2005

EFFECTS OF WEIGHT LOSS ON VISCERAL ADIPOSITY AND METABOLIC ADAPTATIONS IN DIABETIC VERSUS NON-DIABETIC WOMEN

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ABSTRACT OF DISSERTATION

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ABSTRACT OF DISSERTATION

A dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Graduate School at the University of Kentucky

By

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Lexington, Kentucky

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ABSTRACT OF DISSERTATION

EFFECTS OF WEIGHT LOSS ON VISCERAL ADIPOSITY AND METABOLIC ADAPTATIONS IN DIABETIC VERSUS NON-DIABETIC WOMEN

Obesity increases the risk for the development of cardiovascular disease, type 2 diabetes and other co-morbid conditions. Type 2 diabetes also is often associated with excessive visceral abdominal fat. Weight loss in obese individuals decreases the risk for developing the co-morbid conditions. Individuals with type 2 diabetes often have a greater difficulty in controlling these complications compared to individuals without type 2 diabetes.

The purpose of this study was to evaluate adherence to a medically-supervised low-energy diet (LED) weight loss program and changes in body composition and metabolic parameters after weight loss in women with and without type 2 diabetes. Subjects consisted of Caucasian women, between the ages of 40 to 65 years, with BMIs between 30 and 45 kg/m^2. There was no significant difference in BMI between the groups at study initiation (38.1 kg/m^2, diabetics (DM) and 36.0 kg/m^2, non-diabetics (NDM), $p=0.2314$). All subjects participated in the HMR® Program for 16 weeks. Twenty-nine subjects completed the weight loss phase (18 diabetics, 11 non-diabetics) and were evaluated for change in weight, body composition, and blood parameters. Data were analyzed by repeated-measures ANCOVA and student's t-tests using SAS® version 8.02. DM and NDM lost 11.7% and 16% of body weight, respectively ($p=0.6474$). Results indicate DM has more total lean tissue ($p=0.004$), more total body fat ($p=0.04$), more total abdominal tissue ($p=0.001$), more visceral adipose tissue ($p=0.001$) and lost less percent body fat ($p=0.04$) than NDM after 16 weeks of weight loss. After weight loss there was no significant difference in leptin, ghrelin or adiponectin levels. DM had greater insulin ($p=0.05$), HOMA-IR ($p<0.0001$), glucose ($p<0.0001$), HbA1c ($p<0.0001$), resistin ($p=0.04$) and PAI-1 ($p=0.02$). There were no differences after weight loss in lipid levels, blood pressure, diet compliance or exercise.

The data show that medically-supervised LEDs are safe and effective for treating obesity in individuals with type 2 diabetes. Cardiovascular risk factors improved in both NDM and DM subjects with weight loss. The findings also suggest that insulin and metabolically dysfunctional lean tissue may play a critical role in the complex axes affecting changes in body composition and inflammation in individuals with type 2 diabetes.

KEY WORDS: Type 2 Diabetes, Obesity, Weight Loss, Body Composition, Low-Energy Diet (LED)

Elizabeth C. Konz

July 5, 2005

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DEDICATION

This dissertation is dedicated to my family,

Marsha Konz

Jennifer Konz-Alt

and

Fredric and Susan Konz

ACKNOWLEDGMENTS

So many individuals have helped me during my graduate studies in so many different ways, and I would like to thank all of them for their patience, encouragement and support. First, I must thank my Dissertation Chair and mentor, Dr. James W. Anderson, for his guidance through my graduate work. He has provided me with several unique opportunities to enhance my intellect and my research skills. Next I would like to thank my Dissertation Committee consisting of Dr. Geza Bruckner, Dr. Linda Chen, Dr. Thomas Garrity, and Dr. Raymond Reynolds. These individuals have given me continued support over the many years at the University of Kentucky and I could have never finished without them. I would also like to thank the Director of the Graduate Center for Nutritional Sciences, Dr. Lisa Cassis, and the Director of Graduate Studies, Dr. Reto Asmis.

I also wish to express my appreciation to all the people who have supported my research endeavors at the University of Kentucky. First, I would like to thank Dr. Linda Chen for her outstanding work at the University of Kentucky and her commitment and dedication towards students. She has provided me encouragement and strength which I needed for this process. Next, I would like to acknowledge Dr. Raymond Reynolds for his help in mentoring and providing medical support for the patients in my study. His expertise and wit have made my research experience positive and fun. I would also like to acknowledge, Dr. Nancy Kukulinsky, Dr. Thomas Getchell and the rest of the administration and staff of the General Clinical Research Center. These individuals provided me with necessary financial support and resources to conduct my research and also invaluable educational experiences.

Dr. Linda Gotthelf and Dr. Larry Stiffler and the rest of the HMR® team for their financial and research support. And a special thanks to all of the wonderful women who participated in my study (who remain anonymous for reasoning of confidentiality purposes). I could have never completed my research without their extremely hard work and determination. It was a pleasure to get to know every one of my research subjects and I pray for their continued success.

Most importantly, however, I must thank my family and friends for their instrumental assistance in this process. I would like to thank my mom, Marsha Konz for the encouragement and emotional support that she has provided to me in this process. I must thank my dad, Fredric Konz, and his wife, Susan Konz, for their patience and financial support which allowed me to complete my goals and to make a better life for myself. Finally, I have to thank my sister, Jennifer Konz-Alt, for being my best friend and providing a listening ear when I needed it.

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CHAPTER ONE

Introduction

Statement of the Problem

Obesity plays a pivotal role in the development of type 2 diabetes with approximately 75 percent of individuals with type 2 diabetes mellitus being obese (1-3). With the increasing prevalence of obesity it is not surprising that in the 1990's the prevalence of type 2 diabetes increased by one-third (4;5). According to the Centers for Disease Control, 97% of adults with diabetes have one or more lipid abnormalities (6). Individuals with type 2 diabetes often have a collective group of cardiovascular risk factors referred to as the metabolic syndrome. These risk factors include insulin resistance, hypertension, elevated triglycerides, low HDL-cholesterol, endothelial dysfunction, a prothrombotic state, and abdominal and visceral obesity (7). Complications of diabetes include blindness, kidney disease, heart disease, stroke, peripheral vascular disease and neuropathy (8). Using data from the Nurses Health Study (9), it was estimated that as much as 80% of the incidence of type 2 diabetes could be attributed to the combined effect of inactivity and overweight / obesity (8).

Objectives and Hypotheses

Primary Objectives: To determine changes in body composition and hormonal levels in obese individuals with type 2 diabetes compared to matched obese individuals without type 2 diabetes after the completion of a structured low-energy diet weight loss program. The hypotheses are as follows:

1. Obese individuals with type 2 diabetes will lose less body weight than obese individuals without type 2 diabetes.

2. Obese individual with type 2 diabetes will lose a greater proportion of abdominal fat as visceral adipose tissue compared to obese individuals without type 2 diabetes.

3. Plasma ghrelin levels in response to weight loss will not increase as much in individuals with type 2 diabetes as compared with individuals without type 2 diabetes.

4. Plasma leptin levels in response to weight loss will not decrease as much in individuals with type 2 diabetes as compared with individuals without type 2 diabetes.

Secondary Objectives: To determine changes in hormonal, metabolic and lipid levels in obese individuals with type 2 diabetes compared to obese individuals without type 2 diabetes after the completion of a structured low-energy diet weight loss program. The hypotheses are as follows:

1. Obese individuals with type 2 diabetes will have a greater decrease in insulin, interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α) and C-reactive protein (CRP) compared to obese individuals without type 2 diabetes.

2. Obese individuals with type 2 diabetes will have a greater decrease in serum triglyceride, plasma activator inhibitor-1 (PAI-) and serum C-reactive (CRP) compared to obese individuals without type 2 diabetes.

3. Obese individuals with type 2 diabetes will have a greater increase in plasma adiponectin compared to obese individuals without type 2 diabetes.

4. Obese individuals with type 2 diabetes will have a reduction in plasma resistin compared to obese individuals without type 2 diabetes.

CHAPTER TWO

Background and Review of Literature

Obesity

Obesity is increasing in epidemic proportions in the United States and around the world and has become a major global health concern (10;11). Almost two-thirds of adults in the United States are overweight or obese (10). Table 2.1 outlines the body mass index (BMI) criteria for assessing obesity where BMI is an individual's body weight in kilograms divided by their height in meters squared (kg/m^2). Obesity and adipose tissue are associated with several co-morbid conditions. Figure 2.1 outlines environmental and genetic contributions to health problems associated with obesity. Specifically, obesity plays a pivotal role in the development of type 2 diabetes with approximately 75 percent of individuals with type 2 diabetes mellitus being obese (1-3). With the increasing prevalence of obesity it is not surprising that in the 1990's the prevalence of type 2 diabetes increased by one-third (4;5). More than 18 million Americans have diabetes which accounts for 6.3% of the United States population (12). In 2002, diabetes was the sixth leading cause of death listed on U.S. death certificates (13). Table 2.2 lists the top ten leading causes of death in the United States in 2002. According to the Centers for Disease Control, 97% of adults with diabetes have one or more lipid abnormalities (6). Individuals with type 2 diabetes often have a collective group of cardiovascular risk factors referred to as the metabolic syndrome. These risk factors include insulin resistance, hypertension,

elevated triglycerides, low HDL-cholesterol, endothelial dysfunction, a prothrombotic state, and abdominal and visceral obesity (7). As shown in Table 2.2 co-morbid conditions associated with type 2 diabetes are also some of the leading causes of death in the United States. These include the number one leading cause of death, diseases of the heart and the third leading cause of death, cerebrovascular diseases.

Type 2 Diabetes Mellitus

Type 2 diabetes, is characterized by a combination of insulin resistance which is compounded by deficient insulin secretion (14;15). The most common form of type 2 diabetes is a heterogeneous disorder with genetic and environmental factors contributing to a dual defect involving β-cell dysfunction and insulin resistance (16). In muscle and fat cells, insulin enhances the recruitment of glucose transport proteins (GLUT-4) to the cell surface, thereby increasing glucose uptake into the cell in the postprandial state (16). The impairment in glucose transport that is characteristic of the insulin resistance of obesity and type 2 diabetes can worsen as a result of hyperglycemia (16). Hyperglycemia "down regulates" the synthesis of GLUT-4 proteins and inhibits the intrinsic activity of these proteins (16). Hyperglycemia also inhibits insulin gene expression and insulin secretion, particularly by impairing glucose-stimulated insulin secretion (16). Regardless of the pathoetiology of type 2 diabetes, any elevation in glycemic levels will secondarily result in increased insulin resistance and decreased insulin secretion (17).

Coronary Heart Disease, Dyslipidemia, and Type 2 Diabetes

A. Coronary Heart Disease (CHD)

Coronary heart disease (CHD) is the leading cause of death in the United States (18). Observational studies have shown that overweight, obesity and excess abdominal fat are directly related to cardiovascular risk factors and are associated with increased morbidity and mortality (19-24). Obesity itself may possibly be the greatest risk for the development of CHD (25) and is probably a more significant risk factor for individuals with type 2 diabetes (26;27). Type 2 diabetes is also an independent risk factor for CHD in both men and women (7). The Framingham Study found that individuals with diabetes had a two- to three-fold increase risk of CHD compared with individuals without diabetes (28). Other risk factors leading to the development of CHD include an elevated total cholesterol, low-density lipoprotein (LDL)-cholesterol, triglycerides, blood pressure, fibrinogen and insulin (29), and low levels of high-density lipoprotein (HDL)-cholesterol (22).

Coronary heart disease is responsible for approximately 80% of deaths in persons with diabetes (27). A study conducted by Gu et al. (30) using data from the National Health and Nutrition Examination Study (NHANES) looked at the change in mortality from CHD over the last 30 years. The age-adjusted mortality rates from heart disease decreased 36.4% and 13.1% for men without diabetes and men with diabetes, respectively. Women without diabetes also displayed a 27% decrease in mortality from CHD; however, women with type 2 diabetes had a 23% increase in age-adjusted heart disease mortality. Other studies have found that diabetic women in the US have a 3-fold risk of developing CHD (31). This indicates that diabetes

appears to be one of the greatest risk factors for CHD, especially in women (28;30;32).

B. Dyslipidemia

1. Total Cholesterol

Individuals are considered to have high total cholesterol with levels >200 mg/dl and are especially at risk when levels are ≥240 mg/dl (33). Manson et al.. (34) has determined that for every 1% increase in total cholesterol, an individuals risk for the development of CHD increases by approximately 2 to 3 %. In a similar finding, Stamler et al. (35) stated that for every 1 mg/dl increase in total cholesterol that CHD risk increased by 2%. Men and women with a BMI >25 kg/m^2 are associated with having higher levels of total serum cholesterol (36;37). In women, the incidence of hypercholesterolemia also increases with increasing BMI (38). Several large longitudinal studies provide evidence that overweight, obesity and weight gain are associated with increased cholesterol levels (39-41). In addition to higher body weight and BMI, the pattern of fat distribution appears to affect cholesterol levels independently of total body weight. Total cholesterol levels are usually higher in persons with predominant abdominal obesity, defined as a waist-to-hip circumference ratio of ≥0.8 for women and ≥1.0 for men (42).

2. Triglycerides

Triglyceride levels have been shown to have a strong association with BMI in both cross-sectional and longitudinal studies for both men and women (36;37). Triglyceride levels ≥ 150 mg/dl are considered to be high and puts an individual at increased risk for developing CHD (3). One study separated adults into three age

groups (20 to 44 years, 45 to 59 years, and 60 to 74 years) and found that individuals with a BMI $\geq$ 30 kg/m^2 is associated with increasing triglyceride levels compared with individuals with a BMI $\leq$ 21 kg/m^2. The difference in triglycerides between the higher and lower BMI groups, ranged from 61 to 65 mg/dl in women (36) and 62 to 118 mg/dl in men (37).

3. LDL-Cholesterol

A serum LDL-cholesterol concentration of $\geq$ 160 mg/dl is considered to be high and an independent risk factor for CHD (3). This lipoprotein is the predominant atherogenic lipoprotein and is therefore the primary target of cholesterol-lowering therapy by diet, physical activity and drug therapy. Law et al. (43) concluded that for either a 1% increase or 1 mg/dl increase of LDL-cholesterol that an individuals risk for CHD increased by 1%. Cross-sectional data suggest a 10-unit difference in BMI, from 20 kg/m^2 to 30 kg/m^2, is associated with LDL-cholesterol levels that are higher by 10 to 20 mg/dl (36;37). According to extensive epidemiological data, a 10 mg/dl rise in LDL-cholesterol corresponds to approximately a 10 percent increase in CHD risk over a period of 5 to 10 years (43).

4. HDL-Cholesterol

Serum HDL-cholesterol levels are considered to be "good" cholesterol and are negatively associated with risk for developing coronary heart disease. HDL-cholesterol is believed to be able to "pull" cholesterol out of the cells and transport peripheral cholesterol back to the liver for catabolism. This is often referred to as "reverse cholesterol transport." Recommended levels for men are HDL-cholesterol levels of $\geq$ 45 mg/dl and for women $\geq$ 55 mg/dl, but the protective level for HDL is $\geq$

60 mg/dl (3). Cross-sectional studies have reported that HDL-cholesterol levels are lower in men and women with higher BMI (44;45). A low HDL-cholesterol level leads to a higher LDL:HDL ratio that enhances the risk of CHD. Longitudinal studies have found that changes in BMI are associated with changes in HDL-cholesterol. A BMI change of 1 unit is associated with an HDL-cholesterol change of 1.1 mg/dl for young adult men and an HDL-cholesterol change of 0.69 mg/dl for young adult women (46). Frick et al. (47) concluded that for every 1% decrease in HDL-cholesterol an individual's risk of CHD increased by 3.1%. Stamler et al. (35) reached similar findings in that there is a 2% to 3% increase in the risk of developing CHD for every 1 mg/dl decrease in HDL-cholesterol.

C. Type 2 Diabetes and Dyslipidemia

According to the Centers for Disease Control, 97% of adults with diabetes have one or more lipid abnormalities (6). Table 2.3 lists the ATP III clinical identification requirements for an individual to be diagnosed with the metabolic syndrome (48). The presence of the metabolic syndrome is equal to a risk for vascular disease with that of a high-risk LDL-cholesterol concentration of 150 to 220 mg/dl (49). Individuals with the metabolic syndrome often have elevations in C-reactive protein and plasminogen activator inhibitor-1 (PAI-1) indicating proinflammatory and prothrombotic states (48).

Individuals with type 2 diabetes usually do not have LDL-cholesterol levels different from those in non-diabetic patients. However, the LDL-cholesterol particles in individuals with diabetes are usually small, dense, and oxidized LDL-cholesterol and of particular interest in the risk for CHD. Clinical studies have shown that these

lipoprotein particles are particularly atherogenic and tend to be present in greater proportion in hypertriglyceridemic patients with insulin resistance associated with abdominal obesity (50-53). Triglyceride levels are often increased and HDL-cholesterol decreased in individuals with type 2 diabetes as well, which may be the best predictor of vascular disease in these subjects (54).

Longitudinal epidemiological studies have shown that the risk for cardiovascular disease mortality in type 2 diabetic subjects is at least twice that of persons without diabetes and that this relative risk is generally higher in women than in men (28;55).

Abdominal Obesity and Body Composition

Abdominal obesity is a distinct and independent risk factor for the development of type 2 diabetes (1;29;56-58). Abdominal obesity, particularly visceral adipose tissue, increases both metabolic disorders and the cardiovascular risks of dyslipidemia, hypertension, and cardiovascular disease (19;20;59-62). Visceral fat accumulation is influenced by factors such as age, menopause, stress, smoking, alcohol consumption, socioeconomic status and genetic factors (63;64). Specifically, accumulation of visceral adipose tissue at the L4-L5 level, characterized by waist circumferences of above 110 cm^2 for women and approximately 125 cm^2 is associated with distinct elevations in the risk factors for cardiovascular disease and type 2 diabetes (65;66). Other studies have shown that type 2 diabetes is associated with more accumulation of visceral abdominal fat compared with obese non-diabetic subjects with similar body weight (67;68).

Several studies have reported that weight loss induces a greater proportion of fat losses as visceral fat compared to subcutaneous fat. Yip et al. (69) reported that non-diabetic women lost 16.5 $\pm$ 6.6 kg, with a 28.3% reduction in total abdominal adipose tissue, a 31% reduction in visceral adipose tissue and a 26.0% reduction in subcutaneous adipose tissue. Zamboni et al. (70) reported that obese women with a weight loss of 6.6 kg visceral fat by decreased 40% while subcutaneous fat was reduced 23%. Limited research is available in individuals with type 2 diabetes; however, Takami et al. (71) found similar results in individuals with type 2 diabetes. These individuals with a minimal weight loss of 2-3 kg lost 25.8% of their abdominal fat as visceral adipose tissue and 17.2% as subcutaneous abdominal tissue. Others also showed that obese subjects with an initial abundance of visceral fat do not lose more weight but lose more visceral fat than subjects with less visceral fat (63). One may speculate that since individuals with type 2 diabetes have a greater proportion of their abdominal tissue as visceral fat that these individuals should lose more weight as visceral adipose tissue then obese individuals of the same body weight with less visceral adipose tissue.

Due to the increase in health risks related to obesity and particularly obesity with type 2 diabetes, it is important that these individuals lose the excess body fat to decrease the associated metabolic abnormalities accompanying type 2 diabetes mellitus. These metabolic disturbances decrease with weight loss (72); however, obese individuals with type 2 diabetes often have greater difficulty losing weight than obese individuals without type 2 diabetes (73-75). This phenomenon is not fully understood. Several contributing factors could be responsible for the difficulties for

individuals with type 2 diabetes. One potential contributing factor in losing weight could be that often individuals with type 2 diabetes have followed demanding diet regimens for many years and have "diet fatigue" making it difficult for these individuals to follow a rigorous energy-deficient diet. Also, diabetic individuals are often on medications to control the metabolic abnormalities and consequently these same medications may promote weight gain. Oral anti-diabetes agents sulfonylureas, meglitinides, and thiazolidinediones and insulin tend to be associated with weight gain (76). The one exception to this is the use of metformin. Metabolic abnormalities present with type 2 diabetes and visceral adiposity, such as hyperglycemia and hyperinsulinemia, make it more difficult to lose weight and maintain weight lost. This may also include abnormalities in non-glucose regulatory hormones affecting energy balance. Another possible factor for this could be the way in which the body regulates energy balance through the central nervous system (CNS). The CNS plays a fundamental role in the regulation of body weight and energy balance by: 1. affecting feeding behavior and physical activity; 2. affecting the autonomic nervous system controlling various aspects of metabolism, and 3. affecting the neuroendocrine system by controlling the secretion of hormones (77). The hormones of the neuroendocrine system used in the body weight regulation and energy balance are quite complex and the cascade of events causing certain individuals to be in a state of either positive or negative energy balance are still not fully understood. Some of the hormones involved in this complex system include leptin, ghrelin, insulin, neuropeptide Y, and growth hormone. Overall, a disruption in

this complex neuroendocrine pathway will affect the mechanisms by which body weight and energy balance are regulated.

Adipose and Stomach Hormones

A. Leptin

The hormone leptin, a product of the ob gene, is named leptin from the Greek word "leptos" meaning thin (78). The most important variable that determines circulating leptin concentrations is body fat mass (79). Leptin is produced predominantly in subcutaneous adipose tissue compared with visceral adipose tissue (80). Its role is to increase energy expenditure and inhibit food intake by decreasing the release of neuropeptide Y from the hypothalamus (81). If leptin levels are low during a period of positive energy balance an individual is prone to obesity (82). However, leptin levels have been found to be significantly greater in obese than non-obese subjects (78;80;83). Recent data have indicated that this is likely the result of desensitization for the leptin signal, now referred to as leptin resistance (78;84). Leptin production occurs after increases in insulin in response to feeding and a decrease in leptin concentrations follows decreases in insulin during fasting (85;86).

Leptin levels decrease by approximately 20 to 40% when individuals lose approximately 10% of their body weight (87-89). In individuals with type 2 diabetes, leptin levels do not drop as dramatically. Williams et al. (90) found that with an approximate 7.4% weight loss leptin levels decreased 20% in individuals with type 2 diabetes. These researchers also noted that leptin levels increased after sulfonylureas were reinitiated. Because leptin has been found to inhibit food intake and increase

energy expenditure, the administration of leptin is thought to be a potential pharmacotherapy for obesity. However, since leptin is produced by adipose tissue, leptin levels are often high in obese individuals and does not suppress food intake (87). Pharmacologic trials of the administration of leptin into obese individuals to reduce food intake subsequently were not able to reduce body weight, most likely due to some biological change that occurs over time to the excess of leptin in the body(91). Another possible explanation is leptin's interactions with other neuroendocrine hormones that affect body weight regulation.

B. Ghrelin

The hormone ghrelin, which is thought to play an important role in this complex energy balance system, is an endogenous ligand for the growth-hormone secretagogue receptor (GHS-R) (92). Ghrelin was named for its ability to provoke growth hormone secretion (the suffix "ghre" means grow) (93). Ghrelin has profound orexigenic, adipogenic, and somatotropic properties, increasing food intake and body weight.

Ghrelin has been found to be produced primarily in the stomach and then secreted into the blood stream (94). Within the stomach, ghrelin is produced by enteroendocrine cells in the oxyntic mucosa (93-98). The orexigenic actions of intracerebroventricular ghrelin appear to be meditated through hypothalamic neuropeptide Y (NPY) and agouti-related protein circuits (99). States of positive energy balance are associated with a decrease in ghrelin levels. Tschöp et al. (100) found that circulating ghrelin levels are decreased in individuals with obesity. Other studies have found that these levels are also decreased during acute overfeeding (100-

102). On the contrary, an increase in circulating ghrelin levels have been observed in fasting patients and in chronic under-nutrition such as with individuals with anorexia nervosa (96;103). Pre-meal rise of circulating ghrelin levels suggest it has a role as a hunger signal triggering meal initiation and this signal could be mediated by GHS-R subtypes (104). Tschöp et al. (100) also observed that ambient ghrelin levels in lean Pima Indians was significantly lower than obese Caucasians and that obese Pima Indians had even lower fasting plasma ghrelin levels. Pima Indians were used in this study due to their high rate of obesity and type 2 diabetes. Fasting ghrelin levels were also found to be negatively correlated with fasting plasma levels of insulin and leptin. In response to weight loss, Cummings et al. (105) found plasma ghrelin levels to increase approximately 24 percent.

Several mechanisms for the interaction between leptin and ghrelin have been postulated in the complex neuroendocrine system of energy balance. One suggested mechanism is the activation of neuropeptide Y (106). NPY stimulates food intake and promotes the net deposition of adipose mass (107). Leptin acts to inhibit NPY, while ghrelin activates NPY in the hypothalamus. The antagonistic action is suggested by comparison of levels with obese and lean states. Leptin levels are higher in obese individuals compared with non-obese individuals, whereas ghrelin levels are lower in obese compared to lean individuals. The levels of leptin and ghrelin in obese verses lean adults are demonstrated in Figures 2.2a and 2.2b, respectively.

The evidence is inconclusive related to alterations of leptin levels in type 2 diabetes (90;108-111). After weight loss leptin levels dramatically decline. This is

mostly likely do to the changes in abdominal adipose tissue. However, we speculate that individuals with type 2 diabetes would exhibit less of a decline in serum leptin concentrations compared with obese subjects since diabetic individuals should lose a greater proportion of their body fat as visceral fat compared with that of subcutaneous adipose tissue, where leptin is predominantly produced. Figure 2.3 shows leptin levels in individuals with and without type 2 diabetes before and after weight loss. We predict that subjects in this study will follow the same pattern resulting in a smaller decrease in leptin levels in women with type 2 diabetes than obese women without type 2 diabetes.

Limited information is available on changes in ghrelin level for individuals with type 2 diabetes with or without weight loss. Boden et al. (112) found that diabetic subjects on a low-carbohydrate diet lost 1.65 kg in 14 days and that insulin and leptin levels were statistically significantly lower at the end of the low-carbohydrate diet than before the diet, while ghrelin levels increased marginally. Figure 2.4 illustrates currently available data and our hypothesized response for fasting ghrelin levels after weight loss in obese type 2 diabetic women. Because Tschöp et al. (100) also found that Pima Indians had lower ghrelin levels than Caucasians, we hypothesized that obese women with type 2 diabetes will have lower fasting ghrelin levels than that of obese women without type 2 diabetes. As stated earlier, Cummings et al. (105) found that ghrelin levels increased after weight loss. Therefore, it is hypothesized that ghrelin levels will rise less dramatically in individuals with type 2 diabetes than individuals without type 2 diabetes.

Insulin Resistance

Besides the variations in the neuroendocrine hormones, other important metabolic variations exist as a consequence of obesity and type 2 diabetes. Many of these are associated with the excessive accumulation of abdominal adipose tissue. An increase in serum insulin levels is the most obvious in individuals with type 2 diabetes. Insulin is an anti-lipolytic hormone which stimulates glucose uptake and triglyceride biosynthesis. Insulin levels have been found to decrease in obese diabetic and non-diabetic individuals during weight loss (113-116) reflecting an increase in insulin sensitivity. Insulin sensitivity has a critical role in diabetes and is inversely related to degree of obesity.

Methods to test insulin sensitivity are often time-consuming and very expensive. The hyperinsulinemic insulin clamp, the "gold standard" for measuring insulin sensitivity, requires four hours of subject time and involves several intravenous lines, two infusions and about 40 blood glucose and insulin measurements (117). A simplified technique the homeostasis model assessment (HOMA-IR) has been found to be correlated with the hyperinsulinemic-euglycemic clamp technique (118;119). The HOMA-IR method for the determination of insulin-sensitivity derives an estimate of insulin sensitivity from the mathematical modeling of fasting plasma glucose and insulin concentrations (120).

Inflammatory and Thrombotic Cytokines

A. Tumor necrosis factor-alpha (TNF-α), Interleukin-6 (IL-6), C-reactive protein (CRP), Plasminogen activating inhibitor-1 (PAI-1)

Adipose tissue is an important organ which produces cytokines that are involved in inflammatory and thrombotic pathways. Examples of such cytokines include tumor necrosis factor- alpha (TNF-α), interleukin-6 (IL-6), C-reactive protein (CRP), and plasminogen activating inhibitor-1 (PAI-1) (121). It has been proposed that these "adipokines" may be an important factor linking central obesity to other risk components of the metabolic syndrome (122).

Subcutaneous adipose tissue produces the cytokines TNF-α (123) and IL-6 (124). TNF-α, a pro-inflammatory cytokine, is associated with insulin resistance and is correlated with the amount of body fat accumulation (125). Obese individuals express 2.5-fold more TNF-α mRNA in subcutaneous fat tissue than lean controls, with a significant correlation between TNF-α mRNA and BMI (126;127). Dandona et al. (128) found a strong positive correlation between TNF-α mRNA expression in fat tissue and the level of insulin. The TNF-α system is complex and is often associated with increased energy expenditure and weight loss (129;130); however, data on the circulating levels of TNF-α in obese and individuals with type 2 diabetes are conflicting (129;130). IL-6 is believed to increase the level of CRP seen in obesity (131-133). IL-6 and CRP are increased in obesity (134) and are acute phase reactants associated with inflammation and an increased risk for cardiovascular disease (135) and may also play a role in insulin resistance (136).

Bastard et al. (136) found that weight loss in obese non-diabetic individuals slightly, but significantly decreased IL-6 levels from 2.78 pg/ml to 2.32 pg/ml ($p = 0.05$) after a weight loss of approximately 5-6 kg. A similar nonsignificant decline in CRP levels was also observed. Before weight loss, CRP levels were 6.3 ± 1.1 mg/l while after weight loss levels decreased to 4.3 ± 0.9 mg/l ($p = 0.14$). An increase in insulin levels, as seen in type 2 diabetes, have also been found to amplify the production of proinflammatory cytokines (137).

Other metabolic alterations exist in individuals with type 2 diabetes increasing cardiovascular disease risk. Increased levels of PAI-1 have been associated with obesity (138) insulin resistance and type 2 diabetes (139). The Insulin Resistance Atherosclerosis Study (IRAS) (140) found that plasma CRP and PAI-1 levels were higher in insulin-resistant subjects who later developed type 2 diabetes than in subjects who did not. Circulating PAI-1 levels are also elevated in patients with cardiovascular disease and may affect the progression of this disease (141). Individuals with type 2 diabetes often have abnormally high serum triglyceride levels and plasminogen activator inhibitor-1 (PAI-1) (142;143). In plasma, PAI-1 promotes clot formation, which plays a key role in the pathogenesis of myocardial infarction, stroke, and other cardiovascular events (144-147). Excessive serum insulin associated with type 2 diabetes and visceral adipose tissue, inhibits the mobilization of nonesterified fatty acids by decreasing the rate of lipolysis and consequently increasing the rate of resynthesis of triglycerides from nonesterified fatty acids that are formed from lipolysis (148). The presence of visceral adiposity, insulin resistance and type 2 diabetes also increases the levels of PAI-1 (149;150). Metabolic products

such as triglycerides, free fatty acids, glucose, insulin, and TNF-α can stimulate PAI-1 release from fat and other tissues (151-159). Both visceral and subcutaneous adipose tissue express PAI-1 (138); however, PAI-1 is primarily secreted by visceral adipose tissue (160). PAI-1 increases thrombosis and decreases the breakdown of blood clotting leading to greater adhesion of platelets to the endothelial wall (150). Weight loss decreases both triglyceride and PAI-1 levels in obese and type 2 diabetic individuals (161;162).

B. Adiponectin

Adiponectin a recently discovered 244-amino acid, adipose-specific protein (163) is found in high concentrations in peripheral circulation (164). Adiponectin is primarily released by subcutaneous adipose tissue compared with visceral adipose tissue (165). Adiponectin secretion is stimulated by insulin (78) and it has been shown that serum levels of adiponectin correlate with systemic insulin sensitivity (166). It is believed that reduced levels of adiponectin may play a role in the pathogenesis of obesity and type 2 diabetes (166); however, a physiological role has not been fully established.

Decreased adiponectin concentrations are associated with insulin resistance and hyperinsulinemia (78). In contrast to leptin, adiponectin levels are significantly reduced not only in obese subjects (122;167;168), but also in patients with some of the disease states associated with obesity, such as type 2 diabetes (168;169) and coronary heart disease (170). In addition, high adiponectin concentrations are associated with a reduced risk of type 2 diabetes (171). Adiponectin levels are

inversely associated with central or overall adiposity, as well as hyperlipidemia and insulin resistance independently of BMI (172;173).

Data are inconsistent in the literature as to adiponectin and its correlations between various metabolic markers. Yamamoto et al. (172) found that plasma adiponectin was negatively correlated with BMI, systolic and diastolic blood pressure, fasting plasma glucose, insulin, insulin resistance, total cholesterol, LDL-cholesterol, triglycerides and uric acid and positively correlated with HDL-cholesterol in normal-weight subjects. Cnop et al. (174) found similar results. These researchers found plasma adiponectin concentration was negatively correlated with BMI, percentage of body fat, fasting insulin concentration, and plasma triglycerides but positively with HDL (174).

Shetty et al. (175), found a positive correlation of adiponectin with HDL and a negative correlation adiponectin with triglycerides, CRP, and PAI.. However, there was no association between adiponectin with total cholesterol, LDL-cholesterol and TNF-α. Consistent with Shetty and colleagues, other data indicate that adiponectin has been associated with markers of inflammation, such as CRP and TNF-α (176;177). Overall, this adipocyte-derived cytokine may exert anti-inflammatory, anti-fibrotic and anti-atherogenic effects and may be beneficial in the treatment of insulin resistance, diabetes, vascular complications and atherosclerosis (178).

Research findings vary related to weight reduction and adiponectin change in non-diabetic and diabetic patients (179). Valsamakis et al. (180) found a 27% increase in serum adiponectin ($p= 0.04$) with a 5.4% weight loss in Caucasian non-diabetic women. In contrast, Wolfe et al. (181) concluded that after a weight loss of

3.4 $\pm$ 2.1 kg weight loss adiponectin concentrations decreased significantly by 16.2% (p=0.04). Finally, Monzillo et al. (182) found that adiponectin levels increased significantly in subjects with type 2 diabetes (p=0.01), but not in individuals with impaired glucose tolerance or normal glucose tolerance.

C. Resistin

Resistin is a member of the newly discovered cysteine-rich secretory protein family referred to as RELM or FIZZ. Resistin is more highly expressed in both abdominal visceral and subcutaneous adipose tissue compared with adipose tissue from other areas of the body (183). Several small studies have reported that circulating resistin levels are increased in human obesity (184-187) and diabetes (188-192). A study in rats conducted by Shuldiner (193) demonstrated that obesity induced by diet as well as in genetic models of obesity and insulin resistance is associated with increased resistin levels (193). Resistin has also been found to increase blood glucose and insulin concentrations in mice (193). Furthermore, resistin gene expression is markedly down-regulated by treatment with the anti-diabetic drugs thiazolidinediones, which improve target-tissue sensitivity to insulin. A possible role for resistin in the inflammatory processes is suggested (78).

Steppan et al. (194) have proposed that resistin is increased in type 2 diabetes and suggested that it is a potential link between obesity and insulin resistance. However, the role of resistin in obesity and insulin resistance in humans is controversial. Youn et al. (190) found that there is more serum resistin protein in obese than lean individuals; however resistin concentrations were elevated in patients with type 2 diabetes but were not associated with insulin resistance or obesity. These

researchers also found that BMI is a significant predictor of insulin resistance, but resistin adjusted for BMI was not. On the contrary, Silha et al. (195) demonstrated a significant correlation between resistin levels and HOMA-IR in obese subjects independent of BMI. Overall, there is controversy about whether if resistin plays a role in insulin resistance or is just associated with obesity.

The effect of weight loss on resistin levels has also shown conflicting results and the majority of the studies have been conducted in non-diabetic subjects only. Valsamakis et al. (180) found a 16.8% decrease in serum resistin ($p=0.02$) with a 5.4% weight loss in Caucasian non-diabetic women. Similarly, Azuma et al. (185) found that in non-diabetic individuals who lost 1 kg or more of fat mass, resistin levels decreased significantly ($-17 \pm 19\%$, $p<.0.01$). In contrast Wolfe et al. (181) did not find a significant change in resistin in healthy, normal weight women after weight loss. And finally, Monzillo et al. (182) found that in insulin-resistant individuals there was no significant change in resistin levels after a weight loss of 6.9 ± 0.1 kg. Figure 2.5 provides a schematic summary of the adiposity and stomach signals on their positive or negative effects on weight and cardiovascular risk.

Weight Loss

A. Very-Low-Energy Diets (VLED) and Low-Energy Diets (LED)

Very-low energy diets (VLED) and low-energy diets (LED) are medically-supervised diet programs. VLEDs provide 500 to 800 kcal/day, whereas low-energy diets (LED) provide 800 to 1200 kcal/day. The active phase of these programs commonly lasts from 12 to 16 weeks. During this time, VLEDs promote a weight loss of approximately 14 to 23 kg and 9 to 13 kg with LEDs. In three of the four

studies comparing VLEDs to hypocaloric-balanced diets, VLEDs resulted in 4 to 12 kg greater weight loss than the reduced-energy diets consisting of 1,000 to 1,800 kcal/day at the end of the active weight loss phase (196-198). These comprehensive, medically-supervised diets have been found safe and appropriate for the treatment of obesity in individuals with type 2 diabetes (199), however, due to increased expense of the VLED, LED are commonly used in clinical practice (200).

Often individuals who follow conventional weight reducing diet techniques lose minimal amounts of body weight. For example, Markovic et al. (161) found a 6.2 $\pm$ 0.4 kg weight loss with a caloric restriction of 1,000 kcal/day. Metz et al. (201) found that women lost 4.8 $\pm$ 3.0 kg following a 10-week prepared meal plan and individuals following a 10-week self-selected mixed-food plan lost 2.8 $\pm$ 2.8 kg. Faith et al. (202) summarized weight loss treatment by behavior therapy and conventional reducing diet techniques. They reported more positive results from the 5 studies they summarized and concluded that individuals lost 8.5 kg during a 21.3 week treatment.

Individuals with type 2 diabetes have a more difficult time losing weight with the conventional and behavioral approaches to weight loss compared to non-diabetics. McCarron et al. (203) found that with a prepared meal plan (Campbell's Center for Nutrition and Wellness meal program [CCNW]) women with type 2 diabetes lost 4.8 $\pm$ 3.0 kg and individuals who consumed a self-selected diet based on exchange lists lost 2.8 $\pm$ 2.8 kg of body weight. In a continuation of the study, Pi-Sunyer et al. (73) compared the CCNW and self-selected diet programs in individuals with type 2 diabetes and found that weight losses were 3.4 $\pm$ 3.1 kg and 2.9 $\pm$ 2.8 kg,

respectively. Wing et al. (204) found similar results in individuals with type 2 diabetes. During a 16-week energy restricted diet, subjects lost 4.7 $\pm$ 3.9 kg of body weight. In one study type 2 diabetic women were able to lose as much weight as non-diabetic subjects (6.8 kg); however, the type 2 diabetic subjects were not able to maintain the weight loss as well as the non-diabetic women (75).

B. Type 2 Diabetes Mellitus and Weight Loss

Treatment goals for individuals with type 2 diabetes are to promote weight loss and to improve glycemic control, thus the initial treatment choice for individuals who are overweight or obese with type 2 diabetes is weight loss. Weight loss improves insulin sensitivity due to increased non-oxidative glucose disposal (205). Consequently, type 2 diabetic individuals display improved glycemic control and reduce insulin resistance with weight loss (206;207). Weight loss in these individuals will also lower blood pressure and improve their serum lipid concentrations (208).

Several researchers have shown that VLED treatment may be beneficial in obese type 2 diabetics, both from weight and glycemic control points of view (113;199;209;210). Previous studies have shown that during VLED treatment, reduction in blood glucose levels occurs rapidly with the first 7 to 14 days (199;210). Capstick et al. (211) found that after a 12 week VLED program with type 2 diabetics that blood glucose levels fell rapidly at the onset of the VLED. The median fasting and postprandial blood glucose levels fell by 25% and 20% respectively after 2 days of treatment. There was a significant decrease in weight, waist circumference, HbA1c, systolic blood pressure, fasting plasma insulin, and total cholesterol and triglyceride levels. All subjects discontinued using insulin and the use of oral diabetic

agents decrease dramatically. Moreover, reduction in waist circumference following a VLED treatment is also important. As recent data suggest, a high waist circumference increases the risk of cardiovascular disease (212).

In a quantitative analysis of individuals with type 2 diabetes and the use of LED therapy, Anderson et al. (213) found that a greater weight loss was associated with a significant increase in HDL-cholesterol values (+3.9, 95% CI, 0.1 to 7.8) while lesser weight loss was associated with a significant decrease in HDL-cholesterol values (-5.9, 95% CI, -9.4 to -2.3). This is consistent with our previous analysis conducted in individuals without type 2 diabetes (25).

Greenfield et al. (214) reported that a 10-day total fast with weight loss of 5.1% of initial body weight decreased fasting plasma glucose values in type 2 diabetic subjects by 64% (from 17.2 mmol/L to 6.1 mmol/L). Anderson et al. (213) quantified 10 studies of subjects treated with a VLED for 4 to 6 weeks. Subjects lost 9.6% of initial body weight and after 2 weeks of VLED treatment, fasting plasma glucose decreased by approximately 50% of their fasting plasma glucose. This decrease in plasma glucose remained throughout the VLED treatment. Anderson et al. (213) also quantified the fasting plasma glucose response in type 2 diabetes during LED weight loss programs. The results indicated that fasting plasma glucose values decrease approximately 30% with a weight loss of 10 kg. However, consistent with previous studies (113;209), they concluded that greater weight loss was associated with greater improvements in plasma glucose values. Anderson and Konz (25) estimated that for every 1 kg of weight loss in individuals with type 2 diabetes you can expect approximately a 0.2 mM (3.6 mg/dl) decrease in fasting glucose concentrations.

The importance of alleviating these co-morbid risk factors associated with type 2 diabetes has stimulated the research presented here to evaluate the effects of a low-energy diet (LED) weight loss program on the health risk factors associated with type 2 diabetes.

Table 2.1 Classification of Body Mass Index (BMI) to Assess Obesity.

WHO Classification	**Popular Description**	**BMI (kg/m^2)**	**Risk of Co-Morbidities**
Underweight	Thin	< 18.5	Low (but risk of other problems increased)
Healthy Weight	Normal	18.5 - 24.9	Average
Overweight		> 25.0	
Pre-obese	Overweight	25.0 - 29.9	Increased
Obese Class I	Mild Obesity	30.0 - 34.9	Moderate
Obese Class II	Moderate Obesity	35.0 - 39.9	Severe
Obese Class III	Severe Obesity	> 40.0	Very severe

Table 2.2 Deaths and Percentage of Total Deaths for the 10 Leading Causes of Death: United States, 2002. Taken from the National Vital Statistics Report (13).

Rank	Cause of Death	# of Deaths	Percentage of Total Deaths
	All causes	2,443,387	100
1	Diseases of heart	696,947	28.5
2	Malignant neoplasms	557,271	22.8
3	Cerebrovascular diseases	162,672	6.7
4	Chronic lower respiratory diseases	124,816	5.1
5	Accidents (unintentional injuries	106,742	4.4
6	Diabetes Mellitus	73,249	3
7	Influenza and pneumonia	65,681	2.7
8	Alzheimer's disease	58,866	2.4
9	Nephritis, nephrotic syndrome and nephrosis	40,974	1.7
10	Septicemia	33,865	1.4

Table 2.3 ATP III Clinical Identification of the Metabolic Syndrome (48).

Risk Factor	Defining Level
Abdominal obesity, given as waist circumference	
Men	>102 cm (>40 inches)
Women	>88 cm (>35 inches)
Triglycerides	≥150 mg/dL
HDL cholesterol	
Men	<40 mg/dL
Women	<50 mg/dL
Blood pressure	≥130 / ≥85 mmHg
Fasting glucose	≥110 mg/dL

Figure 2.1 Pathogenesis of Health Problems Associated with Obesity. Adapted from Bray (215).

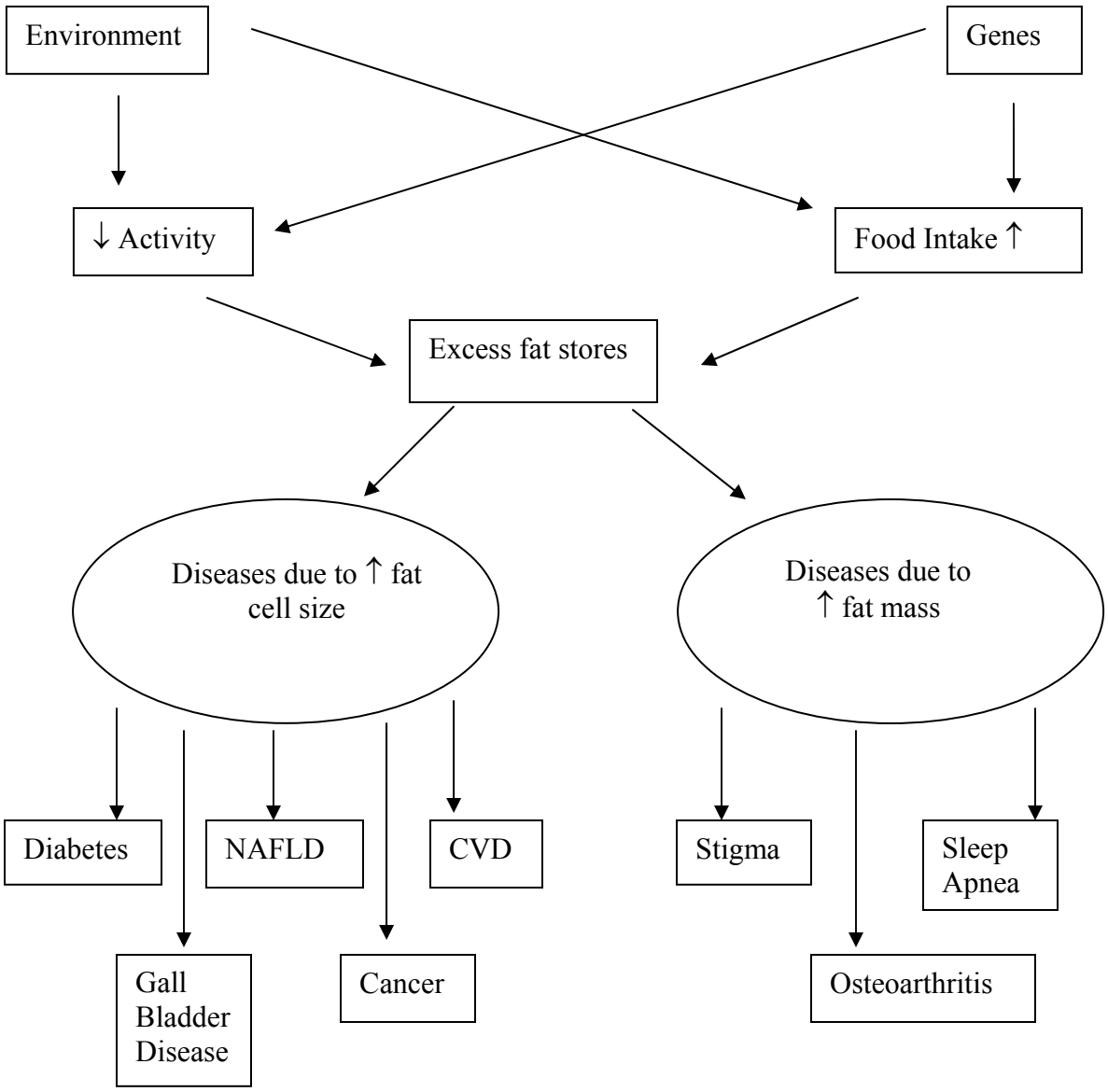
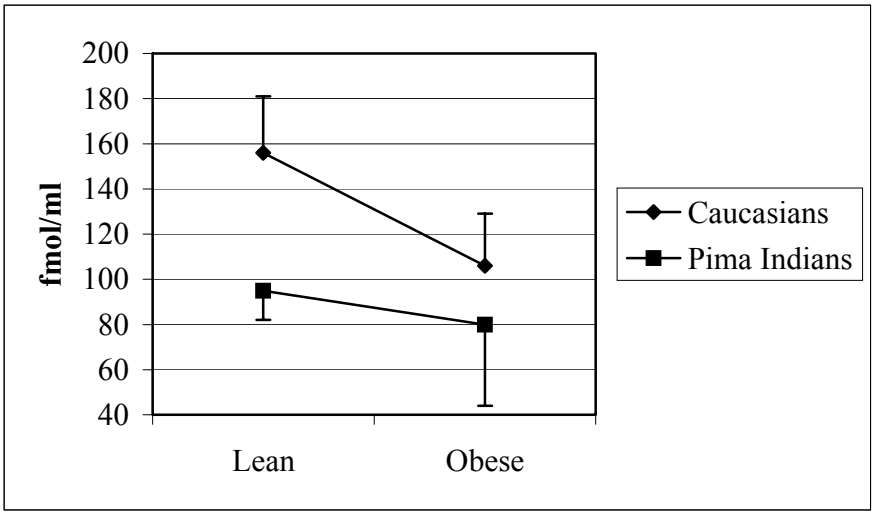


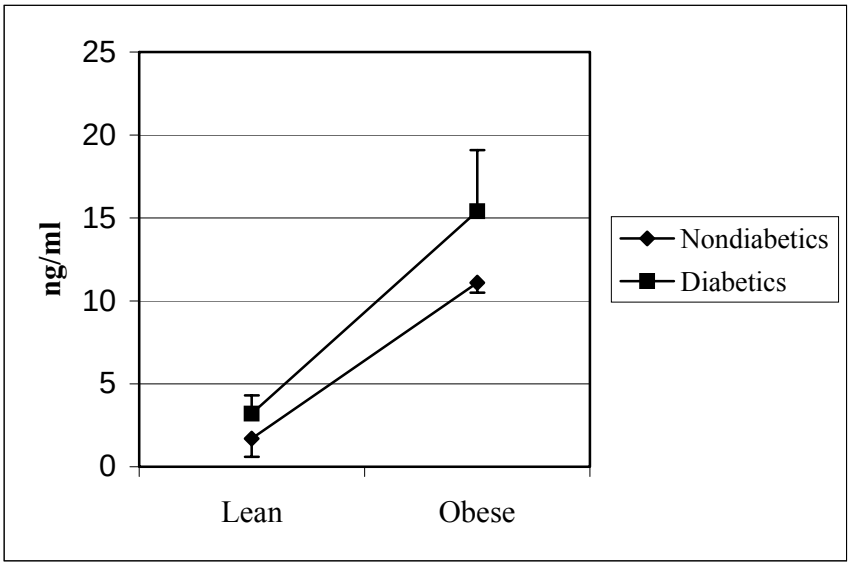
Figure 2.2 Serum Ghrelin (a) and Leptin (b) Levels in Lean and Obese Individuals With and Without Type 2 Diabetes.

(a) Ghrelin



*Data from Tschöp et al. (100)

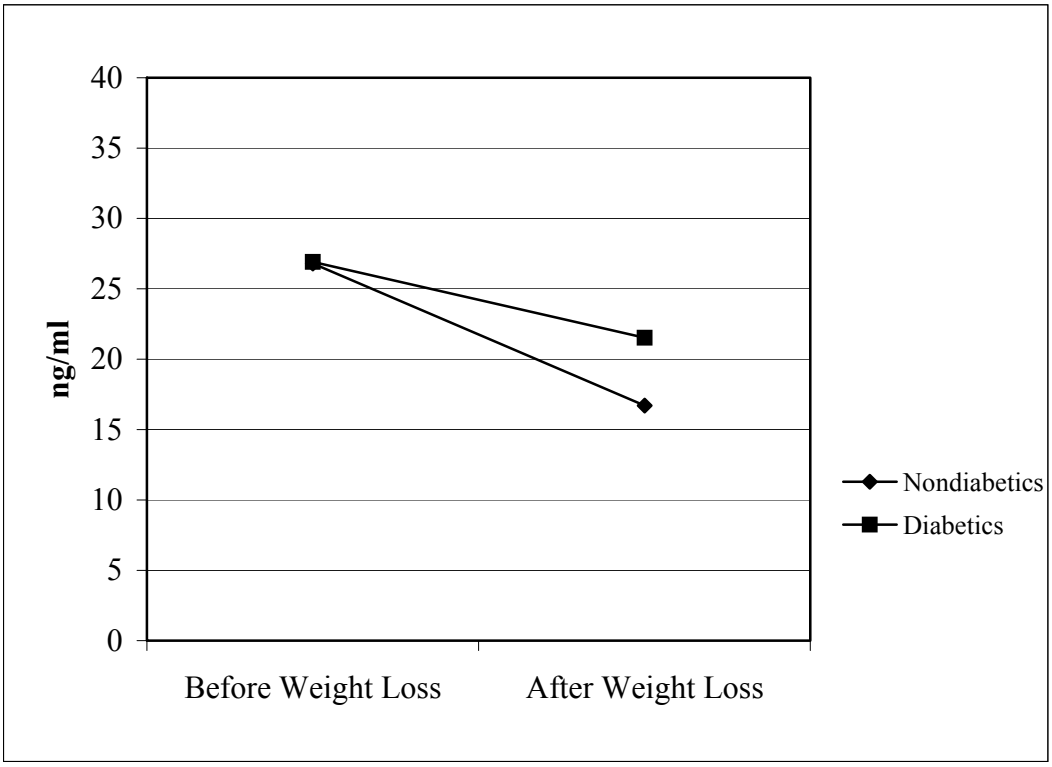
(b) Leptin



*Data from Misra et al. (216)

*Leptin values are expressed as square root transformations

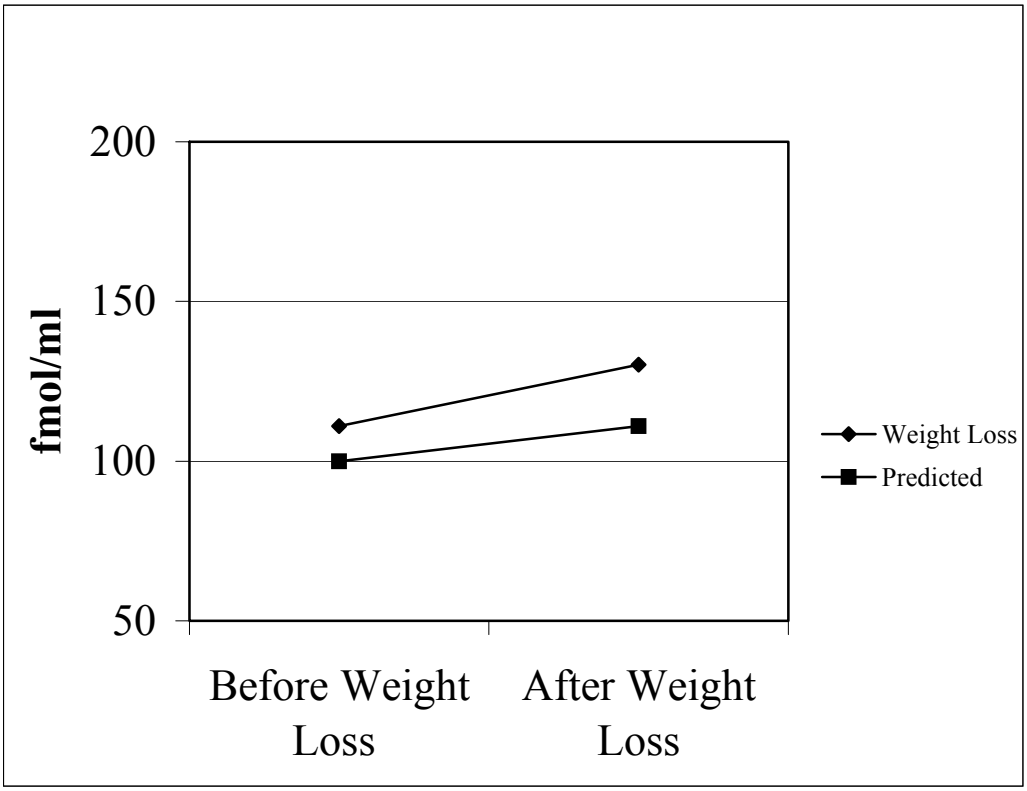
Figure 2.3 Changes in Leptin Response to Weight Loss.



* Data for Non-diabetic individuals (Cummings et al.) (105)

* Data for Diabetic individuals (Williams et al.) (90)

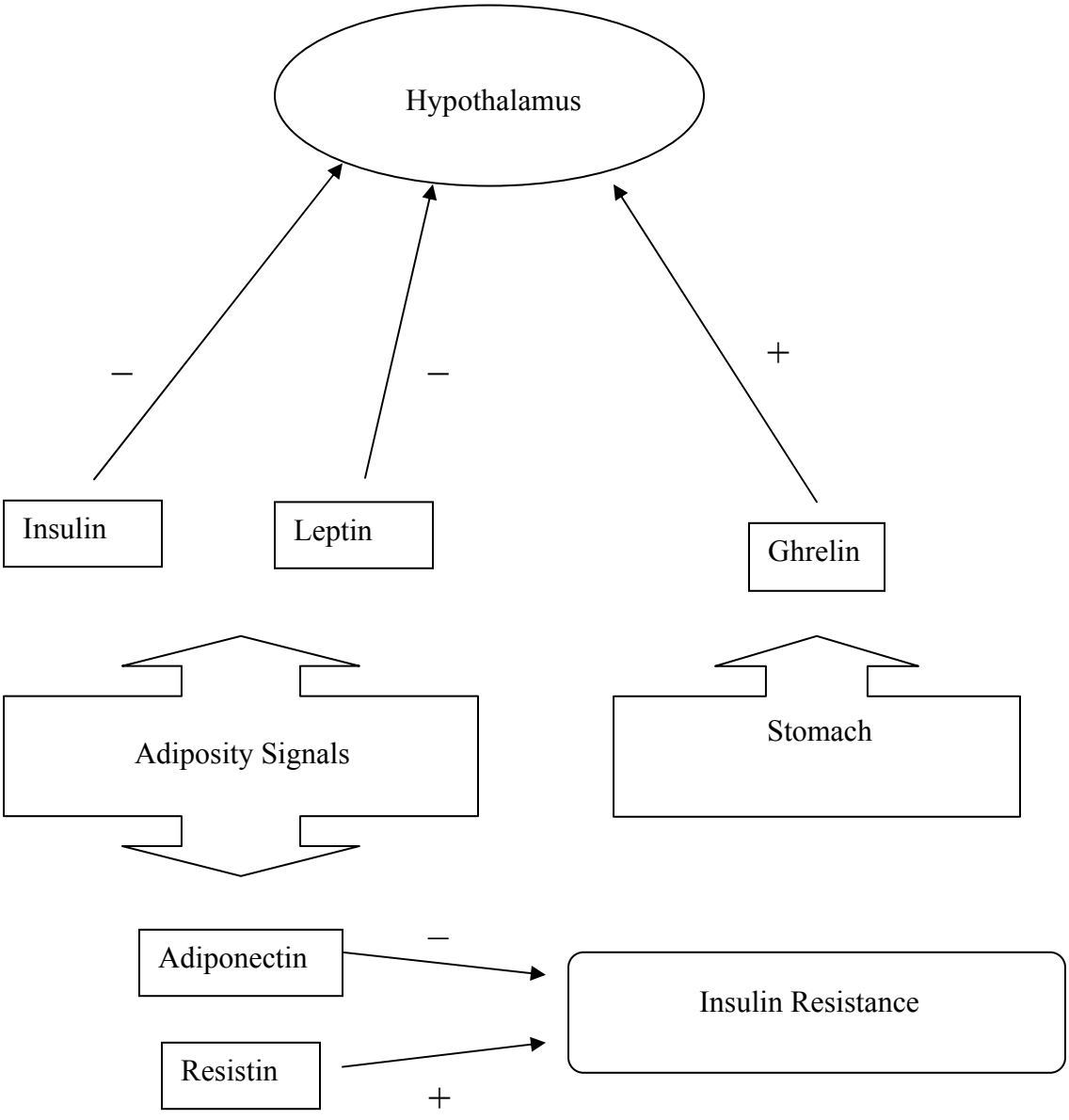
Figure 2.4 Changes in Ghrelin Response to Weight Loss.



* Data for weight loss taken from Cummings et al. (105)

* Predicted is the hypothesized response before and after weight loss in obese individuals with type 2 diabetes.

Figure 2.5 Schematic Summary of Hormone and Adipokines on the Hypothalamus.



CHAPTER THREE

Experimental Design and Methods

Overview

Obese, Caucasian women with and without type 2 diabetes participated in the study. Subjects were between the ages of 40 and 65 years with a BMI between 30 and 45 kg/m^2. Subjects without type 2 diabetes mellitus were matched with women with type 2 diabetes for age and BMI. Subjects participated in a 16-week medically-supervised low-energy diet (LED) weight loss program after a 2 to 4-week run-in period to determine body composition, current metabolic parameters, and to regulate diabetic medications.

Study Participants

Caucasian women with a BMI between 30 and 45 kg/m^2, between the ages of 40 and 65 years were recruited to participate in the study. Subjects were not currently dieting or taking weight loss medications. The health of each subject was stable without severe coronary artery disease, cerebrovascular disease or recent myocardial infarction.

A. Inclusion Criteria

- Women ages 40 to 65 years;
- Caucasian; and
- BMI 30 to 45 kg/m^2.

B. Exclusion Criteria

- Pregnancy, lactation or plans to become pregnant in the next 6 months;

- TSH $\geq$6 μU/ml;
- Severe coronary artery disease, cerebrovascular disease or recent myocardial infarction or any other serious medical condition;
- Recent history of alcohol abuse with current intake of $\geq$ 2 drinks per day;
- Use of weight reducing agents, such as phentermine, sibutramine, orlistat, bupropion, or an herbal weight loss product within the last eight weeks;
- Psychosis or other major psychiatric problems including severe depression;
- Chronic corticosteroid therapy;
- Chronic use of non-steroidal anti-inflammatory drugs (NSAIDs) or COX inhibitors which include the following: Advil®, Aleve®, Naprosyn®, Celebrex®, Voltaren®, Lodine®, Indocin®, Orudis®, Oruvail®, Daypro®, Relafen®, Clinoril®, Tolectin®, Vioxx®, or Bextra® ;
- Currently taking thiazolidinedione medications (Rosiglitizone, Pioglitazone);
- Uncontrolled hypertension with:
    - systolic blood pressure >140 mmHg; or
    - diastolic blood pressure >90 mmHg
- Those who, in the opinion of the principal investigator, have a risk of non-compliance with study procedures.

C. Exclusion criteria specific for subjects with type 2 diabetes

- HbA1c < 6.0% or >10%.

D. Exclusion criteria specific for subjects without type 2 diabetes

- A combination of 2 or more of the following:
    - Triglyceride >150 mg/dl

- HDL <50 mg/dl
- High blood pressure (systolic blood pressure >130 mmHg, diastolic blood pressure >85 mmHg); or
- Fasting blood glucose levels >110 mg/dL (6.1 mmol/L).

Participation of Women and Members of Minority Groups

Caucasian women were selected for study because approximately 80 percent of participants in our community who attend the Health Management Resources weight-loss program are Caucasian women. Body composition for various ethnic groups is also different. Weinsier et al. (217) found despite similar weight losses, Caucasian women lost a greater percentage of abdominal fat as intraabdominal fat and less subcutaneous abdominal fat compared with black women; therefore to reduce heterogeneity in this pilot study only Caucasian subjects were recruited.

Participation of Children

Children did not partake in this study because they do not meet the entry criteria of the study. Also, the body composition of prepubertal individuals is different from adults and thus the changes would not be comparable.

Recruiting Potential Subjects

Participants were recruited by newspaper advertisements in Lexington Kentucky and surrounding communities. Announcements were posted in the Medical Center of the University of Kentucky. In addition, physicians at University of Kentucky Medical Center were asked to inform obese patients of the study for their possible recruitment. Potential research candidates were screened by phone to determine the individual's age, gender, and general health status. Subjects were then

asked to attend an Orientation at HMR and if the subject was still interested a screening visit was scheduled.

Weight Loss Protocol

Research subjects participated in the Health Management Resources (HMR®) weight loss program. HMR® is a commercial medically-supervised low-energy diet (LED) program consisting of dietary supplements and entrees providing complete nutrition. Table 3.1 lists the macronutrient composition of the HMR® 800 supplements for the LED consisting of 800 kcal/day if five shakes are consumed. Individuals attending HMR® are categorized into risk groups depending on initial BMI, age, medical history and presence of other co-morbid conditions associated with obesity such as hypertension, coronary heart disease, and diabetes. In this research study, subjects met the requirements of the medically-supervised risk group and were prescribed the minimum 800 kcal/day LED. Subjects consumed only HMR® products during the sixteen-week weight-loss phase allowing for control over dietary intake. Individuals participated in either the 3 + 2 HMR® program which consists of a minimum of 3 HMR 800® shakes and 2 entrees or consumed a minimum of five shakes per day. During the LED program, two HMR® vitamins were prescribed each day. Patients had the option to supplement with other HMR weight loss products as well such as Benefit Bar® or HMR Chicken soup®.

The HMR® program (218) insists that individuals attend weekly classes and make midweek phone calls to aid in the individual's accountability for their weight loss. Individuals must also keep daily records of the number of meal replacements consumed, caloric intake, and daily physical activity. This information is collected

by the health educator and recorded into a form referred to as "Patient at a Glance". Other information collected in the Patient at a Glance form is if the individual meet the requirements of The Triple Imperative™. Figure 3.1 explains the requirements for an individual to meet The Triple Imperative™. The Triple Imperative™ includes the skills that control the highest degree of variability in an individual's weight loss efforts. Finally, the number of days the individual meets their daily requirements of meal replacements, physical activity and not consuming food products not on the diet are recorded on the Patient at a Glance form. This is referred to as the number of days "in the box." The most common side effects of a LED program include dizziness, low energy, bowel changes, muscle cramps and cold intolerance (218).

Weight Loss Safety

The use of a LED in this population has been determined to be safe. For example, a woman 5'2" would not be at risk for the following reasons:

1. If this woman had a BMI of 30 kg/m^2 her body weight would be approximately 164 lbs or 74.5 kg. At an optimal BMI of 22 kg/m^2 her ideal body weight would be 122 lbs.
2. Using the recommended equations for women between the ages of 31 to 60 by the World Health Organization (WHO)(219) for estimating basal metabolic rate (BMR): BMR = (0.0342 X 74.5 kg + 3.5377) X 240 kcal/day = 1461 kcal/day
3. For the given body weight, the amount of energy burned walking one mile can be calculated by: Body weight (lbs) X 2/3 = kcal/mile

   164 X 2/3 = 109 kcal/mile

   This would result in approximately 765 kcal energy expenditure per week.

4. The total daily energy needs would equal 2226 kcal. When you subtract the 800-1000 kcal provided by the dietary supplements, the individual is in a caloric deficit of 1326 kcal. This caloric restriction would approximate a 2.5 lb per week weight loss. With an anticipated 2.5 lb. per week weight loss the individual would be expected to lose 40 lbs or approximately 15% of their initial body weight. This would result in an anticipated end body weight of 124 lbs and thus the individual would not be at risk during this study.

Study Procedures

Table 3.2 outlines procedures completed at each visit throughout the trial. Visits are described according to week of the study. Week -3 is the screening visit and is considered Baseline. Week -1 is the first visit at the General Clinical Research Center to obtain Baseline body composition and blood measurements. This visit is sometime prior to the initiation of the weight loss diet. Week 0 is the initiation of the weight loss diet. Weeks 1 through 16 are the weeks the subjects are active in the weight loss program.

Body Composition Analysis

Body composition analysis was conducted at the University of Kentucky General Clinical Research Center (GCRC) and the Diagnostic Radiology Department at the University of Kentucky Medical Center. Total and regional body composition was measured with dual-energy x-ray absorptiometry (DEXA), air displacement plethysmography (BOD POD®) and computer tomography (CT) scans. As shown in Table 2, body composition analysis was conducted at weeks -1, 8, and 16 for DEXA and BOD POD® and at weeks -1 and 16 for CT.

A. Dual-Energy X-Ray Absorptiometry (DEXA)

The procedure for the DEXA scan was that as Kamel et al. (220) who used a standard whole body DEXA examination, which included total body and three regional measurements of trunk (chest, abdomen and pelvis), arms and legs to analyze body composition according to the three-compartment model (fat mass, lean mass and bone mineral content). The standard soft tissue analysis was performed using the software provided by the manufacturer. The GE Lunar Prodigy™ (Madison, WI) was used to conduct the scans. Total body fat was estimated for each subject in kilograms. Subjects were informed not to wear any metal for the scan. The scan takes approximately 12 minutes.

B. Air Displacement Plethysmography (BOD POD®)

The procedure to determine total body volume and percent body fat using the BOD POD® requires subjects will sit quietly in a specifically designed chamber (Life Measurement Instruments, Concord, CA) using an air displacement technique. The BOD POD® chamber has a clear plastic window at the level of the subjects' face so that they may view the room outside of the chamber and receive directions by hand gestures from the technician. The first two air displacement measurements consist of the subject sitting quietly for approximately one minute. The third measurement their thoracic lung volume measurements are determined using a spirometer technique. This technique requires the subject to breath normally into a plastic tube for 2 inhalations and one exhalation followed by 3 puffs. The total measurement times took approximately 5-10 minutes.

C. Computer Tomography (CT)

The visceral and subcutaneous abdominal fat masses were determined by abdominal CT scans by the department of Diagnostic Radiology at the University of Kentucky Medical Center using a Siemens Somatom Plus 4 and a Plus 10 (Munich, Germany). Computer tomography procedures were followed as performed by Akazawa et al. (221), for the determination of the separation of abdominal fat tissues. The CT scan was performed at the L4-L5 lumbar with the subject resting in the supine position. The total area of the cross-sectional fat region (i.e., including both subcutaneous and visceral fat) at the umbilical level were traced inside the skin to calculate the total number of pixels showing CT values between -50 and -150 HU. The visceral fat area was traced manually along the inside of the abdominal wall and the number of pixels showing the same range of CT values will be calculated for this region. The reading of the abdominal scans was conducted by a radiology resident at the University of Kentucky Medical Center.

Body Weight, Waist Circumference and Blood Pressure

Body weight was measured on an electronic scale to the nearest 0.1 pound. Waist circumference was be determined by obtaining the minimum circumference (minimum circumference between the lower-rib margin and the iliac crest, mid-waist) and the maximum hip circumference while standing with their heels together. This was conducted by the same person at the screening visit and the final visit at the GCRC. Blood pressure, measured using a sphygmomanometer, was obtained at the screening visit and at each visit to the GCRC. At the weight loss clinic, a registered

nurse measured body weight and blood pressures of each subject prior to each weekly behavioral HMR® class.

Physical Exams and Blood Analysis

Physical examinations including a health history and an electrocardiogram (ECG) were conducted at the screening visit at the Metabolic Research Group (MRG) and at the final visit at the GCRC. Limited physical examinations were performed at weeks 4, 8, and 12. The physical exams performed at HMR® were conducted by both attending physicians and medical residents. Fasting blood samples were taken at the GCRC at weeks -1, 8, and 16 and analyzed at the laboratory for a complete metabolic panel, a lipid profile, a complete blood count with differential and platelets (CBC), and measurements of ghrelin, leptin, insulin, interleukin-6 (IL-6), tumor necrosis factor- alpha (TNF-α), plasminogen activator inhibitor-1 (PAI-1), C-reactive protein (CRP), adiponectin, resistin, HbA1c, and follicle-stimulating hormone (FSH). At weeks 4 and 12 standard safety blood tests consisting of a complete metabolic profile, lipid profile and CBC were taken at HMR®. At week -3, the screening visit blood tests consisting of a complete metabolic profile, lipid profile, and CBC were taken along with TSH to check for thyroid defects.

Screening and safety laboratory measurements were conducted by Quest Diagnostics and LabCorp. Leptin, adiponectin, resistin, IL-6, TNF-α, CRP and FSH values were determined by the General Clinical Research Center Core Laboratory. Leptin, adiponectin, high sensitivity IL-6 and high sensitivity TNF-α were analyzed with Elisa assays from R & D Systems (Minneapolis, MN) and resistin, CRP and FSH were analyzed using Elisa techniques from ALPCO Diagnostics (Windham,

NH). Total ghrelin and total plasminogen activating inhibitor-1 were analyzed by LINCO Diagnostic Services, Inc. (St. Charles, MO). Total ghrelin was analyzed with RIA in pg/ml. Total PAI-1 was analyzed by Human Adipokine Lincoplex in pg/ml. Insulin, complete metabolic panel and lipid profiles were analyzed by the University of Kentucky Clinical Laboratory.

Statistical Analysis

The contrast of interest used to determine effect size was the differences in the amount of body weight that obese women with type 2 diabetes compared to obese women without type 2 diabetes lose after a weight-reducing LED. This contrast is likely to also give meaningful trends in ghrelin and body composition. Data are not available to provide adequate means and standard deviations to determine these contrasts. However, the present research will be able to provide a solid basis for further research and hypothesis development in these areas.

Power analysis was conducted using a two-sample t-test to determine the number of subjects required for the study. After review of the literature regarding changes in body weight in obese women with type 2 diabetes and obese women without type 2 diabetes, means of 9.2 kg and 12.3 kg change in body weight were used to determine power with a standard deviation of 3.8. The test was 1-sided and utilized a power of 0.8 and an alpha of .05. The power analysis revealed that with a beta of .80, 20 subjects would be needed in each group to find significance. We choose 25 subjects to participate in each group to allow for less than a 20 percent attrition rate.

Analysis of baseline scores of the dependent variables was analyzed using a one-way ANOVA to determine if obese individuals with type 2 diabetes and obese individuals without type 2 diabetes mellitus are comparable.

The original statistical analysis of the primary outcome variables body weight, decreased leptin response and increased ghrelin response were to be analyzed by repeated-measures analysis using the PROC MIXED model of SAS version 8.02. The variable of initial body weight and several of the other outcome measurements such as subcutaneous and visceral adipose tissue were determined to be significantly different at baseline. Thus, the PROC MIXED model was not an appropriate analysis for this study. Instead we modified the mixed model to include baseline as a covariate and thus used analysis of covariance (ANCOVA) to determined changes in the outcomes. The ANCOVA analysis is a combined regression analysis with an analysis of variance and thus takes differences in baseline values into account. All primary and secondary outcome variables were analyzed by ANCOVA analysis. Two-sample student's t-test assuming unequal variances were also used to determine if there were absolute differences in the outcome variables for each time point since the sample sizes for each group were not the same. Pearson's correlation was used to determine relationships between variables at week 16.

Table 3.1 Nutrient Compositions of the HMR® Dietary Supplements Based on the Consumption of 5 Packets per Day.

Nutrient	HMR 800
Calories, kcal	800
Protein, g	80
Carbohydrate, g	97
Fat, g	10
Fiber, g	2 to 5
Cholesterol, g	65
Sodium, mg	1250

Table 3.2 Outline of the Procedures and Measurements Taken Throughout the Clinical Trial.

Week	-3	-2	-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
Body Weight, Waist Circumference and Blood Pressure	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Physical Exam	X							X[a]				X[a]				X[a]				X
Blood Tests	X[b]		X[c]	X[d]				X[d]				X[c]				X[d]				X[c]
Body Composition			X									X[e]								X

[a] Limited medical visits will be conducted at week 4, 8, and 12.
[b] Includes dietary history, screening and safety blood tests consisting of a complete metabolic profile, lipid profile, CBC with differentiation and platelets, HbA1c and FSH.
[c] Includes a complete metabolic panel, lipid profile, CBC with differentiation and platelets, ghrelin, leptin, insulin, HOMA-IR, adiponectin, resistin, IL-6, TNF-α, tPAI-1, CRP, HbA1c, and FSH.
[d] Includes screening and safety blood tests consisting of a complete metabolic profile, lipid profile, and CBC with differentiation and platelets. At week 4 and 12 this will be taken at the HMR facility.
[e] Includes only DXA and BOD POD® at week 8, DEXA and CT scans will both be conducted at weeks -1 and 16.

Figure 3.1 Requirements of The Triple Imperative™ which the HMR® Program Considers the Skills Necessary to Control the Greatest Degree of Variability in an Individual's Weight Management Efforts.

The Triple Imperative™

1. Minimum of 2,000 calories of physical activity (PA) per week.

2. Minimum of 35 servings of vegetables and fruits per week
   (for Healthy Solutions® and Maintenance only, not considered for this study)

3. Use of meal replacements

   - Weight loss: minimum of 35 meal replacements per week
   - Maintenance: minimum of 14 meal replacements per week

CHAPTER FOUR

Results

Participant Characteristics

Forty-two subjects were screened for the study. Of these 42 subjects, 8 subjects failed the screening criteria and 32 subjects were randomized into the study. One individual chose not to participate in the study prior to randomization. Three individuals discontinued from the study, one due to family issues and the others were not committed to the weight loss diet. Twenty-nine subjects have completed the study. The attrition rate for this study was 9.4%.

Table 4.1 presents characteristics of the study participants who completed the study. Eleven Caucasian non-diabetic females without the metabolic syndrome between the ages of 40 to 57 years and 18 Caucasian diabetic females between the ages of 41 to 64 years were recruited for the study. The mean Body Mass Index (BMI) was 36.1 $\pm$ kg/m^2 and 38.0 kg/m^2, for non-diabetic and diabetic subjects, respectively. The mean Body Mass Index (BMI) for completers was 36.1 $\pm$ 3.9 kg/m^2 and 38.1 $\pm$ 3.7 kg/m^2 for non-diabetic and diabetic women, respectively. Study participants were matched for age and BMI.

Weight Loss

In a completer's analysis, non-diabetic subjects lost 15.4 kg of body weight resulting in a 16.0% decrease. Diabetic subjects lost 12.2 kg of body weight resulting in an 11.7% decrease. The average and the range of weight lost in kg are demonstrated in Figure 4.1 for completers. Figure 4.2 shows the percent reduction in body weight at weeks 0, 4, 8, 12, and 16. Analysis with two-sample t-test found

diabetic subjects weighed significantly more than non-diabetic subjects prior to weight loss, 105.6 kg and 96.4 kg (p=0.04), respectively. After initial weight was adjusted using ANCOVA, there was no significant difference in the total body weight in kg at baseline (p=0.5694), week 16 (p=0.6474) or percent weight loss (p=0.2621) after 16 weeks of weight loss between the two groups.

Using the intention-to-treat (ITT) or last-observation-carried-forward (LOCF) analyses, there was no significant difference in baseline weight between non-diabetic and diabetic subject, 96.4 kg and 104.5 kg, respectively (p=0.1087). However, using the ITT analysis weight losses were significantly different between non-diabetic and diabetic subjects. Non-diabetic subjects lost significantly more weight (-16.0%) than diabetic subjects (-10.9%, p=0.0029).

Body Mass Index (BMI)

Body mass index (BMI) was one of the parameters used to match the non-diabetic and diabetic subjects. In completer's there was no significant difference in BMI values between non-diabetic and diabetic subjects before weight loss, 36.1 kg/m^2 and 38.1 kg/m^2, respectively(p=0.2314). Baseline BMI values for ITT subjects were not significantly different, 36.1 kg/m2 and 38.0 kg/m2, for non-diabetic and diabetic subjects, respectively (p=0.2329). After 16-weeks of weight loss both groups were still considered to be obese. The non-diabetic completer subjects had reduced their BMI to 30.1 kg/m^2 which was a 16.7% reduction; while diabetic completer subjects reduced their BMI to 33.0 kg/m^2 which was a 13.3% reduction. There was no significant difference in BMI between the groups at week 16

(p=0.0720). ANCOVA analysis found no significance difference between the groups at week 0 (p=0.2216) or at week 16 (p=0.0608).

In non-diabetic subjects, BMI was positively correlated with leptin (p=0.0018), insulin (p=0.0466), and HOMA-IR (p=0.0362). In diabetic subjects, BMI was positively correlated with leptin (p=0.0018) and there was trend that BMI was positively correlated with insulin (p=0.0654), HOMA-IR (p=0.0950), and CRP (p=0.0697). In diabetic subjects, BMI was positively correlated with percent body fat (p=0.0176), subcutaneous adipose tissue (p=0.0114), visceral adipose tissue (p=0.003), and total fat (p<0.0001). In non-diabetic subjects, BMI was positively correlated with percent body fat (p=0.0079), subcutaneous adipose tissue (p<0.0001), and total fat (p<0.0001) and was approaching a significant positive correlation with visceral adipose tissue (p=0.0604). BMI was approaching a significant positive correlation with lean tissue in non-diabetic (p=0.0612), but not in diabetic subjects (p=0.3523).

Body Composition Measurements

A. Dual-Energy X-Ray Absorptiometry (DEXA)

Dual-energy x-ray absorptiometry (DEXA) was used to measure total percent body fat; percent body fat in the trunk; total fat; total fat in the trunk; total lean tissue; and total lean tissue in the trunk. Values of all body composition baseline values and changes throughout the study are shown in Table 4.2.

1. Percent Body Fat-Total

Total percent body fat determined by DEXA found that non-diabetic subjects had significantly greater percent body fat compared to diabetic subjects, 49.9% and

45.9% (p=0.0036), respectively. Figure 4.3 illustrates the percent body fat determined by DEXA at week 0, week 8 and week 16. There was a significant difference in the change of percent body fat between non-diabetic and diabetic subjects. Non-diabetic subjects decreased by 7.4, while diabetic subjects percent body fat decreased by 4.2 (p=0.043). This is apparent since there is no significant difference in total percent body fat between non-diabetic and diabetic subjects at week 16, 42.6% and 42.1% (p=0.8416), respectively. Adjusting for baseline percent body fat levels, ANCOVA analysis found no significant difference between groups after 16 weeks of weight loss.

In diabetic subjects percent body fat was positively correlated with subcutaneous adipose tissue (p=0.0035) and total fat (p=0.0001) and negatively correlated with lean tissue (p=0.0185). There was no correlation between percent body fat and visceral adipose tissue (p=0.1363) in diabetic subjects. Percent body fat was also found to be positively correlated with leptin (p=0.0011) in diabetic subjects, but no significant correlation was found between percent body fat and resistin (p=0.7121), ghrelin (p=0.6273), or HOMA-IR (p=0.4128). In non-diabetic subjects percent body fat was positively correlated with subcutaneous adipose tissue (p=0.0282), visceral adipose tissue (p=0.0350) and total fat (p=0.0151), but was not correlated with lean tissue (p=0.3568). Percent body fat was found to be positively correlated with leptin (p=0.0455), but not correlated with resistin (p=0.9718) in non-diabetic subjects. A trend that percent body fat was negatively correlated with ghrelin (p=0.0995) and HOMA-IR (p=0.0673) was observed in the non-diabetic subjects.

Percent body fat was not found to be correlated with CRP, IL-6, TNF-α, or adiponectin in either diabetic or non-diabetic subjects.

2. Percent Body Fat-Trunk

Percent body fat in the trunk of non-diabetic and diabetic subjects was significantly different at baseline, 51.2% and 47.3% (p=0.0135), respectively. Non-diabetic subjects significantly decreased their percent body fat in the trunk compared to diabetic subjects, -8.0% and 4.1% (p=0.0495), respectively. As found with total percent body fat, there was no significant difference in the percent body fat found in the trunk between non-diabetic and diabetic subjects at week 16, 43.2% and 43.2% (p=0.9765), respectively. This is consistent with the ANCOVA analysis that found no significant difference between the groups at week 16 (p=0.4258). Figure 4.4 shows the percent trunk fat determined by DEXA of study completers at week 0, week 8 and week 16.

3. Total Fat

The DEXA measurements found no significant difference in total fat at baseline between non-diabetics and diabetic subjects, 47.4 kg and 47.3 kg (p=0.9693), respectively. Figure 4.5 illustrates total body fat in kg determined by DEXA at week 0, week 8 and week 16. There was also no significant difference found at week 16 for non-diabetics and diabetic subjects, 33.6 kg and 37.8 kg (p=0.1816), respectively. However, percent change in total fat was found to be significant after 16 weeks of weight loss. Non-diabetic subjects decreased their total fat by 29.3% while diabetic subjects decreased their total fat by 20.6% (p=0.0295). These results are consistent with the ANCOVA analysis. After adjusting for baseline fat levels at 16 weeks there

was a significant difference in total fat content between non-diabetic and diabetic subjects (p=0.0338). Total fat was positively correlated with lean tissue in non-diabetic subjects (p=0.05), but not in diabetic subjects (p=0.9333).

4. Trunk Fat

The amount of fat in the trunk determined by DEXA measurements found that there was no significant difference at baseline between non-diabetic and diabetic subjects, 24.7 kg and 25.8 kg (p=0.4977), respectively. At week 16 a significant difference was found in the amount of trunk fat between the groups. Non-diabetic subjects had 16.7 kg of trunk fat and diabetic subjects had 20.6 kg of trunk fat (p=0.0353). The percent change in trunk fat was found to be significantly difference between the groups. Non-diabetic subjects decreased trunk fat by 32.1% and diabetic subjects decreased trunk fat by 20.8% (p=0.0495). ANCOVA analysis found that at week 16 the amount of trunk fat between the groups was approaching significance (p=0.0584). Figure 4.6 shows the amount of trunk fat at week 0, week 8 and week 16 in individuals who completed the study.

5. Total Lean Tissue

The total amount of lean tissue in the body was measured by DEXA. Figure 4.7 illustrates total lean tissue in kg determined by DEXA at week 0, week 8 and week 16. At baseline non-diabetic subject had significantly lower total lean tissue than diabetic subjects, 44.6 kg and 53.2 kg (p=0.0018), respectively. This finding was also true at week 16. Non-diabetic subjects had 42.1 kg of lean tissue and diabetic subjects had 49.3 kg (p=0.0036). The percent change in total lean tissue however was not significant after 16 weeks of weight loss (p=0.5430). After

adjusting for baseline measurement, ANCOVA analysis found no significant difference between the groups at week 16 (p=0.8661).

6. Trunk Lean Tissue

The amount of lean tissue found in the trunk was significantly lower in non-diabetic than diabetic subjects, 22.6 kg and 28.5 kg (p=0.0013), respectively. A significant difference in amount of lean tissue in the trunk was also found at week 16. Non-diabetics had 20.9 kg of lean tissue in the trunk while diabetics had 25.7 kg (p=0.0005). The percent change in lean tissue in the trunk was found not to be significantly difference between non-diabetic and diabetic subjects after 16 weeks of weight loss, -7.1% and -7.8% (p=0.8548), respectively. After adjusting for baseline values, ANCOVA found that there was no significant difference between the groups at baseline (p=0.1876) or at week 16 (p=0.1141). Figure 4.8 shows the amount of lean tissue in the trunk at week 0, week 8 and week 16 for individuals who completed the study.

7. Total Trunk Tissue

The total amount of trunk tissue at baseline was significantly lower in non-diabetic than diabetic subjects, 47.3 kg and 56.8 kg (p=0.024), respectively. A significant difference in the amount of total trunk tissue was also found at week 16. Non-diabetic subjects had 37.7 kg of tissue in the trunk while diabetic subjects had 46.2 kg (p=0.001). Figure 4.9 shows the total trunk tissue at week 0, week 8 and week 16. The percent change in total trunk tissue was not found was significantly different after 16 weeks of weight loss, -20.2% and -16.7% (p=0.36), respectively. After adjusting for baseline values, ANCOVA analysis found that there was not

significant difference between the groups at baseline (p=0.1145). However, after adjusting for baseline values, non-diabetic subjects were found to have significantly less trunk tissue than diabetic subjects (p=0.0123).

B. Air Displacement Plethysmography (BOD POD®)

1. Percent Body Fat

There was no significant difference between non-diabetic and diabetic subjects in total percent body fat as determined by air displacement plethysmography using the BOD POD® prior to weight loss (52.7% and 49.6%, respectively p=0.0924). Figure 4.10 shows percent body fat determined by air displacement plethysmography at week 0, week 8 and week 16. After 16 weeks of weight loss non-diabetic subjects decreased their percent body fat to 40.2% and diabetic subjects decreased percent body fat to 43.9% (p=0.1308). However, using ANCOVA procedures and adjusting for initial percent body fat diabetic subjects lost significantly less percent body fat than non-diabetic subjects (p=0.0091).

2. Total Fat

The BOD POD® measurements found no significant difference in total fat at baseline between non-diabetics and diabetic subjects, 49.7 kg and 50.1 kg (p=0.9093), respectively. Figure 4.11 illustrates total body fat in kg determined by BOD POD® at week 0, week 8 and week 16. There was significant difference found at week 16 for non-diabetics and diabetic subjects, 32.1 kg and 39.2 kg (p=0.0433), respectively. Percent change in total fat was also found to be significantly different after 16 weeks of weight loss. Non-diabetic subjects decreased their total fat by 35.9% while diabetic subjects decreased their total fat by 21.8% (p=0.0042). These results are

consistent with the ANCOVA analysis. After adjusting for baseline fat levels at 16 weeks there was a significant difference in total fat content between non-diabetic and diabetic subjects (p=0.0074).

3. Total Lean

The total amount of lean tissue in the body was measured by BOD POD®. Figure 4.12 illustrates total lean tissue in kg determined by BOD POD® at week 0, week 8 and week 16. At baseline non-diabetic subject had significantly lower total lean tissue than diabetic subjects, 46.1 kg and 52.1 kg (p=0.0148), respectively. This finding was not true at week 16. Non-diabetic subjects had 46.8 kg of lean tissue and diabetic subjects had 49.7 kg (p=0.2433). The percent change in total lean tissue however was significant after 16 weeks of weight loss (p=0.0273). Non-diabetic subjects increased lean tissue mass by 1.9%; while diabetic lean tissue mass decreased by 4.8%. After adjusting for baseline measurement, ANCOVA analysis was approaching a significant difference between the groups at week 16 (p=0.0532).

C. Computer Tomography (CT)

1. Total Abdominal Fat

The total amount of abdominal adipose tissue in cm^2 at week 0 and week 16 determined by computer tomography is illustrated in Figure 4.13. At baseline, there was no significant difference in the amount of total abdominal adipose tissue between non-diabetic and diabetic subjects at baseline, 717.7 cm^2 and 730.4 cm^2 (p=0.7833), respectively. Non-diabetic subjects lost 15.4 kg of body weight with a 30.0% reduction in total abdominal tissue (p=0.1595), while diabetic subjects lost 12.2 kg of body weight with a 23.5% reduction in total adipose tissue (p=0.1595), as shown in

Table 4.2. After 16 weeks of weight loss there was no significant difference in the amount of total abdominal fat in non-diabetic and diabetic subjects, 508.7 cm^2 and 555.0 cm^2 (p=0.3603), respectively. ANCOVA analysis adjusting for baseline found not significant difference between the groups after 16 weeks of weight loss (p=0.2131). Figure 4.15 reveals the change in subcutaneous, visceral and total abdominal fat loss by abdominal computer tomography.

2. Visceral Adipose Tissue

The amount of visceral adipose tissue in cm^2 at week 0 and week 16 for non-diabetic and diabetic subjects is shown in Figure 4.14. At baseline diabetic subjects had significantly greater amounts of visceral adiposity compared with non-diabetic subjects prior to weight loss, 208.3 cm^2 and 177.4 cm^2 (p=0.0009), respectively. This was also true after 16 weeks of weight loss. Diabetic subjects had 132.4 cm^2 of visceral adipose tissue while non-diabetics subjects had 79.4 cm^2 of visceral adipose tissue (p=0.0036). There was no significant difference in the percentage reduction in visceral adipose tissue between non-diabetic and diabetic subjects, 33.3% and 34.3% (p=0.8749), respectively. The ANCOVA analysis also indicated that after adjusting for baseline values, the amount of visceral adipose tissue was not significantly different at week 16 between non-diabetic and diabetic subjects, 109.7 $cm^2 \pm 9.4$ and 113.9 $cm^2 \pm 7.0$ (p=0.7457), respectively.

Visceral adipose tissue was not correlated with insulin, HOMA-IR, resistin or ghrelin in either diabetic or non-diabetic subjects, but was positively correlated with leptin in both diabetic (p=0.0325) and non-diabetic (p=0.0046) subjects.

3. Subcutaneous Adipose Tissue

The amount of subcutaneous adipose tissue in cm^2 at week 0 and week 16 for non-diabetic and diabetic subjects is shown in Figure 4.14. Unlike the visceral adipose tissue stores, subcutaneous tissue stores were not significantly different prior to the study. Non-diabetics had 600.3 cm^2 subcutaneous adipose tissue and diabetic subjects 522.1 cm^2 (p=0.0879). After 16 weeks of weight loss, non-diabetic subjects lost a significantly greater percentage of subcutaneous adipose tissue than diabetic subjects, 29.0% and 18.2% (p=0.0333), respectively. There was no significant difference in the amount of subcutaneous adipose tissue at week 16 between the non-diabetic and diabetic groups, 422.6 cm^2 and 429.4 cm^2 (p=0.8769), respectively. However, when the 16 week subcutaneous adipose tissue stores were adjusted for baseline, diabetic subjects had significantly greater subcutaneous adipose stores than non-diabetic subjects. The adjusted values for non-diabetic subjects were 393.0 cm^2 and 444.8 cm^2 for diabetic subjects (p=0.0394).

Subcutaneous adipose tissue was positively correlated with insulin (p=0.0423) and HOMA-IR (p=0.0379) in non-diabetic subjects, but not in diabetic subjects. In non-diabetic subjects, subcutaneous adipose tissue was found to be positively correlated with leptin (p=0.0005) and in diabetic subjects a positive correlation was approaching significance (p=0.0675). Subcutaneous adipose tissue was positively correlated with CRP (p=0.0154) in diabetic subjects but no correlation was observed in the non-diabetic subjects (p=0.9820). Subcutaneous adipose tissue was not found to be correlated to adiponection in diabetic subjects (p=0.2385) but a negative correlation was observed in the non-diabetic subjects (p=0.0309).

Before weight loss non-diabetic subjects visceral to subcutaneous fat ratio (V/S) was 0.20, while diabetics had a significantly higher ratio of 0.43 (p=0.0005). The rat%io of both groups decreased with weight loss; however, diabetic subjects had a significantly greater ratio of visceral to subcutaneous adipose tissue. The ratios were 0.19 and 0.33 for non-diabetics and diabetics respectively (p=0.003). There was no significant difference in either non-diabetic (p=0.6446) or diabetic (p=0.1350) subjects in the change of the V/S ratio after weight loss.

D. Waist Circumference

Waist circumference measurements were not significantly different prior to weight loss between non-diabetic and diabetic subjects (110.5 cm, 117.9 cm, p=0.1648). Figure 4.14 displays the absolute waist circumference in centimeters for diabetic and non-diabetic individuals at week 0 and week 16. Figure 4.15 shows that total change in centimeters and percent change in waist circumference for diabetic and non-diabetic subjects. After 16-weeks of weight loss non-diabetics decreased waist circumference by 16.4%, while diabetic subjects decreased waist circumference by 7.8% (p=0.0103). The non-diabetic subjects waist circumference at week 16 was 91.3 cm and the diabetic subjects waist circumference was 106.1 cm and was found to be a significant difference (p=0.0004). After the ANCOVA analysis and adjusting for baseline values, non-diabetic subjects significantly had smaller waist circumferences than diabetic subjects (93.0 $\pm$ 2.8 and 106.7 $\pm$ 2.3, p=0.0012), respectively.

Blood Parameters

A. Insulin / HOMA-IR

As expected, individuals with type 2 diabetes had significantly different serum insulin and HOMA-IR results than individuals without type 2 diabetes. Figure 4.18 and Figure 4.19 displays insulin and HOMA-IR results for week 0, week 8 and week 16, respectively. Prior to weight loss diabetic insulin levels were 21.0 μU/ml while non-diabetic individuals insulin levels were 14.4 μU/ml ($p=0.0447$). After 16 weeks of weight loss, insulin levels decreased by 30.1% and 28.7% in non-diabetic and diabetic subjects respectively. The ANCOVA calculation found that after adjusting for baseline insulin, there was no difference between diabetic and non-diabetics with weight loss ($p=0.2637$). HOMA-IR levels were also significantly different at baseline, 5.3 and 7.9 ($p<0.0001$), for non-diabetics and diabetics respectively. HOMA-IR increased by 1.8% in non-diabetic subjects and decreased by 10.2% in diabetic subjects ($p=0.0007$). ANCOVA analysis revealed no significant different HOMA-IR after 16 weeks of weight loss ($p=0.1764$). Baseline insulin and HOMA-IR values and changes are shown in Table 4.3.

In diabetic subjects, insulin was negatively correlated with resistin ($p=0.0309$) and approaching a negative correlation with ghrelin ($p=0.0843$). Insulin was not associated with body composition measurements in the diabetic subjects but was positively correlated with subcutaneous adipose tissue ($p=0.0423$) and total fat ($p=0.0436$) in non-diabetic subjects. A trend for a positively correlation between insulin and percent body fat was also observed. Insulin was not correlated with CRP, IL-6, TNF-α or adiponectin in either diabetic or non-diabetic subjects. The only

correlation observed with insulin in the non-diabetic subjects was HOMA-IR ($p<0.001$).

B. Glucose and HbA1c

Serum glucose and HbA1c levels were significantly higher before and after weight loss in diabetic versus non-diabetic subjects. Figure 4.20 and Figure 4.21 illustrates glucose and HbA1c levels, respectively, at week 0, week 8 and week 16. At baseline non-diabetic subjects glucose levels were 98.8 mg/dl and diabetic glucose levels were 187.2 mg/dl ($p<0.0001$). After 16 weeks of weight loss, glucose levels were still significantly lower in non-diabetic subjects than diabetic subjects, 92.9 mg/dl and 136.6 mg/dl ($p<0.0001$), respectively. However, after adjusting for baseline glucose levels, ANCOVA analysis found no significant difference in glucose levels at week 16 ($p=0.1941$). HbA1c measurements are reflected in the glucose levels as well. HbA1c measurements were also significantly higher before and after weight loss in diabetic versus non-diabetic subjects. At baseline non-diabetic subjects HbA1c was 5.2% and diabetic subjects had HbA1c levels of 8.1% ($p<0.0001$). After 16 weeks of weight loss, non-diabetic subjects HbA1c remained unchanged at 5.3% and diabetic subjects decreased HbA1c levels to 6.5%. This difference was still found to be significant using t-tests ($p<0.0001$). However, similar to glucose levels, after adjusting for baseline HbA1c levels, ANCOVA analysis found no significant difference in HbA1c levels at week 16 ($p=0.7051$). Baseline glucose and HbA1c values and changes are shown in Table 4.3.

C. Leptin

At baseline, although not significant, non-diabetic subjects had greater plasma leptin levels than diabetic subjects, 64039.2 pg/ml and 50457.5 pg/ml (p=0.142), respectively. Plasma leptin levels decreased by 66.9% in non-diabetic patients and 46.1% in diabetic subjects (p=0.018). There was no significant difference in leptin levels between the groups at week 0, week 8 or week 16; however, the ANCOVA analysis when adjusting week 8 and week 16 for baseline leptin levels became significant at week 16. Non-diabetic subjects leptin levels were 16546 pg/ml $\pm$ 3734.0 and for diabetic subjects 29812 pg/ml $\pm$ 2890.2 (p=0.0105). Figure 4.22 illustrates the change in leptin levels in both non-diabetic and diabetic subjects at week 0, week 8 and week 16. Baseline leptin values and changes are shown in Table 4.4.

Leptin was not correlated to HOMA-IR in non-diabetic (p=0.4624) subjects but was approaching a significant correlation in diabetic subjects (p=0.0872). In non-diabetic subjects leptin was negatively correlated with adiponectin (p=0.0425), but no correlation was observed in diabetic subjects (p=0.3219). Leptin was also correlated positively to weight in both diabetic (p=0.0110) and non-diabetic subjects (p=0.0139). No other correlations with leptin were observed.

D. Ghrelin

Plasma ghrelin levels increased by 22.5% and 26.1%, in non-diabetic and diabetic subjects respectively. At week 0, diabetic subjects had significantly lower ghrelin levels than the non-diabetic subjects, 643.6 pg/ml and 837.8 pg/ml (p=0.0425), respectively. However, after adjusting for baseline ghrelin levels

ANCOVA determined that after 16 weeks of weight loss there was no significant difference between the groups (p=0.8305). Figure 4.23 depicts the ghrelin levels at week 0, week 8, and week 16 for diabetic and non-diabetic subjects. Baseline ghrelin values and changes are shown in Table 4.4.

Ghrelin was positively correlated with adiponectin in diabetic subjects (p=0.0125), but no correlation was observed in the non-diabetic subjects (p=0.1711). Ghrelin was not found to be correlated with any of the other outcome measurements.

E. Adiponectin

Plasma adiponectin levels were significantly lower in diabetic subjects than non-diabetic subjects, 11532.0 ng/ml and 6701.4 ng/ml (p=0.0326), respectively at baseline. During the study, adiponectin levels decreased in non-diabetic subjects by 17.2% and increased by 15.3% in diabetic subjects (p=0.005). The adiponectin levels at week 16 were 10743.5 ng/ml for non-diabetic subjects and 7698.2 ng/ml (p=0.1013). ANCOVA analysis agreed with the description statistics that after adjusting for baseline there was no significant difference between to two groups after 16 weeks of weight loss (p=0.4197). Figure 4.24 illustrates the change in adiponectin levels in both non-diabetic and diabetic subjects at week 0, week 8 and week 16. Baseline adiponectin values and changes are shown in Table 4.4.

Adiponectin was positively correlated with ghrelin in the diabetic subjects (p=0.0125) and negatively correlated with leptin in the non-diabetic subjects (p=0.01425). No other correlations were observed with adiponectin levels in either diabetic or non-diabetic subjects.

F. Resistin

Plasma resistin levels were significantly different at the beginning of the study between non-diabetic and diabetic subjects, 4.6 ng/ml and 5.7 ng/ml (p=0.0358), respectively. The levels of resistin did not change after weight loss. Resistin levels of the non-diabetic subjects was 4.7 ng/ml and for diabetic subjects 6.1 ng/ml. Descriptive statistics state that these levels were still significantly different at week 16 (p=0.039). The percent change was -0.2% and 10.0% for non-diabetic and diabetic subjects respectively (p=0.2605). After adjusting for baseline levels, ANCOVA analysis revealed that at week 16 there was not a significant difference between the two groups (p=0.127). Figure 4.25 shows the change in resistin levels in both non-diabetic and diabetic subjects at week 0, week 8 and week 16. Baseline resistin values and changes are shown in Table 4.4.

Resistin was negatively correlated to insulin (p=0.0309) and HOMA-IR (p=0.0038) in diabetic subjects but no correlation was observed in non-diabetic subjects. No other correlations were observed with resistin in either diabetic or non-diabetic subjects.

G. Interleukin-6 (IL-6)

At baseline, high sensitivity IL-6 levels were approaching significance with non-diabetic having higher IL-6 levels than diabetic subjects, 4.0 pg/ml and 2.3 pg/ml (p=0.057), respectively. IL-6 levels decreased in both non-diabetic and diabetic subjects, -1.0 and -0.3 pg/ml (p=0.2520), respectively. The percent change for non-diabetic subjects was 0.3%, while for diabetic subjects IL-6 levels decreased by 4.5% (p=0.4258). ANCOVA analysis found no significant difference in IL-6 level between

non-diabetic and diabetic at week 16 after adjusting for baseline measurements, 3.0 pg/ml and 2.0 pg/ml (p=0.0961), respectively. Baseline IL-6 values and changes are shown in Table 4.4. IL-6 was not found to be correlated to any of the outcome measurements in either diabetic or non-diabetic subjects.

H. Tumor Necrosis Factor-α (TNF-α)

There was no significant difference in TNF-α levels prior to weight loss, 1.2 pg/ml and 1.3 pg/ml (p=0.286) for non-diabetic and diabetic subjects respectively. Overall, there was no change in serum high sensitivity TNF-α levels in either non-diabetic or diabetic subjects (0.3 and 0.0 respectively p=0.1560). At week 16 no significant difference in absolute TNF-α levels. The percent change for non-diabetics was 25.1% and 10.1% for diabetics (p=0.2556). ANCOVA analysis further verified this non-significance in TNF-α levels between the groups after weight loss (p=0.3795). Baseline TNF-α values and changes are shown in Table 4.4.

TNF-α was approaching a significant correlation with CRP in diabetic subjects (p=0.0915), but not in the non-diabetic subjects (p=0.5691). There were no other correlations observed between TNF-α and any of the other outcome measurements.

I. Plasminogen Activating Inhibitor-1 (PAI-1)

Figure 4.26 shows PAI-1 levels for week 0, week 8 and week 16. There was no significant difference between non-diabetic and diabetic subjects on baseline plasma total plasminogen activating inhibitor-1 (PAI-1), 9696.9 pg/ml and 12219.39 pg/ml (p=0.1132), respectively. At week 16 a significant difference was seen between the two groups, 5768.6 pg/ml and 7736.5 pg/ml (p=0.0105), for non-diabetic

and diabetic subjects respectively. However, no significant decrease was observed with the percent decreases in PAI-1 levels. There was a 26.2% decrease in non-diabetic subjects and a 25.4% decrease in the diabetic subjects (p=0.4819). ANCOVA analysis found a close significance between the two groups at week 16 after adjusting for baseline values (p=0.057). Baseline PAI-1 values and changes are shown in Table 4.4.

PAI-1 levels were positively correlated with percent body (p=0.0073) and negatively correlated with lean tissue (p=0.0681) in diabetic subjects. PAI-1 was approaching a significant negative correlation with lean tissue in the non-diabetics (p=0.0893), but no correlation was observed with percent body fat (p=0.6397). In diabetic subjects a negative correlation between PAI-1 and ghrelin was approaching significance (p=0.0673). This was not observed in the non-diabetic subjects (p=0.9366).

J. C-Reactive Protein (CRP)

There were no significant difference in serum high sensitivity CRP levels at baseline, 7162.4 ng/ml and 6346.4 ng/ml (p=0.3419), for non-diabetic and diabetics respectively. There was no significant difference in the level of CRP at week 16, 5288.1 ng/ml and 4262.2 ng/ml (p=0.3622), respectively for non-diabetics and diabetic subjects. Percent reduction in CRP levels decreased by 33.1% and 21.2% in non-diabetic and diabetic subjects non-significantly (p=0.4637). ANCOVA analysis for adjusting baseline confirms there was no significant difference between the two groups (p=0.7404). Baseline CRP values and changes are shown in Table 4.4.

CRP was positively correlated to subcutaneous adipose tissue in diabetic subjects (p=0.0154), but not in non-diabetic subjects (p=0.9820). CRP was approaching a significant positive correlation to BMI in diabetic subjects (p=0.0697), but not in non-diabetic subjects (p=0.7675). No other correlations with CRP were observed in either the diabetic or non-diabetic subjects.

K. Follicle-Stimulating Hormone (FSH)

Serum follicle stimulating hormone (FSH) levels were not significantly different in non-diabetic and diabetic subjects at the beginning of the study (42.9mIU/ml, 26.4 mIU/ml, p=0.0596). Both groups increased FSH levels during the study. FSH levels increased by 19.5% in non-diabetic subjects and 32.5% in diabetic subjects (p=0.2231). FSH levels at week 16 were also not found to be significantly different between non-diabetic and diabetic subjects, 50.4 mIU/ml and 31.5 mIU/ml (p=0.0573), respectively. ANCOVA analysis verified this non-significant finding at week 16 (p=0.6825). Baseline FSH values and changes are shown in Table 4.3.

L. Lipids

1. Total Cholesterol

Figure 4.27 exhibits total cholesterol levels for diabetic and non-diabetic individuals at week 0, week 8 and week 16. There was no significant difference in total cholesterol levels in non-diabetic and diabetic subjects before or after the weight loss phase. Total cholesterol levels decreased in both non-diabetic and diabetic subjects. Total cholesterol in non-diabetic subjects decreased by 41.2 mg/dl, resulting in a -17.9%. Although there was no significant difference in total cholesterol (p=0.3011) or percent change (p=0.1581) in total cholesterol levels between groups

before or after weight loss, diabetic subjects saw only a 14.4 mg/dl decrease, resulting in a -7.4%. ANCOVA analysis confirmed the t-test and found no significant difference between total cholesterol levels at week 16 (p=0.2223). Baseline cholesterol values and changes are shown in Table 4.5.

2. Low-Density Lipoprotein Cholesterol (LDL-Cholesterol)

LDL-cholesterol levels at week 0, week 8 and week 16 for diabetic and non-diabetic individuals are illustrated in Figure 4.28. There was no significant difference in LDL-cholesterol levels at baseline between non-diabetic and diabetic subjects, 128 mg/dl and 122.6 mg/dl (p=0.5099), respectively. Non-diabetic subjects LDL-cholesterol levels decreased by 13.6%, while diabetic subjects had a 6.9% increase (p=0.0925). ANCOVA analysis adjusting for baseline LDL-cholesterol levels found no significant difference between groups at week 16. Baseline LDL-cholesterol values and changes are shown in Table 4.5.

3. High-Density Lipoprotein Cholesterol (HDL-Cholesterol)

HDL-cholesterol levels at week 0, week 8 and week 16 are shown in Figure 4.29. Non-diabetic subjects had significantly higher HDL-cholesterol levels than diabetic subjects at baseline, 52.1 mg/dl and 37.8 mg/dl (p=0.0009), respectively. At week 16, there was no significant difference in HDL-cholesterol levels between the groups (p=0.135). After weight loss, percent change in HDL-cholesterol levels was significantly different between non-diabetic and diabetic subjects. High-density lipoprotein cholesterol levels decreased by 16.2% in non-diabetics and increased by 0.9% in diabetic subjects (p=0.0001). Adjusting for baseline HDL-cholesterol levels,

ANCOVA analysis found no significant difference between the groups at week 16 (p=0.217). Baseline HDL-cholesterol values and changes are shown in Table 4.5.

4. Triglycerides

Triglyceride levels at week 0, week 8 and week 16 are shown in Figure 4.30 for diabetic and non-diabetic subjects. At baseline diabetic subjects had significantly higher triglyceride levels than non-diabetic subjects, 228.8 mg/dl and 125.1 mg/dl (p=0.0012), respectively. At week 16 non-diabetic subjects triglyceride levels were still significantly lower than diabetic subjects, 100.0 mg/dl and 146.3 mg/dl (p=0.0359), respectively. There was no significant difference in the percent decrease in triglyceride levels after weight loss between non-diabetic subjects and diabetic subjects, -13.1% and -34.5% (p=0.0734), respectively. As stated previously, diabetic subjects had significantly greater triglyceride levels prior to weight and after adjusting for baseline, ANCOVA analysis found no significant difference between the groups at week 16 (p=0.8693). Baseline triglyceride values and changes are shown in Table 4.5.

Blood Pressure

Systolic blood pressure levels were not significantly different in non-diabetic and diabetic subjects at baseline, 117.6 mmHg and 122.6 mmHg (p=0.1224), respectively. After 16 weeks of weight loss systolic blood pressure was not significantly different between non-diabetic and diabetic subjects, 118.4 mmHg and 122.1 mmHg (p=0.4043), respectively. Diastolic blood pressure levels were also not significantly different in non-diabetic and diabetic subjects at baseline, 73.5 mmHg and 77.8 mmHg (p=0.1505), respectively. Week 16 diastolic blood

pressures were not significantly different between non-diabetic and diabetic subjects, 73.8 mmHg and 75.2 mmHg (p=0.6811), respectively. Baseline systolic and diastolic blood pressure levels and their changes are shown in Table 4.5.

Dietary Compliance

Dietary compliance was accessed by self-reported meal replacement use and physical activity expenditure which was recorded by HMR personnel in the Patient at a Glance form. According to the Patient at a Glance form, both diabetic and non-diabetic subjects complied with the HMR program. Figure 4.31 shows the average number of meal replacements, entrees, bars and total meal replacements consumed for diabetic and non-diabetic subjects at week 16. There was no significant difference in the number of meal replacements consumed. Figure 4.32 illustrates the average weekly number of kcal expended by physical activity at week 0, week 8 and week 16 by diabetic and non-diabetic subjects. There was no significant difference in the amount of physical activity reported between the groups. There also was no significant difference in weekly attendance, mid-week phone call, number of days "in the box", and in meeting the Triple Imperative™.

Table 4.1 Baseline Characteristics of Subjects who Completed the Study. (Mean $\pm$ SD)

Variable	Non-Diabetic	Diabetic
Number enrolled	11	18
Age (years)	50.5 $\pm$ 5.6	52.4 $\pm$ 6.7
Weight (kg)	96.4 $\pm$ 13.3	105.6 $\pm$ 12.6
Body mass index (kg/m^2)	36.1 $\pm$ 3.9	38.1 $\pm$ 3.7

Table 4.2 Baseline Values and Absolute and Percentage Change from Week 0 at 16 Weeks for Body Composition Measurements of Study Completers. Data were analyzed by unadjusted student's t-tests and are expressed as mean (SE). Statistical probability of $p<0.05$ was considered to be significant. *Significantly different between non-diabetic and diabetic subjects.

Variable	Non-Diabetic (n=11)			Diabetic (n=18)		
	Week 0	Change	% Change	Week 0	Change	% Change
DXA % Total Body Fat	49.9 (0.8)	-7.4 (1.0)	N/A	45.9* (1.0)	-4.2* (1.1)	N/A
DXA % Trunk Fat	51.2 (1.0)	-8.0 (1.6)	N/A	47.3* (1.1)	-4.1* (1.6)	N/A
DXA Total Fat (kg)	47.4 (2.3)	-13.8 (1.2)	-29.3 (2.4)	47.3 (1.7)	-9.5* (1.3)	-20.6* (2.9)
DXA Trunk Fat (kg)	24.7 (1.4)	-8.0 (1.1)	-32.1 (3.9)	25.8 (0.8)	-5.3* (1.0)	-20.8* (3.8)
DXA Total Lean (kg)	44.6 (1.6)	-2.5 (0.8)	-5.4 (1.6)	53.2* (1.9)	-3.9 (1.2)	-6.9 (1.9)
DXA Trunk Lean (kg)	22.6 (0.9)	-1.7 (0.5)	-7.1 (2.2)	28.5* (1.3)	-2.7 (1.2)	-7.8 (3.2)
DXA Trunk Tissue (kg)	47.3 (2.8)	-9.6 (1.2)	-20.2 (2.1)	56.8* (2.8)	-10.6 (2.7)	-16.7 (3.1)
BOD POD® (% Body Fat)	52.7 (1.4)	-12.5 (1.4)	N/A	49.6 (1.0)	-5.7* (1.1)	N/A
BOD POD® Total Fat (kg)	49.7 (2.5)	-17.6 (1.5)	-35.9 (3.0)	50.1 (1.7)	-10.9* (1.6)	-21.8* (3.3)
BOD POD® Total Lean (kg)	46.1 (1.7)	0.7 (1.1)	1.9 (2.5)	52.1* (1.6)	-2.4* (1.6)	-4.8* (1.2)
CT Total Abdominal Fat (sq cm^2)	717.7 (34.5)	-208.9 (20.8)	-30.0 (3.7)	730.4 (30.0)	-175.4 (20.3)	-23.5 (2.5)
CT Visceral Fat (sq cm^2)	177.4 (11.5)	-38.0 (5.4)	-33.3 (4.6)	208.3* (17.7)	-75.9* (11.4)	-34.3 (4.0)
CT Subcutaneous Fat (sq cm^2)	600.3 (32.2)	-170.9 (21.5)	-29.0 (4.0)	522.1 (28.3)	-99.5* (11.0)	-18.2* (1.9)
Waist Circumference (cm)	110.5 (5.0)	-19.2 (4.0)	-16.4 (2.7)	117.9 (2.7)	-11.9 (2.4)	-7.8* (1.1)

Table 4.3 Baseline Values and Changes from Week 0 at 16 Weeks for Fasting Glucose and Insulin Resistance Measurements of Study Completers. Data were analyzed by unadjusted student's t-tests and are expressed as mean (SE). Statistical probability of $p<0.05$ was considered to be significant. *Significantly different between non-diabetic and diabetic subjects.

Variable	Non-Diabetic (n=11)			Diabetic (n=18)		
	Week 0	Change	% Change	Week 0	Change	% Change
Insulin (mU/ml)	14.4 (2.8)	-5.5 (3.0)	-30.1 (11.8)	21.0* (2.4)	-7.8 (2.1)	-28.7 (7.2)
HOMA-IR	5.3 (0.1)	0.1 (0.1)	1.8 (1.9)	7.9* (0.4)	-0.9* (0.3)	-10.2* (2.5)
Glucose (mg/dl)	104.0 (3.0)	-5.9 (1.9)	-5.5 (1.7)	187.2* (15.6)	-50.6* (12.5)	-22.0* (4.5)
HbA1c	5.2 (0.2)	0.1 (0.1)	N/A	8.1* (0.4)	-1.6* (0.4)	N/A

Table 4.4 Baseline Values and Absolute and Percentage Change from Week 0 at 16 Weeks for Fasting Cytokines and FSH of Study Completers. Data were analyzed by unadjusted student's t-tests and are expressed as mean (SE). Statistical probability of $p<0.05$ was considered to be significant. *Significantly different between non-diabetic and diabetic subjects.

Variable	Non-Diabetic (n=11)			Diabetic (n=18)		
	Week 0	Change	% Change	Week 0	Change	% Change
Leptin (pg/ml)	64039.2 (7328.7)	-44075.3 (5463.6)	-66.9 (5.9)	50457.5 (4988.8)	-22734.3* (3479.4)	-46.1* (5.7)
Ghrelin (pg/ml)	837.8 (90.0)	173.8 (108.9)	22.5 (13.7)	643.6* (57.0)	166.4 (40.5)	26.1 (5.2)
Adiponectin (ng/ml	11532.0 (1894.0)	-1875.5 (968.3)	-17.2 (9.6)	6701.4* (640.9)	996.8* (410.5)	15.3* (4.8)
Resistin (ng/ml)	4.6 (0.3)	0.1 (0.2)	-0.2 (5.0)	5.6* (0.5)	0.4 (0.4)	10.0 (7.2)
IL-6 (pg/ml)	4.0 (1.0)	-1.0 (1.0)	0.3 (22.7)	2.3 (0.3)	-0.3 (0.3)	-4.5 (10.8)
TNFα (pg/ml)	1.2 (0.1)	0.3 (0.2)	25.1 (17.8)	1.3 (0.1)	0.0 (0.1)	10.1 (13.7)
PAI-1 (pg/ml)	9696.9 (1646.9)	-3928.3 (1338.8)	-26.2 (12.4)	12219.4 (1171.6)	-4556.6 (1341.9)	-25.4 (10.6)
CRP (ng/ml)	7162.4 (1653.9)	-1784.9 (758.6)	-33.1 (8.2)	6346.4 (1073.5)	-1720.3 (675.2)	-21.2 (9.4)
FSH (mlU/ml)	42.9 (8.3)	7.5 (3.5)	19.5 (9.6)	26.4 (5.7)	5.1 (1.9)	32.5 (13.8)

Table 4.5 Baseline Values and Changes from Week 0 at 16 Weeks for Fasting Lipid Values and Blood Pressure of Study Completers. Data were analyzed by unadjusted student's t-tests and are expressed as mean (SE). Statistical probability of $p<0.05$ was considered to be significant. *Significantly different between non-diabetic and diabetic subjects.

Variable	Non-Diabetic (n=11)			Diabetic (n=18)		
	Week 0	Change	% Change	Week 0	Change	% Change
Cholesterol (mg/dL)	214.0 (12.5)	-41.2 (12.0)	-17.9 (5.5)	201.9 (3.1)	-14.4 (2.8)	-7.3 (4.0)
LDL-Cholesterol (mg/dL)	128.6 (10.2)	-23.8 (9.8)	-13.6 (8.4)	122.6 (2.9)	1.6 (3.2)	6.9 (3.0)
HDL-Cholesterol (mg/dL)	59.4 (2.5)	-8.5 (2.2)	-16.2 (3.8)	47.6* (2.5)	-0.1* (1.0)	0.9* (2.9)
Triglycerides (mg/dL)	125.1 (20.0)	-25.1 (16.0)	-13.1 (9.4)	228.8* (20.1)	-82.5* (16.7)	-34.5 (6.1)
Systolic Blood Pressure (mmHg)	117.6 (2.7)	9.8 (2.4)	0.7 (2.8)	122.6 (3.0)	-2.3 (3.9)	6.0 (3.3)
Diastolic Blood Pressure (mmHg)	73.5 (1.2)	0.4 (2.1)	0.6 (2.8)	77.8 (2.0)	-2.6 (3.2)	3.3 (4.2)

Figure 4.1 Average and Individual Weight Losses in Non-Diabetic and Diabetic Subjects Who Completed the HMR® Weight Loss Program.

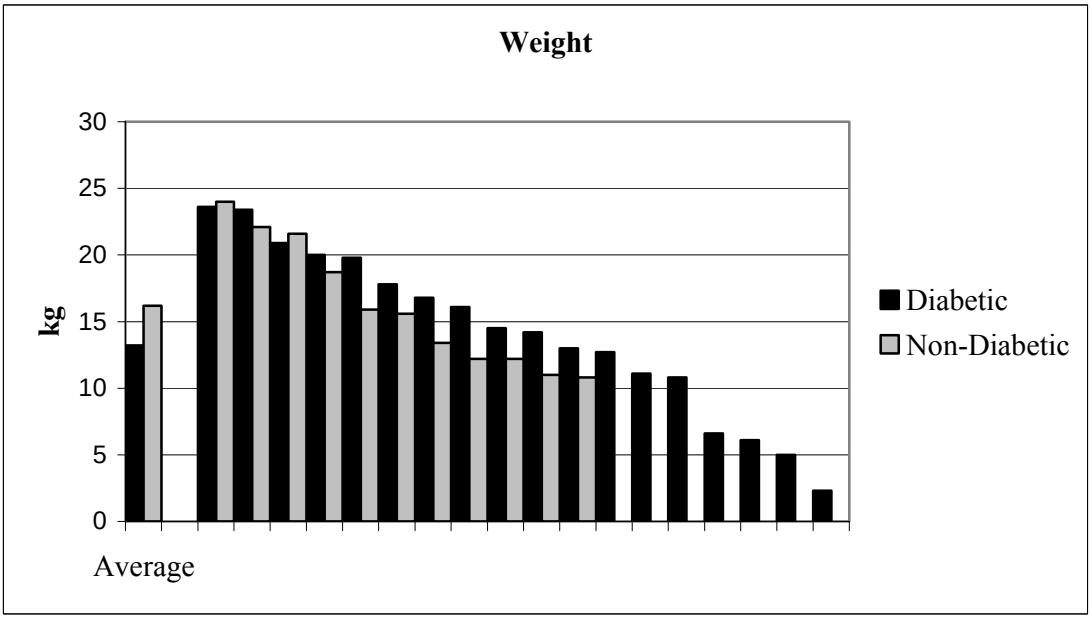
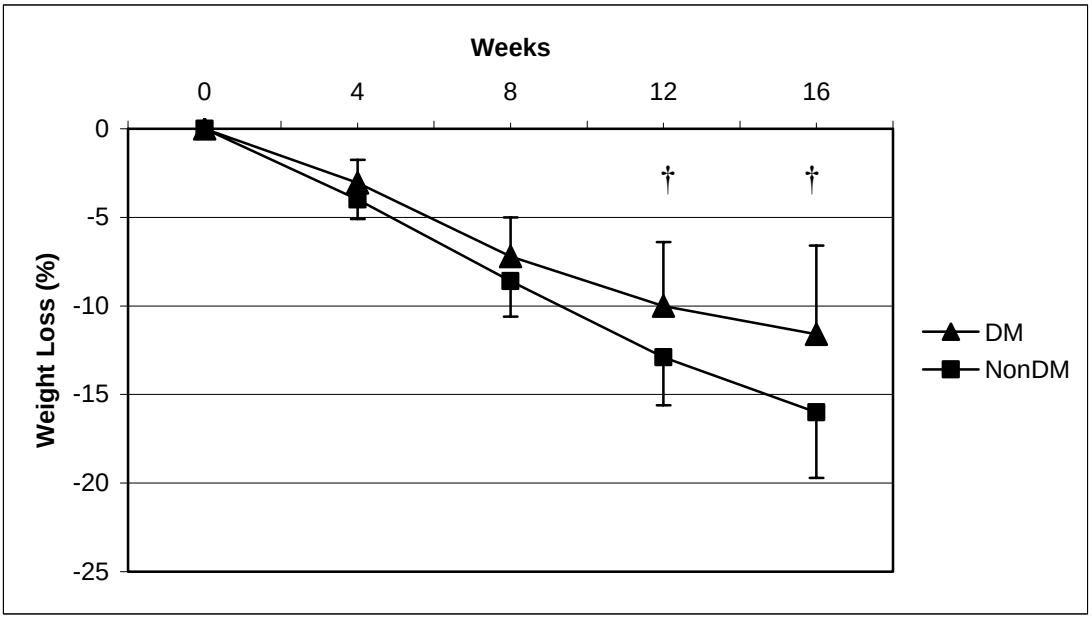
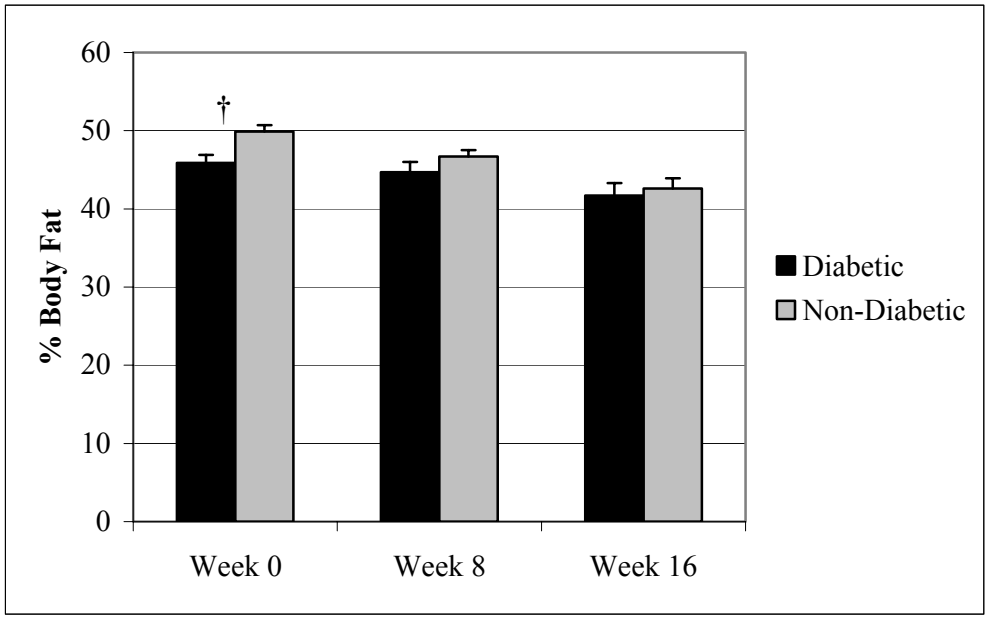


Figure 4.2 Percent Weight Loss of Non-Diabetic and Diabetic Subjects Who Completed the HMR® Weight Loss Program.



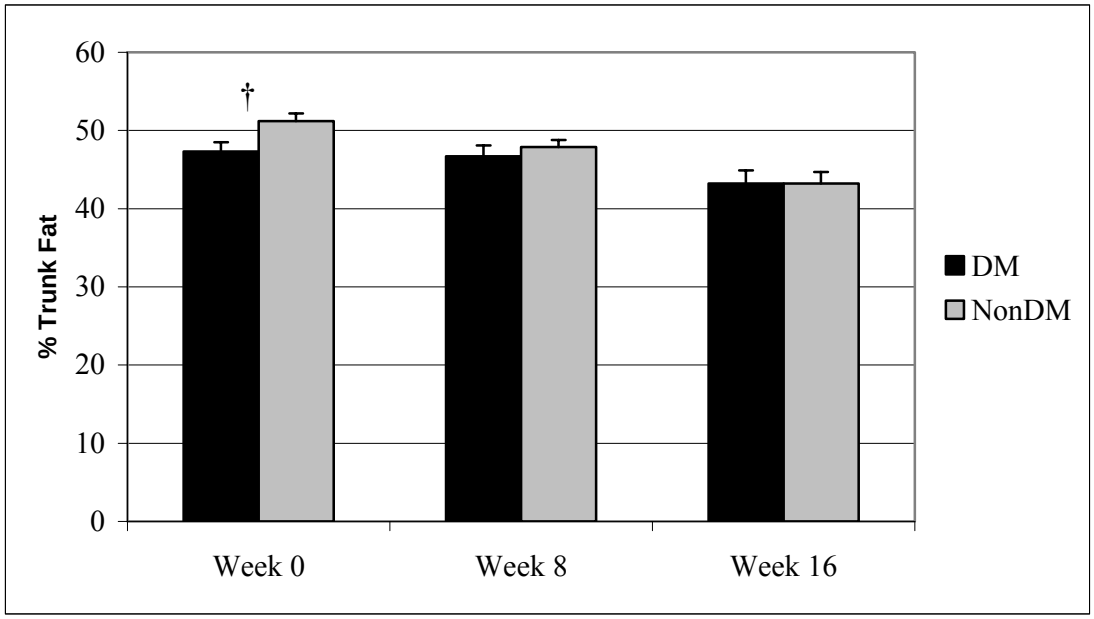
† Unadjusted analysis conducted by student's t-test found to be significantly different between diabetic and non-diabetic subjects.
‡ Adjusted analysis conducted by ANCOVA for week 16 found to be significantly different between diabetic and non-diabetic subjects.
Statistically probability of $p<0.05$ was considered to be significant.

Figure 4.3 Percent Body Fat Determined by DEXA of Study Completers.



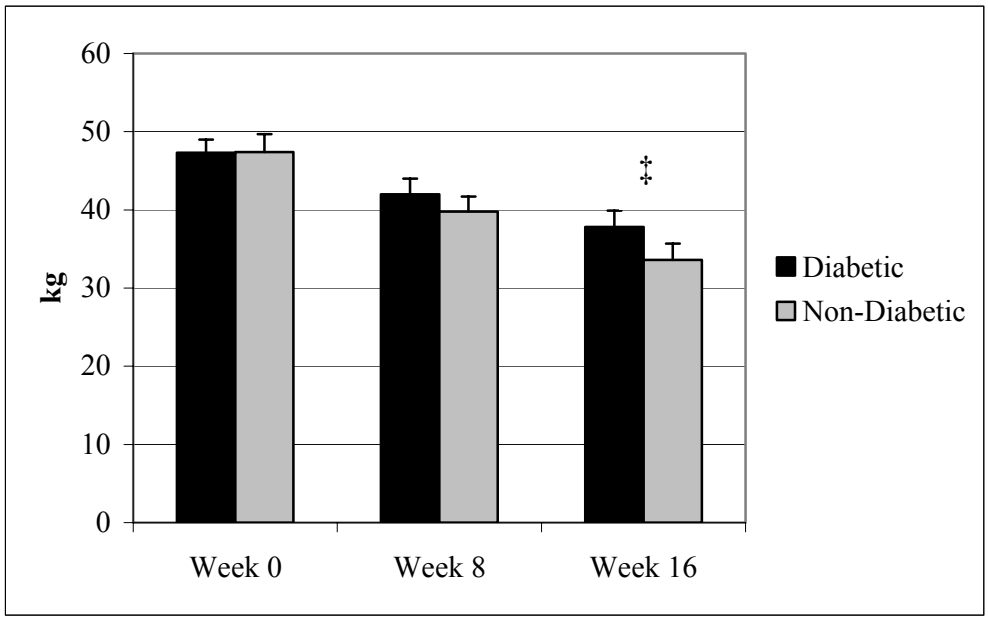
† Unadjusted analysis conducted by student's t-test found to be significantly different between diabetic and non-diabetic subjects.
‡ Adjusted analysis conducted by ANCOVA for week 16 found to be significantly different between diabetic and non-diabetic subjects.
Statistical probability of $p<0.05$ was considered to be significant.

Figure 4.4 Percent Trunk Fat Determined by DEXA for Study Completers.



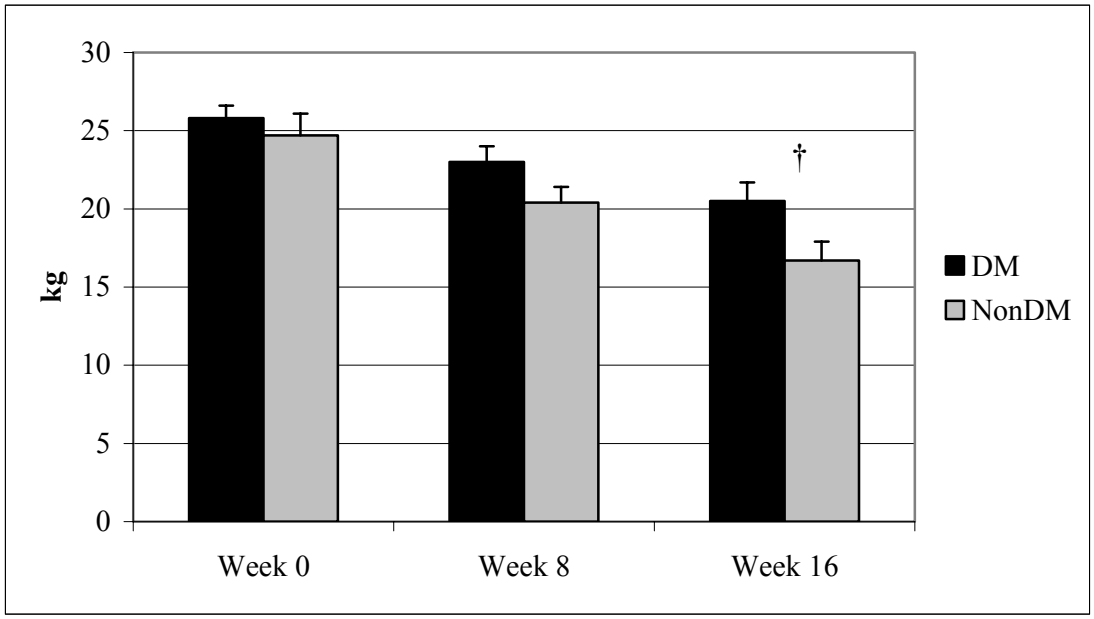
† Unadjusted analysis conducted by student's t-test found to be significantly different between diabetic and non-diabetic subjects.
‡ Adjusted analysis conducted by ANCOVA for week 16 found to be significantly different between diabetic and non-diabetic subjects.
Statistical probability of $p<0.05$ was considered to be significant.

Figure 4.5 Total Body Fat in kg Determined by DEXA of Study Completers.



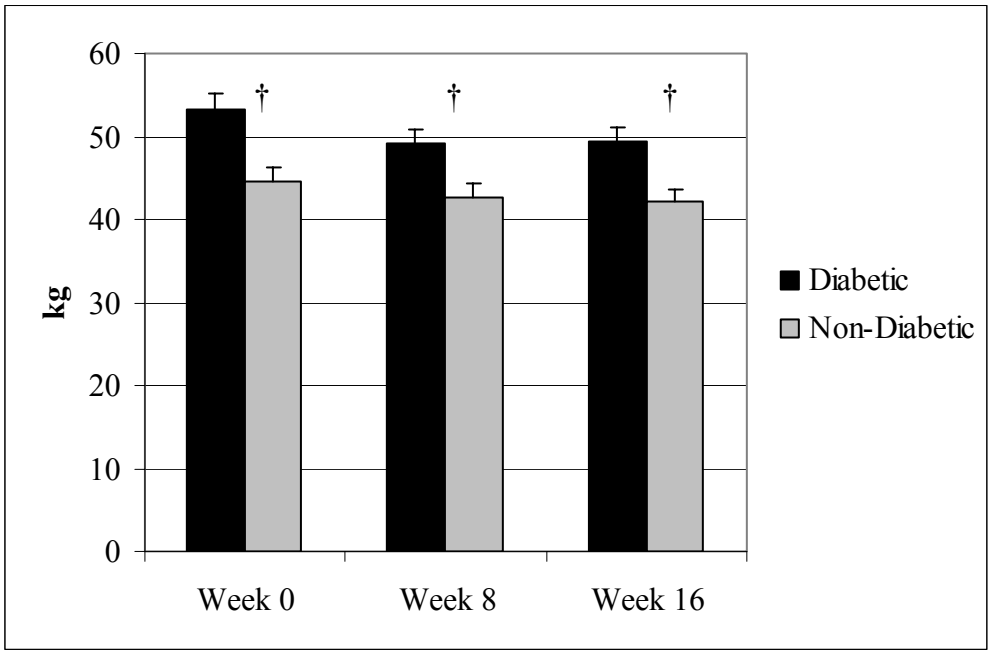
† Unadjusted analysis conducted by student's t-test found to be significantly different between diabetic and non-diabetic subjects.
‡ Adjusted analysis conducted by ANCOVA for week 16 found to be significantly different between diabetic and non-diabetic subjects.
Statistical probability of $p<0.05$ was considered to be significant.

Figure 4.6 Trunk Fat in kg Determined by DEXA for Study Completers.



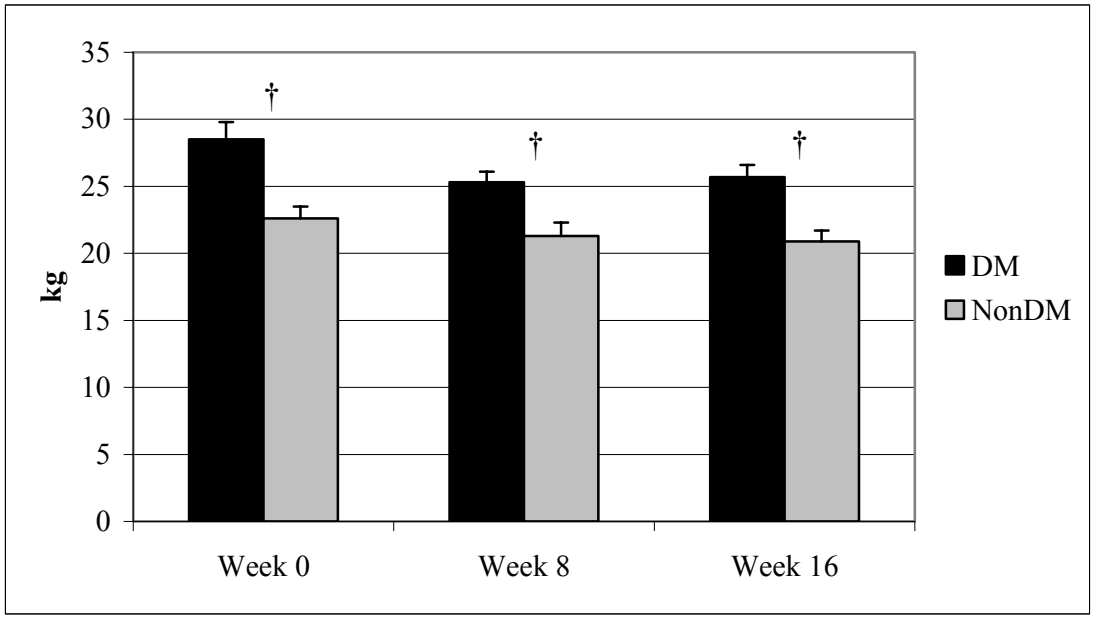
† Unadjusted analysis conducted by student's t-test found to be significantly different between diabetic and non-diabetic subjects.
‡ Adjusted analysis conducted by ANCOVA for week 16 found to be significantly different between diabetic and non-diabetic subjects.
Statistical probability of $p<0.05$ was considered to be significant.

Figure 4.7 Total Lean Tissue in kg Determined by DEXA of Study Completers.



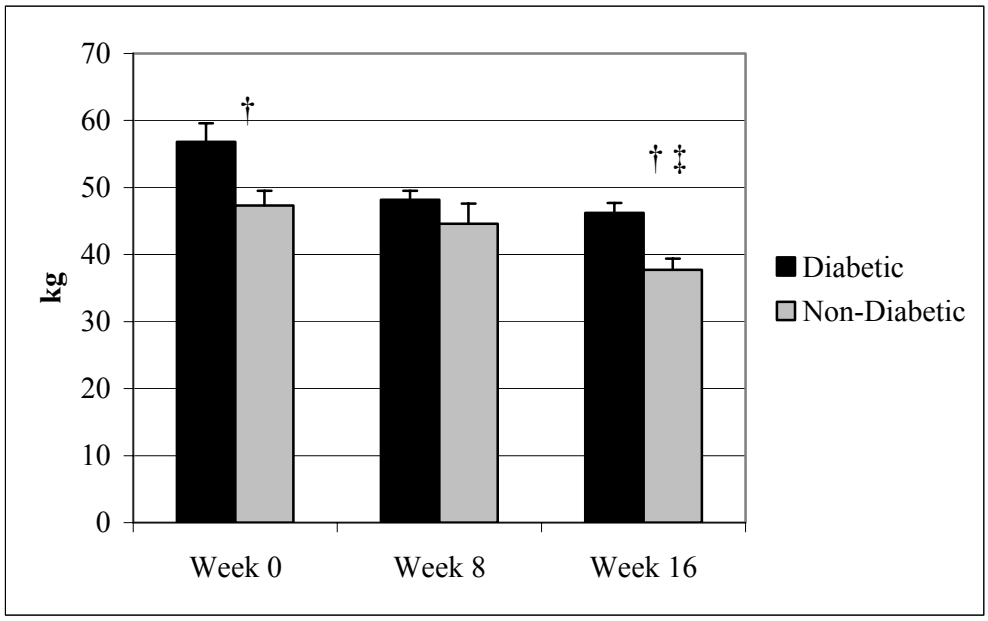
† Unadjusted analysis conducted by student's t-test found to be significantly different between diabetic and non-diabetic subjects.[a]
‡ Adjusted analysis conducted by ANCOVA for week 16 found to be significantly different between diabetic and non-diabetic subjects.[b]
Statistical probability of $p<0.05$ was considered to be significant.[c]

Figure 4.8 Trunk Lean Tissue in kg Determined by DEXA of Study Completers.



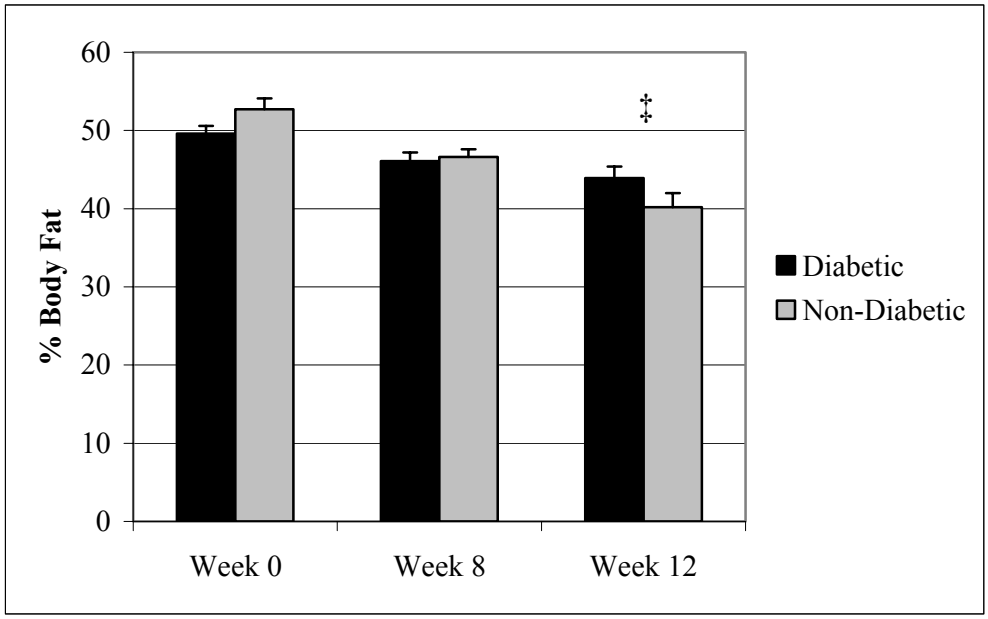
† Unadjusted analysis conducted by student's t-test found to be significantly different between diabetic and non-diabetic subjects.
‡ Adjusted analysis conducted by ANCOVA for week 16 found to be significantly different between diabetic and non-diabetic subjects.
Statistical probability of $p<0.05$ considered to be significant.

Figure 4.9 Total Trunk Tissue Determined by DEXA of Study Completers.



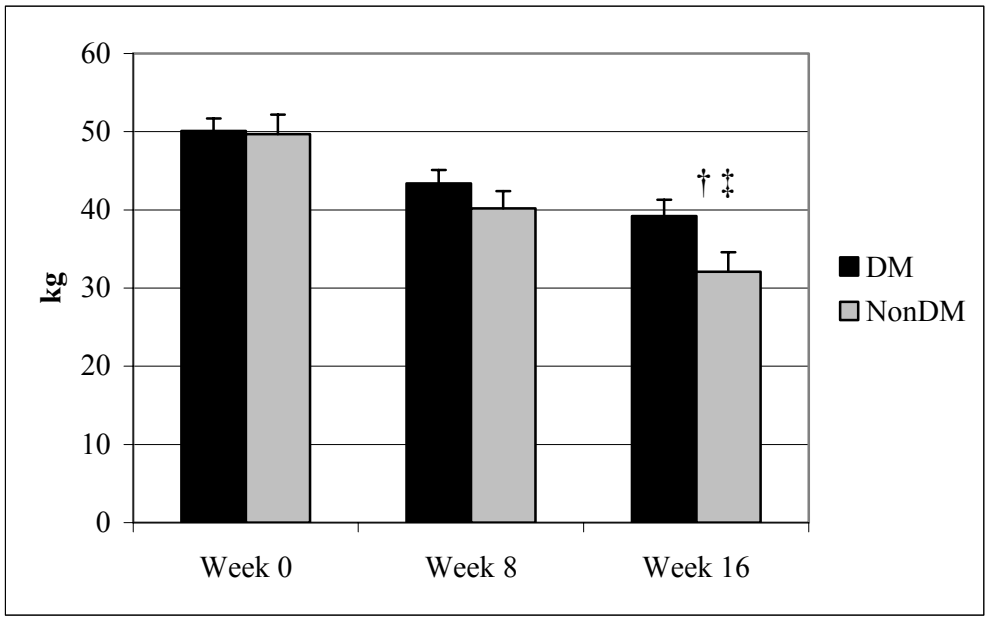
† Unadjusted analysis conducted by student's t-test found to be significantly different between diabetic and non-diabetic subjects.
‡ Adjusted analysis conducted by ANCOVA for week 16 found to be significantly different between diabetic and non-diabetic subjects.
Statistical probability of $p<0.05$ was considered to be significant.

Figure 4.10 Percent Body Fat Determined by Air Displacement Plethysmography (BOD POD®) of Study Completers.



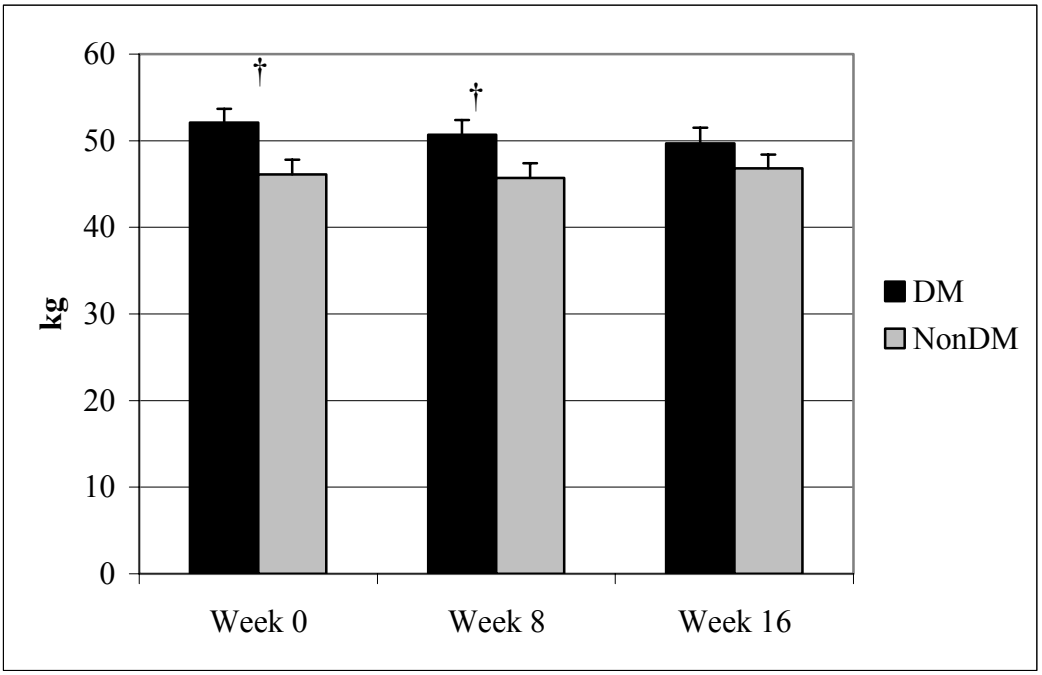
† Unadjusted analysis conducted by student's t-test found to be significantly different between diabetic and non-diabetic subjects.
‡ Adjusted analysis conducted by ANCOVA for week 16 found to be significantly different between diabetic and non-diabetic subjects.
Statistical probability of $p<0.05$ was considered to be significant.

Figure 4.11 Total Fat in kg Determined by BOD POD® of Study Completers.



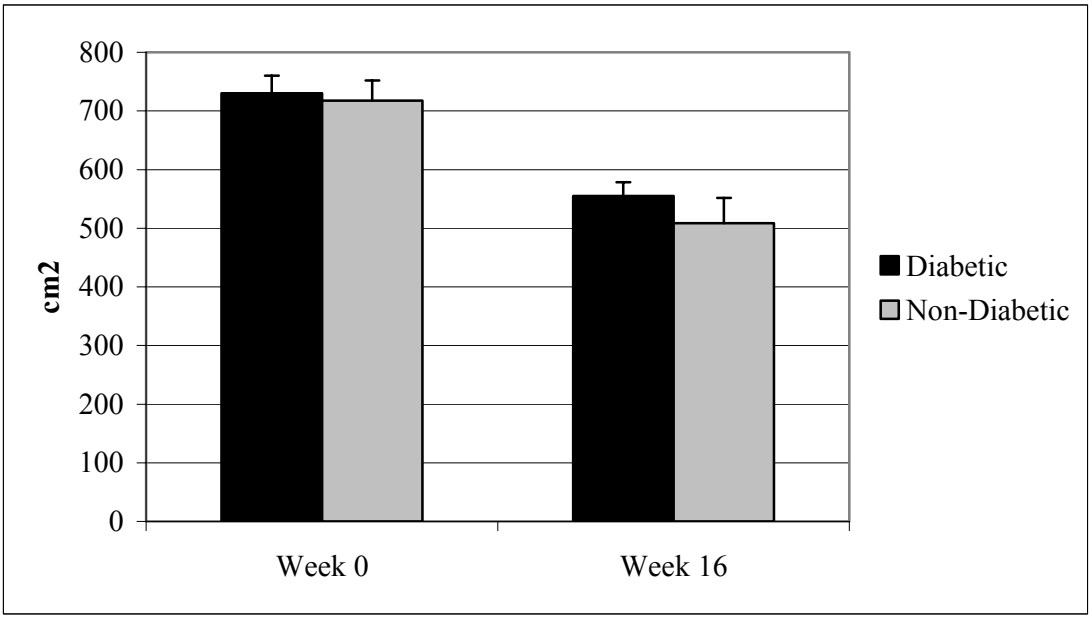
† Unadjusted analysis conducted by student's t-test found to be significantly different between diabetic and non-diabetic subjects.
‡ Adjusted analysis conducted by ANCOVA for week16 found to be significantly different between diabetic and non-diabetic subjects.
Statistical probability of $p<0.05$ was considered to be significant.

Figure 4.12 Total Lean Tissue Determined by BOD POD® of Study Completers.



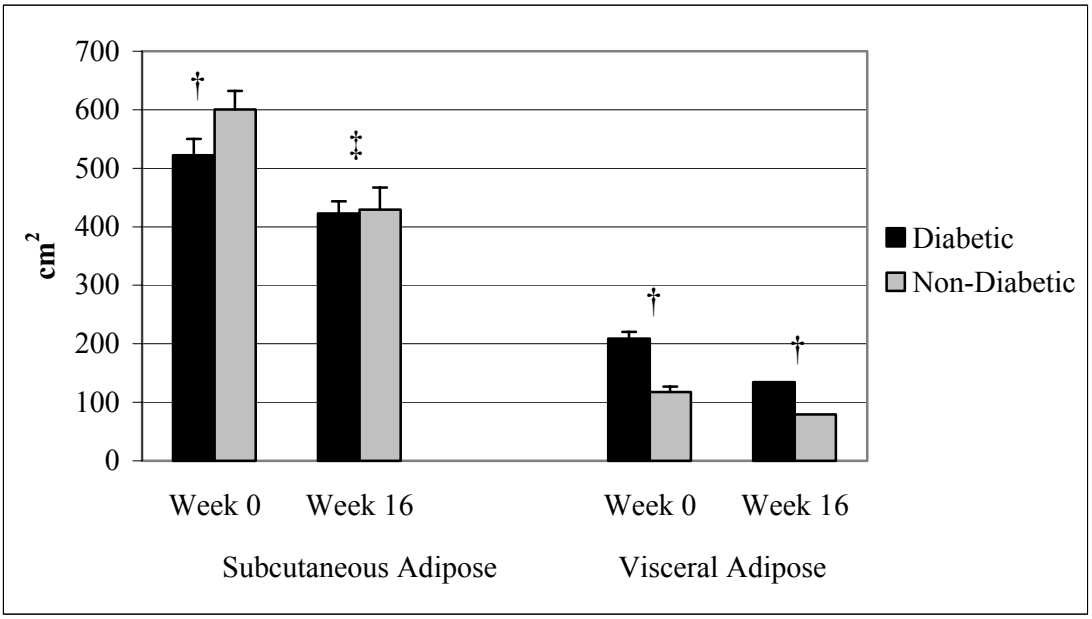
† Unadjusted analysis conducted by student's t-test found to be significantly different between diabetic and non-diabetic subjects.
‡ Adjusted analysis conducted by ANCOVA for week 16 found to be significantly different between diabetic and non-diabetic subjects.
Statistical probability of $p<0.05$ was considered to be significant.

Figure 4.13 Total Abdominal Adipose Tissue Determined by Computer Tomography of Study Completers.



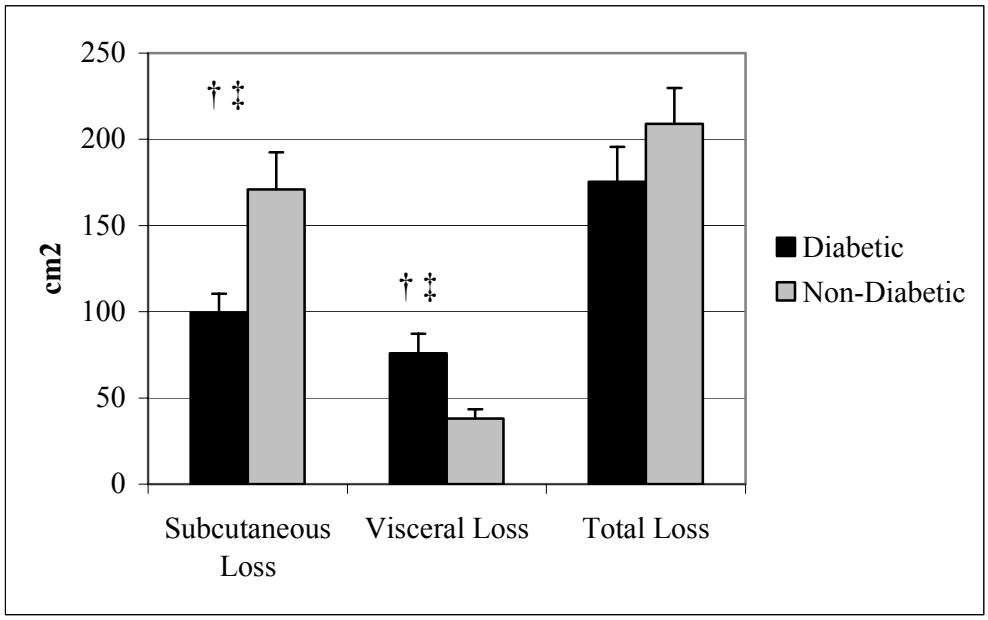
† Unadjusted analysis conducted by student's t-test found to be significantly different between diabetic and non-diabetic subjects.
‡ Adjusted analysis conducted by ANCOVA for week 16 found to be significantly different between diabetic and non-diabetic subjects.
Statistical probability of $p<0.05$ was considered to be significant.

Figure 4.14 Total Subcutaneous and Visceral Adipose Tissue in Study Completers.



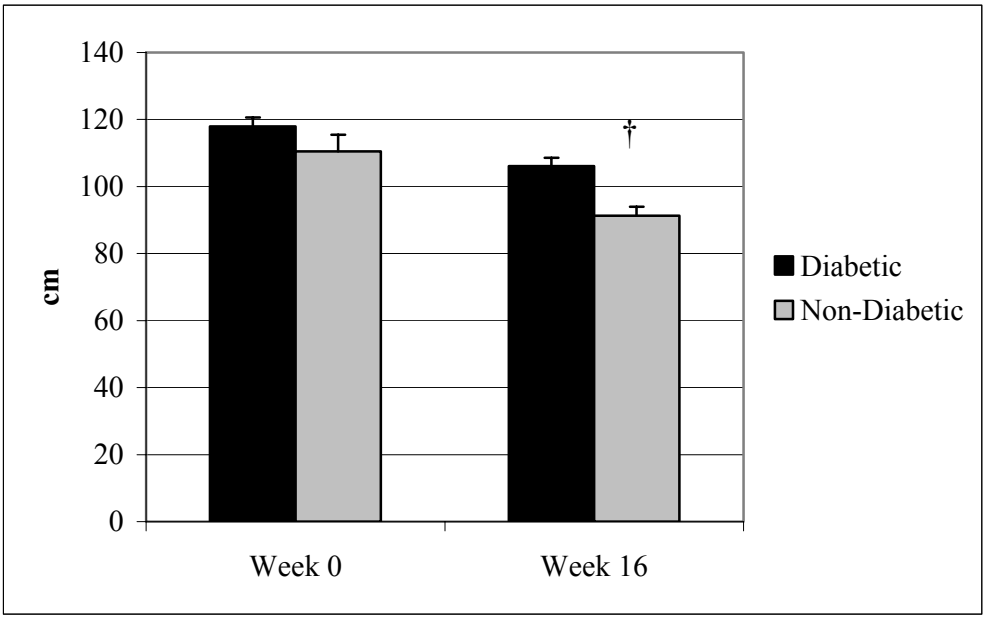
† Unadjusted analysis conducted by student's t-test found to be significantly different between diabetic and non-diabetic subjects.
‡ Adjusted analysis conducted by ANCOVA for week 16 found to be significantly different between diabetic and non-diabetic subjects.
Statistical probability of $p<0.05$ was considered to be significant.

Figure 4.15 Subcutaneous, Visceral and Total Abdominal Fat Loss Determined by Computer Tomography of Study Completers.



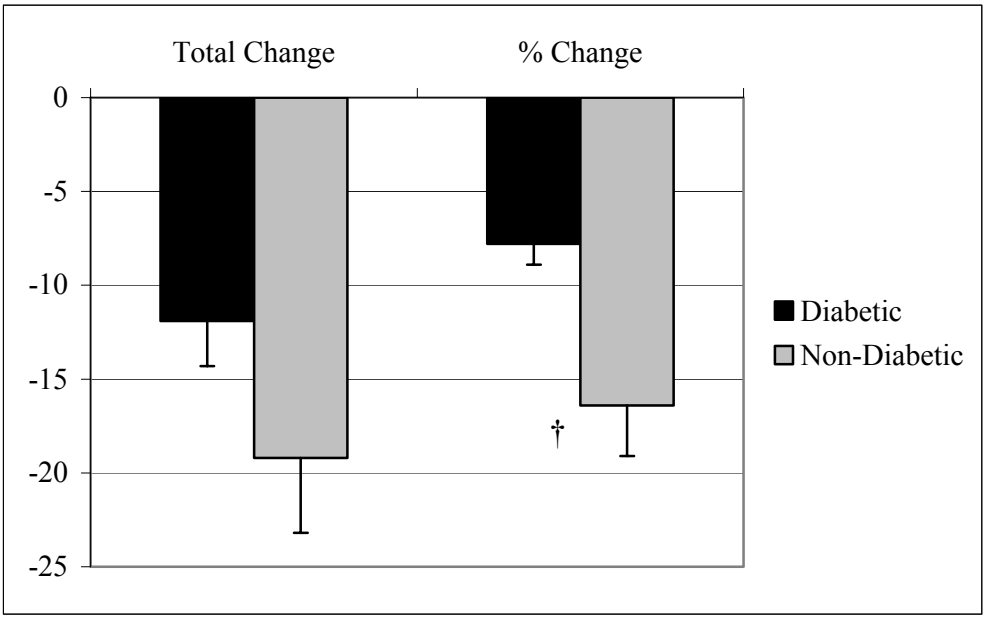
† Unadjusted analysis conducted by student's t-test found to be significantly different between diabetic and non-diabetic subjects.
‡ Adjusted analysis conducted by ANCOVA for week 16 found to be significantly different between diabetic and non-diabetic subjects.
Statistical probability of $p<0.05$ was considered to be significant.

Figure 4.16 Waist Circumference of Study Completers.



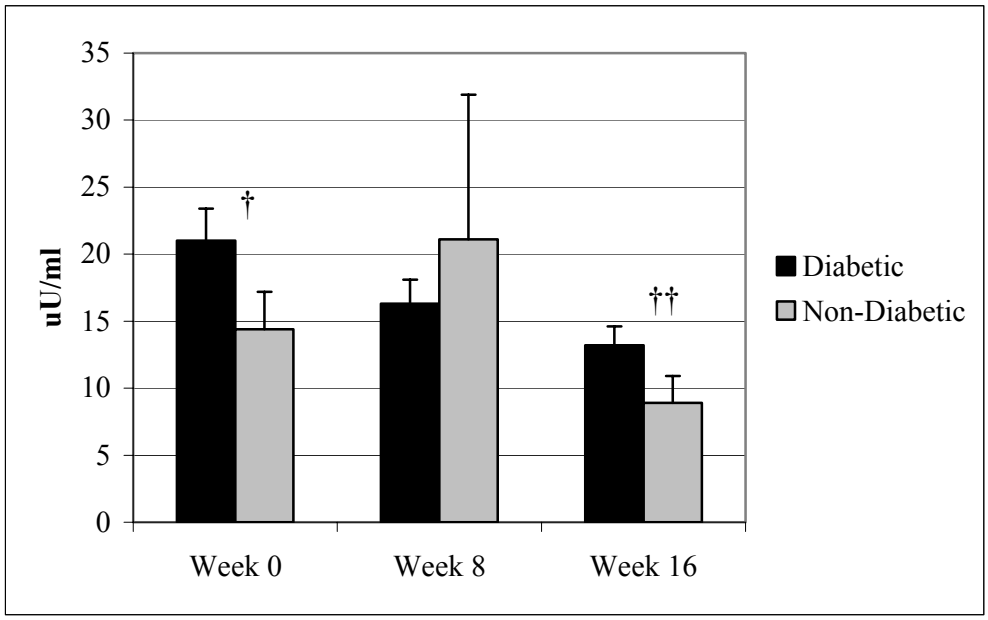
† Unadjusted analysis conducted by student's t-test found to be significantly different between diabetic and non-diabetic subjects.
‡ Adjusted analysis conducted by ANCOVA for week 16 found to be significantly different between diabetic and non-diabetic subjects.
Statistical probability of $p<0.05$ was considered to be significant.

Figure 4.17 Percent Reduction in Waist Circumference and Total Change in Centimeters of Study Completers.



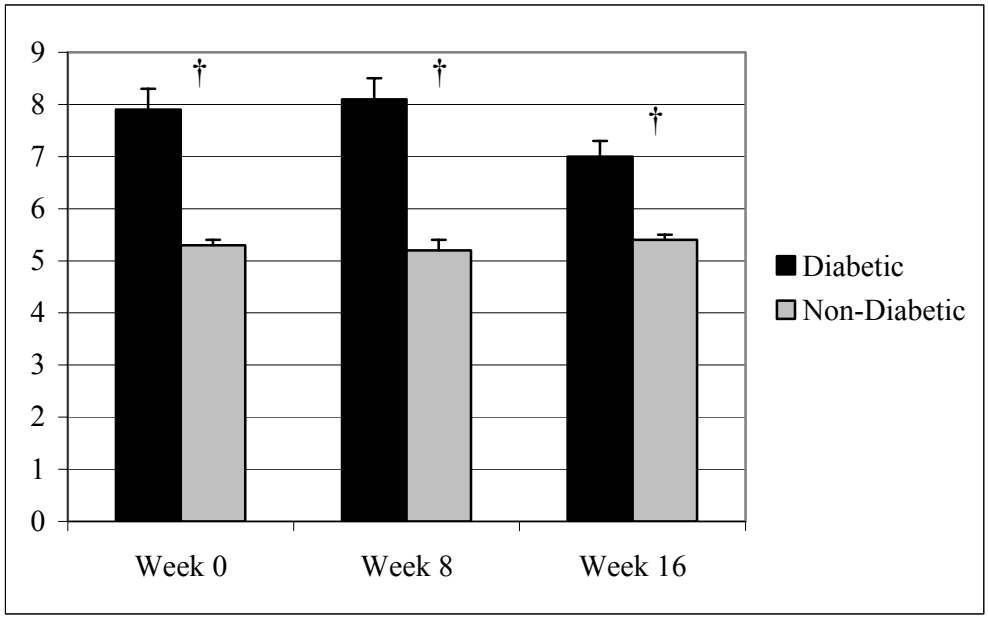
† Unadjusted analysis conducted by student's t-test found to be significantly different between diabetic and non-diabetic subjects.
‡ Adjusted analysis conducted by ANCOVA for week 16 found to be significantly different between diabetic and non-diabetic subjects.
Statistical probability of $p<0.05$ was considered to be significant.

Figure 4.18 Insulin Levels at Week 0, Week 8 and Week 16 of Study Completers. (Mean ± SE)



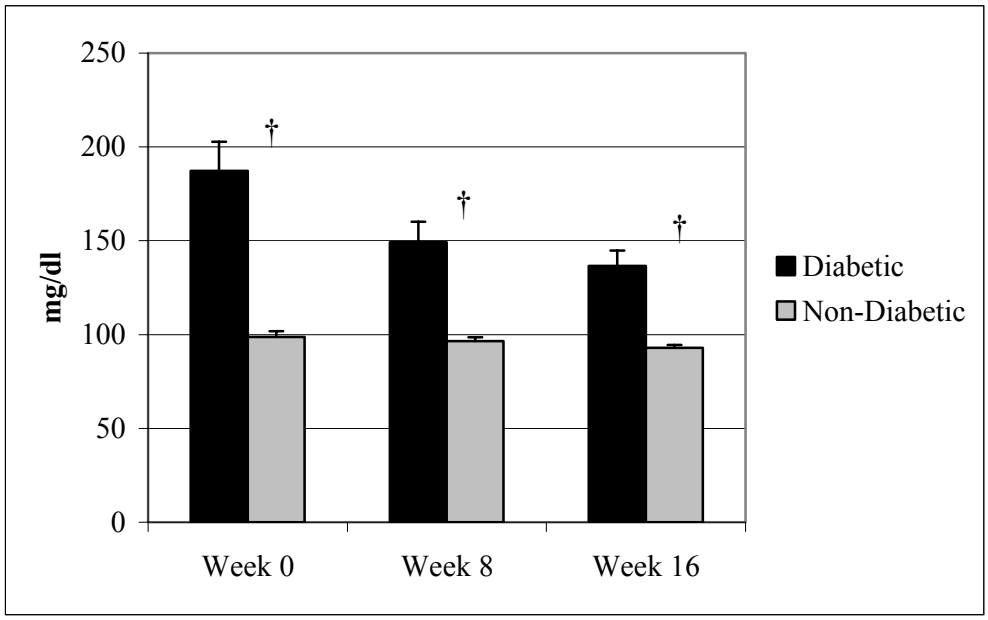
† Unadjusted analysis conducted by student's t-test found to be significantly different between diabetic and non-diabetic subjects.
‡ Adjusted analysis conducted by ANCOVA for week 16 found to be significantly different between diabetic and non-diabetic subjects.
Statistical probability of $p<0.05$ was considered to be significant.

Figure 4.19 HOMA-IR Results at Week 0, Week 8 and Week 16 of Study Completers. (Mean ± SE)



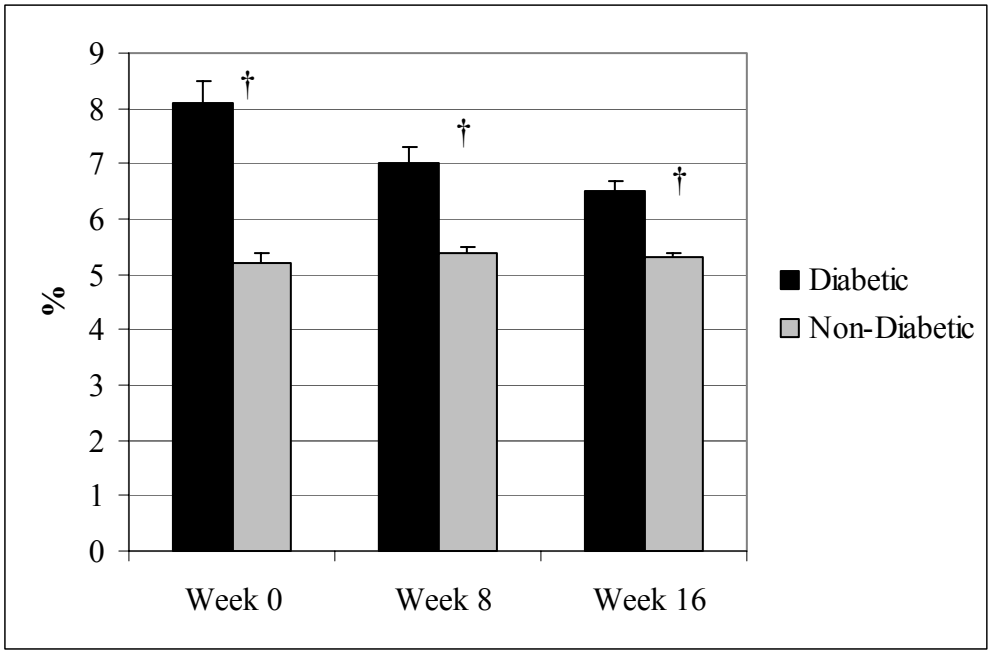
† Unadjusted analysis conducted by student's t-test found to be significantly different between diabetic and non-diabetic subjects.
‡ Adjusted analysis conducted by ANCOVA for week 16 found to be significantly different between diabetic and non-diabetic subjects.
Statistical probability of $p<0.05$ was considered to be significant.

Figure 4.20 Glucose Levels at Week 0, Week 8 and Week 16 of Study Completers. (Mean ± SE)



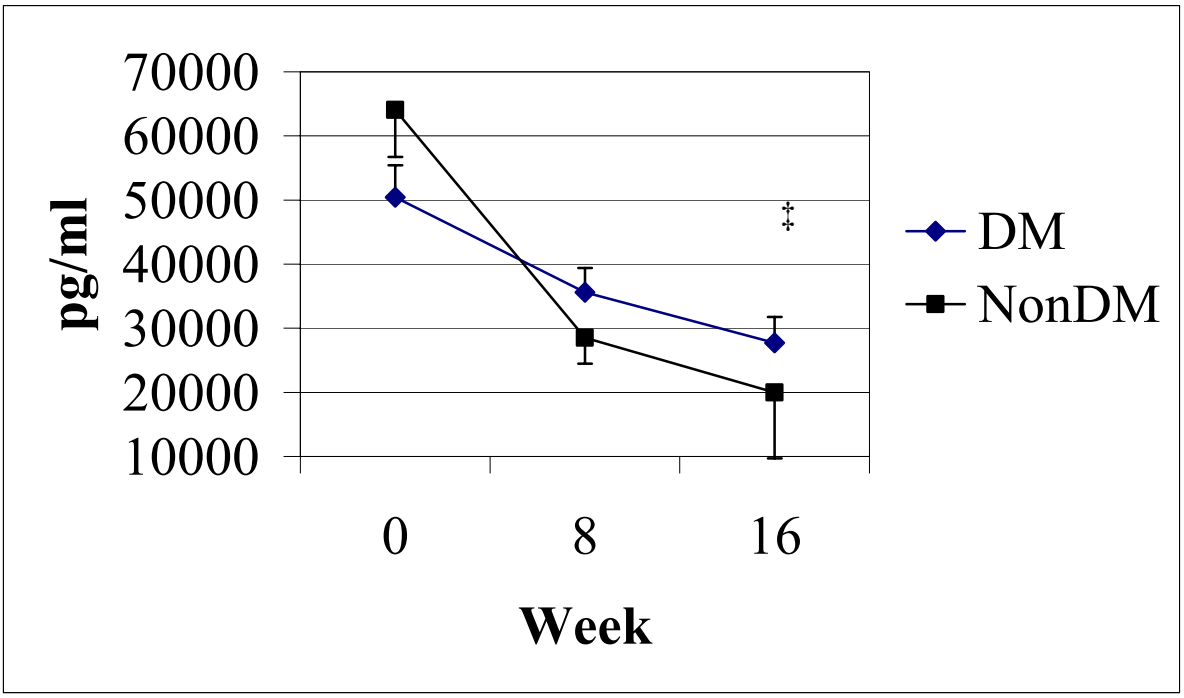
† Unadjusted analysis conducted by student's t-test found to be significantly different between diabetic and non-diabetic subjects.
‡ Adjusted analysis conducted by ANCOVA for week 16 found to be significantly different between diabetic and non-diabetic subjects.
Statistical probability of $p<0.05$ was considered to be significant.

Figure 4.21 HbA1c Values at Week 0, Week 8 and Week 16 of Study Completers. (Mean ± SE)



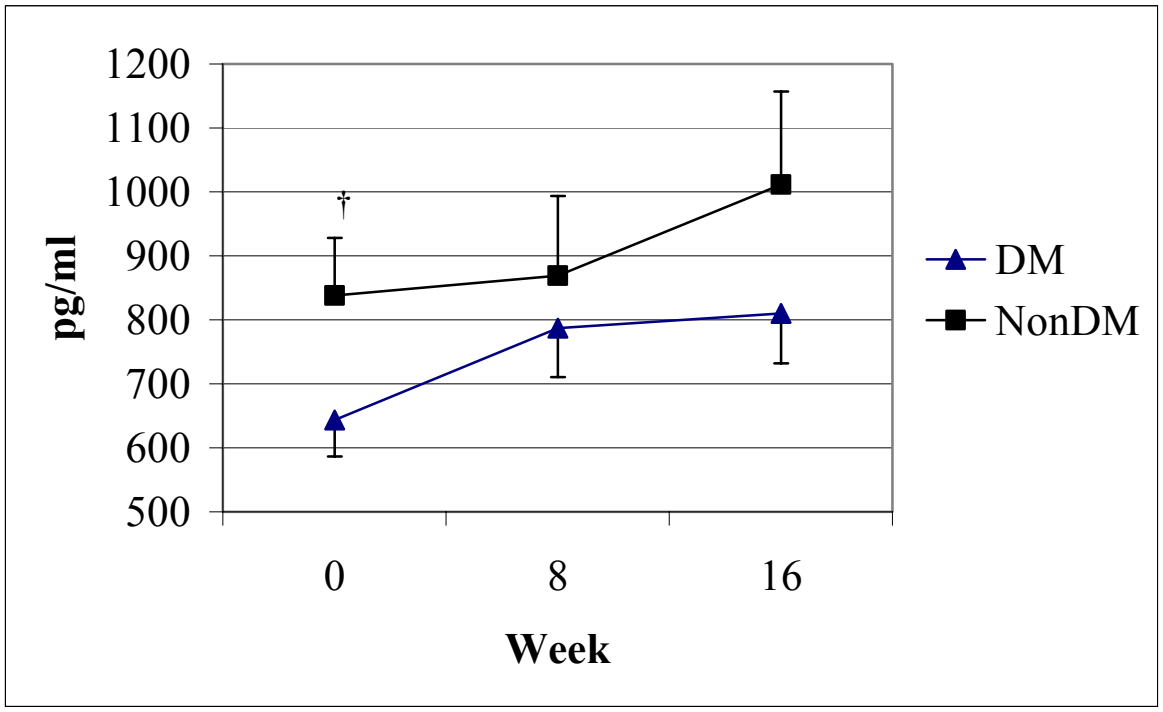
† Unadjusted analysis conducted by student's t-test found to be significantly different between diabetic and non-diabetic subjects.
‡ Adjusted analysis conducted by ANCOVA for week 16 found to be significantly different between diabetic and non-diabetic subjects.
Statistical probability of $p<0.05$ was considered to be significant.

Figure 4.22 Leptin Levels at Week 0, Week 8 and Week 16 of Study Completers. (Mean± SE)



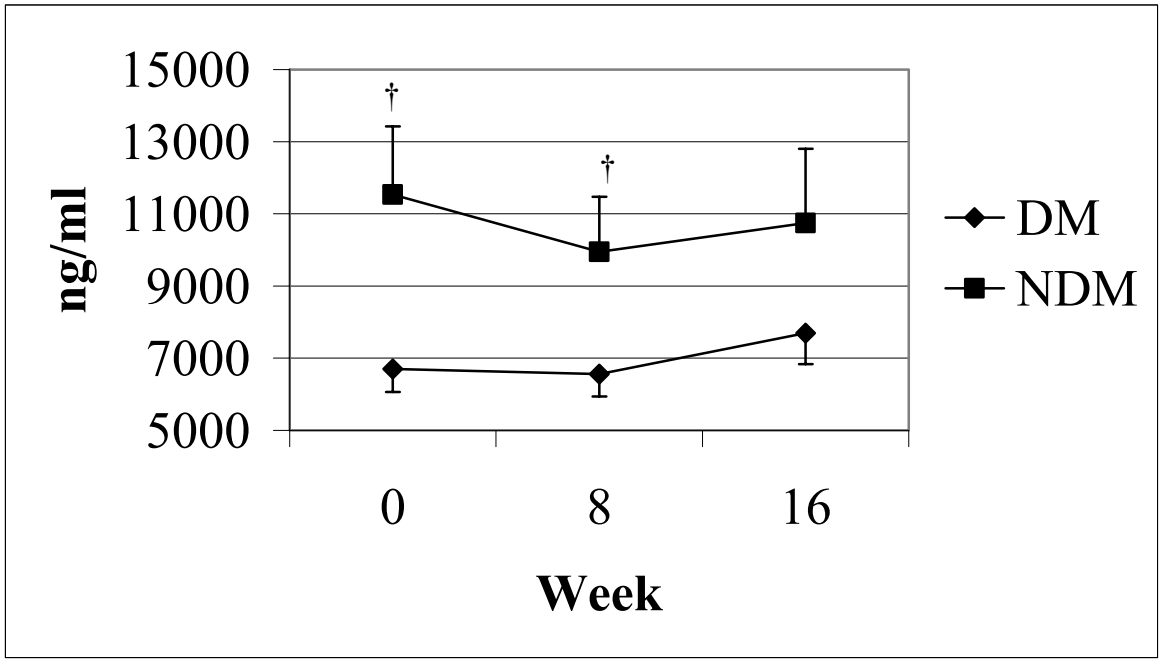
† Unadjusted analysis conducted by student's t-test found to be significantly different between diabetic and non-diabetic subjects.
‡ Adjusted analysis conducted by ANCOVA for week 16 found to be significantly different between diabetic and non-diabetic subjects.
Statistical probability of $p<0.05$ was considered to be significant.

Figure 4.23 Ghrelin Levels at Week 0, Week 8 and Week 16 of Study Completers. (Mean ± SE)



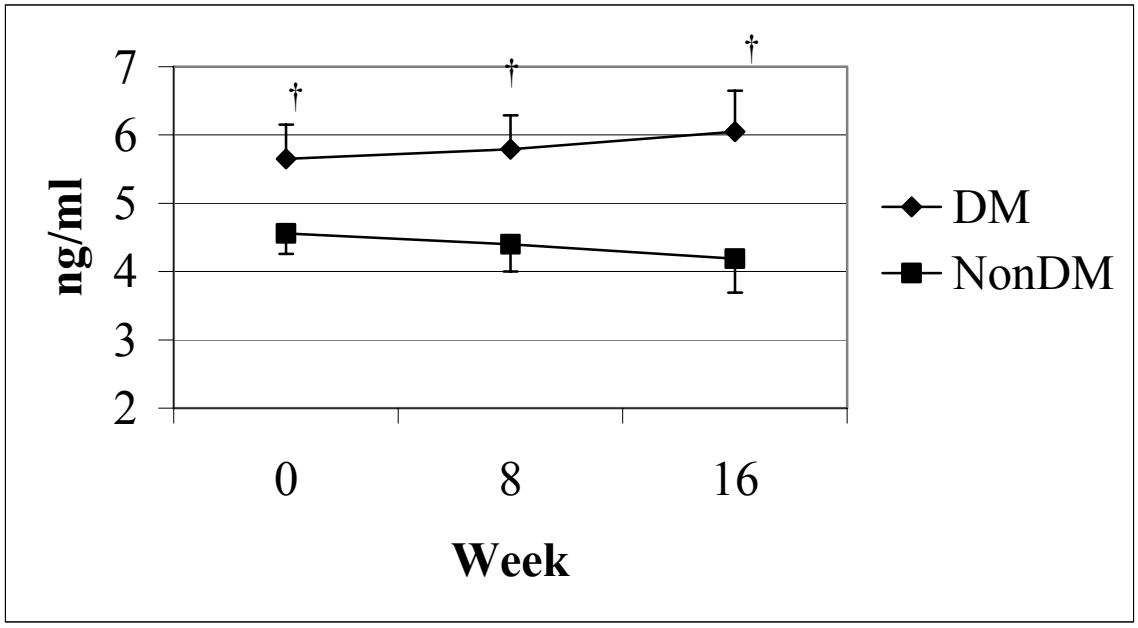
† Unadjusted analysis conducted by student's t-test found to be significantly different between diabetic and non-diabetic subjects.
‡ Adjusted analysis conducted by ANCOVA for week 16 found to be significantly different between diabetic and non-diabetic subjects.
Statistical probability of $p<0.05$ was considered to be significant.

Figure 4.24 Adiponectin Levels at Week 0, Week 8 and Week 16 of Study Completers. (Mean ± SE)



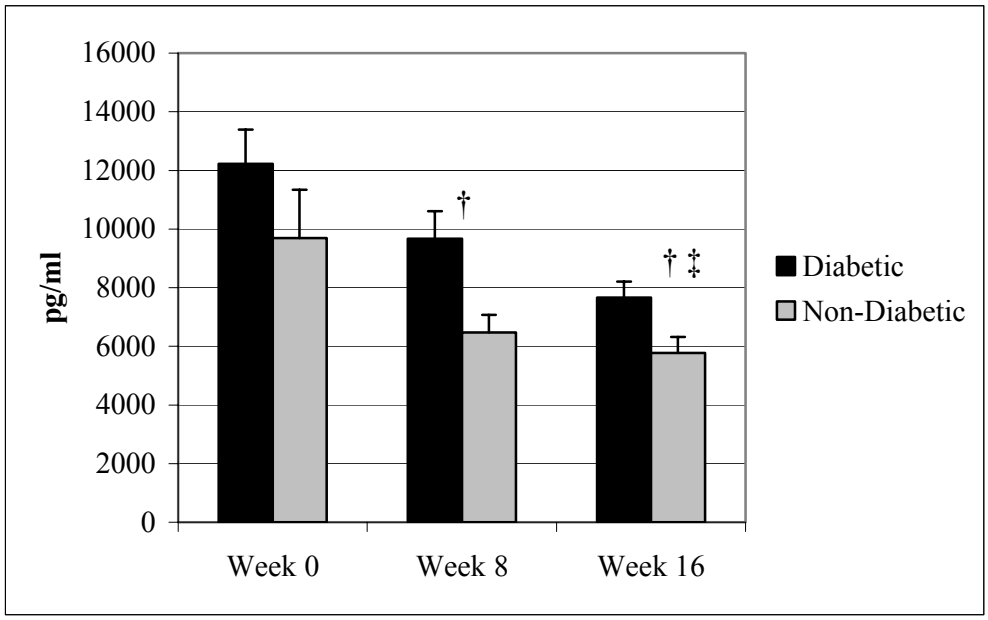
† Unadjusted analysis conducted by student's t-test found to be significantly different between diabetic and non-diabetic subjects.
‡ Adjusted analysis conducted by ANCOVA for week 16 found to be significantly different between diabetic and non-diabetic subjects.
Statistical probability of $p<0.05$ was considered to be significant.

Figure 4.25 Resistin Levels at Week 0, Week 8 and Week 16 of Study Completers. (Mean ± SE)



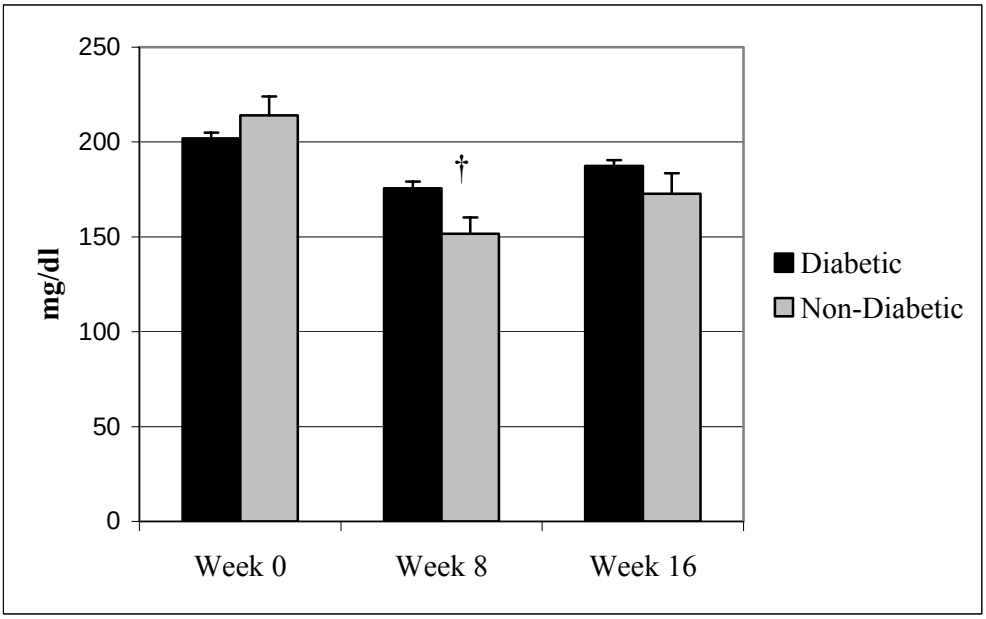
† Unadjusted analysis conducted by student's t-test found to be significantly different between diabetic and non-diabetic subjects.
‡ Adjusted analysis conducted by ANCOVA for week 16 found to be significantly different between diabetic and non-diabetic subjects.
Statistical probability of $p<0.05$ was considered to be significant.

Figure 4.26 Total Plasminogen Activating Inhibitor-1 (PAI-1) Levels at Week 0, Week 8 and Week 16 of Study Completers. (Mean ± SE)



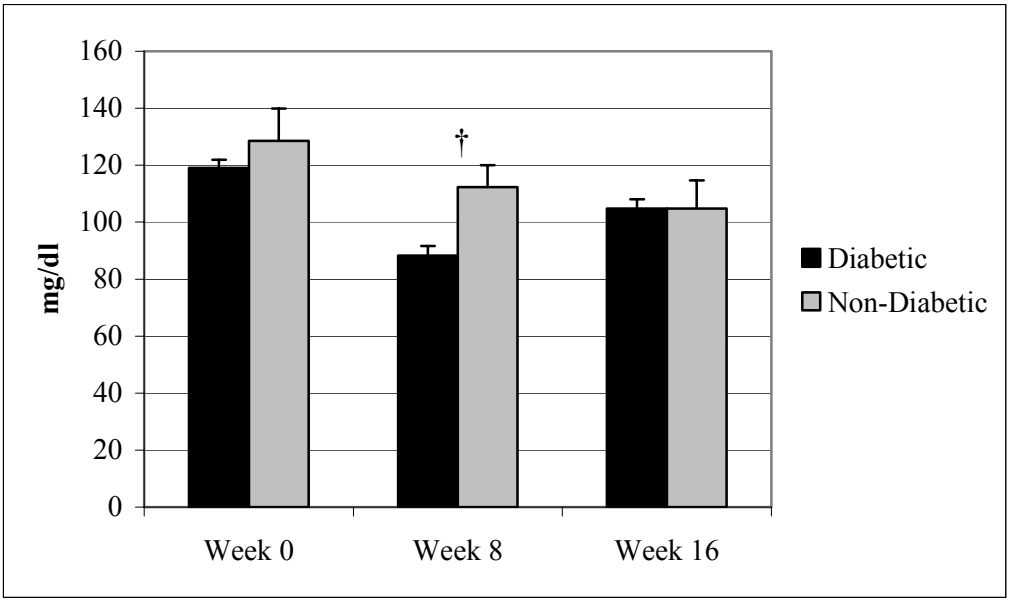
† Unadjusted analysis conducted by student's t-test found to be significantly different between diabetic and non-diabetic subjects.
‡ Adjusted analysis conducted by ANCOVA for week 16 found to be significantly different between diabetic and non-diabetic subjects.
Statistical probability of $p<0.05$ was considered to be significant.

Figure 4.27 Total Cholesterol Levels at Week 0, Week 8 and Week 16 of Study Completers. (Mean ± SE)



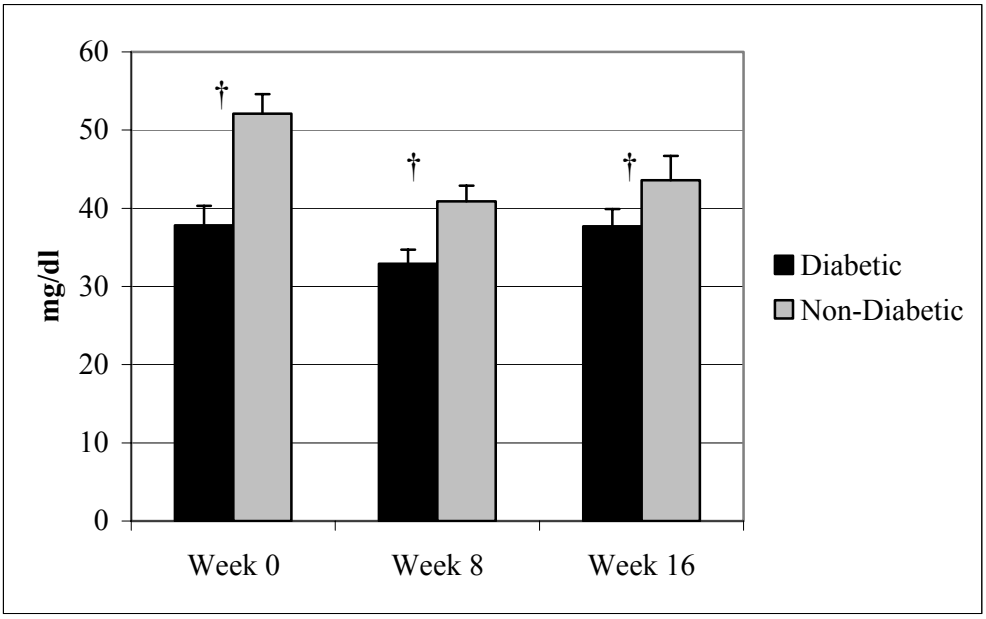
† Unadjusted analysis conducted by student's t-test found to be significantly different between diabetic and non-diabetic subjects.
‡ Adjusted analysis conducted by ANCOVA for week 16 found to be significantly different between diabetic and non-diabetic subjects.
Statistical probability of $p<0.05$ was considered to be significant.

Figure 4.28 LDL-cholesterol Levels at Week 0, Week 8 and Week 16 of Study Completers. (Mean ± SE)



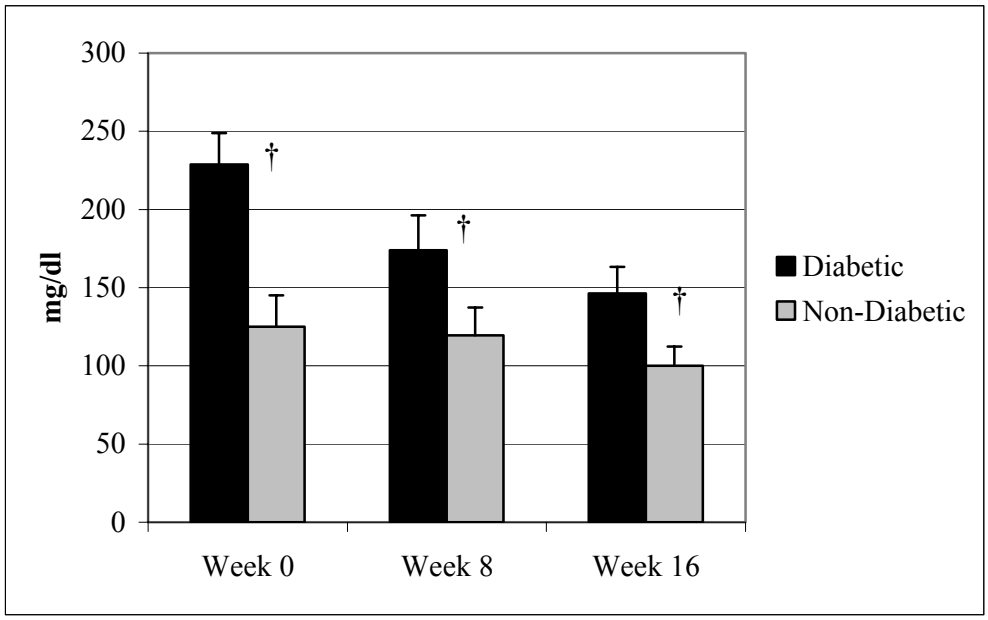
† Unadjusted analysis conducted by student's t-test found to be significantly different between diabetic and non-diabetic subjects.
‡ Adjusted analysis conducted by ANCOVA for week 16 found to be significantly different between diabetic and non-diabetic subjects.
Statistical probability of $p<0.05$ was considered to be significant.

Figure 4.29 HDL-cholesterol at Week 0, Week 8 and Week 16 of Study Completers. (Mean ± SE)



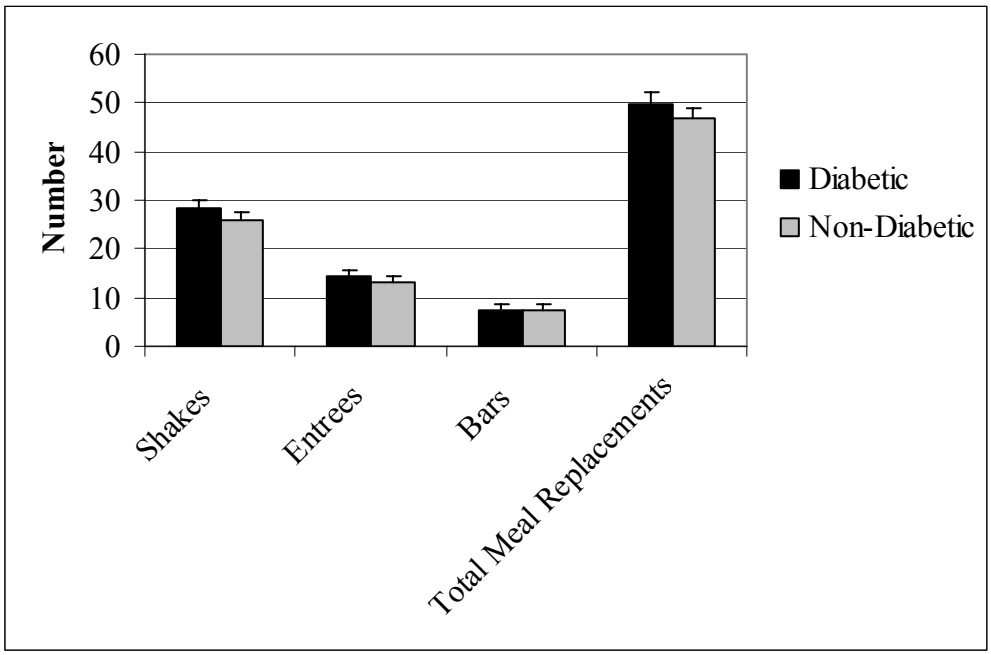
† Unadjusted analysis conducted by student's t-test found to be significantly different between diabetic and non-diabetic subjects.
‡ Adjusted analysis conducted by ANCOVA for week 16 found to be significantly different between diabetic and non-diabetic subjects.
Statistical probability of $p<0.05$ was considered to be significant.

Figure 4.30 Triglyceride Levels at Week 0, Week 8 and Week 16 of Study Completers. (Mean ± SE)



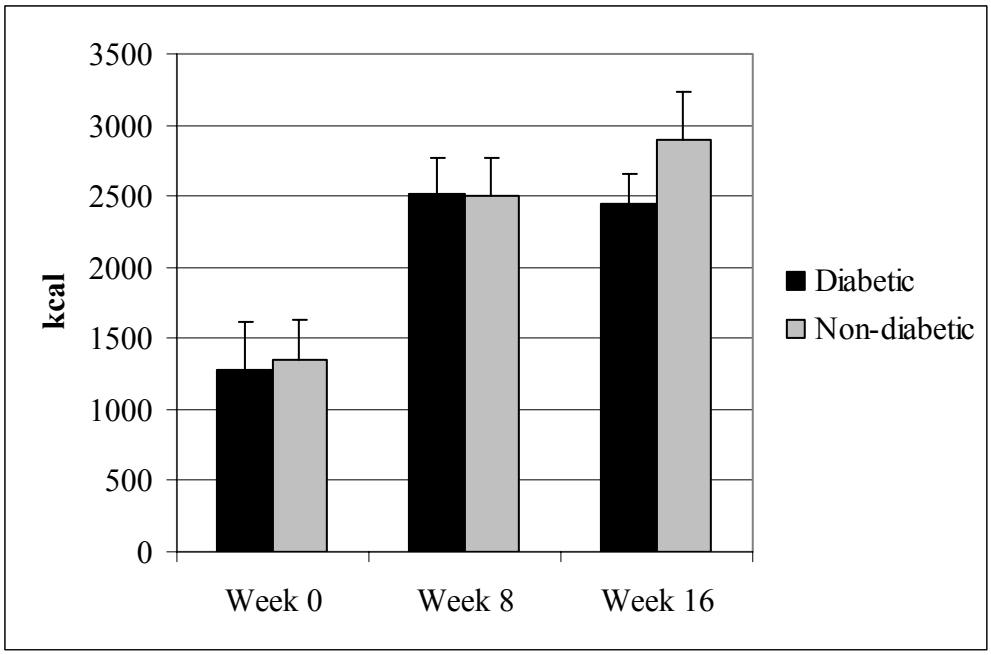
† Unadjusted analysis conducted by student's t-test found to be significantly different between diabetic and non-diabetic subjects.
‡ Adjusted analysis conducted by ANCOVA for week 16 found to be significantly different between diabetic and non-diabetic subjects.
Statistical probability of $p<0.05$ was considered to be significant.

Figure 4.31 Meal Replacement Use for Diabetic and Non-Diabetic Subjects. The Average at Week 16 of Study Completers. (Mean ± SE)



† Unadjusted analysis conducted by student's t-test found to be significantly different between diabetic and non-diabetic subjects.
‡ Adjusted analysis conducted by ANCOVA for week 16 found to be significantly different between diabetic and non-diabetic subjects.
Statistical probability of $p<0.05$ was considered to be significant.

Figure 4.32 Average Weekly Physical Activity for Diabetic and Non-Diabetic Subjects at Week 0, Week 8, and Week 16 as Reported and Recorded into the Patient at a Glance Data Sheets of Study Completers. (Mean ± SE)



† Unadjusted analysis conducted by student's t-test found to be significantly different between diabetic and non-diabetic subjects.
‡ Adjusted analysis conducted by ANCOVA for week 16 found to be significantly different between diabetic and non-diabetic subjects.
Statistical probability of $p<0.05$ was considered to be significant.

CHAPTER FIVE

Discussion

The overall goal of the present study was to assess differences after weight loss in body composition and other metabolic parameters in women with type 2 diabetes compared to women without type 2 diabetes. Individuals with type 2 diabetes are at increased risk of morbidity and mortality and thus the importance of eliminating these co-morbid conditions associated with obesity and type 2 diabetes are of utmost importance in improving overall health and quality of life. This study attempted to decipher why women with type 2 diabetes often have a more difficult time losing weight, the differences between diabetic and non-diabetic individuals in body composition changes, specifically changes in abdominal visceral and subcutaneous adipose changes, changes in proinflammatory and prothrombotic markers and, finally, in improvements of lipid levels.

Weight Loss

The primary hypothesis that obese individuals with type 2 diabetes would lose less body weight than obese women without type 2 diabetes was not fully supported by analyses of women who completed the study. As stated previously, individuals with type 2 diabetes have a more difficult time losing weight with the conventional and behavioral approaches to weight loss compared with non-diabetic individuals (73;203;204). We found that women with type 2 diabetes, after adjusting for initial body weight, lost less weight, but not significantly so compared to women without type 2 diabetes in a medically-supervised weight loss program. Non-diabetic subjects

lost 15.4 kg of body weight and diabetic subjects lost 12.2 kg of body weight. The BMI changes were consistent with body weight changes. There was no significant difference in BMI units in diabetic or non-diabetic subjects before or after the weight loss phase indicating that diabetic subjects lost similar amount of weight to the non-diabetic subjects.

The intention-to-treat (ITT) or last-observation-carried-forward (LOCF) analyses indicated that diabetic subjects were not able to lose as much percentage body weight as the non-diabetic subjects. All of the non-diabetic subjects completed the 16-week weight loss program, while 3 of the diabetic subjects terminated the program early. The fact that all individuals who ended the program early were diabetic subjects could explain why previous researcher (73;203;204) have concluded that individuals with type 2 diabetes often have a greater difficulty losing weight than non-diabetic subjects.

The results of this study demonstrate that for women who complete a structured, medically-supervised low-energy diet (LED) weight loss program, there is no significant difference in success of weight loss. We also concluded that medically-supervised LED weight loss programs are a safe and effective method of weight loss for women with type 2 diabetes. In the present study, women with type 2 diabetes who completed the study consumed the same amount of shakes, entrees, bars and total meal replacements as non-diabetics.

Individuals with type 2 diabetes have an increased risk for cardiovascular disease (222), peripheral vascular disease (222) and peripheral neuropathy (222), often increasing the difficulty to initiate and maintain physical activity. The ability of

individuals with type 2 diabetes to perform the required physical activity in this medically-supervised LED may help explain the success in weight loss observed in these individuals. As seen in the results of physical activity, non-diabetic and diabetic women both consistently attended weekly classes and made their mid-week phone calls. At 16 weeks both groups had an average of 6.6 days that were "in the box" and the majority of individuals were able to following the Triple Imperative™ requirements. Osteoarthritis is also common in obese individuals with and without type 2 diabetes, often making physical activity more painful. In this study 4 women with type 2 diabetes had arthritis and another 5 reported back, leg and joint pain. One subject with type 2 diabetes had Charcot's or neuropathic joint disease, which is a progressive destructive arthritis associated with loss of pain sensation, proprioception, or both (223). This woman had 2 toes amputated and was still able to do most of the required physical activity. One woman without type 2 diabetes reported having arthritis and 2 subjects without type 2 diabetes reported back, leg and joint pain. Despite the higher incidence of arthritis and joint pain in the subjects with type 2 diabetes, there was no difference in the amount of physical activity conducted. At week 8 and week 16, both non-diabetic and diabetic women were doing more than the minimum 2000 kcal required by the HMR® program.

Anderson et al. (224) found that VLED and LED were safe and effective methods of weight loss for individuals with diabetes. In a study of 40 subjects with type 2 diabetes, subjects lost an average of 15.7 kg with a decrease in insulin use, anti-diabetes and hypertensive medications with no serious side effects. Reynolds et al. (225) also found that medically-supervised VLED and LED were safe and

effective methods of weight loss for individuals with diabetes. In a retrospective review of consecutive patients enrolled in these programs, it was found that there was no difference in the amount of weight loss in non-diabetic and diabetic subjects who completed 12 weeks of the weight loss program (225). These results are consistent with the findings of the present study. Other researchers have also found VLEDs to be safe and effective for individuals with type 2 diabetes (226-230).

Body Composition Measurements

Various procedures for body composition analysis cannot be compared directly due to different underlying principles. DEXA uses a 3-compartment body composition model consisting of bone mineral content, fat and lean tissue, while BOD POD® is based on a 2-compartment model based on body density (231). Comparison between these body composition techniques generally yield high correlations for percent body fat but may differ in the absolute values obtained (231). Weyers et al. (231) studied body composition changes after weight loss using DEXA and BOD POD® measurements. These researchers found that there was no significant differences in changes in percent body fat, fat mass and fat-free mass in response to weight loss between the methods. However, Hendel et al. (232) explained the differences in percent body fat between DEXA and BOD POD® could be due to incomplete scanning of the entire body using DEXA which would account for errors in the DEXA estimates of percent body fat. In the present study DEXA scanning of the obese subjects was incomplete. The DEXA scan was originally made for non-obese women to measure bone mineral density and was not designed for larger individuals. Many of the women in the present study did not completely fit on

the table. The majority of the scans had one or both of the arms slightly missing from the scan/ body composition calculations. The CT technique and results also differ from DEXA and BOD POD®. This procedure produces radiographic images of the abdomen which allows for differentiation between subcutaneous and visceral adipose tissue accumulation. The CT results are not expressed as a percentage or mass (e.g., kg), but in area (cm^2). Although the results of these procedures cannot be directly compared, trends in their findings can be useful to validate the changes in body composition.

It must be noted that in the present study, though the methods of body composition can not be directly compared, the results of the data were very consistent between the body composition measurements. This has provided strength in the study design and provided further confirmation of the results.

Baseline Comparison of Body Composition

The hypothesis that obese individuals with type 2 diabetes will lose a greater proportion of abdominal fat as visceral abdominal fat compared to obese individuals without type 2 diabetes was examined. Several body composition measurements were conducted to examine changes in the amount and type of adipose tissue following weight loss in the study subjects. Dual-energy x-ray absorptiometry (DEXA) was used to measure total percent body fat; percent body fat in the trunk; total fat; total fat in the trunk; total lean tissue; and total tissue in the trunk. Air-displacement plethysmography (BOD POD®) was used to measure percent body fat, and abdominal computer tomography (CT) was used to measure total abdominal adipose tissue and subcutaneous and visceral abdominal adipose tissue.

Diabetic individuals have more lean tissue and less fat than non-diabetic individuals. Diabetic individuals also have less abdominal subcutaneous adipose tissue than non-diabetic individuals. However, diabetic individuals have significantly more visceral adipose tissue than non-diabetic individuals. Diabetic subjects have significantly more total lean tissue ($p=0.002$) than non-diabetic subjects. Adjusting for differences in body weight, diabetic subjects have a non-significantly higher percentage of lean body tissue with DEXA and BOD POD® measurements. Results from our measurements are consistent with those from the literature.

It is unclear why diabetic subjects have relatively more lean tissue than non-diabetic subjects. This could somehow be related to the insulin resistant state and impaired metabolism of glucose and fatty acids by skeletal muscle in type 2 diabetes(233-235). One possible explanation for dysregulation of local lipolytic activity and development of insulin resistance in skeletal muscle may be due to an inverse relationship between intramuscular triglyceride content and insulin resistance (236). Kelley et al. (237) found that mitochondria tended to be smaller and have a reduced activity of complex 1 of the electron transport chain in individuals with type 2 diabetes. The researchers concluded that this impaired functional capacity of mitochondria may be a major determinant in the pathogenesis of skeletal muscle insulin resistance in type 2 diabetic individuals. Mitochondrial dysfunction in skeletal muscle in individuals with type 2 diabetes has been reported by other researchers as well (238-240).Glucose toxicity alters protein function through glycosylation of tissue proteins and may decrease enzyme and other vital protein functions (241;242). In the present study, the greater amount of lean tissues in the

women with type 2 diabetes could contribute to the variations in adipose tissue concentrations and insulin resistance compared with the women without type 2 diabetes.

The fat mass of diabetic subjects is relatively lower than that for non-diabetic subjects. Diabetic subjects have a non-significant lower percentage of body fat than non-diabetic subjects by DEXA and BOD POD®. In addition, diabetic subjects have less truncal fat and less subcutaneous fat by CT than non-diabetic subjects. Our results are similar to those reported by Halvatsiotis (243). Halvatsiotis et al. (243) compared baseline body composition measurements of individuals with type 2 diabetes to weight-matched controls. Although not significant, DEXA measurements of lean mass (FFM) in kg found that diabetic subjects had slightly greater total lean tissue than the non-diabetic subjects. Total fat mass was found to be significantly greater in non-diabetic subjects then the diabetic subjects. There was no significant difference in the amount of total abdominal adipose tissue determined by CT and diabetic subjects had significantly greater visceral adipose tissue at baseline than the non-diabetic subjects. The results of these baseline findings are consistent in the study population of the present study. In contrast, Markovic et al. (161) assessed early and late changes in lipid levels induced by energy restriction versus fat loss in obese individuals with and without type 2 diabetes. Percent of total abdominal fat determined by DEXA and waist circumference was not found to be different prior to weight loss.

Body Composition Changes with Weight Loss

With weight loss, diabetic subjects lose slightly more lean tissue than non-diabetic subjects by DEXA and BOD POD®. These changes are consistent after adjusting for baseline difference in body weight. Diabetic subjects also lose less total and truncal fat as measured by DEXA, BOD POD® and CT than non-diabetic subjects. While diabetic subjects lose equivalent amounts of visceral adipose tissue, as a percentage of weight loss on initial values, the absolute loss of visceral adipose tissue is greater in diabetic than non-diabetic subjects is unclear.

DEXA measurements found diabetic subjects had significantly more total lean tissue than non-diabetic subjects after 16 weeks of weight loss ($p=0.004$). The percentage change in total lean tissue was not significantly different after 16 weeks of weight loss. This was also found after adjusting for baseline measurements, ANCOVA analysis found no significant difference between the groups at week 16. Unlike the DEXA results, analysis of total lean tissue after 16 weeks of weight loss with BOD POD® found no significant difference in the amount of total lean tissue in non-diabetic and diabetic subjects. The percent change in total lean tissue however found diabetics subjects lost significantly more lean tissue than non-diabetic ($p=0.027$). ANCOVA analysis, adjusting for baseline values was approaching significance at week 16 with diabetic subjects having more lean tissue than non-diabetic subjects. The differences between the DEXA and BOD POD® are most likely due to incomplete scanning of the subjects in the DEXA analysis. The overall results indicate that diabetic subjects had more total lean tissue than non-diabetic subjects after weight loss.

Percent and Total Body Fat

Total percent body fat was measured by DEXA and BOD POD®. The DEXA analysis indicated that after 16 weeks of weight loss diabetic subjects lost significantly less percent body fat than non-diabetic subjects (p=0.043). However, after adjusting for baseline values there was no significant difference in absolute percent body fat between non-diabetic and diabetic subjects after 16 weeks of weight loss. BOD POD® analysis found no significant difference in the amount of percent body fat lost between non-diabetic and diabetic subjects. However, after adjusting for baseline values, ANCOVA analysis found that diabetic subjects lost significantly less percent body fat than non-diabetic subjects (p=0.009). Differences between DEXA and BOD POD® results have already been discussed. The overall conclusion is diabetic subjects lost less percent body fat than non-diabetic subjects, but not after adjusting for baseline values. Diabetic and non-diabetic subjects had the same amount of percent body fat after weight loss.

DEXA measurements of total fat indicated no significant difference in total body fat at week 16 between non-diabetic and diabetic subjects. Non-diabetics significantly decreased their percentage change in total body fat compared to diabetic subjects after 16 weeks of weight loss (p=0.029). After adjusting for baseline values diabetic subjects had significantly greater total fat than non-diabetic subjects (p=0.007). BOD POD® measurements of total fat found diabetic subjects had more total body fat at week 16 than non-diabetic subjects (p=0.043). Non-diabetic subjects significantly decreased their percentage change in total fat compared to diabetic subjects (p=0.004). After adjusting for baseline values diabetic subjects had

significantly more total fat than non-diabetic subjects after 16 weeks of weight loss ($p=0.007$). Overall, results indicate that diabetic subjects had more total body fat than non-diabetic subjects and diabetic subjects did not decrease their total body fat as much as non-diabetic subjects after 16 weeks of weight loss.

Our observations in percentage body fat and total fat are similar to Funkhouser et al. (244). In a study conducted by Funkhouser et al. (244) these researchers found that in 19 healthy obese women, a 13.1 kg weight loss resulted in a -5.9 percent of body fat analyzed by DEXA. These results are consistent with the non-diabetic subjects studied in the present study. Blaak et al. (245) studied 27 women and 8 men with type 2 diabetes and compared body composition changes after a VLED. The researchers found that with a 12.0 kg weight loss, percentage of body fat determined by underwater weighing decreased by -5.4. This is consistent with the findings of Funkhouser et al. (244) and the present findings in the non-diabetic subjects. Underwater weighing is based on a 2-compartment model as is the BOD POD®. Comparing the present results of diabetic subjects using the BOD POD® analysis to Funkhouser and et al. (244) findings, the diabetic subjects in the present study lost more percentage body fat per kg of weight loss.

Abdominal Adipose Tissue

Abdominal fat was determined by DEXA and CT measurements after 16 weeks of weight loss. DEXA measurements found that at week 16 diabetic subjects had significantly more trunk fat than non-diabetic subjects ($p=0.035$). The percentage change in trunk fat was significantly lower in diabetic than non-diabetic subjects ($p=0.05$). Diabetic subjects had significantly more lean tissue in the trunk than non-

diabetic subjects after 16 weeks of weight loss (0.0005). The percentage change in lean tissue in the trunk was not found to be significantly different between non-diabetic and diabetic subjects. The amount of total trunk tissue determined by DEXA found that diabetic subjects had significantly more than non-diabetic subjects (p=0.001). The percentage change in trunk tissue was not found to be different in diabetic than non-diabetic subjects. After adjusting for baseline values diabetic subjects had significantly more total trunk tissue than non-diabetic subjects (p=0.12). Analysis of total abdominal adipose tissue by CT was found not to be significantly different between diabetic and non-diabetic subjects after 16 weeks of weight loss. After adjusting for baseline there was no difference in the amount of total abdominal tissue between diabetic and non-diabetic subjects. Waist circumferences were significantly greater in diabetic than non-diabetic subjects after 16 weeks of weight loss (p=0.0004). The percentage change in waist circumference was significantly less in diabetic than non-diabetic subjects after 16 weeks of weight loss (p=0.0103). After adjusting for baseline values diabetic subjects had significantly greater waist circumferences than non-diabetic subjects (p=0.001). Overall, the results of the total abdominal tissue found that diabetic subjects had significantly more abdominal tissue than non-diabetic subjects after 16 weeks of weight loss. These results are consistent with Stoney et al. (246) who compared regional body fat distribution in women with and without type 2 diabetes. The results indicated that total body fat were similar between the two groups, the women with type 2 diabetes had significantly less lower-body fat, greater waist circumferences and abdominal fat than the women without type 2 diabetes. These researchers concluded that a reduced capacity to deposit

and/or conserve lower-body fat may be an independent factor associated with the metabolic manifestations of the insulin resistance syndrome in women with type 2 diabetes.

Visceral and subcutaneous adipose tissue measurements were by CT. After 16 weeks of weight loss diabetic subjects had significantly greater amount of visceral adipose tissue than non-diabetic subjects ($p=0.004$). After adjusting for baseline values there was no significant difference in the amount of visceral adipose tissue in diabetic and non-diabetic subjects. After 16 weeks of weight loss there was no significant difference in the amount of subcutaneous adipose tissue between diabetic and non-diabetic subjects. After adjusting for baseline values diabetic subjects had significantly greater subcutaneous adipose tissue than non-diabetic subjects ($p=0.034$). Overall, the changes in visceral adipose tissue were not significantly different between the groups after weight loss, but diabetic subjects had significantly greater visceral adipose tissue stores than the non-diabetic subjects. After 16 weeks of weight loss there was no difference in subcutaneous adipose tissue stores in diabetic and non-diabetic subjects. After adjusting for baseline values diabetic subjects had significantly less subcutaneous adipose tissue than non-diabetic subjects ($p=0.0394$). The explanations for these differences are uncertain. To determine the number of subjects needed to see if there was a difference in percentage change in visceral adipose tissue a sample size calculation was conducted. Using a power of 0.8 and an alpha of 0.05, the sample size to determine differences in percentage change of visceral adipose tissue between diabetic and non-diabetic subjects would require 4070 subjects per group for a total of 8140 subjects. After 16 weeks of weight loss there

was no significant difference in the amount of subcutaneous adipose tissue between diabetic and non-diabetic subjects. This greater number of subjects needed to determine this difference suggests that percentage of visceral adipose tissue change with weight loss is the same in diabetic and non-diabetic subjects. A sample size determination of percentage change in subcutaneous adipose tissue with the same power and alpha would be 17 subjects for each group for a total of 34 subjects. This lower number reflects the significant difference found in subcutaneous adipose tissue in the present study.

Despres and Lamarche (247) suggested that a visceral fat accumulation greater than 130 cm^2 could be associated with a decrease in insulin sensitivity. In the present study both diabetic and non-diabetics had visceral fat accumulation greater than this, 208.3 cm^2 and 177.42 cm^2, respectively. It should be noted that Karelis et al. (248) also found that metabolically healthy obese women had significantly higher visceral adipose accumulation (141 ± 53 cm^2). Despres and Lamarche (65) also concluded that abdominal visceral fat accumulation greater than 100 cm^2 was associated with increased risk factor for coronary heart disease. Williams et al. (249) found similar results in pre- and postmenopausal women and found that intra-abdominal fat accumulation greater than 110 cm^2 were at an increased risk for coronary heart disease. In the present study, after weight loss visceral adipose tissue accumulation was still greater than 130 cm^2 in diabetic subjects (132.4 cm^2), while the non-diabetics had decreased their visceral fat accumulation to 79.4 cm^2. Thus, the diabetic subjects in the present study are at a greater risk of developing coronary heart disease than the non-diabetic subjects.

Karelis et al. (248) compared body composition in women considered to be metabolically healthy but obese to obese individuals with risks for the metabolic syndrome. These researchers found that despite similar levels of total body fatness, metabolically healthy obese individuals showed 49% less visceral adipose tissue (as measured from CT) than at-risk subjects with the metabolic syndrome. The metabolically healthy women showed a more favorable lipid profile, including lower fasting triglycerides, higher HDL-cholesterol and lower glucose and insulin concentrations. These results agree with findings of other researchers (250;251) that the amount of visceral fat is an important factor associated with variations in insulin sensitivity. Excessive visceral fat has been associated with a decrease in insulin sensitivity, which could lead to an increase risk of cardiovascular disease (252). In the study by Karelis et al. (248)the higher levels of insulin sensitivity in the metabolically healthy but obese individuals may be due to lower amount of visceral fat despite the presence of large amount of total body fatness. In the present study, there was no significant difference in the change in abdominal visceral adipose tissue between non-diabetic and diabetic subjects. The diabetic subjects had significantly more visceral adipose tissue at baseline and after 16 weeks of weight which would account for their decrease in insulin sensitivity.

Miyashita et al. (253) found that individuals consuming a low-carbohydrate diet of approximately 1000 kcal/day with a 9 kg weight loss, visceral-to-subcutaneous adipose tissue ratio (V/S) was significantly decreased from 0.69 to 0.47 ($p<0.05$). The amount of carbohydrate used in this diet is consistent with the carbohydrate content used in the HMR® program. In the present study, before weight loss non-

diabetic subjects had a V/S ratio of 0.20 while diabetic subjects had a significantly higher ratio of 0.43. Both groups significantly decreased the V/S ratio to 0.19 and 0.33 for non-diabetic and diabetics respectively; however, there was no significant difference in the amount of change.

Effects of Weight Loss in Ghrelin Values

The hypothesis that plasma ghrelin levels in response to weight loss would not increase as much in individuals with type 2 diabetes as compared with individuals without type 2 diabetes was supported at week 16 after ghrelin values were adjusted for baseline. However, diabetic subjects had significantly lower ghrelin levels at baseline. Figure 4.11 depicting the rise of ghrelin levels due to weight loss, is consistent with the predicted levels in Figure 2.4. Overall, despite nonsignificant differences after 16 weeks of weight loss, women with type 2 diabetes continually had lower levels of ghrelin and both groups did not increase ghrelin levels to normal.

Current research involving this newly discovered hormone is inconclusive and incomplete. Recent studies show that levels of ghrelin (254;255) are inversely related to insulin resistance; visceral adipose tissue accumulation is believed to down-regulate ghrelin (254). Pöykkö et al. (256;257) measured fasting plasma ghrelin concentrations in 1,045 individuals of the Oulu Project Elucidating Risk of Atherosclerosis (OPERA) study. The mean fasting plasma ghrelin concentration of the study cohort was 668 pg/ml (range 117-1513). Results indicated that ghrelin levels were lower in subjects with type 2 diabetes, which is consistent with previous studies (100;258). This study also demonstrated adiposity to be an important determinant of ghrelin concentrations. Therefore, the lower ghrelin concentrations in

type 2 diabetic subjects could be due to their higher adiposity. The results of the study suggested that low ghrelin is independently associated with elevated blood pressure level and insulin concentration and the prevalence of type 2 diabetes. Similar to Pöykkö and colleagues (256;257), Katsuki et al. (259) evaluated 18 obese and 18 non-obese patients with type 2 diabetes to investigate ghrelin's possible role in abdominal adiposity, insulin levels and insulin resistance in individuals with type 2 diabetes. These researchers found that ghrelin levels are significantly associated with abdominal adiposity, fasting serum levels of insulin and insulin resistance in patients with type 2 diabetes. However, instead of adiposity as the determinant of ghrelin concentration, they concluded that hyperinsulinemia associated with insulin resistance decreases plasma levels of active ghrelin in patients with type 2 diabetes. Other research has also concluded that insulin is the prime regulator of ghrelin concentrations and that insulin may be the lead candidate for a long-term mediator of ghrelin responses to weight change (260;261).

In other studies, the association of ghrelin to visceral adipose tissue and insulin has not been shown. Hansen et al. (262) studied eight obese Caucasian women with a mean age of 48.6 $\pm$ 3.5 years attending a 6-month weight loss course organized by The Danish Heart Association. These researchers found that individuals lost 5% of their initial body weight, resulting in an 8% reduction in total body fat and that plasma ghrelin levels increased by 12%. The increase in ghrelin was positively correlated to the weight reduction but not to the decrease in intra-abdominal fat area, plasma insulin or leptin. The possibly discrepancy between these results and other studies could be due to the small sample size and also not including individuals with

type 2 diabetes into the study. It may be that the genetic factors that predispose certain individuals to type 2 diabetes may also affect an individual's ghrelin production and metabolic responses. Purnell et al. (261) examined the relationship of ghrelin levels to body composition and parameters of glucose and lipid metabolism. They found no relationship of ghrelin to percentage body fat, total fat mass, lean mass, intraabdominal fat or leptin levels. They concluded that ghrelin levels best reflect body weight rather than specific amounts of fat or body fat distribution and that ghrelin levels correlated negatively with insulin and positively with insulin resistance. These results could explain why individuals with type 2 diabetes have lower ghrelin levels than non-diabetic individuals.

There are currently no published studies directly examining the effects of weight loss on ghrelin levels in individuals with type 2 diabetes. It has been postulated that ghrelin may function as an adiposity signal contributing to weight regain in post-obese subjects, as evidenced by the increase in circulating ghrelin levels that accompanies voluntary or disease-induced weight loss (96;105;262). The present study found that individuals with type 2 diabetes had significantly lower ghrelin concentrations prior to weight loss which is in agreement with other studies (256;257;259;261).

Effects of Weight Loss in Leptin Levels

The hypothesis that plasma leptin levels in response to weight loss will not decrease as much in individuals with type 2 diabetes as compared with individuals without type 2 diabetes was not supported by this study. In the present study, plasma leptin levels decreased by 66.9% in non-diabetic subjects and 46.1% in diabetic

subjects. After adjusting for baseline measurements, leptin levels were still found to be significantly lower in non-diabetic subjects than diabetic subjects after 16 weeks of weight loss ($p=0.0105$).

There are conflicting reports as to whether plasma leptin is associated with total body, subcutaneous or visceral adipose tissue (263-269). Recent studies have suggested that it is subcutaneous adipose tissue and not visceral adipose tissue which shows a close association with serum or plasma leptin (263;264;266;270). Vettor et al. (34) found that in 15 obese women and 10 normal control women that leptin concentrations were highly significantly correlated with BMI and total and subcutaneous adipose tissue and significantly less with visceral adipose mass. Kobayashi et al. (271) found that in women abdominal subcutaneous adipose tissue mass was a more important determinant of serum leptin than was visceral fat mass and no relationship between serum leptin levels and lipid parameters of total cholesterol, LDL-cholesterol, HDL-cholesterol and triglyceride levels were shown.

In contrast, Ronnemaa et al. (269) suggested that visceral adipose tissue was of special importance in the regulation of leptin levels after investigating 23 healthy identical twin pairs. A study by Gower et al. (272) also showed that in 54 postmenopausal women, visceral adipose tissue was independently related to serum leptin levels after adjusting for subcutaneous adipose tissue, leg fat and lean mass. The conflicting results between researchers as to whether leptin is more closely associated with subcutaneous or visceral adipose tissue are most likely due to the small sample sizes of the studies. Another explanation for the contradictory findings

is that subcutaneous adipose makes up a greater proportion of abdominal adipose tissue than visceral adipose tissue and thus may skew the results.

Results of the present study show that individuals with type 2 diabetes may have alterations in leptin production and metabolic effects in the body. It is known that fasting leptin levels correlate with fasting insulin concentrations (273) and thus may be one of the target points of the complex axis of metabolic disturbances found in individuals with type 2 diabetes, leading to increased risk of other co-morbid conditions such as coronary heart disease.

Effects of Weight Loss in Inflammatory Cytokines

Findings regarding the hypothesis that obese individuals with type 2 diabetes will have a greater decrease in insulin, IL-6, TNF-α or CRP levels in individuals with type 2 diabetes or without type 2 diabetes were not what was expected. First, obviously, women with type 2 diabetes had higher insulin levels prior to weight loss; however, analysis found that there was no difference between the groups at 16 weeks. In the present study, insulin levels decreased by 30.1% and 28.7% in non-diabetic and diabetic subjects, respectively. These results are consistent with previous findings that insulin levels decrease in both obese diabetic and non-diabetic individuals during weight loss (113-116). The importance of reducing insulin concentrations has been apparent. Insulin has been shown to play a role in the long-term regulation of body adiposity (274) and also may mediate the production and effects of cytokines such as ghrelin (261), leptin (86;275), and CRP (140).

In the present study no difference was found in IL-6, TNF-α or CRP before or after weight loss. Levels of these inflammatory cytokines all decreased with weight

loss but non-significantly. Subjects were told not to consume anti-inflammatory medications during the study. These medications obviously effect the cytokine levels of IL-6, TNF-α and CRP. It was originally thought that levels of these cytokines would be increased in obese individuals but significantly greater in obese individuals with type 2 diabetes. Of the 29 subjects in the present study, 15 subjects took anti-inflammatory medications throughout the study. Ten of the subjects taking anti-inflammatory medications were diabetic and 5 non-diabetic. The majority of individuals took over-the-counter aspirin, ibuprofen or Tylenol. However, 6 individuals took either Vioxx® or Celebrex® during the study. The use of these medications can explain why there was no difference found in IL-6, TNF-α or CRP levels before or after the 16 weeks of weight loss.

Putz et al. (276) has stated that CRP concentrations are elevated in obesity and may be the effect of IL-6 release from adipocytes and higher insulin resistant states (140). Hak et al. (140) found that CRP is elevated in subjects with the metabolic syndrome and appears to progressively increase when glucose metabolism deteriorates. Mc Laughlin et al. (277) also found that CRP concentrations are elevated in obese and/or hyperinsulinemic individuals. These researchers show that CRP levels were higher in obese individuals with insulin resistance compared to obese individuals without insulin resistance. After weight loss CRP concentrations decreased only in the insulin resistant women. These researchers concluded that CRP concentrations are elevated predominantly in obese individuals who are also insulin resistant and fall parallel with weight loss-associated improvements in insulin resistance. The relation between CRP concentrations and insulin resistance is

independent of obesity. In the present study, if subjects had not taken anti-inflammatory medications one would expect that the women with type 2 diabetes would have seen a greater decline in CRP levels as their insulin resistance improved as shown from the improved HOMA-IR values.

Xenachis et al. (278) studied 48 morbidly obese subjects who were placed on an 800 kcal formula diet and found that TNF-α levels decreased with weight loss. Dandona et al. (279) found that serum TNF-α concentrations are greater in obese versus lean subjects before and after weight loss. The fall in serum TNF-α concentrations may contribute to the restoration of insulin sensitivity in obese patients who lose weight (280). These results agree with several other studies that serum TNF-α levels decrease with body weight reduction (281;282). TNF-α has been proposed as a mediator of obesity-related insulin resistance (127;283). Katsuki et al. (125) found that TNF-α concentrations were significantly higher in obese individuals with type 2 diabetes as compared to non-obese or non-obese individuals with type 2 diabetes. After weight loss, TNF-α levels significantly decreased in subjects with type 2 diabetes but were unchanged in both the non-obese and non-obese subjects with type 2 diabetes. These researchers suggest that serum TNF-α level may play an important role in the mechanism of insulin resistance associated with obesity. So, as found with CRP concentrations, TNF-α concentrations may play a greater role in insulin sensitivity than adiposity with insulin sensitivity.

Esposito et al. (284) studied 120 healthy obese women to determine the effect of a lifestyle and weight loss program on its effects of vascular inflammatory markers. As with other researchers (136;282), IL-6 levels were found to be correlated

with body weight. Serum IL-6 concentrations were found to decrease with weight loss. Kopp et al. (285) also found similar results in individuals with varying degrees of glucose intolerance after weight loss with gastroplastic surgery. At baseline these researchers found that IL-6 concentrations were more closely related to HbA1c, whereas CRP concentrations were more closely related to glucose-stimulated insulin release. The inflammatory markers of IL-6, CRP and TNF-α were all significantly correlated with insulin resistance. After gastroplastic surgery, a significant weight reduction was produced and levels of IL-6 and CRP were also significantly reduced.

Effects of Weight Loss in Thrombotic Cytokines

The hypothesis that obese individual with type 2 diabetes will have a greater decrease in serum triglyceride, PAI-1 and resistin compared to obese individuals without type 2 diabetes had varying findings. Triglyceride levels were significantly greater in individuals with type 2 diabetes. This is to be expected since triglyceride levels >150 mg/dl was one of the exclusion criteria used to exclude a non-diabetic subject from the study. Also, visceral adipose tissue mass has a positive relationship with triglycerides (286-288) and an inverse relationship with serum HDL-cholesterol (288), while subcutaneous adipose tissue does not have any correlation (269). Contrary to these findings, Kobayashi et al. (271) studied 26 men and 26 women and found that visceral adipose tissue mass had a positive relationship with serum total cholesterol and LDL-cholesterol; however, visceral adipose tissue mass was only associated with triglycerides in men and not women. These findings are consistent with other studies (24;289). Despite the triglyceride exclusion criteria for non-diabetic subjects in the present study, it could be speculated that the higher

triglyceride levels seen in the diabetic subjects could be due to significantly more visceral adipose tissue and less subcutaneous adipose tissue than the non-diabetic subjects. However, after adjusting for baseline there was no significant difference between the groups after 16 weeks of weight loss. Obese subjects did have a greater decrease in serum triglyceride levels but they were not different after adjusting initial values. Non-diabetic subjects decreased triglyceride levels by 15.1 mg/dl resulting in a 13.1% decrease. Diabetic subjects decreased triglyceride levels by 82.5 mg/dl resulting in a 34.5% decrease in triglyceride levels. These results are consistent with many other findings. Serum triglyceride levels decreased from approximately 15% to as much as 50% during VLED treatment, depending upon initial levels (229;230;290-292).

Marckmann et al. (162) found that weight loss decreases PAI-1 levels in individuals with and without type 2 diabetes. The results of the present study found that PAI-1 levels were not significantly different between diabetic and non-diabetic subjects, but PAI-1 levels did decrease in both diabetic and non-diabetic women. At the end of the weight loss phase PAI-1 levels in diabetic subjects were approaching statistically greater significance than non-diabetic subjects. With adequate sample size a significant difference in PAI-1 levels are expected. A rationale for the increase in PAI-1 levels in the diabetic subjects is most likely associated with increased growth factors such as insulin and TNF-α along with metabolic products such as triglycerides, free fatty acids, and glucose, all of which can stimulate PAI-1 expression (151-155;158;293;294).

Skurk et al. (295) found that IL-6, leptin and adiponectin are associated with impaired fibrinolysis in overweight hypertensive humans. In the present study, diabetic subjects had higher insulin and lower leptin and adiponectin levels than their non-diabetic counterparts, which may provide evidence of an association between body fatness, insulin, leptin and adiponectin as key regulators of risk for developing cardiovascular disease. Also, in a study of obese children and adolescents, Ikezaki et al. (254) found that down-regulation of ghrelin secretion may be a consequence of higher insulin resistance associated with visceral fat accumulation and elevated PAI-1 concentrations. In the present study baseline ghrelin levels were significantly lower in diabetic subjects than non-diabetes and were still lower after 16 weeks of weight loss and thus may further have contributed to the higher insulin resistance, greater visceral fat mass and elevated PAI-1 concentrations in the diabetic subjects.

Several small studies have reported that circulating resistin levels are increased in human obesity (184-187) and diabetes (188-192); however, other data dispute these findings (296-298). Previous studies of the effect of weight loss on resistin levels have also been controversial. The results of the present study are consistent with Wolfe et al. (181) and Monzillo et al. (182) in that no significant reduction was found in resistin levels with weight loss. In the present study, plasma resistin levels were significantly greater in individuals with type 2 diabetes than in individuals without type 2 diabetes which is consistent with the findings of Steppan and colleagues (194). However, with weight loss resistin levels did not decrease in either group. Silha et al. (195) found that there was a significant correlation between resistin levels and HOMA-IR in obese subjects independent of BMI. These results

may indicate that resistin levels are a predictor for type 2 diabetes. Resistin seems to reflect insulin resistance despite an individual's BMI. This would explain why levels did not decrease with weight loss but rather is an independent factor associated with a risk for developing type 2 diabetes.

Shetty et al. (175) found a negative correlation between serum resistin and HDL, a positive correlation of serum resistin to CRP; these correlations remained significant after adjusting for type 2 diabetes. The results also indicated that the positive association of resistin to CRP also remained significant despite adjustments for sex and BMI, suggesting that resistin's proinflammatory properties may be independent of overall obesity. However, resistin's association with inflammatory markers appear to be independent of BMI, suggesting that resistin may have a direct proinflammatory role or mediate its effects via yet-to-be discovered obesity-independent mechanism.

Heilbronn et al. (299) found that serum resistin concentrations were increased in response to supraphysiological doses of insulin in both obese and obese diabetic subjects. Although the effect was modest, it suggests that resistin expression may be acutely regulated by insulin. These results indicate that resistin concentrations were up-regulated by insulin concentration thus implying that higher fasting insulin concentrations should result in higher serum resistin concentrations. That study however, does not support a role for resistin as a major mediator of insulin sensitivity in humans.

Stejskal et al. (300) examined differences in resistin levels among persons with type 2 diabetes, with systemic inflammation and healthy persons. The study

found that in the healthy subjects there was a significant correlation between leptin and resistin; however, in individuals with type 2 diabetes no significant correlation was found between resistin, insulin sensitivity markers, BMI or leptin. The researchers concluded that concentrations of resistin in persons with type 2 diabetes do not differ from concentrations of healthy subjects. This is consistent with the findings of the present study. No significant difference was found between the obese diabetic subjects and non-diabetic subjects at week 16 after adjusting for initial resistin levels.

Effects of Weight Loss in Adiponectin Values

The hypothesis that obese individuals with type 2 diabetes will have a greater increase in plasma adiponectin compared to obese individuals without type 2 diabetes is reflected by the current findings of adiponectin levels. As expected, women with type 2 diabetes had significantly lower adiponectin levels at the beginning of the study. After adjusting for baseline there was no significant difference between adiponectin levels after weight loss. An interesting point to recognize is that as expected, adiponectin levels increased in women with type 2 diabetes after weight loss, but although non-significantly, decreased in obese women without type 2 diabetes. These results are consistent with Monzillo et al. (182) who also found that adiponectin levels increased in individuals with type 2 diabetes but not in individuals without type 2 diabetes or who had impaired glucose intolerance without type 2 diabetes. Wolfe et al. (181) also found in normal, healthy weight individuals that adiponectin levels decreased significantly with weight loss.

In a study of Pima Indians, Krafoff et al. (301) examined the relationship of adiponectin to a variety of markers of inflammation and endothelial dysfunction and assessed the relationship of these markers to a later incidence of diabetes. This research provided further in vivo evidence that adiponectin concentrations correlated with markers of inflammation and endothelial dysfunction (170). They concluded that adiponectin is negatively correlated with markers of inflammation in vivo. Moreover, once adiposity is taken into account, these other markers have little or no predictive value for the development of diabetes. Thus, adiponectin may be an important link between adiposity and inflammation and type 2 diabetes. Stejskal et al. (302) conducted a study consisting of 109 persons with type 2 diabetes and concluded that individuals with type 2 diabetes have lower adiponectin concentrations in serum than patients with a high risk of atherosclerotic complications without type 2 diabetes. These researchers also concluded that adiponectin may be a novel marker of metabolic control in persons with a high risk of cardiovascular complications of atherosclerosis.

Shetty et al. (175) found that adiponectin's association with HDL and PAI-1 was independent of BMI, which suggests adiponectin may mediate some effects of adiposity, but whether central obesity or other unrecognized pathways might play a regulatory role remains to be seen. They found that in subjects with diabetes or who are at risk of developing diabetes, adiponectin is negatively correlated with BMI, triglycerides, CRP, PAI-1 and tPA, suggesting that adiponectin may act as an anti-inflammatory mediator with respect to CRP, PAI-1 and tPA. These findings are consistent with prior data that adiponectin levels correlate negatively with

inflammation and endothelial dysfunction (303). Shetty et al. (175)were the first to find a negative correlation with adiponectin to PAI-1, which is also associated with insulin resistance and the metabolic syndrome (304). This provides another possible mode for adiponectin in affecting the metabolic syndrome-induced morbidity and mortality.

Satoh et al. (305) found that the ratio of leptin-to-adiponectin may be a potential atherogenic index in obese type 2 diabetic patients. These researchers compared 98 non-obese individuals with type 2 diabetes to 60 obese individuals with type 2 diabetes to see if there were differences in predicting atherosclerosis between the groups. These researchers found that obese individuals with type 2 diabetes have significantly higher leptin-to-adiponectin ratios then the non-obese type 2 diabetic subjects. In the present study no significant difference was found in leptin-to-adiponectin ratios between the obese women with or without type 2 diabetes at any time point; however, ratios of leptin-to-adiponectin significantly decreased for both groups with weight loss. An interesting finding is that of the 30 obese females Satoh et al.(305) analyzed, in individuals with a BMI of 27.4 $kg/m^2 \pm 0.35$, the leptin-to-adiponectin ratio was 2.59 ± 0.20. This is very close to the results in both the non-diabetic and diabetic subjects in the present study after 16 week of weight loss. Non-diabetics had a BMI of 30.1 kg/m^2 and had a leptin-to-adiponectin ratio of 2.6 ± 0.6, while diabetic subjects with a BMI of 33.0 kg/m^2 had a ratio 4.0 ± 0.5.

Effects of Weight Loss in Lipid Levels and Blood Pressure

The fact that total cholesterol, LDL-cholesterol and triglycerides decrease with weight loss is established and systematically reduces an individual's risk for

coronary heart disease (224;306;307). Anderson and Konz (25) concluded that for every 1 kg reduction in body weight, serum total cholesterol will decrease by 0.99% or 2.28 mg/dl, LDL-cholesterol will decrease by approximately 0.68% or 0.91 mg/dl, and triglycerides will decrease by 1.93% or 1.54 mg/dl. Weight loss also often decreases HDL-cholesterol levels in women (308). In the present study reductions in serum total cholesterol and triglyceride values were seen in both non-diabetic and diabetic subjects. LDL-cholesterol values decreased in the non-diabetic subjects but increased in the diabetic subjects. This occurrence is explained by reporting that in several individuals, LDL-cholesterol raised dramatically. This was most likely due to release of fatty acids from adipose tissue and lack of LDL-receptors on the liver to clear the excess fatty acids from the blood stream.

It is recognized that in approximately 85 percent of individuals with hypertension, blood pressure decreases in a linear fashion with weight loss (306). The present study did not find any changes in systolic or diastolic blood pressure measurements. This is due to both non-diabetic and diabetic individuals being excluded if they had uncontrolled hypertension. Some subjects were on medications to control hypertension but after weight loss the medications were either lowered or discontinued.

Follicle-Stimulating Hormone Analysis

Female sex steroid hormone concentrations regulate adipose tissue mass (309). Menopausal status can be a determinant of body composition changes in women, predominantly in an increase in visceral fat mass, particularly in the abdomen (310). It has also been postulated that changes in sex hormones may also be caused

by an indirect mechanism related to insulin resistance (310). To eliminate menopausal and sex hormone concentrations as confounding variable in the present study, follicle-stimulating hormone levels were measured.

The population in the present study consisted predominantly of post-menopausal women. Normal FSH levels are considered to be within the range of 3 to 10 mIU/ml. Basal FSH levels generally rise in the third decade of life through the first few years after menopause due to physiologic and biochemical changes that reduce negative feedback controls on FSH production. Menopause is associated with substantially increased FSH levels, usually greater than 40 mIU/ml (311). However, in perimenopausal women the absolute value cannot be relied upon to establish the true onset of menopause (312;313). In the present study, non-diabetic subjects at baseline had FSH levels of 42.9 mIU/ml and diabetic subjects had levels of 26.4 mIU/ml, indicating that the majority of the subjects were either perimenopausal or menopausal. After analysis of the present FSH levels there was no significant difference between non-diabetic and diabetic subjects at any point throughout the study, indicating that FSH levels could not explain body composition differences between the two groups. FSH levels increased in both groups with weight loss. One could suppose that FSH levels would decrease with weight loss indicating improved fertility status. A possible explanation for FSH levels increasing in the present study could be due to metabolic and biochemical changes that occur with menopause; additional changes in their body composition were not able to compensate for their age and natural progression of menopause.

Study Limitations

It is recognized that there are several limitations to this study that could be addressed in future. The first and primary limitation is the sample size. The sample size was calculated to include 25 subjects with type 2 diabetes and 25 subjects without type 2 diabetes to allow a 20% attrition rate. This means that 20 subjects in both groups needed to complete the study to meet the sample size calculations. Some of the results were approaching significance and may have become significant if enough subjects were recruited for the study. The sample size was not met due to financial and resource limitations on the part of HMR®.

The second limitation is controlling study subjects medication use. The primary importance of this was a subject's use of non-steroidal anti-inflammatory drugs (NSAIDs). During the phone screen and during the initial screening visit, it was stressed to potential study participants that chronic use of anti-inflammatory medications was not allowed during the study. However, approximately half of the study participants reported use of NSAIDs to the nurses at the HMR® program. For any clinical study dealing with individuals on an outpatient basis, it is understood to contain variables that are uncontrollable by the principal investigator and research team. The results of the study would have been stronger if the study subjects' use of anti-inflammatory, hypertension and hyperlipidemia medications were better controlled.

The third limitation to the study regards determining if individuals with type 2 diabetes have a more difficult time losing weight than individuals without type 2 diabetes; a weight loss protocol in which more individuals in the general population

could participate would have been beneficial. This study was able to find that medically-supervised programs were safe and effective for individuals with type 2 diabetes but does not explain why under "normal" dieting experiences individuals often do not lose much weight. A study consisting of a reduced-calorie diet and meal replacements along with encouraged physical activity and record keeping would be better suited to determine this hypothesis. Many individuals are not able to participate in medically-supervised weight loss programs due to location or cost. Instead, providing a reduced-calorie diet with meal replacements could be implemented so that issues of cost or location of a diet program is not a deterring factor for individuals to partake in a weight loss program.

Another limitation is that many of the outcome measurements were significantly different between the groups from the outset. Subjects were matched for BMI and age, but there were significant differences in initial body weight and amounts of abdominal fat. In a flawless study there would not have been any variations in the groups prior to weight loss. However, with the limits of time and financial resources it was not feasible to recruit individuals and match every outcome parameter.

CHAPTER SIX

Overall Summary and Conclusion

With the increasing prevalence of obesity throughout the world, type 2 diabetes mellitus is dramatically rising as well. Type 2 diabetes is a leading contributor to the risk of coronary heart disease, kidney disease, blindness, stroke, peripheral vascular disease and neuropathy (8). It is of utmost importance in our society to decrease morbidity and mortality in these individuals and to increase their quality of life.

The purpose of this study was to evaluate adherence to a medically-supervised LED weight loss program and changes in body composition and metabolic parameters after weight loss in women with and without type 2 diabetes. Previous studies have investigated the effects of weight loss on changes in body composition, adipose tissue hormones, and cytokines in obese individuals, but none has directly compared differences in non-diabetic and diabetic subjects undergoing a medically-supervised low-energy diet weight loss program (HMR®). It is known that individuals with type 2 diabetes often have a more difficult time losing weight. The important question is if individuals with type 2 diabetes have a greater difficulty in behavioral and environmental cues to lose weight or if metabolic and biochemical adaptations occur in these individuals, making them metabolically dysfunctional to lose weight.

Vijan et al. (314) surveyed and conducted focus groups in suburban and urban individuals with type 2 diabetes to evaluate barriers against adherence to following dietary recommendations in this patient population. Overall, these patients seemed

more likely to cooperate with pharmaceutical diabetes management than with self-care behaviors such as dietary modification or home glucose monitoring. The patients stated that even moderate dietary modifications were more cumbersome than taking anti-diabetic oral agents. An even stricter diet that promotes weight loss and thus likely to lead to more substantial benefits was seen as having a burden similar to that of twice-daily insulin injections. The cost of a diabetes diet was also barrier mentioned in these focus groups. In the present study, both non-diabetic and diabetic women who completed the 16-week medically-supervised LED weight loss program successfully lost weight. Non-diabetics subject lost 15.4 kg resulting in a 16% decrease in body weight and diabetic subjects lost 12.2 kg resulting in an 11.7% decrease in body weight. However, diabetic women in the study were more likely to drop from the weight loss program and once these women were included in the analysis (intention-to-treat analysis), diabetic subjects overall did not lose as much weight as non-diabetic subjects. There are several possible reasons for these results. It is known that in individuals with type 2 diabetes adherence rates to diet and exercise are low (315-318). Many factors that may influence dietary adherence include personal motivation (319), holidays and other social gatherings (177;319), scheduling issues (319), cravings to eat inappropriate foods (177), lack of family support (177), perceived high cost of the diet (320), and displeasure at eating the recommended foods (320). The subjects in the present study underwent a highly rigorous medically-supervised LED weight loss program and thus the women with type 2 diabetes may have had a more difficult time following the diet.

The next question related to possible differences in body composition and metabolic variations between the diabetic and non-diabetic women, which may explain differences in how diabetic and non-diabetic individuals lose weight. First, although the measurements of the DEXA and BOD POD® varied, overall results indicated that the diabetic women had more lean tissue than the non-diabetic women. The higher levels of lean tissue may be related to the insulin resistant state and impaired glucose and fatty acids by skeletal muscle in type 2 diabetes. The women with type 2 diabetes also lost less percent body fat and total body fat mass than the women without type 2 diabetes. More significantly is where, and what type of body fat was decreased in these subjects. It has been well established that abdominal obesity increases the risk of type 2 diabetes (1;29;56-58). In the present study, prior to weight loss there was no difference between the diabetic and non-diabetic women in waist circumference. However, non-diabetic women decreased their waist circumferences significantly more than diabetic women. Although there was no significant difference in the amount of visceral and subcutaneous fat loss after initial adjustment for baseline values it is still important to note that diabetic women had a significantly greater amount of absolute abdominal visceral fat mass than the non-diabetic women before and after equivalent amounts of weight loss. Visceral fat has been shown to be associated with a decrease in insulin sensitivity (252). The higher amounts of insulin may be one of the key initial stimuli for the metabolic disruptions found in obesity causing the increased risk for the other co-morbid diseases associated with obesity and type 2 diabetes mellitus.

Although the changes in insulin and insulin sensitivity (determined by HOMA-IR) overtime were not significantly different between the two groups in the present study, diabetic individuals still had higher insulin levels and higher insulin resistance than their obese counterparts, despite losing weight. Insulin is thought to increase several stomach and adipose tissue hormones and cytokines causing increased inflammation and thrombotic events in this population, as was in the present study. The production of the adipose tissue derived hormone leptin increases in the presence of higher serum insulin levels. After weight loss leptin levels were still consistently higher in the diabetic subjects than in the non-diabetic subjects. The stomach derived hormone, ghrelin, is also inversely related to insulin resistance and visceral adipose tissue accumulation is believed to down-regulate ghrelin (254). The excess of visceral adipose tissue in the diabetic women even after weight loss would explain why ghrelin levels were lower after weight loss in these women than in the non-diabetic women.

The risk of coronary heart disease is increased by proinflammatory and prothrombotic cytokines such as TNF-α, IL-6, CRP, and PAI-1. Although there were no significant changes in the present study, the proinflammatory cytokines, TNF-α, IL-6 and CRP increase with greater serum insulin levels. These cytokines are known to up-regulate and down-regulate each other and most likely play an additional role in this complex system of body fat accumulation and mobilization. The prothrombotic protein PAI-1 plays a key role in the pathogenesis of myocardial infarction, stroke, and other vascular events (137-140) and is increased with insulin resistance and type 2 diabetes. In the present study, PAI-1 levels decreased in both diabetic and non-

diabetic women. Although not statistically significant, PAI-1 levels were higher in diabetic women than non-diabetic women after weight loss. These results indicate that even though diabetic subjects decreased PAI-1 levels with weight loss, they were still at a greater risk of cardiovascular disease than the non-diabetic women.

Resistin and adiponectin are recently studied adipose tissue derived hormones, believed to play a role in insulin resistance and either promote cardiovascular risk factors, as in the case of resistin, or have anti-inflammatory properties and reduce the risk of cardiovascular disease, as with adiponectin. Adiponectin levels were significantly lower in the diabetic subjects at baseline and increased with weight loss, demonstrating an improvement in cardiovascular disease risk. These results were consistent with findings of Monzillo et al.(182). There was non-significant reduction in adiponectin levels in the non-diabetic women after weight loss. Although these results were non-significant, Wolfe et al.(181) also found that in normal, healthy weight individuals' adiponectin levels decreased significantly with weight loss. In the present study, we may have seen this as well with a larger study population. These results may be due to a decrease in adiposity and not reflect an increase in cardiovascular disease risk. It has been proposed that resistin increases in individuals with type 2 diabetes and is a potential link between obesity and insulin resistance. In the present study resistin levels were significantly greater in diabetic women than non-diabetic women. However, resistin levels did not decrease in either group with weight loss. This data are consistent with Steppan and colleagues (178), but this theory is still controversial.

Overall, the results of the present study found that medically-supervised LED weight loss programs are safe and effective for treating obesity in individuals with type 2 diabetes. Lipid profiles and cardiovascular risk factors improved in both non-diabetic and diabetic subjects with weight loss. The findings also suggest that insulin may play a critical role in the complex axis affecting changes in body composition and inflammation in individuals with type 2 diabetes. Further research should focus on the effects of body composition, adipose tissue hormones, and inflammatory cytokines in levels of insulin control of individuals with type 2 diabetes mellitus.

APPENDIX A

Patient Screening Information

Patient Screening Information

Subject Number	Category	Enrolled	Randomized	Age	BMI	Screen Date	Comments
001	NonDM	Yes	HMR	55	38.5	1/21/2003	
002	DM	No	No	46	33	1/28/2003	Couldn't follow diet
003	DM	Yes	HMR	55	44.5	1/28/2003	
004	DM	Yes	HMR	43	44.6	2/21/2003	
005	NonDM	Yes	HMR	50	30.6	3/4/2003	
006	DM	No	No	46	48	3/11/2003	>BMI
006	DM	No	No	54	43	3/18/2003	Graves Disease
007	DM	Yes	HMR	52	39	4/4/2003	
008	DM	Yes	HMR	54	32.5	4/24/2003	
009	DM	Yes	HMR	61	41.5	5/6/2003	
010	DM	Yes	HMR	54	35.5	5/8/2003	
011	DM	No	No	41	36.5	5/9/2003	Type 1.5 Diabetes
012	DM	Yes	HMR	48	34.5	5/12/2003	
013	NonDM	Yes	HMR	51	36	6/6/2003	
014	DM	Yes	HMR	58	38	6/11/2003	
015	DM	Yes	HMR	52	33.5	6/12/2003	
016	NonDM	Yes	No	43	44.5	6/13/2003	
017	DM	Yes	HMR	54	32	7/7/2003	
018	DM	Yes	HMR	53	35	7/18/2003	
019	NonDM	No	No	49	38	7/21/2003	Metabolic Syndrome
020	DM	Yes	HMR	58	45	7/28/2003	
021	DM	Yes	No	54	41	7/25/2003	
022	DM	No	No	53	36	8/1/2003	Need to increase HbA1c
023	DM	Yes	HMR	41	38.5	8/6/2003	
024	NonDM	Yes	HMR	53	32	9/3/2003	
025	DM	Yes	HMR	64	36	9/4/2003	
026	NonDM	Yes	HMR	52	31.7	10/17/2003	
027	NonDM	No	HMR	40	43	11/20/2003	Hypothyroidism
028	NonDM	Yes	HMR	40	42	12/15/2003	
029	NonDM	Yes	HMR	55	39.5	12/16/2003	
030	DM	Yes	HMR	57	42.5	2/25/2004	
031	DM	Yes	HMR	48	36	3/2/2004	
032	NonDM	Yes	HMR	52	39	3/25/2004	
033	NonDM	Yes	HMR	57	38.6	3/30/2004	
034	DM	Yes	HMR	60	43.8	3/31/2004	
035	NonDM	No	No	59	40	4/1/2004	Prediabetic
036	DM	Yes	HMR	51	37.2	4/14/2004	
037	NonDM	Yes	HMR	51	32.2	4/28/2004	
038	DM	Yes	HMR	44	34.7	5/10/2004	
039	DM	Yes	HMR	57	39.1	5/18/2004	
040	NonDM	Yes	HMR	40	36.6	5/19/2004	
041	DM	Yes	HMR	41	40.5	5/20/2004	

APPENDIX B

Weight and Body Composition Measurements Data Tables

Non-Diabetic Subjects weight in kg

Non-Diabetic Subjects

Pt. #	Screen	Wk1	Wk2	Wk3	Wk4	Wk5	Wk6	Wk7	Wk8	Wk9	Wk10	Wk11	Wk12	Wk13	Wk14	Wk15	Wk16
001	103.2	101.8	100.9	100.5	99.8	99.3	98.0	98.9	95.7	95.5	94.5	93.2	92.7	91.8	91.8	89.8	90.7
005	73.5	71.6	70.7	69.8	69.1	68.9	68.0	68.0	66.4	65.7	65.5	64.8	63.9	63.6	63.4	62.7	62.5
013	95.0	92.7	91.8	91.1	90.0	89.8	88.6	88.4	87.3	86.4	85.5	84.8	84.1	83.4	82.7	82.0	81.6
024	98.5	95.9	94.1	92.7	91.4	90.0	88.6	87.5	85.9	85.9	82.3	80.7	79.5	78.6	78.2	76.6	74.5
026	78.7	84.3	83.2	81.6	80.5	79.8	77.7	76.8	75.0	75.5	73.0	72.3	71.4	70.5	69.5	69.1	68.0
028	117.5	118.9	115.9	115.0	113.4	111.8	110.5	108.0	107.0	106.4	103.9	103.2	100.9	100.9	98.9	96.8	95.9
029	101.1	99.8	99.1	97.3	97.0	94.8	94.5	92.3	92.7	91.1	90.2	89.1	88.0	86.8	86.6	86.4	85.2
032	103.5	105.2	103.6	102.7	101.4	100.7	99.3	98.0	97.3	94.8	95.2	94.5	93.2	93.6	93.0	92.3	91.4
033	105.1	101.8	100.2	98.4	97.5	96.1	94.8	93.9	93.2	91.8	90.7	90.5	88.9	88.9	88.0	87.0	86.4
037	81.1	80.2	78.4	77.0	75.7	74.5	72.7	71.8	71.6	70.9	69.8	69.1	68.4	67.7	67.5	65.9	65.5
040	102.7	98.9	97.5	95.2	93.9	92.3	91.1	90.5	88.6	87.3	86.1	85.5	84.1	84.1	83.0	80.5	80.7
Average	96.4	95.6	94.1	92.9	91.8	90.7	89.4	88.5	87.3	86.5	85.1	84.3	83.2	82.7	82.0	80.8	80.2
Count	11.0	11.0	11.0	11.0	11.0	11.0	11.0	11.0	11.0	11.0	11.0	11.0	11.0	11.0	11.0	11.0	11.0
SD	13.3	13.0	12.7	12.7	12.6	12.4	12.4	12.1	12.1	11.8	11.7	11.7	11.4	11.6	11.3	11.2	11.2
SE	4.0	3.9	3.8	3.8	3.8	3.7	3.8	3.6	3.6	3.6	3.5	3.5	3.4	3.5	3.4	3.4	3.4
95% LCI	88.5	87.9	86.6	85.3	84.3	83.4	82.1	81.4	80.2	79.5	78.2	77.4	76.4	75.9	75.3	74.2	73.6
95% UCI	104.2	103.2	101.6	100.4	99.2	98.0	96.8	95.7	94.5	93.4	92.1	91.2	89.9	89.6	88.7	87.4	86.8

Diabetic subjects weight in kg (WD = withdrew)

Diabetic Subjects

Pt. #	Screen	Wk1	Wk2	Wk3	Wk4	Wk5	Wk6	Wk7	Wk8	Wk9	Wk10	Wk11	Wk12	Wk13	Wk14	Wk15	Wk16
003	122.2	120.7	121.1	118.4	116.8	115.9	113.9	113.2	112.3	111.6	110.5	110.0	108.9	108.0	108.0	107.3	108.0
004	110.7	110.7	109.1	108.4	107.5	107.1	105.5	104.6	102.1	103.0	102.3	WD					
007	115.5	111.8	110.2	109.3	107.7	106.4	104.8	103.4	100.9	99.1	98.6	97.0	96.4	94.5	93.4	93.0	91.8
008	95.7	101.1	100.0	100.7	98.0	96.1	95.7	95.7	94.1	93.6	93.2	93.2	93.0	92.7	92.7	93.4	93.4
009	112.1	108.0	107.7	105.7	105.5	103.4	103.2	103.4	102.7	102.0	100.2	100.0	99.1	100.0	97.7	96.8	99.1
010	100.6	97.7	96.6	95.9	95.9	94.8	93.6	93.2	92.1	92.1	90.7	90.7	91.1	WD			
012	76.6	74.3	73.6	73.2	71.8	71.4	71.4	71.1	70.0	69.3	69.8	68.6	69.1	69.1	69.8	70.0	70.0
014	103.2	101.8	101.4	100.2	98.9	97.3	96.1	94.5	93.9	93.2	92.3	92.0	90.7	90.7	90.0	89.1	88.6
015	82.9	81.6	80.0	80.5	78.6	78.6	77.5	78.2	WD								
017	88.6	84.1	83.6	84.1	81.6	83.0	80.5	79.1	77.0	78.0	77.0	75.9	75.0	73.9	73.0	73.0	71.8
018	97.1	96.4	95.2	94.3	93.0	91.8	90.5	88.0	87.3	86.1	84.3	83.6	83.2	82.5	80.2	78.6	77.3
020	98.9	95.2	95.2	93.4	94.1	93.6	92.3	92.6	93.0	93.0	93.5	93.9	93.3	92.7	92.7	92.7	92.7
023	111.1	111.4	109.5	108.9	108.2	106.4	106.8	105.2	103.4	103.4	102.7	102.0	101.1	101.1	101.1	100.7	100.0
025	98.2	95.0	95.0	92.5	93.0	91.6	89.3	89.1	88.0	88.0	87.5	85.7	86.1	85.9	86.6	87.3	85.5
030	122.9	119.8	118.2	116.6	116.1	115.2	114.1	113.9	111.4	110.9	110.7	110.7	108.9	108.6	107.3	106.6	106.8
031	114.1	113.4	112.3	112.0	114.5	112.0	112.5	111.6	110.5	109.8	111.6	109.8	109.5	110.5	108.9	110.0	109.1
034	115.6	112.7	110.7	108.9	107.5	106.1	105.2	103.0	101.8	100.2	99.1	97.7	95.7	95.7	93.6	93.2	92.3
036	98.1	96.6	95.2	94.1	92.0	91.1	90.2	89.5	90.2	89.3	88.4	88.6	88.2	87.5	87.3	87.0	87.3
038	101.9	98.9	98.0	96.6	95.0	93.4	93.2	91.6	90.9	89.8	88.6	88.0	86.6	86.6	84.8	85.7	84.1
039	106.8	105.7	103.4	102.7	101.6	99.8	98.6	97.0	95.5	94.8	93.4	92.5	91.4	90.9	89.1	87.7	86.8
041	122.5	119.1	116.1	115.5	113.9	113.9	112.0	108.2	108.2	105.7	103.9	103.0	101.6	101.6	101.6	101.6	101.6
Average	104.5	102.7	101.5	100.6	99.6	98.5	97.5	96.5	96.3	95.6	94.9	93.8	93.1	92.9	92.1	91.9	91.5
Count	21	21	21	21	21	21	21	21	20	20	20	19	19	18	18	18	18
SD	12.7	12.6	12.4	12.0	12.4	12.0	12.0	11.7	11.1	10.8	10.9	11.1	10.8	11.2	11.1	11.1	11.5
SE	2.8	2.8	2.7	2.6	2.7	2.6	2.6	2.6	2.5	2.4	2.4	2.5	2.5	2.7	2.6	2.6	2.7
95% LCI	97.2	96.1	95.3	94.4	93.2	92.3	91.3	91.3	90.8	90.2	89.1	88.1	88.1	86.9	86.7	86.3	-5.3
95% UCI	110.0	108.1	106.8	105.7	104.9	103.6	102.6	101.5	101.1	100.4	99.7	98.8	97.9	98.1	97.2	97.0	96.8

Percent Weight Loss and Change in kg for Non-Diabetic and Diabetic Completed and ITT Subjects. ITT (Intention-To-Treat) Indicates Last Weight Change Carried Forward for All Study Participants. (WD = withdrew)

Non-Diabetic Subjects

Pt. #	Scrn Wt	Wk 1	Wk 4	Chg	% Chg	Wk 8	Chg	% Chg	Wk 12	Chg	% Chg	Wk 16	Chg	ITT Chg	% Chg	ITT % Chg
001	103.2	101.8	99.8	-2.0	-2.0	95.7	-6.1	-6.0	92.7	-9.1	-8.9	90.7	-11.1	-11.1	-10.9	-10.9
005	73.5	71.6	69.1	-2.5	-3.5	66.4	-5.2	-7.3	63.9	-7.7	-10.8	62.5	-9.1	-9.1	-12.7	-12.7
013	95.0	92.7	90.0	-2.7	-2.9	87.3	-5.5	-5.9	84.1	-8.6	-9.3	81.6	-11.1	-11.1	-12.0	-12.0
024	98.5	95.9	91.4	-4.5	-4.7	85.9	-10.0	-10.4	79.5	-16.4	-17.1	74.5	-21.4	-21.4	-22.3	-22.3
026	78.7	84.3	80.5	-3.9	-4.6	75.0	-9.3	-11.1	71.4	-13.0	-15.4	68.0	-16.4	-16.4	-19.4	-19.4
028	117.5	118.9	113.4	-5.5	-4.6	107.0	-11.8	-9.9	100.9	-18.0	-15.1	95.9	-23.0	-23.0	-19.3	-19.3
029	101.1	99.8	97.0	-2.7	-2.7	92.7	-7.0	-7.1	88.0	-11.8	-11.8	85.2	-14.5	-14.5	-14.6	-14.6
032	103.5	105.2	101.4	-3.9	-3.7	97.3	-8.0	-7.6	93.2	-12.0	-11.4	91.4	-13.9	-13.9	-13.2	-13.2
033	105.1	101.8	97.5	-4.3	-4.2	93.2	-8.6	-8.5	88.9	-13.0	-12.7	86.4	-15.5	-15.5	-15.2	-15.2
037	81.1	80.2	75.7	-4.5	-5.7	71.6	-8.6	-10.8	68.4	-11.8	-14.7	65.5	-14.8	-14.8	-18.4	-18.4
040	102.7	98.9	93.9	-5.0	-5.1	88.6	-10.2	-10.3	84.1	-14.8	-14.9	80.7	-18.2	-18.2	-18.4	-18.4
Average	96.4	95.6	91.8	-3.8	-4.0	87.3	-8.2	-8.6	83.2	-12.4	-12.9	80.2	-15.4	-15.4	-16.0	-16.0
Count	11.0	11.0	11.0	11.0	11.0	11.0	11.0	11.0	11.0	11.0	11.0	11.0	11.0	11.0	11.0	11.0
SD	13.3	13.0	12.6	1.1	1.1	12.1	2.1	2.0	11.4	3.2	2.7	11.2	4.3	4.3	3.7	3.7
SE	4.0	3.9	3.8	0.3	0.3	3.6	0.6	0.6	3.4	1.0	0.8	3.4	1.3	1.3	1.1	1.1
95% LCI	88.5	87.9	84.3	-4.4	-4.6	80.2	-9.5	-9.8	76.4	-14.2	-14.5	73.6	-17.9	-17.9	-18.2	-18.2
95% UCI	104.2	103.2	99.2	-3.1	-3.3	94.5	-7.0	-7.5	89.9	-10.5	-11.3	86.8	-12.8	-12.8	-13.8	-13.8
Diabetic Subjects																
003	122.2	120.7	116.8	-3.9	-3.2	112.3	-8.4	-7.0	108.9	-11.8	-9.8	108.0	-12.7	-12.7	-10.5	-10.5
004	110.7	110.7	107.5	-3.2	-2.9	102.1	-8.6	-7.8	102.3	-8.4	-7.6	WD		-8.4		-7.6
007	115.5	111.8	107.7	-4.1	-3.7	100.9	-10.9	-9.8	96.4	-15.5	-13.8	91.8	-20.0	-20.0	-17.9	-17.9
008	95.7	101.1	98.0	-3.2	-3.1	94.1	-7.0	-7.0	93.0	-8.2	-8.1	93.4	-7.7	-7.7	-7.6	-7.6
009	112.1	108.0	105.5	-2.5	-2.3	102.7	-5.2	-4.8	99.1	-8.9	-8.2	99.1	-8.9	-8.9	-8.2	-8.2
010	100.6	97.7	95.9	-1.8	-1.8	92.1	-5.6	-5.7	91.1	-6.6	-6.8	WD		-6.6		-6.8
012	76.6	74.3	71.8	-2.5	-3.4	70.0	-4.3	-5.8	69.1	-5.2	-7.0	70.0	-4.3	-4.3	-5.8	-5.8
014	103.2	101.8	98.9	-3.0	-2.9	93.9	-8.0	-7.8	90.7	-11.1	-10.9	88.6	-13.2	-13.2	-12.9	-12.9
015	82.9	81.6	78.6	-3.0	-3.7	78.2	-3.4	-4.2	WD					-3.4		-4.2
017	88.6	84.1	81.6	-2.5	-3.0	77.0	-7.0	-8.4	75.0	-9.1	-10.8	71.8	-12.3	-12.3	-14.6	-14.6
018	97.1	96.4	93.0	-3.4	-3.5	87.3	-9.1	-9.4	83.2	-13.2	-13.7	77.3	-19.1	-19.1	-19.8	-19.8
020	98.9	95.2	94.1	-1.1	-1.2	93.0	-2.3	-2.4	93.3	-1.9	-2.0	92.7	-2.5	-2.5	-2.6	-2.6
023	111.1	111.4	108.2	-3.2	-2.9	103.4	-8.0	-7.1	101.1	-10.2	-9.2	100.0	-11.4	-11.4	-10.2	-10.2
025	98.2	95.0	93.0	-2.0	-2.2	88.0	-7.0	-7.4	86.1	-8.9	-9.3	85.5	-9.5	-9.5	-10.0	-10.0
030	122.9	119.8	116.1	-3.6	-3.0	111.4	-8.4	-7.0	108.9	-10.9	-9.1	106.8	-13.0	-13.0	-10.8	-10.8
031	114.1	113.4	114.5	1.1	1.0	110.5	-3.0	-2.6	109.5	-3.9	-3.4	109.1	-4.3	-4.3	-3.8	-3.8
034	115.6	112.7	107.5	-5.2	-4.6	101.8	-10.9	-9.7	95.7	-17.0	-15.1	92.3	-20.5	-20.5	-18.1	-18.1
036	98.1	96.6	92.0	-4.5	-4.7	90.2	-6.4	-6.6	88.2	-8.4	-8.7	87.3	-9.3	-9.3	-9.6	-9.6
038	101.9	98.9	95.0	-3.9	-3.9	90.9	-8.0	-8.0	86.6	-12.3	-12.4	84.1	-14.8	-14.8	-14.9	-14.9
039	106.8	105.7	101.6	-4.1	-3.9	95.5	-10.2	-9.7	91.4	-14.3	-13.5	86.8	-18.9	-18.9	-17.8	-17.8
041	122.5	119.1	113.9	-5.2	-4.4	108.2	-10.9	-9.2	101.6	-17.5	-14.7	101.6	-17.5	-17.5	-14.7	-14.7
Average	104.5	102.7	99.6	-3.1	-3.0	95.4	-7.3	-7.0	93.6	-10.2	-9.7	91.5	-12.2	-11.3	-11.7	-10.9
Count	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	20.0	20.0	20.0	18.0	18.0	21.0	18.0	21.0
SD	12.7	12.6	12.4	1.4	1.3	11.5	2.6	2.2	10.7	4.1	3.5	11.5	5.5	5.6	5.0	5.1
SE	2.8	2.8	2.7	0.3	0.3	2.5	0.6	0.5	2.4	0.9	0.8	2.7	1.3	1.2	1.2	1.1
95% LCI	97.2	94.2	-8.4	-3.6	94.9	-12.2	-8.1	92.6	-14.8	-11.5	89.9	-17.5	-14.2	-13.3	-13.2	-2.2
95% UCI	110.0	108.1	104.9	-2.5	-2.5	100.3	-6.2	-6.1	98.2	-8.4	-8.2	96.8	-9.6	-8.9	-9.4	-8.7

Change and Percent Change in BMI (kg/m^2) for Non-Diabetic and Diabetic Subjects. (WD = withdrew)

Non-Diabetic Subjects

Pt. #	Screen BMI	Final BMI	Chg BMI	%Chg
001	39.0	34.3	4.7	-12.1
005	30.6	26.0	4.6	-14.9
013	35.9	30.9	5.1	-14.1
024	31.2	23.6	7.6	-24.4
026	31.7	27.4	4.3	-13.7
028	43.1	35.2	7.9	-18.4
029	39.5	33.3	6.2	-15.7
032	39.2	34.6	4.6	-11.8
033	38.6	31.7	6.9	-17.8
037	32.2	26.0	6.2	-19.3
040	36.6	28.7	7.8	-21.5
Average	36.1	30.1	6.0	-16.7
Count	11.0	11.0	11.0	11.0
SD	4.2	4.0	1.4	4.0
SE	1.3	1.2	0.4	1.2
95% LCI	33.7	27.8	5.2	-19.0
95% UCI	38.6	32.5	6.8	-14.4

Diabetic Subjects

003	44.8	39.6	5.2	-11.6
004	44.6	WD		
007	41.1	32.7	8.4	-20.5
008	31.6	30.9	0.8	-2.4
009	39.9	35.3	4.6	-11.6
010	35.5	WD		
012	33.0	30.1	2.8	-8.6
014	39.0	33.5	5.5	-14.1
015	33.5	WD		
017	32.0	25.9	6.1	-19.0
018	34.5	27.5	7.1	-20.4
020	41.2	38.6	2.6	-6.2
023	38.4	34.5	3.8	-10.0
025	36.0	31.4	4.7	-13.0
030	42.4	36.9	5.6	-13.1
031	36.1	34.5	1.6	-4.4
034	43.8	34.9	8.8	-20.2
036	37.1	33.0	4.1	-11.0
038	34.7	28.6	6.1	-17.5
039	39.2	31.9	7.3	-18.7
041	40.5	33.6	6.9	-17.1
Average	38.0	33.0	5.1	-13.3
Count	21.0	18.0	18.0	18.0
SD	4.1	3.6	2.2	5.6
SE	0.9	0.8	0.5	1.3
95% LCI	36.3	31.3	4.1	-15.9
95% UCI	38.1	33.0	5.1	-13.3

Total Percent Body Fat Determined by DEXA.

Non-Diabetic Subjects

Pt #	DEXA % Total Fat Wk0	Wk8	Chg	Wk16	Chg
001	50.8	47.1	-3.7	45.2	-5.6
005	47.1	44.2	-2.9	39.9	-7.2
013	49.5	45.9	-3.6	44.8	-4.7
024	48.1	42.1	-6.0	32.3	-15.8
026	48.9	48.8	-0.1	41.4	-7.5
028	54.2	48.3	-5.9	45.9	-8.3
029	47.5	44.6	-2.9	41.2	-6.3
032	53.4	49.6	-3.8	46.6	-6.8
033	51.0	49.3	-1.7	46.9	-4.1
037	52.3	49.0	-3.3	42.3	-10.0
040	46.5	44.7	-1.8	41.6	-4.9
Average	49.9	46.7	-3.2	42.6	-7.4
Count	11.0	11.0	11.0	11.0	11.0
SD	2.6	2.5	1.7	4.2	3.3
SE	0.8	0.8	0.5	1.3	1.0
95% LCI	48.4	45.2	-4.3	40.1	-9.3
95% UCI	51.5	48.2	-2.2	45.0	-5.4

Diabetic Subjects

003	46.8	53.7	6.9	53.1	6.3
004	56.1	53.2	-2.9	WD	
007	38.2	41.5	3.3	38.5	0.3
008	47.1	50.1	3.0	48.0	0.9
009	49.6	44.9	-4.7	44.9	-4.7
012	49.5	49.4	-0.1	49.3	-0.2
014	46.2	45.8	-0.4	40.4	-5.8
017	39.0	37.3	-1.7	32.6	-6.4
018	42.1	34.3	-7.8	28.1	-14.0
020	45.5	43.8	-1.7	41.8	-3.7
023	54.6	53.1	-1.5	51.0	-3.6
025	51.1	48.9	-2.2	47.0	-4.1
030	49.7	47.1	-2.6	44.1	-5.6
031	44.0	43.6	-0.4	40.3	-3.7
034	43.4	47.7	4.3	44.6	1.2
036	48.4	46.6	-1.8	44.1	-4.3
038	43.6	36.5	-7.1	31.8	-11.8
039	44.6	41.2	-3.4	36.6	-8.0
041	42.9	39.4	-3.5	34.8	-8.1
Average	46.4	45.2	-1.3	41.7	-4.2
Count	19.0	19.0	19.0	18.0	18.0
SD	4.7	5.7	3.7	7.0	4.8
SE	1.1	1.3	0.8	1.6	1.1
95% LCI	44.3	42.6	-2.9	38.5	-6.4
95%UCI	48.6	47.7	0.4	44.9	-2.0

Percent Trunk Fat Determined by DEXA.

Non-Diabetic Subjects

Pt #	DEXA %Trunk Fat Wk0	Wk8	Chg	Wk16	Chg
001	46.7	48.6	1.9	47.5	0.8
005	51.3	48.7	-2.6	42.6	-8.7
013	51.4	46.0	-5.4	45.4	-6.0
024	51.3	43.3	-8.0	31.0	-20.3
026	48.9	49.5	0.6	39.9	-9.0
028	56.3	50.0	-6.3	47.8	-8.5
029	47.2	42.4	-4.8	39.9	-7.3
032	54.7	50.5	-4.2	46.7	-8.0
033	52.6	49.8	-2.8	47.4	-5.2
037	54.8	51.8	-3.0	42.7	-12.1
040	48.0	46.6	-1.4	43.8	-4.2
Average	51.2	47.9	-3.3	43.2	-8.0
Count	11	11	11	11	11
SD	3.2	3.0	2.9	5.0	5.2
SE	1.0	0.9	0.9	1.5	1.6
95% LCI	49.3	46.2	-5.0	40.2	-11.1
95% UCI	53.1	49.7	-1.5	46.1	-5.0

Diabetic Subjects

003	43.1	54.9	11.8	55.0	11.9
004	56.9	52.2	-4.7	WD	
007	38.8	44.9	6.1	42.2	3.4
008	47.8	52.4	4.6	50.0	2.2
009	49.9	43.9	-6.0	43.7	-6.2
012	52.8	52.6	-0.2	52.3	-0.5
014	48.5	49.1	0.6	42.5	-6.0
017	43.8	43.1	-0.7	37.9	-5.9
018	46.4	35.9	-10.5	29.0	-17.4
020	46.6	45.3	-1.3	43.4	-3.2
023	57.9	55.3	-2.6	52.6	-5.3
025	52.5	51.1	-1.4	47.8	-4.7
030	51.2	48.4	-2.8	45.3	-5.9
031	44.4	45.0	0.6	39.8	-4.6
034	40.2	49.0	8.8	46.2	6.0
036	50.8	49.3	-1.5	46.6	-4.2
038	45.1	35.2	-9.9	30.2	-14.9
039	46.3	43.1	-3.2	37.4	-8.9
041	45.0	42.3	-2.7	36.1	-8.9
Average	47.8	47.0	-0.8	43.2	-4.1
Count	19	19	19	18	18
SD	5.1	5.7	5.6	7.3	7.0
SE	1.2	1.3	1.3	1.7	1.6
95% LCI	45.5	44.4	-3.3	39.9	-7.3
95% UCI	50.1	49.6	1.7	46.6	-0.8

Total Body Fat in kg Determined by DEXA.

Non-Diabetic Subjects

Pt #	Wk0	Wk8	Chg	%Chg	Wk16	Chg	%Chg
001	50.8	44.4	-6.5	-12.7	40.4	-10.4	-20.5
005	33.4	28.5	-4.9	-14.7	24.5	-9.0	-26.9
013	46.1	39.4	-6.7	-14.4	36.4	-9.7	-21.1
024	45.6	35.3	-10.4	-22.7	23.6	-22.0	-48.2
026	40.8	35.6	-5.2	-12.7	27.2	-13.6	-33.3
028	62.4	49.2	-13.2	-21.1	43.1	-19.4	-31.0
029	47.7	40.6	-7.1	-14.9	34.6	-13.1	-27.4
032	53.7	46.9	-6.8	-12.7	41.1	-12.6	-23.5
033	52.6	45.1	-7.5	-14.3	39.5	-13.2	-25.0
037	41.9	34.7	-7.2	-17.3	26.9	-15.0	-35.8
040	46.2	38.3	-7.8	-17.0	32.7	-13.5	-29.2
Average	47.4	39.8	-7.6	-15.9	33.6	-13.8	-29.3
Count	11	11	11	11	11	11	11
SD	7.6	6.2	2.3	3.4	7.1	3.9	7.9
SE	2.3	1.9	0.7	1.0	2.1	1.2	2.4
95% LCI	42.9	36.2	-9.0	-17.9	29.4	-16.1	-34.0
95% UCI	51.9	43.5	-6.2	-13.9	37.8	-11.5	-24.6

Diabetic Subjects

003	55.6	58.9	3.3	6.0	56.4	0.8	1.5
004	55.8	52.4	-3.4	-6.1	WD		
007	41.1	34.7	-6.4	-15.6	34.7	-6.4	-15.6
008	44.6	46.1	1.5	3.5	43.8	-0.8	-1.7
009	53.0	45.1	-8.0	-15.0	43.5	-9.6	-18.0
012	36.8	33.6	-3.2	-8.7	33.0	-3.8	-10.2
014	47.7	42.3	-5.4	-11.3	35.0	-12.7	-26.6
017	33.5	28.7	-4.8	-14.3	23.2	-10.3	-30.7
018	40.3	29.4	-10.8	-26.9	21.4	-18.9	-46.9
020	44.0	39.0	-5.0	-11.4	38.7	-5.3	-12.1
023	59.3	54.0	-5.3	-8.9	50.1	-9.3	-15.6
025	49.0	42.8	-6.2	-12.6	39.8	-9.1	-18.6
030	59.8	51.8	-7.9	-13.3	46.7	-13.1	-21.9
031	49.4	46.9	-2.5	-5.1	43.6	-5.8	-11.7
034	48.6	47.9	-0.7	-1.4	39.8	-8.7	-18.0
036	47.0	40.7	-6.3	-13.4	37.5	-9.5	-20.2
038	43.6	32.6	-11.0	-25.3	26.4	-17.2	-39.5
039	46.8	38.4	-8.4	-18.0	31.5	-15.3	-32.7
041	51.0	42.2	-8.7	-17.1	34.8	-16.1	-31.7
Average	47.7	42.5	-5.2	-11.3	37.8	-9.5	-20.6
Count	19	19	19	19	18	18	18
SD	7.1	8.5	3.8	8.4	9.0	5.5	12.4
SE	1.6	1.9	0.9	1.9	2.1	1.3	2.9
95% LCI	44.5	38.7	-6.9	-15.1	33.6	-12.0	-26.3
95% UCI	50.9	46.3	-3.5	-7.5	42.0	-7.0	-14.8

Trunk Fat in kg Determined by DEXA.

Non-Diabetic Subjects

Pt #	Wk0	Wk8	Chg	%Chg	Wk16	Chg	%Chg
001	21.6	22.0	0.4	1.9	20.6	-1.0	-4.5
005	19.0	16.0	-3.0	-15.8	13.0	-6.0	-31.4
013	25.0	19.8	-5.2	-20.8	17.8	-7.2	-28.9
024	24.7	17.9	-6.9	-27.7	10.9	-13.8	-55.8
026	20.4	17.8	-2.6	-12.7	11.6	-8.9	-43.4
028	36.9	28.2	-8.8	-23.7	23.0	-13.9	-37.7
029	23.6	18.9	-4.7	-19.9	17.3	-6.4	-26.9
032	27.0	22.8	-4.2	-15.4	19.9	-7.1	-26.1
033	26.7	22.9	-3.7	-13.9	19.5	-7.2	-26.8
037	23.4	19.1	-4.3	-18.3	13.6	-9.8	-41.9
040	23.6	18.7	-4.9	-20.6	16.5	-7.1	-30.0
Average	24.7	20.4	-4.3	-17.0	16.7	-8.0	-32.1
Count	11	11	11	11	11	11	11
SD	4.7	3.4	2.3	7.7	4.0	3.6	13.0
SE	1.4	1.0	0.7	2.3	1.2	1.1	3.9
95% LCI	21.9	18.4	-5.7	-21.5	14.4	-10.2	-39.8
95% UCI	27.5	22.4	-3.0	-12.5	19.1	-5.9	-24.5

Diabetic Subjects

003	27.5	30.3	2.8	10.1	31.3	3.8	13.9
004	27.9	24.5	-3.4	-12.2	WD		
007	25.6	24.4	-1.1	-4.4	21.6	-3.9	-15.4
008	23.2	25.5	2.2	9.7	23.8	0.6	2.7
009	24.8	21.7	-3.1	-12.4	19.4	-5.4	-21.9
012	21.6	19.7	-1.9	-8.8	19.1	-2.5	-11.6
014	26.3	23.7	-2.6	-9.9	19.1	-7.2	-27.3
017	21.4	18.3	-3.1	-14.5	15.4	-6.0	-28.1
018	25.4	16.3	-9.0	-35.7	11.6	-13.8	-54.3
020	24.1	22.2	-1.8	-7.6	21.7	-2.4	-9.8
023	31.5	29.4	-2.0	-6.4	30.3	-1.2	-3.8
025	27.2	23.6	-3.6	-13.2	21.2	-6.0	-22.1
030	34.6	27.8	-6.7	-19.5	24.5	-10.1	-29.3
031	26.2	25.6	-0.6	-2.3	21.8	-4.4	-16.8
034	25.7	24.6	-1.1	-4.2	20.2	-5.5	-21.3
036	25.7	22.4	-3.4	-13.1	21.0	-4.7	-18.4
038	23.4	15.4	-8.0	-34.3	12.4	-11.0	-46.9
039	23.5	19.5	-3.9	-16.8	15.8	-7.6	-32.5
041	27.7	22.9	-4.7	-17.1	18.9	-8.7	-31.6
Average	26.0	23.0	-2.9	-11.2	20.5	-5.3	-20.8
Count	19	19	19	19	18	18	18
SD	3.2	4.0	3.0	11.5	5.1	4.2	16.3
SE	0.7	0.9	0.7	2.6	1.2	1.0	3.8
95% LCI	24.5	21.2	-4.2	-16.4	18.1	-7.3	-28.3
95% UCI	27.4	24.9	-1.6	-6.0	22.9	-3.4	-13.3

Total Lean Tissue in kg Determined by DEXA.

Non-Diabetic Subjects

Pt #	Wk0	Wk8	Chg	%Chg	Wk16	Chg	%Chg
001	46.5	47.2	0.7	1.4	46.2	-0.2	-0.5
005	35.3	33.7	-1.6	-4.5	34.7	-0.6	-1.6
013	44.4	43.9	-0.5	-1.2	42.1	-2.4	-5.3
024	46.3	45.5	-0.8	-1.8	46.7	0.4	0.8
026	40.2	34.7	-5.5	-13.7	35.9	-4.3	-10.7
028	49.9	50.2	0.2	0.5	47.9	-2.0	-4.1
029	50.0	47.5	-2.5	-4.9	46.4	-3.5	-7.1
032	43.8	44.5	0.6	1.5	44.0	0.1	0.3
033	48.2	43.6	-4.6	-9.5	42.0	-6.2	-12.8
037	35.8	33.7	-2.1	-5.9	34.4	-1.4	-3.9
040	50.4	44.5	-5.9	-11.7	43.0	-7.3	-14.6
Average	44.6	42.6	-2.0	-4.5	42.1	-2.5	-5.4
Count	11.0	11.0	11.0	11.0	11.0	11.0	11.0
SD	5.4	5.8	2.4	5.3	5.0	2.6	5.3
SE	1.6	1.8	0.7	1.6	1.5	0.8	1.6
95% LCI	41.4	39.2	-3.4	-7.7	39.2	-4.0	-8.6
95% UCI	47.8	46.1	-0.6	-1.4	45.1	-1.0	-2.3

Diabetic Subjects

003	61.4	48.1	-13.2	-21.6	47.1	-14.2	-23.2
004	41.5	44.1	2.6	6.3	WD		
007	66.9	55.4	-11.6	-17.3	52.8	-14.1	-21.1
008	46.9	42.5	-4.3	-9.3	44.3	-2.6	-5.6
009	50.5	52.1	1.6	3.1	49.6	-0.9	-1.8
012	35.7	32.6	-3.1	-8.8	31.9	-3.8	-10.7
014	53.0	47.3	-5.7	-10.8	48.9	-4.2	-7.9
017	50.0	45.6	-4.4	-8.7	45.3	-4.7	-9.3
018	52.4	53.6	1.1	2.2	51.9	-0.5	-0.9
020	50.5	47.6	-2.9	-5.7	51.5	1.0	1.9
023	46.3	44.6	-1.7	-3.6	44.9	-1.4	-2.9
025	44.3	42.0	-2.2	-5.0	42.3	-2.0	-4.5
030	57.6	55.1	-2.5	-4.3	56.2	-1.4	-2.5
031	59.6	57.2	-2.4	-4.1	61.6	1.9	3.3
034	61.5	50.0	-11.6	-18.8	47.0	-14.6	-23.7
036	47.5	44.1	-3.5	-7.3	44.9	-2.7	-5.6
038	53.8	54.3	0.5	1.0	54.1	0.3	0.5
039	55.2	51.7	-3.5	-6.4	51.5	-3.8	-6.8
041	64.5	61.4	-3.1	-4.8	61.7	-2.8	-4.3
Average	52.6	48.9	-3.7	-6.5	49.3	-3.9	-6.9
Count	19.0	19.0	19.0	19.0	18.0	18.0	18.0
SD	8.1	6.7	4.3	7.2	7.1	5.1	8.1
SE	1.9	1.5	1.0	1.7	1.7	1.2	1.9
95% LCI	49.0	45.9	-5.6	-9.8	46.0	-6.3	-10.7
95% UCI	56.2	51.9	-1.7	-3.3	52.6	-1.6	-3.2

Trunk Lean Tissue in kg Determined by DEXA.

Non-Diabetic Subjects

Pt #	Wk0	Wk8	Chg	%Chg	Wk16	Chg	%Chg
001	23.6	22.5	-1.2	-4.9	21.9	-1.7	-7.2
005	17.2	16.0	-1.2	-6.7	16.8	-0.3	-2.0
013	22.8	22.5	-0.4	-1.6	20.6	-2.3	-10.0
024	22.4	22.5	0.0	0.1	23.4	1.0	4.5
026	20.7	17.2	-3.5	-16.8	17.6	-3.1	-14.8
028	27.8	27.4	-0.4	-1.4	24.1	-3.7	-13.2
029	25.6	24.9	-0.7	-2.8	25.1	-0.6	-2.2
032	21.6	21.6	-0.1	-0.3	21.9	0.3	1.2
033	23.5	22.4	-1.0	-4.4	20.8	-2.6	-11.3
037	18.4	17.0	-1.5	-7.9	17.6	-0.8	-4.6
040	24.8	20.5	-4.3	-17.2	20.2	-4.6	-18.4
Average	22.6	21.3	-1.3	-5.8	20.9	-1.7	-7.1
Count	11	11	11	11	11	11	11
SD	3.1	3.5	1.4	6.1	2.7	1.7	7.1
SE	0.9	1.0	0.4	1.8	0.8	0.5	2.2
95% LCI	20.8	19.3	-2.1	-9.4	19.3	-2.7	-11.3
95% UCI	24.4	23.4	-0.5	-2.2	22.5	-0.6	-2.9
Diabetic Subjects							
003	36.2	24.1	-12.1	-33.4	24.7	-11.5	-31.6
004	20.4	0.9	-19.5	-95.6	WD		
007	40.1	29.3	-10.7	-26.8	28.7	-11.3	-28.3
008	24.3	22.0	-2.3	-9.4	22.7	-1.6	-6.6
009	23.9	26.8	2.9	12.0	23.9	0.0	-0.2
012	18.8	17.2	-1.6	-8.5	16.8	-2.0	-10.8
014	27.3	23.8	-3.5	-13.0	25.0	-2.3	-8.3
017	26.8	23.3	-3.5	-13.2	24.3	-2.5	-9.4
018	28.5	28.5	0.0	0.0	27.7	-0.8	-3.0
020	27.1	26.2	-0.9	-3.3	27.8	0.7	2.6
023	22.0	22.8	0.9	3.9	26.2	4.3	19.4
025	23.8	21.7	-2.1	-9.0	22.4	-1.5	-6.1
030	32.2	28.8	-3.4	-10.5	28.6	-3.6	-11.1
031	31.9	30.3	-1.6	-5.0	32.1	0.2	0.7
034	38.1	25.0	-13.1	-34.5	22.8	-15.3	-40.2
036	24.2	22.1	-2.1	-8.7	23.1	-1.0	-4.2
038	27.7	27.6	-0.1	-0.4	28.2	0.4	1.5
039	26.5	24.9	-1.6	-6.0	25.6	-0.9	-3.3
041	33.0	30.1	-2.8	-8.5	32.4	-0.5	-1.6
Average	28.0	24.0	-4.1	-14.2	25.7	-2.7	-7.8
Count	19	19	19	19	18	18	18
SD	5.9	6.5	5.7	22.9	3.8	4.9	13.8
SE	1.3	1.5	1.3	5.2	0.9	1.2	3.2
95% LCI	25.4	21.0	-6.6	-24.5	24.0	-5.0	-14.2
95% UCI	30.7	26.9	-1.5	-3.9	27.5	-0.5	-1.4

Total Trunk Tissue in kg Determined by DEXA.

Non-Diabetic Subjects

Pt #	Wk0	Wk8	Chg	%Chg	Wk16	Chg	%Chg
001	45.2	44.5	-0.8	-1.7	42.6	-2.7	-5.9
005	36.1	32.0	-4.2	-11.5	29.8	-6.3	-17.4
013	47.9	42.3	-5.6	-11.7	38.3	-9.5	-19.9
024	47.2	40.3	-6.8	-14.5	34.4	-12.8	-27.1
026	41.1	35.0	-6.1	-14.8	29.9	-11.2	-27.3
028	64.7	55.5	-9.2	-14.3	47.1	-17.6	-27.2
029	49.3	43.8	-5.4	-11.0	42.4	-6.9	-14.0
032	48.6	44.4	-4.2	-8.7	41.8	-6.8	-14.0
033	50.1	45.4	-4.8	-9.5	40.3	-9.8	-19.6
037	41.8	68.4	26.6	63.5	31.2	-10.6	-25.4
040	48.4	39.3	-9.1	-18.9	36.8	-11.6	-24.0
Average	47.3	44.6	-2.7	-4.8	37.7	-9.6	-20.2
Count	11	11	11	11	11	11	11
SD	7.2	9.9	10.0	23.1	5.8	3.9	6.9
SE	2.2	3.0	3.0	7.0	1.7	1.2	2.1
95% LCI	43.1	38.7	-8.6	-18.5	34.3	-12.0	-24.3
95% UCI	51.6	50.5	3.2	8.8	41.1	-7.3	-16.1

Diabetic Subjects

003	63.7	54.4	-9.3	-14.6	56.1	-7.6	-12.0
004	48.3	46.4	-1.9	-3.9	WD		
007	65.6	53.8	-11.9	-18.1	50.4	-15.3	-23.3
008	47.5	47.5	0.0	-0.1	46.6	-1.0	-2.0
009	48.7	48.5	-0.2	-0.4	43.3	-5.5	-11.2
012	40.4	36.9	-3.5	-8.7	35.9	-4.5	-11.2
014	53.7	47.5	-6.2	-11.6	44.2	-9.6	-17.8
017	48.2	41.6	-6.7	-13.8	39.7	-8.5	-17.7
018	53.9	44.8	-9.1	-16.8	39.2	-14.6	-27.1
020	51.2	48.4	-2.7	-5.3	49.5	-1.7	-3.2
023	53.4	52.3	-1.2	-2.2	56.5	3.1	5.7
025	51.0	45.3	-5.7	-11.2	43.5	-7.5	-14.6
030	66.8	56.7	-10.1	-15.1	53.1	-13.7	-20.5
031	58.1	55.9	-2.2	-3.8	53.9	-4.2	-7.2
034	63.8	49.6	-14.2	-22.3	43.0	-20.8	-32.6
036	94.6	44.4	-50.1	-53.0	44.1	-50.4	-53.3
038	51.1	43.0	-8.1	-15.9	40.6	-10.6	-20.6
039	49.9	44.4	-5.5	-11.1	41.4	-8.5	-17.0
041	60.6	53.1	-7.5	-12.4	51.3	-9.3	-15.3
Average	56.3	48.1	-8.2	-12.7	46.2	-10.6	-16.7
count	19	19	19	19	18	18	18
SD	11.7	5.2	10.9	11.6	6.2	11.5	13.0
SE	2.7	1.2	2.5	2.7	1.5	2.7	3.1
95% LCI	51.1	45.8	-13.1	-17.9	43.4	-15.8	-22.7
95% UCI	61.6	50.5	-3.3	-7.4	49.1	-5.3	-10.7

Percent Body Fat Determined by BOD POD®.

Non-Diabetic Subjects

Pt #	Wk0	Wk8	Chg	Wk16	Chg
001	64.9	48.4	-16.5	50.1	-14.8
005	49.3	43.6	-5.7	38.7	-10.6
013	52.3	46.7	-5.6	31.4	-20.9
024	49.3	41.4	-8.0	31.2	-18.2
026	52.0	46.7	-5.3	36.3	-15.7
028	55.4	52.3	-3.1	45.6	-9.8
029	49.8	47.0	-2.9	41.4	-8.4
032	51.1	46.8	-4.3	45.5	-5.6
033	54.5	49.2	-5.3	44.2	-10.3
037	51.6	48.8	-2.7	38.7	-12.8
040	49.0	42.2	-6.8	39.0	-10.0
Average	52.7	46.6	-6.0	40.2	-12.5
Count	11.0	11.0	11.0	11.0	11.0
SD	4.6	3.2	3.8	5.9	4.5
SE	1.4	1.0	1.2	1.8	1.4
95% LCI	50.0	44.7	-8.3	36.7	-15.1
95% UCI	55.4	48.5	-3.8	43.7	-9.8

Diabetic Subjects

003	56.5	53.0	-3.5	54.2	-2.3
004	58.9	57.0	-1.9	WD	
007	55.8	48.0	-7.8	44.7	-11.1
008	46.3	48.6	2.3	49.0	2.7
009	48.1	47.4	-0.6	44.0	-4.1
012	50.9	52.8	1.9	50.9	0.0
014	52.4	46.4	-6.0	45.8	-6.6
017	45.3	41.1	-4.2	34.5	-10.7
018	46.2	38.6	-7.6	31.3	-14.9
020	47.8	46.8	-1.0	44.6	-3.2
023	55.1	52.3	-2.8	50.1	-5.0
025	53.8	48.2	-5.7	49.8	-4.0
031	46.3	45.3	-1.0	42.9	-3.4
034	54.7	47.9	-6.9	45.7	-9.0
036	49.6	46.7	-2.9	45.9	-3.7
038	45.4	40.5	-4.9	36.7	-8.8
039	45.8	41.3	-4.5	41.3	-4.5
041	43.7	38.6	-5.1	35.0	-8.7
Average	50.1	46.7	-3.5	43.9	-5.7
Count	18.0	18.0	18.0	17.0	17.0
SD	4.7	5.2	3.0	6.4	4.4
SE	1.1	1.2	0.7	1.5	1.1
95% LCI	48.0	44.3	-4.8	40.9	-7.8
95% UCI	52.3	49.1	-2.1	46.9	-3.6

Total Fat in kg Determined by BOD POD®.

Non-Diabetic Subjects

Pt #	Wk0	Wk8	Chg	Wk16	Chg
001	56.1	46.0	-10.1	45.1	-11.0
005	35.2	28.3	-6.9	24.0	-11.2
013	48.8	40.3	-8.5	25.5	-23.3
024	47.1	34.9	-12.1	22.7	-24.3
026	43.6	34.3	-9.3	23.9	-19.8
028	65.5	54.1	-11.3	43.1	-22.4
029	50.2	42.9	-7.3	34.8	-15.3
032	52.4	44.7	-7.7	40.6	-11.8
033	56.8	45.3	-11.5	37.4	-19.3
037	41.7	34.8	-6.8	25.0	-16.7
040	49.7	36.6	-13.0	30.9	-18.8
Average	49.7	40.2	-9.5	32.1	-17.6
Count	11.0	11.0	11.0	11.0	11.0
SD	8.2	7.3	2.2	8.4	4.8
SE	2.5	2.2	0.7	2.5	1.5
95% LCI	44.9	35.9	-10.8	27.1	-20.5
95% UCI	54.5	44.5	-8.2	37.1	-14.8

Diabetic Subjects

003	56.5	58.9	2.4	58.4	1.9
004	65.1	58.6	-6.5	57.4	-7.7
007	55.8	47.8	-8.0	40.2	-15.6
008	44.0	44.8	0.8	45.1	1.2
009	52.2	48.0	-4.2	42.6	-9.6
010	54.1	WD			
012	38.4	36.6	-1.8	34.4	-4.0
014	54.1	43.0	-11.1	39.8	-14.3
015	38.6	WD			
017	39.2	31.7	-7.6	24.3	-14.9
018	44.2	33.1	-11.1	23.8	-20.4
020	46.4	41.8	-4.6	41.2	-5.2
023	60.6	53.5	-7.2	49.4	-11.2
025	51.9	42.2	-9.6	42.2	-9.7
031	52.6	49.3	-3.3	46.6	-6.0
034	62.3	48.3	-13.9	41.1	-21.2
036	48.5	41.3	-7.2	39.3	-9.2
038	45.6	36.3	-9.2	30.6	-15.0
039	48.3	38.8	-9.5	32.0	-16.3
041	50.9	41.6	-9.3	35.2	-15.7
Average	50.5	44.2	-6.7	40.2	-10.7
Count	20.0	18.0	18.0	18.0	18.0
SD	7.6	7.8	4.3	9.5	6.6
SE	1.7	1.8	1.0	2.2	1.6
95% LCI	47.1	40.6	-8.7	35.8	-13.8
95% UCI	53.8	47.8	-4.7	44.6	-7.7

Total Lean Tissue Determined by BOD POD®.

Non-Diabetic Subjects

Pt #	Wk0	Wk8	Chg	Wk16	Chg
001	46.1	49.0	2.9	44.8	-1.3
005	36.2	36.6	0.4	38.0	1.8
013	44.5	46.0	1.5	55.6	11.1
024	48.3	49.5	1.2	50.2	1.9
026	40.2	39.2	-1.0	41.8	1.6
028	52.7	49.5	-3.2	51.4	-1.3
029	50.5	48.4	-2.1	49.4	-1.1
032	50.2	50.9	0.6	48.6	-1.6
033	47.4	46.8	-0.6	47.3	-0.1
037	39.2	36.5	-2.6	39.5	0.3
040	51.7	50.1	-1.6	48.3	-3.4
Average	46.1	45.7	-0.4	46.8	0.7
Count	11.0	11.0	11.0	11.0	11.0
SD	5.5	5.5	1.9	5.3	3.8
SE	1.7	1.7	0.6	1.6	1.1
95% LCI	42.8	42.4	-1.5	43.7	-1.5
95% UCI	49.3	48.9	0.7	50.0	3.0

Diabetic Subjects

003	52.6	52.2	-0.4	49.4	-3.2
004	45.5	43.3	-2.2	43.3	-2.2
007	55.8	51.8	-3.9	49.8	-6.0
008	51.1	47.4	-3.7	47.0	-4.1
009	56.3	53.2	-3.2	54.1	-2.2
010	44.8	WD			
012	37.0	32.8	-4.2	33.2	-3.8
014	49.2	49.7	0.5	47.1	-2.1
015	44.5	WD			
017	47.4	45.4	-2.0	46.1	-1.4
018	51.5	52.7	1.2	52.2	0.8
020	50.6	47.5	-3.1	51.1	0.5
023	49.4	48.7	-0.7	49.2	-0.3
025	44.5	45.5	1.0	42.5	-2.0
031	61.0	59.5	-1.5	62.1	1.1
034	51.5	52.7	1.1	48.8	-2.7
036	49.3	47.2	-2.1	40.4	-8.9
038	54.8	53.4	-1.4	52.8	-1.9
039	57.2	55.2	-2.0	53.7	-3.5
041	66.8	66.2	-0.6	65.3	-1.5
Average	51.0	50.2	-1.5	49.3	-2.4
Count	20.0	18.0	18.0	18.0	18.0
SD	6.6	7.0	1.7	7.4	2.4
SE	1.5	1.6	0.4	1.7	0.6
95% LCI	48.2	47.0	-2.3	45.9	-3.5
95% UCI	53.9	53.5	-0.7	52.8	-1.3

Change in Subcutaneous and Visceral Adipose Tissue Stores for Non-Diabetic and Diabetic Subjects.

Non-Diabetic Subjects

Pt #	Subcut-aneous Fat 1 (sq cm)	Subcut-aneous Fat 2 (sq cm)	%Chg	Chg (sq cm)	Visceral Fat 1 (sq cm)	Visceral Fat 2 (sq cm)	%Chg	Chg (sq cm)	Total Abdominal Fat Loss (sq cm)
001	655.1	538.8	-17.8	-116.3	122.9	98.9	-19.5	-24.0	-140.3
005	411.2	320.1	-22.2	-91.1	144.9	90.6	-37.5	-54.3	-145.4
013	638.2	516.9	-19.0	-121.3	84.2	74.8	-11.1	-9.4	-130.7
024	539.3	224.5	-58.4	-314.8	63.5	25.6	-59.7	-37.9	-352.8
026	613.8	361.9	-41.0	-252.0	62.4	35.5	-43.2	-26.9	-278.9
028	767.6	595.7	-22.4	-171.9	111.3	63.6	-42.8	-47.7	-219.6
029	507.8	429.3	-15.4	-78.4	167.4	104.5	-37.6	-62.9	-141.3
032	716.3	577.3	-19.4	-139.0	176.2	123.9	-29.7	-52.3	-191.3
033	697.6	504.6	-27.7	-193.0	141.4	103.4	-26.8	-37.9	-230.9
037	521.5	317.7	-39.1	-203.8	103.8	91.6	-11.8	-12.2	-216.0
040	534.5	336.1	-37.1	-198.4	113.8	60.8	-46.6	-53.0	-251.4
Average	600.3	429.3	-29.0	-170.9	117.4	79.4	-33.3	-38.0	-208.9
Count	11	11.0	11.0	11.0	11.0	11.0	11.0	11.0	11.0
SD	106.8	124.3	13.3	71.4	38.2	30.5	15.2	17.9	69.1
SE	32.2	37.5	4.0	21.5	11.5	9.2	4.6	5.4	20.8
95% LCI	537.1	355.9	-36.9	-213.1	94.9	61.4	-42.2	-48.6	-249.8
95% UCI	663.4	502.799	-21.2	-128.7	140.0	97.4	-24.3	-27.4	-168.1

Diabetic Subjects

003	603.0	530.1	-12.1	-72.9	326.1	228.9	-29.8	-97.1	-170.0
007	552.2	435.5	-21.1	-116.8	304.2	152.0	-50.0	-152.2	-269.0
008	491.9	462.7	-6.0	-29.3	84.7	90.1	6.4	5.5	-23.8
009	590.3	511.0	-13.4	-79.3	185.1	133.2	-28.0	-51.9	-131.2
012	393.6	336.0	-14.6	-57.6	179.0	136.1	-24.0	-43.0	-100.6
014	644.1	482.7	-25.1	-161.4	188.8	116.9	-38.1	-71.9	-233.3
017	376.3	277.6	-26.2	-98.8	232.7	113.0	-51.4	-119.7	-218.4
018	490.0	329.4	-32.8	-160.6	167.0	73.4	-56.1	-93.6	-254.2
020	545.1	504.7	-7.4	-40.4	160.8	139.8	-13.1	-21.1	-61.4
023	699.0	549.0	-21.5	-150.0	174.8	132.0	-24.5	-42.8	-192.9
025	536.8	436.3	-18.7	-100.5	121.3	81.6	-32.7	-39.7	-140.2
030	412.4	300.6	-27.1	-111.9	322.4	249.7	-22.6	-72.7	-184.6
031	347.5	374.0	7.6	26.5	228.1	183.4	-19.6	-44.7	-18.3
034	745.3	554.7	-25.6	-190.6	254.8	111.6	-56.2	-143.2	-333.8
036	563.3	432.1	-23.3	-131.2	154.7	108.5	-29.9	-46.2	-177.4
038	414.9	352.6	-15.0	-62.2	203.7	105.3	-48.3	-98.4	-160.6
039	636.9	431.2	-32.3	-205.7	124.0	66.1	-46.7	-58.0	-263.6
041	354.6	306.3	-13.6	-48.3	337.8	161.9	-52.1	-175.9	-224.2
Average	522.1	422.6	-18.2	-99.5	208.3	132.4	-34.3	-75.9	-175.4
Count	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.0
SD	120.2	90.1	8.3	46.5	75.0	49.5	17.0	48.2	85.9
SE	28.3	21.2	1.9	11.0	17.7	11.7	4.0	11.4	20.3
95% LCI	466.5	380.9	-22.1	-121.0	173.7	109.6	-42.1	-98.2	-215.1
95% UCI	577.6	464.2	-14.4	-78.0	243.0	155.3	-26.4	-53.7	-135.7

Change and Percent Change in Waist Circumference (cm) for Non-Diabetic and Diabetic Subjects.

Non-Diabetic Subjects

Pt #	Wk0	Wk16	Total Change	%Chg
001	100.3	99.1	-1.3	-1.3
005	90.2	76.2	-14.0	-15.5
013	104.1	91.4	-12.7	-12.2
024	104.1	82.6	-21.6	-20.7
026	86.4	77.5	-8.9	-10.3
028	132.1	95.3	-36.8	-27.9
029	114.3	101.6	-12.7	-11.1
032	121.9	101.6	-20.3	-16.7
033	139.7	91.4	-48.3	-34.5
037	116.8	96.5	-20.3	-17.4
040	105.4	91.4	-14.0	-13.3
Average	110.5	91.3	-19.2	-16.4
Count	11.0	11.0	11.0	11.0
SD	16.5	9.0	13.2	9.0
SE	5.0	2.7	4.0	2.7
95% LCI	100.8	86.0	-26.9	-21.7
95% UCI	120.2	96.6	-11.4	-11.1

Diabetic Subjects

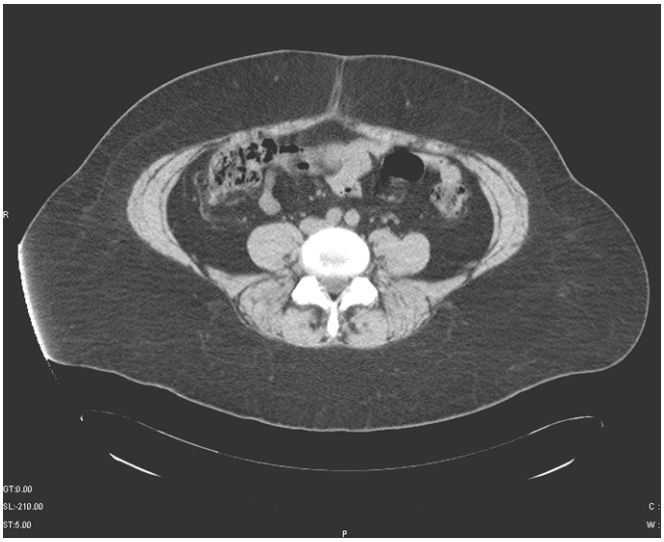
003	128.3	124.5	-3.8	-3.0
004	134.6	WD		
007	137.2	114.3	-22.9	-16.7
008	101.6	102.9	1.3	1.3
009	102.9	99.1	-3.8	-3.7
010	111.8	WD		
012	101.6	95.3	-6.3	-6.2
014	123.2	114.3	-8.9	-7.2
015	104.1	WD		
017	106.7	96.5	-10.2	-9.5
018	118.1	95.3	-22.9	-19.4
020	118.1	116.8	-1.3	-1.1
023	121.9	109.2	-12.7	-10.4
025	104.1	96.5	-7.6	-7.3
030	127.0	124.5	-2.5	-7.6
031	120.7	119.4	-1.3	-8.0
034	139.7	104.1	-35.6	-7.2
036	104.1	94.0	-10.2	-8.0
038	121.9	99.1	-22.9	-8.4
039	125.7	105.4	-20.3	-8.5
041	121.9	99.1	-22.9	-8.7
Average	117.9	106.1	-11.9	-7.8
Count	21.0	18.0	18.0	18.0
SD	12.1	10.4	10.3	4.8
SE	2.7	2.5	2.4	1.1
95% LCI	112.7	101.3	-16.7	-10.0
95% UCI	123.1	110.9	-7.2	-5.5

APPENDIX C

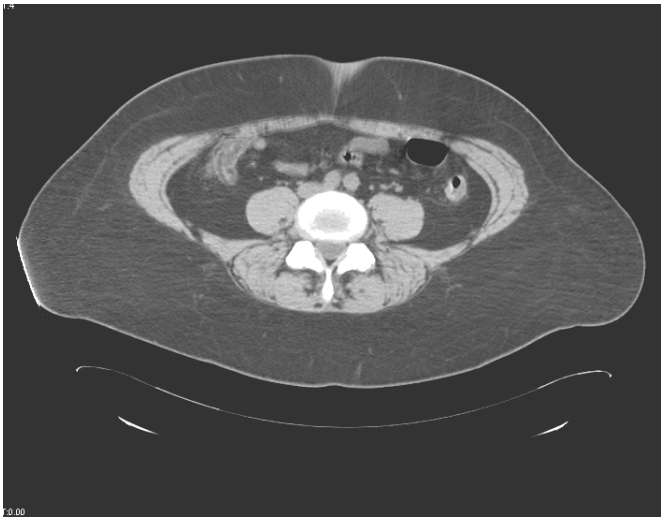
Computer Tomography Scans

Patient # 001

Scan 1

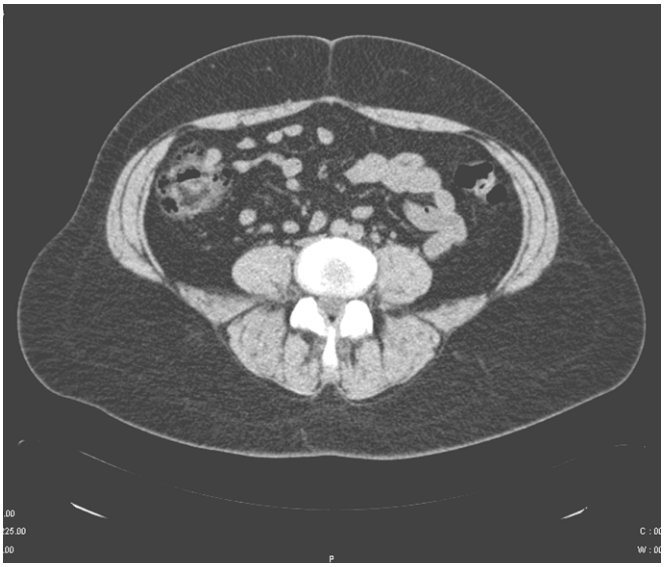


Scan 2

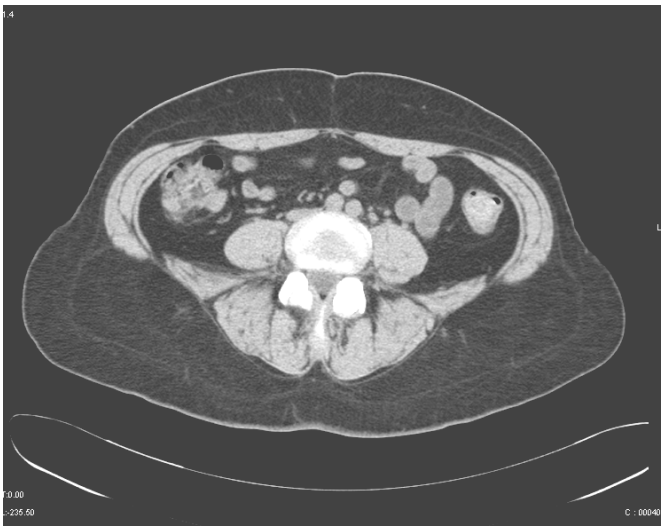


Patient # 005

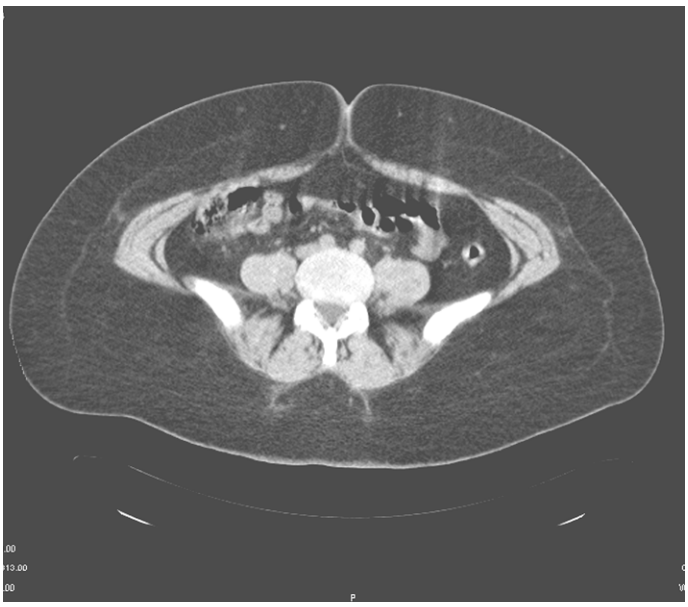
Scan 1



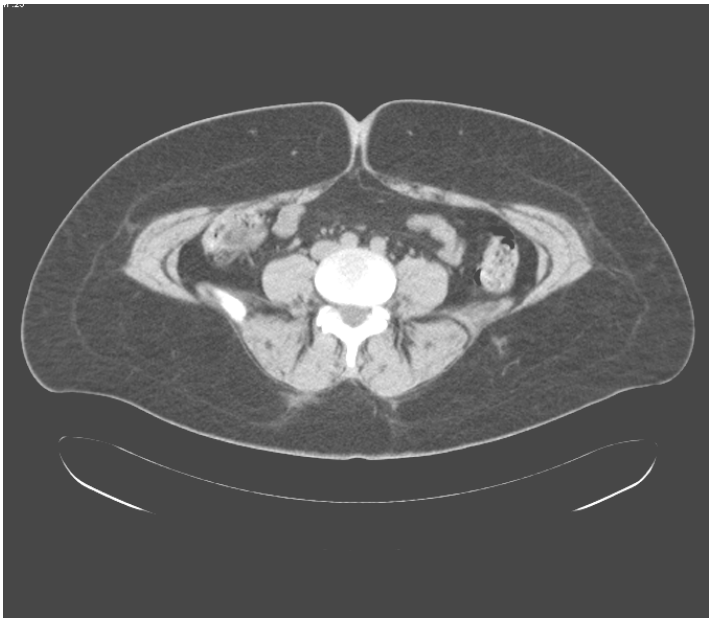
Scan 2



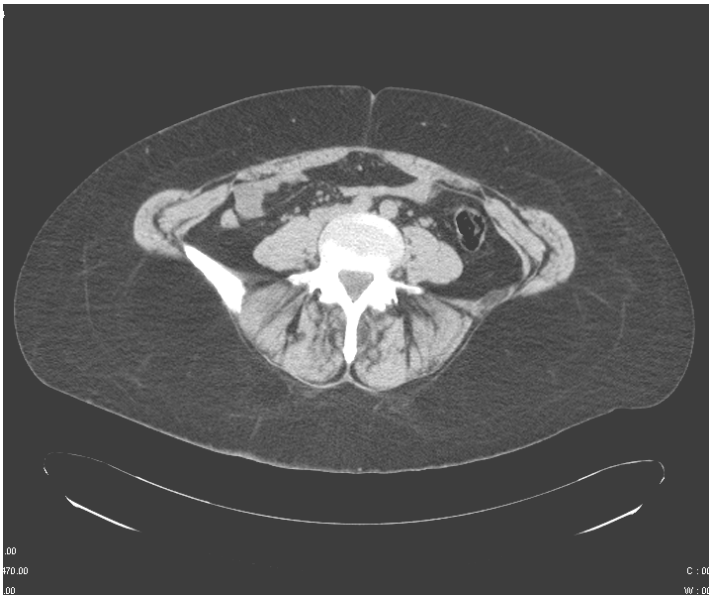
Patient #013



Scan 2



Patient # 024



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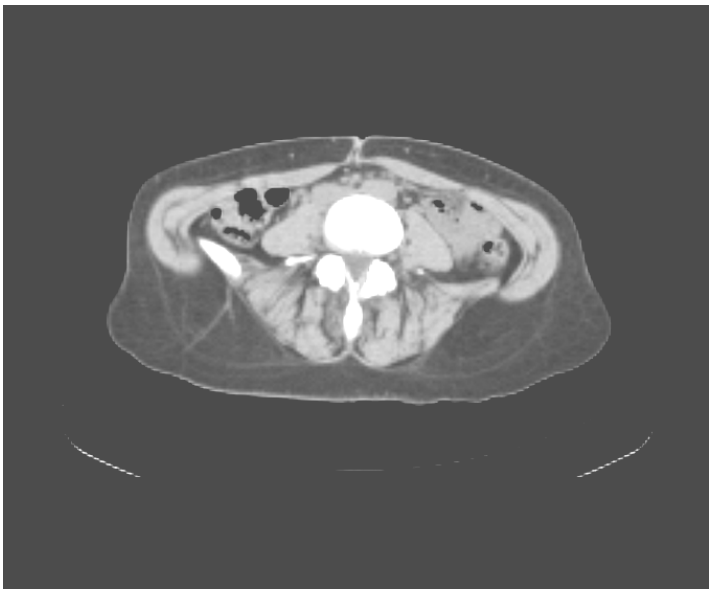
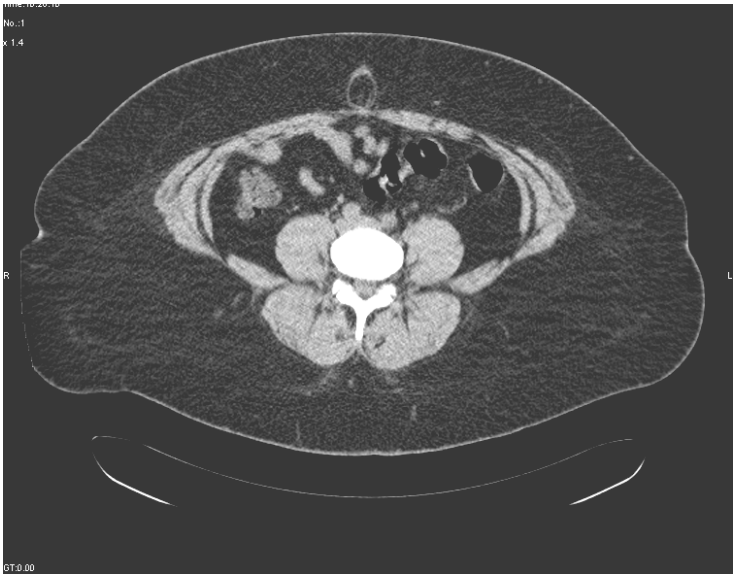


Patient #028

Scan 1



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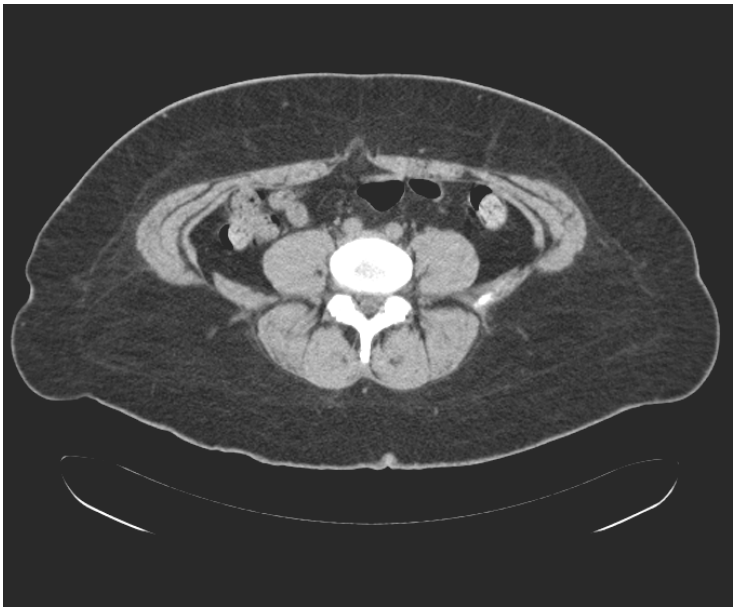
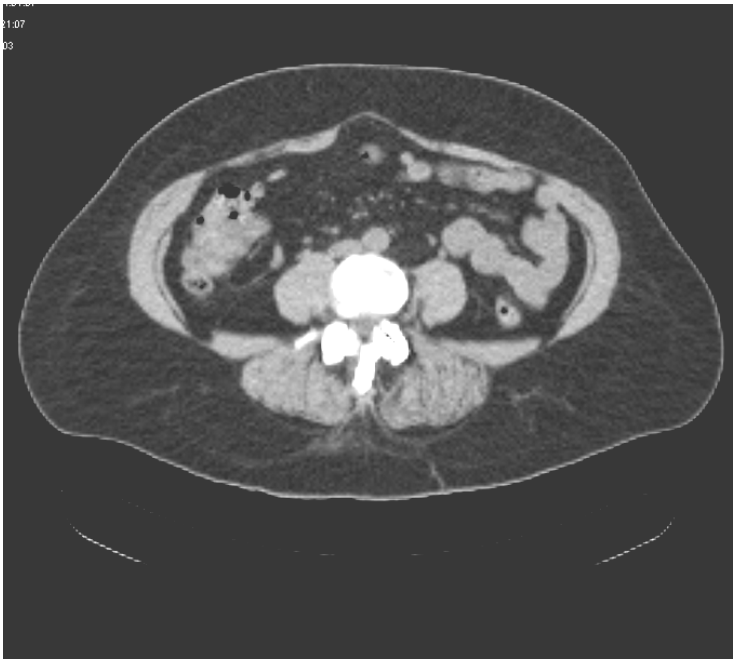


Patient # 029

Scan 1



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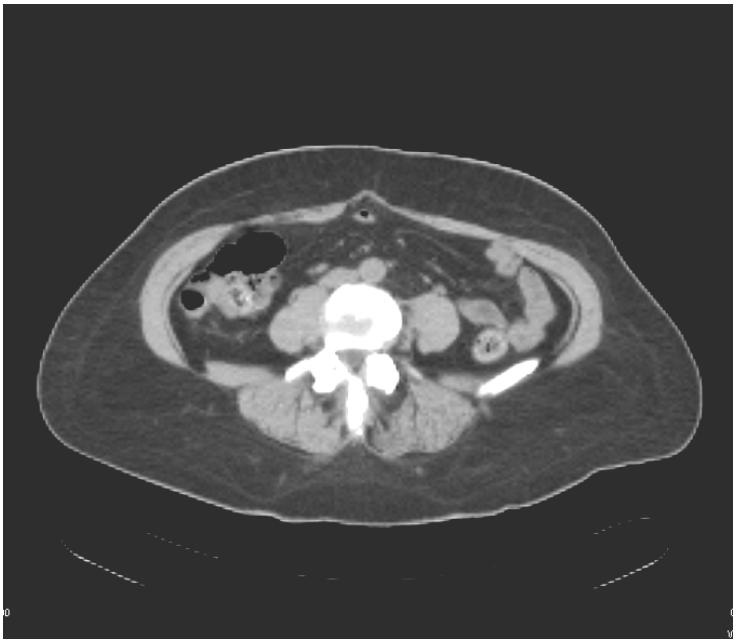
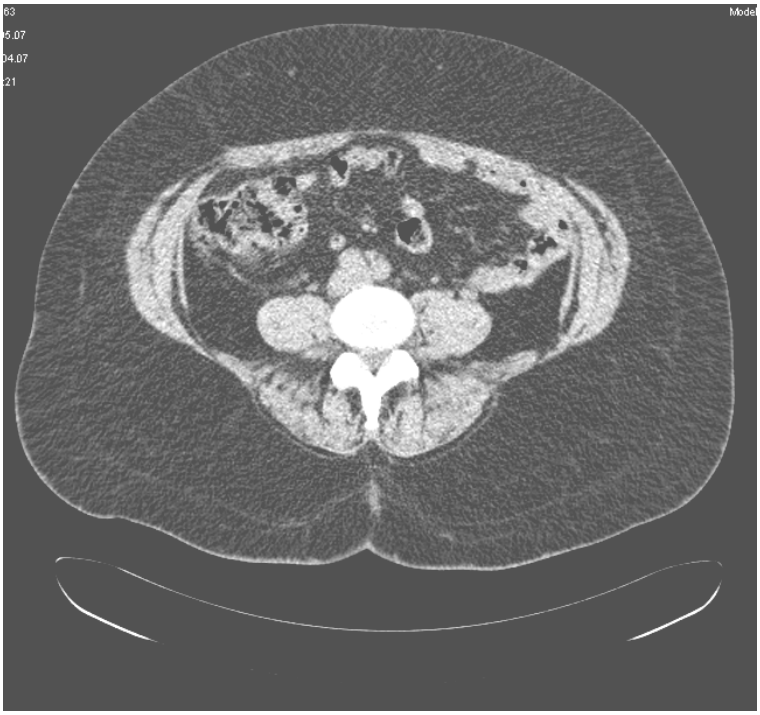


Patient #033

Scan 1



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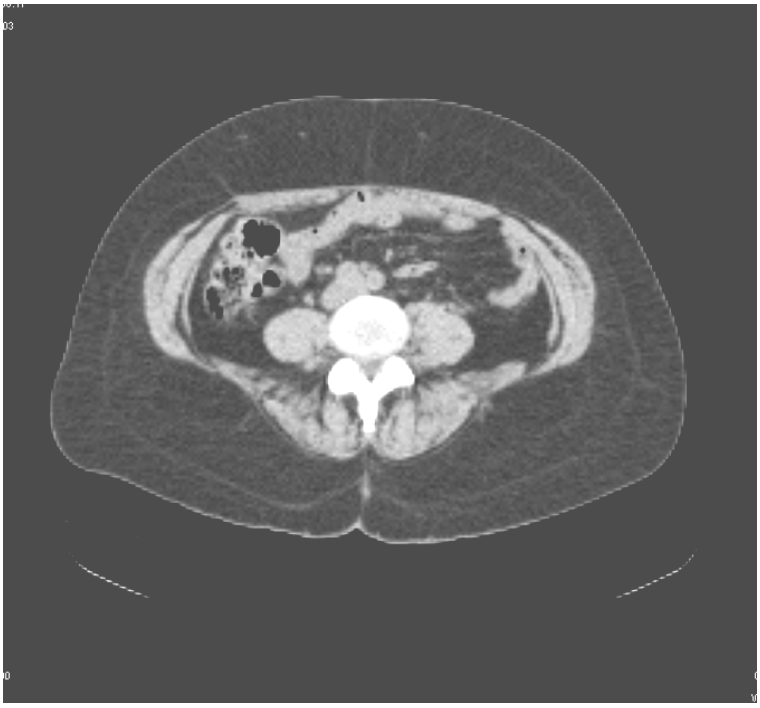
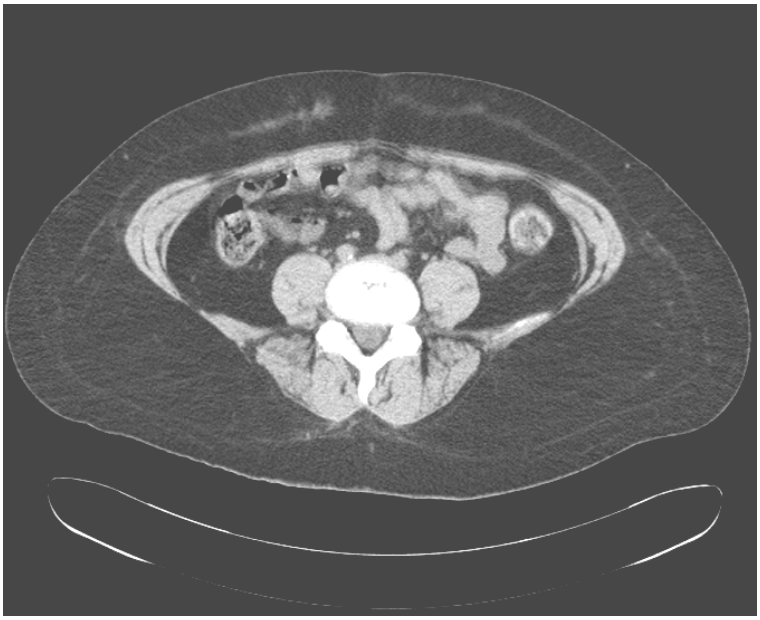


Patient #037

Scan 1



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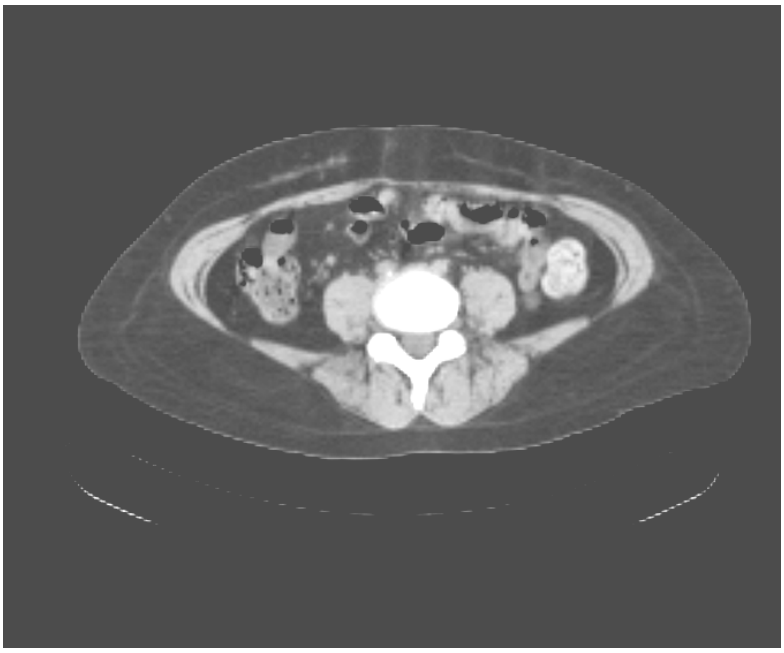
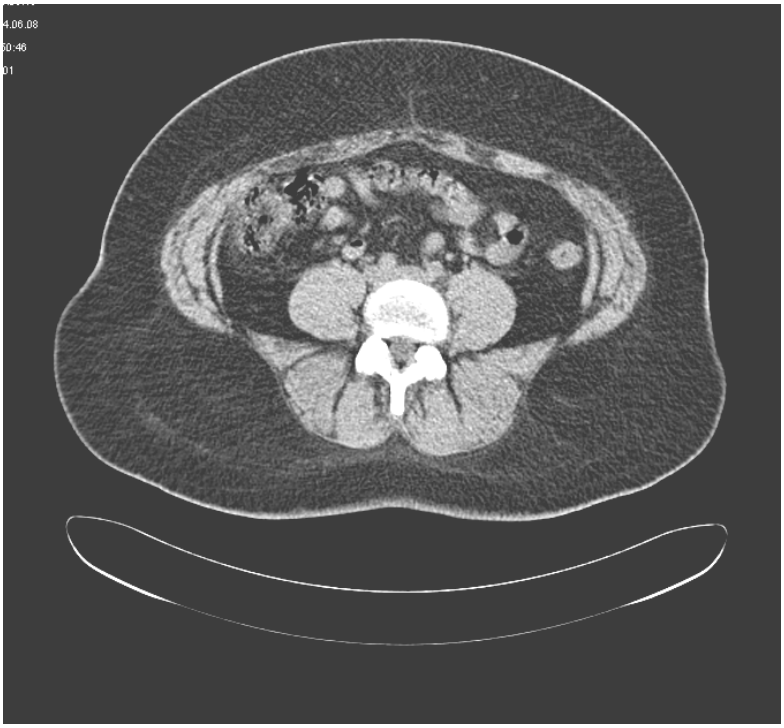


Patient # 040

Scan 1



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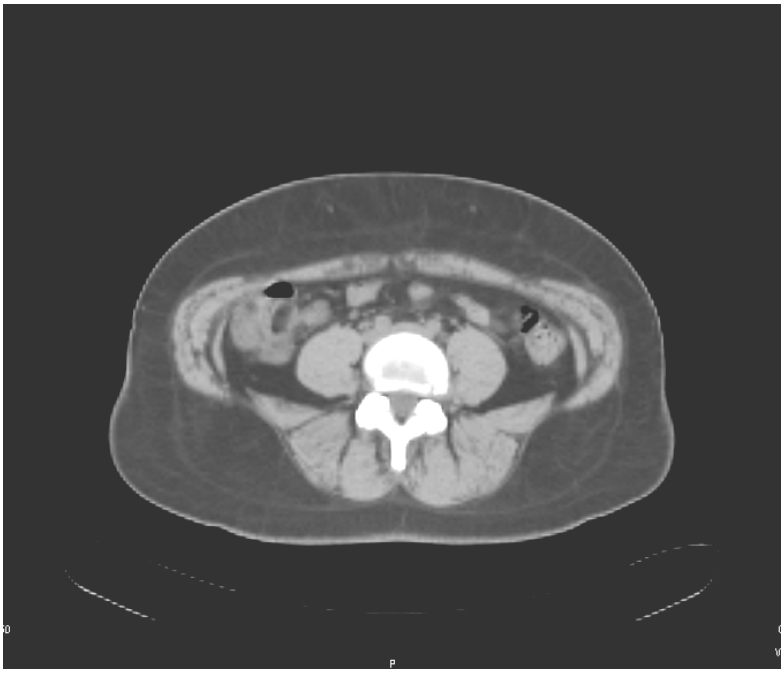
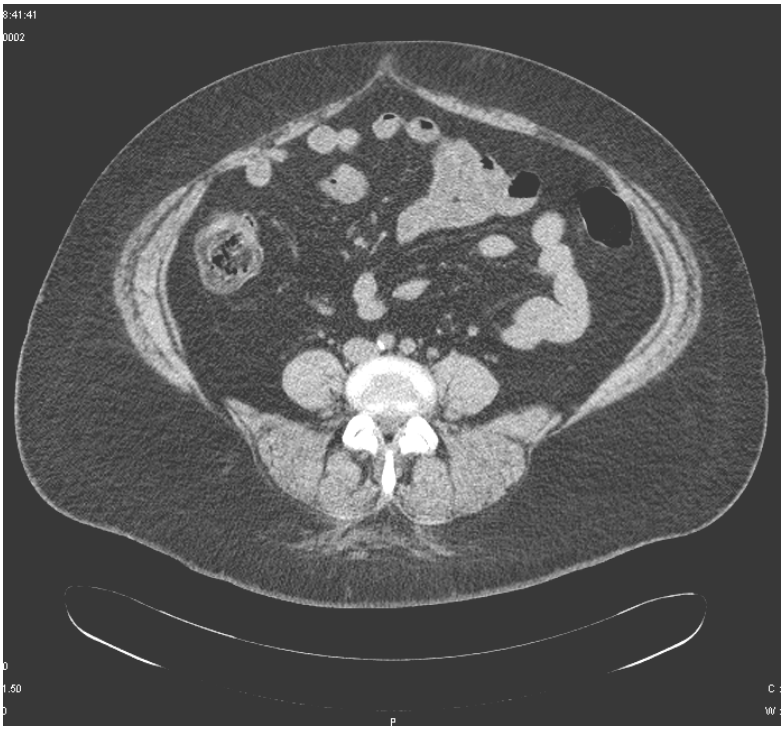


Patient #003

Scan 1



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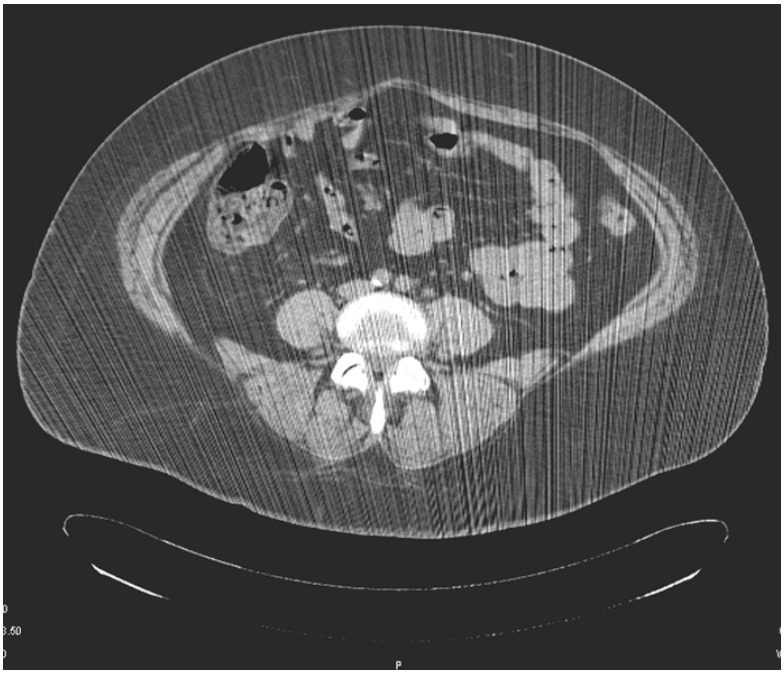

Patient #008

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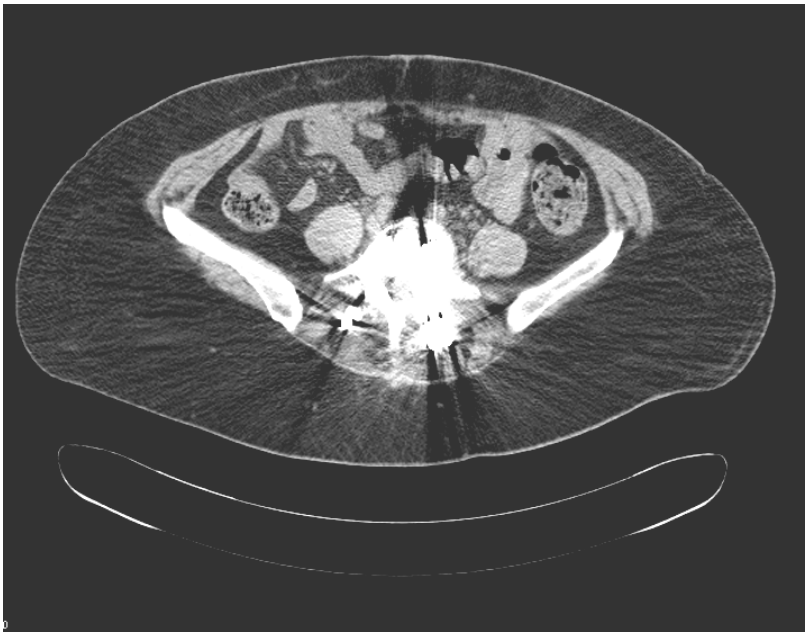

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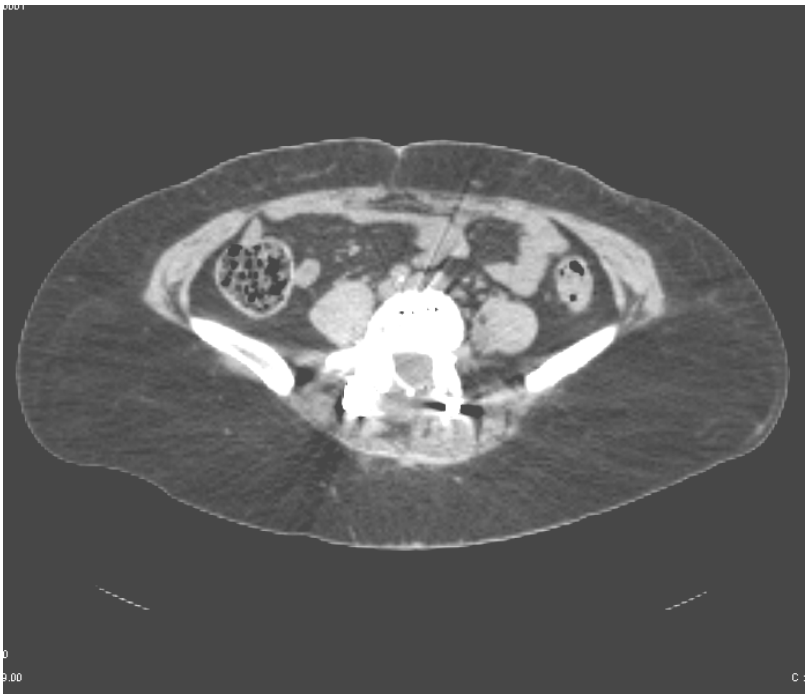
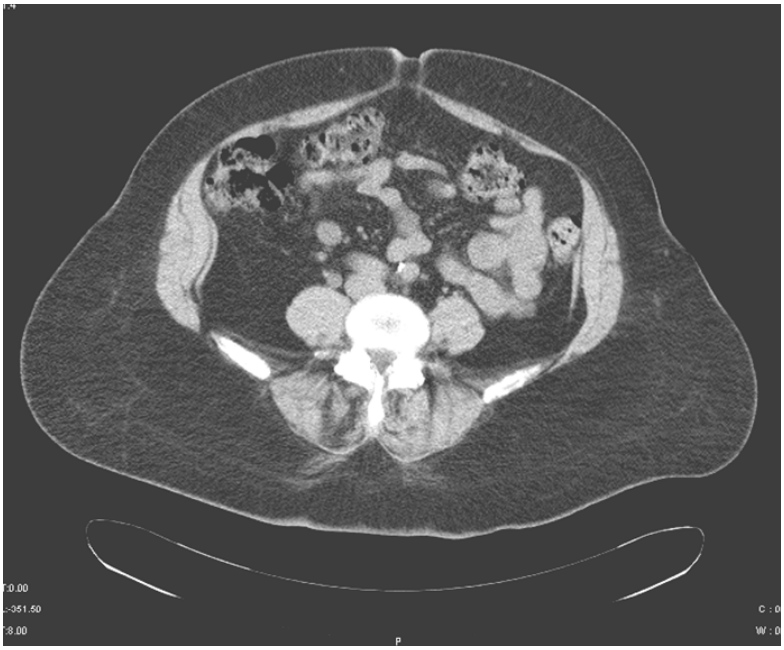


Patient #009

Scan 1



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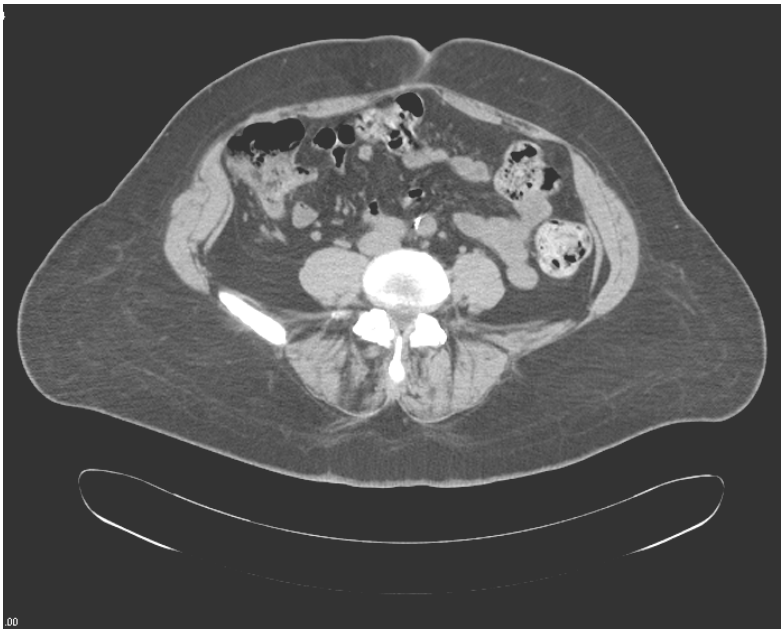
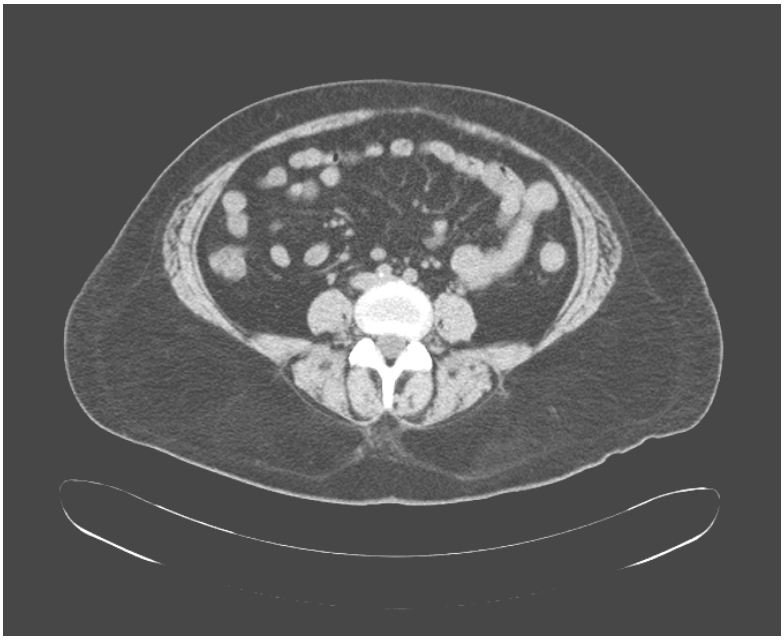


Patient # 012

Scan 1



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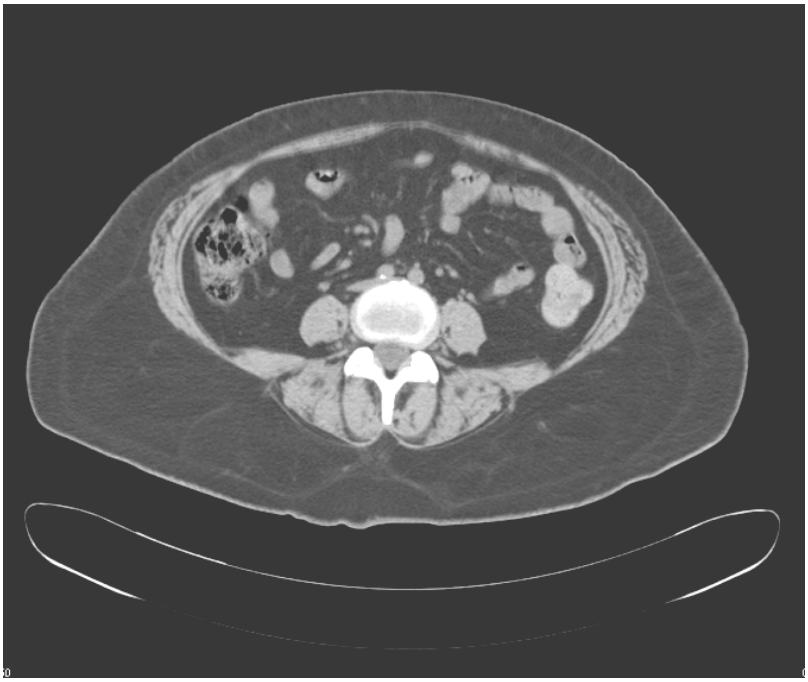

Patient # 014

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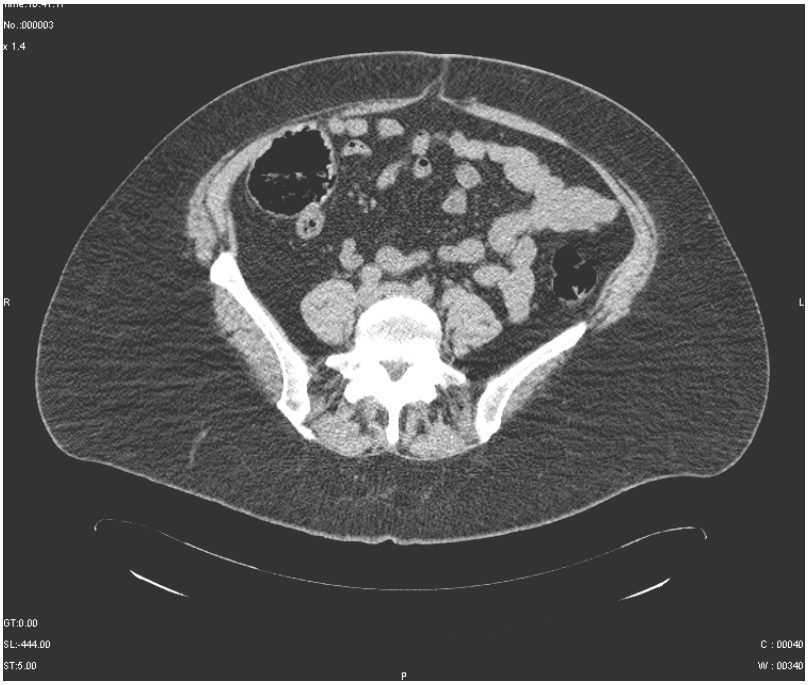

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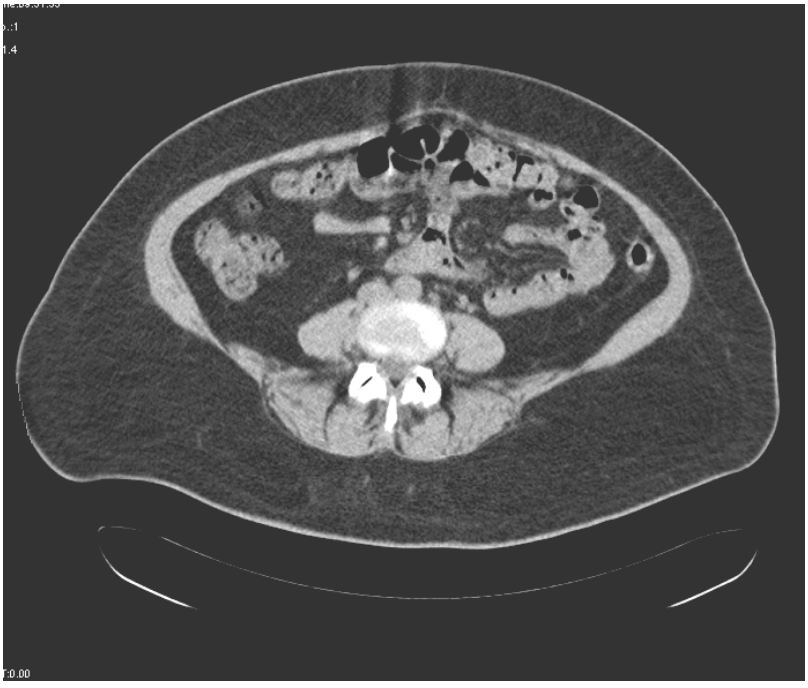
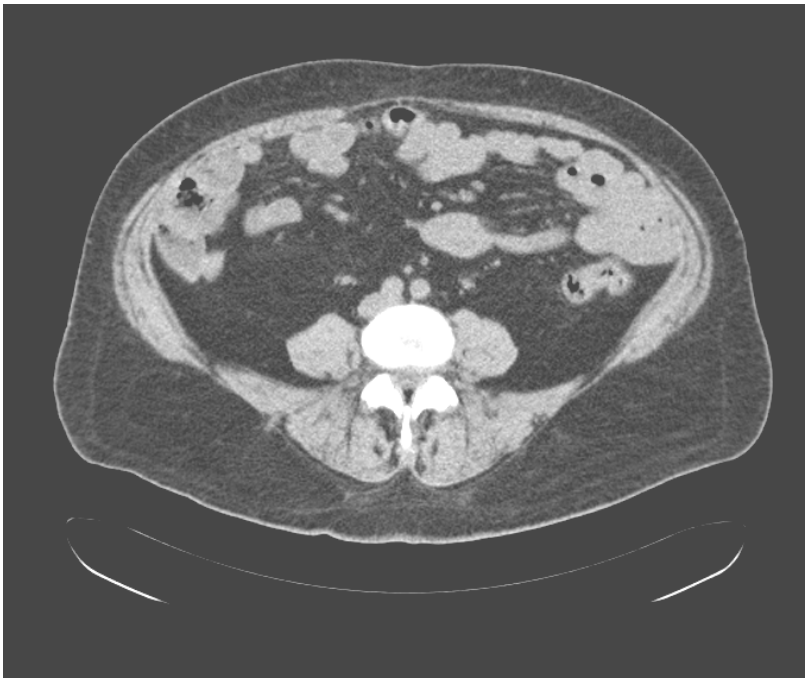


Patient #017

Scan 1



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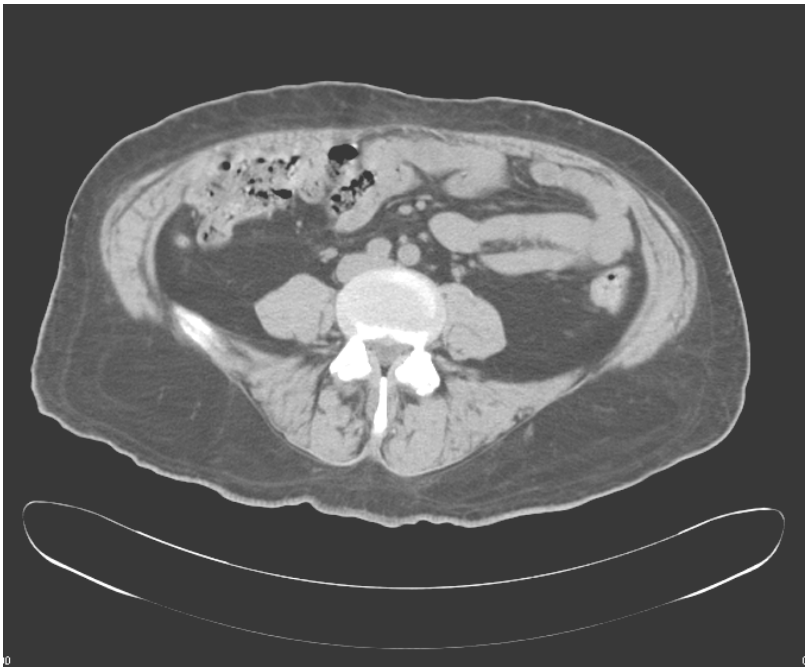
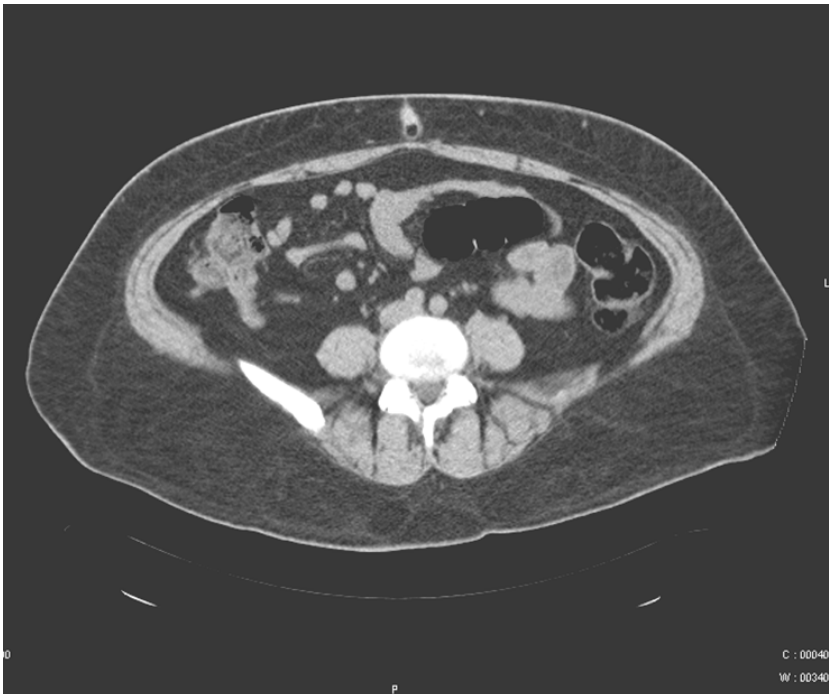
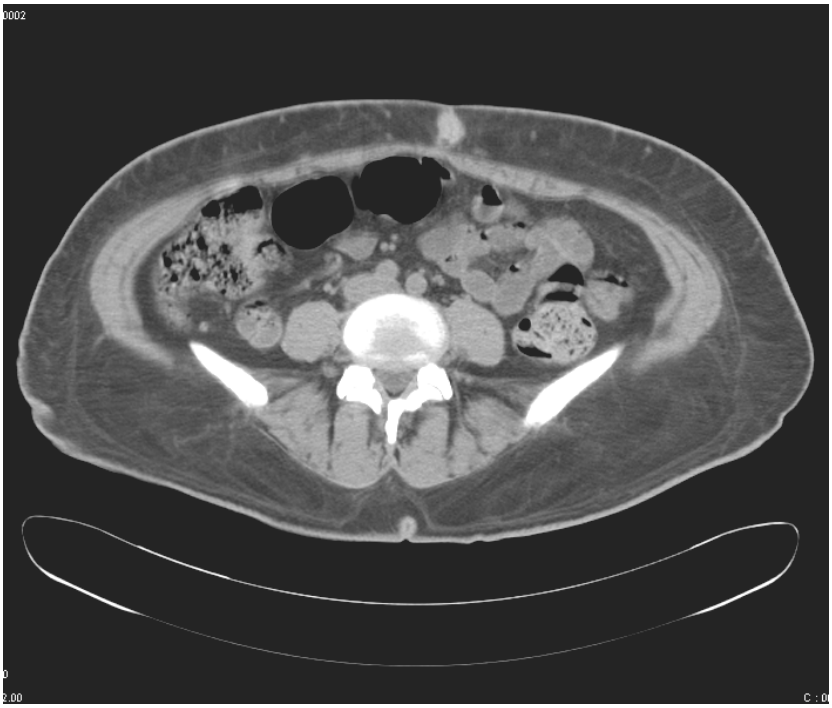


Patient # 018

Scan 1

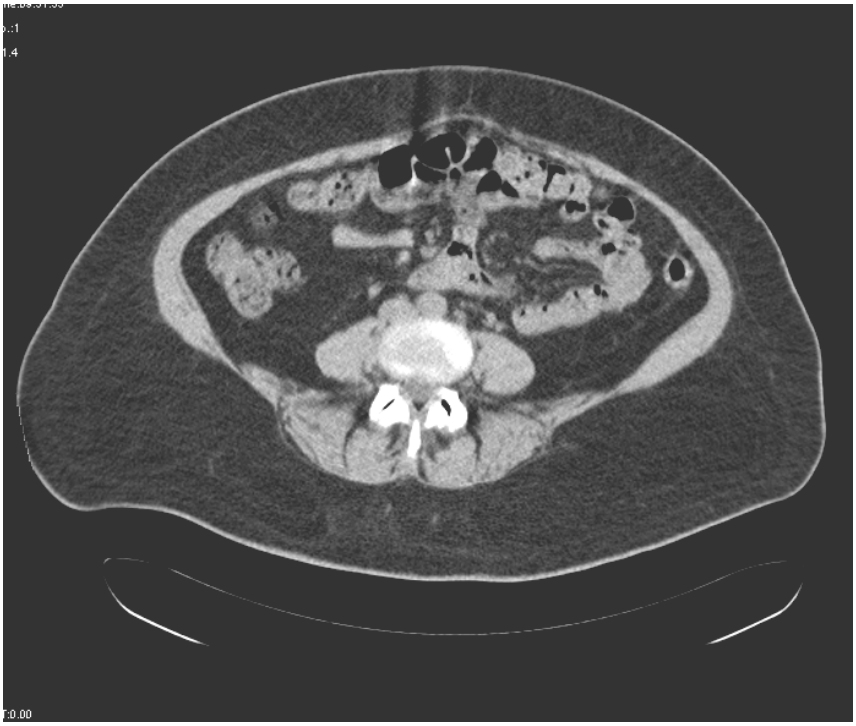


Scan 2



Patient # 020

Scan 1



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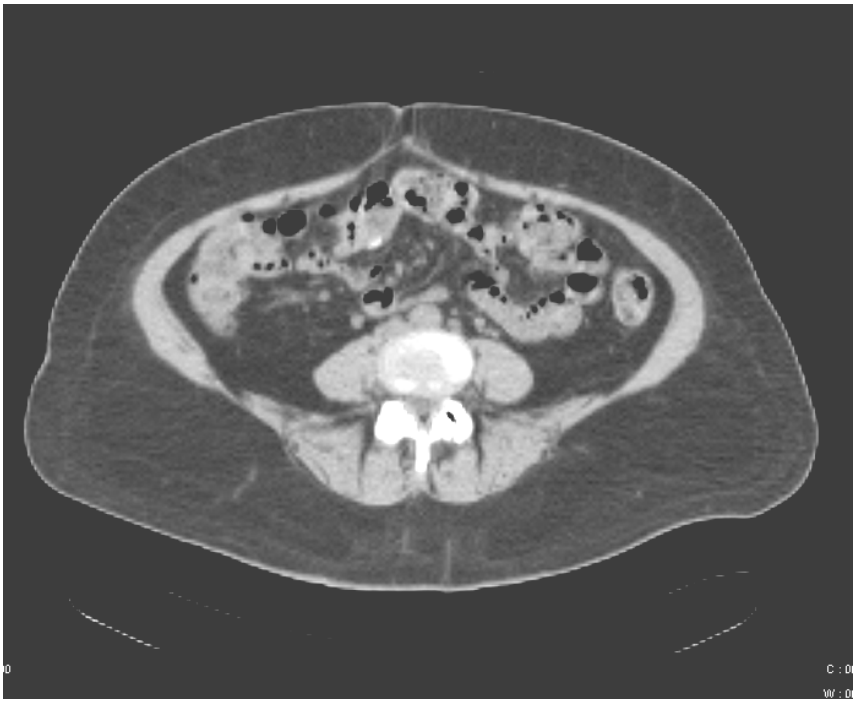
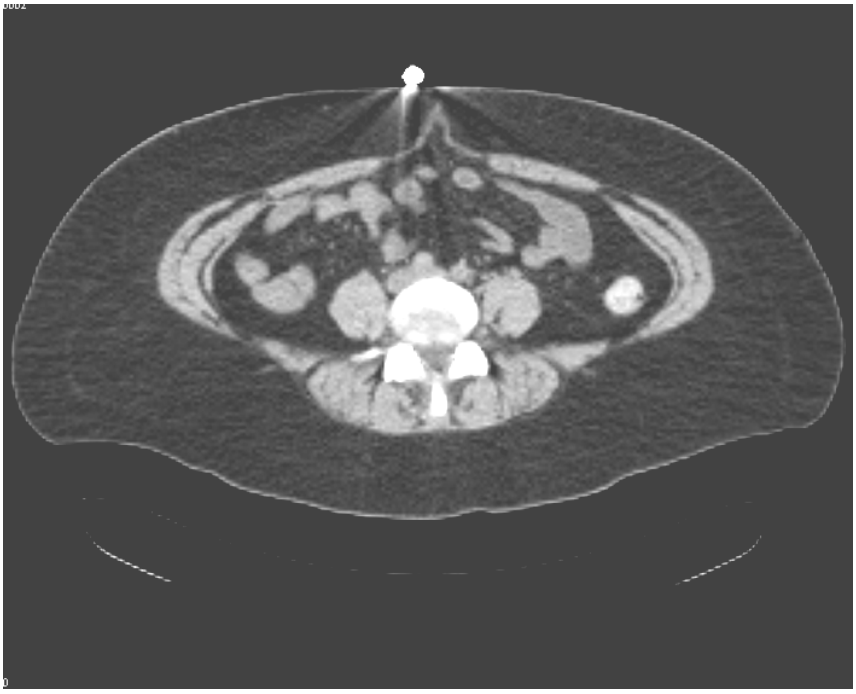


Patient # 023

Scan 1



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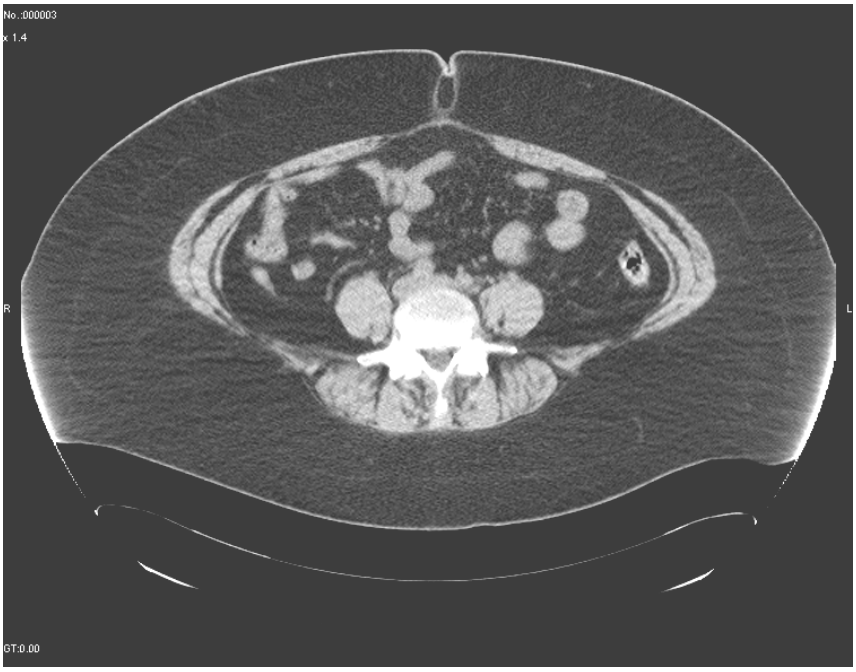
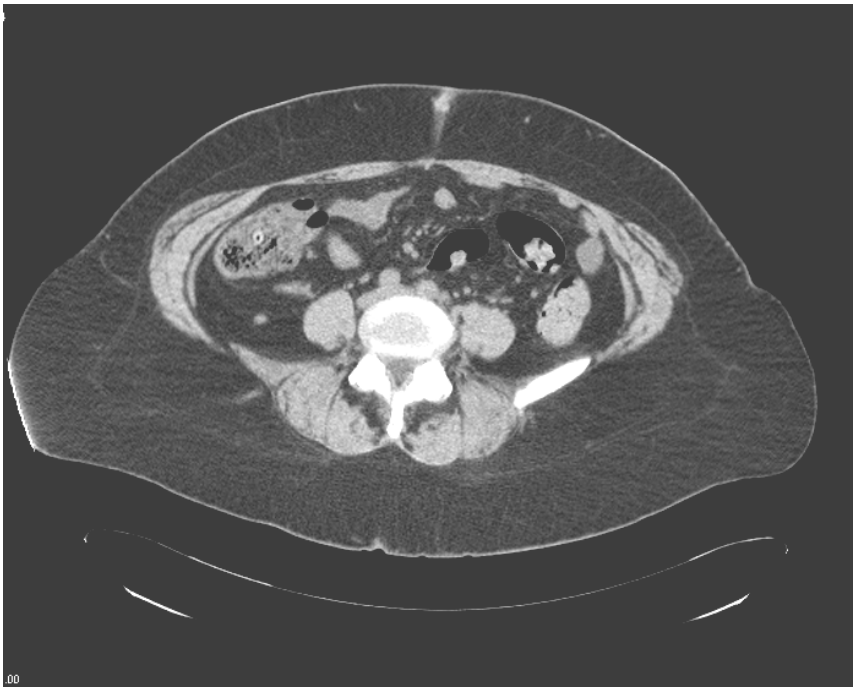


Patient # 025

Scan 1



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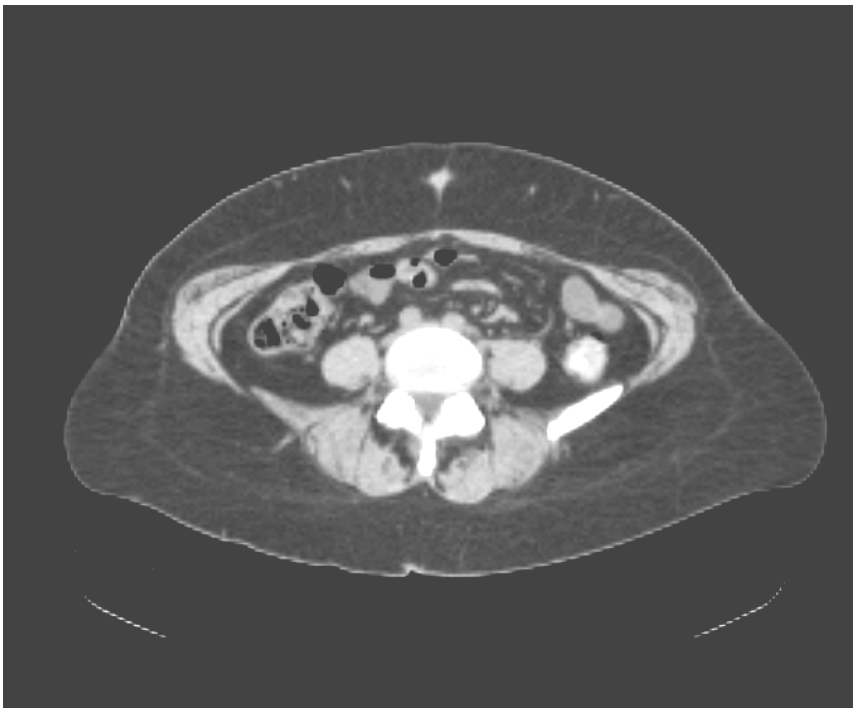
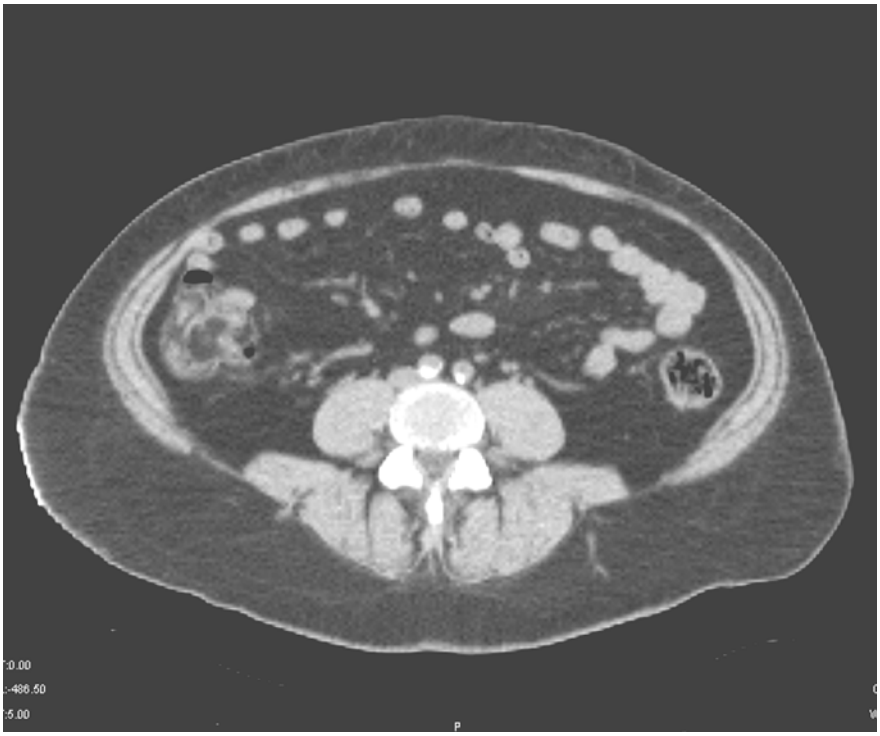
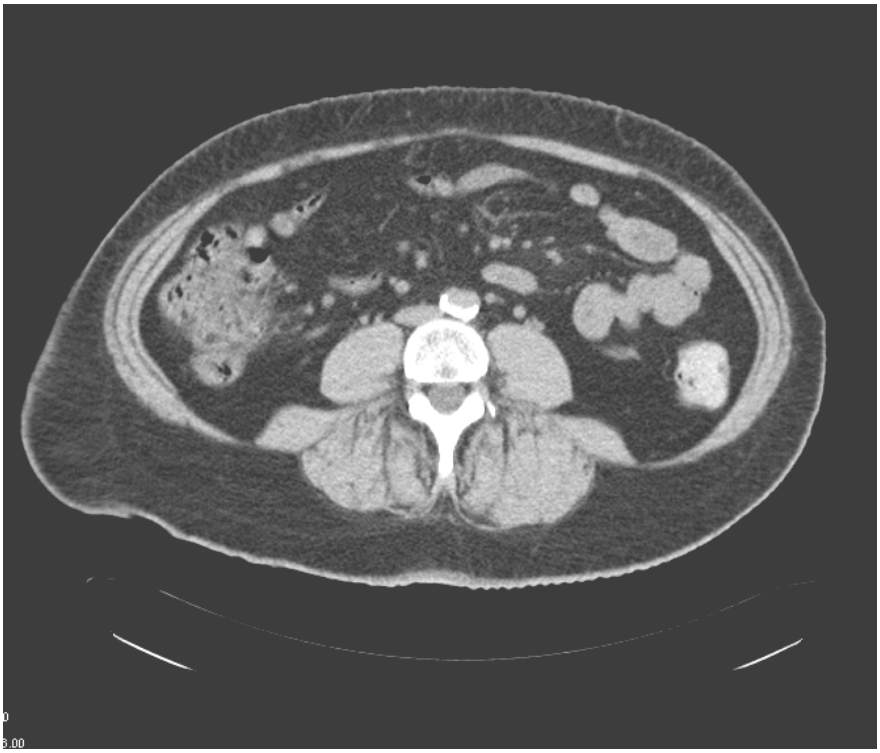


Patient # 030

Scan 1

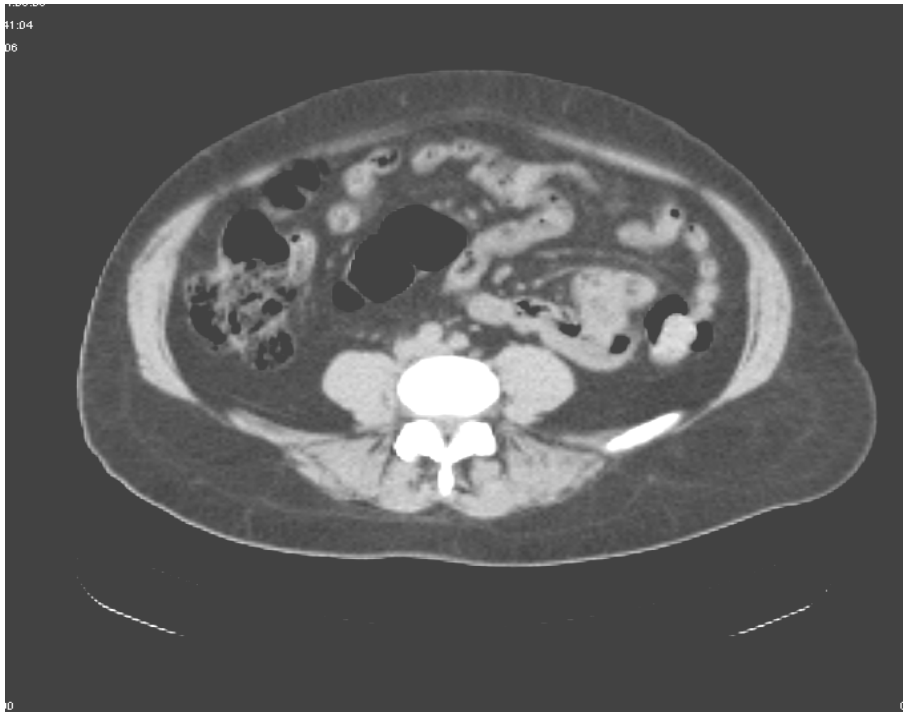


Scan 2

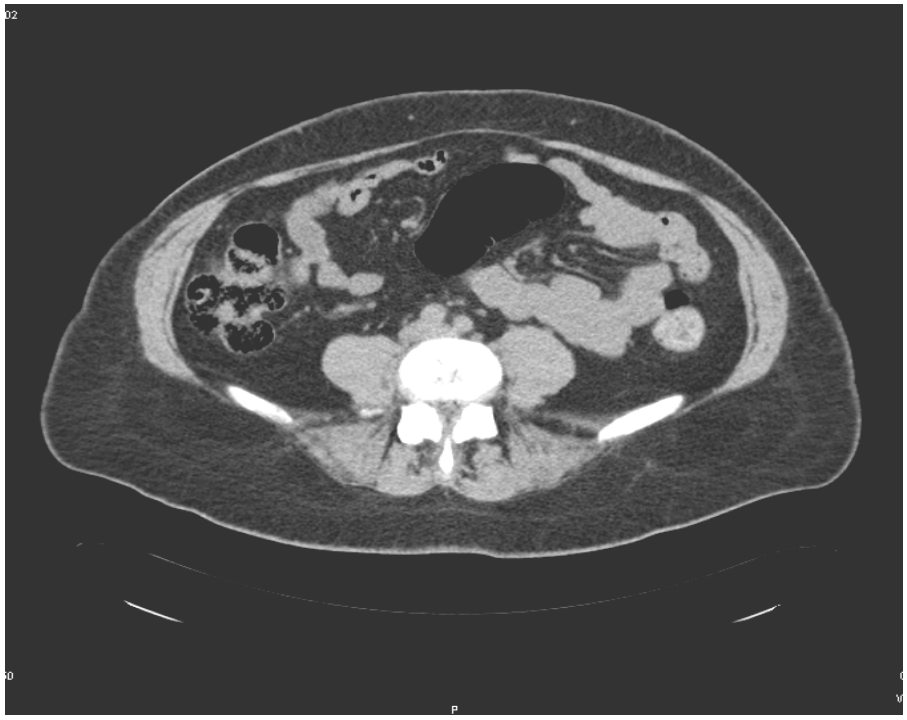


Patient # 31

Scan 1

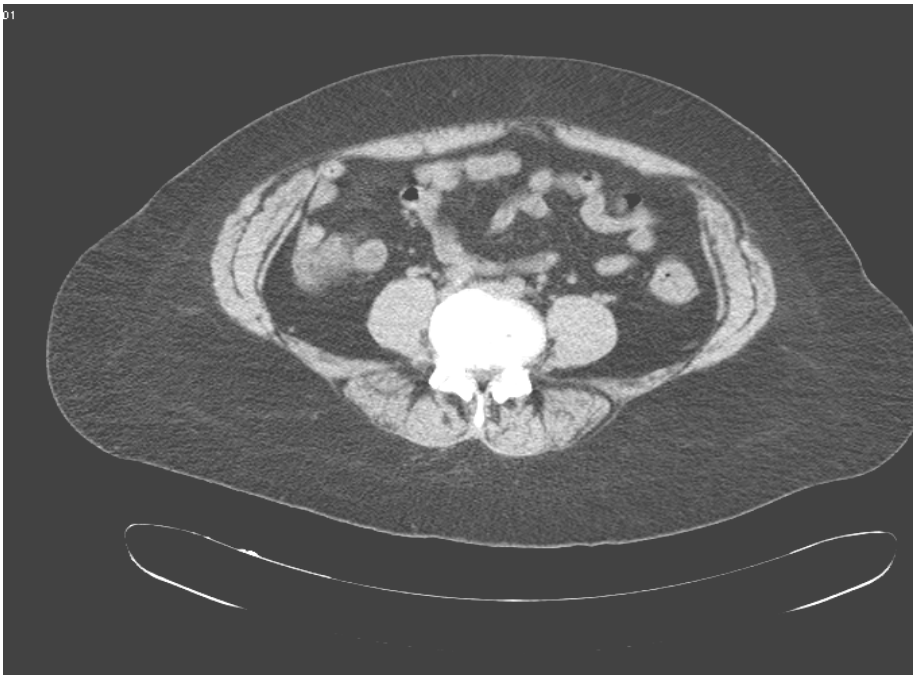


Scan 2

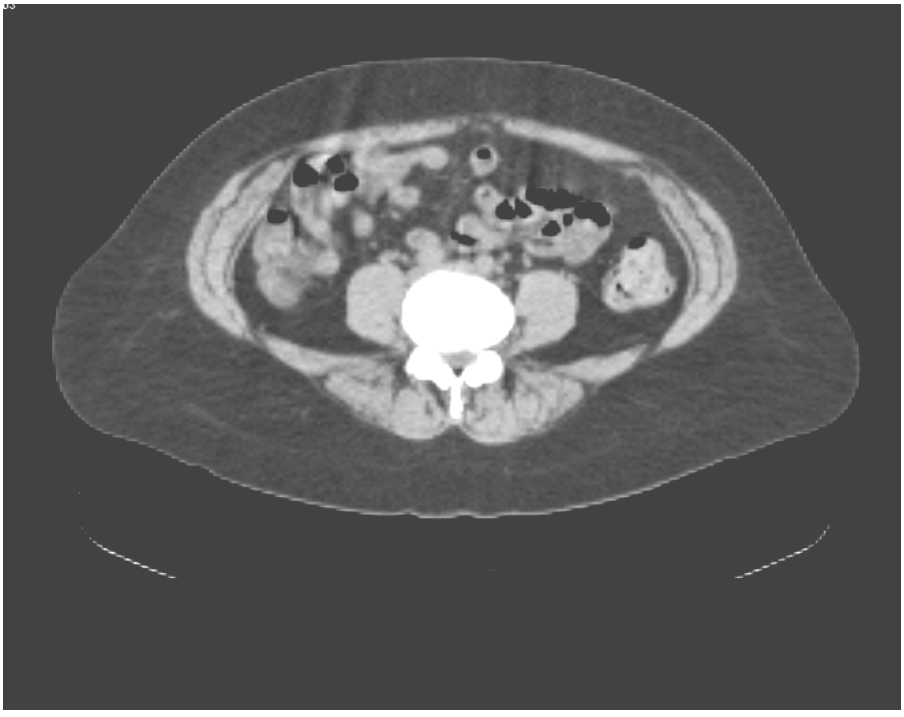


Patient # 036

Scan 1

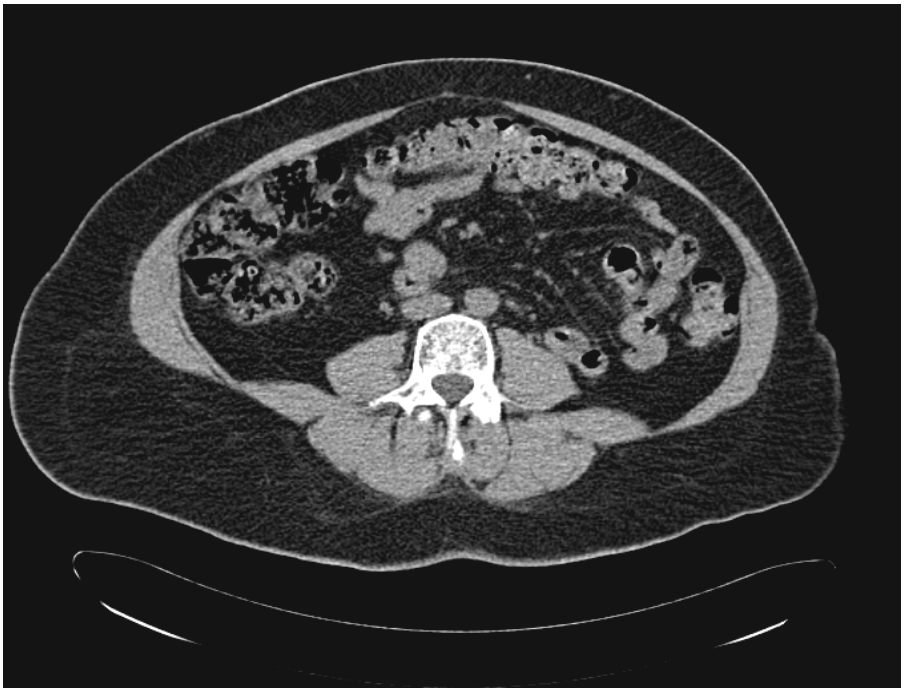


Scan 2

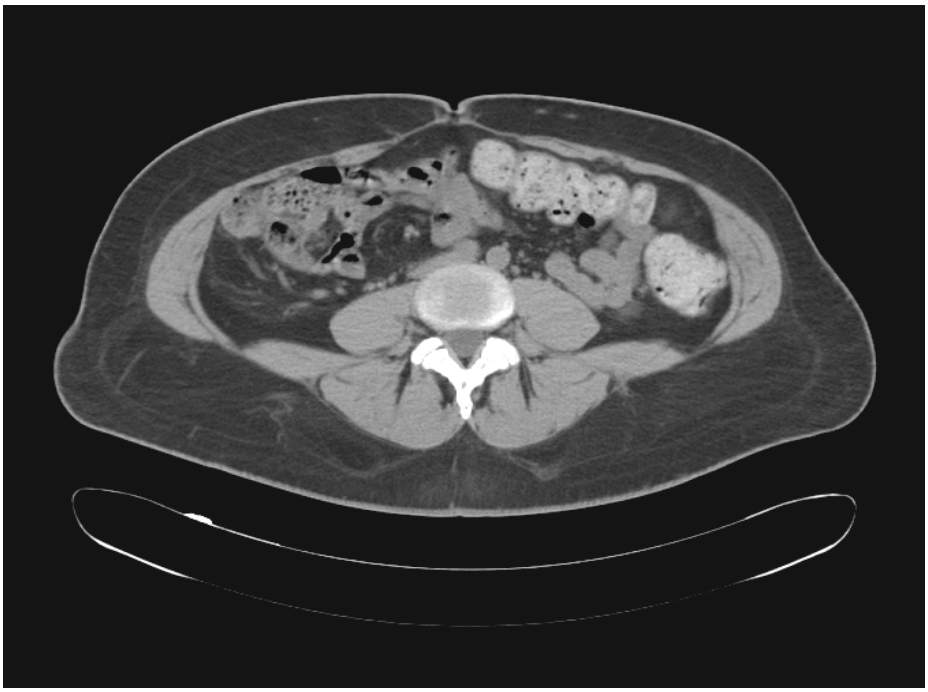


Patient # 038

Scan 1

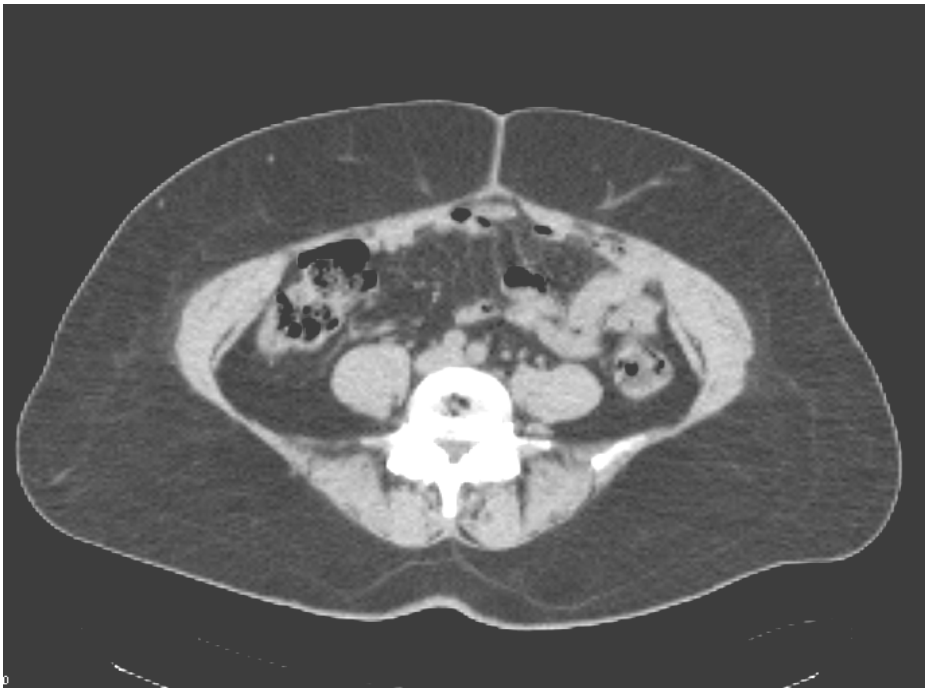


Scan 2

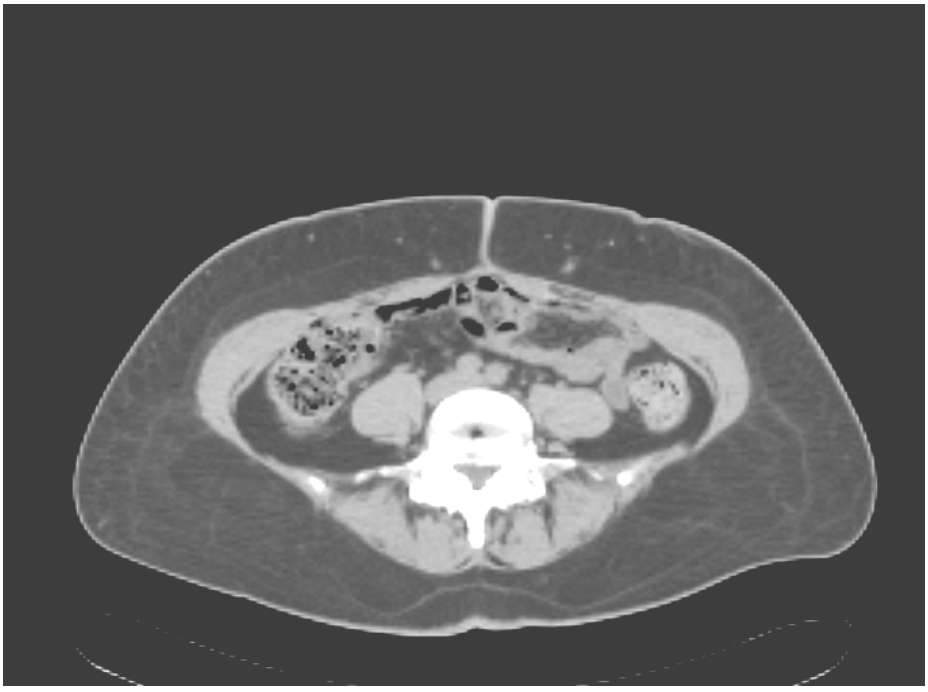


Patient # 039

Scan 1

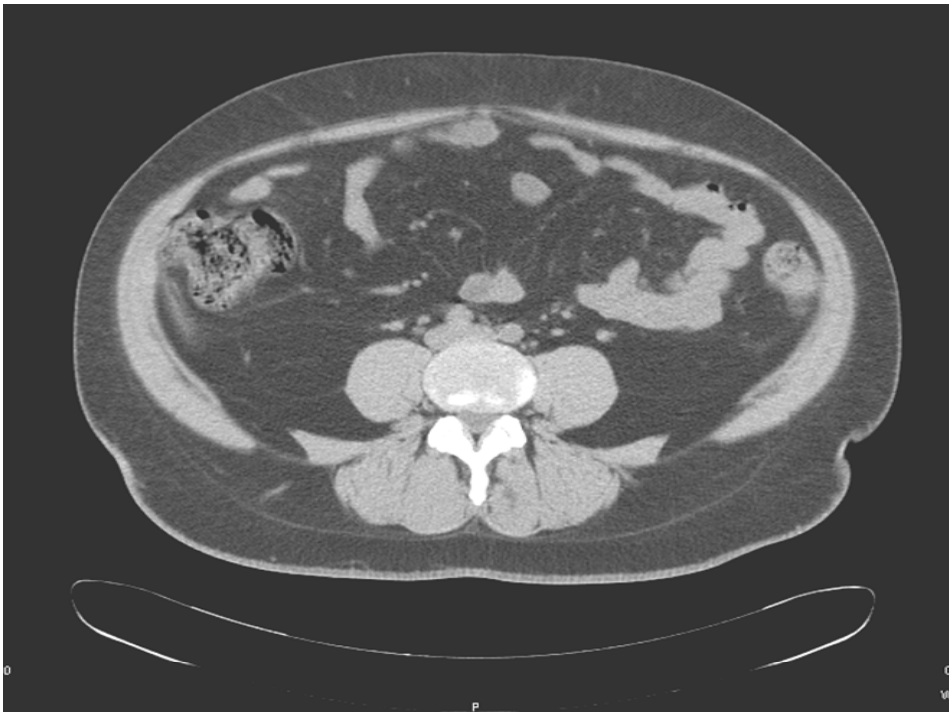


Scan 2

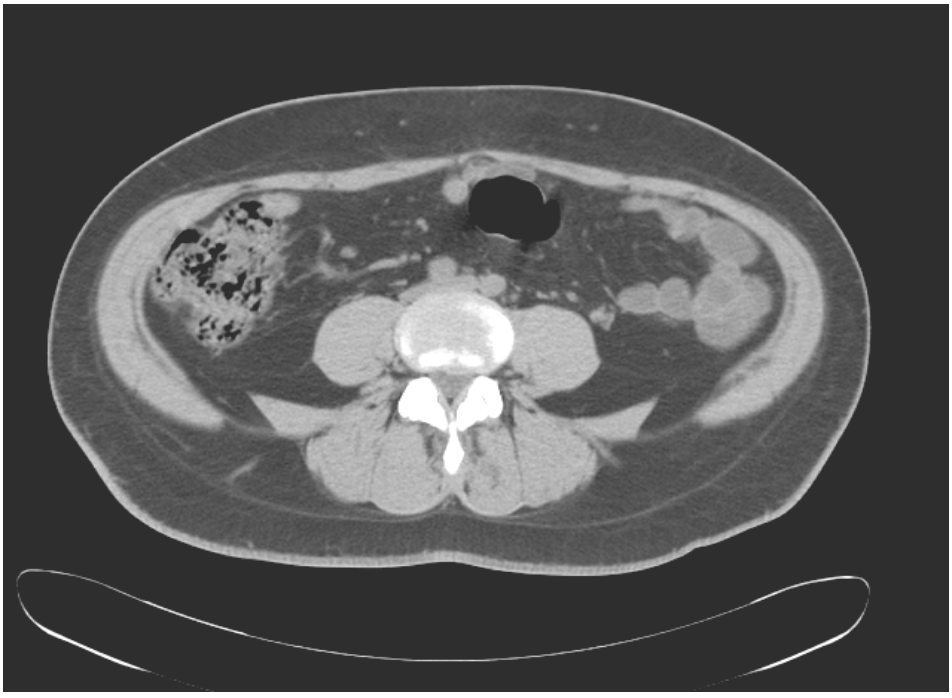


Patient # 041

Scan 1



Scan 2



APPENDIX D

Laboratory Data and Blood Pressure Tables

Insulin (μU/ml) and HOMA-IR.

026	9.8	6.6	6.8	-3.0	-30.6	4.9	5.0	5.6	0.7	14.3
028	17.1	11.7	27.6	10.5	61.4	4.9	4.5	5.4	0.5	10.2
029	27.8	12.5	6.9	-20.9	-75.2	5.7	5.2	5.5	-0.2	-3.5
032	15.7	13.2	8.6	-7.1	-45.2	5.5	5.5	5.7	0.2	3.6
033	9.1	13.8	8.6	-0.5	-5.5	6.0	5.6	6.1	0.1	1.7
037	7.2	7.9	3.9	-3.3	-45.8	5.5	5.5	5.4	-0.1	-1.8
040	34.7	11.3	8.6	-26.1	-75.2	5.6	5.9	5.4	-0.2	-3.6
Average	14.4	21.1	8.9	-5.5	-30.1	5.3	5.2	5.4	0.1	1.8
Count	11	11	11	11	11	11	11	11	11	11
SD	9.4	35.9	6.6	10.0	39.0	0.4	0.5	0.5	0.3	6.5
SE	2.8	10.8	2.0	3.0	11.8	0.1	0.2	0.1	0.1	1.9
95% LCI	8.8	-0.1	4.9	-11.4	-53.2	5.0	4.9	5.1	-0.1	-2.0
95% UCI	19.9	42.3	12.8	0.4	-7.0	5.6	5.5	5.7	0.3	5.6
Diabetic Subjects										
003	33.3	*22.8*	12.3	-21.0	-63.1	8.6	8.8	*8.0*	-0.6	-7.6
004	14.0	19.4	WD			5.5	7.6	WD		
007	27.8	26.2	20.5	-7.3	-26.3	11.5	11.4	7.3	-4.2	-36.5
008	*22.1*	22.1	18.6	-3.5	-15.8	6.0	5.8	6.4	0.4	6.7
009	11.5	9.9	7.5	-4.0	-34.8	6.8	7.5	6.3	-0.5	-7.4
010	14.9	13.9	WD			3.2	3.7	WD		
012	11.8	10.2	10.8	-1.0	-8.5	9.5	9.3	8.7	-0.8	-8.4
014	11.3	6.0	6.3	-5.0	-44.2	8.6	7.9	7.7	-0.9	-10.5
017	4.8	7.1	5.0	0.2	4.2	8.6	10.1	8.7	0.1	1.2
018	7.3	7.6	8.6	1.3	17.8	9.5	9.4	7.9	-1.6	-16.8
020	18.2	20.5	26.3	8.1	44.5	9.6	9.8	7.8	-1.8	-18.8
023	13.9	15.5	9.4	-4.5	-32.4	5.1	5.8	5.0	-0.1	-2.0
025	15.9	11.3	12.0	-3.9	-24.5	5.8	6.2	5.5	-0.3	-5.2
030	41.4	29.4	20.5	-20.9	-50.5	6.3	6.5	5.7	-0.6	-9.5
031	31.9	22.1	15.0	-16.9	-53.0	8.9	9.2	9.0	0.1	1.1
034	34.9	28.6	10.0	-24.9	-71.3	6.4	6.0	6.1	-0.3	-4.7
036	22.5	21.6	21.8	-0.7	-3.1	6.5	6.5	6.2	-0.3	-4.6
038	23.7	12.1	11.0	-12.7	-53.6	9.6	10.4	7.2	-2.4	-25.0
039	17.0	11.7	9.3	-7.7	-45.3	7.3	7.0	5.9	-1.4	-19.2
041	28.2	9.2	12.2	-16.0	-56.7	8.3	8.8	6.9	-1.4	-16.9
Average	20.3	16.4	13.2	-7.8	-28.7	7.6	7.9	7.0	-0.9	-10.2
Count	20	20	18	18	18	20	20	18	18	18
SD	10.0	7.4	6.0	9.0	30.6	2.0	2.0	1.2	1.1	10.5
SE	2.2	1.7	1.4	2.1	7.2	0.4	0.4	0.3	0.3	2.5
95% LCI	16.0	13.1	10.4	-12.0	-42.8	6.7	7.0	6.5	-1.4	-15.1
95% UCI	24.7	19.6	15.9	-3.6	-14.6	8.5	8.7	7.6	-0.4	-5.4

*Italized numbers are taken from baseline or are interpolated

*Baseline Insulin was never taken

Glucose (mg/dl) and HbA1c (%).

024	87	88	84	86	-2	-2.3	5.2	5.2	4.9	5	-0.2	-3.8
026	102	97	94	91	-6	-6.2	4.9	5	5.6	5.5	0.5	10.0
028	89	92	88	*90*	-2	-2.2	4.9	4.5	5.4	5.1	0.6	13.3
029	98	121	107	101	-20	-16.5	5.7	5.2	5.5	5.5	0.3	5.8
032	88	101	95	93	-8	-7.9	5.5	5.5	5.7	5.5	0	0.0
033	91	101	100	99	-2	-2.0	6	5.6	6.1	5.8	0.2	3.6
037	95	102	104	91	-11	-10.8	5.5	5.5	5.4	5.4	-0.1	-1.8
040	95	104	94	98	-6	-5.8	5.6	5.9	5.4	5.5	-0.4	-6.8
Average	90.5	98.8	96.5	92.9	-5.9	-5.5	5.3	5.2	5.4	5.3	0.1	2.9
Count	11	11	11	11	11	11	11	11	11	11	11	11.0
SD	6.9	10.0	6.9	5.3	6.3	5.7	0.4	0.5	0.5	0.4	0.4	8.1
SE	2.1	3.0	2.1	1.6	1.9	1.7	0.1	0.2	0.1	0.1	0.1	2.5
95% LCI	86.4	92.9	92.4	89.8	-9.6	-8.9	5.0	4.9	5.1	5.1	-0.1	-1.9
95% UCI	94.7	104.7	100.5	96.0	-2.2	-2.2	5.6	5.5	5.7	5.5	0.4	7.7

Diabetic Subjects

003	194	186	194	150	-36	-19.4	8.6	8.8	*8.0*	7.1	-1.7	-19.3
004	158	159	123	WD			6.9	6.8	6.6	WD		
007	278	251	129	*129*	-122	-48.6	11.5	11.4	7.3	6.3	-5.1	-44.7
008	106	118	144	127	9	7.6	6	5.8	6.4	5.8	0	0.0
009	148	148	123	120	-28	-18.9	6.8	7.5	6.3	6.3	-1.2	-16.0
010	86	104	112	WD			5.9	5.8	5	WD		
012	192	228	209	221	-7	-3.1	9.5	9.3	8.7	9.1	-0.2	-2.2
014	129	118	125	117	-1	-0.8	8.6	7.9	7.7	6.9	-1	-12.7
015	116	229	203	WD			7.8	7.8	7.8	WD		
017	239	213	215	171	-42	-19.7	8.6	10.1	8.7	8.3	-1.8	-17.8
018	270	257	177	141	-116	-45.1	9.5	9.4	7.9	5.9	-3.5	-37.2
020	256	253	176	199	-54	-21.3	9.6	9.8	7.8	6.5	-3.3	-33.7
023	92	106	96	93	-13	-12.3	5.1	5.8	5	5.6	-0.2	-3.4
025	107	103	101	104	1	1.0	5.8	6.2	5.5	5.5	-0.7	-11.3
030	113	113	118	108	-5	-4.4	6.3	6.5	5.7	5.9	-0.6	-9.2
031	299	254	260	173	-81	-31.9	8.9	9.2	9	8.2	-1	-10.9
034	126	137	134	111	-26	-19.0	6.4	6	6.1	5.8	-0.2	-3.3
036	134	155	128	131	-24	-15.5	6.5	6.5	6.2	6.2	-0.3	-4.6
038	207	299	142	129	-170	-56.9	9.6	10.4	7.2	6.1	-4.3	-41.3
039	145	156	103	95	-61	-39.1	7.3	7	5.9	5.8	-1.2	-17.1
041	154	274	113	139	-135	-49.3	8.3	8.8	6.9	6.4	-2.4	-27.3
Average	169.0	183.9	148.8	136.6	-50.6	-22.0	7.8	7.9	6.9	6.5	-1.6	-17.3
Count	21	21	21	18	18	18	21	21	21	18	18	18.0
SD	65.8	64.9	45.1	35.0	53.1	19.2	1.7	1.7	1.2	1.0	1.5	14.0
SE	14.4	14.2	9.8	8.2	12.5	4.5	0.4	0.4	0.3	0.2	0.4	3.3
95% LCI	140.8	156.1	129.5	120.4	-75.2	-30.9	7.1	7.2	6.4	6.1	-2.3	-23.8
95% UCI	197.2	211.6	168.1	152.7	-26.1	-13.2	8.5	8.7	7.5	7.0	-0.9	-10.9

*Italized numbers are taken from baseline or are interpolated

Leptin (pg/ml).

Non-Diabetic Subjects

Pt #	Wk0	Wk8	Chg	%Chg	Wk16	Chg	%Chg
001	76857.0	35942.0	-40915.0	-53.2	31043.0	-45814.0	-59.6
005	24193.0	11439.0	-12754.0	-52.7	11829.0	-12364.0	-51.1
013	70440.0	42643.0	-27797.0	-39.5	28810.0	-41630.0	-59.1
024	21333.0	4854.9	-16478.1	-77.2	3600.4	-17732.6	-83.1
026	61113.0	14550.0	-46563.0	-76.2	7948.0	-53165.0	-87.0
028	70044.0	38438.0	-31606.0	-45.1	20491.0	-49553.0	-70.7
029	83162.0	27309.0	-55853.0	-67.2	20336.0	-62826.0	-75.5
032	44642.0	40347.0	-4295.0	-9.6	36394.0	-8248.0	-18.5
033	97736.0	43021.0	-54715.0	-56.0	28139.0	-69597.0	-71.2
037	79602.0	28989.0	-50613.0	-63.6	15360.0	-64242.0	-80.7
040	75309.0	25931.0	-49378.0	-65.6	15652.0	-59657.0	-79.2
Average	64039.2	28496.7	-35542.5	-55.1	19963.9	-44075.3	-66.9
Count	11	11	11	11	11	11	11
SD	24306.5	13260.5	18120.8	19.2	10277.7	21811.0	19.6
SE	7328.7	3998.2	5463.6	5.8	3098.8	6576.3	5.9
95% LCI	49675.0	20660.3	-46251.1	-66.4	13890.1	-56964.8	-78.5
95% UCI	78403.4	36333.2	-24833.8	-43.7	26037.6	-31185.8	-55.3

Diabetic Subjects

003	99158.0	59641.0	-39517.0	-39.9	65975.0	-33183.0	-33.5
007	77182.0	28778.0	-48404.0	-62.7	21360.0	-55822.0	-72.3
008	65464.0	66748.0	1284.0	2.0	49138.0	-16326.0	-24.9
009	43165.0	31262.0	-11903.0	-27.6	27345.0	-15820.0	-36.7
012	37725.0	32710.0	-5015.0	-13.3	30725.0	-7000.0	-18.6
014	49215.0	21045.0	-28170.0	-57.2	18771.0	-30444.0	-61.9
017	19062.0	11843.0	-7219.0	-37.9	9753.2	-9308.8	-48.8
018	22560.0	8340.3	-14219.7	-63.0	4971.7	-17588.3	-78.0
020	34362.0	31749.0	-2613.0	-7.6	35767.0	1405.0	4.1
023	80411.0	44664.0	-35747.0	-44.5	39618.0	-40793.0	-50.7
025	47855.0	16929.0	-30926.0	-64.6	20158.0	-27697.0	-57.9
030	49427.0	25866.0	-23561.0	-47.7	25230.0	-24197.0	-49.0
031	62561.0	45601.0	-16960.0	-27.1	57793.0	-4768.0	-7.6
034	65451.0	31922.0	-33529.0	-51.2	21178.0	-44273.0	-67.6
036	50571.0	36567.0	-14004.0	-27.7	37836.0	-12735.0	-25.2
038	30331.0	16147.0	-14184.0	-46.8	11388.0	-18943.0	-62.5
039	39519.0	18614.0	-20905.0	-52.9	9089.0	-30430.0	-77.0
041	34216.0	12488.0	-21728.0	-63.5	12922.0	-21294.0	-62.2
Average	50457.5	30050.8	-20406.7	-40.7	27723.2	-22734.3	-46.1
Count	18	18	18	18	18	18	18
SD	21165.8	16166.2	13589.7	20.2	17225.5	14761.9	24.2
SE	4988.8	3810.4	3203.1	4.8	4060.1	3479.4	5.7
95% LCI	40679.4	22582.4	-26684.8	-50.0	19765.4	-29553.9	-57.3
95% UCI	60235.6	37519.2	-14128.6	-31.4	35681.0	-15914.6	-34.9

Ghrelin (pg/ml).

Non-Diabetic Subjects

Pt #	Wk0	Wk8	Chg	%Chg	Wk16	Chg	%Chg
001	1089.0	814.0	-275.0	-25.3	855.0	-234.0	-21.5
005	1159.0	1136.0	-23.0	-2.0	1057.0	-102.0	-8.8
013	614.0	487.0	-127.0	-20.7	1363.0	749.0	122.0
024	1411.0	1709.0	298.0	21.1	1773.0	362.0	25.7
026	783.0	788.0	5.0	0.6	701.0	-82.0	-10.5
028	766.0	883.0	117.0	15.3	942.0	176.0	23.0
029	605.0	474.0	-131.0	-21.7	531.0	-74.0	-12.2
032	590.0	521.0	-69.0	-11.7	515.0	-75.0	-12.7
033	778.0	814.0	36.0	4.6	954.0	176.0	22.6
037	1016.0	1456.0	440.0	43.3	1900.0	884.0	87.0
040	405.0	475.0	70.0	17.3	537.0	132.0	32.6
Average	837.8	868.8	31.0	1.9	1011.6	173.8	22.5
Count	11.0	11.0	11.0	11.0	11.0	11.0	11.0
SD	298.6	413.8	201.5	21.2	482.3	361.0	45.4
SE	90.0	124.8	60.7	6.4	145.4	108.9	13.7
95% LCI	661.4	624.3	-88.1	-10.6	726.6	-39.5	-4.4
95% UCI	1014.3	1113.4	150.1	14.5	1296.7	387.2	49.3

Diabetic Subjects

003	1196.0	986.0	-210.0	-17.6	1041.0	-155.0	-13.0
007	418.0	641.0	223.0	53.3	564.0	146.0	34.9
008	864.0	786.0	-78.0	-9.0	1253.0	389.0	45.0
009	1226.0	1758.0	532.0	43.4	1698.0	472.0	38.5
012	449.0	567.0	118.0	26.3	497.0	48.0	10.7
014	546.0	777.0	231.0	42.3	724.0	178.0	32.6
017	792.0	1423.0	631.0	79.7	1158.0	366.0	46.2
018	771.0	943.0	172.0	22.3	1148.0	377.0	48.9
020	511.0	578.0	67.0	13.1	537.0	26.0	5.1
023	587.0	631.0	44.0	7.5	650.0	63.0	10.7
025	455.0	598.0	143.0	31.4	618.0	163.0	35.8
030	554.0	586.0	32.0	5.8	647.0	93.0	16.8
031	656.0	739.0	83.0	12.7	707.0	51.0	7.8
034	582.0	766.0	184.0	31.6	881.0	299.0	51.4
036	535.0	656.0	121.0	22.6	471.0	-64.0	-12.0
038	541.0	666.0	125.0	23.1	858.0	317.0	58.6
039	437.0	517.0	80.0	18.3	619.0	182.0	41.6
041	465.0	545.0	80.0	17.2	510.0	45.0	9.7
Average	643.6	786.8	143.2	23.6	810.1	166.4	26.1
Count	18.0	18.0	18.0	18.0	18.0	18.0	18.0
SD	241.9	324.6	191.0	22.4	331.0	171.9	21.9
SE	57.0	76.5	45.0	5.3	78.0	40.5	5.2
95% LCI	531.9	636.9	55.0	13.2	657.2	87.0	16.0
95% UCI	755.4	936.8	231.5	33.9	963.0	245.9	36.2

Adiponectin (ng/ml).

Non-Diabetic Subjects

Pt #	WK0	WK8	Chg	%Chg	WK16	Chg	%Chg
001	9480.4	9196.3	-284.1	-3.0	11637.0	2156.6	22.7
005	12229.0	10637.0	-1592.0	-13.0	12708.0	479.0	3.9
013	7701.8	6987.2	-714.6	-9.3	5586.5	-2115.3	-27.5
024	25779.0	23125.0	-2654.0	-10.3	26121.0	342.0	1.3
026	18372.0	11072.0	-7300.0	-39.7	13382.0	-4990.0	-27.2
028	5245.0	5345.6	100.6	1.9	5060.7	-184.3	-3.5
029	8831.0	9290.2	459.2	5.2	11969.0	3138.0	35.5
032	6340.7	6323.9	-16.8	-0.3	5843.1	-497.6	-7.8
033	12793.0	11745.0	-1048.0	-8.2	11190.0	-1603.0	-12.5
037	14818.0	11324.0	-3494.0	-23.6	9643.1	-5174.9	-34.9
040	5261.8	4384.8	-877.0	-16.7	5038.3	-223.5	-4.2
Average	11532.0	9948.3	-1583.7	-10.6	10743.5	-788.5	-4.9
count	11	11	11	11	11	11	11
SD	6281.7	5054.9	2239.8	12.8	6053.5	2589.6	21.2
SE	1894.0	1524.1	675.3	3.9	1825.2	780.8	6.4
95% LCI	7819.7	6961.0	-2907.3	-18.2	7166.1	-2318.8	-17.4
95% UCI	15244.2	12935.5	-260.1	-3.1	14320.9	741.9	7.6

Diabetic Subjects

003	7805.6	8977.0	1171.4	15.0	8315.9	510.3	6.5
007	7833.7	6868.3	-965.4	-12.3	6963.8	-869.9	-11.1
008	13429.0	13640.0	211.0	1.6	17796.0	4367.0	32.5
009	7147.8	8007.1	859.3	12.0	9263.5	2115.7	29.6
012	5300.9	5477.5	176.6	3.3	6245.8	944.9	17.8
014	7758.7	7002.7	-756.0	-9.7	8276.0	517.3	6.7
017	6930.1	6188.7	-741.4	-10.7	6665.8	-264.3	-3.8
018	8100.3	8089.9	-10.4	-0.1	14381.0	6280.7	77.5
020	3730.7	5056.9	1326.2	35.5	4932.9	1202.2	32.2
023	10988.0	9312.6	-1675.4	-15.2	10590.0	-398.0	-3.6
025	6924.8	5695.5	-1229.3	-17.8	6525.8	-399.0	-5.8
030	3614.6	3424.9	-189.7	-5.2	4016.4	401.8	11.1
031	7425.9	7397.9	-28.0	-0.4	7733.7	307.8	4.1
034	6944.8	6978.3	33.5	0.5	7453.9	509.1	7.3
036	5312.1	5759.2	447.1	8.4	5854.3	542.2	10.2
038	3640.2	3368.7	-271.5	-7.5	4464.9	824.7	22.7
039	5862.1	4515.7	-1346.4	-23.0	6688.5	826.4	14.1
041	1876.1	2285.7	409.6	21.8	2399.3	523.2	27.9
Average	6701.4	6558.1	-143.3	-0.2	7698.2	996.8	15.3
count	18	18	18	18	18	18	18
SD	2719.2	2618.6	848.5	14.8	3657.9	1741.6	20.5
SE	640.9	617.2	200.0	3.5	862.2	410.5	4.8
95% LCI	5445.2	5348.4	-535.3	-7.0	6008.4	192.2	5.9
95% UCI	7957.6	7767.9	248.7	6.6	9388.0	1801.4	24.8

Resistin (ng/ml).

Non-Diabetic Subjects

Pt #	WK0	WK8	Chg	%Chg	WK16	Chg	%Chg
001	4.1	3.9	-0.2	-5.1	3.6	-0.5	-11.9
005	5.4	5.6	0.2	4.3	6.6	1.3	23.3
013	5.3	4.6	-0.6	-12.0	5.9	0.6	12.1
024	3.4	3.4	0.0	0.0	3.1	-0.3	-7.4
026	3.0	2.9	-0.1	-3.3	2.7	-0.3	-10.0
028	3.7	3.1	-0.6	-16.2	2.9	-0.8	-21.6
029	5.0	4.4	-0.6	-12.0	5.3	0.3	6.0
032	5.2	5.3	0.1	1.9	5.2	0.0	0.0
033	5.1	5.5	0.4	7.8	4.9	-0.2	-3.9
037	3.9	2.7	-1.2	-30.8	3.2	-0.7	-17.9
040	6.1	7.0	0.9	14.8	7.9	1.8	29.5
Average	4.6	4.4	-0.2	-4.6	4.7	0.1	-0.2
Count	11	11	11	11	11	11	11
SD	1.0	1.4	0.6	12.7	1.7	0.8	16.4
SE	0.3	0.4	0.2	3.8	0.5	0.2	5.0
95% LCI	4.0	3.6	-0.5	-12.1	3.7	-0.4	-9.9
95% UCI	5.1	5.2	0.2	2.9	5.7	0.6	9.5
Diabetic Subjects							
003	5.1	5.3	0.2	3.9	4.7	-0.4	-7.8
007	3.5	3.9	0.4	11.4	4.2	0.7	20.0
008	3.5	4.0	0.5	13.1	3.6	0.0	1.4
009	3.8	3.8	0.1	1.6	4.6	0.8	22.4
012	3.8	3.5	-0.3	-7.9	3.4	-0.4	-10.6
014	8.9	6.7	-2.2	-24.7	11.6	2.7	30.0
017	9.2	9.1	-0.1	-1.4	6.8	-2.4	-26.0
018	5.6	8.8	3.3	58.4	5.9	0.3	5.2
020	3.5	2.8	-0.7	-20.0	2.4	-1.1	-31.4
023	10.2	9.0	-1.2	-11.8	9.8	-0.4	-3.9
025	7.0	8.5	1.5	20.7	7.2	0.1	2.0
030	5.1	5.1	0.0	0.0	5.5	0.4	7.8
031	7.1	4.1	-3.0	-42.3	4.6	-2.5	-35.2
034	6.3	5.0	-1.3	-20.6	6.6	0.3	4.8
036	5.4	5.0	-0.4	-7.4	7.7	2.3	42.6
038	4.3	4.7	0.4	9.3	5.3	1.0	23.3
039	5.9	10.4	4.5	76.3	8.5	2.6	44.1
041	3.5	4.6	1.1	31.4	6.7	3.2	91.4
Average	5.6	5.8	0.1	5.0	6.1	0.4	10.0
count	18	18	18	18	18	18	18
SD	2.1	2.3	1.8	28.8	2.3	1.6	30.6
SE	0.5	0.5	0.4	6.8	0.6	0.4	7.2
95% LCI	4.7	4.7	-0.7	-8.3	5.0	-0.3	-4.1
95% UCI	6.6	6.9	1.0	18.3	7.1	1.1	24.1

IL-6 (pg/ml).

Non-Diabetic Subjects

Pt #	Wk0	Wk8	Chg	%Chg	Wk16	Chg	%Chg
001	6.5	3.0	-3.5	-53.8	2.0	-4.5	-69.2
005	11.0	12.6	1.6	14.5	2.3	-8.7	-79.1
013	7.6	3.5	-4.1	-53.9	5.9	-1.7	-22.4
024	1.2	0.8	-0.4	-33.3	1.2	0.0	0.0
026	0.9	1.6	0.7	86.0	1.1	0.3	30.2
028	2.1	1.3	-0.8	-36.5	1.1	-1.0	-48.8
029	5.2	5.2	-0.1	-1.2	3.4	-1.8	-35.1
032	2.4	3.5	1.1	46.0	5.6	3.3	137.6
033	3.0	2.4	-0.6	-19.5	2.0	-1.0	-31.9
037	1.1	1.2	0.1	9.9	0.9	-0.2	-20.7
040	2.9	2.5	-0.4	-15.2	7.1	4.2	143.1
Average	4.0	3.4	-0.6	-5.2	3.0	-1.0	0.3
Count	11	11	11	11	11	11	11
SD	3.2	3.3	1.8	42.9	2.2	3.5	75.4
SE	1.0	1.0	0.5	12.9	0.7	1.0	22.7
95% LCI	2.1	1.5	-1.6	-30.5	1.6	-3.1	-44.3
95% UCI	5.9	5.4	0.5	20.2	4.3	1.0	44.9

Diabetic Subjects

003	2.5	1.7	-0.8	-32.8	2.4	-0.1	-3.6
007	2.4	1.6	-0.8	-34.3	2.0	-0.4	-16.3
008	0.5	0.9	0.4	80.0	0.6	0.1	20.0
009	2.1	1.4	-0.7	-33.3	1.4	-0.7	-33.3
012	5.3	3.0	-2.3	-43.4	2.6	-2.7	-50.9
014	3.8	6.1	2.3	60.5	4.5	0.7	18.4
017	3.2	1.2	-2.0	-62.5	1.1	-2.1	-65.6
018	2.0	1.9	-0.1	-5.0	2.1	0.1	5.0
020	2.5	3.0	0.5	20.2	0.7	-1.8	-72.3
023	1.7	1.8	0.1	4.1	1.5	-0.2	-12.9
025	2.5	3.6	1.1	44.0	2.8	0.3	12.0
030	0.8	2.4	1.6	194.0	0.8	-0.1	-9.6
031	1.7	1.7	0.0	1.8	1.9	0.2	12.4
034	2.8	3.1	0.3	10.9	2.3	-0.5	-16.7
036	1.7	3.9	2.2	131.0	4.1	2.4	144.0
038	1.8	1.5	-0.3	-16.2	1.5	-0.3	-16.2
039	1.2	1.2	-0.1	-5.7	1.4	0.1	11.5
041	2.1	1.5	-0.6	-26.3	2.0	-0.1	-6.2
Average	2.3	2.3	0.0	15.9	2.0	-0.3	-4.5
Count	18	18	18	18	18	18	18
SD	1.1	1.3	1.2	65.5	1.1	1.1	46.0
SE	0.3	0.3	0.3	15.4	0.3	0.3	10.8
95% LCI	1.7	1.7	-0.5	-14.3	1.5	-0.8	-25.7
95% UCI	2.8	2.9	0.6	46.2	2.5	0.2	16.8

TNF-α (pg/ml).

Non-Diabetic Subjects

Pt #	Wk0	Wk8	Chg	%Chg	Wk16	Chg	%Chg
001	1.0	1.0	0.0	0.0	0.8	-0.2	-20.0
005	0.6	0.6	0.0	0.0	0.5	-0.1	-16.7
013	1.1	0.9	-0.2	-18.2	3.2	2.1	190.9
024	1.0	0.9	-0.1	-10.0	0.9	-0.1	-10.0
026	1.6	1.8	0.2	12.5	1.8	0.2	12.5
028	1.0	1.4	0.4	40.0	1.2	0.2	20.0
029	0.8	0.8	0.0	0.0	1.1	0.3	37.5
032	1.7	2.5	0.8	47.1	2.4	0.7	41.2
033	2.1	2.2	0.1	4.8	2.1	0.0	0.0
037	1.6	1.8	0.2	12.5	1.5	-0.1	-6.3
040	1.1	1.3	0.2	18.2	1.4	0.3	27.3
Average	1.2	1.4	0.1	9.7	1.5	0.3	25.1
Count	11	11	11	11	11	11	11
SD	0.5	0.6	0.3	19.7	0.8	0.7	58.9
SE	0.1	0.2	0.1	5.9	0.2	0.2	17.8
95% LCI	1.0	1.0	0.0	-1.9	1.1	-0.1	-9.7
95% UCI	1.5	1.7	0.3	21.3	2.0	0.7	60.0

Diabetic Subjects

003	2.7	1.6	-1.1	-40.7	1.6	-1.1	-40.7
007	0.8	2.2	1.4	175.0	2.5	1.7	212.5
008	0.7	0.8	0.1	14.3	0.7	0.0	0.0
009	0.9	0.8	-0.1	-11.1	0.8	-0.1	-11.1
012	1.1	1.2	0.1	9.1	1.1	0.0	0.0
014	1.0	1.1	0.1	10.0	1.1	0.1	10.0
017	1.0	1.2	0.2	20.0	0.8	-0.2	-20.0
018	1.2	2.9	1.7	141.7	1.2	0.0	0.0
020	0.9	1.0	0.1	11.1	0.9	0.0	0.0
023	1.5	1.3	-0.2	-13.3	1.3	-0.2	-13.3
025	1.2	1.3	0.1	8.3	0.9	-0.3	-25.0
030	1.7	1.7	0.0	0.0	1.5	-0.2	-11.8
031	1.4	1.6	0.2	14.3	1.4	0.0	0.0
034	2.1	1.4	-0.7	-33.3	1.8	-0.3	-14.3
036	1.3	1.5	0.2	15.4	1.2	-0.1	-7.7
038	1.5	1.2	-0.3	-20.0	3.0	1.5	100.0
039	1.7	1.7	0.0	0.0	1.4	-0.3	-17.6
041	1.4	1.7	0.3	21.4	1.7	0.3	21.4
Average	1.3	1.5	0.1	17.9	1.4	0.0	10.1
Count	18	18	18	18	18	18	18
SD	0.5	0.5	0.6	54.4	0.6	0.6	58.2
SE	0.1	0.1	0.1	12.8	0.1	0.1	13.7
95% LCI	1.1	1.2	-0.2	-7.2	1.1	-0.2	-16.8
95% UCI	1.6	1.7	0.4	43.0	1.7	0.3	37.0

PAI-1 (pg/ml).

Non-Diabetic Subjects

Pt #	WK0	WK8	Chg	%Chg	WK16	Chg	%Chg
001	21192.0	7827.0	-13365.0	-63.1	7661.0	-13531.0	-63.8
005	16080.0	8098.0	-7982.0	-49.6	9977.0	-6103.0	-38.0
013	10022.0	7425.0	-2597.0	-25.9	5972.0	-4050.0	-40.4
024	3218.0	2937.0	-281.0	-8.7	5895.0	2677.0	83.2
026	3719.0	4118.0	399.0	10.7	3022.0	-697.0	-18.7
028	10336.0	5944.0	-4392.0	-42.5	4832.0	-5504.0	-53.3
029	12603.0	6030.0	-6573.0	-52.2	4602.0	-8001.0	-63.5
032	10626.0	6573.0	-4053.0	-38.1	5849.0	-4777.0	-45.0
033	7729.0	7712.0	-17.0	-0.2	5918.0	-1811.0	-23.4
037	5669.0	9759.0	4090.0	72.1	4220.0	-1449.0	-25.6
040	5472.0	4790.0	-682.0	-12.5	5507.0	35.0	0.6
Average	9696.9	6473.9	-3223.0	-19.1	5768.6	-3928.3	-26.2
Count	11.0	11.0	11.0	11.0	11.0	11.0	11.0
SD	5462.3	1976.9	4808.0	38.3	1833.8	4440.2	41.2
SE	1646.9	596.1	1449.7	11.5	552.9	1338.8	12.4
95% LCI	6468.9	5305.6	-6064.3	-41.7	4685.0	-6552.3	-50.5
95% UCI	12924.9	7642.2	-381.7	3.5	6852.3	-1304.3	-1.8

Diabetic Subjects

003	27176.0	9939.0	-17237.0	-63.4	7348.0	-19828.0	-73.0
007	13191.0	7025.0	-6166.0	-46.7	6703.0	-6488.0	-49.2
008	8644.0	15782.0	7138.0	82.6	8785.0	141.0	1.6
009	13658.0	8239.0	-5419.0	-39.7	5878.0	-7780.0	-57.0
012	14005.0	10869.0	-3136.0	-22.4	13471.0	-534.0	-3.8
014	11542.0	10878.0	-664.0	-5.8	10481.0	-1061.0	-9.2
017	10914.0	5415.0	-5499.0	-50.4	5047.0	-5867.0	-53.8
018	14837.0	3073.0	-11764.0	-79.3	2527.0	-12310.0	-83.0
020	8496.0	8552.0	56.0	0.7	5864.0	-2632.0	-31.0
023	3939.0	6090.0	2151.0	54.6	8733.0	4794.0	121.7
025	8776.0	9780.0	1004.0	11.4	7521.0	-1255.0	-14.3
030	12986.0	18662.0	5676.0	43.7	9615.0	-3371.0	-26.0
031	14014.0	13739.0	-275.0	-2.0	8212.0	-5802.0	-41.4
034	9419.0	9984.0	565.0	6.0	7363.0	-2056.0	-21.8
036	10011.0	11778.0	1767.0	17.7	8716.0	-1295.0	-12.9
038	18391.0	12643.0	-5748.0	-31.3	7154.0	-11237.0	-61.1
039	7812.0	5080.0	-2732.0	-35.0	8102.0	290.0	3.7
041	12138.0	6575.0	-5563.0	-45.8	6410.0	-5728.0	-47.2
Average	12219.4	9672.4	-2547.0	-11.4	7662.8	-4556.6	-25.4
Count	18.0	18.0	18.0	18.0	18.0	18.0	18.0
SD	4970.7	3959.5	5893.2	42.9	2327.5	5693.2	44.9
SE	1171.6	933.3	1389.0	10.1	548.6	1341.9	10.6
95% LCI	9923.0	7843.2	-5269.5	-31.2	6587.5	-7186.7	-46.1
95% UCI	14515.7	11501.6	175.5	8.4	8738.0	-1926.5	-4.7

CRP (ng/ml).

Non-Diabetic Subjects

Pt #	Wk0	Wk8	Chg	%Chg	Wk16	Chg	%Chg
001	2147.9	1017.1	-1130.8	-52.6	608.6	-1539.3	-71.7
005	14358.0	8260.6	-6097.4	-42.5	7383.5	-6974.5	-48.6
013	2964.0	1121.0	-1843.0	-62.2	1563.0	-1401.0	-47.3
024	1212.0	1197.7	-14.3	-1.2	441.5	-770.5	-63.6
026	1964.2	3106.3	1142.1	58.1	1371.3	-592.9	-30.2
028	11892.0	11293.0	-599.0	-5.0	5375.3	-6516.7	-54.8
029	1082.5	887.7	-194.8	-18.0	689.8	-392.7	-36.3
032	10030.0	10766.0	736.0	7.3	11131.0	1101.0	11.0
033	12359.0	8616.3	-3742.7	-30.3	10110.0	-2249.0	-18.2
037	14165.0	11203.0	-2962.0	-20.9	14207.0	42.0	0.3
040	6612.1	5830.4	-781.7	-11.8	6272.2	-339.9	-5.1
Average	7162.4	5754.5	-1408.0	-16.3	5377.6	-1784.9	-33.1
Count	11	11	11	11	11	11	11
SD	5485.2	4419.6	2137.4	32.9	4878.2	2605.5	27.2
SE	1653.9	1332.6	644.4	9.9	1470.8	785.6	8.2
95% LCI	3920.9	3142.7	-2671.1	-35.7	2494.8	-3324.6	-49.2
95% UCI	10404.0	8366.3	-144.9	3.2	8260.4	-245.1	-17.0

Diabetic Subjects

003	10609.0	7786.4	-2822.6	-26.6	10797.0	188.0	1.8
007	8146.9	5569.1	-2577.8	-31.6	5091.2	-3055.7	-37.5
008	596.7	379.0	-217.7	-36.5	625.6	28.9	4.8
009	4276.5	1402.2	-2874.3	-67.2	1815.7	-2460.8	-57.5
012	3287.0	944.5	-2342.5	-71.3	642.7	-2644.3	-80.4
014	7992.1	8748.4	756.3	9.5	11408.0	3415.9	42.7
017	2519.6	2437.5	-82.1	-3.3	1395.9	-1123.7	-44.6
018	5047.3	4446.4	-600.9	-11.9	2509.4	-2537.9	-50.3
020	16671.0	8128.6	-8542.4	-51.2	6101.9	-10569.1	-63.4
023	11248.0	10267.0	-981.0	-8.7	8016.4	-3231.6	-28.7
025	1408.8	3420.2	2011.4	142.8	1672.5	263.7	18.7
030	1042.8	5332.1	4289.3	411.3	1854.2	811.4	77.8
031	10144.0	9065.7	-1078.3	-10.6	5914.5	-4229.5	-41.7
034	12299.0	8895.8	-3403.2	-27.7	10251.0	-2048.0	-16.7
036	1497.3	9023.7	7526.4	502.7	803.5	-693.8	-46.3
038	8112.9	2573.5	-5539.4	-68.3	7736.7	-376.2	-4.6
039	4335.7	3011.1	-1324.6	-30.6	3918.8	-416.9	-9.6
041	5001.3	2653.7	-2347.6	-46.9	2716.1	-2285.2	-45.7
Average	6346.4	5226.9	-1119.5	31.9	4626.2	-1720.3	-21.2
Count	18	18	18	18	18	18	18
SD	4554.4	3273.9	3518.9	162.4	3684.5	2864.6	39.9
SE	1073.5	771.7	829.4	38.3	868.5	675.2	9.4
95% LCI	4242.4	3714.5	-2745.2	-43.1	2924.0	-3043.7	-39.6
95% UCI	8450.5	6739.4	506.2	106.9	6328.3	-396.9	-2.7

FSH (mIU/ml).

Non-Diabetic Subjects

Pt #	Wk0	Wk8	Chg	%Chg	Wk16	Chg	%Chg
001	28.1	30.7	2.6	9.3	35.6	7.5	26.7
005	53.6	59.3	5.7	10.6	50.6	-3.0	-5.6
013	19.1	18.6	-0.5	-2.6	21.5	2.4	12.6
024	88.5	96.4	7.9	8.9	93.5	5.0	5.6
026	76.7	108.1	31.4	40.9	103.6	26.9	35.1
028	8.1	7.0	-1.1	-13.6	8.2	0.1	1.2
029	56.8	72.3	15.5	27.3	81.2	24.4	43.0
032	46.8	97.9	51.1	109.2	41.7	-5.1	-10.9
033	63.8	84.3	20.5	32.1	64.3	0.5	0.8
037	23.0	48.8	25.8	112.2	46.1	23.1	100.4
040	7.4	7.7	0.3	4.1	7.8	0.4	5.4
Average	42.9	57.4	14.5	30.8	50.4	7.5	19.5
Count	11	11	11	11	11	11	11
SD	27.6	37.4	16.5	42.5	32.5	11.7	31.7
SE	8.3	11.3	5.0	12.8	9.8	3.5	9.6
95% LCI	26.6	35.3	4.7	5.7	31.2	0.6	0.7
95% UCI	59.2	79.5	24.2	55.9	69.6	14.4	38.2

Diabetic Subjects

003	37.4	36.7	-0.7	-1.9	37.2	-0.2	-0.5
007	15.5	21.2	5.7	36.8	22.1	6.6	42.6
008	103.6	112.4	8.8	8.5	100.5	-3.1	-3.0
009	40.2	40.0	-0.2	-0.5	41.9	1.7	4.2
012	10.1	30.6	20.5	203.0	31.4	21.3	210.9
014	35.8	42.5	6.7	18.7	37.4	1.6	4.5
017	9.1	17.9	8.8	96.7	22.2	13.1	144.0
018	23.1	28.9	5.8	25.1	26.9	3.8	16.5
020	12.2	16.4	4.2	34.4	14.8	2.6	21.3
023	6.1	6.4	0.3	4.9	6.0	-0.1	-1.6
025	57.4	55.7	-1.7	-3.0	56.8	-0.6	-1.0
030	40.0	47.9	7.9	19.8	59.8	19.8	49.5
031	8.8	18.7	9.9	112.5	9.5	0.7	8.0
034	28.4	42.2	13.8	48.6	50.5	22.1	77.8
036	12.2	16.6	4.4	36.1	12.6	0.4	3.3
038	8.9	7.8	-1.1	-12.4	7.6	-1.3	-14.6
039	16.9	21.9	5.0	29.6	20.7	3.8	22.5
041	9.7	9.7	0.0	0.0	9.7	0.0	0.0
Average	26.4	31.9	5.5	36.5	31.5	5.1	32.5
Count	18	18	18	18	18	18	18
SD	24.3	24.7	5.8	53.1	24.1	8.2	58.5
SE	5.7	5.8	1.4	12.5	5.7	1.9	13.8
95% LCI	15.2	20.4	2.8	12.0	20.4	1.4	5.4
95% UCI	37.6	43.3	8.1	61.0	42.7	8.9	59.5

Total Cholesterol (mg/dl) and LDL-cholesterol (mg/dl).

Non-Diabetic Subjects

Pt #	Screen Chol	Wk0	Wk8	Wk16	Chg	% Chg	Screen LDL	Wk0	Wk8	Wk16	Chg	% Chg
001	208	191	139	221	30	15.7	120	120	75	132	12	10.0
005	266	257	220	255	-2	-0.8	175	185	154	159	-26	-14.1
013	230	248	149	149	-99	-39.9	121	81	65	88	7	8.6
024	231	228	142	162	-66	-28.9	146	159	83	93	-66	-41.5
026	163	227	144	156	-71	-31.3	95	156	94	101	-55	-35.3
028	244	216	159	177	-39	-18.1	143	134	88	118	-16	-11.9
029	141	197	141	134	-63	-32.0	68	127	89	78	-49	-38.6
032	177	*177*	131	143	-34	-19.2	103	*103*	75	87	-16	-15.5
033	267	238	113	175	-63	-26.5	179	175	55	116	-59	-33.7
037	224	230	184	170	-60	-26.1	105	104	98	74	-30	-28.8
040	185	145	147	159	14	9.7	111	71	95	107	36	50.7
Average	212.4	214.0	151.7	172.8	-41.2	-17.9	124.2	128.6	88.3	104.8	-23.8	-13.6
Count	11	11	11	11	11	11	11	11	11	11	11	11
SD	41.5	33.4	28.5	35.6	39.8	18.2	33.8	37.4	25.5	25.3	32.6	27.8
SE	12.5	10.1	8.6	10.7	12.0	5.5	10.2	11.3	7.7	7.6	9.8	8.4
95% LCI	187.9	194.3	134.9	151.8	-64.7	-28.7	104.2	106.6	73.2	89.9	-43.1	-30.0
95% UCI	236.9	233.7	168.6	193.8	-17.6	-7.2	144.2	150.7	103.4	119.8	-4.6	2.8

Diabetic Subjects

003	171	161	141	137	-24	-14.0	66	66	*66*	44	-22	-33.3
004	211	217	224	WD			123	144	157	WD		
007	209	209	171	169	-40	-19.1	99	99	157	97	-2	-2.0
008	223	189	153	295	106	47.5	105	105	70	176	71	67.6
009	250	257	222	241	-16	-6.4	140	140	147	171	31	22.1
010	217	201	214	WD			151	151	75	WD		
012	185	187	157	172	-15	-8.1	125	125	75	120	-5	-4.0
014	261	228	188	191	-37	-14.2	161	161	121	140	-21	-13.0
015	225	192	225	WD			133	118	119	WD		
017	183	157	196	184	27	14.8	50	54	119	111	57	105.6
018	253	252	188	193	-59	-23.3	180	184	137	141	-43	-23.4
020	221	195	175	174	-21	-9.5	*96*	96	90	110	14	14.6
023	232	214	195	194	-20	-8.6	145	142	128	131	-11	-7.7
025	252	236	217	202	-34	-13.5	169	161	158	138	-23	-14.3
030	191	177	174	203	26	13.6	99	101	113	131	30	29.7
031	191	188	188	179	-9	-4.7	97	79	125	97	18	22.8
034	187	176	142	143	-33	-17.6	198	113	89	90	-23	-20.4
036	157	143	187	134	-9	-5.7	87	77	124	77	0	0.0
038	223	194	168	204	10	4.5	150	119	108	141	22	18.5
039	226	213	176	182	-31	-13.7	156	144	122	132	-12	-8.3
041	150	259	122	178	-81	-54.0	83	176	73	123	-53	-30.1
Average	210.4	202.1	182.0	187.5	-14.4	-7.3	124.4	121.7	113.0	120.6	1.6	6.9
Count	21	21	21	18	18	18	21	21	21	18	18	18
SD	31.5	32.0	29.0	37.2	40.0	20.2	38.9	36.1	30.0	32.1	32.6	35.0
SE	3.7	3.7	3.9	2.9	2.8	4.0	3.4	3.5	3.8	3.2	3.2	3.0
95% LCI	203.0	194.9	174.4	181.7	-20.0	-15.2	117.8	114.8	105.5	114.3	-4.6	0.9
95% UCI	217.7	209.4	189.7	193.3	-8.9	0.5	131.0	128.5	120.5	126.8	7.7	12.9

Triglyceride (mg/dl) and HDL-cholesterol (mg/dl).

Non-Diabetic Subjects

Pt #	Screen Triglycerides	Wk0	Wk8	Wk16	Chg	% Chg	Screen HDL	Wk0	Wk8	Wk16	Chg	% Chg
001	158	158	139	110	-48	-30.4	56	42	36	38	-4	-9.5
005	127	117	236	182	65	55.6	66	49	41	*41*	-8	-16.3
013	311	132	177	101	-31	-23.5	47	46	42	41	-5	-10.9
024	59	47	39	46	-1	-2.1	73	60	51	60	0	0.0
026	107	76	68	71	-5	-6.6	46	56	36	41	-15	-26.8
028	161	159	156	89	-70	-44.0	68	50	40	41	-9	-18.0
029	103	82	52	43	-39	-47.6	52	54	42	47	-7	-13.0
032	75	*75*	89	89	14	18.7	59	*59*	38	38	-21	-35.6
033	152	125	110	120	-5	-4.0	58	38	36	35	-3	-7.9
037	183	294	154	150	-144	-49.0	82	67	55	66	-1	-1.5
040	141	111	94	99	-12	-10.8	46	52	33	32	-20	-38.5
Average	143.4	125.1	119.5	100.0	-25.1	-13.1	59.4	52.1	40.9	43.6	-8.5	-16.2
Count	11	11	11	11	11	11	11	11	11	11	11	11
SD	67.3	66.3	59.3	41.2	53.0	31.3	11.8	8.4	6.7	10.4	7.2	12.7
SE	20.3	20.0	17.9	12.4	16.0	9.4	3.6	2.5	2.0	3.1	2.2	3.8
95% LCI	103.6	85.9	84.4	75.7	-56.4	-31.6	52.4	47.1	37.0	37.5	-12.7	-23.7
95% UCI	183.1	164.3	154.5	124.3	6.2	5.4	66.3	57.0	44.9	49.8	-4.2	-8.7

Diabetic Subjects

003	296	296	467	308	12	4.1	46	27	26	31	4	14.8
004	228	228	210	WD			42	37	29	WD		
007	362	362	173	230	-132	-36.5	38	30	23	26	-4	-13.3
008	224	224	152	267	43	19.2	73	71	53	66	-5	-7.0
009	339	339	277	185	-154	-45.4	42	30	28	33	3	10.0
010	106	106	167	WD			45	34	30	WD		
012	119	119	213	92	-27	-22.7	36	32	25	34	2	6.3
014	280	280	169	108	-172	-61.4	44	33	33	29	-4	-12.1
015	241	203	385	ED			45 34	30	WD			
017	342	276	194	119	-157	-56.9	65	48	38	49	1	2.1
018	176	193	112	78	-115	-59.6	38	29	29	36	7	24.1
020	505	368	294	173	-195	-53.0	31	25	26	29	4	16.0
023	145	152	122	106	-46	-30.3	58	42	43	42	0	0.0
025	135	159	128	98	-61	-38.4	56	43	33	44	1	2.3
030	195	168	138	196	28	16.7	53	42	33	33	-9	-21.4
031	215	350	156	212	-138	-39.4	51	39	32	40	1	2.6
034	159	152	134	98	-54	-35.5	47	33	26	33	0	0.0
036	130	148	161	126	-22	-14.9	44	36	31	32	-4	-11.1
038	120	183	83	92	-91	-49.7	49	38	43	45	7	18.4
039	125	142	91	56	-86	-60.6	45	41	36	39	-2	-4.9
041	137	208	68	90	-118	-56.7	40	41	35	37	-4	-9.8
Average	218.0	221.7	185.4	146.3	-82.5	-34.5	47.2	37.2	32.6	37.7	-0.1	0.9
Count	21	21	21	18	18	18	20	21	20	18	18	18
SD	104.1	83.2	98.7	71.8	70.9	25.8	10.1	9.8	7.3	9.4	4.3	12.4
SE	22.7	18.1	21.5	16.9	16.7	6.1	2.2	2.1	1.6	2.2	1.0	2.9
95% LCI	173.5	186.1	143.2	113.2	-115.3	-46.4	42.7	33.0	29.4	33.3	-2.1	-4.8
95% UCI	262.6	257.3	227.6	179.5	-49.7	-22.6	51.6	41.4	35.8	42.0	1.9	6.7

*Italized numbers are interpolated or taken from baseline week

Systolic and Diastolic Blood Pressure Measurements (mmHg).

Non-Diabetic Subjects

Pt #	Screen Systolic	Screen Diastolic	Wk0 S	Wk0 D	Wk4 S	Wk4 D	Wk8 S	Wk8 D	Wk12 S	Wk12 D	Wk16 S	Wk16 D
001	128	68	122	74	100	70	110	72	102	60	112	66
005	120	64	134	80	142	74	120	80	128	84	130	90
013	122	74	108	78	110	74	98	64	100	70	116	66
024	126	72	108	70	108	66	102	70	102	58	114	66
026	122	76	130	80	122	70	110	84	112	70	130	84
028	118	72	110	70	104	74	100	70	118	60	102	74
029	130	78	120	70	100	80	100	60	120	70	140	70
032	114	78	120	70	100	70	110	70	112	70	110	68
033	132	82	110	74	120	80	124	66	152	90	108	72
037	122	78	120	72	130	72	128	70	104	70	130	76
040	122	80	112	70	110	70	112	76	122	84	110	80
Average	123.3	74.7	117.6	73.5	113.3	72.7	110.4	71.1	115.6	71.5	118.4	73.8
Count	11	11	11	11	11	11	11	11	11	11	11	11
SD	5.3	5.4	8.9	4.1	13.7	4.3	10.2	6.9	15.2	10.5	12.1	8.0
SE	1.6	1.6	2.7	1.2	4.1	1.3	3.1	2.1	4.6	3.2	3.6	2.4
95% LCI	120.1	71.5	112.4	71.0	105.1	70.2	104.4	67.0	106.6	65.2	111.2	69.1
95% UCI	126.4	77.9	122.9	75.9	121.4	75.3	116.4	75.2	124.6	77.7	125.5	78.6

Diabetic Subjects

003	130	78	100	68	120	78	130	80	112	80	140	86
004	145	105	140	80	132	90	120	80	WD			
007	122	78	142	88	130	84	118	74	100	70	108	68
008	132	78	130	80	150	86	146	82	120	74	132	80
009	145	90	124	82	132	76	140	80	140	90	150	94
010	138	72	140	84	118	66	120	76	136	74	WD	
012	140	82	138	90	100	76	120	80	134	82	130	70
014	148	72	134	74	110	68	120	60	116	60	122	76
015	158	90	144	88	130	84	78	100	WD			
017	136	78	110	70	120	64	130	70	120	72	126	66
018	136	88	144	86	138	74	130	90	120	80	140	82
020	122	78	110	70	120	70	130	70	126	72	100	80
023	112	72	110	74	110	74	106	70	104	70	110	70
025	132	78	118	78	90	56	100	58	100	60	118	82
030	132	72	138	90	110	80	116	80	124	72	120	70
031	116	68	110	80	112	80	116	72	108	74	120	60
034	118	78	110	74	102	62	110	70	100	62	100	54
036	118	78	124	70	140	90	110	70	140	78	124	74
038	118	76	120	86	108	60	118	74	110	74	118	74
039	124	78	124	80	116	74	128	80	114	78	122	88
041	122	78	120	60	106	70	100	60	110	60	118	80
Average	130.7	79.4	125.2	78.7	118.8	74.4	118.4	75.0	117.6	72.7	122.1	75.2
Count	21	21	21	21	21	21	21	21	19	19	18	18
SD	12.2	8.2	13.7	8.2	14.9	9.6	15.0	9.8	13.1	8.1	13.2	10.0
SE	2.7	1.8	3.0	1.8	3.2	2.1	3.3	2.1	3.0	1.8	3.1	2.4
95% LCI	125.4	75.9	119.4	75.2	112.4	70.3	112.0	70.9	111.7	69.1	116.0	70.6
95% UCI	135.9	82.9	131.1	82.2	125.1	78.5	124.8	79.2	123.5	76.4	128.2	79.8

APPENDIX E

Correlation Analyses

Diabetic Subjects

Pearson Correlation Coefficients, N = 18

	Weight	Leptin	Resistin	Insulin	HOMA-IR
Weight	1.00000	0.58332 0.0110	-0.06395 0.8010	0.31957 0.1961	0.15609 0.5363
Leptin	0.58332 0.0110	1.00000	-0.32905 0.1824	0.38868 0.1109	0.41457 0.0872
Resistin	-0.06395 0.8010	-0.32905 0.1824	1.00000	-0.50912 0.0309	-0.64540 0.0038
Insulin	0.31957 0.1961	0.38868 0.1109	-0.50912 0.0309	1.00000	0.88828 <.0001
HOMA-IR	0.15609 0.5363	0.41457 0.0872	-0.64540 0.0038	0.88828 <.0001	1.00000

Non-Diabetic Subjects

Pearson Correlation Coefficients, N = 11

	Weight	Leptin	Resistin	Insulin	HOMA-IR
Weight	1.00000	0.71257 0.0139	0.43343 0.1829	0.58066 0.0611	0.60139 0.0503
Leptin	0.71257 0.0139	1.00000	0.41352 0.2062	0.22670 0.5026	0.24788 0.4624
Resistin	0.43343 0.1829	0.41352 0.2062	1.00000	-0.13450 0.6934	-0.11060 0.7461
Insulin	0.58066 0.0611	0.22670 0.5026	-0.13450 0.6934	1.00000	0.99801 <.0001
HOMA-IR	0.60139 0.0503	0.24788 0.4624	-0.11060 0.7461	0.99801 <.0001	1.00000

Diabetic Subjects

Pearson Correlation Coefficients, N = 18

	BMI	Leptin	Resistin	Insulin	HOMA-IR
BMI	1.00000	0.59797 0.0088	-0.13450 0.5947	0.44322 0.0654	0.40553 0.0950
Leptin	0.59797 0.0088	1.00000	-0.32905 0.1824	0.38868 0.1109	0.41457 0.0872
Resistin	-0.13450 0.5947	-0.32905 0.1824	1.00000	-0.50912 0.0309	-0.64540 0.0038
Insulin	0.44322 0.0654	0.38868 0.1109	-0.50912 0.0309	1.00000	0.88828 <.0001
HOMA-IR	0.40553 0.0950	0.41457 0.0872	-0.64540 0.0038	0.88828 <.0001	1.00000

Non-Diabetic Subjects

Pearson Correlation Coefficients, N = 11

	BMI	Leptin	Resistin	Insulin	HOMA-IR
BMI	1.00000	0.82402 0.0018	0.31312 0.3485	0.60938 0.0466	0.63385 0.0362
Leptin	0.82402 0.0018	1.00000	0.41352 0.2062	0.22670 0.5026	0.24788 0.4624
Resistin	0.31312 0.3485	0.41352 0.2062	1.00000	-0.13450 0.6934	-0.11060 0.7461
Insulin	0.60938 0.0466	0.22670 0.5026	-0.13450 0.6934	1.00000	0.99801 <.0001
HOMA-IR	0.63385 0.0362	0.24788 0.4624	-0.11060 0.7461	0.99801 <.0001	1.00000

Diabetic Subjects

Pearson Correlation Coefficients, N = 18

	Leptin	Resistin	Insulin	HOMA-IR	Ghrelin	Adiponectin
Leptin	1.00000	-0.32905 0.1824	0.38868 0.1109	0.41457 0.0872	0.03533 0.8893	0.24760 0.3219
Resistin	-0.32905 0.1824	1.00000	-0.50912 0.0309	-0.64540 0.0038	-0.18873 0.4533	-0.04695 0.8532
Insulin	0.38868 0.110	-0.50912 0.0309	1.00000	0.88828 <.0001	-0.41806 0.0843	-0.14652 0.5618
HOMA-IR	0.41457 0.0872	-0.64540 0.0038	0.88828 <.0001	1.00000	-0.38697 0.1126	-0.18609 0.4597
Ghrelin	0.03533 0.8893	-0.18873 0.4533	-0.41806 0.0843	-0.38697 0.1126	1.00000	0.57527 0.0125
Adiponectin	0.24760 0.3219	-0.04695 0.8532	-0.14652 0.5618	-0.18609 0.4597	0.57527 0.0125	1.00000

Non-Diabetic Subjects

Pearson Correlation Coefficients, N = 11

	Leptin	Resistin	Insulin	HOMA-IR	Ghrelin	Adiponectin
Leptin	1.00000	0.41352 0.2062	0.22670 0.5026	0.24788 0.4624	-0.37545 0.2552	-0.61844 0.0425
Resistin	0.41352 0.2062	1.00000	-0.13450 0.6934	-0.11060 0.7461	-0.38078 0.2480	-0.45637 0.1583
Insulin	0.22670 0.5026	-0.13450 0.6934	1.00000	0.99801 <.0001	-0.31998 0.3374	-0.49174 0.1245
HOMA-IR	0.24788 0.4624	-0.11060 0.7461	0.99801 <.0001	1.00000	-0.35775 0.2800	-0.49922 0.1180
Ghrelin	-0.37545 0.2552	-0.38078 0.2480	-0.31998 0.3374	-0.35775 0.2800	1.00000	0.44422 0.1711
Adiponectin	-0.61844 0.0425	-0.45637 0.1583	-0.49174 0.1245	-0.49922 0.1180	0.44422 0.1711	1.00000

Diabetic Subjects

Pearson Correlation Coefficients, N = 18

	BMI	CRP	IL-6	TNF-α	Insulin
BMI	1.00000	0.43709 0.0697	-0.01402 0.9560	-0.02011 0.9369	0.44322 0.0654
CRP	0.43709 0.0697	1.00000	0.25831 0.3007	0.40949 0.0915	-0.18633 0.4591
IL-6	-0.01402 0.9560	0.25831 0.3007	1.00000	0.00698 0.9781	-0.19369 0.4412
TNF-α	-0.02011 0.9369	0.40949 0.0915	0.00698 0.9781	1.00000	0.07350 0.7719
Insulin	0.44322 0.0654	-0.18633 0.4591	-0.19369 0.4412	0.07350 0.7719	1.00000

Non-Diabetic Subjects

Pearson Correlation Coefficients, N = 11

	BMI	CRP	IL-6	TNF-α	Insulin
BMI	1.00000	-0.10754 0.7675	0.25181 0.4551	0.24618 0.4656	0.60938 0.0466
CRP	-0.10754 0.7675	1.00000	-0.05715 0.8754	0.20543 0.5691	0.00026 0.9994
IL-6	0.25181 0.4551	-0.05715 0.8754	1.00000	0.49414 0.1224	-0.13721 0.6875
TNF-α	0.24618 0.4656	0.20543 0.5691	0.49414 0.1224	1.00000	-0.12708 0.7096
Insulin	0.60938 0.0466	0.00026 0.9994	-0.13721 0.6875	-0.12708 0.7096	1.00000

Diabetic Subjects

Pearson Correlation Coefficients, N = 18

	Weight	Leptin	Resistin	Insulin	HOMA-IR
Weight	1.00000	0.58332 0.0110	-0.06395 0.8010	0.31957 0.1961	0.15609 0.5363
Leptin	0.58332 0.0110	1.00000	-0.32905 0.1824	0.38868 0.1109	0.41457 0.0872
Resistin	-0.06395 0.8010	-0.32905 0.1824	1.00000	-0.50912 0.0309	-0.64540 0.0038
Insulin	0.31957 0.1961	0.38868 0.1109	-0.50912 0.0309	1.00000	0.88828 <.0001
HOMA-IR	0.15609 0.5363	0.41457 0.0872	-0.64540 0.0038	0.88828 <.0001	1.00000

Non-Diabetic Subjects

Pearson Correlation Coefficients, N = 11

	Weight	Leptin	Resistin	Insulin	HOMA-IR
Weight	1.00000	0.71257 0.0139	0.43343 0.1829	0.58066 0.0611	0.60139 0.0503
Leptin	0.71257 0.0139	1.00000	0.41352 0.2062	0.22670 0.5026	0.24788 0.4624
Resistin	0.43343 0.1829	0.41352 0.2062	1.00000	-0.13450 0.6934	-0.11060 0.7461
Insulin	0.58066 0.0611	0.22670 0.5026	-0.13450 0.6934	1.00000	0.99801 <.0001
HOMA-IR	0.60139 0.0503	0.24788 0.4624	-0.11060 0.7461	0.99801 <.0001	1.00000

Diabetic Subjects

Pearson Correlation Coefficients, N = 18

	SAT	VAT	Insulin	HOMA-IR	Resistin	Ghrelin
SAT	1.00000	-0.07844 0.7570	0.06746 0.7903	0.03148 0.9013	0.13456 0.5945	0.14492 0.5661
VAT	-0.07844 0.7570	1.00000	0.32018 0.1952	0.28711 0.2480	-0.28494 0.2518	-0.12384 0.6244
Insulin	0.06746 0.7903	0.32018 0.1952	1.00000	0.88828 <.0001	-0.50912 0.0309	-0.41806 0.0843
HOMA-IR	0.03148 0.9013	0.28711 0.2480	0.88828 <.0001	1.00000	-0.64540 0.0038	-0.38697 0.1126
Resistin	0.13456 0.5945	-0.28494 0.2518	-0.50912 0.0309	-0.64540 0.0038	1.00000	-0.18873 0.4533
Ghrelin	0.14492 0.5661	-0.12384 0.6244	-0.41806 0.0843	-0.38697 0.1126	-0.18873 0.4533	1.00000

Non-Diabetic Subjects

Pearson Correlation Coefficients, N = 11

	SAT	VAT	Insulin	HOMA-IR	Resistin	Ghrelin
SAT	1.00000	0.54467 0.0832	0.61906 0.0423	0.62963 0.0379	0.20826 0.5389	-0.45145 0.1634
VAT	0.54467 0.0832	1.00000	0.03378 0.9214	0.06491 0.8496	0.17620 0.6043	-0.31443 0.3463
Insulin	0.61906 0.0423	0.03378 0.9214	1.00000	0.99801 <.0001	-0.13450 0.6934	-0.31998 0.3374
HOMA-IR	0.62963 0.0379	0.06491 0.8496	0.99801 <.0001	1.00000	-0.11060 0.7461	-0.35775 0.2800
Resistin	0.20826 0.5389	0.17620 0.6043	-0.13450 0.6934	-0.11060 0.7461	1.00000	-0.38078 0.2480
Ghrelin	-0.45145 0.1634	-0.31443 0.3463	-0.31998 0.3374	-0.35775 0.2800	-0.38078 0.2480	1.00000

Diabetic Subjects

Pearson Correlation Coefficients, N = 18

	BMI	%BF	SAT	VAT	Fat	Lean
BMI	1.00000	0.56699 0.0176	0.58108 0.0114	0.65818 0.0030	0.81721 <.0001	0.23290 0.3523
%BF	0.56699 0.0176	1.00000	0.66674 0.0035	0.37650 0.1363	0.80252 0.0001	-0.56366 0.0185
SAT	0.58108 0.0114	0.66674 0.0035	1.00000	-0.07844 0.7570	0.59476 0.0092	-0.23720 0.3433
VAT	0.65818 0.0030	0.37650 0.1363	-0.07844 0.7570	1.00000	0.60538 0.0078	0.33578 0.1731
Fat	0.81721 <.0001	0.80252 0.0001	0.59476 0.0092	0.60538 0.0078	1.00000	-0.02126 0.9333
Lean	0.23290 0.3523	-0.56366 0.0185	-0.23720 0.3433	0.33578 0.1731	-0.02126 0.9333	1.00000

Non-Diabetic Subjects

Pearson Correlation Coefficients, N = 11

	BMI	%BF	SAT	VAT	Fat	Lean
BMI	1.00000	0.74983 0.0079	0.94085 <.0001	0.58185 0.0604	0.95563 <.0001	0.58038 0.0612
%BF	0.74983 0.0079	1.00000	0.65655 0.0282	0.63711 0.0350	0.70635 0.0151	0.30799 0.3568
SAT	0.94085 <.0001	0.65655 0.0282	1.00000	0.54467 0.0832	0.95345 <.0001	0.44314 0.1722
VAT	0.58185 0.0604	0.63711 0.0350	0.54467 0.0832	1.00000	0.51832 0.1024	0.00809 0.9812
Fat	0.95563 <.0001	0.70635 0.0151	0.95345 <.0001	0.51832 0.1024	1.00000	0.60202 0.0500
Lean	0.58038 0.0612	0.30799 0.3568	0.44314 0.1722	0.00809 0.9812	0.60202 0.0500	1.00000

Diabetic Subjects

Pearson Correlation Coefficients, N = 18

	Insulin	Weight	BMI
Insulin	1.00000	0.31957 0.1961	0.44322 0.0654
Weight	0.31957 0.1961	1.00000	0.79522 <.0001
BMI	0.44322 0.654	0.79522 <.0001	1.00000

Non-Diabetic Subjects

Pearson Correlation Coefficients, N = 11

	Insulin	Weight	BMI
Insulin	1.00000	0.58066 0.0611	0.60938 0.0466
Weight	0.58066 0.0611	1.00000	0.89177 0.0002
BMI	0.60938 0.0466	0.89177 0.0002	1.00000

Diabetic Subjects

Pearson Correlation Coefficients, N = 18

	Insulin	%BF	SAT	VAT	Fat	Lean
Insulin	1.00000	0.26757 0.2992	0.06746 0.7903	0.32018 0.1952	0.29263 0.2386	0.17826 0.4791
%BF	0.26757 0.2992	1.00000	0.66674 0.0035	0.37650 0.1363	0.80252 0.0001	-0.56366 0.0185
SAT	0.06746 0.7903	0.66674 0.0035	1.00000	-0.07844 0.7570	0.59476 0.0092	-0.23720 0.3433
VAT	0.32018 0.1952	0.37650 0.1363	-0.07844 0.7570	1.00000	0.60538 0.0078	0.33578 0.1731
Fat	0.29263 0.2386	0.80252 0.0001	0.59476 0.0092	0.60538 0.0078	1.00000	-0.02126 0.9333
Lean	0.17826 0.4791	-0.56366 0.0185	-0.23720 0.3433	0.33578 0.1731	-0.02126 0.9333	1.00000

Non-Diabetic Subjects

Pearson Correlation Coefficients, N = 11

	Insulin	%BF	SAT	VAT	Fat	Lean
Insulin	1.00000	0.53063 0.0931	0.61906 0.0423	0.03378 0.9214	0.61609 0.0436	0.38407 0.2436
%BF	0.53063 0.0931	1.00000	0.65655 0.0282	0.63711 0.0350	0.70635 0.0151	0.30799 0.3568
SAT	0.61906 0.0423	0.65655 0.0282	1.00000	0.54467 0.0832	0.95345 <.0001	0.44314 0.1722
VAT	0.03378 0.9214	0.63711 0.0350	0.54467 0.0832	1.00000	0.51832 0.1024	0.00809 0.9812
Fat	0.61609 0.0436	0.70635 0.0151	0.95345 <.0001	0.51832 0.1024	1.00000	0.60202 0.0500
Lean	0.38407 0.2436	0.30799 0.3568	0.44314 0.1722	0.00809 0.9812	0.60202 0.0500	1.00000

Diabetic Subjects

Pearson Correlation Coefficients, N = 18

	Insulin	Leptin	Resistin	Ghrelin	HOMA-IR
Insulin	1.00000	0.38868 0.1109	-0.50912 0.0309	-0.41806 0.0843	0.88828 <.0001
Leptin	0.38868 0.1109	1.00000	-0.32905 0.1824	0.03533 0.8893	0.41457 0.0872
Resistin	-0.50912 0.0309	-0.32905 0.1824	1.00000	-0.18873 0.4533	-0.64540 0.0038
Ghrelin	-0.41806 0.0843	0.03533 0.8893	-0.18873 0.4533	1.00000	-0.38697 0.1126
HOMA-IR	0.88828 <.0001	0.41457 0.0872	-0.64540 0.0038	-0.38697 0.1126	1.00000

Non-Diabetic Subjects

Pearson Correlation Coefficients, N = 11

	Insulin	Leptin	Resistin	Ghrelin	HOMA-IR
Insulin	1.00000	0.22670 0.5026	-0.13450 0.6934	-0.31998 0.3374	0.99801 <.0001
Leptin	0.22670 0.5026	1.00000	0.41352 0.2062	-0.37545 0.2552	0.24788 0.4624
Resistin	-0.13450 0.6934	0.41352 0.2062	1.00000	-0.38078 0.2480	-0.11060 0.7461
Ghrelin	-0.31998 0.3374	-0.37545 0.2552	-0.38078 0.2480	1.00000	-0.35775 0.2800
HOMA-IR	0.99801 <.0001	0.24788 0.4624	-0.11060 0.7461	-0.35775 0.2800	1.00000

Diabetic Subjects

Pearson Correlation Coefficients, N = 18

	Insulin	CRP	IL-6	TNF-α	Adiponectin
Insulin	1.00000	-0.18633 0.4591	-0.19369 0.4412	0.07350 0.7719	-0.14652 0.5618
CRP	-0.18633 0.4591	1.00000	0.25831 0.3007	0.40949 0.0915	-0.07220 0.7759
IL-6	-0.19369 0.4412	0.25831 0.3007	1.00000	0.00698 0.9781	-0.12576 0.6190
TNF-α	0.07350 0.7719	0.40949 0.0915	0.00698 0.9781	1.00000	-0.38637 0.1132
Adiponectin	-0.14652 0.5618	-0.07220 0.7759	-0.12576 0.6190	-0.38637 0.1132	1.00000

Non-Diabetic Subjects

Pearson Correlation Coefficients, N = 11

	Insulin	CRP	IL-6	TNF-α	Adiponectin
Insulin	1.00000	0.00026 0.9994	-0.13721 0.6875	-0.12708 0.7096	-0.49174 0.1245
CRP	0.00026 0.9994	1.00000	-0.05715 0.8754	0.20543 0.5691	-0.36323 0.3022
IL-6	-0.13721 0.6875	-0.05715 0.8754	1.00000	0.49414 0.1224	-0.54031 0.0862
TNF-α	-0.12708 0.7096	0.20543 0.5691	0.49414 0.1224	1.00000	-0.46298 0.1516
Adiponectin	-0.49174 0.1245	-0.36323 0.3022	-0.54031 0.0862	-0.46298 0.1516	1.00000

Diabetic Subjects

Pearson Correlation Coefficients, N = 18

	%BF	Leptin	Resistin	Ghrelin	HOMA-IR
%BF	1.00000	0.72023 0.0011	-0.09666 0.7121	-0.12694 0.6273	0.21251 0.4128
Leptin	0.72023 0.0011	1.00000	-0.32905 0.1824	0.03533 0.8893	0.41457 0.0872
Resistin	-0.09666 0.7121	-0.32905 0.1824	1.00000	-0.18873 0.4533	-0.64540 0.0038
Ghrelin	-0.12694 0.6273	0.03533 0.8893	-0.18873 0.4533	1.00000	-0.38697 0.1126
HOMA-IR	0.21251 0.4128	0.41457 0.0872	-0.64540 0.0038	-0.38697 0.1126	1.00000

Non-Diabetic Subjects

Pearson Correlation Coefficients, N = 11

	%BF	Leptin	Resistin	Ghrelin	HOMA-IR
%BF	1.00000	0.61181 0.0455	-0.01212 0.9718	-0.52210 0.0995	0.56978 0.0673
Leptin	0.61181 0.0455	1.00000	0.41352 0.2062	-0.37545 0.2552	0.24788 0.4624
Resistin	-0.01212 0.9718	0.41352 0.2062	1.00000	-0.38078 0.2480	-0.11060 0.7461
Ghrelin	-0.52210 0.0995	-0.37545 0.2552	-0.38078 0.2480	1.00000	-0.35775 0.2800
HOMA-IR	0.56978 0.0673	0.24788 0.4624	-0.11060 0.7461	-0.35775 0.2800	1.00000

Diabetic Subjects

Pearson Correlation Coefficients, N = 18

	%BF	CRP	IL-6	TNF-α	Adiponectin
%BF	1.00000	0.23269 0.3688	0.24746 0.3383	-0.20420 0.4318	0.14741 0.572
CRP	0.23269 0.3688	1.00000	0.25831 0.3007	0.40949 0.0915	-0.07220 0.7759
IL-6	0.24746 0.3383	0.25831 0.3007	1.00000	0.00698 0.9781	-0.12576 0.6190
TNF-α	-0.20420 0.4318	0.40949 0.0915	0.00698 0.9781	1.00000	-0.38637 0.1132
Adiponectin	0.14741 0.5724	-0.07220 0.7759	-0.12576 0.6190	-0.38637 0.1132	1.00000

Non-Diabetic Subjects

Pearson Correlation Coefficients, N = 11

	%BF	CRP	IL-6	TNF-α	Adiponectin
%BF	1.00000	0.20583 0.5683	-0.09351 0.7845	-0.23333 0.4899	-0.39723 0.2264
CRP	0.20583 0.5683	1.00000	-0.05715 0.8754	0.20543 0.5691	-0.36323 0.3022
IL-6	-0.09351 0.7845	-0.05715 0.8754	1.00000	0.49414 0.1224	-0.54031 0.0862
TNF-α	-0.23333 0.4899	0.20543 0.5691	0.49414 0.1224	1.00000	-0.46298 0.1516
Adiponectin	-0.39723 0.2264	-0.36323 0.3022	-0.54031 0.0862	-0.46298 0.1516	1.00000

Diabetic Subjects

Pearson Correlation Coefficients, N = 18

	SAT	Leptin	Resistin	Ghrelin	HOMA-IR
SAT	1.00000	0.44022 0.0675	0.13456 0.5945	0.14492 0.5661	0.03148 0.9013
Leptin	0.44022 0.0675	1.00000	-0.32905 0.1824	0.03533 0.8893	0.41457 0.0872
Resistin	0.13456 0.5945	-0.32905 0.1824	1.00000	-0.18873 0.4533	-0.64540 0.0038
Ghrelin	0.14492 0.5661	0.03533 0.8893	-0.18873 0.4533	1.00000	-0.38697 0.1126
HOMA-IR	0.03148 0.9013	0.41457 0.0872	-0.64540 0.0038	-0.38697 0.1126	1.00000

Non-Diabetic Subjects

Pearson Correlation Coefficients, N = 11

	SAT	Leptin	Resistin	Ghrelin	HOMA-IR
SAT	1.00000	0.86803 0.0005	0.20826 0.5389	-0.45145 0.1634	0.62963 0.0379
Leptin	0.86803 0.0005	1.00000	0.41352 0.2062	-0.37545 0.2552	0.24788 0.4624
Resistin	0.20826 0.5389	0.41352 0.2062	1.00000	-0.38078 0.2480	-0.11060 0.7461
Ghrelin	-0.45145 0.1634	-0.37545 0.2552	-0.38078 0.2480	1.00000	-0.35775 0.2800
HOMA-IR	0.62963 0.0379	0.24788 0.4624	-0.11060 0.7461	-0.35775 0.2800	1.00000

Diabetic Subjects

Pearson Correlation Coefficients, N = 18

	SAT	CRP	IL-6	TNF-α	Adiponectin
SAT	1.00000	0.56124	0.15238	-0.10988	0.29269
		0.0154	0.5461	0.6643	0.2385
CRP	0.56124	1.00000	0.25831	0.40949	-0.07220
	0.0154		0.3007	0.0915	0.7759
IL-6	0.15238	0.25831	1.00000	0.00698	-0.12576
	0.5461	0.3007		0.9781	0.6190
TNF-α	-0.10988	0.40949	0.00698	1.00000	-0.38637
	0.6643	0.0915	0.9781		0.1132
Adiponectin	0.29269	-0.07220	-0.12576	-0.38637	1.00000
	0.2385	0.7759	0.6190	0.1132	

Non-Diabetic Subjects

Pearson Correlation Coefficients,N = 11

	SAT	CRP	IL-6	TNF-α	Adiponectin
SAT	1.00000	0.00821	0.20746	0.42953	-0.64839
		0.9820	0.5405	0.1874	0.0309
CRP	0.00821	1.00000	-0.05715	0.20543	-0.36323
	0.9820		0.8754	0.5691	0.3022
IL-6	0.20746	-0.05715	1.00000	0.49414	-0.54031
	0.5405	0.8754		0.1224	0.0862
TNF-α	0.42953	0.20543	0.49414	1.00000	-0.46298
	0.1874	0.5691	0.1224		0.1516
Adiponectin	-0.64839	-0.36323	-0.54031	-0.46298	1.00000
	0.0309	0.3022	0.0862	0.1516	

Diabetic Subjects

Pearson Correlation Coefficients, N = 18

	VAT	Leptin	Resistin	Ghrelin	HOMA-IR
VAT	1.00000	0.50514 0.0325	-0.28494 0.2518	-0.12384 0.6244	0.28711 0.2480
Leptin	0.50514 0.0325	1.00000	-0.32905 0.1824	0.03533 0.8893	0.41457 0.0872
Resistin	-0.28494 0.2518	-0.32905 0.1824	1.00000	-0.18873 0.4533	-0.64540 0.0038
Ghrelin	-0.12384 0.6244	0.03533 0.8893	-0.18873 0.4533	1.00000	-0.38697 0.1126
HOMA-IR	0.28711 0.2480	0.41457 0.0872	-0.64540 0.0038	-0.38697 0.1126	1.00000

Non-Diabetic Subjects

Pearson Correlation Coefficients, N = 11

	VAT	Leptin	Resistin	Ghrelin	HOMA-IR
VAT	1.00000	0.78083 0.0046	0.17620 0.6043	-0.31443 0.3463	0.06491 0.8496
Leptin	0.78083 0.0046	1.00000	0.41352 0.2062	-0.37545 0.2552	0.24788 0.4624
Resistin	0.17620 0.6043	0.41352 0.2062	1.00000	-0.38078 0.2480	-0.11060 0.7461
Ghrelin	-0.31443 0.3463	-0.37545 0.2552	-0.38078 0.2480	1.00000	-0.35775 0.2800
HOMA-IR	0.06491 0.8496	0.24788 0.4624	-0.11060 0.7461	-0.35775 0.2800	1.00000

Diabetic Subjects

Pearson Correlation Coefficients, N = 18

	VAT	CRP	IL-6	TNF-α	Adiponectin
VAT	1.00000	0.20013 0.4259	-0.14189 0.5744	0.18429 0.4641	-0.36219 0.1397
CRP	0.20013 0.4259	1.00000	0.25831 0.3007	0.40949 0.0915	-0.07220 0.7759
IL-6	-0.14189 0.5744	0.25831 0.3007	1.00000	0.00698 0.9781	-0.12576 0.6190
TNF-α	0.18429 0.4641	0.40949 0.0915	0.00698 0.9781	1.00000	-0.38637 0.1132
Adiponectin	-0.36219 0.1397	-0.07220 0.7759	-0.12576 0.6190	-0.38637 0.1132	1.00000

Non-Diabetic Subjects

Pearson Correlation Coefficients, N = 11

	VAT	CRP	IL-6	TNF-α	Adiponectin
VAT	1.00000	0.42850 0.2166	0.25319 0.4525	0.15575 0.6475	-0.47394 0.1408
CRP	0.42850 0.2166	1.00000	-0.05715 0.8754	0.20543 0.5691	-0.36323 0.3022
IL-6	0.25319 0.4525	-0.05715 0.8754	1.00000	0.49414 0.1224	-0.54031 0.0862
TNF-α	0.15575 0.6475	0.20543 0.5691	0.49414 0.1224	1.00000	-0.46298 0.1516
Adiponectin	-0.47394 0.1408	-0.36323 0.3022	-0.54031 0.0862	-0.46298 0.1516	1.00000

Diabetic Subjects

Pearson Correlation Coefficients, N = 18

	PAI-1	Weight	BMI	Insulin	HOMA-IR
PAI-1	1.00000	0.01411 0.9557	0.16867 0.5035	0.08314 0.7429	0.06282 0.8044
Weight	0.01411 0.9557	1.00000	0.79522 <.0001	0.31957 0.1961	0.15609 0.5363
BMI	0.16867 0.5035	0.79522 <.0001	1.00000	0.44322 0.0654	0.40553 0.0950
Insulin	0.08314 0.7429	0.31957 0.1961	0.44322 0.0654	1.00000	0.88828 <.0001
HOMA-IR	0.06282 0.8044	0.15609 0.5363	0.40553 0.0950	0.88828 <.0001	1.00000

Non-Diabetic Subjects

Pearson Correlation Coefficients, N = 11

	PAI-1	Weight	BMI	Insulin	HOMA-IR
PAI-1	1.00000	-0.08505 0.8036	-0.04758 0.8895	-0.02725 0.9366	-0.01544 0.9641
Weight	-0.08505 0.8036	1.00000	0.89177 0.0002	0.58066 0.0611	0.60139 0.0503
BMI	-0.04758 0.8895	0.89177 0.0002	1.00000	0.60938 0.0466	0.63385 0.0362
Insulin	-0.02725 0.9366	0.58066 0.0611	0.60938 0.0466	1.00000	0.99801 <.0001
HOMA-IR	-0.01544 0.9641	0.60139 0.0503	0.63385 0.0362	0.99801 <.0001	1.00000

Diabetic Subjects

Pearson Correlation Coefficients, N = 18

	PAI-1	SAT	VAT	%BF	Fat	Lean
PAI-1	1.00000	0.06766 0.7897	0.21083 0.4010	0.62502 0.0073	0.33136 0.1792	-0.43940 0.0681
SAT	0.06766 0.7897	1.00000	-0.07844 0.7570	0.66674 0.0035	0.59476 0.0092	-0.23720 0.3433
VAT	0.21083 0.4010	-0.07844 0.7570	1.00000	0.37650 0.1363	0.60538 0.0078	0.33578 0.1731
%BF	0.62502 0.0073	0.66674 0.0035	0.37650 0.1363	1.00000	0.80252 0.0001	-0.56366 0.0185
Fat	0.33136 0.1792	0.59476 0.0092	0.60538 0.0078	0.80252 0.0001	1.00000	-0.02126 0.9333
Lean	-0.43940 0.0681	-0.23720 0.3433	0.33578 0.1731	-0.56366 0.0185	-0.02126 0.9333	1.00000

Non-Diabetic Subjects

Pearson Correlation Coefficients, N = 11

	PAI-1	SAT	VAT	%BF	Fat	Lean
PAI-1	1.00000	-0.00484 0.9887	0.31444 0.3463	0.15938 0.6397	-0.05084 0.8820	-0.04601 0.8931
SAT	-0.00484 0.9887	1.00000	0.54467 0.0832	0.65655 0.0282	0.95345 <.0001	0.44314 0.1722
VAT	0.31444 0.3463	0.54467 0.0832	1.00000	0.63711 0.0350	0.51832 0.1024	0.00809 0.9812
%BF	0.15938 0.6397	0.65655 0.0282	0.63711 0.0350	1.00000	0.70635 0.0151	0.30799 0.3568
Fat	-0.05084 0.8820	0.95345 <.0001	0.51832 0.1024	0.70635 0.0151	1.00000	0.60202 0.0500
Lean	-0.04601 0.8931	0.44314 0.1722	0.00809 0.9812	0.30799 0.3568	0.60202 0.0500	1.00000

Diabetic Subjects

Pearson Correlation Coefficients, N = 18

	PAI-1	Leptin	Ghrelin	Resistin
PAI-1	1.00000	0.31852 0.1977	-0.44054 0.0673	0.12748 0.6142
Leptin	0.31852 0.1977	1.00000	0.03533 0.8893	-0.32905 0.1824
Ghrelin	-0.44054 0.0673	0.03533 0.8893	1.00000	-0.18873 0.4533
Resistin	0.12748 0.6142	-0.32905 0.1824	-0.18873 0.4533	1.00000

Non-Diabetic Subjects

Pearson Correlation Coefficients, N = 11

	PAI-1	Leptin	Ghrelin	Resistin
PAI-1	1.00000	0.15566 0.6476	0.02727 0.9366	-0.24821 0.4618
Leptin	0.15566 0.6476	1.00000	-0.37545 0.2552	0.41352 0.2062
Ghrelin	0.02727 0.9366	-0.37545 0.2552	1.00000	-0.38078 0.2480
Resistin	-0.24821 0.4618	0.41352 0.2062	-0.38078 0.2480	1.00000

Diabetic Subjects

Pearson Correlation Coefficients, N = 18

	PAI-1	CRP	TNF-α	IL-6	Adiponectin
PAI-1	1.00000	0.03367 0.8945	-0.05453 0.8298	0.31014 0.2104	-0.15436 0.5408
CRP	0.03367 0.8945	1.00000	0.40949 0.0915	0.25831 0.3007	-0.07220 0.7759
TNF-α	-0.05453 0.8298	0.40949 0.0915	1.00000	0.00698 0.9781	-0.38637 0.1132
IL-6	0.31014 0.2104	0.25831 0.3007	0.00698 0.9781	1.00000	-0.12576 0.6190
Adiponectin	-0.15436 0.5408	-0.07220 0.7759	-0.38637 0.1132	-0.12576 0.6190	1.00000

Non-Diabetic Subjects

Pearson Correlation Coefficients, N = 11

	PAI-1	CRP	TNF-α	IL-6	Adiponectin
PAI-1	1.00000	-0.13854 0.7027	-0.35547 0.2834	0.10648 0.7554	0.09340 0.7847
CRP	-0.13854 0.7027	1.00000	0.20543 0.5691	-0.05715 0.8754	-0.36323 0.3022
TNF-α	-0.35547 0.2834	0.20543 0.5691	1.00000	0.49414 0.1224	-0.46298 0.1516
IL-6	0.10648 0.7554	-0.05715 0.8754	0.49414 0.1224	1.00000	-0.54031 0.0862
Adiponectin	0.09340 0.7847	-0.36323 0.3022	-0.46298 0.1516	-0.54031 0.0862	1.00000

APPENDIX F

Patient at a Glance Summary

Non-Diabetic Subjects

Pt #	Wk 1									Wk8 Average									Wk16 Average								
	S	E	B	MR	PA	A	P	Box	TI	S	E	B	MR	PA	A	P	Box	TI	S	E	B	MR	PA	A	P	Box	TI
001	12.0	12.0	0.0	24.0	850.0	1.0	1.0	5.0	0.0	21.0	14.0	3.7	38.7	2336.7	1.0	1.0	6.0	1.0	20.0	12.3	4.0	36.3	2700.0	1.0	1.0	4.0	1.0
005	20.0	12.0	8.5	30.5	1233.0	1.0	1.0	6.0	0.0	29.7	14.7	5.0	49.3	2145.0	1.0	1.0	6.0	1.0	31.0	15.3	8.8	55.2	1872.7	1.0	1.0	6.3	0.7
013	18.0	12.0	4.0	34.0	2012.0	1.0	1.0	6.0	1.0	21.7	14.3	4.3	40.3	2133.7	1.0	1.0	7.0	0.7	21.7	14.0	8.0	43.7	2282.0	1.0	1.0	7.0	1.0
024	18.0	12.0	0.0	31.0	3110.0	1.0	1.0	6.0	1.0	22.7	14.0	1.0	37.3	4571.3	1.0	1.0	7.0	1.0	22.0	14.3	0.0	36.3	5189.0	1.0	1.0	7.0	1.0
026	32.0	0.0	3.0	35.0	540.0	1.0	1.0	6.0	0.0	36.7	1.0	0.0	37.3	2000.0	1.0	1.0	7.0	0.7	37.0	6.7	2.0	45.7	2641.7	1.0	1.0	7.0	1.0
028	39.0	0.0	10.0	49.0	630.0	1.0	1.0	6.0	0.0	35.0	7.3	2.3	44.7	1343.3	1.0	1.0	7.0	0.0	35.0	8.3	9.0	52.3	1739.0	1.0	1.0	7.0	0.7
029	17.0	12.0	3.0	32.0	245.0	1.0	1.0	6.0	0.0	22.8	14.3	4.3	41.5	2041.7	1.0	1.0	7.0	0.7	24.0	15.0	7.3	46.7	2851.7	1.0	1.0	7.0	1.0
032	20.5	12.0	4.0	36.5	494.0	1.0	1.0	6.0	0.0	23.0	15.7	11.5	45.8	2081.0	1.0	1.0	6.7	1.0	26.3	14.7	12.7	54.0	1841.7	1.0	1.0	7.0	0.3
033	20.0	12.0	6.0	38.0	1989.0	1.0	1.0	6.0	0.0	21.3	14.0	15.0	50.3	3028.3	1.0	1.0	7.0	1.0	21.0	16.0	13.0	53.3	3746.7	1.0	1.0	7.0	1.0
037	21.0	12.0	0.0	33.0	1435.0	1.0	1.0	6.0	0.0	23.0	14.3	3.0	40.3	3420.0	1.0	1.0	7.0	1.0	24.0	15.7	11.0	50.7	4480.0	1.0	1.0	7.0	1.0
040	17.0	12.0	4.0	33.0	2355.0	1.0	1.0	6.0	0.0	21.3	14.3	6.7	42.3	2433.3	1.0	1.0	6.3	1.0	20.7	13.7	6.3	40.3	2449.7	1.0	1.0	6.7	1.0
Average	21.3	9.8	3.9	34.2	1353.9	1.0	1.0	5.9	0.2	25.3	12.5	5.2	42.5	2503.1	1.0	1.0	6.7	0.8	25.7	13.3	7.5	46.8	2890.4	1.0	1.0	6.6	0.9
Count	11.0	11.0	11.0	11.0	11.0	11.0	11.0	11.0	11.0	11.0	11.0	11.0	11.0	11.0	11.0	11.0	11.0	11.0	11.0	11.0	11.0	11.0	11.0	11.0	11.0	11.0	11.0
SD	7.6	4.9	3.3	6.1	914.0	0.0	0.0	0.3	0.4	5.7	4.4	4.5	4.5	876.4	0.0	0.0	0.4	0.3	6.0	3.1	4.2	6.9	1125.6	0.0	0.0	0.9	0.2
SE	2.3	1.5	1.0	1.8	275.6	0.0	0.0	0.1	0.1	1.7	1.3	1.3	1.4	264.2	0.0	0.0	0.1	0.1	1.8	0.9	1.3	2.1	339.4	0.0	0.0	0.3	0.1
95% LCI	16.8	6.9	1.9	30.6	813.8	1.0	1.0	5.7	-0.1	21.9	9.9	2.5	39.9	1985.2	1.0	1.0	6.5	0.6	22.2	11.5	5.0	42.7	2225.2	1.0	1.0	6.1	0.7
95% UCI	25.8	12.7	5.8	37.8	1894.0	1.0	1.0	6.1	0.4	28.7	15.1	7.8	45.2	3021.0	1.0	1.0	7.0	1.0	29.2	15.1	9.9	50.9	3555.5	1.0	1.0	7.2	1.0

S=Shakes, E=Entrees, B=Bars, MR=Total Meal Replacements, PA=Physical Activity, A=Attendance

P=Midweek phone call, Box=Number of days in the box, TI=Triple Imperative

Diabetic Subjects

Pt #	Wk 1									Wk8 Average									Wk16 Average								
	S	E	B	MR	PA	A	P	Box	TI	S	E	B	MR	PA	A	P	Box	TI	S	E	B	MR	PA	A	P	Box	TI
003	21.0	14.0	7.0	42.0	2000.0	1.0	1.0	6.0	1.0	21.0	14.3	6.5	39.7	2676.7	1.0	1.0	7.0	1.0	21.0	14.0	4.0	39.0	2358.3	1.0	0.7	6.7	1.0
007	3.0	3.0	2.0	8.0	45.0	1.0	1.0	5.0	0.0	22.3	15.0	12.3	49.7	1591.7	1.0	1.0	6.7	0.0	23.3	16.3	7.0	46.7	1927.7	1.0	1.0	7.0	0.7
008	30.0	4.0	5.0	39.0	350.0	1.0	1.0	5.0	0.0	30.0	14.7	4.0	44.7	1813.3	1.0	1.0	7.0	0.3	21.0	14.0	0.0	35.0	1813.3	0.7	1.0	5.0	0.0
009	18.0	13.0	2.0	33.0	1152.0	1.0	1.0	6.0	0.0	21.3	19.3	6.0	46.7	2647.0	1.0	1.0	6.0	1.0	21.7	18.3	11.0	51.0	2370.0	1.0	1.0	6.3	1.0
012	19.0	12.0	2.0	33.0	885.0	1.0	1.0	6.0	0.0	10.0	8.0	2.5	20.5	885.0	0.3	0.3	2.3	0.0	21.0	23.0	9.0	53.0	2130.0	1.0	0.0	5.0	1.0
014	47.0	4.0	9.0	60.0	980.0	1.0	1.0	6.0	0.0	24.3	21.0	7.0	52.0	2363.3	1.0	1.0	7.0	0.7	29.3	22.0	5.0	56.0	2021.7	1.0	1.0	7.0	0.3
017	18.0	12.0	6.0	36.0	6380.0	1.0	1.0	6.0	1.0	30.0	13.7	12.3	52.3	4366.7	1.0	1.0	7.0	1.0	21.7	16.0	14.3	54.0	3800.0	1.0	1.0	7.0	1.0
018	14.0	10.0	2.0	26.0	1527.0	1.0	1.0	5.0	0.0	21.0	14.3	2.7	38.0	3504.0	1.0	1.0	7.0	1.0	22.3	10.7	5.3	38.3	3020.3	1.0	1.0	6.7	1.0
020	28.0	0.0	0.0	28.0	40.0	1.0	1.0	6.0	0.0	37.3	2.5	1.0	39.3	76.7	0.7	1.0	6.3	0.0	39.3	8.3	1.0	48.3	70.0	0.0	0.7	6.0	0.0
023	32.0	0.0	0.0	32.0	320.0	1.0	1.0	6.0	0.0	42.5	9.7	12.3	64.5	1527.3	1.0	1.0	7.0	0.0	44.0	12.7	15.3	72.0	1516.7	1.0	1.0	7.0	0.7
025	36.5	0.0	7.0	43.5	1835.0	1.0	1.0	6.0	0.0	36.0	1.0	8.7	45.3	3376.3	1.0	1.0	7.0	1.0	36.5	3.0	4.0	42.0	2717.5	1.0	1.0	7.0	1.0
030	20.0	12.0	1.0	33.0	540.0	1.0	1.0	6.0	0.0	26.0	14.3	6.3	46.7	2671.7	1.0	1.0	7.0	1.0	29.0	19.3	12.7	61.0	2855.3	1.0	1.0	7.0	1.0
031	17.0	12.0	7.0	36.0	280.0	1.0	1.0	5.0	0.0	21.0	19.0	2.3	42.3	2266.7	0.7	0.7	6.0	0.3	39.0	18.0	10.0	63.0	2066.7	1.0	1.0	7.0	1.0
034	26.0	10.0	0.0	36.0	540.0	1.0	1.0	6.0	0.0	21.0	14.3	4.3	40.0	4110.0	1.0	1.0	7.0	1.0	24.0	11.0	3.3	38.3	3178.3	1.0	1.0	7.0	1.0
036	20.0	12.0	0.0	22.0	945.0	1.0	1.0	6.0	0.0	21.7	15.3	3.7	40.7	1850.0	1.0	1.0	7.0	0.7	26.0	15.3	8.3	49.7	3478.3	1.0	1.0	7.0	1.0
038	18.0	13.0	7.0	38.0	1890.0	1.0	1.0	6.0	0.0	22.7	15.3	6.7	44.7	2592.3	1.0	1.0	7.0	1.0	25.3	19.3	13.7	58.3	2974.3	1.0	1.0	7.0	1.0
039	26.0	12.0	4.0	40.0	1320.0	1.0	1.0	6.0	0.0	24.3	14.3	7.0	48.3	3533.3	1.0	1.0	7.0	1.0	27.8	14.5	8.0	46.3	3650.0	1.0	1.0	7.0	1.0
041	31.0	11.0	15.0	57.0	2013.0	1.0	1.0	6.0	1.0	42.7	11.3	6.3	59.0	3359.3	1.0	1.0	6.7	1.0	36.7	5.5	2.0	41.0	2022.7	0.7	1.0	7.0	1.0
Average	23.6	8.6	4.2	35.7	1280.1	1.0	1.0	5.8	0.2	26.4	13.2	6.2	45.2	2511.7	0.9	0.9	6.6	0.7	28.3	14.5	7.4	49.6	2442.8	0.9	0.9	6.6	0.8
Count	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.0
SD	9.8	5.1	4.0	11.7	1437.5	0.0	0.0	0.4	0.4	8.5	5.2	3.5	9.3	1110.5	0.2	0.2	1.1	0.4	7.5	5.4	4.7	10.0	892.1	0.3	0.3	0.7	0.3
SE	2.3	1.2	0.9	2.8	338.8	0.0	0.0	0.1	0.1	2.0	1.2	0.8	2.2	261.8	0.0	0.0	0.3	0.1	1.8	1.3	1.1	2.4	210.3	0.1	0.1	0.2	0.1
95% LCI	19.1	6.2	2.4	30.3	616.0	1.0	1.0	5.6	0.0	22.5	10.8	4.6	40.9	1998.7	0.8	0.9	6.0	0.5	24.8	12.0	5.3	45.0	2030.7	0.8	0.8	6.3	0.7
95%UCI	28.1	10.9	6.1	41.1	1944.2	1.0	1.0	6.0	0.3	30.3	15.6	7.8	49.5	3024.8	1.0	1.0	7.1	0.9	31.7	17.0	9.6	54.2	2855.0	1.0	1.0	7.0	1.0

S=Shakes, E=Entrees, B=Bars, MR=Total Meal Replacements, PA=Physical Activity, A=Attendance

P=Midweek phone call, Box=Number of days in the box, TI=Triple Imperative

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VITAE

Elizabeth Catherine Konz

PERSONAL DATA

Birth Date:	February 28, 1973
Place of Birth:	FonDuLac, WI

EDUCATION

Master of Science — Nutrition
Mississippi State University
Starkville, MS

Thesis: *Effects of Consumption of Muscatine Pumice Puree on Serum Apolipoprotein A-1 Concentrations*

Postgraduate Dietetic Internship — Registered Dietitian
Mississippi State University
Starkville, MS

Bachelor of Science — Dietetics
University of Wisconsin – Madison
Madison, WI

PROFESSIONAL EXPERIENCE

UNIVERSITY OF KENTUCKY **Lexington, Kentucky**

Graduate Student and Principal Research Investigator-Metabolic Research Group
1998 to Present

Conducted research and educational outreach related to oxidative stress, obesity, and diabetes. Supported internal medicine and nutrition research and education programs with extramural funding and consistent publication. Directed 8 undergraduate students, research assistants, and research coordinators. Reported to the Director of the Metabolic Research Group.

- Initiated problem-solving research program, which resulted in state and regional recognition in weight loss and weight maintenance.
- Procured $139,454 in extramural grants.
- Developed and presented health information on obesity, cardiovascular disease, and diabetes at health fairs, staff appreciation events, and local community groups.
- Reviewed research and prepared health information for international drug companies, medically supervised weight loss programs, and commercial nutritional supplement outlet stores.
- Authored six refereed journal articles and nine other publications.
- Planned innovative curricula, organized group projects, html online access, and discussion boards to enhance coursework, and facilitated undergraduate education. Developed and taught the following courses to nutrition, dietetics, and pre-med majors:
    - Nutrition and Food Science 510: Advanced Nutrition
    - Nutrition and Food Science 240: Nutrition and Physical Fitness
- Recruited by Department Chair to assume teaching responsibility for professors on leave.
- Consulted on design and information content and answered general email questions for HCF Nutrition Foundation website – www.hcf-nutrition.org
- Served as the Student Representative on the Student Recruitment Committee to encourage US students to attend the Nutritional Sciences Graduate Program at the University. Prepared and presented slide shows, posters, and letters throughout State to promote program.

LEXINGTON COMMUNITY COLLEGE

Lexington, Kentucky

Instructor, 2002 to 2004

Recognized educational opportunity and successfully initiated nutrition coursework at local community college. Taught six semesters. Reported to the Biology Coordinator.

- Identified need, obtained approval, and initiated Nutrition 101: Human Nutrition and Wellness, an online course for undergraduate students.
- Prepared in-class and online lectures using PowerPoint, BlackBoard, and Angel programs.
- Achieved student satisfaction rating of 4.6 for Excellence of Teacher and Excellence of Course.

VETERANS ADMINISTRATION MEDICAL CENTER

Lexington, Kentucky

Preceptor and Mentor, 1998 to 2002

Recruited to mentor undergraduate dietetic students and to assist undergraduate students in research projects. Reported to the Chief of Endocrinology and Director of the Metabolic Research Group.

- Facilitated and mentored undergraduate dietetic students with research projects to help them gain research experience as part of Nutrition and Food Science 591: Special Problems in Food and Nutrition coursework.
- Served as preceptor for clinical practicum experience as part of Nutrition and Food Science 580: Pre-professional Practice in Dietetics.

SPECIAL ACHIEVEMENTS

Recognized for achievement and potential as awarded following stipends, scholarships, and fellowships:

- Oxidative Stress in Nutrition Training Grant • National Institutes of Health DK07778-02 • 2001 to 2004
- TORA Tuition Scholarship • University of Kentucky • 1998 to 2001
- Graduate Research Assistant • University of Kentucky Stipend • 1998-2001 and 2004 to Present

Coordinated Annual Symposia, sponsored by the National Institutes of Health Oxidative Stress and Nutrition Training Grant, on cancer, diabetes, obesity, alcoholism, and cardiovascular disease • Attended by 150 professional, research, and academic personnel • May 6, 2002, April 17, 2003, and May 17, 2004

Worked with Roche Pharmaceutical Company to direct consumer and healthcare professional information and prepare presentations on Orlistat, the Company's weight loss drug.

Reviewed research and publications on medically-supervised low calorie and SCAN Diet Plans for Health Management Resources, a Boston-based weight loss company, and for General Nutrition Centers.

Invited to review research grant proposals and to allocate funding awards as part of the Proposal Review Committee for the General Clinical Research Center • University of Kentucky • 2004 to Present

Prepared public health television advertisement and outreach program to promote milk for healthy nutrition • University of Mississippi • 1997

Completed Massage Therapy Coursework • Capri College • Madison, Wisconsin • 1995 to 1996

Served as Diet Clerk • University of Wisconsin Medical Center • 1994 to 1996

PROFESSIONAL and COMMUNITY INVOLVEMENT

American College of Nutrition • Member • 1999 to Present
American Dietetic Association • Member • 1994 to Present
American Society for Nutritional Sciences • Member • 1999 to Present
Kentucky Dietetic Association • Member • 1998 to Present
North American Association for the Study of Obesity • Member • 1999 to Present
Nutritional Sciences Graduate Student Association • Member • 1998 to Present
Society for Experimental Biology and Medicine • Member • 1999 to Present
American Red Cross • CPR & First Aid Instructor • 1994 to 1996

GRANTS RECEIVED

Clinical Research Feasibility Funds • 2004 to 2005 • $20,000 • General Clinical Research Center • University of Kentucky • National Institutes of Health National Center for Research Resources (NIH-NCRR) M01-RR02602

Effects of Weight Loss on Visceral Adiposity and Metabolic Adaptations in Diabetic versus Non-Diabetic Women • 2002 to 2004 • $71,972 • Principal Investigator • National Institutes of Health M01-RR02602

A 16-Week, Randomized, Double-Blind, Controlled, Parallel Group Study to Compare the Effects of Revival Soy Shakes and Casein Meal Replacement Shakes as Part of an Energy-Restricted Diet for the Treatment of Obesity • 2003 to 2004 • $47482 • Co-Principal Investigator • National Institutes of Health M01-RR02602

PUBLICATIONS – BOOKS or CHAPTERS

Anderson, JW and Konz, EC. *Guidelines for Weight Management and Use of Very-low-calorie Diets and Meal Replacements*. Chapter 19 **Food, Diet, and Obesity**. Ed. David Mela. Woodhead Publishing Lte, Cambridge, England. In Press.

PUBLICATIONS – ARTICLES, ABSTRACTS, REPORTS, or LETTERS TO EDITOR

Konz, EC, Anderson, JW, and Reynolds, LR. *Low-energy Diet Effects on Percentage Weight and Body Fat Changes in Women with and without Type 2 Diabetes Mellitus*. **Obesity Research** 12 (Supplement 1): A36, 2004.

Konz, EC and Anderson, JW. *Effect of an Intensive Weight Loss Program on Long-term Weight Maintenance* **Journal American College of Nutrition** 22(5):468, 2003.

Tharappel, JC, Nalca, A, Owens, A, Ghabrial, L, Konz, E, Glauret, H, and Spear, B. *Cell Proliferation and Apoptosis are Altered in Mice Deficient in the NF-κB p50 Subunit After Treatment with the Peroxisome Proliferator Ciprofibrate*. **Toxicology Science** 75(2):300-308, 2003.

Reynolds, LR, Konz, EC, Frederich, RC, and Anderson, JW. *Rosiglitazone Amplifies the Benefits of Lifestyle Intervention Measures in Long-standing Type 2 Diabetes Mellitus*. **Diabetes Obesity Metabolism** 4(4):270-275, 2002.

Konz, EC and Anderson JW. *Effects of an Intensive Weight Loss Program on Long-term Weight Maintenance and Health Behaviors – Final Report*. **Health Management Resource**, 2002.

Anderson, JW and Konz, EC. *Obesity and Disease Management: Effects of Weight Loss on Co-Morbid Conditions*. **Obesity Research** 9 (Supplement 4):326S-334S, 2001.

Konz, EC and Anderson, JW. *Effects of Weight Gain and Loss on Co-Morbid Conditions*. **Obesity Research** 9 (Supplement 3):166S, 2001.

Reynolds, LR, Strange, K, Anderson JW, and Konz, EC. *Lifestyle Intervention Reduces Multiple Risk Factors in Obese Patients with Poorly Controlled Insulin Requiring Type 2 Diabetes Mellitus*. **Proceedings of the 83rd Annual Endocrine Society**. Abstract P2-572, page 416, 2001.

Anderson, JW, Konz, EC, Frederich, RC, and Wood, CL. *Long-term Weight Maintenance: A Meta-Analysis of US Studies*. **American Journal of Clinical Nutrition** 74:579-584, 2001.

Anderson, JW and Konz, EC. *Benefits and Risk of Anti-Obesity Agents* (Letter to the Editor). **American Journal of Clinical Nutrition** 71:844-845, 2000.

Daly, AE, Konz, EC, Soler, NG, Anderson, JW, Yergler, C, and Carpenter, P. *Successful Long-term Maintenance of Substantial Weight Loss: One Program's Experience*. **Journal American Dietetics Association** 100:1456, 2000.

Konz, EC and Anderson, JW. *Comparison of Weight Loss Strategies*. **Obesity Research** 8 (Supplement 1):77S, 2000.

Anderson, JW, Konz, EC, and Jenkins, DJA. *Health Advantages and Disadvantages of Weight-Reducing Diets: A Computer Analysis and Critical Review*. **Journal of American College of Nutrition** 19:578-590, 2000.

Anderson, JW and Konz, EC. *Orlistat: First of a New Generation of Drugs for the Treatment of Obesity*. **Today's Therapeutic Trends** 17:243-255, 1999.

Anderson, JW, Konz, EC, Frederich, RC, and Wood, CL. *Long-term Weight Maintenance: A Meta-Analysis of US Studies.* **Obesity Research** 7 (Supplement1):43S, 1999.

ADDRESSES, LECTURES, POSTERS, or WORKSHOPS

Body Composition and Metabolic Adaptations in Diabetic versus Non-Diabetic Women after Weight Loss • Graduate Center for Nutritional Sciences Seminar Series • University of Kentucky, Lexington, KY • December 8, 2004

Low-energy Diet Effects on Percentage Weight and Body Fat Changes in Women with and without Type 2 Diabetes • North American Association for the Study of Obesity Conference • Las Vegas, NV • November 14-18, 2004

Effect of an Intensive Weight Loss Program on Long-term Weight Maintenance • American College of Nutrition Conference • Nashville, TN • October 9-12, 2003

Fighting the "Freshman 15" • University of Kentucky 101 – Academic Orientation • University of Kentucky, Lexington, KY • October 3, 2002

Obesity Treatment Approaches • Nutrition and Food Science 101 – Human Nutrition and Wellness • Lexington Community College, Lexington, KY • April 4, 2002

Obesity Treatment Approaches • Nutrition and Food Science 212 – Introductory Nutrition • University of Kentucky, Lexington, KY • March 18 and March 20, 2002

Effects of Weight Gain and Loss on Co-Morbid Conditions • Nutrition Week • San Diego, CA • February 23-27, 2002

Energy Balance and Healthy Body Weight • Nutrition and Food Science 101 – Human Nutrition and Wellness • University of Kentucky, Lexington, KY • October 24, 26, and 29, 2001

Obesity: Classification, Body Composition and Treatment Approaches • Nutrition and Food Science 212 – Introductory to Nutrition • University of Kentucky, Lexington, KY • October 12 and October15, 2001

Effects of Weight Gain and Loss on Co-Morbid Conditions • North American Association for the Study of Obesity Conference • Quebec City, Canada • October 7-10, 2001

Lifestyle Intervention Reduces Multiple Risk Factors in Obese Patients with Poorly Controlled Insulin-Requiring Type 2 Diabetes Mellitus • Proceedings of the 83rd Annual Endocrine Society Meeting • Denver, CO • June 20-23, 2001.

Comparison of Diet and Drug Weight Loss Approaches in Clinical and Research Practices • North American Association for the Study of Obesity Conference • Long Beach, CA • October 29 to November 2, 2000

Eat For the Health of It • University of Kentucky College of Medicine Mini-Medical School • Lexington, KY • September 19, 2000

Obesity Treatment Approaches- The Real Truth • Nutrition and Food Science 510 – Advanced Nutrition • University of Kentucky, Lexington, KY • April 17, 2000

Long-term Weight Maintenance: A Meta-Analysis of US Studies • Veteran's Administration Medical Center Research Week • Lexington, KY • April 17-21, 2000

Fad Diets – Pros and Cons • Annual Endocrinology Conference • Embassy Suites, Lexington, KY • April 7-8, 2000

Obesity Treatment Approaches- The Real Truth • Nursing 842 – Community Health Nursing • University of Kentucky, Lexington, KY • March 22, 2000.

Obesity Treatment: Combating the Diet Craze- The Real Truth • Bluegrass District Dietetic Association • February Seminar • Lexington, KY • February 12, 2000

Long-term Weight Maintenance: A Meta-Analysis of US Studies • North American Association for the Study of Obesity • Charleston, SC • November 14-18, 1999

Long-term Weight Maintenance: A Meta-Analysis of US Studies • University of Kentucky Life Sciences Day • Lexington, KY • November 1, 1999