat germ
1 cup bran
1 cup peanut butter
1/2 cup honey

Mix and slowly add water as needed. Finished bars should have the consistency of an "Eatmore" bar. Place in cookie tray and let set in fridge for 2 hours

BEST FOODS BY CATEGORY

Choosing the right type of nutrient based on the situation and your bodie's needs is an important part in choosing the right foods.

This will take some practice but the "Cheat Sheet" on the opposite page will help with this process. Learn what foods fall into what category and use the food planning sheets and you will be all set.

"Proteins" – Good Choices

Fish
Seafood
Beef
Ham
Pork
Turkey
Chicken
Wild game
Beans (pulse crops)
Dairy
skim milk
yogurt
cottage cheese
low fat cheese
Eggs
Whey protein

For complete list see opposite page

"Fats" – Good Choices

Salmon
Scallops
Shrimp
Nuts
Olive Oil
Winter Squash
Fish Oils
Avacado

For complete list see opposite page

"Carbs" – Definitions Choices

Fruit – all kinds
Vegetables – all kinds
Vegetables with minimal carbohydrates are…

- Leafy vegetables (spinach, lettuce, cabbage)
- Flowering vegetables (broccoli, cauliflower)
- Colored Vegetables (peppers, tomato, carrots)
- Stalk vegetables (bok choy, celery, asparagus)
- Sprouts
- Onions

Highest carbohydrate content for vegetables are…

- Potato
- Yams/sweet potato
- Corn
- Peas
- Beans (legumes and pulse crops)
- Turnip

Bread, Grains and Rices…

- Multigrain
- Whole grain
- Whole wheat
- Oats
- Millett
- Brown Rice
- Basmati Rice
- Cuscus
- Steamed Rice (long grain)

Examples include…

- Whole wheat pasta
- Whole wheat/multi grain bread/wraps/pita's/bagels/ English muffins
- cereals
- Are the preferred choices over white
- All bran
- Granola
- Fiber One
- Shredded Wheat
- Multi Grain Cheerios
- Muslix
- Whole Wheat Bread
- Multi Grain Bread
- Whole Wheat Bagels
- Whole Wheat English Muffins

CHEAT SHEET

Proteins

Back bacon
Turkey Bacon
Lean ham
Egg whites
Eggs (2 whole eggs at one time)
Liquid eggs
Dairy:
Cheese fat free
Cottage cheese, fat free
Probiotic Yogurt – low fat
Milk skim
Whey protein supplement

All fish and seafood fresh or frozen...Must be wild not farmed...ex:

- Salmon
- Halibut
- Trout
- Bass
- Tuna
- Sole
- Char
- Haddock
- Cod
- Sardines
- Anchovies
- Herring
- Kippers
- Mackeral
- Shrimp
- Mussels

Beef

- Sirloin
- Round

Chicken (skinless)
Turkey (skinless)
Ground beef extra lean
Ground turkey
Ground chicken
Lean deli meats (not optimal but ok)
Veal
Pork

- Tenderloin
- Pork chops (trim fat)

Fish

With all meats trim off fat or remove skin

Carbohydrates / Starch

Fruits
(High to Moderate)

- Apple
- Grapefruit
- Orange
- Tangerine
- Peaches
- Berries (all)
- Plums
- Cherries
- Bannana
- Pears
- Peachers
- Nectarine
- Pineapple
- Cantelope
- Honeydew
- Watermelon
- Mango
- Grapes
- Pomegranate
- Kiwi
- Plum
- Lemon
- Limes

Starches (high)
All bran
Bran buds
Fibre first
Kashi go lean
Oat bran
Porridge (old fashioned rolled oats)
Instant unsweetened oatmeal
100% stone ground whole wheat bread (at least 2 grams fibre per slice)
Quinoa
Wheat Germ
Pinto Beans
Rice (basmati, wild, brown, long grain)
Sweet potatoes

Vegetables (low)

- Carrots
- Asparagus
- Avocado (good fats)
- Peppers (hot)
- Green / red peppers
- Mushrooms
- Olives
- Onions
- Radishes
- Spinach
- Tomatoes
- Beans
- Bell peppers
- Broccoli
- Brussel sprouts
- Cabbage
- Cauliflower
- Celery
- Cucumbers
- And others...

Fats

Nuts:

- Almonds
- Walnuts
- Hazelnuts
- Pecans

Cook with:

- Canola oil
- Olive oil
- Grapeseed oil

Soft margarine (nonhydrogenated light)

Peanut butter
Almond butter
Flax (ground)
Hemp Hearts
Salad dressings (low fat, low sugar) or

- make your own with olive oil, lemon, balsamic vinegar

Omega 3 supplements

- Fish oil
- Cod Liver Oil
- Seal Oil

Fresh Basil
Avocado

Proteins w/fats:

- Wild Salmon
- Tuna
- Herring
- Mackeral
- Sardines
- Kippers

Spices

Allspice
Cardamom
Cayenne pepper
Celery seed
Chili Powder
Cinnamon
Coriander
Curry Powder
Garlic
Ginger
Horseradish
Mint
Mustard
Rosemary
Saffron
Wasabi

Smoothie Station

One snack station that can be set up all day long at home or at work is the smoothie station. Smoothies made with protein powder are healthy snacks that can be had any time and only take seconds to create and the possibilities are endless. All that is required is a blender and some ingredients that can be added to the smoothie and blender with several containers (the Magic Bullet works great due to the multiple cups that come with each blender).

That way you can customize your smoothie based on what you like (see list below for healthy options) place them in their cup with either milk or water, add protein powder and simply blend it up to create your own healthy snack. Some basic smoothie recipes form the Definitions recipe book are on the following page to give examples to follow in order to create some of our most popular smoothies.

List of Healthy Smoothie Additions:

- Berries
- Rolled Oats (non cooked)
- Yogurt and Cottage Cheese
- Peanut Butter
- All Bran
- Low Fat Milk
- Protein Powder (Chocolate or Vanilla flavour)

Chocolate PB Banana Oatmeal Smoothie:

1 pack of peanut butter
1 cup of water
1 scoop of whey protein
1 banana
1/4 cup of dry oatmeal
4 ice cubes

Blend and enjoy...

Easy Breakfast Smoothie:

1/2 cup of milk
1 cup of yogurt
1 scoop of whey protein
1 banana or 1/2 cup of berries
4 ice cubes

Blend and enjoy...

POWER FOODS

Power foods are a staple for personal wellness. They come in many forms and can add significantly to a well rounded plate. These foods are some of the same foods that offer our key nutrients like protein, carbohydrates and fats but at the same time can hold special properties which lead to health risk reduction, metabolism or energy.

The goal of the Power Foods chapter is for you the food preparation team to apply these foods to recipes, dinners and snacks as much as possible and share you knowledge with the crew as to why they are beneficial. This is a fun element of the education that allows you to have that little extra bit of knowledge that can truly establish you as a specialized crew.

Nuts:

Nuts, especially almonds in their original form are a great snack; full of good essential fats that unclog arteries, are high in protein, fiber, vitamins and minerals. Don't be confused or sucked in by "salted", "smoked", "honey roasted" or other alternative forms of nuts, these are only glorified pieces of candy; eat them in the form that they grow.

Spinach and Green Vegetables:

Popeye ate spinach so why wouldn't you? With lots of vitamins and minerals; spinach, lettuce, green peppers, brocholi (and other flowering vegetables), peas, Brussels sprouts are the ultimate power food. High in important vitamins and minerals these foods help you stay and feel young while boosting the immune system, preventing cancer, heart disease, strokes etc. the bottom line is just eat your veggies.

Eggs:

High in protein, vitamins A and B12, eggs are quick, healthy and an easy meal to make. The once thought of notion that eggs are high in cholesterol and obviously bad for you is wrong. In fact high cholesterol in the body is due to dietary fat and not as much to do with cholesterol in foods like once thought. Eggs are a fantastic power food; both whole and egg whites fill you up and keep you healthy.

Lean Cuts of White Meat (Turkey, Chicken etc.):

Low fat, high protein iron and other vitamins and minerals not to mention filling lean cuts of meat are the ultimate power food; breakfast, lunch, dinner or snack. Protein is the base of any plan and the cleanest, healthiest most natural source is from lean cuts of meat such as turkey or chicken. Remember to remove any chicken or turkey skin before eating but after cooking (keeps the juices in for more tender meat).

Berries:

Raspberries, strawberries, blueberries etc. are extremely high in antioxidants, fiber and vitamin C that fights against heart disease, aging, prevent cravings and boost ones immune system.

Fish:

Very high in protein, vitamins and minerals, omega 3 fatty acids and is also low in saturated fats and cholesterol. Species high in omega 3 fats and low in mercury include char, herring, mackerel, salmon, sardines and rainbow trout.

Red Meat:

Humans are meant to eat atleast some meat. Cavemen hunted, killed and feasted on animals and our consumption should be no different. High in protein, iron, vitamin B12, red meat is the classic example of a mans power food. Take note red meat is high in saturated fat, cholesterol which can lead to heart disease and arthrosclerosis if over consumed and accompanied by an inactive lifestyle.

Olive Oil (also canola, peanut and sesame oil):

High in good fats and olive oil raises testosterone levels, lowers cholesterol, burns fast and boosts the immune system. Don't be confused with other oils such as hydrogenated vegetable oils, trans fatty acids or margarine.

Tomatoes:

Loaded with vitamins tomatoes prevent the risk of bladder, stomach and colon cancers. Ketchup DOES NOT count as eating tomatoes, for it is loaded down with sugar.

Celery:

Celery has long been known in Chinese medicine to reduce blood pressure; a recent study found that eating 4 sticks of celery a day drops blood pressure 13 percent, so it doesn't take much.

Chicken Soup:

Who hasn't heard that chicken soup is good for soothing colds, flu's and other inflammatory properties? But is their any science behind your grandmother's seemingly random wisdom? A study concluded that ingredients in chicken soup shows that our conventional wisdom is actually right and chicken soup does help fight colds.

Probiotic Yogurt:

Low fat yogurt is high in calcium and protein needed for maintaining healthy bones and muscles. However probiotic yogurt is key because of the microorganisms that benefit our system when eaten. Essentially these live bacteria are within our large intestine that improves our digestive processes. Not all yogurts contain bacterial culture so be sure to check for it.

SPICES

Spices are a great way to improve the taste of food without sugary or fatty calorie dressings or sauces. Used for thousands of years, spices were once considered one of the most valuable trade goods spurring the discovery of North America in an attempt to find a quicker route to India. Aside from their unique flavors spices also have medicinal and wellness benefits. Although not as powerful as real medicine some spices highlighted below are excellent additions to your recipes as they do aid in everything from minor to severe illness.

Allspice:

Potential Health Benefit: an aromatic stimulant helps to relieve indigestion and gas.

Jamaican Jerk Recipe:

Ingredients:
1/2 cup ground allspice berries
1/2t cup packed brown sugar
6 to 8 garlic cloves
4 to 6 Scotch bonnet peppers (hot peppers)
1 tablespoon ground thyme or 2 tablespoons thyme leaves
2 bunches green onions
1 teaspoon cinnamon
1/2 teaspoon nutmeg
Salt and pepper to taste
2 tablespoons soy sauce to moisten

Preparation:

Place allspice, brown sugar, garlic, scotch bonnet peppers, thyme, scallions, cinnamon, nutmeg, salt, pepper, and soy sauce in a food processor and blend until smooth.

Cardamon:

Potential Health Benefit: strong, unique taste. Often used in Indian cooking and Scandinavian baking. Used medicinally to treat infections in teeth and gums, congestion of the lungs, and digestive disorders.

Cayenne pepper:

Potential Health Benefit: Increases metabolism and fat-burning ability by up to 25 per cent.

Celery Seed:

Potential Health Benefit: Used as a homeopathic extract as a diuretic. Believed to help clear toxins from the system. Also used as a mild digestive stimulant.

Chili Powder:

Potential Health Benefit: Relieves achy joints. Research shows that capsaicin, found in chili peppers, has an anti-inflammatory effect, which may help ease arthritic swelling and pain.

Sprinkle a few shakes of chili powder and salt on baked sweet potato fries.

Cinnamon:

Potential Health Benefit: Protects against Type 2 diabetes and heart disease. A 2003 study found that about half a teaspoon lowered blood glucose, cholesterol, and triglyceride levels.

Mix half a teaspoon of cinnamon into your coffee, or jazz up whipped cream with a couple of pinches. (it makes the whipped cream taste better but not healthy)

Coriander:
(also known as cilantro and Chinese parsley)

Potential Health Benefit: Said to assist with clearing the body of lead, aluminum, and mercury. Also said to help relieve anxiety and insomnia.

Curry Powder:

Potential Health Benefit: Safeguards your brain. The yellow curry pigment curcumin may fight Alzheimer's by thwarting development of the disease's signature amyloid brain plaques, says a study.

Whisk 1 1/2 teaspoons mild curry powder into mayonnaise to dress up sandwiches

Garlic:

Potential Health Benefit: Improves your heart's health. Brigham Young University researchers found that garlic consumption can lower total cholesterol and triglyceride levels by an average of 10 percent.

Add minced garlic and chopped cucumber to plain yogurt for a light dip or salad dressing.

Ginger:

Potential Health Benefit: Can inhibit nausea and vomiting that may accompany morning sickness or motion sickness.

Horseradish:

Potential Health Benefit: Used as a digestive stimulant.

Mint:

Potential Health Benefit: Traditionally, mint was used to treat stomach ache and chest pains. It is also a strong diuretic and digestive aid.

Mustard:

There are several kinds of mustard — not just the type you slather on your hot dogs and hamburgers. "Mustard packs" have been used for generations to help relieve respiratory problems.

Rosemary:

Potential Health Benefit: Acts as a stimulant and mild analgesic, and has been used to treat headaches and poor circulation.

Saffron:

Potential Health Benefit: Besides being the world's most expensive spice, saffron has been used to treat depression in Persian traditional medicine. A 2005 study found that saffron may help in cases of mild to moderate depression.

Wasabi:

Potential health perk: Prevents ulcers. A 2004 South Korean study suggests Japanese horseradish can kill ulcer-causing Helicobacter pylori bacteria. Plant chemicals may also prevent tooth decay.

Mix a smidgen of wasabi paste with mashed avocado for a snappier guacamole.

Fruits (60 calories /serving)

Apple	1 small
Banana	1 small or 1/2 large
Blueberries	3/4 cup
Cantaloupe	1 cup cubed
Cherries	1 cup
Dates	3
Grapefruit	1 small or 1/2 large
Grapes	1/2 cup
Honeydew melon	1 cup cubed
Kiwi	1 large
Mango	1/2 cup diced
Mixed fruit	1/2 cup
Nectarine	1
Orange	1 medium
Orange juice	1/2 cup
Peach	1 large
Pineapple	1/2 cup cubed
Pear	1 small
Plums	2
Prunes	3
Raisins	2 tablespoons
Raspberries	1 cup
Strawberries	1 1/2 cups whole
Tangerine	1

Vegetables (50 calories/serving)

Asparagus	1 cup pieces
Broccoli	2 cups florets
Brussels sprouts	1 cup
Carrots	1 cup sliced
Cauliflower	2 cups florets
Celery	2 cups diced
Cherry or grape tomatoes	16
Cucumber	2 cups sliced
Eggplant (cooked)	2 cups
Green beans	1 1/2 cup
Green pepper	2 cups sliced
Kale (cooked)	1 1/2 cup
Lettuce	4 cups shredded
Mushrooms	2 cups whole
Onions	1 cup sliced
Peas, green	2/3 cup
Spinach (cooked)	2 cups
Spinach (raw)	4 cups
Squash (summer)	1 1/5 cup sliced
Tomatillo	1 cup diced
Tomato	2 medium
Vegetable juice	8 ounces

Starchy Carbohydrates (140 calories

Bagel (whole-grain)	1
Barley (cooked)	1cup
Beans	1 cup
Bread (whole-grain)	2 slices
Bulgur (cooked)	1 cup
Cereal (see best foods list)	1 cup
Corn	1 cup
Corn tortillas	1
English muffin (whole-grain)	1
Garbanzos beans	2/3 cup
Kasha (buckwheat groats, cooked)	1 cup
Oatmeal (cooked)	1 cup
Pasta (whole-grain, cooked)	1 cup
Peas	1 1/2 cups
Pita bread (whole-grain)	1 circle
Popcorn (air-popped, plain)	4 cups
Pumpkin (cooked)	3 cups
Rutabagas (cooked)	1 1/2 cups
Rice (brown, cooked)	2/3 cup
Roll (whole-grain)	1 medium
Rye wafer	2 triple crackers
Shredded wheat	2 biscuits
Squash (winter, cooked)	2 cups
Sweet potato (baked)	1 medium
Turnips (cooked)	1 cup

Protein/Dairy (220 calories/ serving)

Beef (lean)	3 ounces
Chicken	6 ounces
Cheese (feta)	1/2 cup
Cheese (low-fat)	3 ounces
Cod	6 ounces
Cottage cheese (1% or lower)	1 cup
Crab	6 ounces
Egg	2 medium
Egg substitute	1 cup
Egg whites	8
Halibut	6 ounces
Lamb, lean cuts no fat	5 ounces
Lentils	1 cup
Milk (skim or 1 percent fat)	2 cups
Pheasant, duck (breast)	6 ounces
Venison	6 ounces
Pork, lean cuts no fat	4 ounces
Salmon	6 ounces
Shrimp	6 ounces
Tofu	1 cup
Tuna (canned in water)	6 ounces
Turkey	6 ounces
Yogurt (fat-free or lite)	2 cups

Fats (90 calories/serving)

Almonds	16 whole
Avocado	1/3
Canola oil	2 teaspoons
Cream cheese	2 tablespoons
Olives	18 large
Olive oil	2 teaspoons
Margarine (olive oil/omega 3)	2 teaspoons
Peanut butter	1 tablespoon
Peanuts	16 whole
Sunflower seeds	2 tablespoon
Walnuts or pecans	8 halves

Star * Point

Weigh and measure all food until you are completely comfortable with what constitutes a serving size. Eating too big of a serving is the number one way an individual will not lose weight so pay careful attention with the scales and cups provided by the study team

As you are undergoing a new training regimen it is necessary to fuel your body. You have three types of days for your training, non-resistance training day, resistance training day, and rest day. This section will outline your specific nutritional demands for your exercise habits. Follow these rules and you will see the potential of your training program. Nutrition is 80% of the battle, stick with it.

A Typical Day of Healthy Eating

Breakfast

It is vital to consume a balanced meal with breakfast to start the day. There are many nutrients that must be consumed with breakfast to provide you with proper energy throughout the day. First, low Glycemic Index carbohydrates are a must (see yellow choices on best foods by category). After sleeping (approx. 8 hours of fasting) your muscle glycogen (stored carbohydrate energy) becomes depleted through the night. Because of this, your body releases the hormone cortisol which is responsible for breaking down stored muscle into glucose for energy. By consuming low GI carbs at breakfast, you will improve glucose tolerance for the rest of the day. This will allow your body to properly use carbohydrates for energy without feeling lethargic or storing excess fat.

Proteins are also a must at this meal. Individuals who exercise must consume a little more protein than the average individual because you are intentionally breaking down muscle by training (which is made up of protein) and therefore need excess in order to allow proper recovery. A high quality whey protein is a good choice as it is absorbed rapidly, which is needed after an 8 hour fast, as well as some solid food proteins to provide a steady stream of amino acids.

Macronutrient breakdown:

· Protein: 40 grams
· Carbs: 50 grams of carbohydrates
· Fats: 1 serving of essential fats

For example a great breakfast is:
· 1/2 cup (dry) oatmeal (add water of course)
· Serving of frozen berries (mixed into the oatmeal)

With:
4 egg whites and 1 whole egg
2 omega-3 fish oil caps or cook eggs in olive oil

Mid-Morning Snack:

Pre determine mid morning snacks (the night before) and make sure you have them before you head out the door. Stock your bag full of good food. You can have bags of almonds or other nuts on hand, fruit or even some dairy products in your fridge at work.

See the "Easy Eating document" (online in the intelligence bank of definitions website) for some more ideas about snacks

• Tip make or buy snacks once a week (see recipes) package them, stock and bring them daily. Your week will go really smooth and you will see tremendous results always your nutrition handy

• Try green tea instead of coffee or diet pop. It has antioxidants and will boost your energy and act as a natural fat burner.

• If you want a protein shake have 1 scoop of protein with water. That will give you 20 grams of protein with no sugary carbs. This will keep your metabolism up but without the risk of spiking insulin levels and storing fat.

Lunch:

Think about lean proteins and your carbs coming in the form of vegetables and fruit. You get an increase in anti-oxidants and vitamins as opposed to breads and grains, so:

- Lunch today should be warm leftovers from last night or prepared meals that are nutritionally balanced and of the right portions
- See sample ideas on "Sample Nutrition Days" section next
- Use the "Best Foods by Category" to plan a meal
- Ask your researchers what to eat!

Tip: cook a large batch on Sundays and portion off into containers and freeze for weekly lunches .

PS - Salad dressings are usually terrible sources of fat and calories. A great salad dressing would be two table spoons of olive oil (excellent source of monounsaturated essential fats) mixed with some vinegar and a pinch of oregano. Spinach is an excellent choice over lettuce because it has a lot more antioxidants, vitamins and minerals. Also condiments of any kind should be used sparingly and always look for low fat low sugar options of ketchup and BBQ sauce. Mayonnaise is not a good choice, mustard is fine.

All seasonings and spices are fine and can add lots of flavor to otherwise dull meals.

MS. Dash has lots of great flavors · If you don't have olive oil or a serving of essential fats from the list then take 2 omega 3 capsules.

Mid Afternoon Snack:

Must have feeding mid afternoon. Fruit, veggies, almonds, yogurt or choose from the list of snacks from out endorsed food list. Mid afternoon snack can be exactly the same size as mid morning snack This snack fires the metabolism up again gives the muscle the energy to repair itself which in-turn burns more fat. A mid afternoon feeding also reduces the tendency to overeat during supper which is when most people break down and lose their commitment to nutrition.

Dinner:

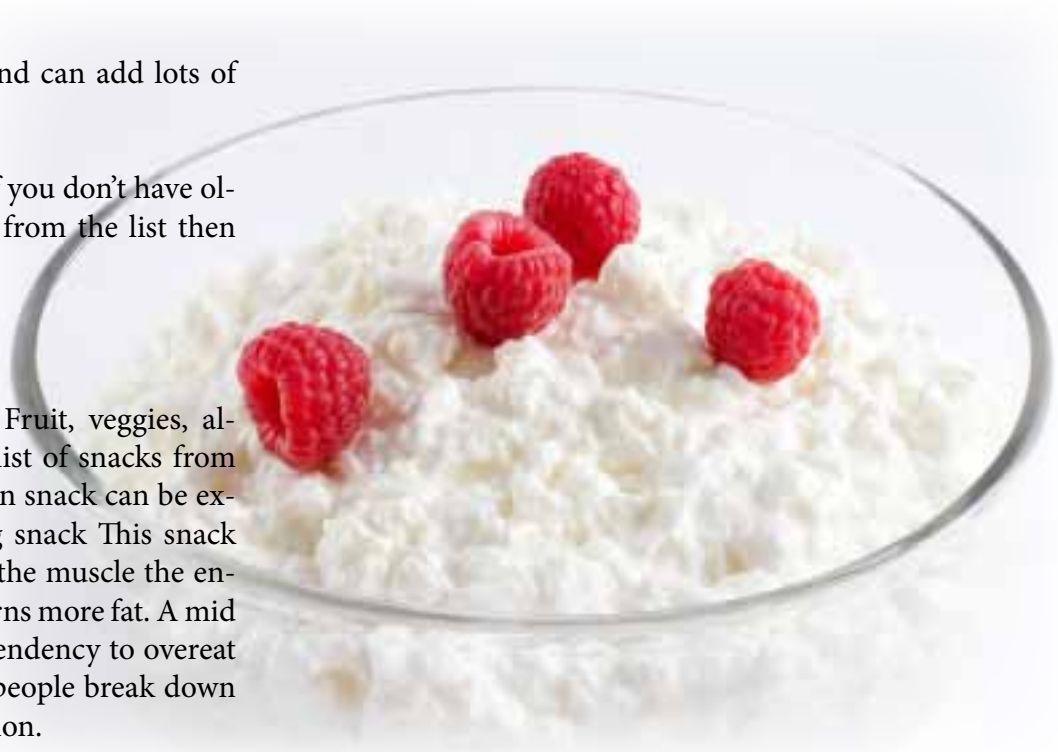
Continue to eat lean protein (see meal planner list), vegetables and a small serving of fruit. Stay away from potatoes, white rice and bread, try yams, brown rice or whole wheat pasta but try and stay away from lots of carbs coming in these forms. In general only have half of a serving of the starchy sources listed in the serving size section as you do not need alot of energy in the form of carbohydrates at that point in the evening.

Remember your supper should essential be a 6-8 oz. of protein with a serving of vegetables the greener the better with only a little bit of high energy carbohydrates because we don't need too much energy at that point in the day).

Pre Bed Time Meal:

1 cup cottage cheese or Greek Yogurt

This is the last meal of the day before a long fast (sleep). Cottage cheese or Greek yogurt are great choices here as it is very slow digested.



Workout Nutrition:

You can complete cardio any time of the day you would like however it is important to understand you must have some food in your system either from a meal or snack before you train.

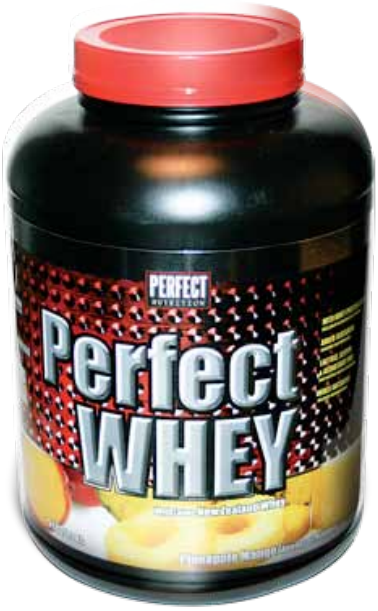
Complete prescribed cardio (if you are supposed to do it that day) after breakfast. If cardio is not prescribed for that day simply begin your day with breakfast.

Cortisol (stress hormone which breaks down muscle) is increased by between 150-400% when cardio is performed in a hypoglycemic state i.e. on an empty stomach (27, 28). This in mind you should always do cardio after breakfast. The intensity dictated in your cardio prescription requires metabolism of both fat and carbohydrates.

For the guidelines of this nutrition plan, this will serve as your pre training meal. For this meal, it is essential to consume high quality protein and carbohydrates that will be used for fuel during exercise. If proper pre workout nutrition is not consumed, your body will rely on other methods (breaking down muscle) in order to provide energy, which will be detrimental to your progress.

Examples of before workout foods could be a peice of fruit, half of a sandwich or can of tuna.

Prior to each resistance training workout, you will be given Branch Chain Amino Acids to help improve gains from the workout.



During Workout Nutrition:

Water – Lots of it and it is advantageous to consume 15 grams of BCAA's during a workout. Doing this will allow these amino acids to be digested and placed in the blood stream where they will be used as a source of fuel during exercise. Using these BCAA's during exercise is beneficial because it causes a glycogen sparing effect, meaning you will break down less muscle glycogen (low levels of muscle glycogen is associated with impaired strength and performance).

If you train at a different time of day please follow these recommendations for during training nutrition at those times.

Post Workout Nutrition:

Post workout shake:

- 2 scoops whey protein (34-38 grams of protein)
- 1 scoop dextrose (20 grams of carbohydrates)

So why do we need to take in protein following a workout? An equation that is necessary to understand is the Protein Balance equation:

Protein Balance = amount of protein synthesized minus the amount of protein broken down.

After a workout, your protein balance is in a negative state because protein synthesis has remained unchanged, however, protein breakdown has gone up as a result of the damage of exercise on your muscles. Because you have used your body's stored carbohydrates for energy the body begins to release the hormone cortisol toward the end of a workout, which breaks down muscle for energy. This hormone must be stopped ASAP, or else protein breakdown will continue to rise. In order to stop this, your body must absorb carbohydrates as fast as possible. The best carbohydrates to do this is dextrose, which is one of the fastest absorbing, high Glycemic index carbohydrates. The workout itselfcauses the body to require an insulin spike which will shuttle nutrients to damaged muscles for repair, and these carbohydrates in the form of dextrose cause the spike to occur. These carbohydrates will help combat the muscle breakdown caused by cortisol and are the fastest way to replenish muscle glycogen, so muscle breakdown is reduced and muscle growth is amplified.

As it has been shown to be advantageous to consume a mixture of both of these nutrients in several scientific studies.

The drink must also contain whey protein. Whey protein is the fasted absorbed source of protein, which immediately is used by your muscles for repair and growth. Also, it has been shown that whey protein and carbohydrates are more effective in replenishing muscle glycogen than carbohydrates alone.

This drink must also contain adequate water. As explained, the goal here is to digest the nutrients as fast as possible. The rate of nutrients emptying the stomach is known as gastric emptying. Having high levels of water is essential after a workout because research has proven that a liquid meal with under 10% solution has been proven to digest as fast as pure water!

Definitions will provide both the BCAA's and the protein shake following the workout to ensure you are following the protocol without any undue expense.

What you should do with this is immediately after the workout, drink half of the mixture, then, for 1 hour, slowly sip on the rest of it. So you fill up the container, drink half the shake immediately, then, fill up the container again with water and keep sipping for 1 hour (its essential for proper nutrient delivery to get a ton of water after a workout.)

We know this sounds confusing so let us summarize:

1) Immediately after: chug half the shake
2) For rest of hour, sip shake slowly

Sample Eating Days

Intervention Group

7am	2 Eggs	Protein
	Omega 3's	Fats
	Whole Wheat Toast 2 slices	Carbs
10am	Protein Powder Shake	Protein
	Banana	Fats
		Carbs
12pm	Chicken (in wrap)	Protein
	Olive Oil Dressing	Fats
	Wrap and Salad	Carbs
3pm	Small Can of Tuna in Olive Oil	Protein
	(oilve oil in tuna)	Fats
	Chopped Veggies	Carbs
6pm	Chicken (Baked or BBQ)	Protein
	Olive Oil Dressing	Fats
	Salad and steamed Veggies	Carbs
9pm	Greek Yogurt 1 portion	Protein
	2 Omega 3's	Fats
	(Greek Yogurt)	Carbs
	Total Calories: 1600	

6am	2 Eggs	Protein
	Hand full of almonds or Omega 3's	Fats
	All Bran w/skim milk (3/4 Cup)	Carbs
9am	Greek Yogurt (1 portion)	Protein
		Fats
	Sliced Peppers (red, green, yellow)	Carbs
12pm	Chicken (6-8oz)	Protein
	Olive Oil Dressing	Fats
	1/2 Cup of Brown Rice and Salad	Carbs
2pm		Protein
	w/peanut butter (1 tbsp)	Fats
	Apple (4oz)	Carbs
4pm	Sirloin Steak (6 oz)	Protein
	Vinaigrette Dressing (1 tbsp)	Fats
	Salad and Steamed Veggies	Carbs
7pm	Cottage Cheese (1/2 cup)	Protein
		Fats
		Carbs
	Total - 1791 Calories per day....	

SAMPLE NUTRITION LOGS

		Protein	
		Fats	
		Carbs	
		Protein	
		Fats	
		Carbs	
		Protein	
		Fats	
		Carbs	
		Protein	
		Fats	
		Carbs	
		Protein	
		Fats	
		Carbs	
		Protein	
		Fats	
		Carbs	
Total Calories:			

You may also use smart phone calorie tracking on online food tracking saftware as long as logs are submitted weekly.

Also remember serving sizes must be written down!!!

You must fill out a nutrition log every week in order to ensure you are on track with your eating plan. Kayla will request this from you each week

Appendix 6

Body Fat Assessment Techniques

Appendix 6: Body Fat Assessment Techniques

Body Fat Assessment Techniques:

The assessment of body fat can be accomplished in many ways including predictive equations, skinfold measurements and advanced imaging techniques. Each of these approaches has benefits and limitations related to cost, time, and accuracy. Due to adipose tissue's metabolic role and its regional characteristics, the determination of total, depot and region specific body fat is relevant for overweight and obese populations. This is exemplified by the increased understanding of the visceral adipose deposit that has had a significant impact on obesity research. Therefore the assessment of regional body fat in comparison with circulating concentration of energy regulating hormones may provide insights into the role of these regional fat depots in the manifestation of obesity related metabolic disease.

Body Mass Index:

BMI is the most cost effective method to evaluate adiposity, it has been shown to have significant weaknesses in accurately determining adiposity. Body mass index, calculated as [(weight (kg) / Height $(m)^2$] classifies degree of body fat as underweight, normal weight, overweight, obese class 1, obese class II and obese class III respectively (**Table**

1). One such weakness of the BMI is that there are no sex specific criteria even though gender differences for body fat percentage have been well documented (Kennedy et al., 2009). BMI does not reflect either the clear accumulation of body fat with age nor the inter-individual difference of body fat percentage among people within the same BMI category. According to dual x-ray absorptiometry body fat percentage measurements, BMI scores can mis-classify by one or even two obesity categories (Geer & Shen, 2009; Machann et al., 2005). Lastly due to the fact that BMI was originally developed in Caucasian populations, the accuracy within various ethnic populations is problematic. These misclassifications of obesity status reduces the identification of those at higher risk of cardiometabolic diseases with lower body fat content (De Lorenzo et al., 2013).

Skin Fold Thickness:

Skin fold calipers have been used to determine body fat percentage, body density, osteoporosis, hypertension, and insulin sensitivity with accuracy. The modern skin fold caliper was designed in 1955 by the Harpenden Corporation in collaboration with Tanner and Whitehouse. The tool was developed to determine thickness of skin of specific regions and apply these values mathematically to determine body fat percentage or body density. Since its inception it has been utilized in numerous studies as a means of testing skin fold thickness and has been adopted by several governing bodies of physiology including the American College of Sports Medicine (ACSM), the National Strength and Conditioning Association (NSCA) and the Canadian Society of Exercise

Physiology (CSEP) for the determination of body fat percentage. As a result, skin fold calipers have become an integral part of the field of kinesiology however due gold standard measures of the CT scan or the more convenient DXA scans research rarely employs the use of skin fold calipers in their assessment of body fat. One of the advantages of skin fold measurement is the ability to distinguish different patterns of adipose distribution from circumference indices or predictive equations (Jackson & Pollock, 2004).

Skin fold calipers have shown a strong statistical correlation with measures of skinfold thickness determined by CT scan, a more accurate assessment than ultrasound, and are significantly less costly to administer then both CT and ultrasound. Although there are challenges with respect to skin compressibility and hydration status among those being tested, skin fold calipers have been shown to be an effective, low cost means of accurately assessing body fat and regional subcutaneous adipose deposits.

Dual-Energy X-Ray Absorptiometry:

Originally designed for determining bone mineral density and diagnosing osteoporosis and other bone diseases, DXA is also used to assess fat and fat-free soft tissue. By measuring the absorption (attenuation) of two X-ray photon energies, which allows for the differentiating of bone from soft tissue (Pietrobelli, Wang, Formica, & Heymsfield, 1998). DXA further separates soft tissue into lean body mass and adipose tissue through providing a comprehensive view of body composition. The estimation of fat tissue may

be influenced by conditions where the ratio of extracellular to intracellular water varies (e.g., due to edema, infancy, or aging), as it is assumed that the hydration of lean soft tissue remains constant.(Pietrobelli et al., 1998; St-Onge, Wang, Horlick, Wang, & Heymsfield, 2004) However, in normal, healthy conditions, a change in hydration of 5% influenced fat estimation by only 1–2.5%.(Lohman, 1984). An additional consideration in obese persons is that body thickness (>25 cm) can result in underestimation of fat mass (Genton, Hans, Kyle, & Pichard, 2002).

DXA is considered to be a convenient, quick (5- to 13-min scan time), and safe modality for body composition assessment. It is used in people of all ages due to its low ionizing radiation, however it is not recommended during pregnancy (H. Wang, Chen, & Eitzman, 2014). When compared to the *in vivo* gold standard four-compartment model has demonstrated shows that DXA's accuracy is within ±5% and is a useful tool for measuring changes in body fat over time (Toombs, Ducher, Shepherd, & De Souza, 2012). More recent improvements, such as increased weight limit of the iDXA scanner bed to 400 lbs, allow heavier individuals to be assessed. In obese individuals whose bodies are wider than the scanner area, scans are typically performed by extrapolating data acquired from the right side of the body. While bilateral symmetry is assumed, half-body scans accurately predict total fat mass, total lean mass, and percent body fat in adults (Tataranni & Ravussin, 1995).

Anthropometric measurements such as body mass index, waist circumference and waist-to-hip ratio are commonly used in large epidemiologic studies. However, these measurements actually assess total fat, and therefore cannot differentiate between

viscerat and subcutaneous fat. (Kaul et al., 2012). Additional commercial software (CoreScan or Hologic's InnerCore, GE Healthcare, Chicago, IL, USA) is now available to measure visceral fat and will add significantly to the data available to obesity research. Technical performance of DXA VF has been demonstrated in both American and Chinese populations. These studies showed a high correlation and small average difference between DXA and CT (Kaul et al., 2012; Lin et al., 2013). Recently, a Korean study showed that visceral fat measured by DXA is highly correlated with the visceral fat measured by CT scan and could be a reliable estimate of visceral fat in Korean population (Choi, Seo, Lee, & Chung, 2015).

Appendix 7

Anthropometric Testing Protocol

Appendix 7: Anthropometric Testing Protocol:

Girth Measurements:

Neck:

The neck measurement is taken immediately above the thyroid cartilage (the Adam's Apple). When recording, you need to make sure the tape is not too tight or too loose, is lying flat on the skin.

Arm Relaxed:

This girth measurement is usually taken on the right side of the body. The arm is relaxed and hanging by the side, and the circumference is taken at the level of the mid-point between the acromion (boney point of shoulder) and the olecranon (boney point of elbow) processes.

Arm Flexed:

This girth measurement is usually taken on the right side of the body. The arm is raised to a horizontal position in the sagittal (forward) plane, with the elbow at about 45 degrees. The subject maximally contracts the biceps muscle, and the largest circumference is measured.

Chest:

This measure is taken at the level of the middle of the sternum (breast-bone), with the tape passing under the arms. After the tape is in position, the arms should be relaxed by the side, and the measurement taken at the end of a normal expiration. When recording, you need to make sure the tape is not too tight or too loose, is lying flat on the skin, and is horizontal, particularly around the back.

Waist:

The waist measurement is taken at the mid point between the lowest rib and the top of the hip bone (illiac crest). Three measurements were taken and the lowest measure was recorded.

Hip:

The hip girth measurement is taken over minimal clothing, at the level of the greatest protrusion of the gluteal (buttock) muscles. The subject stands erect with their weight evenly distributed on both feet and legs slightly parted, making sure not tense the gluteal muscles.

Thigh:

The subject stands erect with their weight evenly distributed on both feet and legs slightly parted. The circumference measure is taken at the level of the mid-point on the lateral (outer side) surface of the thigh, midway between trochanterion (top of the thigh bone, femur) and tibiale laterale (top of the tibia bone). When recording, you need to make sure the tape is not too tight or too loose, is lying flat on the skin, and with the tape horizontal.

Skin Fold Measurements:

Skin fold measurements should be made on the right side of the body with the caliper placed 1-2 cm away from the thumb and finger and perpendicular to the skin fold. The measure should be taken halfway between the crest and the base of the fold. The tester should release the caliper lever so its spring tension is exerted on the skinfold while maintaining the pinch and the reading caliper between 1 to 2 seconds after lever has been released (to allow for adequate skin compression). Measures are taken to the nearest 0.5 mm and the average of three measures are recorded for each site.

Triceps

- Vertical fold
- Posterior midline of the upper arm
- Halfway between the acromion (shoulder) and olecranon processes (elbow)
- Arm held freely to the side of the body

Chest/Pectoral

- Diagonal fold
- Men: one-half the distance between the anterior axillary line (crease of the underarm) and the nipple

Midaxillary

- Horizontal fold taken at the level of the xiphoid/sternal border in the midaxillary line.

Subscapular

- Diagonal fold
- 1 to 2 cm below the inferior angle of the scapula

Suprailiac

- Diagonal fold
- Anterior axillary line (modern technique)
- immediately superior to the iliac crest
- in line with the natural angle of the iliac crest taken

Umbilical

- Vertical (modern technique)
- 2 cm or 1" to the right side of the umbilicus

Thigh

- Vertical fold
- anterior midline of the thigh
- midway between the proximal border of the patella (upper knee) and the inguinal crease (hip)
-

Appendix 8

Fitness Testing Protocol

Appendix 8: Fitness Testing Protocol:

Push-Up Test:

The push-up fitness test (also called the press up test) measures upper body strength and endurance. The standard push was used and began with the hands and toes of each subject touching the floor, with the body and legs in a straight line, feet slightly apart, the arms at shoulder width apart, extended and at a right angles to the body. Keeping the back and knees straight, the subject lowered their body to until their chest touched a tennis ball placed below them on the floor, then returned back to the starting position with the arms extended. This action was repeated, and test continued until subjects were not able to continue without pausing for longer than 2 seconds.

Partial Curl-Up Test:

The curl up test measures abdominal muscular strength and endurance of the abdominals and hip-flexors, important in back support and core stability. The subject laid on am exercise mat with knees flexed, at 90 degrees. Subjects hands were placed by their side and markers were placed on the ground 5 cms from the end of their finger tips which they were required to touch to successfully complete a repetition. The subject was required to raise their trunk in a smooth motion, keeping the arms in position, curling up the desired amount. The trunk was lowered back to the floor so that their shoulder blades

touched the floor. The test was performed at a 2 second repetition tempo, and the maximum number of total sit ups were recorded

Sit and Reach Test:

The sit and reach test is a common measure of flexibility, and specifically measures the flexibility of the lower back and hamstring muscles. This test was first described by Wells and Dillon (1952) and is now widely used as a general test of flexibility. The test involved sitting on the floor with legs stretched out straight ahead. Shoes were removed with the soles of the feet placed flat against the sit and reach box. The subjects locked and pressed their knees flat to the floor with their palms facing downwards, and the hands on top of each other or side by side, the subject reached forward along the measuring line as far as possible. The primary investigator ensured that the hands remained at the same level, (not one reaching further forward than the other). After two practice reaches, the subject reached out and held the stretched position for two seconds while the distance is recorded.

Appendix 9

HREA Approval Letters

Health Research Ethics Authority

Ethics Office
Suite 200, Eastern Trust Building
95 Bonaventure Avenue
St. John's, NL
A1B 2X5

September 6, 2011

Dr. Michael Wahl
17 Green Acre Drive
St. John's, NL A1H 1C3

Dear Dr. Wahl:

Reference #11.327

RE: Adiponectin response to lifestyle intervention in sedentary, middle aged, obese class I men - a randomized control trial

Your application was reviewed by the Health Research Ethics Board at the meeting held on **September 1, 2011**. The board requested the following:

1. The Committee noted that Page 26 of the protocol states that "Contact with potential participants will be recruited through a local advertising and awareness campaign; also the application says "see attached handout", however, no handout was included in the application package.

2. The Committee noted that other than the special consent page on the consent itself which asks for future use of DNA there is no mention of any other longitudinal study. The investigator will be asked to provide clarification on this.

3. The Committee requests clarification on if study codes OR personal identifiers will be kept.

4. The Committee noted that it would be in the investigators best interest to request that participants have a letter from their physician stating that they are capable of taking part in this study.

5. The Committee noted that the title of the protocol could be changed to "Hormone Level Changes with Weight Loss Programs and Physical Activity Improvement In Men Ages 35-55". This will be suggested to the investigator.

6. Will any feedback about abnormal blood values be given to participants or their family doctors?

The consent form version **August 15, 2011** was also reviewed and the board requested specific modifications. Please see the attached scanned document. Please forward a copy of the revised consent form, with changes highlighted, to the HREB office for review.

Please provide the information listed above in a letter to the board; do not revise your application.

The Board has directed that your response and the revised consent form will be reviewed by the Chair.

Please be advised that a response to the aforementioned concerns is expected within three months of the date of this correspondence. If we do not receive a response within this timeframe, the file will automatically be closed by the Chair of the committee.

We look forward to hearing further from you regarding the above outlined issues.

Sincerely,

Patricia Grainger

Patricia Grainger, Acting Vice Chair
Dr. M. Khraishi, MB, B.Ch., FRCPC (Vice-Chair)
Health Research Ethics Board

11.327

Health Research Ethics Authority

July 2011

Consent to Take Part in Research

consider title change.

TITLE: Adiponectin response to lifestyle intervention in sedentary, middle aged, obese class I men

INVESTIGATOR(S): Michael Wahl, Dr. Gerry Mugford, Dr. Majed Khraishi, Dr. Christopher Kovacs

You have been invited to take part in a research study. It is up to you to decide whether to be in the study or not. Before you decide, you need to understand what the study is for, what risks you might take and what benefits you might receive. This consent form explains the study.

The researchers will:

- discuss the study with you
- answer your questions
- keep confidential any information which could identify you personally
- be available during the study to deal with problems and answer questions

If you decide not to take part or to leave the study, you can do so at any time, however signing this consent form requires you return for follow up measures in order to complete the study.

1. Introduction/Background:

The goal of this study is to look at the effects of healthy lifestyle on hormones in men who are middle aged, slightly overweight and don't exercise. This study will use exercise and nutrition guidelines to look at their effect on some of the hormones which maintain healthy body weight. If you enroll in this study you ~~may~~ have to exercise with a trainer at a gym and ~~eat healthy~~ for 3 months as well as have various tests during the study to see how you change during this period of time. This study ~~will help find information that will provide~~ try to find clues to improve treatments of obesity and other diseases related with excess body fat.

healthy eating training

may

2. Purpose of study:

will have a fitness test and may be randomized to....

To determine the effect of structured nutrition and exercise on hormones related to body fat.

3. Description of the study procedures and tests:

Subjects involved in the study will be tested in a series of baseline and follow up measurements at three locations:

Nexus Clinical Research: 120 Stavanger Drive

- Study participants will complete a health habit questionnaire, including questions about smoking, alcohol and food intake patterns.
- You will be asked to come to Nexus Clinical Research for blood sampling each week for fourteen weeks. About 1 table spoon of blood will be drawn each visit. why?
  1 word

Genetics Lab: H4353

- Percent body fat, lean body mass and bone density will be measured ~~by Dr. Sun~~ or a ~~certified staff member~~ using a bone densitometer (lying on a bed, and a scanner will complete the measurement in about 10 to 15 minutes.)
  Is there any radiation? If so describe amount (i.e. similar to x-ray)

Exercise Physiology Lab: PE2005A

- Cardiorespiratory Fitness describe will assessed using a treadmill test. During this test you will be required to run on the treadmill at an increasing pace of 4 intervals. Scores from each level will be recorded to calculate ~~what is called a sub-maximal VO2max~~. your hearts use of oxygen
- You will have your strength measured by using a hand grip test. This requires squeezing a metal grip attached to a gauge. You will also have your leg strength tested by attaching a cable to your foot and extending your leg as hard against the cable.
- Your standing height, body weight, waist, hips, heart rate, blood pressure and temperature will be measured. how? how? - using a reg. measuring tape.
- Body fat will also be measured using skin fold calipers. We will test a series of sites around the body including the arms, legs, and torso. We will also take girth measurements of the arms, neck, chest, shoulders, legs, waist and hips using a measuring tape.

All subjects will be required to undergo baseline and follow up testing as well as weekly blood testing at Nexus Clinical Research.

Intervention Group: Definitions Training Facility, 120 Stavanger Drive
explain this process
Subjects randomized to the intervention group must complete the following interventions as part of the study:

- Nutrition education seminar: This nutrition education will involve a one hour talk to explain proper nutrition. This will be followed by 30 minutes of explaining food logs and what will be required of you during the study. The remaining 30 minutes will be used for handing out information, questions and booking you in for workouts.

- Supervised exercise training - (3) 1 hour sessions per week for 12 week. Subjects chosen for the intervention will receive supervised exercise training with a certified personal trainer for 12 weeks during the study. During this time you will be asked to exercise with the trainer/research assistant 3 times each week. Flexibility in when you want to exercise will be allowed and the trainer will be available between 6 am and 8 pm daily.

- Completion ~~weekly~~ of food logs - ~~(7) days a week for 12 weeks:~~ You will be asked to complete a daily food log to ensure you are eating the right foods. You will ~~also~~ be asked to submit these food logs to your research assistant once a week. for 12 weeks.

4. Length of time:

The study will span 14 weeks from start to finish. All subjects, including those who were not selected for the lifestyle intervention and are part of the "control group" must attend all testing. Baseline and follow up testing is required as well as weekly blood (fasting) testing at the Nexus Research. People who are selected for the lifestyle intervention are required to attend a workout with a personal trainer 3 times a week for 1 hour and record food intake weekly. Exercise sessions and food logging will last for 12 weeks.

After the 14 weeks.

for what exactly?

5. Possible risks and discomforts:

There is little risk when sampling blood. There is a possibility of bruising at the site and a slight chance of infection. There will be a very low dose of X-ray exposure when you receive measurement of percent body fat. + bone density.

Some discomfort from healthy eating may occur in the intervention group. It will be recommended that subjects take one day each week to eat foods which they crave.

Fasting bloodwork. Increased physical activity may cause discomfort. (List all risks given in the protocol).

6. Benefits:

It is not known whether this study will benefit you personally.

However, potential benefits may include:

- Increased physical fitness
- Weight loss
- Nutrition education
- Education on how to exercise properly
- Access to professional lifestyle counseling
- Awareness of physical fitness and body fat percentage

7. Liability statement:

Signing this form gives us your consent to be in this study. It tells us that you understand the information about the research study. When you sign this form, you do not give up your legal rights. Researchers or agencies involved in this research study still have their legal and professional responsibilities.

8. What about my privacy and confidentiality?

Protecting your privacy is an important part of this study. Every effort to protect your privacy will be made. However it cannot be guaranteed. For example we may be required by law to allow access to research records.
A copy of this consent will be put in your health record. If you agree, your family doctor will be told that you are taking part in this study.

When you sign this consent form you give us permission to

- Collect information from you
- Collect information from your health record
- Share information with the people conducting the study
- Share information with the people responsible for protecting your safety

Access to records

The members of the research team will see health and study records that identify you by name.

Other people may need to look at your health records and the study records that identify you by name. This might include the research ethics board. You may ask to see the list of these people. They can look at your records only when one of the research team is present.

Use of records

The research team will collect and use only the information they need for this research study.

This information will include your :

- date of birth
- sex
- address
- contact information
- emergency contact
- medical conditions
- medications
- the results of tests and procedures you had during the study
- information from questionnaires

will this be kept post study? If so, why?

Your name and contact information will be kept secure by the research team in Newfoundland and Labrador. It will not be shared with others without your permission. Your name will not appear in any report or article published as a result of this study.

Information collected for this study will kept for 5 years.

If you decide to withdraw from the study, the information collected up to that time will continue to be used by the research team. It may not be removed. This information will only be used for the purposes of this study

After your part in this study ends, we may continue to review your health records to check that the information we collected is correct.

clarify that you're not accessing medical records.

Information collected and used by the research team will be stored by Michael Wahl the principle investigator of the study who is the person responsible for keeping it secure.

Your access to records

You may ask the primary investigator to see the information that has been collected about you.

9. Compensation:

In the event that you suffer injury as a direct result of taking part in this study, necessary medical treatment will be available at no additional cost to you. -covered by MCP?

10. Questions:

If you have any questions about taking part in this study, you can meet with the investigator who is in charge of the study at this institution. That person is: Michael Wahl

has not been stated anywhere that you plan to extract DNA.

what are your intentions for freezing blood?

- **Future use of tissue/DNA samples:**

In order to preserve a valuable resource, your (tissue/DNA) samples may be stored at the end of this research project. It is possible that these samples may be useful in a future research project which may or may not be related to the current research project. **Any future research would have to be approved by a Research Ethics Board (REB).**

Please tick **one** of the following options:

	I agree that my (tissue/DNA) sample can be used for approved obesity related research projects without contacting me again, but **only if my name* cannot be linked, in any way, to the sample.**
	Under no circumstances may my sample be used for future research. **My sample must be destroyed** at **the end of this present project**.
	I agree that I may be contacted in future to be invited to provide consent for the use of my [tissue/DNA] in any new approved research project.

The committee requested that this be removed.

*Includes name, MCP number or any other identifying information.

The (blood/DNA) sample from this study will be stored at Nexus Clinical Research, 120 Stavanger Drive, St. John's, Newfoundland for 5 years. The data guardian is Michael Wahl. Samples can be withdrawn by consulting Michael Wahl. how? written request/ phone call? . . .

Michael Wahl (709) 746-3355

Or you can talk to someone who is not involved with the study at all, but can advise you on your rights as a participant in a research study. This person can be reached through:

Health Research Ethics Authority (HREA) at 709-777-6974 or
Email: info@hrea.ca

After signing this consent you will be given a copy.

Health Research Ethics Authority

July 2011

Signature Page

Study title:

Name of principal investigator:

To be filled out and signed by the participant:

	Please check as appropriate:
I have read the consent.	Yes { } No { }
I have had the opportunity to ask questions/to discuss this study.	Yes { } No { }
I have received satisfactory answers to all of my questions.	Yes { } No { }
I have received enough information about the study.	Yes { } No { }
I have spoken to Mr. Wahl and he/she has answered my questions	Yes { } No { }
I understand that I am free to withdraw from the study	Yes { } No { }
• at any time	
• without having to give a reason	
I understand that it is my choice to be in the study and that I may not benefit.	Yes { } No { }
I agree to take part in this study.	Yes { } No { }

_____ _____

Signature of participant Date

_____ _____

Signature of witness (if applicable) Date

To be signed by the investigator or person obtaining consent

I have explained this study to the best of my ability. I invited questions and gave answers. I believe that the participant fully understands what is involved in being in the study, any potential risks of the study and that he or she has freely chosen to be in the study.

_____ _____

Signature of investigator/person obtaining consent Date

Telephone number: _____

Health Research Ethics Authority

Ethics Office
Suite 200, Eastern Trust Building
95 Bonaventure Avenue
St. John's, NL
A1B 2X5

September 13, 2011

Dr. Michael Wahl
17 Green Acre Drive
St. John's, NL A1H 1C3

Dear Dr. Wahl:

Reference #11.327

RE: Adiponectin response to lifestyle intervention in sedentary, middle aged, obese class I men - a randomized control trial

This will acknowledge receipt of your correspondence.

This correspondence has been reviewed by the Chair under the direction of the Board. ***Full board approval*** of this research study is granted for one year effective **September 1, 2011.**

This is to confirm that the Health Research Ethics Board reviewed and approved or acknowledged the following documents (as indicated):
E-mail to potential participants, approved
Revised Consent Form dated September 12, 2011, approved
Protocol, approved
Personal & Parental History Questionnaire, approved
Food Intake Questionnaire, approved
Diet Assessment, approved
Workout Grid 1.1, approved
Workout Grid 1.2, approved
Workout Grid 1.3, approved
Workout Grid 3.1, approved
Workout Grid GVT Arms & Shoulders, approved
Workout Grid GVT Chest and Back, approved
Workout Grid GVT Legs, approved
Meal Planner & Best Foods by Category, approved

Nutrient Breakdown, approved

MARK THE DATE

This approval will lapse on **August 31, 2012**. It is your responsibility to ensure that the Ethics Renewal form is forwarded to the HREB office prior to the renewal date. *The information provided in this form must be* ***current to the time of submission*** *and submitted to HREB* ***not less than 30 nor more than 45 days*** *of the anniversary of your approval date.* The Ethics Renewal form can be downloaded from the HREB website http://www.hrea.ca.

The Health Research Ethics Board advises THAT IF YOU DO NOT return the completed Ethics Renewal form prior to date of renewal:

- *Your ethics approval will lapse*
- *You will be required to stop research activity immediately*
- *You may not be permitted to restart the study until you reapply for and receive approval to undertake the study again*

Lapse in ethics approval may result in interruption or termination of funding

It is **your responsibility to seek the necessary approval from the Regional Health Authority or other organization as appropriate.**

Modifications of the protocol/consent are not permitted without prior approval from the Health Research Ethics Board. Implementing changes in the protocol/consent without HREB approval may result in the approval of your research study being revoked, necessitating cessation of all related research activity. Request for modification to the protocol/consent must be outlined on an amendment form (available on the HREB website) and submitted to the HREB for review.

This research ethics board (the HREB) has reviewed and approved the research protocol and documentation as noted above for the study which is to be conducted by you as the qualified investigator named above at the specified site. This approval and the views of this Research Ethics Board have been documented in writing. In addition, please be advised that the Health Research Ethics Board currently operates according to *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans*; *ICH Guidance E6: Good Clinical Practice* and applicable laws and regulations. The membership of this research ethics board is constituted in compliance with the membership requirements for research ethics boards as defined by *Health Canada Food and Drug Regulations Division 5; Part C.*

Notwithstanding the approval of the HREB, the primary responsibility for the ethical conduct of the investigation remains with you.

We wish you every success with your study.

Sincerely,

Patricia Grainger

Patricia Grainger, Acting Vice-Chair
Dr. M. Khraishi, MB, B.Ch., FRCPC (Vice-Chair)
Health Research Ethics Board

C C VP Research c/o Office of Research, MUN
VP Research c/o Patient Research Centre, Eastern Health
HREB meeting date: September 29, 2011

Appendix 10

Subject Consent Forms

Consent to Take Part in Research

TITLE: **Hormone Level Changes with Weight Loss Programs and Physical Activity improvement in Men Ages 35-55.**

INVESTIGATOR(S): Michael Wahl, Dr. Gerry Mugford, Dr. Majed Khraishi, Dr. Christopher Kovacs

You have been invited to take part in a research study. It is up to you to decide whether to be in the study or not. Before you decide, you need to understand what the study is for, what risks you might take and what benefits you might receive. This consent form explains the study.

The researchers will:

- discuss the study with you
- answer your questions
- keep confidential any information which could identify you personally
- be available during the study to deal with problems and answer questions

If you decide not to take part or to leave the study, you can do so at any time, however signing this consent form requires you return for follow up measures in order to complete the study.

You will also be required to submit a letter from your physician stating you are capable of taking part in this study.

1. Introduction/Background:

The goal of this study is to look at the effects of healthy lifestyle on hormones in men who are middle aged, slightly overweight and don't exercise. This study will use exercise and nutrition guidelines to look at their effect on some of the hormones which maintain healthy body weight. If you enroll in this study you will have a fitness test and may be randomized to exercise with a trainer at a gym and engage in healthy eating training for 3 months as well as have various tests during the study to see how you change during this period of time. This study may try to find clues to improve treatments of obesity and other diseases related with excess body fat.

2. Purpose of study:

To determine the effect of structured nutrition and exercise on hormones related to body fat.

3. Description of the study procedures and tests:

Subjects involved in the study will be tested in a series of baseline and follow up measurements at three locations:

Nexus Clinical Research: 120 Stavanger Drive

- Study participants will complete a health habit questionnaire, including questions about smoking, alcohol and food intake patterns.
- You will be asked to come to Nexus Clinical Research for blood sampling at the beginning and the end of the study. About 1 tablespoon of blood will be drawn each visit which will be used to determine if changes in your hormones are occurring during the study**.**
- Feedback regarding abnormal blood values will be reported to the family physician.

Genetics Lab: H4353

- Percent body fat, lean body mass and bone density will be measured using a bone densitometer (lying on a bed, and a scanner will complete the measurement in about 10 to 15 minutes.
- The scan will expose you to radiation levels similar to an x-ray.

Exercise Physiology Lab: PE2005A

- Cardiorespiratory Fitness, which is the ability of the body's circulatory and respiratory systems to supply fuel and oxygen during sustained physical activity, will assessed using a treadmill test. During this test you will be required to run on the treadmill at an increasing pace of 4 intervals. Scores from each level will be recorded to calculate your hearts use of oxygen.
- You will have your strength measured by using a hand grip test. This requires squeezing a metal grip attached to a gauge. You will also have your leg strength tested by attaching a cable to your foot and extending your leg as hard against the cable.
- Your standing height, body weight will be taken using a medical scale. As well girth measurements of your waist and hips will be taken with a standard measuring tape. heart rate and blood pressure will be measured using an automated blood pressure cuff and temperature will be measured using a standard thermometer.

- Body fat will also be measured using skin fold calipers. We will test a series of sites around the body including the arms, legs, and torso. We will also take girth measurements of the arms, neck, chest, shoulders, legs, waist and hips using a measuring tape.

All subjects will be required to undergo baseline and follow up testing.

Intervention Group: Definitions Training Facility, 120 Stavanger Drive

You will have a 50% chance of being allocated to the exercise group. Those involved in the study (both control and intervention group) must complete the following interventions as part of the study:

- Nutrition education seminar: This nutrition education will involve a one hour talk to explain proper nutrition. This will be followed by 30 minutes of explaining food logs and what will be required of you during the study. The remaining 30 minutes will be used for handing out information, questions and booking you in for workouts.

- Completion of food logs - You will be asked to complete a daily food log to ensure you are eating the right foods for 12 weeks. You will be asked to submit these food logs to your research assistant once a week.

Those chosen for the intervention/exercise group will also have to complete:

- Supervised exercise training - (3) 1 hour sessions per week for 12 week. Subjects chosen for the intervention will receive supervised exercise training with a certified personal trainer for 12 weeks during the study. During this time you will be asked to exercise with the trainer/research assistant 3 times each week. Flexibility in when you want to exercise will be allowed and the trainer will be available between 6 am and 8 pm daily.

4. Length of time:

The study will span 12 weeks from start to finish. All subjects, including those who were not selected for the exercise intervention and are part of the "control group" must attend all testing. Baseline and follow up testing after 12 weeks is required. People who are selected for the exercise intervention are required to attend a workout with a personal trainer 3 times a week for 1 hour and record food intake weekly. Control subjects will only be required to record weekly food intake and physical activity. Exercise sessions (for those in the intervention group) and food logging will last for 12 weeks.

5. Possible risks and discomforts:

There is little risk when sampling blood. There is a possibility of bruising at the site and a slight chance of infection. There will be a very low dose of X-ray exposure when you receive measurement of percent body fat and bone density.

Some discomfort from healthy eating may occur. It will be recommended that subjects take one day each week to eat foods which they crave.

Physical activity may also cause discomfort including muscle soreness, acute injury, aggravation of previous injuries, fatigue, disrupted sleep patterns and hunger.

6. Benefits:

It is not known whether this study will benefit you personally.

However, potential benefits may include:

- Increased physical fitness
- Weight loss
- Nutrition education
- Education on how to exercise properly
- Access to professional lifestyle counseling
- Awareness of physical fitness and body fat percentage

7. Liability statement:

Signing this form gives us your consent to be in this study. It tells us that you understand the information about the research study. When you sign this form, you do not give up your legal rights. Researchers or agencies involved in this research study still have their legal and professional responsibilities.

8. What about my privacy and confidentiality?

Protecting your privacy is an important part of this study. Every effort to protect your privacy will be made. However it cannot be guaranteed. For example we may be required by law to allow access to research records.

A copy of this consent will be put in your health record. If you agree, your family doctor will be told that you are taking part in this study.

When you sign this consent form you give us permission to

- Collect information from you
- Collect information from your health record
- Share information with the people conducting the study

- Share information with the people responsible for protecting your safety

Access to records

The members of the research team will see health and study records that identify you by study code. The names associated with the study codes will be separate from the study records and will be accessible by the research team only.

Other people may however need to look at your health records and the study records that identify you by name. This might include the research ethics board. You may ask to see the list of these people. They can look at your records only when one of the research team is present.

Use of records

The research team will collect and use only the information they need for this research study.

This information will be will kept for 5 years and will include your :

- date of birth
- sex
- address
- contact information
- emergency contact
- medical conditions
- medications
- the results of tests and procedures you had during the study
- information from questionnaires

Your name and contact information will be kept secure by the research team in Newfoundland and Labrador. It will not be shared with others without your permission. Your name will not appear in any report or article published as a result of this study.

If you decide to withdraw from the study, the information collected up to that time will continue to be used by the research team. It may not be removed. This information will only be used for the purposes of this study

After your part in this study ends, we may continue to review your health records we collected during the study to check that the information we collected is correct. We will not be accessing your medical records at any time.

Information collected and used by the research team will be stored by Michael Wahl the principle investigator of the study who is the person responsible for keeping it secure.

Study codes will be assigned to each individual record instead of names and kept secure by the research team to avoid identification of your information by those not involved with the study.

Your access to records

You may ask the primary investigator to see the information that has been collected about you.

9. Compensation:

In the event that you suffer injury as a direct result of taking part in this study, necessary medical treatment will be available at no additional cost to you as covered by MCP.

10. Questions:

If you have any questions about taking part in this study, you can meet with the investigator who is in charge of the study at this institution. That person is: Michael Wahl

· **Storage of Blood Samples:**

The (blood) sample from this study will be securely stored at Nexus Clinical Research, 120 Stavanger Drive, St. John's, Newfoundland for 5 years. These samples will not be used for further research outside of the scope of this project. The data guardian is Michael Wahl. Samples can be withdrawn by calling or emailing Michael Wahl using the contact information below.

Michael Wahl (709) 746-3355
mikewahl@definitionsonline.com

Or you can talk to someone who is not involved with the study at all, but can advise you on your rights as a participant in a research study. This person can be reached through:

Health Research Ethics Authority (HREA) at 709-777-6974 or
Email: info@hrea.ca

After signing this consent you will be given a copy.

Signature Page

Study title:

Name of principal investigator:

To be filled out and signed by the participant:

	Please check as appropriate:	
I have read the consent.	Yes { }	No { }
I have had the opportunity to ask questions/to discuss this study.	Yes { }	No { }
I have received satisfactory answers to all of my questions.	Yes { }	No { }
I have received enough information about the study.	Yes { }	No { }
I have spoken to Mr. Wahl and he/she has answered my questions	Yes { }	No { }
I understand that I am free to withdraw from the study	Yes { }	No { }
• at any time		
• without having to give a reason		
I understand that it is my choice to be in the study and that I may not benefit.	Yes { }	No { }
I agree to take part in this study.	Yes { }	No { }

_____ _____

Signature of participant Date

_____ _____

Signature of witness (if applicable) Date

<u>To be signed by the investigator or person obtaining consent</u>

I have explained this study to the best of my ability. I invited questions and gave answers. I believe that the participant fully understands what is involved in being in the study, any potential risks of the study and that he or she has freely chosen to be in the study.

_____ _____

Signature of investigator/person obtaining consent Date

Telephone number: _____

Appendix 11

Subject Recruitment Email

Good afternoon,

We would like to inform you about a study we will be conducting through Memorial University this fall. We are looking for candidates to participate in a study on the effects of weight loss on hormones who meet the following criteria:

- Male
- Age 35-55
- Have a BMI of 30-35
- No medically diagnosed illness including:
    - high cholesterol
    - high blood pressure
    - diabetes
    - kidney disease
    - liver disease

To participate in this study you must be willing to engage in supervised exercise regularly and follow a structured eating plan. You will also be required to have weekly blood testing and complete series of physical fitness and body composition tests at the beginning and the end of the study.

If you are interested in learning more please contact me at any time for specific information on what is involved in the study and it's potential benefits and risks to subjects. You can reach me at: mikewahl@me.com or 746-3355.

Regards,

Mike Wahl
Primary Investigator
mikewahl@me.com

Appendix 12

Food Intake

Questionnaire

Food Intake Questionnaire

DIRECTIONS

How to complete EPAT: For each of the 23 food groups on the chart, circle one box to the right of each food grop that best describes your **usual** eating habits. The correct answer is what you actually eat. If you have trouble choosing between two boxes, circle the one that comes closest.

How much is a serving? Use the serving sizes listed next to the foods to determine the number of servings you eat. **Hint:** one serving is not necessarily the amount you eat at one sitting. If you eat a whole pizza that's 4 servings, not 1.

Adding it all up: You probably eat a variety of foods within each food group. Include the listed foods you eat plus other similar items when you estimate the number of servings.

For example: In an average week, Joe might eat four pancakes for breakfast one weekend morning (4 pancakes = 2 servings). During the week, he has a doughnut at his coffee break about three times a week (3 doughnuts = 3 servings). He seldom eats desserts, but may snack on a large cookie about once a week (1 large cookie = 1 serving). That adds up to 6 servings in the Baked Goods Group. (See the example below.)

FOOD GROUPS AND SERVING SIZES

Baked Goods such as: Doughnuts, sweet rolls, muffins 1 avg. Cakes, coffee cakes□ 1 avg. piece Cookies□□ □ 2 avg. or 1 large Pie□ □ □ 1 avg. edge Granola bars□ □ 1 bar Granola cereals□ □ 1/2 cup Pancakes□ □ 2 avg. Waffles, french toast□ 1 avg.	7 or more servings per week	5-6 servings per week	3-4 servings per week	2 or less serving per week or Never eat	BG

EXAMPLE

SECTION I

PLEASE BEGIN HERE:

FOOD GROUPS AND SERVING SIZES — CIRCLE ONE BOX FOR EACH FOOD GROUP

Convenience Foods such as: Fast-food meat sandwich 1 sandwich All canned, packaged or frozen dinners (except lean, light or diet types) such as pizza, 1/4 med. pizza macaroni and cheese, 1 cup pot pies, etc. 1 avg. pot pie	7 or more servings per week	3-6 servings per week	1-2 servings per week	Less than 1 serving per week or Never eat	CF
(Most other meats are in section II) **Processsed Meats and Untrimmed Red Meats such as:** Bacon□ □ □ 4 slices Bologna, lunch meat□ 2 slices Hot dog, breakfst sausage □avg. Bratwurst□ □ 1 link Reg. or lean hamburger□ 1/4-pound patty (not extra lean) Beef, pork. lamb, veal□ 1 med. slice or with visible fat□ □ 1 med. chop	6 or more servings per week	3-5 servings per week	1-2 servings per week	Less than 1 serving per week or Never eat	UN
Poultry Skin	Always eat poultry with skin	Usually eat poultry with skin	Usually eat poultry without skin	Always eat poultry without skin or Never eat	PS

FOR OFFICE USE ONLY□□ □ W-4□□ X-3□ □ Y-2□ □ Z-1□

SECTION II

FOOD GROUPS AND SERVING SIZES	CIRCLE ONE BOX FOR EACH FOOD GROUP				
Trimmed Red Meats such as: Low-fat lunch meat (e.g. 95% fat-free) 2 slices Pork, beef, lamb, veal without visible fat 1 med. slice or 1 med. chop Extra lean hamburger 1/4-pound patty	Less than 1 serving per week or Never eat OR 8 or more servings per week	1-2 servings per week	3-5 servings per week	6-7 serving per week	TR
Poultry and Fish/Seafood such as: Chicken, turkey☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ 1 med. slice 1 avg. piece or 1/2 cup diced Turkey lunch meat☐ 2 slices Fish fillet☐ ☐ ☐ Tuna☐ ☐ ☐ ☐ ☐ ☐ Crab☐ ☐ ☐ 1 med. 1/2 cup or 1/2 avg. can 1/2 cup or 2 legs☐	2 or less servings per week or Never eat OR 10 or more servings per week	3-4 servings per week	5-6 servings per week	7-9 serving per week	PF
Dairy Foods such as: Ice milk Soft serve Frozen yogurt 1/2 cup or 1 scoop	4 or more servings per week	3 servings per week	2 servings per week	1 or less servings per week or Never use	IM
Skim milk 1% milk Low-fat or non-fat yogurt 1 cup	2 or less servings per week or Never use	3-6 servings per week	7-13 servings per week	14 or more servings per week	SM
Cheeses such as: Don't forget cheese contained in mixed dishes, e.g. sauces, pizza and salad. Mozzarella, part-skim☐ 1 oz. slice "Diet"☐ ☐ ☐ 1 oz. slice "Lite"☐ ☐ ☐ 1 oz. slice. Cottage cheese, ricotta☐ 1/4 cup	Rarely or Never eat OR 7 or more servings per week	1-2 servings per week	3-4 servings per week	5-6 serving per week	CH
Beans such as: kidney beans, lima beans, split peas, or other dried beans or dried peas 1/2 cup cooked	Less than 1 serving per week or Never eat	1-2 servings per week	3-5 servings per week	6 or more servings per week	BE
Preparation Method for Meat, Fish and Poultry Foods cooked with fat (butter, margarine, oil, shortening or lard)	Always prepared with fat or commercial breading	Usually prepared with fat or commercial breading	Usually prepared without fat or commercial breading	Always prepared without fat or commercial breading, or Never eat meat, fish or poultry	P
Preparation Method for Baked Goods	Usually eat commercially prepared	Eat both commercially prepared and homemade from mixes	Usually eat homemade from mixes	Usually eat homemade from scratch	PB

FOR OFFICE USE ONLY☐☐ ☐ W-1☐☐ X-2☐ ☐ Y-3☐ ☐ Z-4☐

CONTINUED ON NEXT PAGE

FOOD GROUPS AND SERVING SIZES	CIRCLE ONE BOX FOR EACH FOOD GROUP				
Eggs (other than those used in baking) 1 whole egg	6 or more servings per week	4-5 servings per week	2-3 servings per week	Less than 2 whole eggs per week, and/ or eat only egg whites or egg substitutes, or Never eat eggs	EG
(Most other dairy desserts are in section II) **Dairy Foods such as:** Ice cream□ 1/2 cup or 1 scoop	3 or more servings per week	1-2 servings per week	Less than 1 serving per week	Never eat	IC
(Most other milks and yoghurts are in section II) Whole milk 2% milk□□ □ 1 cup Regular yoghurt	7 or more servings per week	3-6 servings per week	1-2 serving per week	Less than 1 serving per week or Never eat	WM
(Most other cheeses are in section II) **Cheeses such as:** Don't forget cheese contained in mixed dishes, e.g. sauces, cheeseburgers, pizza and blue cheese dressing. Cheddar, Colby□ □ 1 oz. slice Swiss, Monterey Jack□ 1 oz. slice American, processed cheese 1 oz. slice. Cream cheese, blue cheese 2 Tablespoons	5 or more servings per week	2-4 servings per week	1 servings per week	Never eat	CS
Types of Fats and Oils Used: (In cooking and at the table, but not in baked goods) Include cream and fat used in casseroles as well as spreads on breads, etc.	Always use butter, lard, cream and/or cream substitutes	Usually use butter, lard, cream, cream substitutes, and/or shortening	Usually use margarine, salad dressings, and/or oils	Always use margarine, salad dressings, and/or oils, or Never use any fats or oils	FO
Amount of Visible Fats and Oils: Do not include fats and oils used in cooking or baking here. Do include fats such as: Butter, margarine, lard (as a spread or on vegetables, etc.) 1 teaspoon (1 pat) Oils 1 teaspoon Salad dressing (mayonnaise, french, etc.) 1 Tablespoon Cream (whipped, sour, half and half, or cream substitutes 1 Tablespoon Peanut butter 1 Tablespoon Nuts, seeds (shelled) 1 Tablespoon	6 or more servings per day	5 servings per day	4 servings per day	3 or less servings per day or Never use	AF
	Note: These servings are daily amounts, not weekly.				
Baked Goods such as: Doughnuts, sweet rolls, muffins 1 avg. Cakes, coffee cakes□ 1 avg. piece Cookies□□ □ 2 avg. or 1 large Pie□ □ □ 1 avg. edge Granola bars□ □ 1 bar Granola cereals□ □ 1/2 cup Pancakes□ □ 2 avg. Waffles, french toast□ 1 avg.	Remember breakfast, snacks and coffee breaks!				
	7 or more servings per week	5-6 servings per week	3-4 servings per week	2 or less serving per week or Never eat	BG
Snacks such as: Snack crackers□ □ 12 pieces Chips□ □ □ 12 chips French fries□ □ 1 small order	7 or more servings per week	2-6 servings per week	1 serving per week	Rarely or never eat	SN
Chocolate candy□□ □ □ □ 2 oz. or 1 avg. candy bar	3 or more servings per week	2 servings per week	1 serving per week	Rarely or never eat	CC
FOR OFFICE USE ONLY□□ □ W-4□□ X-3□ □ Y-2□ □ Z-1□					

Note: The servings below are daily amounts, not weekly.

FOOD GROUPS AND SERVING SIZES	CIRCLE ONE BOX FOR EACH FOOD GROUP				
Breads and Other Starchy Foods such as: Bread — 1 avg. slice Dinner roll, bagel — 1 avg. Cereal — 1 cup or 1 small package Rice, Noodles, pasta — 1/2 cup cooked	1 or less servings per day or Never eat	2 servings per day	3 servings per day	4 or more servings per day	BR
Fruits and Vegetables such as: Fruit: fresh or frozen — 1 avg. piece Canned fruit — 1/2 cup (1 avg. serving) Dried fruit — 2 Tablespoons or 2 avg. pieces Vegetable: fresh, frozen or canned — 1/2 cup (1 avg. serving) Lettuce salad — 1 cup (1 small bowl) Potato (baked, mashed, or other) — 1 small or 1/2 cup Juice: fruit or vegetable — 1/2 cup (1 small glass)	1 or less servings per day or Never eat	2-3 servings per day	4-5 servings per day	6 or more serving per day	FV
Alcohol such as: Beer, regular or light□ — 1 can Liquor□ □ □ □ □ □ — 1 cocktail or 1 jigger□ Wine□ □ □ — 1 small glass	5 or more servings per day	3-4 servings per day	1-2 servings per day	Less than 1 serving per day or Never use	AL
FOR OFFICE USE ONLY□□ □	W-1□□	X-2□ □	Y-3□ □	Z-4□	

☐ Check here if you usually add salt at the table.

☐ Check here if you eat more than 5 meals per week in restaurants or fast-food chains.

If you are following a special diet or vegetarian diet, enter name or type of diet here:_____

_____

Please check that you have circled 23 answers and that you have filled in your name and the date.

THANK YOU

DIET ASSESSMENT

ID: ⓪①②③④⑤⑥⑦⑧⑨ ⓪①②③④⑤⑥⑦⑧⑨ ⓪①②③④⑤⑥⑦⑧⑨ (×3 rows)

1. Do you currently take multiple vitamins? (Please report individual vitamins under question 2)

○ No ○ Yes → If yes,
a) How many do you take per week? → ○ 2 or less ○ 3-5 ○ 6-9 ○ 10 or more
b) What specific brand do you usually use? → Specify exact brand and type

2. Not counting multiple vitamins, do you take any of the following preparations:

		How many years?	What dose per day?
a) Vitamin A?	○ No ○ Yes, seasonal only ○ Yes, most months	○ 0-1 yr. ○ 2-4 yrs. ○ 5-9 yrs. ○ 10+ yrs. ○ Don't know	○ Less than 8,000 IU ○ 8,000 to 12,000 IU ○ 13,000 to 22,000 IU ○ 23,000 IU or more ○ Don't know
b) Vitamin C?	○ No ○ Yes, seasonal only ○ Yes, most months	○ 0-1 yr. ○ 2-4 yrs. ○ 5-9 yrs. ○ 10+ yrs. ○ Don't know	○ Less than 400 mg. ○ 400 to 700 mg. ○ 750 to 1250 mg. ○ 1300 mg. or more ○ Don't know
c) Vitamin B6?	○ No ○ Yes → If yes,	○ 0-1 yr. ○ 2-4 yrs. ○ 5-9 yrs. ○ 10+ yrs. ○ Don't know	○ Less than 10 mg. ○ 10 to 39 mg. ○ 40 to 79 mg. ○ 80 mg. or more ○ Don't know
d) Vitamin E?	○ No ○ Yes → If yes,	○ 0-1 yr. ○ 2-4 yrs. ○ 5-9 yrs. ○ 10+ yrs. ○ Don't know	○ Less than 100 IU ○ 100 to 250 IU ○ 300 to 500 IU ○ 600 IU or more ○ Don't know
e) Selenium?	○ No ○ Yes → If yes,	○ 0-1 yr. ○ 2-4 yrs. ○ 5-9 yrs. ○ 10+ yrs. ○ Don't know	○ Less than 8 mcg. ○ 80 to 130 mcg. ○ 140 to 250 mcg. ○ 260 mcg. or more ○ Don't know
f) Iron?	○ No ○ Yes → If yes,	○ 0-1 yr. ○ 2-4 yrs. ○ 5-9 yrs. ○ 10+ yrs. ○ Don't know	○ Less than 51 mg. ○ 51 to 200 mg. ○ 201 to 400 mg. ○ 401 mg. or more ○ Don't know
g) Zinc?	○ No ○ Yes → If yes,	○ 0-1 yr. ○ 2-4 yrs. ○ 5-9 yrs. ○ 10+ yrs. ○ Don't know	○ Less than 25 mg. ○ 25 to 74 mg. ○ 75 to 100 mg. ○ 101 mg. or more ○ Don't know
h) Calcium?	○ No ○ Yes → If yes,	○ 0-1 yr. ○ 2-4 yrs. ○ 5-9 yrs. ○ 10+ yrs. ○ Don't know	○ Less than 400 mg. ○ 400 to 900 mg. ○ 901 to 1300 mg. ○ 1301 mg. or more ○ Don't know

i) Are there other supplements that you take on a regular basis? Please mark if yes:

○ Folic acid ○ Vitamin D ○ B-Complex vitamins ○ Cod liver Oil ○ Omega-3 Fatty-acids ○ Iodine ○ Copper ○ Brewer's Yeast ○ Beta-Carotene ○ Magnesium ○ Other (please specify) →

3. For each food listed, fill in the circle indicating how often on average you have used the amount specified during the past year.

DAIRY FOODS	Never, or less than once per month	1-3 per mo.	1 per week.	2-4 per week.	5-6 per week.	1 per day.	2-3 per day.	4-5 per day.	6+ per day.
	AVERAGE USE LAST YEAR								
Skim or low fat milk (8 oz. glass)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Whole milk (8 oz. glass)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Cream, e.g coffee, whipped (Tbs)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Sour cream (Tbs)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Non-dairy coffee whitener (tsp.)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Sherbet or ice milk (1/2 cup)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Ice cream (1/2 cup)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Yogurt (1 cup)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Cottage or ricotta cheese (1/2 cup)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Cream cheese (1 oz.)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Other cheese, e.g. American, cheddar, etc. plain or as part of a dish (1 slice or 1 oz. serving)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Margarine (pat), added to food or bread; exclude use in cooking	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Butter (pat), added to food or bread; exclude use in cooking	○	○	Ⓦ	○	○	Ⓓ	○	○	○

Please turn to page 2

3. (Continued) Please fill in your average use, ~~during the past year~~, of each specified food.

Please try to average your seasonal use of foods over the entire year. For example, if a food such as cantaloupe is eaten 4 times a week during the approximate 3 weeks it is in season, then the average use would be once per week.

FRUITS	Never, or less than once per month	1-3 per mo.	1 per week.	2-4 per week.	5-6 per week.	1 per day.	2-3 per day.	4-5 per day.	6+ per day.
Raisins (1 oz. or small pack) or grapes	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Prunes (1/2 cup)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Bananas (1)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Cantaloupe (1/4 melon)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Watermelon (1 slice)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Fresh apples or pears (1)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Apple juice or cider (small glass)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Oranges (1)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Orange juice (small glass)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Other fruit juices (small glass)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Grapefruit (1/2)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Grapefruit juice (small glass)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Strawberries, fresh, frozen or canned (1/2 cup)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Blueberries, fresh, frozen or canned (1/2 cup)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Peaches, apricots or plums (1 fresh or 1/2 cup canned)	○	○	Ⓦ	○	○	Ⓓ	○	○	○

VEGETABLES	Never, or less than once per month	1-3 per mo.	1 per week.	2-4 per week.	5-6 per week.	1 per day.	2-3 per day.	4-5 per day.	6+ per day.
Tomatoes (1)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Tomato juice (small glass)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Tomato sauce (small cup) e.g. spaghetti sauce	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Red chili sauce (1 Tbs)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Tofu or soybeans (3-4 oz.)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
String beans (1/2 cup)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Brocolli (1/2 cup)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Cabbage or cole slaw (1/2 cup)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Cauliflower (1/2 cup)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Brussels sprouts (1/2 cup)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Carrots, raw (1/2 carot or 2-4 sticks)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Carrots, cooked (1/2 cup)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Corn (1 ear or 1/2 cup frozen or canned)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Mixed vegetables (1/2 cup)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Beans or lentils, baked or dried (1/2 cup)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Eggplant, zucchini, or other summer squash (1/2 cup)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Yams or sweet potatoes (1/2 cup)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Spinach, cooked (1/2 cup)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Spinach, raw as in salad	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Kale, mustsard or chard greens (1/2 cup)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Iceberg or head lettuce (serving)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Romaine or leaf lettuce (serving)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Celery (4" stick)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Beets (1/2 cup)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Alfalfa sprouts (1/2 cup)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Garlic, fresh or powdered (1 clove or shake)	○	○	Ⓦ	○	○	Ⓓ	○	○	○

EGGS, MEAT, ETC.	Never, or less than once per month	1-3 per mo.	1 per week.	2-4 per week.	5-6 per week.	1 per day.	2-3 per day.	4-5 per day.	6+ per day.
Eggs (1)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Chicken or turkey, with skin (4-6 oz.)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Chicken or turkey, without skin (4-6 oz.)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Bacon (2 slices)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Hot dogs (1)	○	○	Ⓦ	○	○	Ⓓ	○	○	○

Please turn to page 3

3. (Continued) Please fill in your average use, during the past year, of each specified food.

MEATS (CONTINUED)	Never, or less than once per month	1-3 per mo.	1 per week.	2-4 per week.	5-6 per week.	1 per day.	2-3 per day.	4-5 per day.	6+ per day.
Processed meats, e.g. sausage, salami, bologna, etc. (piece or slice)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Liver (3-4 oz.)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Hamburger (1 patty)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Beef, pork, or lamb as a sandwich or mixed dish, e.g. stew, cassorole, lasagne, etc.	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Beef, pork, or lamb as a main dish, e.g. steak, roast, ham, etc. (4-6 oz.)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Canned tuna fish. (3-4 oz.)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Dark meat, fish, e.g. mackerel, salmon sardines, bluefish, swordfish (3-5 oz.)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Other fish (3-5 oz.)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Shrimp, lobster, scallops as a main dish	○	○	Ⓦ	○	○	Ⓓ	○	○	○

BREADS, CEREALS, STARCHES	Never, or less than once per month	1-3 per mo.	1 per week.	2-4 per week.	5-6 per week.	1 per day.	2-3 per day.	4-5 per day.	6+ per day.
Cold breakfast cereal (1 cup)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Cooked oatmeal (1 cup)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Other cooked breakfast cereal (1 cup)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
White bread (slice), including pita bread	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Dark bread (slice)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
English muffins, bagels, or rolls (1)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Muffins or biscuits (1)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Brown rice (1 cup)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
White rice (1 cup)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Pasta, e.g. spaghetti, noodles, etc. (1 cup)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Other grains, e.g. bulgar, kasha couscous, etc. (1 cup)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Pancakes or waffles (serving)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
French fried potatoes (4 oz.)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Potatoes, baked, boiled (1) or mashed (1 cup)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Potato chips or corn chips (small bag or 1 oz.)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Crackers, Triscots, Wheat Thins (1)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Pizza (2 slices)	○	○	Ⓦ	○	○	Ⓓ	○	○	○

		BEVERAGES	Never, or less than once per month	1-3 per mo.	1 per week.	2-4 per week.	5-6 per week.	1 per day.	2-3 per day.	4-5 per day.	6+ per day.
OTHER BEVERAGES Consider the serving size as 1 glass. bottle or can for these carbonated beverages	Low Calorie (sugar-free) types	Low calorie cola, e.g. Tab with caffeine	○	○	Ⓦ	○	○	Ⓓ	○	○	○
		Low calorie caffeine-free cola, e.g. Pepsi Free	○	○	Ⓦ	○	○	Ⓓ	○	○	○
		Other low calorie carbonated beverage, e.g. Fresca, Diet 7-Up, diet ginger ale	○	○	Ⓦ	○	○	Ⓓ	○	○	○
	Regular types (not sugar-free)	Coke, Pepsi, or other Cola with sugar	○	○	Ⓦ	○	○	Ⓓ	○	○	○
		Caffeine free Coke, Pepsi, or other Cola with sugar	○	○	Ⓦ	○	○	Ⓓ	○	○	○
		Other carbonated beverage with sugar, e.g. 7-Up, ginger ale	○	○	Ⓦ	○	○	Ⓓ	○	○	○
	OTHER BEVERAGES	Hawaian Punch, lemonade or other non-carbonated fruit drinks (1 glass, bottle, can)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
		Decaffeinated coffee (1 cup)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
		Coffee (1 cup)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
		Tea (1 cup), not herbal tea	○	○	Ⓦ	○	○	Ⓓ	○	○	○
		Beer (1 glass, bottle, can)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
		Red wine (4 oz. glass)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
		White wine (4 oz. glass)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
		Liquor, e.g. whiskey, gin, etc. (1 glass or shot)	○	○	Ⓦ	○	○	Ⓓ	○	○	○

Please turn to page 4

ID:

3. (Continued) Please fill in your average use, during the past year, of each specified food.

SWEETS, BAKED GOODS, MISCELLANEOUS	Never, or less than once per month	1-3 per mo.	1 per week.	2-4 per week.	5-6 per week.	1 per day.	2-3 per day.	4-5 per day.	6+ per day.
Chocolate (bars or pieces) e.g. Hershey's, M&M's	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Candy bars, e.g. Snickers, Milky Way, Reeses	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Candy without chocolate (1 oz.)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Cookies, home baked (1)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Cookies, ready made (1)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Brownies (1)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Doughnuts (1)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Cake, home baked (slice)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Cake, ready made (slice)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Sweet roll, coffee cake or other pastry, home baked (serving)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Sweet roll, coffee cake or other pastry, ready made (serving)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Pie, home made (slice)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Pie,ready made (slice)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Jams, jellies, preserves, syrup or honey (1 Tbs)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Peanut butter (Tbs)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Popcorn (1 cup)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Nuts (small packet or 1 oz.)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Bran, added to food (1 Tbs)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Wheat Germ (1 Tbs)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Chowder or cream soip (1 cup)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Oil or vinegar dressing, e.g. Italian (1 Tbs)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Mayonaisse or other creamy salad dressing (1 Tbs)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Mustard, dry or prepared(1 Tbs)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Pepper (1 shake)	○	○	Ⓦ	○	○	Ⓓ	○	○	○
Salt (1 shake)	○	○	Ⓦ	○	○	Ⓓ	○	○	○

4. How much of the visible fat on your meats do you remove before eating?

○ Remove all visible fat ○ Remove small part of fat
○ Remove majority ○ Remove none
○ (Don't eat meat)

5. What kind of fat do you usually use for frying and sautéing? (Exclude "Pam"-type spray)

○ Real butter ○ Vegetable oil ○ Lard
○ Margarine ○ Vegetable shortening

6. What kind of fat do you usually use for baking?

○ Real butter ○ Vegetable oil ○ Lard
○ Margarine ○ Vegetable shortening

7. What form of margarine do you usually use?

○ None ○ Stick ○ Tub ○ Spread
○ Low-calorie stick ○ Low-calorie tub

8. How often do you eat food that is fried at home? (e.g. french fries, fried chicken, fried fish)

○ Daily ○ 4-6 times per week
○ 1-3 times per week ○ Less than once a week

9. How often do you eat fried food away from home? (e.g. french fries, fried chicken, fried fish)

○ Daily ○ 4-6 times per week
○ 1-3 times per week ○ Less than once a week

10. How many teaspoons of sugar do you add to your beverages or food each day? → tsp.

11. What type of cooking oil do you usually use? → Specify type and brand

→ Specify type and brand

13. Are there any other important foods that you usually eat at least once per week?

Include, for example: paté, tortillas, yeast, cream sauce, custard, horseradish, parsnips, rhubarb, radishes, fava beans, carrot juice, coconut, avocado, mango, papaya, dried apricots, dates, figs.

(Do not include dried spices and do not list something that has been listed in the previous sections.)

Other foods that you usually use at least once per week	Usual serving size	Servings per week
(a)		
(b)		
(c)		
(d)		

Appendix 13

Dietary Assessment

Diet Assessment

Name: _____ **Date:** _____

Email Address: _____

Medical Hx: _____
_____

Medications: _____

Ht: _____ **Wt:** _____ **BMI:** _____ **Age:** _____ **Wt Hx:** _____

Activity Level: _____ (low/moderate/high)

Occupation: _____
Recreational Activity: _____
Other**:** _____
Possible Barriers to PA: _____

Energy Level: _____(low/moderate/high) **Quality of Sleep:** _____ **Hrs Sleep per Night:** _____
Stress Level: _____ (low/moderate/high) _____
Bowel Health: _____
_____

Nutrition Hx

Allergies/Intolerances: _____

Meal Frequency: _____

Supplements: _____

Fluid Intake (cups/day and types)**:** _____

Take-out/Fast Food: _____

Alcohol: _____

Perceptions of Barriers to Healthy Eating:

_____
_____

Health and Wellness Concerns:

_____
_____
_____
_____

Diet Hx:

Breakfast	**Lunch**	**Supper**
Time:		
Snack	**Snack**	**Snack**
Energy:		

Goals Set:

_____
_____
_____
_____
_____
_____
_____

Notes: